# Package 'MXM'

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Type Package

**Title** Feature Selection (Including Multiple Solutions) and Bayesian Networks

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Maintainer Michail Tsagris <mtsagris@uoc.gr>

**Description** Many feature selection methods for a wide range of response variables, including minimal, statistically-equivalent and equally-predictive feature subsets. Bayesian network algorithms and related functions are also included. The package name 'MXM' stands for "Mens eX Machina", meaning "Mind from the Machine" in Latin. References: a) Lagani, V. and Athineou, G. and Farcomeni, A. and Tsagris, M. and Tsamardinos, I. (2017). Feature Selection with the R Package MXM: Discovering Statistically Equivalent Feature Subsets. Journal of Statistical Software, 80(7). <doi:10.18637/jss.v080.i07>. b) Tsagris, M., Lagani, V. and Tsamardinos, I. (2018). Feature selection for high-dimensional temporal data. BMC Bioinformatics, 19:17. <doi:10.1186/s12859-018-2023-7>. c) Tsagris, M., Borboudakis, G., Lagani, V. and Tsamardinos, I. (2018). Constraint-based causal discovery with mixed data. International Journal of Data Science and Analytics, 6(1): 19-30. <doi:10.1007/s41060-018-0097y>. d) Tsagris, M., Papadovasilakis, Z., Lakiotaki, K. and Tsamardinos, I. (2018). Efficient feature selection on gene expression data: Which algorithm to use? BioRxiv. <doi:10.1101/431734>. e) Tsagris, M. (2019). Bayesian Network Learning with the PC Algorithm: An Improved and Correct Variation. Applied Artificial Intelligence, 33(2):101-123. <doi:10.1080/08839514.2018.1526760>. f) Tsagris, M. and Tsamardinos, I. (2019). Feature selection with the R package MXM. F1000Research 7: 1505. <doi:10.12688/f1000research.16216.2>. g) Borboudakis, G. and Tsamardinos, I. (2019). Forward-Backward Selection with Early Dropping. Journal of Machine Learning Research 20: 1-39. h) The gamma-OMP algorithm for fea2 R topics documented:

ture selection with application to gene expression data. IEEE/ACM Transactions on Computational Biology and Bioinformatics 19(2): 1214-1224. <a href="https://doi.org/10.1109/TCBB.2020.3029952">doi:10.1109/TCBB.2020.3029952</a>>.

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MXM-package

This is an R package that currently implements feature selection methods for identifying minimal, statistically-equivalent and equally-predictive feature subsets. Additionally, the package includes two algorithms for constructing the skeleton of a Bayesian network.

# **Description**

'MXM' stands for Mens eX Machina, meaning 'Mind from the Machine' in Latin. The package provides source code for the SES algorithm and for some appropriate statistical conditional independence tests. (Fisher and Spearman correlation, G-square test are some examples. Currently the response variable can be univariate or multivariate Euclidean, proportions within 0 and 1, compositional data without zeros and ones, binary, nominal or ordinal multinomial, count data (handling also overdispersed and with more zeros than expected), longitudinal, clustered data, survival and casecontrol. Robust versions are also available in some cases and a K-fold cross validation is offered. Bayesian network related algorithms and ridge reression are also included. Read the package's help pages for more details.

MMPC and SES can handle even thousands of variables and for some tests, even many sample sizes of tens of thousands. The user is best advised to check his variables in the beginning. For some regressions, logistic and Poisson for example, we have used C++ codes for speed reasons.

For more information the reader is addressed to

Lagani V., Athineou G., Farcomeni A., Tsagris M. and Tsamardinos I. (2017). Feature Selection with the R Package MXM: Discovering Statistically Equivalent Feature Subsets. Journal of Statistical Software, 80(7), doi:10.18637/jss.v080.i07 and

Tsagris, M. and Tsamardinos, I. (2019). Feature selection with the R package MXM. F1000Research 7: 1505.

### Details

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#### Maintainer

Michail Tsagris <mtsagris@uoc.gr>.

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#### Note

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**Disclaimer:** Professor Tsamardinos is the creator of this package and Dr Lagani supervised Mr Athineou build it. Dr Tsagris is the current maintainer.

#### Author(s)

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#### References

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```
SES, MMPC, fbed.reg, gomp, pc.sel, censIndCR, testIndFisher, testIndLogistic, gSquare, testIndRQ
```

Ancestors and descendants of a node in a directed graph

Returns and plots, if asked, the descendants or ancestors of one or all node(s) (or variable(s))

# **Description**

Returns and plots, if asked, the descendants or ancestors of one or all node(s) (or variable(s))

#### Usage

```
findDescendants(G, node = NULL, graph = FALSE)
findAncestors(G, node = NULL, graph = FALSE)
```

# **Arguments**

G	The graph matrix as produced from pc.or or any other algorithm which pro-
	duces directed graphs.

node A numerical value indicating the node (or variable) whose descendants are to be

returned.

graph A boolean variable. If TRUE the relevant graph will appear (if there are descen-

dants).

#### **Details**

The functions searches for the descendants of some node. This is an S3 class output.

### Value

isAnc	A matrix of the same dimensions as the original graph matrix with 0s and 1s.
	isAnc[i, j] = 1 indicates that the i-th node is an ancestor of the j-th node. If the

assument " and a " in NIII I and a thin material and the section of the just hode. If the

argument "node" is NULL, only this matrix will be returned.

Ganc A matrix of dimensions equal to the number of descendants of the node with 0s

and 1s, if the argument "node" is not NULL.

anc The descendants of the node if the argument "node" is not NULL.

### Author(s)

Anna Roumpelaki

R implementation and documentation: Anna Roumpelaki <anna.roumpelaki@gmail.com>

```
plotnetwork, nei, mb, pc.or
```

# **Examples**

```
# simulate a dataset with continuous data
y = rdag(1000, 10, 0.3)
tru = y$G
x = y$x
mod = pc.con(x)
G = pc.or(mod)$G
plotnetwork(G)
findDescendants(G, 4, graph = FALSE)
findAncestors(G, 4, graph = FALSE)
findAncestors(G)
```

Backward phase of MMPC

Backward phase of MMPC

# **Description**

Backward phase of MMPC.

# Usage

```
mmpcbackphase(target, dataset, max_k = 3, threshold = 0.05, test = NULL, wei = NULL, R = 1)
```

# Arguments

target	The class variable. Provide either a string, an integer, a numeric value, a vector, a factor, an ordered factor or a Surv object. See also Details.
dataset	The data-set; provide either a data frame or a matrix (columns = variables, rows = samples). Alternatively, provide an ExpressionSet (in which case rows are samples and columns are features, see bioconductor for details).
max_k	The maximum conditioning set to use in the conditional indepedence test (see Details). Integer, default value is 3.
threshold	Threshold (suitable values in $(0, 1)$ ) for assessing p-values significance. Default value is $0.05$ .
test	The conditional independence test to use. Type the test without " ", e.g. type testIndFisher, Not "testIndFisher". Default value is NULL. See also CondIndTests.
wei	A vector of weights to be used for weighted regression. The default value is NULL.

R

The number of permutations, set to 1 by default (no permutations based test). There is a trick to avoind doing all permutations. As soon as the number of times the permuted test statistic is more than the observed test statistic is more than 50 (if threshold = 0.05 and R = 999), the p-value has exceeded the significance level (threshold value) and hence the predictor variable is not significant. There is no need to continue do the extra permutations, as a decision has already been made.

#### **Details**

For each of the selected variables (dataset) the function performs conditional independence tests where the conditioning sets are formed from the other variables. All possible combinations are tried until the variable becomes non significant. The maximum size of the conditioning set is equal to max\_k. This is called in the MMPC when the backward phase is requested.

#### Value

A list including:

met A numerical vector of size equal to the number of columns of the dataset.

counter The number of tests performed.

pvalues The maximum **logged p-value** for the association of each predictor variable.

### Author(s)

Ioannis Tsamardinos, Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

#### References

Tsamardinos, Brown and Aliferis (2006). The max-min hill-climbing Bayesian network structure learning algorithm. Machine learning, 65(1), 31-78.

# See Also

```
MMPC, mmhc.skel, CondIndTests, cv.mmpc
```

# **Examples**

```
#simulate a dataset with continuous data
dataset <- matrix(runif(500 * 100, 1, 100), ncol = 100)

#define a simulated class variable
target <- 3 * dataset[, 10] + 2 * dataset[, 100] + 3 * dataset[, 20] + rnorm(500, 0, 5)

# MMPC algorithm
m1 <- MMPC(target, dataset, max_k = 3, threshold = 0.05, test="testIndFisher");
m2 <- MMPC(target, dataset, max_k = 3, threshold = 0.05, test="testIndFisher", backward = TRUE);</pre>
```

```
x <- dataset[, m1@selectedVars]
mmpcbackphase(target, x, test = testIndFisher)</pre>
```

Backward selection regression

Variable selection in regression models with backward selection

# Description

Variable selection in regression models with backward selection

# Usage

```
bs.reg(target, dataset, threshold = 0.05, wei = NULL, test = NULL, user_test = NULL)
```

# Arguments

target	The class variable. Provide either a string, an integer, a numeric value, a vector, a factor, an ordered factor or a Surv object. See also Details. For the gamma regression this must a vector with strictly positive numbers (no zeros allowed).
dataset	The dataset; provide either a data frame or a matrix (columns = variables, rows = samples). In either case, only two cases are available, either all data are continuous, or categorical.
threshold	Threshold (suitable values in $(0, 1)$ ) for assessing p-values significance. Default value is 0.05.
test	The regression model to use. Available options are most of the tests for SES and MMPC. The ones NOT available are "censIndER", "testIndMVreg", "testIndSpearman". If you want to use multinomial or ordinal logistic regression, make sure your target is factor. See also SES and CondIndTests for the tests.
wei	A vector of weights to be used for weighted regression. The default value is NULL. An example where weights are used is surveys when stratified sampling has occured.
user_test	A user-defined conditional independence test (provide a closure type object). Default value is NULL. If this is defined, the "test" argument is ignored.

### **Details**

If the sample size is less than the number of variables a meesage will appear and no backward regression is performed.

# Value

The output of the algorithm is S3 object including:

runtime The run time of the algorithm. A numeric vector. The first element is the user

time, the second element is the system time and the third element is the elapsed

time.

info	A matrix with the non selected variables and their latest test statistics and <b>logged p-values</b> .
mat	A matrix with the selected variables and their latest statistics and <b>logged p-values</b> .
ci_test	The conditional independence test used.
final	The final regression model.

### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

### See Also

```
glm.fsreg, lm.fsreg, bic.fsreg, bic.glm.fsreg, CondIndTests, MMPC, SES
```

### **Examples**

```
set.seed(123)
dataset <- matrix( runif(200 * 10, 1, 100), ncol = 10 )
target <- rnorm(200)
a <- bs.reg(target, dataset, threshold = 0.05, test = "testIndRQ")
b <- bs.reg(target, dataset, threshold = 0.05, test = "testIndReg")
b2 <- bs.reg(target, dataset, threshold = 0.05, test = "testIndFisher")</pre>
```

Backward selection regression for GLMM

Backward selection regression for GLMM

# Description

Backward selection regression for GLMM

# Usage

```
glmm.bsreg(target, dataset, id, threshold = 0.05, wei = NULL, test = "testIndGLMMReg")
```

# Arguments

target	The class variable. This can be a numerical vector with continuous data, binary or discrete valued data. It can also be a factor variable with two levels only.
dataset	The dataset; provide a numerical a matrix (columns = variables, rows = samples).
id	This is a numerical vector of the same size as target denoting the groups or the subjects.

threshold Threshold (suitable values in (0, 1)) for assessing p-values significance. Default

value is 0.05.

wei A vector of weights to be used for weighted regression. The default value is

NULL.

test This is for the type of regression to be used, "testIndGLMMReg", for Gaussian

regression, "testIndGLMMLogistic for logistic regression or "testIndGLMM-

Pois" for Poisson regression.

#### **Details**

If the sample size is less than the number of variables a meesage will appear and no backward regression is performed.

#### Value

The output of the algorithm is S3 object including:

runtime The run time of the algorithm. A numeric vector. The first element is the user

time, the second element is the system time and the third element is the elapsed

time.

info A matrix with the non selected variables and their latest test statistics and logged

p-values.

mat A matrix with the selected variables and their latest statistics and logged p-

values.

final The final regression model.

### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

# References

Eugene Demidenko (2013). Mixed Models: Theory and Applications with R, 2nd Edition. New Jersey: Wiley & Sons.

#### See Also

```
fbed.glmm.reg, ebic.glmm.bsreg, MMPC.glmm
```

### **Examples**

```
## Not run:
require(lme4)
data(sleepstudy)
reaction <- sleepstudy$Reaction
days <- sleepstudy$Days
subject <- sleepstudy$Subject
x <- matrix(rnorm(180 * 200),ncol = 200) ## unrelated predictor variables</pre>
```

```
m1 <- glmm.bsreg(Reaction, x, subject)
m2 <- MMPC.glmm(target = reaction, group = subject, dataset = x)
## End(Not run)</pre>
```

Backward selection regression for GLMM using the eBIC

Backward selection regression for GLMM using the eBIC

# Description

Backward selection regression for GLMM using the eBIC

### Usage

```
ebic.glmm.bsreg(target, dataset, id, wei = NULL, gam = NULL, test = "testIndGLMMReg")
```

# Arguments

target	The class variable. This can be a numerical vector with continuous data, binary or discrete valued data. It can also be a factor variable with two levels only.
dataset	The dataset; provide a numerical a matrix (columns = variables, rows = samples).
id	This is a numerical vector of the same size as target denoting the groups or the subjects.
wei	A vector of weights to be used for weighted regression. The default value is NULL. An example where weights are used is surveys when stratified sampling has occured.
gam	In case the method is chosen to be "eBIC" one can also specify the $gamma$ parameter. The default value is "NULL", so that the value is automatically calculated.
test	This is for the type of regression to be used, "testIndGLMMReg", for Gaussian regression, "testIndGLMMLogistic for logistic regression or "testIndGLMM-Pois" for Poisson regression.

# **Details**

The algorithm is a variation of the usual forward selection. At every step, the most significant variable enters the selected variables set. In addition, only the significant variables stay and are further examined. The non significant ones are dropped. This goes until no variable can enter the set. The user has the option to redo this step 1 or more times (the argument K). In the end, a backward selection is performed to remove falsely selected variables.

### Value

A list including:

runtime The runtime required.

info A matrix with the number of variables and the number of tests performed (or

models fitted) at each round (value of K).

mat A matrix with the selected variables and their eBIC.

### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

#### References

Borboudakis G. and Tsamardinos I. (2019). Forward-backward selection with early dropping. Journal of Machine Learning Research, 20(8): 1-39.

Eugene Demidenko (2013). Mixed Models: Theory and Applications with R, 2nd Edition. New Jersey: Wiley & Sons.

#### See Also

```
fbed.glmm.reg, glmm.bsreg, MMPC.glmm
```

# **Examples**

```
## Not run:
require(lme4)
data(sleepstudy)
reaction <- sleepstudy$Reaction
days <- sleepstudy$Days
subject <- sleepstudy$Subject
x <- matrix(rnorm(180 * 20),ncol = 20) ## unrelated preidctor variables
m1 <- ebic.glmm.bsreg(reaction, x, id = subject)
m2 <- MMPC.glmm(reaction, group = subject, dataset = x)
## End(Not run)</pre>
```

Backward selection regression using the eBIC

Backward selection regression using the eBIC

# Description

Backward selection regression using the eBIC

#### **Usage**

```
ebic.bsreg(target, dataset, test = NULL, wei = NULL, gam = NULL)
```

#### **Arguments**

target The class variable. Provide either a string, an integer, a numeric value, a vector,

a factor, an ordered factor or a Surv object.

dataset The dataset; provide either a data frame or a matrix (columns = variables, rows

= samples).

test The available tests: "testIndReg", "testIndPois", "testIndNB", "testIndLogistic",

"testIndMMReg", "testIndBinom", "censIndCR", "censIndWR", "testIndBeta",

"testIndZIP", "testIndGamma", "testIndNormLog" and "testIndTobit".

wei A vector of weights to be used for weighted regression. The default value is

NULL. It is not suggested when testIndMMReg is used. An example where

weights are used is surveys when stratified sampling has occured.

gam In case the method is chosen to be "eBIC" one can also specify the gamma

parameter. The default value is "NULL", so that the value is automatically cal-

culated.

#### **Details**

The algorithm is a variation of the usual forward selection. At every step, the most significant variable enters the selected variables set. In addition, only the significant variables stay and are further examined. The non significant ones are dropped. This goes until no variable can enter the set. The user has the option to redo this step 1 or more times (the argument K). In the end, a backward selection is performed to remove falsely selected variables.

#### Value

# A list including:

runtime The runtime required.

info A matrix with the number of variables and the number of tests performed (or

models fitted) at each round (value of K).

mat A matrix with the selected variables and their eBIC.

back.rem The variables removed in the backward phase.

back.n.tests The number of models fitted in the backward phase.

#### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

# References

Borboudakis G. and Tsamardinos I. (2019). Forward-backward selection with early dropping. Journal of Machine Learning Research, 20(8): 1-39.

```
fs.reg, bic.fsreg, MMPC
```

### **Examples**

```
dataset <- matrix( runif(100 * 15, 1, 100), ncol = 15 )
target <- rt(100, 10)
a1 <- ebic.bsreg(target, dataset, test = "testIndReg")
target <- rpois(100, 10)
a2 <- ebic.bsreg(target, dataset, test = "testIndPois")</pre>
```

Backward selection with generalised linear regression models

Variable selection in generalised linear regression models with backward selection

# **Description**

Variable selection in generalised linear regression models with backward selection

# Usage

```
glm.bsreg(target, dataset, threshold = 0.05, wei = NULL, test = NULL)
glm.bsreg2(target, dataset, threshold = 0.05, wei = NULL, test = NULL)
```

# Arguments

target	The class variable. Provide either an integer, a numeric value, or a factor. It can also be a matrix with two columns for the case of binomial regression. In this case, the first column is the nubmer of successes and the second column is the number of trials. See also the Details.
dataset	The dataset; provide either a data frame or a matrix (columns = variables, rows = observations). In either case, only two cases are available, either all data are continuous, or categorical.
threshold	Threshold (suitable values in $(0, 1)$ ) for assessing p-values significance. Default value is $0.05$ .
wei	A vector of weights to be used for weighted regression. The default value is NULL. An example where weights are used is surveys when stratified sampling has occured.
test	For "glm.bsreg" this can be "testIndLogistic", "testIndPois", "testIndBinom", testIndReg" or "testIndMMReg". For "glm.bsreg2" this can be "testIndGamma", "testIndNormLog", "testIndQPois" or "testIndQBinom".

# **Details**

This functions currently implements only linear, binomial, binary logistic and Poisson regression. If the sample size is less than the number of variables a meesage will appear and no backward regression is performed.

### Value

The output of the algorithm is S3 object including:

runtime	The run time of the algorithm. A numeric vector. The first element is the user time, the second element is the system time and the third element is the elapsed time.
info	A matrix with the variables and their latest test statistics and <b>logged p-values</b> .
mat	A matrix with the selected variables and their latest test statistic and <b>logged p-value</b> .
ci_test	The conditional independence test used.
final	The final regression model.

# Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

### See Also

```
fs.reg, lm.fsreg, bic.fsreg, bic.glm.fsreg, CondIndTests, MMPC, SES
```

# **Examples**

```
set.seed(123)
#simulate a dataset with continuous data
dataset <- matrix( runif(200 * 10, 1, 100), ncol = 10 )

#define a simulated class variable
target <- rpois(200, 10)
a <- glm.bsreg(target, dataset, threshold = 0.05)

target <- rbinom(200, 1, 0.6)
b <- glm.bsreg(target, dataset, threshold = 0.05)

target <- rgamma(200, 1, 2)
b1 <- glm.bsreg2(target, dataset, threshold = 0.05, test = "testIndGamma")
b2 <- glm.bsreg2(target, dataset, threshold = 0.05, test = "testIndNormLog")</pre>
```

Bayesian Network construction using a hybrid of MMPC and PC Bayesian Network construction using a hybrid of MMPC and PC

# **Description**

Bayesian Network construction using a hybrid of MMPC and PC.

# Usage

```
mmpc.or(x, max_k = 5, threshold = 0.01, test = "testIndFisher", backward = TRUE,
symmetry = TRUE, ini.pvalue = NULL)
```

# **Arguments**

X	A matrix with the variables. The user must know if they are continuous or if they are categorical. If you have a matrix with categorical data, i.e. 0, 1, 2, 3 where each number indicates a category, the minimum number for each variable must be 0. data.frame is also supported, as the dataset in this case is converted into a matrix.
max_k	The maximum conditioning set to use in the conditional indepedence test (see Details of SES or MMPC).
threshold	Threshold (suitable values in $(0, 1)$ ) for assessing p-values significance. Default value is 0.05.
test	The conditional independence test to use. Default value is "testIndFisher". This procedure allows for "testIndFisher", "testIndSPearman" for continuous variables and "gSquare" for categorical variables.
backward	If TRUE, the backward (or symmetry correction) phase will be implemented. This removes any falsely included variables in the parents and children set of the target variable. It calls the link{mmpcbackphase} for this purpose. For perm.ses and wald.ses this is not yet applicable.
symmetry	In order for an edge to be added, a statistical relationship must have been found from both directions. If you want this symmetry correction to take place, leave this boolean variable to TRUE. If you set it to FALSE, then if a relationship between Y and X is detected but not between X and Y, the edge is still added.
ini.pvalue	This is a list with the matrix of the univariate p-values. If you want to run mmhc.skel again, the univariate associations need not be calculated again.

# **Details**

The MMPC is run on every variable. The backward phase (see Tsamardinos et al., 2006) can then take place. After all variables have been used, the matrix is checked for inconsistencies and they are corrected if you want. The "symmetry" argument. Do you want the edge to stay if it was discovered from both variables when they were considered as responses?

# Value

A list including:

ini.pvalue A matrix with the p-values of all pairwise univariate assocations.

Kapa The maximum number of conditioning variables ever observed.

The number of tests MMPC (or SES) performed at each variable.

info Some summary statistics about the edges, minimum, maximum, mean, median

number of edges.

density	The number of edges divided by the total possible number of edges, that is $\#edges / n(n-1)/2$ , where $n$ is the number of variables.
runtime	The run time of the skeleton phase of the algorithm. A numeric vector. The first element is the user time, the second element is the system time and the third element is the elapsed time.
runtime.or	The run time of the PC orientation rules. A numeric vector. The first element is the user time, the second element is the system time and the third element is the elapsed time.
Gini	The adjancency matrix. A value of 1 in $G[i, j]$ appears in $G[j, i]$ also, indicating that i and j have an edge between them.
G	The final adjaceny matrix with the orientations. If $G[i, j] = 2$ then $G[j, i] = 3$ . This means that there is an arrow from node i to node j. If $G[i, j] = G[j, i] = 0$ ; there is no edge between nodes i and j. If $G[i, j] = G[j, i] = 1$ ; there is an (undirected) edge between nodes i and j.
sepset	A list with the separating sets for every value of k.

Bear in mind that the values can be extracted with the \$ symbol, i.e. this is an \$3 class output.

#### Author(s)

Michail Tsagris

R implementation and documentation: Giorgos Athineou <athineou@csd.uoc.gr> and Michail Tsagris <mtsagris@uoc.gr>

### References

Tsamardinos, Brown and Aliferis (2006). The max-min hill-climbing Bayesian network structure learning algorithm. Machine learning, 65(1), 31-78.

Spirtes P., Glymour C. and Scheines R. (2001). Causation, Prediction, and Search. The MIT Press, Cambridge, MA, USA, 3nd edition.

### See Also

```
pc.skel, pc.or, corfs.network
```

# **Examples**

```
y <- rdag2(500, p = 20, nei = 3)
ind <- sample(1:20, 20)
x <- y$x[, ind]
a1 <- mmpc.or(x, max_k = 3, threshold = 0.01, test = "testIndFisher" )
b <- pc.skel( x, alpha = 0.01 )
a2 <- pc.or(b)</pre>
```

Beta regression 21

#### **Description**

Beta regression.

# Usage

```
beta.mod(target, dataset, wei = NULL, xnew= NULL)
```

# **Arguments**

The target (dependent) variable. It must be a numerical vector with proportions, excluding 0s and 1s.

The indendent variable(s). It can be a vector, a matrix or a dataframe with continuous only variables, a data frame with mixed or only categorical variables. If this is NULL, a beta distribution is fitted, no covariates are present.

A vector of weights to be used for weighted regression. The default value is NULL. An example where weights are used is surveys when stratified sampling has occured.

If you have new values for the predictor variables (dataset) whose target variable

you want to predict insert them here. If you put the "dataset" or leave it NULL.

### Details

xnew

The beta regression is fitted. The "beta.reg" is an internal wrapper function and is used for speed up purposes. It is not to be called directly by the user unless they know what they are doing.

#### Value

A list including:

be The estimated coefficients of the model.

phi The estimated precision parameter.

loglik The log-likelihood of the regression model. est The estimated values if xnew is not NULL.

#### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

# References

Ferrari S.L.P. and Cribari-Neto F. (2004). Beta Regression for Modelling Rates and Proportions. Journal of Applied Statistics, 31(7): 799-815.

```
beta.regs, testIndBeta, reg.fit, ridge.reg
```

#### **Examples**

```
y <- rbeta(300, 3, 5)
x \leftarrow matrix(rnorm(300 * 2), ncol = 2)
a1 <- beta.mod(y, x)
w \leftarrow runif(300)
a2 \leftarrow beta.mod(y, x, w)
```

BIC based forward selection

Variable selection in regression models with forward selection using BIC

### **Description**

Variable selection in regression models with forward selection using BIC

# Usage

```
bic.fsreg(target, dataset, test = NULL, wei = NULL, tol = 2, ncores = 1)
```

# **Arguments**

target

The class variable. Provide either a string, an integer, a numeric value, a vector, a factor, an ordered factor or a Surv object. See also Details.

dataset

test

The dataset; provide either a data frame or a matrix (columns = variables, rows = samples). The data can be either euclidean, categorical or both.

The regression model to use. Available options are "testIndReg" for normal linear regression, "testIndBeta" for beta regression, "censIndCR" or "censIndWR" for Cox proportional hazards and Weibull regression respectively, "testIndLogistic" for binomial, multinomial or ordinal regression, "testIndPois" for poisson regression, "testIndNB" for negative binomial regression, "testIndZIP" for zero inflated poisson regression, "testIndRQ" for quantile regression, "testIndGamma" for gamma regression, "testIndNormLog" for linear regression with the log-link (non negative data), "testIndTobit" for Tobit regression. If you want to use multinomial or ordinal logistic regression, make sure your target is factor. See also SES and CondIndTests for the tests.

A vector of weights to be used for weighted regression. The default value is NULL. It is not suggested when robust is set to TRUE. An example where weights are used is surveys when stratified sampling has occured.

tol

The difference bewtween two successive values of the stopping rule. By default this is is set to 2. If for example, the BIC difference between two succesive models is less than 2, the process stops and the last variable, even though significant does not enter the model.

wei

ncores

How many cores to use. This plays an important role if you have tens of thousands of variables or really large sample sizes and tens of thousands of variables and a regression based test which requires numerical optimisation. In other cammb it will not make a difference in the overall time (in fact it can be slower). The parallel computation is used in the first step of the algorithm, where univariate associations are examined, those take place in parallel. We have seen a reduction in time of 50% with 4 cores in comparison to 1 core. Note also, that the amount of reduction is not linear in the number of cores.

#### **Details**

If the current 'test' argument is defined as NULL or "auto" and the user\_test argument is NULL then the algorithm automatically selects the best test based on the type of the data. Particularly:

- if target is a factor, the multinomial or the binary logistic regression is used. If the target has two values only, binary logistic regression will be used.
- if target is a ordered factor, the ordinal regression is used.
- if target is a numerical vector or a matrix with at least two columns (multivariate) linear regression is used.
- if target is discrete numerical (counts), the poisson regression conditional independence test is used. If there are only two values, the binary logistic regression is to be used.
- if target is a Surv object, the Survival conditional independence test (Cox regression) is used.

### Value

The output of the algorithm is S3 object including:

runtime The run time of the algorithm. A numeric vector. The first element is the user

time, the second element is the system time and the third element is the elapsed

time.

mat A matrix with the variables and their latest test statistics and p-values.

info A matrix with the selected variables, and the BIC of the model with that and all

the previous variables.

ci\_test The conditional independence test used.

final The final regression model.

### Author(s)

Michail Tsagris

R implementation and documentation: Giorgos Athineou <athineou@csd.uoc.gr> Michail Tsagris <mtsagris@uoc.gr>

#### References

Tsamardinos I., Aliferis C. F. and Statnikov, A. (2003). Time and sample efficient discovery of Markov blankets and direct causal relations. In Proceedings of the 9th ACM SIGKDD international conference on Knowledge discovery and data mining (pp. 673-678).

```
glm.fsreg, lm.fsreg, bic.glm.fsreg, CondIndTests, MMPC, SES
```

### **Examples**

```
set.seed(123)
dataset <- matrix( runif(200 * 20, 1, 100), ncol = 20 )
target <- 3 * dataset[, 10] + 2 * dataset[, 15] + 3 * dataset[, 20] + rnorm(200, 0, 5)

a1 <- bic.fsreg(target, dataset, tol = 4, ncores = 1, test = "testIndReg" )
a3 <- MMPC(target, dataset, ncores = 1)
target <- round(target)
b1 <- bic.fsreg(target, dataset, tol = 2, ncores = 1, test = "testIndReg" )</pre>
```

BIC based forward selection with generalised linear models

Variable selection in generalised linear models with forward selection based on BIC

# **Description**

Variable selection in generalised linear models with forward selection based on BIC

# Usage

```
bic.glm.fsreg( target, dataset, wei = NULL, tol = 0, ncores = 1)
bic.mm.fsreg( target, dataset, wei = NULL, tol = 0, ncores = 1)
bic.gammafsreg(target, dataset, wei = NULL, tol = 0, ncores = 1)
bic.normlog.fsreg(target, dataset, wei = NULL, tol = 0, ncores = 1)
```

# **Arguments**

target	The class variable. It can be either a vector with binary data (binomial regression), counts (poisson regression). If none of these is identified, linear regression is used.
dataset	The dataset; provide either a data frame or a matrix (columns = variables, rows = samples). These can be continous and or categorical.
wei	A vector of weights to be used for weighted regression. The default value is NULL. It is not suggested when robust is set to TRUE.
tol	The difference bewtween two successive values of BIC. By default this is is set to 2. If for example, the BIC difference between two succesive models is less than 2, the process stops and the last variable, even though significant does not enter the model.

ncores

How many cores to use. This plays an important role if you have tens of thousands of variables or really large sample sizes and tens of thousands of variables and a regression based test which requires numerical optimisation. In other cammb it will not make a difference in the overall time (in fact it can be slower). The parallel computation is used in the first step of the algorithm, where univariate associations are examined, those take place in parallel. We have seen a reduction in time of 50% with 4 cores in comparison to 1 core. Note also, that the amount of reduction is not linear in the number of cores.

#### Details

Forward selection via the BIC is implemented. A variable which results in a reduction of BIC will be included, until the reduction is below a threshold set by the user (argument "tol").

#### Value

The output of the algorithm is S3 object including:

runtime	The run time of the algorithm. A numeric vector. The first element is the user time, the second element is the system time and the third element is the elapsed time.
mat	A matrix with the variables and their latest test statistics and <b>logged p-values</b> .
info	A matrix with the selected variables, and the BIC of the model with that and all the previous variables.
ci_test	The conditional independence test used.
final	The final regression model.

#### Author(s)

Michail Tsagris

R implementation and documentation: Giorgos Aathineou <athineou@csd.uoc.gr> Michail Tsagris <mtsagris@uoc.gr>

### See Also

```
fs.reg, lm.fsreg, bic.fsreg, CondIndTests, MMPC, SES
```

# **Examples**

```
set.seed(123)
dataset <- matrix( runif(200 * 20, 1, 100), ncol = 20 )
target <- 3 * dataset[, 10] + 2 * dataset[, 15] + 3 * dataset[, 20] + rnorm(200, 0, 5)
a1 <- bic.glm.fsreg(target, dataset, tol = 2, ncores = 1 )
a2 <- bic.glm.fsreg( round(target), dataset, tol = 2, ncores = 1 )
y <- target  ; me <- median(target)  ; y[ y < me ] <- 0  ; y[ y >= me ] <- 1
a3 <- bic.glm.fsreg( y, dataset, tol = 2, ncores = 1 )</pre>
```

Bootstrap bias correction for the performance of the cross-validation procedure  $Bootstrap\ bias\ correction\ for\ the\ performance\ of\ the\ cross-validation\ procedure$ 

## Description

Bootstrap bias correction for the performance of the cross-validation procedure.

#### Usage

```
bbc(predictions, target, metric = "auc.mxm", conf = 0.95, B = 1000)
```

### Arguments

predictions A matrix with the predictived values.

target A vector with the target variable, survival object, factor (ordered or unordered)

or a numerical vector.

metric The possible values are:

a) Binary target: "auc.mxm" (area under the curve), "fscore.mxm" (F-score), "prec.mxm" (precision), "euclid\_sens.spec.mxm" (Euclidean distance of sensitivity and specificity), "spec.mxm" (specificity), "sens.mxm" (sensitivity), "acc.mxm"

(accuracy, proportion of correct classification).

b) Multinomial target: "acc\_multinom.mxm" (accuracy, proportion of correct

classification).

c) Ordinal target: "ord\_mae.mxm" (mean absolute error).

d) Continuous target: "mae.mxm" (MAE with continuous target), "mse.mxm" (mean squared error), "pve.mxm" (percentage of variance explained).

e) Survival target "ci.mxm" (concordance index for Cox regression), "ciwr.mxm" (concordance index for Weibull regression). g) Count target "poisdev.mxm".

h) Binomial target "binomdev.mxm" (deviance of binomial regression).

The "nbdev.mxm" (negative binomial deviance) is missing. For more informa-

tion on these see cv. ses. boldNote that they come with "".

conf A number between 0 and 1, the confidence level.

B The number of bootstrap replicates. The default number is 1000.

### **Details**

Upon completion of the cross-validation, the predicted values produced by all predictive models across all folds is collected in a matrix P of dimensions  $n \times M$ , where n is the number of samples and M the number of trained models or configurations. Sampled with replacement a fraction of rows (predictions) from P are denoted as the in-sample values. On average, the newly created set will be comprised by 63.2% of the original individuals (The probability of sampling, with replacement, a sample of n numbers from a set of n numbers is  $1 - \left(1 - \frac{1}{n}\right)^n \simeq 1 - \frac{1}{e} = 0.632$ ), whereas

the rest 36.8% will be random copies of them. The non re-sampled rows are denoted as out-of-sample values. The performance of each model in the in-sample rows is calculated and the model (or configuration) with the optimal performance is selected, followed by the calculation of performance in the out-of-sample values. This process is repeated B times and the average performance is returned.

Note, that the only computational overhead is with the repetitive re-sampling and calculation of the predictive performance, i.e. no model is fitted nor trained. The final estimated performance usually underestimates the true performance, but this negative bias is smaller than the optimistic uncorrected performance.

Note, that all metrics are for maximization. For this reason "mse.mxm", "mae.mxm", "ord\_mae.mxm", "poisdev.mxm", "binomdev.mxm" are multiplied by -1.

#### Value

### A list including:

out.perf The B out sampled performances. Their mean is the "bbc.perf" given above.

The bootstrap bias corrected performance of the chosen algorithm, model or configuration.

The (1- conf)% confidence interval of the BBC performance. It is based on the empirical or percentile method for bootstrap samples. The lower and upper 2.5% of the "out.perf".

# Author(s)

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>.

### References

Ioannis Tsamardinos, Elissavet Greasidou and Giorgos Borboudakis (2018). Bootstrapping the out-of-sample predictions for efficient and accurate cross-validation. Machine Learning (To appear).

```
https://link.springer.com/article/10.1007/s10994-018-5714-4
```

# See Also

```
cv.ses, cv.gomp
```

## **Examples**

```
predictions <- matrix(rbinom(200 * 100, 1, 0.7), ncol = 100)
target <- rbinom(200, 1, 0.5)
bbc(predictions, target, metric = "auc.mxm")</pre>
```

Calculation of the constant and slope for each subject over time

Calculation of the constant and slope for each subject over time

# Description

Calculation of the constant and slope for each subject over time.

# Usage

```
group.mvbetas(x, id, reps)
```

#### **Arguments**

X	The dataset; provide a numerical a matrix. This should contain longitudinal data. Each variable is a column, and rows are longitudinal data.
id	This is a numerical vector denoting the subjects. Its length must be equal to the number of rows of the x matrix.
reps	This is a numerical vector with the time points. Its length must be equal to the number of rows of the x matrix.

### **Details**

This function is used internally in SES and MMPC and does calculations required bys the first step of the **Static-Longitudinal** scenario of Tsagris, Lagani and Tsamardinos (2018). The measurements of each subject are regressed againt time. So, for each subject, we get the constant and intercept over time and this is repated for very feature.

# Value

A matrix. The first r (= length(unique(id)), the nubmer of subjects) rows contain the constants and the other r rows contain the slopes.

#### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

# References

Tsagris M., Lagani V., & Tsamardinos I. (2018). Feature selection for high-dimensional glmm data. BMC bioinformatics, 19(1), 17.

McCullagh, Peter, and John A. Nelder. Generalized linear models. CRC press, USA, 2nd edition, 1989.

```
fbed.gee.reg, glmm.bsreg, MMPC.glmm
```

#### **Examples**

```
## assume these are longitudinal data, each column is a variable (or feature) x <- matrix( rnorm(100 \star 30), ncol = 30 ) id <- rep(1:20, each = 5) ## 20 subjects reps <- rep( seq(4, 12, by = 2), 20) ## 5 time points for each subject a <- group.mvbetas(x, id, reps) dim(a) ## 5 100 ## these are the regression coefficients of the first subject's values on the ## reps (which is assumed to be time in this example) a[c(1, 21), 1] coef( lm( x[id == 1, 1] \sim reps[1:5] ) )
```

Certificate of exclusion from the selected variables set using SES or MMPC Certificate of exclusion from the selected variables set using SES or MMPC

### Description

Information on why one ore more variables were not selected.

#### Usage

```
certificate.of.exclusion(xIndex, sesObject = NULL, mmpcObject = NULL)
certificate.of.exclusion2(xIndex, mmpc2object)
```

# **Arguments**

xIndex A numerical vector with the indices of the predictor variables.

sesObject If you ran SES, wald.ses or perm.ses, give the whole SES object here, otherwise

leave it NULL.

mmpcObject If you ran MMPC, wald.mmpc or prm.mmpc, give the whole MMPC object

here, otherwise leave it NULL.

mmpc2object If you ran mmpc2, give the whole MMPC object here.

#### Value

A list with the conditioning variables (if any), the test statistic and the logarithm of the p-value. In case a variable has been selected a message appears.

# Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

**MMPC** 

### **Examples**

```
set.seed(123)
#simulate a dataset with continuous data
dataset <- matrix(runif(100 * 100, 1, 100), ncol = 100)</pre>
#define a simulated class variable
target <- 3 * dataset[, 10] + 2 * dataset[, 100] + 3 * dataset[, 20] + rnorm(100, 0, 5)</pre>
# define some simulated equivalences
dataset[, 15] <- dataset[, 10] + rnorm(100, 0, 2)
dataset[, 100] <- dataset[, 100] + rnorm(100, 0, 2)</pre>
dataset[, 20] <- dataset[, 100] + rnorm(100, 0, 2)</pre>
# run the SES algorithm
mod1 <- SES(target, dataset, max_k = 5, threshold = 0.05, test = "testIndFisher",</pre>
hash = TRUE, hashObject = NULL);
mod2 <- MMPC(target, dataset, max_k = 5, threshold = 0.05, test = "testIndFisher",</pre>
hash = TRUE, hashObject = NULL);
certificate.of.exclusion(c(10, 15, 30, 45, 20), mod1)
certificate.of.exclusion(c(10, 15, 30, 45, 20), NULL, mod2)
```

Check Markov equivalence of two DAGs

Check Markov equivalence of two DAGs

# **Description**

Check Markov equivalence of two DAGs.

### Usage

```
equivdags(g1, g2)
```

### **Arguments**

g1	The matrix of a DAG or a partially directed graph as produced from pc.or or
	any other algorithm

The matrix of a DAG or a partially directed graph as produced from pc.or or any other algorithm.

### **Details**

Two DAGs are Markov equivalent if a) they have the same adjancencies (regardlsee of the mark, arrowhead, tail or nothing) and b) they have the same unshielded colliders.

### Value

A list including:

apofasi A boolean variable, TRUE of FALSE.

mes A message specyfying the result, the dimensions of the adjacency matrices do

not match for example, or the number of adjancencies is not the same, they do

not share the same unshilded colliders, or they are Markov equivalent.

### Author(s)

Michail Tsagris

R implementation and documentation: Giorgos Athineou <athineou@csd.uoc.gr> and Michail Tsagris <mtsagris@uoc.gr>

#### References

Tsamardinos, Brown and Aliferis (2006). The max-min hill-climbing Bayesian network structure learning algorithm. Machine learning, 65(1), 31-78.

#### See Also

```
pc.or, mmhc.skel, pc.con
```

# **Examples**

```
y <- rdag(1000, 10, 0.3)
tru <- y$G
x <- y$x
mod <- pc.con(x)

eg <- dag2eg(y$G) ## make it essential graph first
est <- pc.or(mod)$G

equivdags(est, tru)</pre>
```

Check whether a directed graph is acyclic

Check whether a directed graph is acyclic

# **Description**

Check whether a directed graph is acyclic.

# Usage

```
is.dag(dag)
```

# **Arguments**

dag

A square matrix representing a directed graph which contains either 0, 1 or 0, 2, and 3. In the first canse where G[i, j] = 1, means there is an arrow from node i to node j. In the second case G[i, j] = 2 and G[j, i] = 3 means that there is an arrow from node i to node j, where the 2 iindcates the arrohead and the 3 inducates the arrowtail.

#### **Details**

The topological sort is performed. If it cannot be performed, NAs are returned. Hence, the functions checks for NAs.

### Value

A logical value, TRUE if the matrix represents a DAG and FALSE otherwise.

### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

#### References

Chickering, D.M. (1995). A transformational characterization of equivalent Bayesian network structures. Proceedings of the 11th Conference on Uncertainty in Artificial Intelligence, Montreal, Canada, 87-98.

#### See Also

```
topological_sort, dag2eg, pc.or
```

# **Examples**

```
# simulate a dataset with continuous data
# simulate a dataset with continuous data
G <- rdag(100, 20, 0.3)$G
is.dag(G) ## TRUE</pre>
```

CondInditional independence tests

MXM Conditional independence tests

# **Description**

Currently the **MXM** package supports numerous tests for different types of target (dependent) and predictor (independent) variables. The target variable can be of continuous, discrete, categorical and of survival type. As for the predictor variables, they can be continuous, categorical or mixed.

The **testIndFisher** and the **gSquare** tests have two things in common. They do not use a model implicitly (i.e. estimate some beta coefficients), even though there is an underlying assumed one. Secondly they are pure tests of independence (again, with assumptions required).

As for the other tests, they share one thing in common. For all of them, two parametric models must be fit. The null model containing the conditioning set of variables alone and the alternative model containing the conditioning set and the candidate variable. The significance of the new variable is assessed via a log-likelihood ratio test with the appropriate degrees of freedom. All of these tests which are available for SES and MMPC are summarized in the below table.

Target variable	Predictor variables	Available tests	Short explanation
Continuous	Continuous	testIndFisher	Partial correlation
Continuous	Continuous	testIndMMFisher	Robust partial correlation
Continuous	Continuous	testIndSpearman	Partial correlation
Continuous	Mixed	testIndMMReg	MM regression
Continuous	Mixed	testIndRQ	Median regression
Proportions	Continuous	testIndFisher	Partial correlation
Proportions	Continuous	testIndMMFisher	Robust partial correlation
Proportions	Continuous	testIndSpearman	Partial correlation
Proportions	Mixed	testIndReg	Linear regression
Proportions	Mixed	testIndMMReg	MM regression
Proportions	Mixed	testIndRQ	Median regression
Proportions	Mixed	testIndBeta	Beta regression
Proportions	Mixed	testIndQbinom	Quasi binomial regression
Strictly positive	Mixed	testIndIGreg	Inverse Gaussian regression
Strictly positive	Mixed	testIndGamma	Gamma regression
Non negative	Mixed	testIndNormLog	Gaussian regression with log link
Strictly Positive	Mixed	censIndWR	Weibull regression
Strictly Positive	Mixed	censIndER	Exponential regression
Strictly Positive	Mixed	censIndLLR	Log-logistic regression
Successes \& totals	Mixed	testIndBinom	Binomial regression
Discrete	Mixed	testIndPois	Poisson regression
Discrete	Mixed	testIndZIP	Zero Inflated
			Poisson regression
Discrete	Mixed	testIndNB	Negative binomial regression
Discrete	Mixed	testIndQPois	Quasi Poisson regression
Factor with two	Mixed	testIndLogistic	Binary logistic regression
levels or binary		Ç	, ,
Factor with two	Mixed	testIndQBinom	Quasi binomial regression
levels or binary			
Factor with more	Mixed	testIndMultinom	Multinomial logistic regression
than two levels			
(unordered)			
Factor with more than	Mixed	testIndOrdinal	Ordinal logistic regression
two levels (ordered)			

Categorical	Categorical	gSquare	G-squared test of independence
Categorical	Categorical	testIndMultinom	Multinomial logistic regression
Categorical	Categorical	testIndOrdinal	Ordinal logistic regression
Survival	Mixed	censIndCR	Cox regression
Survival	Mixed	censIndWR	Weibull regression
Survival	Mixed	censIndER	Exponential regression
Survival	Mixed	censIndLLR	Log-logistic regression
Left censored	Mixed	testIndTobit	Tobit regression
Case-control	Mixed	testIndClogit	Conditional logistic regression
Multivariate continuous	Mixed	testIndMVreg	Multivariate linear regression
Compositional data	Mixed	testIndMVreg	Multivariate linear regression
(no zeros)		after multivariate	
		logit transformation	
Longitudinal/clustered	Continuous	testIndGLMMReg	Linear mixed models
Clustered	Continuous	testIndLMM	Fast linear mixed models
Binary longitudinal	Continuous	testIndGLMMLogistic	Logistic mixed regression
and clustered			
Count longitudinal	Continuous	testIndGLMMPois	Poisson mixed regression
and clustered			
Positive longitudinal	Continuous	testIndGLMMNormLog	GLMM with Gaussian regression
and clustered			and log link
Non negative longitudinal	Continuous	testIndGLMMGamma	GLMM with Gamma regression
and clustered			and log link
Longitudinal/clustered	Continuous	testIndGEEReg	GEE with Gaussian regression
Binary longitudinal	Continuous	testIndGEELogistic	GEE with logistic regression
and clustered			
Count longitudinal	Continuous	testIndGEEPois	GEE with Poisson regression
and clustered			
Positive longitudinal	Continuous	testIndGEENormLog	GEE with Gaussian regression
and clustered	~ .		and log link
Non negative longitudinal	Continuous	testIndGEEGamma	GEE with Gamma regression
and clustered	<i>a</i>	A TOLIMACD	and log link
Clustered survival	Contiunous	testIndGLMMCR	Mixed effects Cox regression
Circular	Continuous	testIndSPML	Circular-linear regression

# **Details**

These tests can be called by SES, MMPC, wald.mmpc or individually by the user. In all regression cases, there is an option for weights.

# Log-likelihood ratio tests

1. **testIndFisher**. This is a standard test of independence when both the target and the set of predictor variables are continuous (continuous-continuous). When the joint multivariate normality of all the variables is assumed, we know that if a correlation is zero this means that the two variables are independent. Moving in this spirit, when the partial correlation between the target variable and the new predictor variable conditioning on a set of (predictor) variables is zero, then we have evidence to say they are independent as well. An easy way to

calculate the partial correlation between the target and a predictor variable conditioning on some other variables is to regress the both the target and the new variable on the conditioning set. The correlation coefficient of the residuals produced by the two regressions equals the partial correlation coefficient. If the robust option is selected, the two aforementioned regression models are fitted using M estimators (Marona et al., 2006). If the target variable consists of proportions or percentages (within the (0, 1) interval), the logit transformation is applied beforehand.

- 2. **testIndSpearman**. This is a non-parametric alternative to **testIndFisher** test. It is a bit slower than its competitor, yet very fast and suggested when normality assumption breaks down or outliers are present. In fact, within SES, what happens is that the ranks of the target and of the dataset (predictor variables) are computed and the **testIndSpearman** is aplied. This is faster than applying Fisher with M estimators as described above. If the target variable consists of proportions or percentages (within the (0, 1) interval), the logit transformation is applied beforehand.
- 3. **testIndReg**. In the case of target-predictors being continuous-mixed or continuous-categorical, the suggested test is via the standard linear regression. In this case, two linear regression models are fitted. One with the conditioning set only and one with the conditioning set plus the new variable. The significance of the new variable is assessed via the F test, which calculates the residual sum of squares of the two models. The reason for the F test is because the new variable may be categorical and in this case the t test cannot be used. It makes sense to say, that this test can be used instead of the **testIndFisher**, but it will be slower. If the robust option is selected, the two models are fitted using M estimators (Marona et al. 2006). If the target variable consists of proportions or percentages (within the (0, 1) interval), the logit transformation is applied beforehand.
- 4. **testIndRQ**. An alternative to **testIndReg** for the case of continuous-mixed (or continuous-continuous) variables is the **testIndRQ**. Instead of fitting two linear regression models, which model the expected value, one can choose to model the median of the distribution (Koenker, 2005). The significance of the new variable is assessed via a rank based test calibrated with an F distribution (Gutenbrunner et al., 1993). The reason for this is that we performed simulation studies and saw that this type of test attains the type I error in contrast to the log-likelihood ratio test. The benefit of this regression is that it is robust, in contrast to the classical linear regression. If the target variable consists of proportions or percentages (within the (0, 1) interval), the logit transformation is applied beforehand.
- 5. **testIndBeta**. When the target is proportion (or percentage, i.e., between 0 and 1, not inclusive) the user can fit a regression model assuming a beta distribution. The predictor variables can be either continuous, categorical or mixed. The procedure is the same as in the **testIndReg** case.
- 6. **Alternatives to testIndBeta**. Instead of **testIndBeta** the user has the option to choose all the previous to that mentioned tests by transforming the target variable with the logit transformation. In this way, the support of the target becomes the whole of R^d and then depending on the type of the predictors and whether a robust approach is required or not, there is a variety of alternative to beta regression tests.
- 7. **testIndIGreg**. When you have non negative data, i.e. the target variable takes positive values (including 0), a suggested regression is based on the the inverse gaussian distribution. The link function is not the inverse of the square root as expected, but the logarithm. This is to ensure that the fitted values will be always be non negative. The predictor variables can be either continuous, categorical or mixed. The significance between the two models is assessed via the

log-likelihood ratio test. Alternatively, the user can use the Weibull regression (**censIndWR**), gamma regression (**testIndGamma**) or Gaussian regression with log link (**testIndNormLog**).

- 8. **testIndGamma**. This is an alternative to **testIndIGreg**.
- 9. **testIndNormLog**. This is a second alternative to **testIndIGreg**.
- 10. testIndPois. When the target is discrete, and in specific count data, the default test is via the Poisson regression. The predictor variables can be either continuous, categorical or mixed. The procedure is the same as in all the previously regression model based tests, i.e. the log-likelihood ratio test is used to assess the conditional independence of the variable of interest.
- testIndNB. As an alternative to the Poisson regression, we have included the Negative binomial regression to capture cases of overdispersion. The predictor variables can be either continuous, categorical or mixed.
- 12. **testIndQPois**. This is a better alternative for discrete target, better than the **testIndPois** and than the **testIndNB**, because it can capture both cases of overdispersion and undersidpesrion.
- 13. **testIndZIP**. When the number of zeros is more than expected under a Poisson model, the zero inflated poisson regression is to be employed. The predictor variables can be either continuous, categorical or mixed.
- 14. **testIndLogistic**. When the target is categorical with only two outcomes, success or failure for example, then a binary logistic regression is to be used. Whether regression or classification is the task of interest, this method is applicable. The advantage of this over a linear or quadratic discriminant analysis is that it allows for categorical predictor variables as well and for mixed types of predictors.
- testIndQBinom. This is an alternative to either the testIndLogistic or especially the testInd-Beta.
- 16. testIndMultinom. If the target has more than two outcomes, but it is of nominal type, there is no ordering of the outcomes, multinomial logistic regression will be employed. Again, this regression is suitable for classification purposes as well and it to allows for categorical predictor variables.
- 17. **testIndOrdinal**. This is a special case of multinomial regression, in which case the outcomes have an ordering, such as **not satisfied**, **neutral**, **satisfied**. The appropriate method is ordinal logistic regression.
- 18. **testIndBinom**. When the target variable is a matrix of two columns, where the first one is the number of successes and the second one is the number of trials, binomial regression is to be used.
- 19. **gSquare**. If all variables, both the target and predictors are categorical the default test is the G-square test of independence. It is similar to the chi-squared test of independence, but instead of using the chi-squared metric between the observed and estimated frequencies in contingency tables, the Kullback-Leibler divergence of the observed from the estimated frequencies is used. The asymptotic distribution of the test statistic is a chi-squared distribution on some appropriate degrees of freedom. The target variable can be either ordered or unordered with two or more outcomes.
- 20. **Alternatives to gSquare**. An alternative to the **gSquare** test is the **testIndLogistic**. Depending on the nature of the target, binary, un-ordered multinomial or ordered multinomial the appropriate regression model is fitted.

- 21. **censIndCR**. For the case of time-to-event data, a Cox regression model is employed. The predictor variables can be either continuous, categorical or mixed. Again, the log-likelihood ratio test is used to assess the significance of the new variable.
- 22. **censIndWR**. A second model for the case of time-to-event data, a Weibull regression model is employed. The predictor variables can be either continuous, categorical or mixed. Again, the log-likelihood ratio test is used to assess the significance of the new variable. Unlike the semi-parametric Cox model, the Weibull model is fully parametric.
- 23. **censIndER**. A third model for the case of time-to-event data, an exponential regression model is employed. The predictor variables can be either continuous, categorical or mixed. Again, the log-likelihood ratio test is used to assess the significance of the new variable. This is a special case of the Weibull model.
- 24. **testIndClogit**. When the data come from a case-control study, the suitable test is via conditional logistic regression.
- 25. **testIndMVreg**. In the case of multivariate continuous targets, the suggested test is via a multivariate linear regression. The target variable can be compositional data as well. These are positive data, whose vectors sum to 1. They can sum to any constant, as long as it the same, but for convenience reasons we assume that they are normalised to sum to 1. In this case the additive log-ratio transformation (multivariate logit transformation) is applied beforehand.
- 26. **testIndSPML**. With a circular target, the projected bivariate normal distribution (Presnell et al., 1998) is used to perform regression.

# Tests for clustered/longitudinal data

- testIndGLMMReg, testIndGLMM, testIndGLMMPois & testIndGLMMLogistic. In the
  case of a longitudinal or clustered targets (continuous, proportions, binary or counts), the
  suggested test is via a (generalised) linear mixed model. testIndGLMMCR stands for mixed
  effects Cox regression.
- testIndGEEReg, testIndGEELogistic, testIndGEEPois, testIndGEENormLog and testIndGEEGamma.
   In the case of a longitudinal or clustered targets (continuous, proportions, binary, counts, positive, strictly positive), the suggested test is via GEE (Generalised Estimating Equations).

### Wald based tests

The available tests for wald.ses and wald.mmpc are listed below. Note, that only continuous predictors are allowed.

Target variable	Available tests	Short explanation
Continuous	waldMMReg	MM regression
Proportions	waldMMReg	MM regression
		after logit transformation
Proportions	waldBeta	Beta regression
Non negative	waldIGreg	Inverse Gaussian regression
Strictly positive	waldGamma	Gamma regression
Non negative	waldNormLog	Gaussian regression with log link
Successes \& totals	testIndBinom	Binomial regression
Discrete	waldPois	Poisson regression
Discrete	waldSpeedPois	Poisson regression

Discrete	waldZIP	Zero Inflated Poisson regression
Discrete	waldNB	Negative binomial regression
Factor with two	waldLogistic	Logistic regression
levels or binary		
Factor with more than	waldOrdinal	Ordinal logistic regression
two levels (ordered)		
Left censored	waldTobit	Tobit regression
Case-control	Mixed	testIndClogit
		Conditional logistic regression
Survival	waldCR	Cox regression
Survival	waldWR	Weibull regression
Survival	waldER	Exponential regression
Survival	waldLLR	Log-logistic regression

# Permutation based tests

The available tests for perm.ses and perm.mmpc are listed below. Note, that only continuous predictors are allowed.

Target variable	Available tests	Short explanation
Continuous	permFisher	Pearson correlation
Continuous	permMMFisher	Robust Pearson correlation
Continuous	permDcor	Distance correlation
Continuous	permReg	Linear regression
Proportions	permReg	Linear regression
		after logit transformation
Proportions	permBeta	Beta regression
Non negative	permIGreg	Inverse Gaussian regression
Strictly positive	permGamma	Gamma regression
Non negative	permNormLog	Gaussian regression with log link
Non negative	permWR	Weibull regression
Successes \& totals	permBinom	Binomial regression
Discrete	permPois	Poisson regression
Discrete	permZIP	Zero Inflated
		Poisson regression
Discrete	permNB	Negative binomial regression
Factor with two	permLogistic	Binary logistic regression
levels or binary		
Factor with more than two levels (nominal)	permMultinom	Multinomial logistic regression
Factor with more than	permOrdinal	Ordinal logistic regression
two levels (ordered)	permoramar	Ordinal logistic regression
Left censored	permTobit	Tobit regression
Survival	permCR	Cox regression
Survival	permWR	Weibull regression
Survival	permER	Exponential regression
Survival	permLLR	Log-logistic regression
Survivar	permeen	Log logistic regression

# Author(s)

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# References

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Conditional independence regression based tests

Conditional independence regression based tests

# **Description**

Conditional independence regression based tests.

### Usage

```
cond.regs(target, dataset, xIndex, csIndex, test = NULL, wei = NULL, ncores = 1)
glmm.condregs(target, reps = NULL, id, dataset, xIndex, csIndex, test, wei = NULL,
slopes = FALSE, ncores = 1)
gee.condregs(target, reps = NULL, id, dataset, xIndex, csIndex, test, wei = NULL,
correl = "echangeable", se = "jack", ncores = 1)
```

### **Arguments**

wei

target The target (dependent) variable. It must be a numerical vector.

dataset The indendent variable(s). For the "univregs" this can be a matrix or a dataframe

with continuous only variables, a data frame with mixed or only categorical variables. For the "wald.univregs", "perm.univregs", "score.univregs" and "rint.regs"

this can only by a numerical matrix.

xIndex The indices of the variables whose association with the target you want to test.

csIndex The index or indices of the variable(s) to condition on. If this is 0, the the

function univregs will be called.

For the "cond.regs" one of the following: **testIndBeta**, **testIndReg**, **testInd-**

Logistic, testIndOrdinal, testIndPois, testIndQPois, testIndZIP, testIndNB, testIndClogit, testIndBinom, testIndQBinom, testIndIGreg, censIndCR, censIndWR, censIndER, censIndLLR, testIndMMReg, testIndMVreg, testIndMultinom, testIndTobit, testIndGamma, testIndNormLog or testIndSPML for a circu-

lar target.

For the "glmm.condregs" one of the following: testIndLMReg, testIndGLMM-Logistic, testIndGLMMPois, testIndGLMMOrdinal, testIndGLMMGamma or testIndGLMMNormLog.

For the "gee.condregs" one of the following: **testIndGEEReg**, **testIndGEELogistic**, **testIndGEEPois**, **testIndGEEGamma** or **testIndGEENormLog**.

Note that in all cases you must give the name of the test, without " ".

A vector of weights to be used for weighted regression. The default value is

NULL. An example where weights are used is surveys when stratified sampling

has occured.

ncores How many cores to use. This plays an important role if you have tens of thou-

sands of variables or really large sample sizes and tens of thousands of variables and a regression based test which requires numerical optimisation. In other cases it will not make a difference in the overall time (in fact it can be slower). The parallel computation is used in the first step of the algorithm, where univariate associations are examined, those take place in parallel. We have seen a reduction in time of 50% with 4 cores in comparison to 1 core. Note also, that the amount

of reduction is not linear in the number of cores.

id A numerical vector of the same length as target with integer valued numbers,

such as 1, 2, 3,... (zeros, negative values and factors are not allowed) specifying the clusters or subjects. This argument is for the rint.regs (see details for more

information).

reps If you have measurements over time (lognitudinal data) you can put the time here

(the length must be equal to the length of the target) or set it equal to NULL.

(see details for more information).

slopes Should random slopes for the ime effect be fitted as well? Default value is

FALSE.

correl The correlation structure. For the Gaussian, Logistic, Poisson and Gamma regression this can be either "exchangeable" (compound symmetry, suitable for

clustered data) or "ar1" (AR(1) model, suitable for longitudinal data).

se

The method for estimating standard errors. This is very important and crucial. The available options for Gaussian, Logistic, Poisson and Gamma regression are: a) 'san.se', the usual robust estimate. b) 'jack': if approximate jackknife variance estimate should be computed. c) 'j1s': if 1-step jackknife variance estimate should be computed and d) 'fij': logical indicating if fully iterated jackknife variance estimate should be computed. If you have many clusters (sets of repeated measurements) "san.se" is fine as it is astmpotically correct, plus jacknife estimates will take longer. If you have a few clusters, then maybe it's better to use jacknife estimates.

The jackknife variance estimator was suggested by Paik (1988), which is quite suitable for cases when the number of subjects is small (K < 30), as in many biological studies. The simulation studies conducted by Ziegler et al. (2000) and Yan and Fine (2004) showed that the approximate jackknife estimates are in many cases in good agreement with the fully iterated ones.

# **Details**

This function is more as a help function for MMPC, but it can also be called directly by the user. In some, one should specify the regression model to use and the function will perform all simple regressions, i.e. all regression models between the target and each of the variables in the dataset. The function does not check for zero variance columns, only the "univregs" and related functions do.

If you want to use the GEE methodology, make sure you load the library geepack first.

### Value

A list including:

stat The value of the test statistic.

pvalue The **logarithm of the p-value** of the test.

### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

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#### See Also

```
univregs, SES, MMPC, CondIndTests, reg.fit, ridge.reg
```

### **Examples**

```
y <- rpois(100, 15)
x <- matrix( rnorm(100 * 10), ncol = 10)
a1 <- univregs(y, x, test = testIndPois)
a4 <- cond.regs(y, as.data.frame(x), xIndex = 1:9, csIndex = 10, test = testIndPois)</pre>
```

Conditional independence test for binary, categorical or ordinal data

Conditional independence test for binary, categorical or ordinal class variables

# **Description**

The main task of this test is to provide a p-value PVALUE for the null hypothesis: feature 'X' is independent from 'TARGET' given a conditioning set CS. The pvalue is calculated by comparing a logistic model based on the conditioning set CS against a model whose regressor are both X and CS. The comparison is performed through a chi-square test with the aproprirate degrees of freedom on the difference between the deviances of the two models.

# Usage

```
testIndLogistic(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
testIndMultinom(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
testIndOrdinal(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
testIndQBinom(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
permLogistic(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL,
threshold = 0.05, R = 999)
permMultinom(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL,
threshold = 0.05, R = 999)
permOrdinal(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL,
```

```
threshold = 0.05, R = 999)

waldLogistic(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)

waldQBinom(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)

waldOrdinal(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
```

### **Arguments**

target A numeric vector containing the values of the target variable. For the "testInd-

Logistic" this can either be a binary numerical variable or a factor variable. The factor variable can have two values (binary logistic regression), more than two values (multinomial logistic regression) or it can be an ordered factor with more than two values (ordinal regression). The last one is for example, factor(x, ordered = TRUE). The "waldBinary" is the Wald test version of the binary logistic regression. The "waldOrdinal" is the Wald test version of the ordinal regression.

dataset A numeric matrix or data frame, in case of categorical predictors (factors), con-

taining the variables for performing the test. Rows as samples and columns as features. In the cases of "waldBinary", "waldOrdinal" this is strictly a matrix.

xIndex The index of the variable whose association with the target we want to test.

csIndex The indices of the variables to condition on. If you have no variables set this

equal to 0.

wei A vector of weights to be used for weighted regression. The default value is

NULL. An example where weights are used is surveys when stratified sampling

has occured.

univariateModels

Fast alternative to the hash object for univariate test. List with vectors "pvalues" (p-values), "stats" (statistics) and "flags" (flag = TRUE if the test was successful) representing the univariate association of each variable with the target. Default

value is NULL.

hash A boolean variable which indicates whether (TRUE) or not (FALSE) to use the

hash-based implementation of the statistics of SES. Default value is FALSE. If TRUE you have to specify the stat\_hash argument and the pvalue\_hash argu-

ment.

stat\_hash A hash object which contains the cached generated statistics of a SES run in the

current dataset, using the current test.

pvalue\_hash A hash object which contains the cached generated p-values of a SES run in the

current dataset, using the current test.

threshold Threshold (suitable values in (0, 1)) for assessing p-values significance.

R The number of permutations, set to 999 by default. There is a trick to avoind do-

ing all permutations. As soon as the number of times the permuted test statistic is more than the observed test statistic is more than 50 (if threshold = 0.05 and

R = 999), the p-value has exceeded the significance level (threshold value) and hence the predictor variable is not significant. There is no need to continue do the extra permutations, as a decision has already been made.

# **Details**

The testIndQBinom does quasi binomial regression which is suitable for binary targets and proportions including 0 and 1.

If hash = TRUE, testIndLogistic requires the arguments 'stat\_hash' and 'pvalue\_hash' for the hash-based implementation of the statistic test. These hash Objects are produced or updated by each run of SES (if hash == TRUE) and they can be reused in order to speed up next runs of the current statistic test. If "SESoutput" is the output of a SES run, then these objects can be retrieved by SESoutput@hashObject\$stat\_hash and the SESoutput@hashObject\$pvalue\_hash.

Important: Use these arguments only with the same dataset that was used at initialization. For all the available conditional independence tests that are currently included on the package, please see "?CondIndTests".

The log-likelihood ratio test used in "testIndLogistic" requires the fitting of two models. The Wald test used in waldBinary" and "waldOrdinal" requires fitting of only one model, the full one. The significance of the variable is examined only. Only continuous (or binary) predictor variables are currently accepted in this test.

The testIndQBinom can also be used with percentages, see testIndBeta for example.

### Value

### A list including:

pvalue A numeric value that represents the logarithm of the generated p-value.

stat A numeric value that represents the generated statistic.

stat\_hash The current hash object used for the statistics. See argument stat hash and de-

tails. If argument hash = FALSE this is NULL.

pvalue\_hash The current hash object used for the p-values. See argument stat\_hash and de-

tails. If argument hash = FALSE this is NULL.

#### Note

This test uses the function multinom (package nnet) for multinomial logistic regression, the function clm (package ordinal) for ordinal logit regression and the function glm (package stats) for binomial regression.

# Author(s)

Vincenzo Lagani and Ioannis Tsamardinos

R implementation and documentation: Vincenzo Lagani <vlagani@csd.uoc.gr>, Giorgos Athineou <athineou@csd.uoc.gr> and Michail Tsagris <mtsagris@uoc.gr>

#### References

Vincenzo Lagani, George Kortas and Ioannis Tsamardinos (2013), Biomarker signature identification in "omics" with multiclass outcome. Computational and Structural Biotechnology Journal, 6(7):1-7.

McCullagh, Peter, and John A. Nelder. Generalized linear models. CRC press, USA, 2nd edition, 1989

### See Also

```
SES, gSquare, CondIndTests
```

# **Examples**

```
#simulate a dataset with categorical data
dataset_m \leftarrow matrix( sample(c(0, 1, 2), 20 * 100, replace = TRUE), ncol = 20)
#initialize categorical target
target_m <- dataset_m[, 20]</pre>
#remove target from the dataset
dataset_m <- dataset_m[, -20]</pre>
#run the conditional independence test for the nominal class variable
testIndMultinom(target_m, dataset_m, xIndex = 14, csIndex = c(1, 2))
#run the conditional independence test for the ordinal class variable
testIndOrdinal( factor(target_m, ordered = TRUE), dataset_m,
xIndex = 14, csIndex = c(1, 2))
#run the SES algorithm using the testIndLogistic conditional independence test
#for the ordinal class variable
sesObject <- SES(factor(target_m, ordered=TRUE), dataset_m, max_k = 3,</pre>
threshold = 0.05, test = "testIndOrdinal")
#simulate a dataset with binary data
dataset_b \leftarrow matrix(sample(c(0,1), 50 * 20, replace = TRUE), ncol = 20)
#initialize binary target
target_b <- dataset_b[, 20]</pre>
#remove target from the dataset
dataset_b <- dataset_b[, -20]</pre>
#run the conditional independence test for the binary class variable
testIndLogistic( target_b, dataset_b, xIndex = 14, csIndex = c(1, 2) )
#run the MMPC algorithm using the testIndLogistic conditional independence test
#for the binary class variable
mmpcObject <- MMPC(target_b, dataset_b, max_k = 3, threshold = 0.05,
test = "testIndLogistic")
```

Conditional independence test for case control data

Conditional independence test based on conditional logistic regression for case control studies

# Description

The main task of this test is to provide a p-value PVALUE for the null hypothesis: feature 'X' is independent from 'TARGET' given a conditioning set CS. The pvalue is calculated by comparing a conditional logistic regression model based on the conditioning set CS against a model whose regressors are both X and CS. The comparison is performed through a chi-square test with the appropriate degrees of freedom on the difference between the deviances of the two models. This is suitable for a case control design

# Usage

```
testIndClogit(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
permClogit(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL,
threshold = 0.05, R = 999)
```

# **Arguments**

wei

target	A matrix with two columns, the first one must be 0 and 1, standing for $0 = \text{control}$ and $1 = \text{case}$ . The second column is the id of the patients. A numerical variable, for example $c(1,2,3,4,5,6,7,1,2,3,4,5,6,7)$ .
dataset	A numeric matrix or a data.frame in case of categorical predictors (factors), containing the variables for performing the test. Rows as samples and columns as features.
xIndex	The index of the variable whose association with the target we want to test.

csIndex The indices of the variables to condition on. If you have no variables set this equal to 0.

A vector of weights to be used for weighted regression. The default value is

NULL and it should stay NULL as weights are ignored at the conditional logistic regression. See the **survival** package for more information about conditional logistic regression.

### univariateModels

Fast alternative to the hash object for univariate test. List with vectors "pvalues" (p-values), "stats" (statistics) and "flags" (flag = TRUE if the test was successful) representing the univariate association of each variable with the target. Default value is NULL.

hash A boolean variable which indicates whether (TRUE) or not (FALSE) to use tha

hash-based implementation of the statistics of SES. Default value is FALSE. If TRUE you have to specify the stat\_hash argument and the pvalue\_hash argu-

ment.

stat\_hash A hash object which contains the cached generated statistics of a SES run in the

current dataset, using the current test.

pvalue\_hash A hash object which contains the cached generated p-values of a SES run in the

current dataset, using the current test.

threshold Threshold (suitable values in (0, 1)) for assessing p-values significance.

R The number of permutations, set to 999 by default. There is a trick to avoind do-

ing all permutations. As soon as the number of times the permuted test statistic is more than the observed test statistic is more than 50 (if threshold = 0.05 and R = 999), the p-value has exceeded the significance level (threshold value) and hence the predictor variable is not significant. There is no need to continue do

the extra permutations, as a decision has already been made.

### **Details**

If hash = TRUE, testIndClogit requires the arguments 'stat\_hash' and 'pvalue\_hash' for the hash-based implementation of the statistic test. These hash Objects are produced or updated by each run of SES (if hash == TRUE) and they can be reused in order to speed up next runs of the current statistic test. If "SESoutput" is the output of a SES run, then these objects can be retrieved by SESoutput@hashObject\$stat\_hash and the SESoutput@hashObject\$pvalue\_hash.

Important: Use these arguments only with the same dataset that was used at initialization. For all the available conditional independence tests that are currently included on the package, please see "?CondIndTests".

This is for case control studies. The log-likelihood for a conditional logistic regression model equals the log-likelihood from a Cox model with a particular data structure. When a well tested Cox model routine is available many packages use this "trick" rather than writing a new software routine from scratch, and this is what the "clogit" function in the "survival" package does. In detail, a stratified Cox model with each case/control group assigned to its own stratum, time set to a constant, status of 1=case 0=control, and using the exact partial likelihood has the same likelihood formula as a conditional logistic regression. The "clogit" routine creates the necessary dummy variable of times (all 1) and the strata, then calls the function "coxph".

Note that this function is a bit sensitive and prone to breaking down for some reason which I have not yet figured out. In case of singular design matrix it will work, it identifies the problem and handles it internally like most regression functions do. However, problems can still occur.

# Value

A list including:

pvalue A numeric value that represents the logarithm of the generated p-value due to

the conditional logistic regression (see reference below).

stat A numeric value that represents the generated statistic due to the conditional

logistic regression (see reference below).

stat\_hash The current hash object used for the statistics. See argument stat\_hash and details. If argument hash = FALSE this is NULL.

pvalue\_hash The current hash object used for the p-values. See argument stat\_hash and de-

tails. If argument hash = FALSE this is NULL.

### Author(s)

Vincenzo Lagani, Ioannis Tsamardinos, Giorgos Athineou and Michail Tsagris

R implementation and documentation: Giorgos Athineou <athineou@csd.uoc.gr>, Vincenzo Lagani <vlagani@csd.uoc.gr> and Michail Tsagris <mtsagris@uoc.gr>

#### References

Michell H. Gail, Jay H. Lubin and Lawrence V. Rubinstein (1980). Likelihood calculations for matched case-control studies and survival studies with tied death times. Biometrika 68:703-707.

### See Also

```
SES, testIndLogistic, censIndCR, censIndWR
```

# **Examples**

```
#simulate a dataset with continuous data
dataset <- matrix( rnorm(100 * 7), nrow = 100 )
#the target feature is the last column of the dataset as a vector
case <- rbinom(100, 1, 0.6)
ina <- which(case == 1)
ina <- sample(ina, 50)
case[-ina] = 0
id <- rep(1:50, 2)
target <- cbind(case, id)

results <- testIndClogit(target, dataset, xIndex = 4, csIndex = 1)
results

#run the SES algorithm using the testIndClogit conditional independence test
a <- MMPC(target, dataset, max_k = 3, threshold = 0.01, test = "testIndClogit")</pre>
```

Conditional independence test for circular data

Circular regression conditional independence test for circular class dependent variables and continuous predictors.

# Description

The main task of this test is to provide a p-value PVALUE for the null hypothesis: feature 'X' is independent from 'TARGET' given a conditioning set CS. The pvalue is calculated by comparing a Beta regression model based on the conditioning set CS against a model whose regressor are both X and CS. The comparison is performed through a log-likelihood ratio test using circular regression with 2 degrees of freedom.

### Usage

testIndSPML(target, dataset, xIndex, csIndex, wei = NULL, univariateModels = NULL, hash = FALSE, stat\_hash = NULL, pvalue\_hash = NULL)

### **Arguments**

target A numerical vector with the data expressed in radians, or a 2 column matrix

with the cosine and sine of the response (i.e. unit vector). See examples for

more information on this.

dataset A numeric matrix with the variables for performing the test. Rows as samples

and columns as features. currently this test accepts only continuous variables.

xIndex The index of the variable whose association with the target we want to test.

csIndex The indices of the variables to condition on. If you have no variables set this

equal to 0.

wei This is not used in this test.

univariateModels

Fast alternative to the hash object for univariate test. List with vectors "pval-

ues" (p-values), "stats" (statistics) representing the univariate association of each

variable with the target. Default value is NULL.

hash A boolean variable which indicates whether (TRUE) or not (FALSE) to use tha

hash-based implementation of the statistics of SES. Default value is FALSE. If TRUE you have to specify the stat hash argument and the pvalue hash argument

ment.

stat\_hash A hash object which contains the cached generated statistics of a SES run in the

current dataset, using the current test.

pvalue\_hash A hash object which contains the cached generated p-values of a SES run in the

current dataset, using the current test.

### **Details**

If hash = TRUE, testIndSPML requires the arguments 'stat\_hash' and 'pvalue\_hash' for the hash-based implementation of the statistic test. These hash Objects are produced or updated by each run of SES (if hash == TRUE) and they can be reused in order to speed up next runs of the current statistic test. If "SESoutput" is the output of a SES run, then these objects can be retrieved by SESoutput@hashObject\$stat\_hash and the SESoutput@hashObject\$pvalue\_hash.

Important: Use these arguments only with the same dataset that was used at initialization. For all the available conditional independence tests that are currently included on the package, please see "?CondIndTests".

The log-likelihood ratio test used in "testIndSPML" requires the fitting of two models. The significance of the variable is examined and Only continuous (or binary) predictor variables are currently accepted in this test.

### Value

A list including:

pvalue	A numeric value that represents the logarithm of the generated p-value due to Beta regression (see reference below).
stat	A numeric value that represents the generated statistic due to Beta regression (see reference below).
stat_hash	The current hash object used for the statistics. See argument stat_hash and details. If argument hash = FALSE this is NULL.
pvalue_hash	The current hash object used for the logged p-values. See argument stat_hash

and details. If argument hash = FALSE this is NULL.

# Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

### References

Presnell Brett, Morrison Scott P. and Littell Ramon C. (1998). Projected multivariate linear models for directional data. Journal of the American Statistical Association, 93(443): 1068-1077.

### See Also

```
univregs, SES, testIndReg, CondIndTests
```

# Examples

```
y <- runif(100, - pi, pi) ## suppose these are radians x \leftarrow matrix( rnorm(100 * 3), ncol = 3) testIndSPML(y1, x, csIndex = 1, xIndex = 2) ## alternatively y1 <- cbind(cos(y), sin(y)) ## a matrix with two columns testIndSPML(y1, x, csIndex = 1, xIndex = 2)
```

Conditional independence test for longitudinal and clustered data using GEE

Linear mixed models conditional independence test for longitudinal class variables

# **Description**

The main task of this test is to provide a p-value PVALUE for the null hypothesis: feature 'X' is independent from 'TARGET' given a conditioning set CS. The pvalue is calculated by comparing a linear model based on the conditioning set CS against a model with both X and CS. The comparison is performed through an F test the appropriate degrees of freedom on the difference between the deviances of the two models. This test accepts a longitudinal target and longitudinal, categorical, continuous or mixed data as predictor variables.

### Usage

```
testIndGEEReg(target, reps = NULL, group, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL,
correl = "exchangeable", se = "jack")

testIndGEELogistic(target, reps = NULL, group, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL,
correl = "exchangeable", se = "jack")

testIndGEEPois(target, reps = NULL, group, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL,
correl = "exchangeable", se = "jack")

testIndGEEGamma(target, reps = NULL, group, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL,
correl = "exchangeable", se = "jack")

testIndGEENormLog(target, reps = NULL, group, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL,
correl = "exchangeable", se = "jack")
```

#### Arguments

target	A numeric vector containing the values of the target variable. If the values are proportions or percentages, i.e. strictly within 0 and 1 they are mapped into R using log( target/(1 - target)). In both cases a linear mixed model is applied. It can also be a binary variable (binary logistic regression) or a discrete, counts (Poisson regression), thus fitting generalised linear mixed models.
reps	A numeric vector containing the time points of the subjects. It's length is equal to the length of the target variable. If you have clustered data, leave this NULL.
group	A numeric vector containing the subjects or groups. It must be of the same length as target.
dataset	A numeric matrix or data frame, in case of categorical predictors (factors), containing the variables for performing the test. Rows as samples and columns as features.
xIndex	The index of the variable whose association with the target we want to test.
csIndex	The indices of the variables to condition on. If you have no variables set this equal to 0.
wei	A vector of weights to be used for weighted regression. The default value is NULL. It is mentioned in the "geepack" that weights is not (yet) the weight as in sas proc genmod, and hence is not recommended to use.

### univariateModels

Fast alternative to the hash object for univariate test. List with vectors "pvalues" (p-values), "stats" (statistics) and "flags" (flag = TRUE if the test was successful) representing the univariate association of each variable with the target. Default value is NULL.

hash A boolean variable which indicates whether (TRUE) or not (FALSE) to use tha

hash-based implementation of the statistics of SES. Default value is FALSE. If TRUE you have to specify the stat\_hash argument and the pvalue\_hash argu-

ment.

stat\_hash A hash object which contains the cached generated statistics of a SES run in the

current dataset, using the current test.

pvalue\_hash A hash object which contains the cached generated p-values of a SES run in the

current dataset, using the current test.

correl The correlation structure. For the Gaussian, Logistic, Poisson and Gamma re-

gression this can be either "exchangeable" (compound symmetry, suitable for clustered data) or "ar1" (AR(1) model, suitable for longitudinal data). For the ordinal logistic regression its only the "exchangeable" correlation sturcture.

se The method for estimating standard errors. This is very important and crucial.

The available options for Gaussian, Logistic, Poisson and Gamma regression are: a) 'san.se', the usual robust estimate. b) 'jack': if approximate jackknife variance estimate should be computed. c) 'j1s': if 1-step jackknife variance estimate should be computed and d) 'fij': logical indicating if fully iterated jackknife variance estimate should be computed. If you have many clusters (sets of repeated measurements) "san.se" is fine as it is astmpotically correct, plus jacknife estimates will take longer. If you have a few clusters, then maybe it's better

to use jacknife estimates.

The jackknife variance estimator was suggested by Paik (1988), which is quite suitable for cases when the number of subjects is small (K < 30), as in many biological studies. The simulation studies conducted by Ziegler et al. (2000) and Yan and Fine (2004) showed that the approximate jackknife estimates are in

many cases in good agreement with the fully iterated ones.

# Details

If hash = TRUE, testIndGEE requires the arguments 'stat\_hash' and 'pvalue\_hash' for the hash-based implementation of the statistic test. These hash Objects are produced or updated by each run of SES (if hash == TRUE) and they can be reused in order to speed up next runs of the current statistic test. If "SESoutput" is the output of a SES.temp run, then these objects can be retrieved by SESoutput@hashObject\$stat\_hash and the SESoutput@hashObject\$pvalue\_hash.

Important: Use these arguments only with the same dataset that was used at initialization. For all the available conditional independence tests that are currently included on the package, please see "?CondIndTests".

This test is for longitudinal and clustered data. Bear in mind that the time effect, for the longitudinal data case, is linear. It could be of higer order as well, but this would be a hyper-parameter, increasing the complexity of the models to be tested.

Make sure you load the library geepack first.

### Value

A list including:

pvalue A numeric value that represents the logarithm of the generated p-value due to

the (generalised) linear mixed model (see reference below).

stat	A numeric value that represents the generated statistic due to the (generalised) linear mixed model (see reference below).
stat_hash	The current hash object used for the statistics. See argument stat_hash and details. If argument hash = FALSE this is NULL.
pvalue_hash	The current hash object used for the p-values. See argument stat_hash and details. If argument hash = FALSE this is NULL.

# Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

### References

Liang K.Y. and Zeger S.L. (1986). Longitudinal data analysis using generalized linear models. Biometrika, 73(1): 13-22.

Prentice R.L. and Zhao L.P. (1991). Estimating equations for parameters in means and covariances of multivariate discrete and continuous responses. Biometrics, 47(3): 825-839.

Heagerty P.J. and Zeger S.L. (1996) Marginal regression models for clustered ordinal measurements. Journal of the American Statistical Association, 91(435): 1024-1036.

Paik M.C. (1988). Repeated measurement analysis for nonnormal data in small samples. Communications in Statistics-Simulation and Computation, 17(4): 1155-1171.

Ziegler A., Kastner C., Brunner D. and Blettner M. (2000). Familial associations of lipid profiles: A generalised estimating equations approach. Statistics in medicine, 19(24): 3345-3357

Yan J. and Fine J. (2004). Estimating equations for association structures. Statistics in medicine, 23(6): 859-874.

Eugene Demidenko (2013). Mixed Models: Theory and Applications with R, 2nd Edition. New Jersey: Wiley & Sons.

Tsagris, M., Lagani, V., & Tsamardinos, I. (2018). Feature selection for high-dimensional glmm data. BMC bioinformatics, 19(1), 17.

# See Also

```
SES.glmm, MMPC.glmm, CondIndTests
```

# **Examples**

```
library("geepack", quietly = TRUE)
y <- rnorm(150)
x <- matrix(rnorm(150 * 5), ncol = 5)
id <- sample(1:20, 150, replace = TRUE)
testIndGEEReg(y, group = id, dataset = x, xIndex = 1, csIndex = 3)</pre>
```

Conditional independence test for longitudinal and clustered data using GLMM

Linear mixed models conditional independence test for longitudinal class variables

# **Description**

The main task of this test is to provide a p-value PVALUE for the null hypothesis: feature 'X' is independent from 'TARGET' given a conditioning set CS. The pvalue is calculated by comparing a linear model based on the conditioning set CS against a model with both X and CS. The comparison is performed through an F test the appropriate degrees of freedom on the difference between the deviances of the two models. This test accepts a longitudinal target and longitudinal, categorical, continuous or mixed data as predictor variables.

### Usage

```
testIndGLMMReg(target, reps = NULL, group, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL,
pvalue_hash = NULL, slopes = FALSE)
testIndGLMMLogistic(target, reps = NULL, group, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL,
pvalue_hash = NULL, slopes = FALSE)
testIndGLMMPois(target, reps = NULL, group, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL,
pvalue_hash = NULL, slopes = FALSE)
testIndGLMMNB(target, reps = NULL, group, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL,
pvalue_hash = NULL, slopes = FALSE)
testIndGLMMGamma(target, reps = NULL, group, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL,
pvalue_hash = NULL, slopes = FALSE)
testIndGLMMNormLog(target, reps = NULL, group, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL,
pvalue_hash = NULL, slopes = FALSE)
testIndGLMMOrdinal(target, reps = NULL, group, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL,
pvalue_hash = NULL, slopes = FALSE)
testIndGLMMCR(target, reps = NULL, group, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL,
pvalue_hash = NULL, slopes = FALSE)
```

testIndLMM(target, reps = NULL, group, dataset, xIndex, csIndex, wei = NULL, univariateModels = NULL, hash = FALSE, stat\_hash = NULL, pvalue\_hash = NULL, slopes = FALSE)

### **Arguments**

A numeric vector containing the values of the target variable. If the values are

proportions or percentages, i.e. strictly within 0 and 1 they are mapped into R using log( target/(1 - target) ). In both cases a linear mixed model is applied. It can also be a binary variable (binary logistic regression) or a discrete, counts (Poisson regression), thus fitting generalised linear mixed models. In the case of

"testIndGLMMOrdinal" this must be an ordered factor.

reps A numeric vector containing the time points of the subjects. It's length is equal

to the length of the target variable. If you have clustered data, leave this NULL.

This is not applied in ordinal and Cox regression.

group A numeric vector containing the subjects or groups. It must be of the same

length as target.

dataset A numeric matrix or data frame, in case of categorical predictors (factors), con-

taining the variables for performing the test. Rows as samples and columns as

features.

xIndex The index of the variable whose association with the target we want to test.

csIndex The indices of the variables to condition on. If you have no variables set this

equal to 0.

wei A vector of weights to be used for weighted regression. The default value is

NULL. An example where weights are used is surveys when stratified sampling

has occured.

univariateModels

Fast alternative to the hash object for univariate test. List with vectors "pvalues" (p-values), "stats" (statistics) and "flags" (flag = TRUE if the test was successful) representing the univariate association of each variable with the target. Default

value is NULL.

hash A boolean variable which indicates whether (TRUE) or not (FALSE) to use tha

hash-based implementation of the statistics of SES. Default value is FALSE. If TRUE you have to specify the stat\_hash argument and the pvalue\_hash argu-

ment.

stat\_hash A hash object which contains the cached generated statistics of a SES run in the

current dataset, using the current test.

pvalue\_hash A hash object which contains the cached generated p-values of a SES run in the

current dataset, using the current test.

slopes A boolean variable which indicates whether (TRUE) to or not (FALSE) random

slopes in the time effect as well. By deault random intercepts are considered.

This is not applied in ordinal and Cox regression.

### **Details**

If hash = TRUE, testIndGLMM requires the arguments 'stat\_hash' and 'pvalue\_hash' for the hash-based implementation of the statistic test. These hash Objects are produced or updated by each run of SES (if hash == TRUE) and they can be reused in order to speed up next runs of the current statistic test. If "SESoutput" is the output of a SES.temp run, then these objects can be retrieved by SESoutput@hashObject\$stat\_hash and the SESoutput@hashObject\$pvalue\_hash.

Important: Use these arguments only with the same dataset that was used at initialization. For all the available conditional independence tests that are currently included on the package, please see "?CondIndTests".

This test is for longitudinal and clustered data. Bear in mind that the time effect, for the longitudinal data case, is linear. It could be of higer order as well, but this would be a hyper-parameter, increasing the complexity of the models to be tested.

The testIndLMM is used for linear mixed models with no weights, no slopes and no reps. This is a random intercepts model only. The advantage of this function is that it is tens of times faster than testIndGLMM.

### Value

# A list including:

pvalue	A numeric value that represents the logarithm of the generated p-value due to the (generalised) linear mixed model (see reference below).
stat	A numeric value that represents the generated statistic due to the (generalised) linear mixed model (see reference below).
stat_hash	The current hash object used for the statistics. See argument stat_hash and details. If argument hash = FALSE this is NULL.
pvalue_hash	The current hash object used for the p-values. See argument stat_hash and de-

# Author(s)

Vincenzo Lagani, Ioannis Tsamardinos, Michail Tsagris and Giorgos Athineou

tails. If argument hash = FALSE this is NULL.

R implementation and documentation: Giorgos Athineou <athineou@csd.gr>, Vincenzo Lagani <vlagani@csd.uoc.gr> and Michail Tsagris <mtsagris@uoc.gr>

# References

Eugene Demidenko (2013). Mixed Models: Theory and Applications with R, 2nd Edition. New Jersey: Wiley & Sons.

Jose Pinheiro Jose and Douglas Bates. Mixed-effects models in S and S-PLUS. Springer Science & Business Media, 2006.

### See Also

SES.glmm, MMPC.glmm, CondIndTests

# **Examples**

```
y <- rnorm(150)
x <- matrix(rnorm(150 * 5), ncol = 5)
id <- sample(1:20, 150, replace = TRUE)
testIndGLMMReg(y, group = id, dataset = x, xIndex = 1, csIndex = 3)
testIndLMM(y, group = id, dataset = x, xIndex = 1, csIndex = 3)</pre>
```

Conditional independence test for proportions/percentages

Beta regression conditional independence test for proportions/percentage class dependent variables and mixed predictors

# **Description**

The main task of this test is to provide a p-value PVALUE for the null hypothesis: feature 'X' is independent from 'TARGET' given a conditioning set CS. The pvalue is calculated by comparing a Beta regression model based on the conditioning set CS against a model whose regressor are both X and CS. The comparison is performed through a chi-square test with the appropriate degrees of freedom on the difference between the deviances of the two models.

# Usage

```
testIndBeta(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)

permBeta(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL,
threshold = 0.05, R = 999)

waldBeta(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
```

# **Arguments**

target	A numeric vector containing the values of the target variable. They must be percentages or proportions, i.e. within the (0, 1) interval. Currently 0 and/or 1 values are not allowed.
dataset	A numeric matrix or data frame, in case of categorical predictors (factors), containing the variables for performing the test. Rows as samples and columns as features. In the case of "waldBeta" this is strictly a matrix.
xIndex	The index of the variable whose association with the target we want to test.
csIndex	The indices of the variables to condition on. If you have no variables set this equal to $0$ .
wei	A vector of weights to be used for weighted regression. The default value is NULL. An example where weights are used is surveys when stratified sampling has occured.

univariateModels

Fast alternative to the hash object for univariate test. List with vectors "pvalues" (p-values), "stats" (statistics) and "flags" (flag = TRUE if the test was successful) representing the univariate association of each variable with the target. Default

value is NULL.

hash A boolean variable which indicates whether (TRUE) or not (FALSE) to use tha

hash-based implementation of the statistics of SES. Default value is FALSE. If TRUE you have to specify the stat\_hash argument and the pvalue\_hash argument and the pvalue\_hash argument.

ment.

stat\_hash A hash object which contains the cached generated statistics of a SES run in the

current dataset, using the current test.

pvalue\_hash A hash object which contains the cached generated p-values of a SES run in the

current dataset, using the current test.

threshold (suitable values in (0, 1)) for assessing p-values significance.

R The number of permutations, set to 999 by default. There is a trick to avoind do-

ing all permutations. As soon as the number of times the permuted test statistic is more than the observed test statistic is more than 50 (if threshold = 0.05 and R = 999), the p-value has exceeded the significance level (threshold value) and hence the predictor variable is not significant. There is no need to continue do

the extra permutations, as a decision has already been made.

#### **Details**

If hash = TRUE, testIndBeta requires the arguments 'stat\_hash' and 'pvalue\_hash' for the hash-based implementation of the statistic test. These hash Objects are produced or updated by each run of SES (if hash == TRUE) and they can be reused in order to speed up next runs of the current statistic test. If "SESoutput" is the output of a SES run, then these objects can be retrieved by SESoutput@hashObject\$stat\_hash and the SESoutput@hashObject\$pvalue\_hash.

Important: Use these arguments only with the same dataset that was used at initialization. For all the available conditional independence tests that are currently included on the package, please see "?CondIndTests". An alternative regression to this is "testIndReg" and "testIndRQ". In these two latter cases, the logit transformation is first applied to the target variable.

The log-likelihood ratio test used in "testIndBeta" requires the fitting of two models. The Wald test used in "waldBeta" requires fitting of only one model, the full one. The significance of the variable is examined only. Only continuous (or binary) predictor variables are currently accepted in this test.

The testIndOBinom is another alternative to use.

#### Value

A list including:

pvalue A numeric value that represents the logarithm of the generated p-value due to

Beta regression (see reference below).

stat A numeric value that represents the generated statistic due to Beta regression

(see reference below).

stat\_hash The current hash object used for the statistics. See argument stat\_hash and de-

tails. If argument hash = FALSE this is NULL.

pvalue\_hash The current hash object used for the logged p-values. See argument stat\_hash and details. If argument hash = FALSE this is NULL.

### Author(s)

Vincenzo Lagani, Ioannis Tsamardinos, Michail Tsagris and Giorgos Athineou

R implementation and documentation: Giorgos Athineou <athineou@csd.uoc.gr>, Vincenzo Lagani <vlagani@csd.uoc.gr> and Michail Tsagris <mtsagris@uoc.gr>

### References

Ferrari S.L.P. and Cribari-Neto F. (2004). Beta Regression for Modelling Rates and Proportions. Journal of Applied Statistics, 31(7): 799-815.

### See Also

```
testIndQBinom, SES, testIndReg, testIndRQ, testIndFisher, CondIndTests
```

# **Examples**

```
#simulate a dataset with continuous data
dataset <- matrix(runif(100 * 10, 1, 1000), ncol = 10 )
#the target feature is the last column of the dataset as a vector
target <- dataset[, 10]
dataset <- dataset[, -10]
target <- target / (max(target) + 2 )

testIndBeta(target, dataset, xIndex = 4, csIndex = 9)

#run the MMPC algorithm using the testIndBeta conditional independence test
mmpcObject <- MMPC(target, dataset, max_k = 3, threshold = 0.05, test = "testIndBeta")</pre>
```

Conditional independence test for the static-longitudinal scenario

Conditional independence test for the static-longitudinal scenario

# **Description**

The main task of this test is to provide a p-value PVALUE for the null hypothesis: feature 'X' is independent from 'TARGET' given a conditioning set CS. The pvalue is calculated by comparing a logistic model based on the conditioning set CS against a model whose regressor are both X and CS. The comparison is performed through a chi-square test with the aproprirate degrees of freedom on the difference between the deviances of the two models.

### **Usage**

```
testIndTimeLogistic(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)

testIndTimeMultinom(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
```

# **Arguments**

target

A numeric vector containing the values of the target variable. For the "testInd-Logistic" this can either be a binary numerical variable or a factor variable. The factor variable can have two values (binary logistic regression), more than two values (multinomial logistic regression) or it can be an ordered factor with more than two values (ordinal regression). The last one is for example, factor(x, ordered = TRUE). The "waldBinary" is the Wald test version of the binary logistic regression. The "waldOrdinal" is the Wald test version of the ordinal regression.

dataset A numeric matrix with the constants and slopes stack one upo the other. The first r rows are the constants and the rest of the rows contains the slopes. In

some the matrix can be calculated using the group.mvbetas function.

xIndex The index of the variable whose association with the target we want to test.

csIndex The indices of the variables to condition on. If you have no variables set this

equal to 0.

wei A vector of weights to be used for weighted regression. The default value is

NULL. An example where weights are used is surveys when stratified sampling

has occured.

univariateModels

Fast alternative to the hash object for univariate test. List with vectors "pvalues" (p-values), "stats" (statistics) and "flags" (flag = TRUE if the test was successful) representing the univariate association of each variable with the target. Default

value is NULL.

hash A boolean variable which indicates whether (TRUE) or not (FALSE) to use the

hash-based implementation of the statistics of SES. Default value is FALSE. If TRUE you have to specify the stat\_hash argument and the pvalue\_hash argument.

ment.

stat\_hash A hash object which contains the cached generated statistics of a SES run in the

current dataset, using the current test.

pvalue\_hash A hash object which contains the cached generated p-values of a SES run in the

current dataset, using the current test.

### **Details**

This conditional independence test is devised for the static-longitudinal scenario of Tsagris, Lagani and Tsamardinos (2018). The idea is that you have many features of longitudinal data for many subjects. For each subject you have calculated the coefficients of a simple linear regression over time and this is repeated for each feature. In the end, assuming p features, you have p constants and p slopes for each subject, each constant and slope refers to a feature for a subject.

### Value

A list including:

pvalue A numeric value that represents the logarithm of the generated p-value.

stat A numeric value that represents the generated statistic.

stat\_hash The current hash object used for the statistics. See argument stat\_hash and de-

tails. If argument hash = FALSE this is NULL.

pvalue\_hash The current hash object used for the p-values. See argument stat\_hash and de-

tails. If argument hash = FALSE this is NULL.

### Note

This test uses the function multinom (package nnet) for multinomial logistic regression, the function clm (package ordinal) for ordinal logit regression and the function glm (package stats) for binomial regression.

# Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

### References

Tsagris M., Lagani V., & Tsamardinos I. (2018). Feature selection for high-dimensional temporal data. BMC bioinformatics, 19(1), 17.

Vincenzo Lagani, George Kortas and Ioannis Tsamardinos (2013), Biomarker signature identification in "omics" with multiclass outcome. Computational and Structural Biotechnology Journal, 6(7):1-7.

McCullagh, Peter, and John A. Nelder. Generalized linear models. CRC press, USA, 2nd edition, 1989

#### See Also

```
SES, gSquare, CondIndTests
```

### **Examples**

```
## assume these are longitudinal data, each column is a variable (or feature) x \leftarrow matrix( rnorm(400 * 50), ncol = 50 ) id \leftarrow rep(1:80, each = 5) ## 80 subjects reps \leftarrow rep( seq(4, 12, by = 2), 80) ## 5 time points for each subject dataset \leftarrow group.mvbetas(x, id, reps) ## these are the regression coefficients of the first subject's values on the ## reps (which is assumed to be time in this example) target \leftarrow rbinom(80, 1, 0.5) testIndTimeLogistic(target, dataset, xIndex = 1, csIndex = 0) testIndTimeLogistic(target, dataset, xIndex = 1, csIndex = 2)
```

Conditional independence tests counting the number of times a possible collider d-separates two nodes

Many conditional independence tests counting the number of times a

possible collider d-separates two nodes

# **Description**

Many conditional independence tests counting the number of times a possible collider d-separates two nodes .

# Usage

```
condis(ind1, ind2, cs1, cs2, Var, dat, type = "pearson", rob = FALSE, max_k = 2, R = 1)
```

# **Arguments**

ind1	The index of the one variable to be considered.
ind2	The index of the other variable to be considered.
cs1	The index or indices of the conditioning set of variable(s). These are the neighbours of node ind1.
cs2	The index or indices of the conditioning set of variable(s). These are the neighbours of node ind2.
Var	The index of the possible collider.
dat	A numerical matrix or a data.frame with numerical, binary, nominal and ordinal variables only.
type	This is either "pearson", "spearman", "cat", "distcor", "ci.mm" or "ci.fast".
rob	In case you want robust estimation of the Pearson correlation prior to applying the conditional independence test. This is activated only when type = "pearson".
max_k	The maximum number of conditioning variables to consider. It can be the case that each node ind1 and ind2 has 10 neighbours. We should try all possible combinations of the neighbours of ind1 and then of ind2. To reduce the computational cost we search the subsets with at most max_k variables.
R	This is used by most tests, except for type = "ci.mm" and type = "ci.fast".

### **Details**

This is to be used in the conservative version of Rule 0 of the Pc algorithm. When one wants to know whether a variable is a possible collider, Ramsey, Spirtes and Zhang (2005) propose to perform the following action. For every unshilded triple (X, Y, Z) check all subsets of X's possible parents and of Z's poissible parents. a) If Y is NOT in any such set conditional on which, X are independent orient X - Y - Z as X -> Y <- Z. b) If Y is in ALL sets conditional on which, X and Z are independent, leave X - Y - Z as it is, i.e. a non-collider. c) Mark the triple X - Y - Z as "unfaitfull" otherwise. This modification leads to the so called conservative PC (CPC) algorithm.

A few years later, Colombo and Maathuis (2014) suggested a modification of the previous action, called the majority rule. If Y is less than 50% of thet sets that render X and Z independent orient X - Y - Z as X -> Y <- Z. If Y is found in exactly 50% of sets that render X and Z independent, this triple is marked as "ambiuous". This modification leads the so called majority rule PC (MPC) algorithm.

This function we have implemented here, does exactly this. It applies tests to many subsets and returns a matrix with two columns. The first one contains 0 or 1 and the second is the p-value. A value of 0 indicates absence of the possible collider from the set that produced that p-value, whereas a value of 1 indicates its presence in the set.

This way, we can measure the proportion of times the possible collider Y was in a subset that rendered X and Z independent.

# Value

A matrix with two columns. The second one is the logarithm of the p-value. The first one contains 0s and 1s. The value of 0 means that the candidate collider was not in that set which produced the relevant p-value, whereas a value of 1 indicates that it was a member of that conditioning set.

### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

# References

Ramsey, J., Zhang, J., Spirtes, P., 2006. Adjacency-faithfulness and conservative causal inference. Proceedings of the 22nd Annual Conference on Uncertainty in Artificial Intelligence (UAI 2006). https://arxiv.org/ftp/arxiv/papers/1206/1206.6843.pdf

Colombo, Diego, and Marloes H. Maathuis (2014). Order-independent constraint-based causal structure learning. The Journal of Machine Learning Research 15(1): 3741–3782.

### See Also

```
SES, MMPC, testIndLogistic
```

### **Examples**

Conditional independence tests for continous univariate and multivariate data

Linear (and non-linear) regression conditional independence test for continous univariate and multivariate response variables

# **Description**

The main task of this test is to provide a p-value PVALUE for the null hypothesis: feature 'X' is independent from 'TARGET' given a conditioning set CS. The pvalue is calculated by comparing a linear regression model based on the conditioning set CS against a model whose regressor are both X and CS. The comparison is performed through an F test the appropriate degrees of freedom on the difference between the deviances of the two models.

# Usage

```
testIndReg(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
testIndRQ(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
testIndMVreg(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
testIndMMReg(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
waldMMReg(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
permReg(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL,
threshold = 0.05, R = 999)
permMMReg(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL,
threshold = 0.05, R = 999)
permRQ(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL,
threshold = 0.05, R = 999)
permMVreg(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL,
threshold = 0.05, R = 999)
```

### **Arguments**

target A numeric vector containing the values of the target variable. If the values are

proportions or percentages, i.e. strictly within 0 and 1 they are mapped into R using log(target/(1 - target)). In the case of testIndMVreg, the same takes place

true. See details for more information.

dataset A numeric matrix or data frame, in case of categorical predictors (factors), con-

taining the variables for performing the test. Rows as samples and columns as features. In the cases of "waldIGreg" and "waldMMreg" this is strictly a matrix.

xIndex The index of the variable whose association with the target we want to test.

csIndex The indices of the variables to condition on. If you have no variables set this

equal to 0.

wei A vector of weights to be used for weighted regression. The default value is

NULL. An example where weights are used is surveys when stratified sampling has occured. They are not take into account in the robust regression via MM

estimation (testIndMMReg and permMMreg).

univariateModels

Fast alternative to the hash object for univariate test. List with vectors "pvalues" (p-values) and "stats" (statistics) representing the univariate association of each

variable with the target. Default value is NULL.

hash A boolean variable which indicates whether (TRUE) or not (FALSE) to use tha

hash-based implementation of the statistics of SES. Default value is FALSE. If TRUE you have to specify the stat\_hash argument and the pvalue\_hash argument.

ment.

stat\_hash A hash object which contains the cached generated statistics of a SES run in the

current dataset, using the current test.

pvalue\_hash A hash object which contains the cached generated p-values of a SES run in the

current dataset, using the current test.

threshold Threshold (suitable values in (0, 1)) for assessing p-values significance.

R The number of permutations, set to 999 by default. There is a trick to avoind do-

ing all permutations. As soon as the number of times the permuted test statistic is more than the observed test statistic is more than 50 (if threshold = 0.05 and R = 999), the p-value has exceeded the signifiance level (threshold value) and hence the predictor variable is not significant. There is no need to continue do

the extra permutations, as a decision has already been made.

### **Details**

If hash = TRUE, all three tests require the arguments 'stat\_hash' and 'pvalue\_hash' for the hash-based implementation of the statistic test. These hash Objects are produced or updated by each run of SES (if hash == TRUE) and they can be reused in order to speed up next runs of the current statistic test. If "SESoutput" is the output of a SES run, then these objects can be retrieved by SESoutput@hashObject\$stat\_hash and the SESoutput@hashObject\$pvalue\_hash.

Important: Use these arguments only with the same dataset that was used at initialization.

TestIndReg offers linear regression.

testIndMMReg offers robust linear MM estimation regression.

TestIndRQ offers quantile (median) regression as a robust alternative to linear regression.

In both cases, if the dependent variable consists of proportions (values between 0 and 1) the logit transformation is applied and the tests are applied then.

testIndMVreg is for multivariate continuous response variables. Compositional data are positive multivariate data and each vector (observation) sums to the same constant, usually taken 1 for convenience. A check is performed and if such data are found, the additive log-ratio (multivariate logit) transformation (Aitchison, 1986) is applied beforehand. Zeros are not allowed.

For all the available conditional independence tests that are currently included on the package, please see "?CondIndTests".

The Wald test used in "waldMMReg" requires fitting of only one model, the full one. The significance of the variable is examined only. Only continuous (or binary) predictor variables are currently accepted in this test.

#### Value

# A list including:

pvalue	A numeric value that represents the logarithm of the generated p-value due to linear regression (see reference below).
stat	A numeric value that represents the generated statistic due to linear regression (see reference below).
stat_hash	The current hash object used for the statistics. See argument stat_hash and details. If argument hash = FALSE this is NULL.
pvalue_hash	The current hash object used for the p-values. See argument stat_hash and details. If argument hash = FALSE this is NULL.

# Author(s)

Vincenzo Lagani, Ioannis Tsamardinos, Michail Tsagris and Giorgos Athineou

R implementation and documentation: Giorgos Athineou <athineou@csd.gr>, Vincenzo Lagani <vlagani@csd.uoc.gr> and Michail Tsagris <mtsagris@uoc.gr>

### References

Draper, N.R. and Smith H. (1988). Applied regression analysis. New York, Wiley, 3rd edition.

Hampel F. R., Ronchetti E. M., Rousseeuw P. J., and Stahel W. A. (1986). Robust statistics: the approach based on influence functions. John Wiley & Sons.

Koenker R.W. (2005). Quantile regression. New York, Cambridge University Press.

Sadovski A. (1974). L1-norm fit of a straight line. Applied Statistics, 23(2):244-248.

Yohai, V. J. (1987). High breakdown-point and high efficiency robust estimates for regression. The Annals of Statistics, 15(2): 642-656.

Mardia, Kanti, John T. Kent and John M. Bibby. Multivariate analysis. Academic press, 1979.

John Aitchison. The Statistical Analysis of Compositional Data, Chapman & Hall; reprinted in 2003, with additional material, by The Blackburn Press.

### See Also

testIndRQ, testIndFisher, testIndSpearman, CondIndTests

### **Examples**

```
#simulate a dataset with continuous data
dataset <- matrix(runif(100 * 50, 1, 100), ncol = 50 )
#the target feature is the last column of the dataset as a vector
target <- dataset[, 50]
dataset <- dataset[, -50]

testIndReg(target, dataset, xIndex = 44, csIndex = 10)
testIndRPg(target, dataset, xIndex = 44, csIndex = 10)
testIndRQ(target, dataset, xIndex = 44, csIndex = 10)
testIndIGreg(target, dataset, xIndex = 44, csIndex = 10)

#run the MMPC algorithm using the testIndReg conditional independence test
m1 <- MMPC(target, dataset, max_k = 3, threshold = 0.05, test = "testIndReg")
m2 <- MMPC(target, dataset, max_k = 3, threshold = 0.05, test = "testIndRQ")</pre>
```

Conditional independence tests for count data

Regression conditional independence test for discrete (counts) class dependent variables

# Description

The main task of this test is to provide a p-value PVALUE for the null hypothesis: feature 'X' is independent from 'TARGET' given a conditioning set CS. The pvalue is calculated by comparing a Poisson regression model based on the conditioning set CS against a model whose regressor are both X and CS. The comparison is performed through a chi-square test with the appropriate degrees of freedom on the difference between the deviances of the two models. The models supported here are poisson, zero inlftaed poisson and negative binomial.

# Usage

```
testIndPois(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)

testIndNB(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)

testIndZIP(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)

testIndQPois(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
```

```
permPois(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL,
threshold = 0.05, R = 999)

permNB(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL,
threshold = 0.05, R = 999)

permZIP(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL,
threshold = 0.05, R = 999)

waldPois(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)

waldNB(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)

waldZIP(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
```

### **Arguments**

target A numeric vector containing the values of the target variable.

dataset A numeric matrix or data frame, in case of categorical predictors (factors), con-

taining the variables for performing the test. Rows as samples and columns as features. In the cases of "waldPois", "waldNB" and "waldZIP" this is strictly a

matrix.

xIndex The index of the variable whose association with the target we want to test.

csIndex The indices of the variables to condition on. If you have no variables set this

equal to 0.

wei A vector of weights to be used for weighted regression. The default value is

NULL. An example where weights are used is surveys when stratified sampling

has occured.

univariateModels

Fast alternative to the hash object for univariate test. List with vectors "pvalues" (p-values), "stats" (statistics) and "flags" (flag = TRUE if the test was successful) representing the univariate association of each variable with the target. Default

value is NULL.

hash A boolean variable which indicates whether (TRUE) or not (FALSE) to use tha

hash-based implementation of the statistics of SES. Default value is FALSE. If TRUE you have to specify the stat\_hash argument and the pvalue\_hash argu-

ment.

stat\_hash A hash object which contains the cached generated statistics of a SES run in the

current dataset, using the current test.

pvalue\_hash A hash object which contains the cached generated p-values of a SES run in the

current dataset, using the current test.

threshold Threshold (suitable values in (0, 1)) for assessing p-values significance.

The number of permutations, set to 999 by default. There is a trick to avoind do-

ing all permutations. As soon as the number of times the permuted test statistic is more than the observed test statistic is more than 50 (if threshold = 0.05 and R = 999), the p-value has exceeded the significance level (threshold value) and hence the predictor variable is not significant. There is no need to continue do

the extra permutations, as a decision has already been made.

# **Details**

If hash = TRUE, all three tests require the arguments 'stat\_hash' and 'pvalue\_hash' for the hash-based implementation of the statistic test. These hash Objects are produced or updated by each run of SES (if hash == TRUE) and they can be reused in order to speed up next runs of the current statistic test. If "SESoutput" is the output of a SES run, then these objects can be retrieved by SESoutput@hashObject\$stat\_hash and the SESoutput@hashObject\$pvalue\_hash.

Important: Use these arguments only with the same dataset that was used at initialization. For all the available conditional independence tests that are currently included on the package, please see "?CondIndTests".

If you have overdispersion, the variance is higher than the mean, a negative binomial is to be used. If you have more zeros than expected under a Poisson model, not overdispersion, then zero inlfated Poisson is to be used. Bear in mind that if you have a small number of zeros, there is no reason to use this model. If for example you have count data but no, or 1 zeros, this will not work.

The log-likelihood ratio test used in "testIndPois", "testIndNB" and "testIndZIP" requires the fitting of two models. The Wald test used in "waldPois", "waldNB" and "waldZIP" requires fitting of only one model, the full one. The significance of the variable is examined only. Only continuous (or binary) predictor variables are currently accepted in this test.

The testIndQPois does quasi Poisson regression. The benefit of this regression is that it works for over and under dispersed data. Negative Binomial works for over dispersed data, but not for under dispersed data. In addition it is fast.

### Value

### A list including:

pvalue A numeric value that represents the logarithm of the generated p-value due to

the count data regression (see references below).

stat A numeric value that represents the generated statistic due to Poisson regres-

sion(see reference below).

stat\_hash The current hash object used for the statistics. See argument stat\_hash and de-

tails. If argument hash = FALSE this is NULL.

pvalue\_hash The current hash object used for the p-values. See argument stat\_hash and de-

tails. If argument hash = FALSE this is NULL.

### Author(s)

Vincenzo Lagani, Ioannis Tsamardinos, Michail Tsagris and Giorgos Athineou

R implementation and documentation: Giorgos Athineou <athineou@csd.uoc.gr>, Vincenzo Lagani <vlagani@csd.uoc.gr> and Michail Tsagris <mtsagris@uoc.gr>

### References

McCullagh P., and Nelder J.A. (1989). Generalized linear models. CRC press, USA, 2nd edition.

Lambert D. (1992). Zero-inflated Poisson regression, with an application to defects in manufacturing. Technometrics, 34(1):1-14.

Joseph M.H. (2011). Negative Binomial Regression. Cambridge University Press, 2nd edition.

#### See Also

```
testIndReg, testIndNB, testIndZIP, gSquare, CondIndTests
```

# **Examples**

```
#simulate a dataset with continuous data
dataset <- matrix(runif(100 * 20, 1, 50), ncol = 20 )
#the target feature is the last column of the dataset as a vector
target <- rpois(100, 10)
results <- testIndPois(target, dataset, xIndex = 14, csIndex = 10)
results

#run the SES algorithm using the testIndPois conditional independence test
m1 <- MMPC(target, dataset, max_k = 3, threshold = 0.05, test = "testIndPois");
m2 <- MMPC(target, dataset, max_k = 3, threshold = 0.05, test = "testIndNB");</pre>
```

Conditional independence tests for left censored data

Conditional independence test for survival data

# Description

The main task of this test is to provide a p-value PVALUE for the null hypothesis: feature 'X' is independent from 'TARGET' given a conditioning set CS. This test can based on the Cox (semi-parametric) regression or on the Weibull (parametric) regression.

# Usage

```
testIndTobit(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
waldTobit(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
permTobit(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL,
threshold = 0.05, R = 999)
```

### **Arguments**

target A Survival object (class Surv from package survival) with left censored data.

This test works with responses that are left censored. See the examples below (the command Surv or the final example in the survreg documentation of the "survival" package) for more information on how to create the target variable.

dataset A numeric matrix or data frame, in case of categorical predictors (factors), con-

taining the variables for performing the test. Rows as samples and columns as features. In the cases of "waldTobit" and "permTobit" this is strictly a matrix.

xIndex The index of the variable whose association with the target we want to test.

csIndex The indices of the variables to condition on. If you have no variables set this

equal to 0.

wei A vector of weights to be used for weighted regression. The default value is

NULL. An example where weights are used is surveys when stratified sampling

has occured.

univariateModels

Fast alternative to the hash object for univariate test. List with vectors "pvalues" (p-values), "stats" (statistics) and "flags" (flag = TRUE if the test was successful) representing the univariate association of each variable with the target. Default

value is NULL.

hash A boolean variable which indicates whether (TRUE) or not (FALSE) to use the

hash-based implementation of the statistics of SES. Default value is FALSE. If TRUE you have to specify the stat hash argument and the pvalue hash argument

ment.

stat\_hash A hash object which contains the cached generated statistics of a SES run in the

current dataset, using the current test.

pvalue\_hash A hash object which contains the cached generated p-values of a SES run in the

current dataset, using the current test.

threshold Threshold (suitable values in (0, 1)) for assessing p-values significance.

R The number of permutations, set to 999 by default. There is a trick to avoind

doing all permutations. As soon as the number of times the permuted test statistic is more than the observed test statistic is more than 50 (in this example case), the p-value has exceeded the significance level (threshold value) and hence the predictor variable is not significant. There is no need to continue do the extra

permutations, as a decision has already been made.

# **Details**

Tobit regression is performed. The implied model is Gaussian with left censored data.

If hash = TRUE, censIndCR, censIndWR and censIndER require the arguments 'stat\_hash' and 'pvalue\_hash' for the hash-based implementation of the statistic test. These hash Objects are produced or updated by each run of SES (if hash == TRUE) and they can be reused in order to speed up next runs of the current statistic test. If "SESoutput" is the output of a SES run, then these objects can be retrieved by SESoutput@hashObject\$stat\_hash and the SESoutput@hashObject\$pvalue\_hash.

Important: Use these arguments only with the same dataset that was used at initialization.

For all the available conditional independence tests that are currently included on the package, please see "?CondIndTests".

The log-likelihood ratio test used in "testIndTobit" requires the fitting of two models. The Wald test used in "waldTobit", requires fitting of only one model, the full one. The significance of the variable is examined only. Only continuous (or binary) predictor variables are currently accepted in this test.

#### Value

## A list including:

pvalue A numeric value that represents the logarithm of the generated p-value.

stat A numeric value that represents the generated statistic.

stat\_hash The current hash object used for the statistics. See argument stat\_hash and de-

tails. If argument hash = FALSE this is NULL.

pvalue\_hash The current hash object used for the p-values. See argument stat\_hash and de-

tails. If argument hash = FALSE this is NULL.

#### Note

This test uses the functions "survreg" and Surv of the package survival and the function anova (analysis of variance) of the package stats.

### Author(s)

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

## References

Tobin James (1958). Estimation of relationships for limited dependent variables. Econometrica. 26(1): 24-36.

### See Also

```
SES, censIndWR, testIndFisher, gSquare, testIndLogistic, Surv, anova, CondIndTests
```

### **Examples**

```
require(survival, quietly = TRUE)  x \leftarrow \text{matrix}(\text{rnorm}(100 * 30), \text{ncol} = 30) \\ y \leftarrow x[, 1] - x[, 2] + \text{rnorm}(100, 5) \\ y[y < 0] < 0 \\ y \leftarrow \text{survival}::Surv(y, y>0, type = 'left')  #run the censIndCR conditional independence test testIndTobit(y, x, xIndex = 12, csIndex = c(5, 7, 4)) waldTobit(y, x, xIndex = 12, csIndex = c(5, 7, 4)) permTobit(y, x, xIndex = 12, csIndex = c(5, 7, 4), R = 499)
```

```
#run the SES algorithm using the censIndCR conditional independence #test for the survival class variable a \leftarrow MMPC(y, x, max_k = 2, threshold = 0.05, test = "testIndTobit")
```

Conditional independence tests for positive data

Regression conditional independence test for positive response variables.

# Description

The main task of this test is to provide a p-value PVALUE for the null hypothesis: feature 'X' is independent from 'TARGET' given a conditioning set CS. The pvalue is calculated by comparing a Poisson regression model based on the conditioning set CS against a model whose regressor are both X and CS. The comparison is performed through a chi-square test with the appropriate degrees of freedom on the difference between the deviances of the two models. The models supported here are poisson, zero inlftaed poisson and negative binomial.

## Usage

```
testIndGamma(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
testIndNormLog(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
testIndIGreg(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
permGamma(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL,
threshold = 0.05, R = 999)
permNormLog(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL,
threshold = 0.05, R = 999)
permIGreg(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL,
threshold = 0.05, R = 999)
waldGamma(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
waldNormLog(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
```

```
waldIGreg(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
```

### Arguments

target A numeric vector containing the values of the target variable. For the Gamma

based tests, the values must be strictly greater than zero. For the NormLog case,

zeros can be included.

dataset A numeric matrix or data frame, in case of categorical predictors (factors), con-

taining the variables for performing the test. Rows as samples and columns as features. In the cases of "waldPois", "waldNB" and "waldZIP" this is strictly a

matrix.

xIndex The index of the variable whose association with the target we want to test.

csIndex The indices of the variables to condition on. If you have no variables set this

equal to 0.

wei A vector of weights to be used for weighted regression. The default value is

NULL. An example where weights are used is surveys when stratified sampling

has occured.

univariateModels

Fast alternative to the hash object for univariate test. List with vectors "pvalues" (p-values), "stats" (statistics) and "flags" (flag = TRUE if the test was successful) representing the univariate association of each variable with the target. Default

value is NULL.

hash A boolean variable which indicates whether (TRUE) or not (FALSE) to use tha

hash-based implementation of the statistics of SES. Default value is FALSE. If TRUE you have to specify the stat\_hash argument and the pvalue\_hash argu-

ment

stat\_hash A hash object which contains the cached generated statistics of a SES run in the

current dataset, using the current test.

pvalue\_hash A hash object which contains the cached generated p-values of a SES run in the

current dataset, using the current test.

threshold Threshold (suitable values in (0, 1)) for assessing p-values significance.

R The number of permutations, set to 999 by default. There is a trick to avoind do-

ing all permutations. As soon as the number of times the permuted test statistic is more than the observed test statistic is more than 50 (if threshold = 0.05 and R = 999), the p-value has exceeded the signifiance level (threshold value) and hence the predictor variable is not significant. There is no need to continue do

the extra permutations, as a decision has already been made.

### **Details**

If hash = TRUE, all three tests require the arguments 'stat\_hash' and 'pvalue\_hash' for the hash-based implementation of the statistic test. These hash Objects are produced or updated by each run of SES (if hash = TRUE) and they can be reused in order to speed up next runs of the current statistic test. If "SESoutput" is the output of a SES run, then these objects can be retrieved by SESoutput@hashObject\$stat\_hash and the SESoutput@hashObject\$pvalue\_hash.

Important: Use these arguments only with the same dataset that was used at initialization. For all the available conditional independence tests that are currently included on the package, please see "?CondIndTests".

For the testIndGamma and testIndNormLog the F test is used and not the log-likelihood ratio test because both of these regression models have a nuisance parameter. The testIndNormLog can be seen as a non linear Gaussian model where the conditional mean is related with the covariate(s) via an exponential function.

TestIndIGreg fits an inverse gaussian distribution with a log link. The testIndIGreg has some problems due to problems in R's implementation of the inverse gaussian regression with a log link.

### Value

### A list including:

pvalue A numeric value that represents the logarithm of the generated p-value due to

the count data regression (see references below).

stat A numeric value that represents the generated statistic due to Poisson regres-

sion(see reference below).

stat\_hash The current hash object used for the statistics. See argument stat\_hash and de-

tails. If argument hash = FALSE this is NULL.

pvalue\_hash The current hash object used for the p-values. See argument stat\_hash and de-

tails. If argument hash = FALSE this is NULL.

### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

#### References

McCullagh P., and Nelder J.A. (1989). Generalized linear models. CRC press, USA, 2nd edition.

### See Also

```
testIndReg, testIndNB, testIndZIP, gSquare, CondIndTests
```

### **Examples**

```
#simulate a dataset with continuous data
dataset <- matrix( rnorm(200 * 20, 1, 5), ncol = 20 )
#the target feature is the last column of the dataset as a vector
target <- rgamma(200, 1, 3)
testIndGamma(target, dataset, xIndex = 14, csIndex = 10)
testIndNormLog(target, dataset, xIndex = 14, csIndex = 10)
#run the MMPC algorithm using the testIndPois conditional independence test
m1 <- MMPC(target, dataset, max_k = 3, threshold = 0.05, test = "testIndGamma");
m2 <- MMPC(target, dataset, max_k = 3, threshold = 0.05, test = "testIndNormLog");</pre>
```

Conditional independence tests for sucess rates

Binomial regression conditional independence test for success rates (binomial)

## **Description**

The main task of this test is to provide a p-value PVALUE for the null hypothesis: feature 'X' is independent from 'TARGET' given a conditioning set CS. The pvalue is calculated by comparing a binomial logistic regression model based on the conditioning set CS against a model whose regressor are both X and CS. The comparison is performed through a chi-square test with the appropriate degrees of freedom on the difference between the deviances of the two models.

### Usage

```
testIndBinom(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
permBinom(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL,
threshold = 0.05, R = 999)
waldBinom(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL , hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
```

### **Arguments**

target	A matrix with two two columns, the first one is the number of successes, the cases (integer) and the second one is the totals (integers).
dataset	A numeric matrix or data frame, in case of categorical predictors (factors), containing the variables for performing the test. Rows as samples and columns as features. In the case of "waldBinom" this is strictly a matrix.
xIndex	The index of the variable whose association with the target we want to test.
csIndex	The indices of the variables to condition on. If you have no variables set this equal to $0$ .
wei	A vector of weights to be used for weighted regression. The default value is NULL and should stay as is, since the totals (second column of the target) is used as weights.
univariateModels	

univariateModels

Fast alternative to the hash object for univariate test. List with vectors "pvalues" (p-values), "stats" (statistics) and "flags" (flag = TRUE if the test was successful) representing the univariate association of each variable with the target. Default value is NULL.

hash A boolean variable which indicates whether (TRUE) or not (FALSE) to use tha

hash-based implementation of the statistics of SES. Default value is FALSE. If TRUE you have to specify the stat\_hash argument and the pvalue\_hash argument.

ment.

stat\_hash A hash object which contains the cached generated statistics of a SES run in the

current dataset, using the current test.

pvalue\_hash A hash object which contains the cached generated p-values of a SES run in the

current dataset, using the current test.

threshold Threshold (suitable values in (0, 1)) for assessing p-values significance.

R The number of permutations, set to 999 by default. There is a trick to avoind do-

ing all permutations. As soon as the number of times the permuted test statistic is more than the observed test statistic is more than 50 (if threshold = 0.05 and R = 999), the p-value has exceeded the significance level (threshold value) and hence the predictor variable is not significant. There is no need to continue do

the extra permutations, as a decision has already been made.

#### **Details**

If hash = TRUE, all three tests require the arguments 'stat\_hash' and 'pvalue\_hash' for the hash-based implementation of the statistic test. These hash Objects are produced or updated by each run of SES (if hash == TRUE) and they can be reused in order to speed up next runs of the current statistic test. If "SESoutput" is the output of a SES run, then these objects can be retrieved by SESoutput@hashObject\$stat\_hash and the SESoutput@hashObject\$pvalue\_hash.

Important: Use these arguments only with the same dataset that was used at initialization. For all the available conditional independence tests that are currently included on the package, please see "?CondIndTests".

If you have overdispersion, the variance is higher than the mean, a negative binomial is to be used. If you have more zeros than expected under a Poisson model, not overdispersion, then zero inlfated Poisson is to be used. This is in fact a logistic reression where the target is the ratio of successes divided by the totals and the weights are the totals.

The log-likelihood ratio test used in "testIndBinom" requires the fitting of two models. The Wald test used in "waldBinom" requires fitting of only one model, the full one. The significance of the variable is examined only. Only continuous (or binary) predictor variables are currently accepted in this test.

### Value

A list including:

pvalue A numeric value that represents the logarithm of the generated p-value due to

the count data regression (see references below).

stat A numeric value that represents the generated statistic due to Poisson regres-

sion(see reference below).

stat\_hash The current hash object used for the statistics. See argument stat\_hash and de-

tails. If argument hash = FALSE this is NULL.

pvalue\_hash The current hash object used for the p-values. See argument stat\_hash and de-

tails. If argument hash = FALSE this is NULL.

### Author(s)

Vincenzo Lagani, Ioannis Tsamardinos, Giorgos Athineou and Michail Tsagris.

R implementation and documentation: Giorgos Athineou <athineou@csd.uoc.gr>, Vincenzo Lagani <vlagani@csd.uoc.gr> and Michail Tsagris <mtsagris@uoc.gr>

### References

McCullagh P., and Nelder J.A. (1989). Generalized linear models. CRC press, USA, 2nd edition.

### See Also

```
testIndLogistic, testIndBeta, testIndReg, CondIndTests
```

### **Examples**

```
#simulate a dataset with continuous data
dataset <- matrix(runif(200 * 20, 1, 50), ncol = 20 )
#the target feature is the last column of the dataset as a vector
y <- rbinom(200, 10, 0.6)
N <- sample(11:20, 200, replace = TRUE)
target <- cbind(y, N)
testIndBinom(target, dataset, xIndex = 14, csIndex = 10)
#run the MMPC algorithm using the testIndPois conditional independence test
a <- MMPC(target, dataset, max_k = 3, threshold = 0.05, test = "testIndBinom")</pre>
```

```
Conditional independence tests for survival data

Conditional independence test for survival data
```

## Description

The main task of this test is to provide a p-value PVALUE for the null hypothesis: feature 'X' is independent from 'TARGET' given a conditioning set CS. This test can based on the Cox (semi-parametric) regression or on the Weibull (parametric) regression.

## Usage

```
censIndCR(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)

censIndWR(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)

censIndER(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
```

```
censIndLLR(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
permCR(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL,
threshold = 0.05, R = 999)
permWR(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL,
threshold = 0.05, R = 999)
permER(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL,
threshold = 0.05, R = 999)
permLLR(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL,
threshold = 0.05, R = 999)
waldCR(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
waldWR(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
waldER(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL, pvalue_hash = NULL)
```

### Arguments

target A Survival object (class Surv from package survival) containing the time to

event data (time) and the status indicator vector (event). View Surv documenta-

tion for more information.

dataset A numeric matrix or data frame, in case of categorical predictors (factors), con-

taining the variables for performing the test. Rows as samples and columns as features. In the cases of "waldCR", "waldWR", "waldER", "waldCR", "permWR", "waldER", "w

"permER" and "permLLR" this is strictly a matrix.

xIndex The index of the variable whose association with the target we want to test.

csIndex The indices of the variables to condition on.

wei A vector of weights to be used for weighted regression. The default value is

NULL. An example where weights are used is surveys when stratified sampling

has occured.

univariateModels

Fast alternative to the hash object for univariate test. List with vectors "pvalues" (p-values), "stats" (statistics) and "flags" (flag = TRUE if the test was successful) representing the univariate association of each variable with the target. Default value is NULL.

hash A boolean variable which indicates whether (TRUE) or not (FALSE) to use the

hash-based implementation of the statistics of SES. Default value is FALSE. If TRUE you have to specify the stat\_hash argument and the pvalue\_hash argument.

ment.

stat\_hash A hash object which contains the cached generated statistics of a SES run in the

current dataset, using the current test.

pvalue\_hash A hash object which contains the cached generated p-values of a SES run in the

current dataset, using the current test.

threshold (suitable values in (0, 1)) for assessing p-values significance.

R The number of permutations, set to 999 by default. There is a trick to avoind

doing all permutations. As soon as the number of times the permuted test statistic is more than the observed test statistic is more than 50 (in this example case), the p-value has exceeded the significance level (threshold value) and hence the predictor variable is not significant. There is no need to continue do the extra

permutations, as a decision has already been made.

#### **Details**

The censIndCR implies the Cox (semiparametric) regression, the censIndWR the Weibull (parametric) regression and the censIndER the exponential (parametric) regression, which is a special case of the Weibull regression (when shape parameter is 1). **Note**: When there are observations with zero values (time=0) the Weibull and Exponential regressions will not work. Only Cox regression will run. The censIndLLR is the log-logistic regression. This is a pure AFT model, unlike Weibull which is either a proportional hazards model or and AFT.

If hash = TRUE, censIndCR, censIndWR, censIndER and censIndLLR require the arguments 'stat\_hash' and 'pvalue\_hash' for the hash-based implementation of the statistic test. These hash Objects are produced or updated by each run of SES (if hash == TRUE) and they can be reused in order to speed up next runs of the current statistic test. If "SESoutput" is the output of a SES run, then these objects can be retrieved by SESoutput@hashObject\$stat\_hash and the SESoutput@hashObject\$pvalue\_hash.

Important: Use these arguments only with the same dataset that was used at initialization.

For all the available conditional independence tests that are currently included on the package, please see "?CondIndTests".

The log-likelihood ratio test used in "censIndCR", "censIndWR" and "censIndER" requires the fitting of two models. The Wald tests used in "waldCR", "waldWR" and "waldER" requires fitting of only one model, the full one. The significance of the variable is examined only. Only continuous (or binary) predictor variables are currently accepted in this test.

### Value

A list including:

pvalue A numeric value that represents the logarithm of the generated p-value.

stat A numeric value that represents the generated statistic.

stat\_hash The current hash object used for the statistics. See argument stat\_hash and de-

tails. If argument hash = FALSE this is NULL.

pvalue\_hash The current hash object used for the p-values. See argument stat\_hash and details. If argument hash = FALSE this is NULL.

### Note

This test uses the functions coxph and Surv of the package survival and the function anova (analysis of variance) of the package stats.

### Author(s)

R implementation and documentation: Vincenzo Lagani «vlagani@csd.uoc.gr», Giorgos Athineou «athineou@csd.uoc.gr»

#### References

V. Lagani and I. Tsamardinos (2010). Structure-based variable selection for survival data. Bioinformatics Journal 16(15): 1887-1894.

Cox, D.R. (1972) Regression models and life-tables. J. R. Stat. Soc., 34, 187-220.

Scholz, F. W. (2001). Maximum likelihood estimation for type I censored Weibull data including covariates. ISSTECH-96-022, Boeing Information & Support Services.

Smith, R. L. (1991). Weibull regression models for reliability data. Reliability Engineering & System Safety, 34(1), 55-76.

#### See Also

```
SES, censIndWR, testIndFisher, gSquare, testIndLogistic, Surv, anova, CondIndTests
```

### **Examples**

```
#create a survival simulated dataset
dataset <- matrix(runif(400 * 20, 1, 100), nrow = 400, ncol = 20)
dataset <- as.data.frame(dataset);</pre>
timeToEvent <- numeric(400)</pre>
event <- numeric(400)
ca <- numeric(400)
for(i in 1:400) {
 timeToEvent[i] <- dataset[i, 1] + 0.5 * dataset[i, 10] + 2 * dataset[i, 15] + runif(1, 0, 3);</pre>
 event[i] \leftarrow sample(c(0, 1), 1)
 ca[i] <- runif(1, 0, timeToEvent[i] - 0.5)</pre>
 if(event[i] == 0) timeToEvent[i] = timeToEvent[i] - ca[i]
}
require(survival, quietly = TRUE)
#init the Surv object class feature
target <- Surv(time = timeToEvent, event = event)</pre>
#run the censIndCR conditional independence test
censIndCR( target, dataset, xIndex = 12, csIndex = c(5, 7, 4) )
# run the SESC algorithm
## Not run:
```

```
ses1 <- SES(target, dataset, max_k = 1, threshold = 0.05, test = "censIndCR");
ses2 <- SES(target, dataset, max_k = 1, threshold = 0.05, test = "censIndWR");
## End(Not run)</pre>
```

Conditional independence tests with and without permutation p-value

Conditional independence test for continuous class variables with and without permutation based p-value

## **Description**

The main task of this test is to provide a permutation based p-value PVALUE for the null hypothesis: feature 'X' is independent from 'TARGET' given a conditioning set CS.

## Usage

```
condi(ind1, ind2, cs, dat, type = "pearson", rob = FALSE, R = 1)
dist.condi(ind1, ind2, cs, dat, type = NULL, rob = FALSE, R = 499)
cat.ci(ind1, ind2, cs, dat, type, rob = FALSE, R = 1)
```

# Arguments

ind1	The index of the one variable to be considered.
ind2	The index of the other variable to be considered.
CS	The index or indices of the conditioning set of variable(s). If you have no variables set this equal to 0.
dat	A matrix with the data. In the case of "cat.ci" the minimum must be $0$ , i.e. the data must be like $0$ , $1$ , $2$ and NOT $1$ , $2$ , $3$ There is a C++ code behind and the minimum must be $0$ .
type	Do you want the Pearson (type = "pearson") or the Spearman (type = "spearman") correlation to be used. For "dist.condi" this is an obsolete argument but it requires to exist when it is used in the PC algorithm.
	For "cat.ci" this should be a vector with the levels, the number of distinct (different) values of each categorical variable. Its length is equal to the number of variables used in the test (2 + the number of conditioning variables).
rob	If you choose type="pearson" then you can sapecify whether you want a robust version of it. For "dist.condi" and "cat.ci" this is an obsolete argument but it requires to exist when it is used in the PC algorithm.
R	If $R = 1$ then the asymptotic p-value is calculated. If $R > 1$ a permutation based p-value is returned. For the distance correlation based test, this is set to 499 by default and is used in the partial correlation test only.

### **Details**

This test is currently designed for usage by the PC algorithm. The Fisher conditional independence test which is based on the Pearson or Spearman correlation coefficients is much faster than the distance based (partial) correlation test.

The distance correlation can handle non linear relationships as well. The p-value for the partial distance correlation is calculated via permutations and is slow.

#### Value

A vector including the test statistic, it's associated p-value and the relevant degrees of freedom. In the case of a permutation based p-value, the returned test statistic is the observed test statistic divided by the relevant degrees of freedom (Pearson and Spearman correlation coefficients only). This is for the case of ties between many permutation based p-values. The PC algorithm choose a pair of variables based on the p-values. If they are equal it will use the test statistic.

### Author(s)

Michail Tsagris

R implementation and documentation: Giorgos Athineou <athineou@csd.uoc.gr> and Michail Tsagris <mtsagris@uoc.gr>

#### References

Hampel F. R., Ronchetti E. M., Rousseeuw P. J., and Stahel W. A. (1986). Robust statistics: the approach based on influence functions. John Wiley & Sons.

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#### See Also

```
testIndFisher, testIndSpearman, pc.skel, gSquare, CondIndTests
```

## **Examples**

```
#simulate a dataset with continuous data
dataset <- matrix(runif(500 * 5, 1, 100), ncol = 5 )
testIndFisher(dataset[, 1], dataset[, -1], xIndex = 1, csIndex = 2)
condi(ind1 = 1, ind2 = 2, cs = 3, dataset, R = 1)
condi(ind1 = 1, ind2 = 2, cs = 3, dataset, R = 999)</pre>
```

```
dist.condi(ind1 = 1, ind2 = 2, 0, dataset)

dist.condi(ind1 = 1, ind2 = 2, cs = 3, dataset, R = 99)
```

Constraint based feature selection algorithms

SES: Feature selection algorithm for identifying multiple minimal, statistically-equivalent and equally-predictive feature signatures MMPC: Feature selection algorithm for identifying minimal feature subsets

### Description

SES algorithm follows a forward-backward filter approach for feature selection in order to provide minimal, highly-predictive, statistically-equivalent, multiple feature subsets of a high dimensional dataset. See also Details. MMPC algorithm follows the same approach without generating multiple feature subsets.

### Usage

```
SES(target, dataset, max_k = 3, threshold = 0.05, test = NULL, ini = NULL,
wei = NULL, user_test = NULL, hash = FALSE, hashObject = NULL,
ncores = 1, backward = FALSE)
MMPC(target, dataset, max_k = 3, threshold = 0.05, test = NULL, ini = NULL,
wei = NULL, user_test = NULL, hash = FALSE, hashObject = NULL,
ncores = 1, backward = FALSE)
wald.ses(target, dataset, max_k = 3, threshold = 0.05, test = NULL, ini = NULL,
wei = NULL, user_test = NULL, hash = FALSE, hashObject = NULL,
ncores = 1, backward = FALSE)
wald.mmpc(target, dataset, max_k = 3, threshold = 0.05, test = NULL, ini = NULL,
wei = NULL, user_test = NULL, hash = FALSE, hashObject = NULL,
ncores = 1, backward = FALSE)
perm.ses(target, dataset, max_k = 3, threshold = 0.05, test = NULL, ini = NULL,
wei = NULL, user_test = NULL, hash=FALSE, hashObject = NULL,
R = 999, ncores = 1, backward = FALSE)
perm.mmpc(target, dataset, max_k = 3, threshold = 0.05, test = NULL, ini = NULL,
wei = NULL, user_test = NULL, hash=FALSE, hashObject = NULL,
R = 999, ncores = 1, backward = FALSE)
```

#### **Arguments**

target

The class variable. Provide either a string, an integer, a numeric value, a vector, a factor, an ordered factor or a Surv object. See also Details.

dataset The data-set; provide either a data frame or a matrix (columns = variables, rows

= samples).

max\_k The maximum conditioning set to use in the conditional indepedence test (see

Details). Integer, default value is 3.

threshold Threshold (suitable values in (0, 1)) for assessing p-values significance. Default

value is 0.05.

test The conditional independence test to use. Default value is NULL. See also

CondIndTests.

This is a supposed to be a list. After running SES or MMPC with some hyperini

parameters you might want to run SES again with different hyper-parameters. To avoid calculating the univariate associations (first step of SES and of MMPC) again, you can extract them from the first run of SES and plug them here. This can speed up the second run (and subequent runs of course) by 50%. See the

details and the argument "univ" in the output values.

A vector of weights to be used for weighted regression. The default value is wei

NULL. An example where weights are used is surveys when stratified sampling

has occured.

A user-defined conditional independence test (provide a closure type object). user\_test

Default value is NULL. If this is defined, the "test" argument is ignored.

A boolean variable which indicates whether (TRUE) or not (FALSE) to store the

statistics calculated during SES execution in a hash-type object. Default value

is FALSE. If TRUE a hashObject is produced.

hashObject A List with the hash objects generated in a previous run of SES or MMPC. Each

time SES runs with "hash=TRUE" it produces a list of hashObjects that can be

re-used in order to speed up next runs of SES or MMPC.

Important: the generated hashObjects should be used only when the same dataset

is re-analyzed, possibly with different values of max k and threshold.

The number of permutations, set to 999 by default. There is a trick to avoind do-

ing all permutations. As soon as the number of times the permuted test statistic is more than the observed test statistic is more than 50 (if threshold = 0.05 and R = 999), the p-value has exceeded the signifiance level (threshold value) and hence the predictor variable is not significant. There is no need to continue do

the extra permutations, as a decision has already been made.

How many cores to use. This plays an important role if you have tens of thouncores

> sands of variables or really large sample sizes and tens of thousands of variables and a regression based test which requires numerical optimisation. In other cases it will not make a difference in the overall time (in fact it can be slower). The parallel computation is used in the first step of the algorithm, where univariate associations are examined, those take place in parallel. We have seen a reduction in time of 50% with 4 cores in comparison to 1 core. Note also, that the amount

of reduction is not linear in the number of cores.

If TRUE, the backward (or symmetry correction) phase will be implemented.

This removes any falsely included variables in the parents and children set of

the target variable. It calls the link{mmpcbackphase} for this purpose.

hash

R

backward

### **Details**

The SES function implements the Statistically Equivalent Signature (SES) algorithm as presented in "Tsamardinos, Lagani and Pappas, HSCBB 2012".

The MMPC function implements the MMPC algorithm as presented in "Tsamardinos, Brown and Aliferis. The max-min hill-climbing Bayesian network structure learning algorithm".

he output value "univ" along with the output value "hashObject" can speed up the computations of subsequent runs of SES and MMPC. The first run with a specific pair of hyper-parameters (threshold and max\_k) the univariate associations tests and the conditional independence tests (test statistic and **natural logarithm of their corresponding p-values**) are stored and returned. In the next run(s) with different pair(s) of hyper-parameters you can use this information to save time. With a few thousands of variables you will see the difference, which can be up to 50%. For the non robust correlation based tests, the difference may not be significant though, because the unconditional correlation coefficients are calculated very efficiently.s.

The max\_k option: the maximum size of the conditioning set to use in the conditioning independence test. Larger values provide more accurate results, at the cost of higher computational times. When the sample size is small (e.g., < 50 observations) the max\_k parameter should be say 3, otherwise the conditional independence test may not be able to provide reliable results.

If the dataset (predictor variables) contains missing (NA) values, they will automatically be replaced by the current variable (column) mean value with an appropriate warning to the user after the execution.

If the target is a single integer value or a string, it has to corresponds to the column number or to the name of the target feature in the datase. In any other case the target is a variable that is not contained in the dataset.

If the current 'test' argument is defined as NULL or "auto" and the user\_test argument is NULL then the algorithm automatically selects the best test based on the type of the data. Particularly:

- if the target is a factor, the multinomial or the binary logistic regression is used. If the target has two values only, binary logistic regression will be used.
- if target is a ordered factor, ordinal regression is used in the logistic test. Hence, if you want to use multinomial or ordinal logistic regression, make sure your target is factor.
- if target is a numerical vector and the dataset is a matrix or a data.frame with continuous variables, the Fisher conditional independence test is used. If the dataset is a data.frame and there are categorical variables, linear regression is used.
- if target is discrete numerical (counts), the Poisson regression conditional independence test is used. If there are only two values, the binary logistic regression is to be used.
- if target is a Surv object, a Survival conditional independence test is used.
- if target is a matrix with at least 2 columns, the multivariate linear regression is used.
- if target is a 2 column matrix whose columns are the number of successes and the number of trials (first and second column respectively) the testIndBinom should be used.

Conditional independence test functions to be pass through the user\_test argument should have the same signature of the included test. See testIndFisher for an example.

For all the available conditional independence tests that are currently included on the package, please see CondIndTests. If two or more p-values are below the machine epsilon (.Machine\$double.eps which is equal to 2.220446e-16), all of them are set to 0. To make the comparison or the ordering

feasible we use the logarithm of the p-value. The max-min heuristic though, requires comparison and an ordering of the p-values. Hence, all conditional independence tests calculate the logarithm of the p-value.

If there are missing values in the dataset (predictor variables) columnwise imputation takes place. The median is used for the continuous variables and the mode for categorical variables. It is a naive and not so clever method. For this reason the user is encouraged to make sure his data contain no missing values.

If you have percentages, in the (0, 1) interval, they are automatically mapped into R by using the logit transformation. If you set the test to **testIndBeta**, beta regression is used. If you have compositional data, positive multivariate data where each vector sums to 1, with NO zeros, they are also mapped into the Euclidean space using the additive log-ratio (multivariate logit) transformation (Aitchison, 1986).

If you use testIndSpearman (argument "test"), the ranks of the data calculated and those are used in the caclulations. This speeds up the whole procedure.

As a rule of thumb you can try this. If for example you have counts and want to see which model fits best, there are two ways. Calculate the mean and the variance. If they are similar, use the Poisson instead of the negative binomial as it is much faster. If you are not convinced, you can either use the negative binomial or do the following simulation study.

# x <- matrix(rnorm(n \* 1000), ncol = 1000) # a <- Rfast::univglms(y, x) # hist(a[, 2]) ## histogram of the p-values

If the histogram shows a uniform distribution, use the Poisson regression. If the histogram is not uniform, then repeat the simulation but with a negative binomial distribution. If the histogram is again not flat, then another model is necessary. If the data come from a Poisson or negative binomial, the histogram with a negative binomial regressino will be flat. If the data come a from a negative binomial, the histogram with a Poisson will not be uniform.

On the same page, if you have many zeros, try Rfast::zip.mle and see whether there are grounds to to facilitate the use of a zero inflated Poisson model. Otherwise, do a simulation study like before.

### Value

The output of the algorithm is an object of the class 'SESoutput' for SES or 'MMPCoutput' for MMPC including:

selectedVars The selected variables, i.e., the signature of the target variable. selectedVarsOrder

The order of the selected variables according to increasing pvalues.

queues A list containing a list (queue) of equivalent features for each variable included in selected Vars. An equivalent signature can be built by selecting a single feature

from each queue. Featured only in SES.

signatures A matrix reporting all equivalent signatures (one signature for each row). Fea-

tured only in SES.

hashObject The hashObject caching the statistic calculated in the current run.

pvalues For each feature included in the dataset, this vector reports the strength of its

association with the target in the context of all other variable. Particularly, this vector reports the max p-values found when the association of each variable

with the target is tested against different conditional sets. Lower values indicate higher association. Note that these are the logged p-values, natural logarithm of the pvalues, and not the p-values.

stats The statistics corresponding to "pvalues" (higher values indicates higher associ-

ation).

univ This is a list with the univariate associations; the test statistics and their cor-

responding logged p-values. This list is very important for subsequent runs of SES with different hyper-parameters. After running SES with some hyper-parameters you might want to run SES again with different hyper-parameters. To avoid calculating the univariate associations (first step of SES or MMPC) again, you can take this list from the first run of SES and plug it in the argument "ini" in the next run(s) of SES or MMPC. This can speed up the second run (and subequent runs of course) by 50%. See the argument "univ" in the output values.

max\_k The max\_k option used in the current run.
threshold The threshold option used in the current run.

n.tests If you have set hash = TRUE, then the number of tests performed by SES or

MMPC will be returned. If you have not set this to TRUE, the number of uni-

variate associations will be returned. So be careful with this number.

runtime The run time of the algorithm. A numeric vector. The first element is the user

time, the second element is the system time and the third element is the elapsed

time.

test The character name of the statistic test used.

Generic Functions implemented for SESoutput Object:

plot(object=SESoutput, mode="all")

Plots the generated pvalues (using barplot) of the current SESoutput object in

comparison to the threshold.

Argument mode can be either "all" or "partial" for the first 500 pvalues of the

object.

## Note

The packages required by the SES and MMPC algorithm operations are:

quantreg: for the quantile (median) regression

**MASS**: for negative binomial regression and simple ordinal regression **nnet**: also require(stats) and require(MASS) for the testIndLogistic test **survival**: for the censIndCR, censIndWR and the censIndER tests

doParallel: for parallel computations

**lme4**: for (generalised) linear mixed models

Rfast: for many fast functions.

### Author(s)

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R implementation and documentation: Giorgos Athineou <athineou@csd.uoc.gr> Vincenzo Lagani <vlagani@csd.uoc.gr>

### References

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Brown, L. E., Tsamardinos, I., & Aliferis, C. F. (2004). A novel algorithm for scalable and accurate Bayesian network learning. Medinfo, 711-715.

Tsamardinos, Brown and Aliferis (2006). The max-min hill-climbing Bayesian network structure learning algorithm. Machine learning, 65(1), 31-78.

### See Also

```
CondIndTests, cv.ses
```

## **Examples**

```
set.seed(123)
#simulate a dataset with continuous data
dataset <- matrix(runif(100 * 50, 1, 100), ncol = 50)
#define a simulated class variable
target <- 3 * dataset[, 10] + 2 * dataset[, 15] + 3 * dataset[, 20] + rnorm(100, 0, 5)</pre>
# define some simulated equivalences
dataset[, 16] <- dataset[, 10] + rnorm(100, 0, 2)
dataset[, 17] <- dataset[, 15] + rnorm(100, 0, 2)
# run the SES algorithm
sesObject <- SES(target , dataset, max_k = 5, threshold = 0.05, test = "testIndFisher",
hash = TRUE, hashObject = NULL);
# get the queues with the equivalences for each selected variable
sesObject@queues
#get the generated signatures
sesObject@signatures;
# re-run the SES algorithm with the same or different configuration
# under the hash-based implementation of retrieving the statistics
# in the SAME dataset (!important)
hashObj <- sesObject@hashObject;</pre>
sesObject2 <- SES(target, dataset, max_k = 2, threshold = 0.01, test = "testIndFisher",
hash = TRUE, hashObject = hashObj);
```

```
# get the run time
sesObject@runtime;
sesObject2@runtime;
# MMPC algorithm
mmpcObject <- MMPC(target, dataset, max_k = 3, threshold = 0.05, test="testIndFisher");</pre>
mmpcObject@selectedVars
mmpcObject@runtime
```

Constraint based feature selection algorithms for longitudinal and clustered data SES.glmm/SES.gee: Feature selection algorithm for identifying multiple minimal, statistically-equivalent and equally-predictive feature signatures with correlated data

### **Description**

SES.glmm algorithm follows a forward-backward filter approach for feature selection in order to provide minimal, highly-predictive, statistically-equivalent, multiple feature subsets of a high dimensional dataset. See also Details. MMPC.glmm algorithm follows the same approach without generating multiple feature subsets. They are both adapted to longitudinal target variables.

## Usage

```
SES.glmm(target, reps = NULL, group, dataset, max_k = 3, threshold = 0.05,
test = NULL, ini = NULL, wei = NULL, user_test = NULL, hash = FALSE,
hashObject = NULL, slopes = FALSE, ncores = 1)
MMPC.glmm(target, reps = NULL, group, dataset, max_k = 3, threshold = 0.05,
test = NULL, ini = NULL, wei = NULL, user_test = NULL, hash = FALSE,
hashObject = NULL, slopes = FALSE, ncores = 1)
MMPC.gee(target, reps = NULL, group, dataset, max_k = 3, threshold = 0.05,
test = NULL, ini = NULL, wei = NULL, user_test = NULL, hash = FALSE,
hashObject = NULL, correl = "exchangeable", se = "jack", ncores = 1)
SES.gee(target, reps = NULL, group, dataset, max_k = 3, threshold = 0.05,
test = NULL, ini = NULL, wei = NULL, user_test = NULL, hash = FALSE,
hashObject = NULL, correl = "exchangeable", se = "jack", ncores = 1)
```

## **Arguments**

target	The class variable. Provide a vector with continuous (normal), binary (binomial)
	or discrete (Poisson) data.

A numeric vector containing the time points of the subjects. It's length is equal to the length of the target variable. If you have clustered data, leave this NULL.

reps

A numeric vector containing the subjects or groups. It must be of the same group

legnth as target.

dataset The dataset; provide either a data frame or a matrix (columns = variables, rows

= samples). Currently, only continuous datasets are supported.

The maximum conditioning set to use in the conditional indepedence test (see max\_k

Details). Integer, default value is 3.

threshold Threshold (suitable values in (0, 1)) for assessing p-values significance. Default

value is 0.05.

The conditional independence test to use. Default value is NULL. Currently, test

the only available conditional independence tests are the "testIndGLMMLogistic", "testIndGLMMPois", "testIndGLMMGamma", "testIndGLMMNormLog", "testIndGLMMOrdinal", "testIndGLMMReg", "testIndLMM" and "testIndGLMMCR" for generalised linear mixed models. For the GEE, the available tests are "testIndGEEReg", "testIndGEEPois", "testIndGEELogistic", "testIndGEEGamma" and "testIndGEENorm-

Log".

ini This is a supposed to be a list. After running SES or MMPC with some hyper-

parameters you might want to run SES again with different hyper-parameters. To avoid calculating the univariate associations (first step of SES and of MPPC) again, you can extract them from the first run of SES and plug them here. This can speed up the second run (and subequent runs of course) by 50%. See the

details and the argument "univ" in the output values.

A vector of weights to be used for weighted regression. The default value is wei

NULL.

A user-defined conditional independence test (provide a closure type object). user\_test

Default value is NULL. If this is defined, the "test" argument is ignored.

hash A boolean variable which indicates whether (TRUE) or not (FALSE) to store the

statistics calculated during SES execution in a hash-type object. Default value

is FALSE. If TRUE a hashObject is produced.

hashObject A List with the hash objects generated in a previous run of SES.glmm. Each

time SES runs with "hash=TRUE" it produces a list of hashObjects that can be

re-used in order to speed up next runs of SES.

Important: the generated hashObjects should be used only when the same dataset

is re-analyzed, possibly with different values of max\_k and threshold.

slopes Should random slopes for the ime effect be fitted as well? Default value is

FALSE.

se

correl The correlation structure. For the Gaussian, Logistic, Poisson and Gamma re-

gression this can be either "exchangeable" (compound symmetry, suitable for clustered data) or "ar1" (AR(1) model, suitable for longitudinal data). For the

ordinal logistic regression its only the "exchangeable" correlation sturcture.

The method for estimating standard errors. This is very important and crucial. The available options for Gaussian, Logistic, Poisson and Gamma regression

are: a) 'san.se': the usual robust estimate. b) 'jack': approximate jackknife variance estimate. c) 'j1s': if 1-step jackknife variance estimate and d) 'fij': fully

iterated jackknife variance estimate. If you have many clusters (sets of repeated

measurements) "san.se" is fine as it is asympotically correct, plus jacknife estimates will take longer. If you have a few clusters, then maybe it's better to use jacknife estimates.

The jackknife variance estimator was suggested by Paik (1988), which is quite suitable for cases when the number of subjects is small (K < 30), as in many biological studies. The simulation studies conducted by Ziegler et al. (2000) and Yan and Fine (2004) showed that the approximate jackknife estimates are in many cases in good agreement with the fully iterated ones.

ncores

How many cores to use. This plays an important role if you have tens of thousands of variables or really large sample sizes and tens of thousands of variables and a regression based test which requires numerical optimisation. In other cases it will not make a difference in the overall time (in fact it can be slower). The parallel computation is used in the first step of the algorithm, where univariate associations are examined, those take place in parallel. We have seen a reduction in time of 50% with 4 cores in comparison to 1 core. Note also, that the amount of reduction is definetely not linear in the number of cores.

### **Details**

The SES.glmm function implements the Statistically Equivalent Signature (SES) algorithm as presented in "Tsamardinos, Lagani and Pappas, HSCBB 2012" adapted to longitudinal data. The citation for this is "Tsagris, Lagani and tsamardinos, (2018)". These functions presented here are for the **temporal-lonitudinal scenario**.

The MMPC function mplements the MMPC algorithm as presented in "Tsamardinos, Brown and Aliferis. The max-min hill-climbing Bayesian network structure learning algorithm" adapted to longitudinal data.

The output value "univ" along with the output value "hashObject" can speed up the computations of subesequent runs of SES and MMPC. The first run with a specific pair of hyper-parameters (threshold and max\_k) the univariate associations tests and the conditional independence tests (test statistic and logarithm of their corresponding p-values) are stored and returned. In the next run(s) with different pair(s) of hyper-parameters you can use this information to save time. With a few thousands of variables you will see the difference, which can be up to 50%.

The max\_k option: the maximum size of the conditioning set to use in the conditioning independence test. Larger values provide more accurate results, at the cost of higher computational times. When the sample size is small (e.g., <50 observations) the max\_k parameter should be  $\le5$ , otherwise the conditional independence test may not be able to provide reliable results.

If the dataset contains missing (NA) values, they will automatically be replaced by the current variable (column) mean value with an appropriate warning to the user after the execution.

If the target is a single integer value or a string, it has to corresponds to the column number or to the name of the target feature in the dataset. In any other case the target is a variable that is not contained in the dataset.

If the current 'test' argument is defined as NULL or "auto" and the user\_test argument is NULL then the algorithm automatically selects only available, which is testIndGLMMReg.

Conditional independence test functions to be pass through the user\_test argument should have the same signature of the included test. See "?testIndFisher" for an example.

For all the available conditional independence tests that are currently included on the package, please see "?CondIndTests".

If two or more p-values are below the machine epsilon (.Machine\$double.eps which is equal to 2.220446e-16), all of them are set to 0. To make the comparison or the ordering feasible we use the logarithm of the p-value. The max-min heuristic though, requires comparison and an ordering of the p-values. Hence, all conditional independence tests calculate the logarithm of the p-value.

If there are missing values in the dataset (predictor variables) columnwise imputation takes place. The median is used for the continuous variables and the mode for categorical variables. It is a naive and not so clever method. For this reason the user is encouraged to make sure his data contain no missing values.

If you have percentages, in the (0, 1) interval, they are automatically mapped into R by using the logit transformation and a linear mixed model is fitted. If you have binary data, logistic mixed regression is applied and if you have discrete data (counts), Poisson mixed regression is applied.

If you want to use the GEE methodology, make sure you load the library geepack first.

### Value

The output of the algorithm is an object of the class 'SES.glmm.output' for SES.glmm or 'MMPC.glmm.output' for MMPC.glmm including:

selectedVars The selected variables, i.e., the signature of the target variable. selectedVarsOrder

The order of the selected variables according to increasing pvalues.

queues A list containing a list (queue) of equivalent features for each variable included

in selected Vars. An equivalent signature can be built by selecting a single feature

from each queue. Featured only in SES.

signatures A matrix reporting all equivalent signatures (one signature for each row). Fea-

tured only in SES.

hashObject The hashObject caching the statistic calculted in the current run.

pvalues For each feature included in the dataset, this vector reports the strength of its

association with the target in the context of all other variables. Particularly, this vector reports the max p-values found when the association of each variable with the target is tested against different conditional sets. Lower values indicate

higher association. Note that these are the logarithm of the p-values.

stats The statistics corresponding to "pvalues" (higher values indicates higher associ-

ation).

univ This is a list with the univariate associations. The test statistics and their cor-

responding **logged p-values**. This list is very important for subsequent runs of SES with different hyper-parameters. After running SES with some hyper-parameters you might want to run SES again with different hyper-parameters. To avoid calculating the univariate associations (first step of SES or MMPC) again, you can take this list from the first run of SES and plug it in the argument "ini" in the next run(s) of SES or MMPC. This can speed up the second run (and subequent runs of course) by 50%. See the argument "univ" in the output values.

max\_k The max\_k option used in the current run.

threshold The threshold option used in the current run.

n.tests If you have set hash = TRUE, then the number of tests performed by SES or

MMPC will be returned. If you have not set this to TRUE, the number of uni-

variate associations will be returned. So be careful with this number.

runtime The run time of the algorithm. A numeric vector. The first element is the user

time, the second element is the system time and the third element is the elapsed

time.

slope Whether random slopes for the time effects were used or not, TRUE or FALSE.

Generic Functions implemented for SESoutput Object:

plot(object=SES.glmm.output, mode="all")

Plots the generated pvalues (using barplot) of the current SESoutput object in comparison to the threshold. Argument mode can be either "all" or "partial" for the first 500 pvalues of the object.

### Author(s)

Ioannis Tsamardinos, Vincenzo Lagani

R implementation and documentation: Giorgos Athineou <athineou@csd.uoc.gr> Vincenzo Lagani <vlagani@csd.uoc.gr>

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### See Also

CondIndTests, testIndGLMMReg

## **Examples**

```
## Not run:
require(lme4)
data(sleepstudy)
reaction <- sleepstudy$Reaction
days <- sleepstudy$Days
subject <- sleepstudy$Subject
x <- matrix(rnorm(180 * 200),ncol = 200) ## unrelated predictor variables
m1 <- SES.glmm(target = reaction, reps = days, group = subject, dataset = x)
m2 <- MMPC.glmm(target = reaction, reps = days, group = subject, dataset = x)
## End(Not run)</pre>
```

Constraint based feature selection algorithms for multiple datasets

ma.ses: Feature selection algorithm for identifying multiple minimal, statistically-equivalent and equally-predictive feature signatures with multiple datasets ma.mmpc: Feature selection algorithm for identifying minimal feature subsets with multiple datasets

### **Description**

SES algorithm follows a forward-backward filter approach for feature selection in order to provide minimal, highly-predictive, statistically-equivalent, multiple feature subsets of two or more high dimensional datasets. See also Details. MMPC algorithm follows the same approach without generating multiple feature subsets.

### Usage

```
ma.ses(target, dataset, ina, statistic = FALSE, max_k = 3, threshold = 0.05,
test = NULL, ini = NULL, user_test = NULL, hash = FALSE, hashObject = NULL,
ncores = 1)

ma.mmpc(target, dataset, ina, statistic = FALSE, max_k = 3, threshold = 0.05,
test = NULL, ini = NULL, user_test = NULL, hash = FALSE, hashObject = NULL,
ncores = 1, backward = FALSE)
```

### **Arguments**

target The class variable. Provide either a string, an integer, a numeric value, a vector,

a factor, an ordered factor or a Surv object. See also Details.

dataset The data-set; provide either a data frame or a matrix (columns = variables, rows

= samples). Alternatively, provide an ExpressionSet (in which case rows are

samples and columns are features, see bioconductor for details).

ina A numerical vector indicating the dataset. The numbers must be 1, 2, 3,...

statistic A boolean variable indicating whether the test statistics (TRUE) or the p-values

should be combined (FALSE). See the details about this.

max\_k The maximum conditioning set to use in the conditional indepedence test (see

Details). Integer, default value is 3.

threshold Threshold (suitable values in (0, 1)) for assessing p-values significance. Default

value is 0.05.

test The conditional independence test to use. Default value is NULL. See also

CondIndTests.

ini This is a supposed to be a list. After running SES or MMPC with some hyper-

parameters you might want to run SES again with different hyper-parameters. To avoid calculating the univariate associations (first step of SES and of MPPC) again, you can extract them from the first run of SES and plug them here. This can speed up the second run (and subequent runs of course) by 50%. See the

details and the argument "univ" in the output values.

user\_test A user-defined conditional independence test (provide a closure type object).

Default value is NULL. If this is defined, the "test" argument is ignored.

hash A boolean variable which indicates whether (TRUE) or not (FALSE) to store the

statistics calculated during SES execution in a hash-type object. Default value

is FALSE. If TRUE a hashObject is produced.

hashObject A List with the hash objects generated in a previous run of SES or MMPC. Each

time SES runs with "hash=TRUE" it produces a list of hashObjects that can be

re-used in order to speed up next runs of SES or MMPC.

Important: the generated hashObjects should be used only when the same dataset

is re-analyzed, possibly with different values of max\_k and threshold.

ncores How many cores to use. This plays an important role if you have tens of thou-

sands of variables or really large sample sizes and tens of thousands of variables and a regression based test which requires numerical optimisation. In other cases it will not make a difference in the overall time (in fact it can be slower). The parallel computation is used in the first step of the algorithm, where univariate associations are examined, those take place in parallel. We have seen a reduction in time of 50% with 4 cores in comparison to 1 core. Note also, that the amount

of reduction is not linear in the number of cores.

backward If TRUE, the backward (or symmetry correction) phase will be implemented.

This removes any falsely included variables in the parents and children set of the target variable. This is an experimental stage, so do not trust too much or

ven better do not use.

### **Details**

This is more at an experimental stage at the present.

The SES function implements the Statistically Equivalent Signature (SES) algorithm as presented in "Tsamardinos, Lagani and Pappas, HSCBB 2012".

The MMPC function mplements the MMPC algorithm as presented in "Tsamardinos, Brown and Aliferis. The max-min hill-climbing Bayesian network structure learning algorithm".

The output value "univ" along with the output value "hashObject" can speed up the computations of subesequent runs of SES and MMPC. The first run with a specific pair of hyper-parameters (threshold and max\_k) the univariate associations tests and the conditional independence tests (test statistic and logarithm of their corresponding p-values) are stored and returned. In the next run(s) with different pair(s) of hyper-parameters you can use this information to save time. With a few thousands of variables you will see the difference, which can be up to 50%. For the non robust correlation based tests, the difference may not be significant though, because the unconditional correlation coefficients are calcualted very efficiently.

The max\_k option: the maximum size of the conditioning set to use in the conditioning independence test. Larger values provide more accurate results, at the cost of higher computational times. When the sample size is small (e.g., < 50 observations) the max\_k parameter should be  $\le 5$ , otherwise the conditional independence test may not be able to provide reliable results.

If the dataset (predictor variables) contains missing (NA) values, they will automatically be replaced by the current variable (column) mean value with an appropriate warning to the user after the execution.

Conditional independence test functions to be pass through the user\_test argument should have the same signature of the included test. See testIndFisher for an example.

For all the available conditional independence tests that are currently included on the package, please see CondIndTests.

If two or more p-values are below the machine epsilon (.Machine\$double.eps which is equal to 2.220446e-16), all of them are set to 0. To make the comparison or the ordering feasible we use the logarithm of the p-value. The max-min heuristic though, requires comparison and an ordering of the p-values. Hence, all conditional independence tests calculate the logarithm of the p-value.

If there are missing values in the dataset (predictor variables) columnwise imputation takes place. The median is used for the continuous variables and the mode for categorical variables. It is a naive and not so clever method. For this reason the user is encouraged to make sure his data contain no missing values.

If you have percentages, in the (0, 1) interval, they are automatically mapped into R by using the logit transformation.

If you use testIndSpearman (argument "test"), the ranks of the data calculated and those are used in the caclulations. This speeds up the whole procedure.

Currently only the testIndFisher and testIndSpearman tests are supported for use in the algorithm.

If the argument **statistic** is set to FALSE, the p-values from the hypothesis test of each dataset are combined via Fisher's meta-analytic approach, that is  $T=-2\sum_{i=1}^k\log p_i$  and T  $\chi^2_{2k}$ . If **statistic** is TRUE, the test statistics are combined as  $T=\frac{\sum_{i=1}^k t_i/se(t_i)}{\sum_{i=1}^k 1/se(t_i)}$  and T N(0,1).

### Value

The output of the algorithm is an object of the class 'SESoutput' for SES or 'MMPCoutput' for MMPC including:

selectedVars The selected variables, i.e., the signature of the target variable.

selectedVarsOrder

The order of the selected variables according to increasing pvalues.

queues A list containing a list (queue) of equivalent features for each variable included

in selectedVars. An equivalent signature can be built by selecting a single feature

from each queue. Featured only in SES.

signatures A matrix reporting all equivalent signatures (one signature for each row). Fea-

tured only in SES.

hashObject The hashObject caching the statistic calculated in the current run.

pvalues For each feature included in the dataset, this vector reports the strength of its

association with the target in the context of all other variables. Particularly, this vector reports the max p-values (on a logarithmic scale) found when the association of each variable with the target is tested against different conditional

sets. Lower values indicate higher association.

stats The statistics corresponding to "pvalues" (higher values indicates higher associ-

ation).

univ This is a list with the univariate associations. The test statistics and their cor-

responding logged p-values, along with their flag (1 if the test was perfromed and 0 otherwise). This list is very important for subsequent runs of SES with different hyper-parameters. After running SES with some hyper-parameters you might want to run SES again with different hyper-parameters. To avoid calculating the univariate associations (first step of SES or MMPC) again, you can take this list from the first run of SES and plug it in the argument "ini" in the next run(s) of SES or MMPC. This can speed up the second run (and subequent runs

of course) by 50%. See the argument "univ" in the output values.

max\_k The max\_k option used in the current run.

threshold The threshold option used in the current run.

runtime The run time of the algorithm. A numeric vector. The first element is the user

time, the second element is the system time and the third element is the elapsed

time.

test The character name of the statistic test used.

Generic Function implemented for SESoutput Object:

plot(object=SESoutput, mode="all")

Plots the generated pvalues (using barplot) of the current SESoutput object in

comparison to the threshold.

Argument mode can be either "all" or "partial" for the first 500 pvalues of the

object.

### Author(s)

Ioannis Tsamardinos, Vincenzo Lagani

R implementation and documentation: Giorgos Athineou <athineou@csd.uoc.gr>, Vincenzo Lagani <vlagani@csd.uoc.gr> and Michail Tsagris <mtsagris@uoc.gr>

#### References

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- I. Tsamardinos, V. Lagani and D. Pappas (2012). Discovering multiple, equivalent biomarker signatures. In proceedings of the 7th conference of the Hellenic Society for Computational Biology & Bioinformatics HSCBB12.

Tsamardinos, Brown and Aliferis (2006). The max-min hill-climbing Bayesian network structure learning algorithm. Machine learning, 65(1), 31-78.

### See Also

```
SES, CondIndTests, cv.ses
```

## **Examples**

```
set.seed(123)
#simulate a dataset with continuous data
dataset <- matrix(runif(400 * 100, 1, 100), ncol = 100)
#define a simulated class variable
target <- 3 * dataset[, 10] + 2 * dataset[, 20] + 3 * dataset[, 30] + rnorm(400, 0, 5)
#define some simulated equivalences
dataset[, 15] <- dataset[, 10] + rnorm(400, 0, 2)</pre>
dataset[, 10] <- dataset[ , 10] + rnorm(400, 0, 2)
dataset[, 25] <- dataset[, 20] + rnorm(400, 0, 2)</pre>
dataset[, 23] <- dataset[, 20] + rnorm(400, 0, 2)</pre>
#run the SES algorithm
a1 <- SES(target , dataset, max_k = 5, threshold = 0.05, test = "testIndFisher",
hash = TRUE, hashObject = NULL)
ina <- rbinom(400, 2, 0.5) + 1
a2 <- ma.ses(target , dataset, ina = ina, max_k = 5, threshold = 0.05, test = "testIndFisher",
hash = TRUE, hashObject = NULL)
a3 <- ma.mmpc(target , dataset, ina = ina, max_k = 5, threshold = 0.05, test = "testIndFisher",
hash = TRUE, hashObject = NULL)
#get the generated signatures
a1@signatures
a2@signatures
a3@selectedVars
```

Correlation based conditional independence tests

Fisher and Spearman conditional independence test for continuous class variables

## **Description**

The main task of this test is to provide a p-value PVALUE for the null hypothesis: feature 'X' is independent from 'TARGET' given a conditioning set CS.

### Usage

```
testIndFisher(target, dataset, xIndex, csIndex, wei = NULL, statistic = FALSE,
univariateModels = NULL, hash = FALSE, stat_hash = NULL,
pvalue_hash = NULL)
testIndMMFisher(target, dataset, xIndex, csIndex, wei = NULL, statistic = FALSE,
univariateModels = NULL, hash = FALSE, stat_hash = NULL,
pvalue_hash = NULL)
testIndSpearman(target, dataset, xIndex, csIndex, wei = NULL, statistic = FALSE,
univariateModels = NULL, hash = FALSE, stat_hash = NULL,
pvalue_hash = NULL)
permFisher(target, dataset, xIndex, csIndex, wei = NULL, statistic = FALSE,
univariateModels = NULL, hash = FALSE, stat_hash = NULL,
pvalue_hash = NULL, threshold = 0.05, R = 999)
permMMFisher(target, dataset, xIndex, csIndex, wei = NULL, statistic = FALSE,
univariateModels = NULL, hash = FALSE, stat_hash = NULL,
pvalue_hash = NULL, threshold = 0.05, R = 999)
permDcor(target, dataset, xIndex, csIndex, wei = NULL, statistic = FALSE,
univariateModels = NULL, hash = FALSE, stat_hash = NULL,
pvalue_hash = NULL, threshold = 0.05, R = 499)
```

### **Arguments**

target	A numeric vector containing the values of the target variable. If the values are proportions or percentages, i.e. strictly within 0 and 1 they are mapped into R using log( target/(1 - target)). This can also be a list of vectors as well. In this case, the metanalytic approach is used.
dataset	A numeric matrix containing the variables for performing the test. Rows as samples and columns as features.
xIndex	The index of the variable whose association with the target we want to test.

csIndex The indices of the variables to condition on. If you have no variables set this

equal to 0.

wei A vector of weights to be used for weighted regression. The default value is

NULL. This is not used with "permDcor".

statistic A boolean variable indicating whether the test statistics (TRUE) or the p-values

should be combined (FALSE). See the details about this. For the permFisher

test this is not taken into account.

univariateModels

Fast alternative to the hash object for univariate test. List with vectors "pvalues" (p-values), "stats" (statistics) and "flags" (flag = TRUE if the test was successful) representing the univariate association of each variable with the target. Default

value is NULL.

hash A boolean variable which indicates whether (TRUE) or not (FALSE) to use the

hash-based implementation of the statistics of SES. Default value is FALSE. If TRUE you have to specify the stat\_hash argument and the pvalue\_hash argument.

ment.

stat\_hash A hash object which contains the cached generated statistics of a SES run in the

current dataset, using the current test.

pvalue\_hash A hash object which contains the cached generated p-values of a SES run in the

current dataset, using the current test.

threshold Threshold (suitable values in (0, 1)) for assessing p-values significance. Default

value is 0.05. This is actually obsolete here, but has to be in order tyo have a

concise list of input arguments across the same family of functions.

R The number of permutations to use. The default value is 999. For the "permD-

cor" this is set to 499.

## **Details**

If hash = TRUE, testIndFisher requires the arguments 'stat\_hash' and 'pvalue\_hash' for the hash-based implementation of the statistic test. These hash Objects are produced or updated by each run of SES (if hash == TRUE) and they can be reused in order to speed up next runs of the current statistic test. If "SESoutput" is the output of a SES run, then these objects can be retrieved by SESoutput@hashObject\$stat\_hash and the SESoutput@hashObject\$pvalue\_hash.

Important: Use these arguments only with the same dataset that was used at initialization.

For all the available conditional independence tests that are currently included on the package, please see "?CondIndTests".

Note that if the testIndReg is used instead the results will not be be the same, unless the sample size is very large. This is because the Fisher test uses the t distribution stemming from the Fisher's z transform and not the t distribution of the correlation coefficient.

BE CAREFUL with testIndSpearman. The Pearson's correlation coefficient is actually calculated. So, you must have transformed the data into their ranks before plugging them here. The reason for this is to speed up the computation time, as this test can be used in SES, MMPC and mmhc.skel. The variance of the Fisher transformed Spearman's correlation is  $\frac{1.06}{n-3}$  and the variance of the Fisher transformed Pearson's correlation coefficient is  $\frac{1}{n-3}$ .

When performing the above tests with multiple datasets, the test statistic and the p-values are combined in a meta-analytic way. Is up to the user to decide whether to use the fixed effects model approach and combine the test statistics (statistic = TRUE), or combine the p-values as Fisher suggested (statistic = FALSE).

The argument R is useful only for the permFisher and permDcor tests. The permDcor test uses the distance correlation instead of the usual Pearson or Spearman correlations.

TestIndMMFisher does a robust estimation of the correlation via MM regression.

### Value

### A list including:

A numeric value that represents the logarithm of the generated p-value due to pvalue Fisher's method (see reference below). stat A numeric value that represents the generated statistic due to Fisher's method (see reference below). The current hash object used for the statistics. See argument stat\_hash and destat\_hash tails. If argument hash = FALSE this is NULL.

pvalue\_hash The current hash object used for the p-values. See argument stat\_hash and de-

tails. If argument hash = FALSE this is NULL.

### Author(s)

Vincenzo Lagani and Ioannis Tsamardinos

R implementation and documentation: Giorgos Athineou <athineou@csd.uoc.gr> Vincenzo Lagani <vlagani@csd.uoc.gr>.

## References

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### See Also

```
testIndSpearman, testIndReg, SES, testIndLogistic, gSquare, CondIndTests
```

### **Examples**

```
#simulate a dataset with continuous data
dataset <- matrix(runif(300 * 50, 1, 1000), nrow = 50 )
#the target feature is the last column of the dataset as a vector
target <- dataset[, 50]
res1 <- testIndFisher(target, dataset, xIndex = 44, csIndex = 10)
res2 <- testIndSpearman(target, dataset, xIndex = 44, csIndex = 10)
res3 <- permFisher(target, dataset, xIndex = 44, csIndex = 10, R = 999)
res4 <- permDcor(target, dataset, xIndex = 44, csIndex = 10, R = 99)
#define class variable (here tha last column of the dataset)
dataset <- dataset[, -50]
#run the MMPC algorithm using the testIndFisher conditional independence test
mmpcObject <- MMPC(target, dataset, max_k = 3, threshold = 0.05, test = "testIndFisher")</pre>
```

```
Cross-Validation for gOMP
```

Cross-Validation for gOMP

## **Description**

The function performs a k-fold cross-validation for identifying the best tolerance values for gOMP.

# Usage

```
cv.gomp(target, dataset, kfolds = 10, folds = NULL, tol = seq(4, 9, by = 1),
task = "C", metric = NULL, metricbbc = NULL, modeler = NULL, test = NULL,
method = "ar2", B = 1)
```

### **Arguments**

target The target or class variable as in SES and MMPC. The difference is that it cannot

accept a single numeric value, an integer indicating the column in the dataset.

dataset The dataset object as in SES and MMPC.

kfolds The number of the folds in the k-fold Cross Validation (integer).

folds The folds of the data to use (a list generated by the function generateCVRuns

TunePareto). If NULL the folds are created internally with the same function.

tol A vector of tolerance values.

task A character ("C", "R" or "S"). It can be "C" for classification (logistic, multi-

nomial or ordinal regression), "R" for regression (robust and non robust linear regression, median regression, (zero inflated) poisson and negative binomial regression, beta regression), "S" for survival regression (Cox, Weibull or exponen-

tial regression).

metric A metric function provided by the user. If NULL the following functions will

be used: auc.mxm, mse.mxm, ci.mxm for classification, regression and survival analysis tasks, respectively. See details for more. If you know what you have put it here to avoid the function choosing somehting else. **Note** that you put

these words as they are, without "".

metricbbc This is the same argument as "metric" with the difference that " " must be placed.

If for example, metric = auc.mxm, here metricbbc = "auc.mxm". The same value must be given here. This argument is to be used with the function bbc which does bootstrap bias correction of the estimated performance (Tsamardinos, Greasidou and Borboudakis, 2018). This argument is valid if the last argu-

ment (B) is more than 1.

modeler A modeling function provided by the user. If NULL the following functions

will be used: glm.mxm, lm.mxm, coxph.mxm for classification, regression and survival analysis tasks, respectively. See details for more. If you know what you have put it here to avoid the function choosing somehting else. **Note** that you

put these words as they are, without "".

test A function object that defines the conditional independence test used in the SES

function (see also SES help page). If NULL, "testIndFisher", "testIndLogistic" and "censIndCR" are used for classification, regression and survival analysis tasks, respectively. If you know what you have put it here to avoid the function choosing somehting else. Not all tests can be included here. "testIndClogit", "testIndMVreg", "testIndIG", "testIndGamma", "testIndZIP" and "testIndTobit"

are anot available at the moment.

method This is only for the "testIndFisher". You can either specify, "ar2" for the adjusted

R-square or "sse" for the sum of squares of errors. The tolerance value in both cases must a number between 0 and 1. That will denote a percentage. If the percentage increase or decrease is less than the nubmer the algorithm stops. An alternative is "BIC" for BIC and the tolerance values are like in all other

regression models.

B How many bootstrap re-samples to draw. This argument is to be used with the function bbc which does bootstrap bias correction of the estimated performance

(Tsamardinos, Greasidou and Borboudakis, 2018). If you have thousands of

samples (observations) then this might not be necessary, as there is no optimistic bias to be corrected. What is the lower limit cannot be told beforehand however. SES and MMPC however were designed for the low sample cases, hence, bootstrap bias correction is perhaps a must thing to do.

### **Details**

For more details see also cy. ses.

### Value

A list including:

cv\_results\_all A list with predictions, performances and selected variables for each fold and each tolerance value. The elements are called "preds", "performances" and "selectedVars".

best\_performance

A numeric value that represents the best average performance.

best\_configuration

A numeric value that represents the best tolerance value.

bbc\_best\_performance

The bootstrap bias corrected best performance if B was more than 1, othwerwise this is NULL.

runtime

The runtime of the cross-validation procedure.

Bear in mind that the values can be extracted with the \$ symbol, i.e. this is an \$3 class output.

# Author(s)

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>.

### References

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### See Also

```
cv.mmpc, gomp.path, bbc
```

### **Examples**

```
## Not run:
set.seed(1234)
# simulate a dataset with continuous data
dataset <- matrix( rnorm(200 * 50), ncol = 50 )
# the target feature is the last column of the dataset as a vector
target <- dataset[, 50]
dataset <- dataset[, -50]
# run a 10 fold CV for the regression task
best_model <- cv.gomp(target, dataset, kfolds = 5, task = "R",
tol = seq(0.001, 0.01,by=0.001), method = "ar2" )
## End(Not run)</pre>
```

Cross-validation for ridge regression

Cross validation for the ridge regression

# **Description**

Cross validation for the ridge regression is performed using the TT estimate of bias (Tibshirani and Tibshirani, 2009). There is an option for the GCV criterion which is automatic.

## Usage

```
ridgereg.cv( target, dataset, K = 10, lambda = seq(0, 2, by = 0.1), auto = FALSE, seed = FALSE, ncores = 1, mat = NULL)
```

# Arguments

target	A numeric vector containing the values of the target variable. If the values are proportions or percentages, i.e. strictly within 0 and 1 they are mapped into R using $log(target/(1 - target))$ .
dataset	A numeric matrix containing the variables. Rows are samples and columns are features.
K	The number of folds. Set to 10 by default.
lambda	A vector with the a grid of values of $\lambda$ to be used.
auto	A boolean variable. If it is TRUE the GCV criterion will provide an automatic answer for the best \$lambda\$. Otherwise k-fold cross validation is performed.
seed	A boolean variable. If it is TRUE the results will always be the same.
ncores	The number of cores to use. If it is more than 1 parallel computing is performed.
mat	If the user has its own matrix with the folds, he can put it here. It must be a matrix with K columns, each column is a fold and it contains the positions of the data, i.e. numbers, not the data. For example the first column is $c(1,10,4,25,30)$ , the second is $c(21,23,2,19,9)$ and so on.

### **Details**

The lm.ridge command in MASS library is a wrapper for this function. If you want a fast choice of  $\lambda$ , then specify auto = TRUE and the  $\lambda$  which minimizes the generalised cross-validation criterion will be returned. Otherise a k-fold cross validation is performed and the estimated performance is bias corrected as suggested by Tibshirani and Tibshirani (2009).

### Value

A list including:

mspe If auto is FALSE the values of the mean prediction error for each value of  $\lambda$ .

lambda If auto is FALSE the  $\lambda$  which minimizes the MSPE.

performance If auto is FALSE the minimum bias corrected MSPE along with the estimate of

bias.

runtime The run time of the algorithm. A numeric vector. The first element is the user

time, the second element is the system time and the third element is the elapsed

time.

### Note

The values can be extracted with the \$ symbol, i.e. this is an \$3 class output.

### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

## References

Hoerl A.E. and R.W. Kennard (1970). Ridge regression: Biased estimation for nonorthogonal problems. Technometrics, 12(1):55-67.

Brown P. J. (1994). Measurement, Regression and Calibration. Oxford Science Publications.

Tibshirani R.J., and Tibshirani R. (2009). A bias correction for the minimum error rate in cross-validation. The Annals of Applied Statistics 3(2): 822-829.

## See Also

```
ridge.reg
```

### **Examples**

```
#simulate a dataset with continuous data
dataset <- matrix(runif(200 * 40, 1, 100), nrow = 200 )
#the target feature is the last column of the dataset as a vector
target <- dataset[, 40]
a1 <- ridgereg.cv(target, dataset, auto = TRUE)
a2 <- ridgereg.cv( target, dataset, K = 10, lambda = seq(0, 1, by = 0.1) )</pre>
```

```
Cross-Validation for SES and MMPC Cross-Validation \ for \ SES \ and \ MMPC
```

## Description

The function performs a k-fold cross-validation for identifying the best values for the SES and MMPC 'max\_k' and 'threshold' hyper-parameters.

### Usage

```
cv.ses(target, dataset, wei = NULL, kfolds = 10, folds = NULL,
alphas = c(0.1, 0.05, 0.01), max_ks = c(3, 2), task = NULL,
metric = NULL, metricbbc = NULL, modeler = NULL, ses_test = NULL,
ncores = 1, B = 1)
cv.mmpc(target, dataset, wei = NULL, kfolds = 10, folds = NULL,
alphas = c(0.1, 0.05, 0.01), max_ks = c(3, 2), task = NULL,
metric = NULL, metricbbc = NULL, modeler = NULL, mmpc_test = NULL,
ncores = 1, B = 1)
cv.waldses(target, dataset, wei = NULL, kfolds = 10, folds = NULL,
alphas = c(0.1, 0.05, 0.01), max_ks = c(3, 2), task = NULL,
metric = NULL, metricbbc = NULL, modeler = NULL, ses_test = NULL,
ncores = 1, B = 1)
cv.waldmmpc(target, dataset, wei = NULL, kfolds = 10, folds = NULL,
alphas = c(0.1, 0.05, 0.01), max_ks = c(3, 2), task = NULL,
metric = NULL, metricbbc = NULL, modeler = NULL, mmpc_test = NULL,
ncores = 1, B = 1)
cv.permses(target, dataset, wei = NULL, kfolds = 10, folds = NULL,
alphas = c(0.1, 0.05, 0.01), max_ks = c(3, 2), task = NULL,
metric = NULL, metricbbc = NULL, modeler = NULL, ses_test = NULL, R = 999,
ncores = 1, B = 1)
cv.permmmpc(target, dataset, wei = NULL, kfolds = 10, folds = NULL,
alphas = c(0.1, 0.05, 0.01), max_ks = c(3, 2), task = NULL,
metric = NULL, metricbbc = NULL, modeler = NULL, mmpc_test = NULL, R = 999,
ncores = 1, B = 1)
```

# Arguments

The target or class variable as in SES and MMPC. The difference is that it cannot accept a single numeric value, an integer indicating the column in the dataset.

dataset The dataset object as in SES and MMPC.

wei A vector of weights to be used for weighted regression. The default value is

NULL.

kfolds The number of the folds in the k-fold Cross Validation (integer).

The folds of the data to use (a list generated by the function generateCVRuns TunePareto). If NULL the folds are created internally with the same function.

A vector of SES or MMPC thresholds hyper parameters used in CV.

max\_ks A vector of SES or MMPC max\_ks parameters used in CV.

A character ("C", "R" or "S"). It can be "C" for classification (logistic, multinomial or ordinal regression), "R" for regression (robust and non robust linear regression, median regression, (zero inflated) poisson and negative binomial regression, beta regression), "S" for survival regression (Cox, Weibull or exponen-

tial regression).

A metric function provided by the user. If NULL the following functions will be used: auc.mxm, mse.mxm, ci.mxm for classification, regression and survival analysis tasks, respectively. See details for more. If you know what you have put it here to avoid the function choosing somehting else. **Note** that you put

these words as they are, without "".

This is the same argument as "metric" with the difference that " " must be placed. If for example, metric = auc.mxm, here metricbbc = "auc.mxm". The same value must be given here. This argument is to be used with the function bbc which does bootstrap bias correction of the estimated performance (Tsamardinos, Greasidou and Borboudakis, 2018). This argument is valid if the last argu-

ment (B) is more than 1.

A modeling function provided by the user. If NULL the following functions will be used: glm.mxm, lm.mxm, coxph.mxm for classification, regression and survival analysis tasks, respectively. See details for more. If you know what you have put it here to avoid the function choosing somehting else. **Note** that you

put these words as they are, without "".

A function object that defines the conditional independence test used in the SES function (see also SES help page). If NULL, "testIndFisher", "testIndLogistic" and "censIndCR" are used for classification, regression and survival analysis tasks, respectively. If you know what you have put it here to avoid the function choosing somehting else. Not all tests can be included here. "testIndClogit", "testIndMVreg", "testIndIG", "testIndGamma", "testIndZIP" and "testIndTobit"

are anot available at the moment.

A function object that defines the conditional independence test used in the MMPC function (see also SES help page). If NULL, "testIndFisher", "testInd-Logistic" and "censIndCR" are used for classification, regression and survival

analysis tasks, respectively.

The number of permutations, set to 999 by default. There is a trick to avoind doing all permutations. As soon as the number of times the permuted test statistic is more than the observed test statistic is more than 50 (if threshold = 0.05 and R = 999), the p-value has exceeded the signifiance level (threshold value) and hence the predictor variable is not significant. There is no need to continue do the extra permutations, as a decision has already been made.

metric

alphas

metricbbc

modeler

ses\_test

mmpc\_test

R

ncores

This argument is valid only if you have a multi-threaded machine.

В

How many bootstrap re-samples to draw. This argument is to be used with the function bbc which does bootstrap bias correction of the estimated performance (Tsamardinos, Greasidou and Borboudakis, 2018). If you have thousands of samples (observations) then this might not be necessary, as there is no optimistic bias to be corrected. What is the lower limit cannot be told beforehand however. SES and MMPC however were designed for the low sample cases, hence, bootstrap bias correction is perhaps a must thing to do.

### **Details**

Input for metric functions: predictions: A vector of predictions to be tested. test\_target: target variable actual values to be compared with the predictions.

The output of a metric function is a single numeric value. **Higher values indicate better performance**. Metric based on error measures should be modified accordingly (e.g., multiplying the error for -1)

The metric functions that are currently supported are:

- auc.mxm: "area under the receiver operator characteristic curve" metric for binary logistic regression.
- acc.mxm: accuracy for binary logistic regression.
- fscore.mxm: F score for binary logistic regression.
- prec.mxm: precision for binary logistic regression.
- euclid\_sens.spec.mxm: Euclidean norm of 1 sensititivy and 1 specificity for binary logistic regression.
- spec.mxm: specificity for logistic regression.
- sens.mxm: sensitivity for logistic regression.
- acc\_multinom.mxm: accuracy for multinomial logistic regression.
- mse.mxm: mean squared error, for robust and non robust linear regression and median (quantile) regression (multiplied by -1).
- pve.mxm: 1 (mean squared error)/( (n 1) \* var(y\_out) ), for non robust linear regression. It is basically the proportion of variance explained in the test set.
- ci.mxm: 1 concordance index as provided in the rcorr.cens function from the suvriva package. This is to be used with the Cox proportional hazards model only.
- ciwr.mxm concordance index as provided in the rcorr.cens function from the survival package. This is to be used with the Weibull regression model only.
- poisdev.mxm: Poisson regression deviance (multiplied by -1).
- nbdev.mxm: Negative binomial regression deviance (multiplied by -1).
- binomdev.mxm: Negative binomial regression deviance (multiplied by -1).
- ord\_mae.mxm: Ordinal regression mean absolute error (multiplied by -1).
- mae.mxm: Mean absolute error (multiplied by -1).
- mci.mxm: Matched concordance index (for conditional logistic regression).

Usage: metric(predictions, test\_target)

Input of modelling functions: train\_target: target variable used in the training procedure. sign\_data: training set. sign\_test: test set.

Modelling functions provide a single vector of predictions obtained by applying the model fit on sign\_data and train\_target on the sign\_test

The modelling functions that are currently supported are:

- glm.mxm: fits a glm for a binomial family (classification task).
- multinom.mxm: fits a multinomial regression model (classification task).
- lm.mxm: fits a linear model (regression task).
- coxph.mxm: fits a cox proportional hazards regression model (survival task).
- weibreg.mxm: fits a Weibull regression model (survival task).
- rq.mxm: fits a quantile (median) regression model (regression task).
- lmrob.mxm: fits a robust linear model (regression task).
- pois.mxm: fits a poisson regression model (regression task).
- nb.mxm: fits a negative binomial regression model (regression task).
- ordinal.mxm: fits an ordinal regression model (regression task).
- beta.mxm: fits a beta regression model (regression task). The predicted values are transformed into R using the logit transformation. This is so that the "mse.mxm" metric function can be used. In addition, this way the performance can be compared with the regression scenario, where the logit is applied and then a regression model is employed.
- clogit: fits a conditionalo logistic regression model.

Usage: modeler(train\_target, sign\_data, sign\_test)

The procedure will be more automated in the future and more functions will be added. The multithreaded functions have been tested and no error has been detected. However, if you spot any suspicious results please let us know.

### Value

A list including:

cv\_results\_all A list with predictions, performances and signatures for each fold and each SES or MMPC configuration (e.g cv\_results\_all[[3]]\$performances[1] indicates the performance of the 1st fold with the 3d configuration of SES or MMPC). In the case of the multi-threaded functions (cvses.par and cvmmpc.par) this is a list with a matrix. The rows correspond to the folds and the columns to the configurations (pairs of threshold and max\_k).

best\_performance

A numeric value that represents the best average performance.

best\_configuration

A list that corresponds to the best configuration of SES or MMPC including id, threshold (named 'a') and max\_k.

bbc\_best\_performance

The bootstrap bias corrected best performance if B was more than 1, othwerwise this is NULL.

runtime

The runtime of the cross-validation procedure.

Bear in mind that the values can be extracted with the \$ symbol, i.e. this is an \$3 class output.

#### Author(s)

R implementation and documentation: Giorgos Athineou <athineou@csd.uoc.gr> and Vincenzo Lagani <vlagani@csd.uoc.gr>

#### References

Ioannis Tsamardinos, Elissavet Greasidou and Giorgos Borboudakis (2018). Bootstrapping the out-of-sample predictions for efficient and accurate cross-validation. Machine Learning (To appear). https://link.springer.com/article/10.1007/s10994-018-5714-4

Harrell F. E., Lee K. L. and Mark D. B. (1996). Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. Statistics in medicine, 15(4), 361-387.

Hanley J. A. and McNeil B. J. (1982). The meaning and use of the area under a receiver operating characteristic (ROC) curve. Radiology, 143(1), 29-36.

Brentnall A. R., Cuzick J., Field J. and Duffy S. W. (2015). A concordance index for matched case-control studies with applications in cancer risk. Statistics in medicine, 34(3), 396-405.

Pedregosa F., Bach F. & Gramfort A. (2017). On the consistency of ordinal regression methods. The Journal of Machine Learning Research, 18(1), 1769-1803.

### See Also

```
SES, CondIndTests, cv.gomp, bbc, testIndFisher, testIndLogistic, gSquare, censIndCR
```

# Examples

```
# simulate a dataset with continuous data
dataset <- matrix( rnorm(100 * 50), ncol = 50 )
# the target feature is the last column of the dataset as a vector
target <- dataset[, 50]
dataset <- dataset[, -50]

# get 50 percent of the dataset as a train set
train_set <- dataset[1:100, ]
train_target <- target[1:100]

# run a 10 fold CV for the regression task
best_model <- cv.ses(target = train_target, dataset = train_set, kfolds = 5, task = "R")
# get the results
best_model$best_configuration</pre>
```

```
best_model$best_performance
```

```
# summary elements of the process. Press tab after each $ to view all the elements and
# choose the one you are intresting in.
# best_model$cv_results_all[[...]]$...
#i.e.
# mse value for the 1st configuration of SES of the 5 fold
abs( best_model$cv_results_all[[ 1 ]]$performances[5] )

best_a <- best_model$best_configuration$a
best_max_k <- best_model$best_configuration$max_k</pre>
```

Cross-validation of the FBED with LMM

Cross-validation of the FBED with LMM

### **Description**

Cross-validation of the FBED with LMM.

#### Usage

### **Arguments**

target	The class variable. This must be a numerical vector with continuous data.
dataset	The dataset; provide a numerical a matrix (columns = variables, rows = observations).
id	This is a numerical vector of the same size as target denoting the groups or the subjects.
prior	If you have prior knowledge of some variables that must be in the variable selection phase add them here. This an be a vector (if you have one variable) or a matrix (if you more variables). This does not work during the backward phase at the moment.
kfolds	The number of the folds in the k-fold Cross Validation (integer).
folds	The folds of the data to use (a list generated by the function generateCVRuns TunePareto). If NULL the folds are created internally with the same function.
alphas	A vector of significance levels to be tested.
ks	A vector of K values to be tested.

### **Details**

The function performs cross-validation for the FBED agortihm with clustered data using the linear mixed model. The k-folds cross-validation is on clusters. Instead of leaving observations, clusters are left aside each time.

### Value

A list including:

list(vars = vars, cv = cv, perf = perf, best = best, runtime = runtime)

vars An array with the number of selected variables for each combination of signifi-

cance level and value of K.

cv An array with the number of selected variables for each combination of signifi-

cance level and value of K.

perf A matrix with the average performance each combination of significance level

and value of K.

best The best significance level and value of K.

runtime The runtime required.

# Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

#### References

Fang Y. (2011). Asymptotic equivalence between cross-validations and Akaike information criteria in mixed-effects models. Journal of data science, 9(1), 15-21.

Eugene Demidenko (2013). Mixed Models: Theory and Applications with R, 2nd Edition. New Jersey: Wiley & Sons.

Borboudakis G. and Tsamardinos I. (2019). Forward-backward selection with early dropping. Journal of Machine Learning Research, 20(8): 1-39.

# See Also

```
fbed.glmm.reg, fbed.gee.reg, MMPC.glmm
```

# **Examples**

```
## Not run:
require(lme4)
data(sleepstudy)
reaction <- sleepstudy$Reaction
subject <- sleepstudy$Subject
x1 <- sleepstudy$Days
x <- matrix(rnorm(180 * 200),ncol = 200) ## unrelated predictor variables
x <- cbind(x1, x)
m <- cv.fbed.lmm.reg(reaction, x, subject)
## End(Not run)</pre>
```

Data simulation from a DAG

Data simulation from a DAG.

### **Description**

Data simulation from a DAG.

# Usage

```
rdag(n, p, s, a = 0, m, A = NULL, seed = FALSE)

rdag2(n, A = NULL, p, nei, low = 0.1, up = 1)

rmdag(n, A = NULL, p, nei, low = 0.1, up = 1)
```

### **Arguments**

n	A number indicating the sample size.
р	A number indicating the number of nodes (or vectices, or variables).
nei	The average number of neighbours.
S	A number in $(0,1)$ . This defines somehow the sparseness of the model. It is the probability that a node has an edge.
a	A number in $(0,1)$ . The defines the percentage of outliers to be included in the simulated data. If $a=0$ , no outliers are generated.
m	A vector equal to the number of nodes. This is the mean vector of the normal distribution from which the data are to be generated. This is used only when $a>0$ so as to define the mena vector of the multivariate normal from which the outliers will be generated.
A	If you already have an an adjacency matrix in mind, plug it in here, otherwise, leave it NULL.
seed	If seed is TRUE, the simulated data will always be the same.
low	Every child will be a function of some parents. The beta coefficients of the parents will be drawn uniformly from two numbers, low and up. See details for more information on this.
up	Every child will be a function of some parents. The beta coefficients of the parents will be drawn uniformly from two numbers, low and up. See details for more information on this.

# **Details**

In the case where no adjacency matrix is given, an  $p \times p$  matrix with zeros everywhere is created. Every element below the diagonal is is replaced by random values from a Bernoulli distribution with probability of success equal to s. This is the matrix B. Every value of 1 is replaced by a uniform value in 0.1, 1. This final matrix is called A. The data are generated from a multivariate normal distribution with a zero mean vector and covariance matrix equal to  $(\mathbf{I}_p - A)^{-1} (\mathbf{I}_p - A)$ , where  $\mathbf{I}_p$ 

is the  $p \times p$  identiy matrix. If a is greater than zero, the outliers are generated from a multivariate normal with the same covariance matrix and mean vector the one specified by the user, the argument "m". The flexibility of the outliers is that you can specify outliers in some variables only or in all of them. For example, m = c(0,0,5) introduces outliers in the third variable only, whereas m = c(5,5,5) introduces outliers in all variables. The user is free to decide on the type of outliers to include in the data.

For the "rdag2", this is a different way of simulating data from DAGs. The first variable is normally generated. Every other variable can be a function of some previous ones. Suppose now that the i-th variable is a child of 4 previous variables. We need for coefficients  $b_j$  to multiply the 4 variables and then generate the i-th variable from a normal with mean  $\sum_{j=1} b_j X_j$  and variance 1. The  $b_j$  will be either positive or negative values with equal probability. Their absolute values ranges between "low" and "up". The code is accessible and you can see in detail what is going on. In addition, every generated data, are standardised to avoid numerical overflow.

The "rmdag" generates data from a BN with continous, ordinal and binary data in proportions 50%, 25% and 25% resepctively on average. This was used in the experiments run by Tsagris et al. (2017). If you want to generate data and then use them in the "pcalg" package with the function "ci.fast2" or "ci.mm2" you should transform the resulting data into a matrix. The factor variables must become numeric starting from 0. See the examples for more on this.

#### Value

A list including:

nout	The number of outliers.
G	The adcacency matrix used. For the "rdag" if $G[i, j] = 2$ , then $G[j, i] = 3$ and this means that there is an arrow from j to i. For the "rdag2" and "rmdag" the entries are either $G[i, j] = G[j, i] = 0$ (no edge) or $G[i, j] = 1$ and $G[j, i] = 0$ (indicating i -> j).
A	The matrix with the with the uniform values in the interval $0.1,1.$ This is returned only by "rdag".
Х	The simulated data.

# Author(s)

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

### References

Tsagris M. (2019). Bayesian network learning with the PC algorithm: an improved and correct variation. Applied Artificial Intelligence, 33(2): 101-123.

Tsagris M., Borboudakis G., Lagani V. and Tsamardinos I. (2018). Constraint-based Causal Discovery with Mixed Data. International Journal of Data Science and Analytics.

Spirtes P., Glymour C. and Scheines R. (2001). Causation, Prediction, and Search. The MIT Press, Cambridge, MA, USA, 3nd edition.

Colombo, Diego, and Marloes H. Maathuis (2014). Order-independent constraint-based causal structure learning. The Journal of Machine Learning Research 15(1): 3741–3782.

### See Also

```
pc.skel, pc.or, ci.mm, mmhc.skel
```

### **Examples**

```
y <- rdag(100, 20, 0.2)
x <- y$x
tru <- y$G

mod <- pc.con(x)
b <- pc.or(mod)
plotnetwork(tru)
dev.new()
plotnetwork(b$G)</pre>
```

Drop all possible single terms from a model using the partial correlation

Drop all possible single terms from a model using the partial correlation

# Description

Drop all possible single terms from a model using the partial correlation.

## Usage

```
cor.drop1(y, x, logged = FALSE)
```

# **Arguments**

Х

y A numerical vector with the response variable.

A numerical matrix or a data frame with the predictor variables. If is is a matrix it is internally transformed into a data frame form, hence the user is advised to supply a data frame in order to save some time. If the number of columns (variables) is higher than the number of rows (observations) the function will

simply not work.

logged If you want the p-values be returned leave this FALSE. If it is TRUE their loga-

rithm is returned.

#### **Details**

This uses R's command drop1 and modifies it so as to calculate the p-value using Fisher's conditional independence test.

### Value

A matrix with two columns, the test statistic values and its associated p-value.

# Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

### See Also

```
glm.bsreg, fbed.reg, mmpcbackphase
```

# **Examples**

```
y <- rnorm(200)
x <- matrix( rnorm(200 * 10), ncol = 10)
cor.drop1(y, x)</pre>
```

eBIC for many regression models

eBIC for many regression models

# Description

eBIC for many regression models.

# Usage

```
ebic.regs(target, dataset, xIndex, csIndex, gam = NULL, test = NULL, wei = NULL,
ncores = 1)
```

# **Arguments**

target	The target (dependent) variable. It must be a numerical vector, a factor or a Surv object.
dataset	The indendent variable(s). This can be a matrix or a dataframe with continuous only variables, a data frame with mixed or only categorical variables.
xIndex	The indices of the variables whose association with the target you want to test.
csIndex	The index or indices of the variable(s) to condition on. If this is 0, the the function univregs will be called.
gam	In case the method is chosen to be "eBIC" one can also specify the $gamma$ parameter. The default value is "NULL", so that the value is automatically calculated.
test	One of the following: testIndBeta, testIndReg, testIndLogistic, testIndOrdinal, testIndPois, testIndZIP, testIndNB, testIndClogit, testIndBinom, testIndIGreg, censIndCR, censIndWR, censIndER, censIndLLR testIndMultinom, testIndTobit, testIndSPML, testIndGamma or testIndNormLog.

Note that in all cases you must give the name of the test, without " ".

wei A vector of weights to be used for weighted regression. The default value is

NULL. An example where weights are used is surveys when stratified sampling

has occured.

ncores How many cores to use. This plays an important role if you have tens of thou-

sands of variables or really large sample sizes and tens of thousands of variables and a regression based test which requires numerical optimisation. In other cases it will not make a difference in the overall time (in fact it can be slower). The parallel computation is used in the first step of the algorithm, where univariate associations are examined, those take place in parallel. We have seen a reduction in time of 50% with 4 cores in comparison to 1 core. Note also, that the amount

of reduction is not linear in the number of cores.

### **Details**

This function is more as a help function for MMPC, but it can also be called directly by the user. In some, one should specify the regression model to use and the function will perform all simple regressions, i.e. all regression models between the target and each of the variables in the dataset. The function does not check for zero variance columns, only the "univregs" and related functions do.

#### Value

A list including:

stat The value of the test statistic.

pvalue The logarithm of the p-value of the test.

# Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

#### References

Chen J. and Chen Z. (2008). Extended Bayesian information criteria for model selection with large model spaces. Biometrika, 95(3): 759-771.

Eugene Demidenko (2013). Mixed Models: Theory and Applications with R, 2nd Edition. New Jersey: Wiley & Sons.

McCullagh, Peter, and John A. Nelder. Generalized linear models. CRC press, USA, 2nd edition, 1989.

#### See Also

```
univregs, SES, MMPC, CondIndTests, reg.fit, ridge.reg
```

### **Examples**

```
y <- rpois(100, 15)
x <- matrix( rnorm(100 * 10), ncol = 10)
a1 <- univregs(y, x, test = testIndPois)
a2 <- perm.univregs(y, x, test = permPois)
a3 <- wald.univregs(y, x, test = waldPois)
a4 <- cond.regs(y, as.data.frame(x), xIndex = 1:4, csIndex = 5, test = testIndPois)</pre>
```

Effective sample size for  $G^2$  test in BNs with case control data Effective sample size for  $G^2$  test in BNs with case control data

### **Description**

Effective sample size for G^2 test in BNs with case control data.

### Usage

```
Ness(propNt, N, K = 10000)
```

## **Arguments**

propNt	A numerical vector with the proportions (distribution) of the (single) selection variable.
N	The sample size of the data.
K	The number of repetitions to be used for estimating the effective sample size.

#### **Details**

When dealing with case control data, spurious correlations or relationships arise. To deal with this one way is to adjust the sample size used in the G^2 test statistic. This function does exactly this, estimates the effective sample size as per the Borboudakis and Tsamardinos (2012) suggestion. The idea is that after learning the skeleton with the usual G^2 test, one should go to the edges and perform a conditional G^2

#### Value

The estimated effective sample size.

### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

## References

Borboudakis G. and Tsamardinos I. (2015). Bayesian Network Learning with Discrete Case-Control Data. 31st Conference on Uncertainty in Artificial Intelligence (UAI), 151-160.

### See Also

```
SES, MMPC, testIndLogistic
```

### **Examples**

```
Ness(c(0.3, 0.7), N = 1000, K = 10000)
```

Estimation of the percentage of Null p-values

Estimation of the percentage of Null p-values

### **Description**

Estimation of the percentage of Null p-values.

## Usage

```
pi0est(p, lambda = seq(0.05, 0.95, by = 0.01), dof = 3)
```

# **Arguments**

p A vector of p-values.

lambda A vector of values of the tuning parameter lambda.

dof Number of degrees of freedom to use when estimating pi\_0 with smoothing

splines.

#### **Details**

The estimated proporiton of null p-values is estimated the algorithm by Storey and Tibshirani (2003).

#### Value

The estimated proportion of non significant (null) p-values. In the paper Storey and Tibshirani mention that the estimate of pi0 is with lambda=1, but in their R code they use the highest value of lambda and thus we do the same here.

# Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

## References

Storey J.D. and Tibshirani R. (2003). Statistical significance for genome-wide experiments. Proceedings of the National Academy of Sciences, 100: 9440-9445.

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## See Also

```
conf.edge.lower, bn.skel.utils, mmhc.skel, pc.skel, corfs.network, local.mmhc.skel
```

# **Examples**

```
## simulate a dataset with continuous data
y <- rdag2(1000, p = 20, nei = 3)
ind <- sample(1:20, 20)
x <- y$x[, ind]
mod <- pc.skel( x, method = "comb.fast", alpha = 0.01 )
pval <- exp(mod$pvalue)
pval <- lower.tri(pval)
pi0est(pval)</pre>
```

Fast MMPC

A fast version of MMPC

# Description

A fast version of MMPC

# Usage

```
mmpc2(target, dataset, prior = NULL, max_k = 3, threshold = 0.05,
test = "testIndLogistic", ini = NULL, wei = NULL, ncores = 1, backward = FALSE)
```

### **Arguments**

target	The class variable. Provide either a string, an integer, a numeric value, a vector, a factor, an ordered factor or a Surv object. See also Details.
dataset	The data-set; provide either a data frame or a matrix (columns = variables, rows = samples).
prior	If you have prior knowledge of some variables that must be in the variable selection phase add them here. This an be a vector (if you have one variable) or a matrix (if you more variables). This does not work during the backward phase at the moment.
max_k	The maximum conditioning set to use in the conditional indepedence test (see Details). Integer, default value is 3.
threshold	Threshold (suitable values in $(0, 1)$ ) for assessing p-values significance. Default value is 0.05.
test	One of the following: "testIndBeta", "testIndReg", "testIndRQ", "testIndLogistic", "testIndMultinom", "testIndOrdinal", "testIndPois", "testIndQPois", "testIndZIP", "testIndNB", "testIndClogit", "testIndBinom", "testIndQBinom", "testIndIGreg", "censIndCR", "censIndWR", "censIndER", "testIndMMReg", "testIndMVreg", "testIndMultinom", "testIndOrdinal", "testIndTobit", "testIndGamma", "testIndNormLog" or "testIndSPML".

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ini This is a supposed to be a list. To avoid calculating the univariate associations

> (first step of SES, MMPC and of FBED) again, you can extract them from the first run of omne of these algorithms and plug them here. This can speed up the second run (and subequent runs of course) by 50%. See the details and the

argument "univ" in the output values.

wei A vector of weights to be used for weighted regression. The default value is

NULL. An example where weights are used is surveys when stratified sampling

has occured.

How many cores to use. This plays an important role if you have tens of thouncores

> sands of variables or really large sample sizes and tens of thousands of variables and a regression based test which requires numerical optimisation. In other cases it will not make a difference in the overall time (in fact it can be slower). The parallel computation is used in the first step of the algorithm, where univariate associations are examined, those take place in parallel. We have seen a reduction in time of 50% with 4 cores in comparison to 1 core. Note also, that the amount

of reduction is not linear in the number of cores.

backward If TRUE, the backward (or symmetry correction) phase will be implemented.

This removes any falsely included variables in the parents and children set of

the target variable. It calls the link{mmpcbackphase} for this purpose.

#### **Details**

MMPC tests each feature for inclusion (selection). For each featurer it performs a conditional independence tets. Each test requires fitting two regression models, one without the feature and one with the feature included. In this version, we have changed the order of the tests. We find all possible subsets of the already selected features and for each of them we test each feature. This way, only half of the regression models the usual MMPC fits, are fitted. Also, less tests will be performed. It is the same algorithm, with a change in the sequence.

We have seen a 50% in the computational time, but the drawback is that if you want to run MMPC with different value of "max\$\_\$k" and "alpha", this is not possible from here. This function is for oa signle pair of "max\$\_\$k" and "alpha" values. It saves no test statistics, only p-values, no hashing and hence is memory efficient, but contains less information than MMPC.

#### Value

The output of the algorithm is an S3 object including:

selectedVars The selected variables, i.e., the signature of the target variable.

pvalues For each feature included in the dataset, this vector reports the strength of its

> association with the target in the context of all other variable. Particularly, this vector reports the max p-values found when the association of each variable with the target is tested against different conditional sets. Lower values indicate

higher association. Note that these are the logarithm of the p-values

univ A vector with the **logged p-values** of the univariate associations. This vector is

> very important for subsequent runs of MMPC with different hyper-parameters. After running SES with some hyper-parameters you might want to run MM-PCagain with different hyper-parameters. To avoid calculating the univariate

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associations (first step) again, you can take this list from the first run of SES and plug it in the argument "ini" in the next run(s) of MMPC. This can speed up the second run (and subequent runs of course) by 50%. See the argument "univ" in the output values.

kapa\_pval A list with the same number of elements as the max\$\_k\$. Every element in

the list is a matrix. The first row is the **logged p-values**, the second row is the variable whose conditional association with the target variable was tests and the

other rows are the conditioning variables.

max\_k The max\_k option used in the current run.
threshold The threshold option used in the current run.

n. tests The number of tests performed by MMPC will be returned.

runtime The run time of the algorithm. A numeric vector. The first element is the user

time, the second element is the system time and the third element is the elapsed

time.

test The character name of the statistic test used.

#### Author(s)

Ioannis Tsamardinos, Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>.

#### References

Feature Selection with the R Package MXM: Discovering Statistically Equivalent Feature Subsets, Lagani, V. and Athineou, G. and Farcomeni, A. and Tsagris, M. and Tsamardinos, I. (2017). Journal of Statistical Software, 80(7).

Tsamardinos, I., Aliferis, C. F., & Statnikov, A. (2003). Time and sample efficient discovery of Markov blankets and direct causal relations. In Proceedings of the ninth ACM SIGKDD international conference on Knowledge discovery and data mining (pp. 673-678). ACM.

Brown, L. E., Tsamardinos, I., & Aliferis, C. F. (2004). A novel algorithm for scalable and accurate Bayesian network learning. Medinfo, 711-715.

Tsamardinos, Brown and Aliferis (2006). The max-min hill-climbing Bayesian network structure learning algorithm. Machine learning, 65(1), 31-78.

#### See Also

```
MMPC, certificate.of.exclusion2
```

### **Examples**

```
set.seed(123)
#simulate a dataset with continuous data
dataset <- matrix(runif(100 * 40, 1, 100), ncol = 40)
#define a simulated class variable
target <- 3 * dataset[, 10] + 2 * dataset[, 15] + 3 * dataset[, 20] + rnorm(100, 0, 5)</pre>
```

```
m <- median(target)
target[target < m] <- 0
target[abs(target) > 0 ] <- 1

m1 <- mmpc2(target, dataset, max_k = 3, threshold = 0.05, test="testIndLogistic")
m1$selectedVars ## S3 class, $, not @
m1$runtime

m2 <- MMPC(target, dataset, max_k = 3, threshold = 0.05, test="testIndLogistic")
m2@selectedVars ## S3 class, @, not $
m2@runtime</pre>
```

Fast MMPC for longitudinal and clustered data

mmpc.glmm2/mmpc.gee2: Fast Feature selection algorithm for identifying minimal feature subsets with correlated data

### **Description**

SES.glmm algorithm follows a forward-backward filter approach for feature selection in order to provide minimal, highly-predictive, statistically-equivalent, multiple feature subsets of a high dimensional dataset. See also Details. MMPC.glmm algorithm follows the same approach without generating multiple feature subsets. They are both adapted to longitudinal target variables.

### Usage

```
mmpc.glmm2(target, reps = NULL, group, dataset, prior = NULL, max_k = 3,
threshold = 0.05, test = NULL, ini = NULL, wei = NULL, slopes = FALSE, ncores = 1)
mmpc.gee2(target, reps = NULL, group, dataset, prior = NULL, max_k = 3,
threshold = 0.05, test = NULL, ini = NULL, wei = NULL, correl = "exchangeable",
se = "jack", ncores = 1)
```

# **Arguments**

The class variable. Provide a vector with continuous (normal), binary (binomial) or discrete (Poisson) data. For the GEE the data must be sorted so that

observations on a cluster are contiguous rows for all entities in the formula.

reps A numeric vector containing the time points of the subjects. It's length is equal

to the length of the target variable. If you have clustered data, leave this NULL. For the GEE the data must be sorted so that observations on a cluster are con-

tiguous rows for all entities in the formula.

group A numeric vector containing the subjects or groups. It must be of the same

length as target. For the GEE the data must be sorted so that observations on a

cluster are contiguous rows for all entities in the formula.

dataset The dataset; provide either a data frame or a matrix (columns = variables, rows

= samples). Currently, only continuous datasets are supported. For the GEE the data must be sorted so that observations on a cluster are contiguous rows for all

entities in the formula.

prior If you have prior knowledge of some variables that must be in the variable se-

lection phase add them here. This an be a vector (if you have one variable) or a

matrix (if you more variables).

max\_k The maximum conditioning set to use in the conditional indepedence test (see

Details). Integer, default value is 3.

threshold Threshold (suitable values in (0, 1)) for assessing p-values significance. Default

value is 0.05.

test The conditional independence test to use. Default value is NULL. Currently,

the only available conditional independence test are the testIndGLMMLogistic, testIndGLMMPois, testIndGLMMGamma, testIndGLMMNormLog and testIndGLMMReg which fit linear mixed models. For the GEE the options are testIndGEELogistic,

testIndGEEPois, testIndGEEGamma, testIndGEENormLog and testIndGEENormLog.

This is a supposed to be a list. After running SES or MMPC with some hyper-parameters you might want to run SES again with different hyper-parameters. To avoid calculating the univariate associations (first step of SES and of MPPC) again, you can extract them from the first run of SES and plug them here. This can speed up the second run (and subequent runs of course) by 50%. See the

details and the argument "univ" in the output values.

wei A vector of weights to be used for weighted regression. The default value is

NULL.

ini

ncores

slopes Should random slopes for the ime effect be fitted as well? Default value is

FALSE.

correl The correlation structure of the GEE. For the Gaussian, Logistic, Poisson and

Gamma regression this can be either "exchangeable" (compound symmetry, suitable for clustered data) or "ar1" (AR(1) model, suitable for longitudinal data). All observations must be ordered according to time within each subject.

See the vignette of **geepack** to understand how.

The method for estimating standard errors. This is very important and crucial. The available options for Gaussian, Logistic, Poisson and Gamma regression

are: a) 'san.se': the usual robust estimate. b) 'jack': approximate jackknife variance estimate. c) 'j1s': if 1-step jackknife variance estimate and d) 'fij': fully iterated jackknife variance estimate. If you have many clusters (sets of repeated measurements) "san.se" is fine as it is asympotically correct, plus jacknife estimates will take longer. If you have a few clusters, then maybe it's better to use

jacknife estimates.

The jackknife variance estimator was suggested by Paik (1988), which is quite suitable for cases when the number of subjects is small (K < 30), as in many biological studies. The simulation studies conducted by Ziegler et al. (2000) and Yan and Fine (2004) showed that the approximate jackknife estimates are in

many cases in good agreement with the fully iterated ones.

How many cores to use. This plays an important role if you have tens of thousands of variables or really large sample sizes and tens of thousands of variables

and a regression based test which requires numerical optimisation. In other cases it will not make a difference in the overall time (in fact it can be slower). The parallel computation is used in the first step of the algorithm, where univariate associations are examined, those take place in parallel. We have seen a reduction in time of 50% with 4 cores in comparison to 1 core. Note also, that the amount of reduction is definetely not linear in the number of cores.

#### **Details**

These are faster versions of MMPC using GLMM or GEE methodologies. See also mmpc2 for more details on the algorithm.

If you want to use the GEE methodology, make sure you load the library geepack first.

#### Value

The output of the algorithm is an object of the class 'SES.glmm.output' for SES.glmm or 'MMPC.glmm.output' for MMPC.glmm including:

selectedVars The selected variables, i.e., the signature of the target variable.

pvalues For each feature included in the dataset, this vector reports the strength of its

association with the target in the context of all other variables. Particularly, this vector reports the max p-values found when the association of each variable with the target is tested against different conditional sets. Lower values indicate

higher association. Note that these are the logarithm of the p-values.

univ A vector with the **logged p-values** of the univariate associations. This vector is

very important for subsequent runs of MMPC with different hyper-parameters. After running SES with some hyper-parameters you might want to run MM-PCagain with different hyper-parameters. To avoid calculating the univariate associations (first step) again, you can take this list from the first run of SES and plug it in the argument "ini" in the next run(s) of MMPC. This can speed up the second run (and subequent runs of course) by 50%. See the argument "univ" in

the output values.

kapa\_pval A list with the same number of elements as the max\$\_k\$. Every element in

the list is a matrix. The first row is the logged p-values, the second row is the variable whose conditional association with the target variable was tests and the

other rows are the conditioning variables.

max\_k The max\_k option used in the current run.

threshold The threshold option used in the current run.

n.tests If you have set hash = TRUE, then the number of tests performed by SES or

MMPC will be returned. If you have not set this to TRUE, the number of uni-

variate associations will be returned. So be careful with this number.

runtime The run time of the algorithm. A numeric vector. The first element is the user

time, the second element is the system time and the third element is the elapsed

time.

test The character name of the statistic test used.

slope Whether random slopes for the time effects were used or not, TRUE or FALSE.

#### Author(s)

Ioannis Tsamardinos, Vincenzo Lagani

R implementation and documentation: Giorgos Athineou <athineou@csd.uoc.gr> Vincenzo Lagani <vlagani@csd.uoc.gr>

#### References

Tsagris, M., Lagani, V., & Tsamardinos, I. (2018). Feature selection for high-dimensional glmm data. BMC bioinformatics, 19(1), 17.

- I. Tsamardinos, M. Tsagris and V. Lagani (2015). Feature selection for longitudinal data. Proceedings of the 10th conference of the Hellenic Society for Computational Biology & Bioinformatics (HSCBB15).
- I. Tsamardinos, V. Lagani and D. Pappas (2012). Discovering multiple, equivalent biomarker signatures. In proceedings of the 7th conference of the Hellenic Society for Computational Biology & Bioinformatics HSCBB12.

Tsamardinos, Brown and Aliferis (2006). The max-min hill-climbing Bayesian network structure learning algorithm. Machine learning, 65(1), 31-78.

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Liang K.Y. and Zeger S.L. (1986). Longitudinal data analysis using generalized linear models. Biometrika, 73(1): 13-22.

Prentice R.L. and Zhao L.P. (1991). Estimating equations for parameters in means and covariances of multivariate discrete and continuous responses. Biometrics, 47(3): 825-839.

Heagerty P.J. and Zeger S.L. (1996) Marginal regression models for clustered ordinal measurements. Journal of the American Statistical Association, 91(435): 1024-1036.

Paik M.C. (1988). Repeated measurement analysis for nonnormal data in small samples. Communications in Statistics-Simulation and Computation, 17(4): 1155-1171.

Ziegler A., Kastner C., Brunner D. and Blettner M. (2000). Familial associations of lipid profiles: A generalised estimating equations approach. Statistics in medicine, 19(24): 3345-3357

Yan J. and Fine J. (2004). Estimating equations for association structures. Statistics in medicine, 23(6): 859-874.

#### See Also

CondIndTests, testIndGLMMReg

## **Examples**

```
## Not run:
require(lme4)
data(sleepstudy)
reaction <- sleepstudy$Reaction
days <- sleepstudy$Days</pre>
```

```
subject <- sleepstudy$Subject
x <- matrix(rnorm(180 * 100), ncol = 100) ## unrelated predictor variables
m1 <- mmpc.glmm2(target = reaction, reps = days, group = subject, dataset = x)
m2 <- MMPC.glmm(target = reaction, reps = days, group = subject, dataset = x)
## End(Not run)</pre>
```

Feature selection using SES and MMPC for classification with longitudinal data Feature selection using SES and MMPC for classification with longitudinal data

# Description

SES algorithm follows a forward-backward filter approach for feature selection in order to provide minimal, highly-predictive, statistically-equivalent, multiple feature subsets of a high dimensional dataset. See also Details. MMPC algorithm follows the same approach without generating multiple feature subsets.

## Usage

```
SES.timeclass(target, reps, id, dataset, \max_k = 3, threshold = 0.05, ini = NULL, wei = NULL, hash = FALSE, hashObject = NULL, ncores = 1)

MMPC.timeclass(target, reps, id, dataset, \max_k = 3, threshold = 0.05, ini = NULL, wei = NULL, hash = FALSE, hashObject = NULL, ncores = 1)
```

# Arguments

target	The class variable. Provide a vector or a factor with discrete numbers indicating the class. Its length is equal to the number of rows of the dataset.
reps	A numeric vector containing the time points of the subjects. Its length is equal to the number of rows of the dataset.
id	A numeric vector containing the subjects or groups. Its length is equal to the number of rows of the dataset.
dataset	The dataset; provide a matrix. Currently, only continuous datasets are supported. The dataset contains longitudinal data, where each column is a variable. The repeated measurements are the samples.
max_k	The maximum conditioning set to use in the conditional indepedence test (see Details). Integer, default value is 3.
threshold	Threshold (suitable values in $(0, 1)$ ) for assessing p-values significance. Default value is $0.05$ .
ini	This is a supposed to be a list. After running SES or MMPC with some hyper-parameters you might want to run SES again with different hyper-parameters. To avoid calculating the univariate associations (first step of SES and of MPPC) again, you can extract them from the first run of SES and plug them here. This

can speed up the second run (and subequent runs of course) by 50%. See the

details and the argument "univ" in the output values.

wei A vector of weights to be used for weighted regression. The default value is

NULL.

hash A boolean variable which indicates whether (TRUE) or not (FALSE) to store the

statistics calculated during SES execution in a hash-type object. Default value

is FALSE. If TRUE a hashObject is produced.

hashObject A List with the hash objects generated in a previous run of SES.glmm. Each

time SES runs with "hash=TRUE" it produces a list of hashObjects that can be

re-used in order to speed up next runs of SES.

Important: the generated hashObjects should be used only when the same dataset

is re-analyzed, possibly with different values of max\_k and threshold.

ncores How many cores to use. This plays an important role if you have tens of thousands of variables or really large sample sizes and tens of thousands of variables

sands of variables or really large sample sizes and tens of thousands of variables and a regression based test which requires numerical optimisation. In other cases it will not make a difference in the overall time (in fact it can be slower). The parallel computation is used in the first step of the algorithm, where univariate associations are examined, those take place in parallel. We have seen a reduction in time of 50% with 4 cores in comparison to 1 core. Note also, that the amount

of reduction is definetely not linear in the number of cores.

#### **Details**

This is SES and MMPC used in the static-longitudinal scenario of Tsagris, Lagani and Tsamardinos (2018). The idea is that you have many features of longitudinal data for many subjects. For each subject you have calculated the coefficients of a simple linear regression over time and this is repeated for each feature. In the end, assuming p features, you have p constants and p slopes for each subject, each constant and slope refers to a feature for a subject. Hence, each new feature consists of two vectors, the constants and the slopes and the feature selection takes place there.

# Value

The output of the algorithm is an object of the class 'SESoutput' for SES or 'MMPCoutput' for MMPC including:

selectedVars The selected variables, i.e., the signature of the target variable. selectedVarsOrder

The order of the selected variables according to increasing pvalues.

queues A list containing a list (queue) of equivalent features for each variable included

in selected Vars. An equivalent signature can be built by selecting a single feature

from each queue. Featured only in SES.

signatures A matrix reporting all equivalent signatures (one signature for each row). Fea-

tured only in SES.

hashObject The hashObject caching the statistic calculated in the current run.

pvalues For each feature included in the dataset, this vector reports the strength of its

association with the target in the context of all other variables. Particularly,

this vector reports the max p-values found when the association of each variable with the target is tested against different conditional sets. Lower values indicate higher association. Note that these are the logged p-values, natural logarithm of the pvalues, and not the p-values.

stats

The statistics corresponding to "pvalues" (higher values indicates higher association).

univ

This is a list with the univariate associations. The test statistics and their corresponding **logged p-values**, along with their flag (1 if the test was perfromed and 0 otherwise). This list is very important for subsequent runs of SES with different hyper-parameters. After running SES with some hyper-parameters you might want to run SES again with different hyper-parameters. To avoid calculating the univariate associations (first step of SES or MMPC) again, you can take this list from the first run of SES and plug it in the argument "ini" in the next run(s) of SES or MMPC. This can speed up the second run (and subequent runs of course) by 50%. See the argument "univ" in the output values.

max\_k The max\_k option used in the current run.
threshold The threshold option used in the current run.

n.tests If you have set hash = TRUE, then the number of tests performed by SES or

MMPC will be returned. If you have not set this to TRUE, the number of uni-

variate associations will be returned. So be careful with this number.

runtime The run time of the algorithm. A numeric vector. The first element is the user

time, the second element is the system time and the third element is the elapsed

time.

test The character name of the statistic test used.

Generic Functions implemented for SESoutput Object:

plot(object=SESoutput, mode="all")

Plots the generated pvalues (using barplot) of the current SESoutput object in

comparison to the threshold.

Argument mode can be either "all" or "partial" for the first 500 pvalues of the object.

### Author(s)

Ioannis Tsamardinos, Vincenzo Lagani

R implementation and documentation: Giorgos Athineou <athineou@csd.uoc.gr> Vincenzo Lagani <vlagani@csd.uoc.gr>

#### References

Tsagris M., Lagani V., & Tsamardinos I. (2018). Feature selection for high-dimensional glmm data. BMC bioinformatics, 19(1), 17.

Vincenzo Lagani, George Kortas and Ioannis Tsamardinos (2013), Biomarker signature identification in "omics" with multiclass outcome. Computational and Structural Biotechnology Journal, 6(7):1-7.

McCullagh, Peter, and John A. Nelder. Generalized linear models. CRC press, USA, 2nd edition, 1989.

## See Also

```
mmpc.timeclass.model
```

# **Examples**

```
## assume these are longitudinal data, each column is a variable (or feature)
dataset <- matrix( rnorm(400 * 30), ncol = 30 )
id <- rep(1:80, each = 5)  ## 80 subjects
reps <- rep( seq(4, 12, by = 2), 80)  ## 5 time points for each subject
## dataset contains are the regression coefficients of each subject's values on the
## reps (which is assumed to be time in this example)
target <- rep(0:1, each = 200)
a <- MMPC.timeclass(target, reps, id, dataset)</pre>
```

Fit a mixture of beta distributions in p-values

Fit a mixture of beta distributions in p-values

# **Description**

Fit a mixture of beta distributions in p-values.

### Usage

```
pval.mixbeta(p)
```

#### Arguments

р

A vector of p-values.

### **Details**

The p-values are assumed to follow a mixture of two beta distributions. The null p-values follow Be(1, 1) and the non-null p-values follow Be( $\xi$ , 1). In the first step, the proportion of true null values using Storey and Tibshirani (2003) is calculated and then MLE is adopted to obtain  $\xi$ . For more information on this see Triantafillou (2014).

#### Value

A vector with the estimated  $\pi_0$  and  $\xi$  values.

### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

### References

Triantafillou S., Tsamardinos I. and Roumpelaki A. (2014). Learning neighborhoods of high confidence in constraint-based causal discovery. In European Workshop on Probabilistic Graphical Models, pp. 487-502.

Storey J.D. and Tibshirani R. (2003). Statistical significance for genome-wide experiments. Proceedings of the National Academy of Sciences, 100: 9440-9445.

#### See Also

```
pc.skel, mmhc.skel, corfs.network, local.mmhc.skel, conf.edge.lower
```

### **Examples**

```
## simulate a dataset with continuous data
y <- rdag2(400, p = 25, nei = 3)
ind <- sample(1:25, 25)
x <- y$x[, ind]
mod <- pc.skel( x, method = "comb.fast", alpha = 0.01 )
pval <- as.vector( mod$pvalue[lower.tri(mod$pvalue)] )
pval.mixbeta(pval)</pre>
```

Forward Backward Early Dropping selection regression

Forward Backward Early Dropping selection regression

### **Description**

Forward Backward Early Dropping selection regression.

# Usage

```
fbed.reg(target, dataset, prior = NULL, ini = NULL, test = NULL, threshold = 0.05,
wei = NULL, K = 0, method = "LR", gam = NULL, backward = TRUE)
```

### **Arguments**

target	The class variable. Provide either a string, an integer, a numeric value, a vector, a factor, an ordered factor or a Surv object.
dataset	The dataset; provide either a data frame or a matrix (columns = variables, rows = samples).
prior	If you have prior knowledge of some variables that must be in the variable selection phase add them here. This an be a vector (if you have one variable) or a matrix (if you more variables). This does not work during the backward phase at the moment.

ini If you already have the test statistics and the p-values of the univariate associ-

ations (the first step of FBED) supply them as a list with the names "stat" and "pvalue" respectively. If you have used the EBIc this list contains the eBIC of the univariate associations. Note, that the "gam" argument must be the same

though.

test The available tests: "testIndReg", "testIndPois", "testIndNB", "testIndLogistic",

"testIndMMReg", "testIndBinom", "censIndCR", "censIndWR", "testIndBeta", "testIndZIP", "testIndGamma, "testIndNormLog", "testIndTobit", "testIndQPois", "testIndQBinom", "testIndFisher" "testIndMultinom", "testIndOrdinal", "testInd-Clogit" and "testIndSPML". Note that not all of them work with eBIC. The only test that does not have "eBIC" and no weights (input argument "wei") is the test

"gSquare". The tests "testIndFisher" and "testIndSPML" have no weights.

threshold Threshold (suitable values in (0, 1)) for assessing p-values significance. Default

value is 0.05.

wei A vector of weights to be used for weighted regression. The default value is

NULL. It is not suggested when robust is set to TRUE. If you want to use the "testIndBinom", then supply the successes in the y and the trials here. An example where weights are used is surveys when stratified sampling has occured.

K How many times should the process be repeated? The default value is 0. You

can also specify a range of values of K, say 0:4 for example.

method Do you want the likelihood ratio test to be performed ("LR" is the default value)

or perform the selection using the "eBIC" criterion (BIC is a special case).

gam In case the method is chosen to be "eBIC" one can also specify the gamma

parameter. The default value is "NULL", so that the value is automatically cal-

culated.

backward After the Forward Early Dropping phase, the algorithm proceeds with a the usual

Backward Selection phase. The default value is set to TRUE. It is advised to perform this step as maybe some variables are false positives, they were wrongly

selected.

The backward phase using likelihood ratio test and eBIc are two different functions and can be called directly by the user. SO, if you want for example to perform a backard regression with a different threshold value, just use these two

functions separately.

#### **Details**

The algorithm is a variation of the usual forward selection. At every step, the most significant variable enters the selected variables set. In addition, only the significant variables stay and are further examined. The non significant ones are dropped. This goes until no variable can enter the set. The user has the option to re-do this step 1 or more times (the argument K). In the end, a backward selection is performed to remove falsely selected variables. Note that you may have specified, for example, K=10, but the maximum value FBED used can be 4 for example.

The "testIndQPois" and "testIndQBinom" do not work for method = "eBIC" as there is no BIC associated with quasi Poisson and quasi binomial regression models.

If you specify a range of values of K it returns the results of fbed.reg for this range of values of K. For example, instead of running fbed.reg with K=0, K=1, K=2 and so on, you can run fbed.reg

with K=0:2 and the selected variables found at K=2, K=1 and K=0 are returned. Note also, that you may specify maximum value of K to be 10, but the maximum value FBED used was 4 (for example).

#### Value

If K is a single number a list including:

univ If you have used the log-likelihood ratio test this list contains the test statistics

and the associated **logged p-values** of the univariate associations tests. If you have used the EBIc this list contains the eBIC of the univariate associations.

Note, that the "gam" argument must be the same though.

res A matrix with the selected variables, their test statistic and the associated **logged** 

p-value.

info A matrix with the number of variables and the number of tests performed (or

models fitted) at each round (value of K). This refers to the forward phase only.

runtime The runtime required.

back.rem The variables removed in the backward phase.

back.n.tests The number of models fitted in the backward phase.

If K is a sequence of numbers a list tincluding:

univ If you have used the log-likelihood ratio test this list contains the test statistics

and the associated p-values of the univariate associations tests. If you have used

the EBIc this list contains the eBIC of the univariate associations.

res The results of fbed.reg with the maximum value of K.

mod A list where each element refers to a K value. If you run FBEd with method

= "LR" the selected variables, their test statistic and their p-value is returned. If you run it with method = "eBIC", the selected variables and the eBIC of the

model with those variables are returned.

### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

#### References

Borboudakis G. and Tsamardinos I. (2019). Forward-backward selection with early dropping. Journal of Machine Learning Research, 20(8): 1-39.

Tsagris, M. and Tsamardinos, I. (2019). Feature selection with the R package MXM. F1000Research 7: 1505

#### See Also

fs.reg, ebic.bsreg, bic.fsreg, MMPC

# **Examples**

```
#simulate a dataset with continuous data
dataset <- matrix( runif(100 * 20, 1, 100), ncol = 20 )
#define a simulated class variable
target <- rt(100, 10)

a1 <- fbed.reg(target, dataset, test = "testIndReg")
y <- rpois(100, 10)
a2 <- fbed.reg(y, dataset, test = "testIndPois")
a3 <- MMPC(y, dataset)</pre>
```

Forward Backward Early Dropping selection regression for big data

Forward Backward Early Dropping selection regression for big data

# Description

Forward Backward Early Dropping selection regression for big data.

# Usage

```
big.fbed.reg(target = NULL, dataset, threshold = 0.01, ini = NULL,
test = "testIndLogistic", K = 0, backward = FALSE)
```

# **Arguments**

target	The class variable. Provide either a string, an integer, a numeric value, a vector, a factor, an ordered factor or a Surv object. This can also be NULL and will be extracted from the big.matrix object "dataset". If you want to use the test "censIndWR", for survival data for example, the target must not contain any censored values.
dataset	The dataset; this is abig.matrix object, where rows denote the samples and columns the features. If "target" is NULL, the first column must be the target. Only continuous variables are allowed. <b>Note:</b> In the case of thest being "gSquare", the dataset should contain the target variable in the last line.
threshold	Threshold (suitable values in $(0, 1)$ ) for assessing p-values significance. Default value is $0.05$ .
ini	If you already have the test statistics and the p-values of the univariate associations (the first step of FBED) supply them as a list with the names "stat" and "pvalue" respectively.
test	The available tests: "testIndFisher", "testIndPois", "testIndLogistic", "censIndWR", "testIndQPois", "testIndMultinom", "gSquare".
K	How many times should the process be repeated? The default value is 0. You can also specify a range of values of K, say 0:4 for example.

backward

After the Forward Early Dropping phase, the algorithm proceeds with the usual Backward Selection phase. The default value is set to TRUE. It is advised to perform this step as maybe some variables are false positives, they were wrongly selected. Pay attention to this, as it will convert the big matrix object with the selected features into a matrix object in R.

The backward phase using likelihood ratio test is a different functions and can be called directly by the user. So, if you want for example to perform a backard regression with a different threshold value, just use that functions separately.

#### **Details**

The algorithm is a variation of the usual forward selection. At every step, the most significant variable enters the selected variables set. In addition, only the significant variables stay and are further examined. The non significant ones are dropped. This goes until no variable can enter the set. The user has the option to re-do this step 1 or more times (the argument K). In the end, a backward selection is performed to remove falsely selected variables. Note that you may have specified, for example, K=10, but the maximum value FBED used can be 4 for example.

**Notes:** The backward phase needs caution, because the big.matrix object with the selected features is turned into a matrix and then the backward selection takes place. In general, this algorithm is to be used with a few tens ,or hundreds of features and millions of rows. It is designed for thin matrices only. The big.gomp on the other hand is designed for thin, fat and matrices with many rows and many columns.

#### Value

If K is a single number a list including:

univ If you have used the log-likelihood ratio test this list contains the test statistics

and the associated p-values of the univariate associations tests. If you have used the EBIc this list contains the eBIC of the univariate associations. Note, that the

"gam" argument must be the same though.

res A matrix with the selected variables, their test statistic and the associated **logged** 

p-value.

info A matrix with the number of variables and the number of tests performed (or

models fitted) at each round (value of K). This refers to the forward phase only.

runtime The runtime required.

back.rem The variables removed in the backward phase.

back.n.tests The number of models fitted in the backward phase.

#### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

## References

Borboudakis G. and Tsamardinos I. (2019). Forward-backward selection with early dropping. Journal of Machine Learning Research, 20(8): 1-39.

#### See Also

```
fs.reg, ebic.bsreg, bic.fsreg, MMPC
```

#### **Examples**

```
## Not run:
#simulate a dataset with continuous data
x <- matrix( runif(10^6 * 50, 1, 100), ncol = 50 )
require(bigmemory)
dataset <- bigmemory::as.big.matrix(x)
#define a simulated class variable
target <- rt(10^6, 10)
a1 <- big.fbed.reg(target, dataset, test = "testIndFisher")
y <- rpois(10^6, 10)
a2 <- big.fbed.reg(y, dataset, test = "testIndPois")
## End(Not run)</pre>
```

Forward Backward Early Dropping selection regression with GEE  $Forward\ Backward\ Early\ Dropping\ selection\ regression\ with\ GEE$ 

### **Description**

Forward Backward Early Dropping selection regression with GEE.

#### Usage

```
fbed.gee.reg(target, dataset, id, prior = NULL, reps = NULL, ini = NULL,
threshold = 0.05, wei = NULL, K = 0, test = "testIndGEEReg",
correl = "exchangeable", se = "jack")
```

### **Arguments**

target The class variable. This can be a numerical vector with continuous data, binary,

discrete or an ordered factor variable. It can also be a factor variable with two levels only. Pay attention to this. If you have ordinal data, then supply an ordered factor variable. The data must be sorted so that observations on a cluster are

contiguous rows for all entities in the formula.

dataset The set of candidate predictor variables provide a numerical matrix or a data frame

in case of categorical variables (columns = variables, rows = samples). In the case of ordinal regression, this can only be a numerical matrix, i.e. only continuous predictor variables. The data must be sorted so that observations on a

cluster are contiguous rows for all entities in the formula.

This is a numerical vector of the same size as target denoting the groups or the

subjects. The data must be sorted so that observations on a cluster are contiguous

rows for all entities in the formula.

prior

If you have prior knowledge of some variables that must be in the variable selection phase add them here. This an be a vector (if you have one variable) or a matrix (if you more variables).

reps

This is a numerical vector of the same size as target denoting the groups or the subjects. If you have longitudinal data and you know the time points, then supply them here. The data must be sorted so that observations on a cluster are contiguous rows for all entities in the formula.

ini

If you already have the test statistics and the logged p-values of the univariate associations (the first step of FBED) supply them as a list with the names "stat" and "pvalue" respectively.

threshold

Threshold (suitable values in (0, 1)) for asymmbsing p-values significance. Default value is 0.05.

wei

A vector of weights to be used for weighted regression. The default value is NULL. It is mentioned in the "geepack" that weights is not (yet) the weight as in sas proc genmod, and hence is not recommended to use.

K

How many times should the process be repated? The default value is 0.

test

This is for the type of regression to be used, "testIndGEEReg", for Gaussian regression, "testIndGEEGamma" for Gamma regression, "testIndGEELogistic for logistic regression, "testIndGEENormLog" for linear regression with a log link, "testIndGEEPois" for Poisson regression or "testIndGEEOrdinal" for ordinal regression.

correl

The correlation structure. For the Gaussian, Logistic, Poisson and Gamma regression this can be either "exchangeable" (compound symmetry, suitable for clustered data) or "ar1" (AR(1) model, suitable for longitudinal data). If you want to use the AR(1) correlation structure you must be careful with the input dat you give. All data (target and dataset) must be sorted according to the id and time points. All observations must be ordered according to time within each subject. See the vignette of **geepack** to understand how. For the ordinal logistic regression its only the "exchangeable" correlation sturcture.

se

The method for estimating standard errors. This is very important and crucial. The available options for Gaussian, Logistic, Poisson and Gamma regression are: a) 'san.se', the usual robust estimate. b) 'jack': if approximate jackknife variance estimate should be computed. c) 'j1s': if 1-step jackknife variance estimate should be computed and d) 'fij': logical indicating if fully iterated jackknife variance estimate should be computed. If you have many clusters (sets of repeated measurements) "san.se" is fine as it is astmpotically correct, plus jacknife estimates will take longer. If you have a few clusters, then maybe it's better to use jacknife estimates.

The jackknife variance estimator was suggested by Paik (1988), which is quite suitable for cases when the number of subjects is small (K < 30), as in many biological studies. The simulation studies conducted by Ziegler et al. (2000) and Yan and Fine (2004) showed that the approximate jackknife estimates are in many cases in good agreement with the fully iterated ones.

#### **Details**

The algorithm is a variation of the usual forward selection. At every step, the most significant variable enters the selected variables set. In addition, only the significant variables stay and are further examined. The non significant ones are dropped. This goes until no variable can enter the set. The user has the option to redo this step 1 or more times (the argument K). In the end, a backward selection is performed to remove falsely selected variables.

Since GEE are likelihood free, all significance tests take place using the Wald test, hence we decided not to have a backward phase. This algorithm is suitable for both clustered and longitudinal (glmm) data.

If you specify a range of values of K it returns the results of fbed.reg for this range of values of K. For example, instead of runnning fbed.reg with K=0, K=1, K=2 and so on, you can run fbed.reg with K=0:2 and the selected variables found at K=2, K=1 and K=0 are returned. Note also, that you may specify maximum value of K to be 10, but the maximum value FBED used was 4 (for example).

For GEE make sure you load the library geepack first.

#### Value

If K is a single number a list including:

res A matrix with the selected variables, their test statistic and the associated **logged** 

p-value.

info A matrix with the number of variables and the number of tests performed (or

models fitted) at each round (value of K).

runtime The runtime required.

If K is a sequence of numbers a list tincluding:

univ If you have used the log-likelihood ratio test this list contains the test statistics

and the associated logged p-values of the univariate associations tests. If you have used the EBIc this list contains the eBIC of the univariate associations.

res The results of fbed.gee.reg with the maximum value of K.

mod A list where each element refers to a K value. If you run FBEd with method

= "LR" the selected variables, their test statistic and their p-value is returned. If you run it with method = "eBIC", the selected variables and the eBIC of the

model with those variables are returned.

### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

#### References

Borboudakis G. and Tsamardinos I. (2019). Forward-backward selection with early dropping. Journal of Machine Learning Research, 20(8): 1-39.

Liang K.Y. and Zeger S.L. (1986). Longitudinal data analysis using generalized linear models. Biometrika, 73(1): 13-22.

Prentice R.L. and Zhao L.P. (1991). Estimating equations for parameters in means and covariances of multivariate discrete and continuous responses. Biometrics, 47(3): 825-839.

Paik M.C. (1988). Repeated measurement analysis for nonnormal data in small samples. Communications in Statistics-Simulation and Computation, 17(4): 1155-1171.

Ziegler A., Kastner C., Brunner D. and Blettner M. (2000). Familial associations of lipid pro

les: A generalised estimating equations approach. Statistics in medicine, 19(24): 3345-3357

Yan J. and Fine J. (2004). Estimating equations for association structures. Statistics in medicine, 23(6): 859-874

Eugene Demidenko (2013). Mixed Models: Theory and Applications with R, 2nd Edition. New Jersey: Wiley & Sons.

The R package geepack vignette.

#### See Also

```
fbed.glmm.reg, glmm.bsreg, MMPC.glmm, fbed.reg
```

#### **Examples**

```
## Not run:
require(lme4)
data(sleepstudy)
reaction <- sleepstudy$Reaction
days <- sleepstudy$Days
subject <- sleepstudy$Subject
x <- matrix(rnorm(180 * 200),ncol = 200) ## unrelated predictor variables
m1 <- fbed.gee.reg(reaction, x, subject)
m2 <- fbed.glmm.reg(reaction, x, subject, backward = FALSE)
## End(Not run)</pre>
```

Forward Backward Early Dropping selection regression with GLMM

Forward Backward Early Dropping selection regression with GLMM

### **Description**

Forward Backward Early Dropping selection regression with GLMM.

#### Usage

```
fbed.glmm.reg(target, dataset, id, prior = NULL, reps = NULL, ini = NULL,
threshold = 0.05, wei = NULL, K = 0, method = "LR", gam = NULL,
backward = TRUE, test = "testIndGLMMReg")
```

#### **Arguments**

target The class variable. This can be a numerical vector with continuous data, binary or discrete valued data. It can also be a factor variable with two levels only. dataset The dataset; provide a numerical a matrix (columns = variables, rows = observations). id This is a numerical vector of the same size as target denoting the groups or the subjects. prior If you have prior knowledge of some variables that must be in the variable selection phase add them here. This an be a vector (if you have one variable) or a matrix (if you more variables). This does not work during the backward phase at the moment. This is a numerical vector of the same size as target denoting the groups or reps the subjects. If you have longitudinal data and you know the time points, then supply them here. ini If you already have the test statistics and the p-values of the univariate associations (the first step of FBED) supply them as a list with the names "stat" and "pvalue" respectively in the case of method = "LR". In the case of method = "eBIC" this is a list with an element called "bic". threshold Threshold (suitable values in (0, 1)) for asmmmbsing p-values significance. Default value is 0.05. wei A vector of weights to be used for weighted regression. The default value is NULL. Κ How many times should the process be repated? The default value is 0. method Do you want the likelihood ratio test to be performed ("LR" is the default value) or perform the selection using the "eBIC" criterion (BIC is a special case). In case the method is chosen to be "eBIC" one can also specify the gamma gam parameter. The default value is "NULL", so that the value is automatically calculated. backward After the Forward Early Dropping phase, the algorithm proceeds with the usual Backward Selection phase. The default value is set to TRUE. It is advised to perform this step as maybe some variables are false positives, they were wrongly selected. The backward phase using likelihood ratio test and eBIc are two different functions and can be called directly by the user. SO, if you want for example to perform a backard regression with a different threshold value, just use these two functions separately. This is for the type of regression to be used, "testIndGLMMReg", for Gaussian test regression, "testIndGLMMLogistic for logistic regression or "testIndGLMM-Pois" for Poisson regression, "testIndGLMMGamma" for Gamma regression and "testIndGLMMNormLog" for Gaussian regression with log link and "testIndGLM-MOrdinal" for ordinal regression.

#### **Details**

The algorithm is a variation of the usual forward selection. At every step, the most significant variable enters the selected variables set. In addition, only the significant variables stay and are further examined. The non significant ones are dropped. This goes until no variable can enter the set. The user has the option to redo this step 1 or more times (the argument K). In the end, a backward selection is performed to remove falsely selected variables.

Bear in mind that for the "gaussian" case, the forward phase takes place using the F test (Wald statistic calibrated against an F distribution). The backward phase though takes place using the log-likelihood ratio test.

If you specify a range of values of K it returns the results of fbed.reg for this range of values of K. For example, instead of runnning fbed.reg with K=0, K=1, K=2 and so on, you can run fbed.reg with K=0:2 and the selected variables found at K=2, K=1 and K=0 are returned. Note also, that you may specify maximum value of K to be 10, but the maximum value FBED used was 4 (for example).

#### Value

If K is a single number a list including:

res A matrix with the selected variables, their test statistic and the associated **logged** 

p-value.

info A matrix with the number of variables and the number of tests performed (or

models fitted) at each round (value of K). This refers to the forward phase only.

runtime The runtime required.

back.rem The variables removed in the backward phase.

back.n.tests The number of models fitted in the backward phase.

If K is a sequence of numbers a list tincluding:

univ If you have used the log-likelihood ratio test this list contains the test statistics

and the associated p-values of the univariate associations tests. If you have used

the EBIc this list contains the eBIC of the univariate associations.

res The results of fbed.glmm.reg with the maximum value of K.

mod A list where each element refers to a K value. If you run FBED with method

= "LR" the selected variables, their test statistic and their p-value is returned. If you run it with method = "eBIC", the selected variables and the eBIC of the

model with those variables are returned.

### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

### References

Borboudakis G. and Tsamardinos I. (2019). Forward-backward selection with early dropping. Journal of Machine Learning Research, 20(8): 1-39.

Eugene Demidenko (2013). Mixed Models: Theory and Applications with R, 2nd Edition. New Jersey: Wiley \& Sons.

#### See Also

```
fbed.gee.reg, glmm.bsreg, MMPC.glmm, cv.fbed.lmm.reg
```

### **Examples**

```
## Not run:
require(lme4)
data(sleepstudy)
reaction <- sleepstudy$Reaction
subject <- sleepstudy$Subject
x <- matrix(rnorm(180 * 200),ncol = 200) ## unrelated predictor variables
m1 <- fbed.glmm.reg(reaction, cbind(x1, x), subject)
m2 <- MMPC.glmm(target = reaction, group = subject, dataset = x)
## End(Not run)</pre>
```

Forward selection regression

Variable selection in regression models with forward selection

# Description

Variable selection in regression models with forward selection

fault value is 0.05.

## Usage

```
fs.reg(target, dataset, ini = NULL, threshold = 0.05, wei = NULL, test = NULL,
user_test = NULL, stopping = "BIC", tol = 2, ncores = 1)
```

#### **Arguments**

target	The class variable. Provide either a string, an integer, a numeric value, a vector, a factor, an ordered factor or a Surv object. See also Details.
dataset	The dataset; provide either a data frame or a matrix (columns = variables, rows = samples). In either case, only two cases are available, either all data are continuous, or categorical.
ini	If you have a set of variables already start with this one. Otherwise leave it NULL.
threshold	Threshold (suitable values in (0, 1)) for asmmmbsing p-values significance. De-

wei A vector of weights to be used for weighted regression. The default value is

NULL. An example where weights are used is surveys when stratified sampling

has occured.

test The regression model to use. Available options are most of the tests for SES and

MMPC. The ones NOT available are "gSquare", "censIndER", "testIndMVreg", "testIndClogit" and "testIndSpearman". If you have continuous predictor variables in matrix form, you can put "testIndFisher" and this is pretty fast. Instead of calcualting partial F-tests, which requires liear regression models to be fit, it

calcualtes partial correlation coefficients and this is much more efficient.

user\_test A user-defined conditional independence test (provide a closure type object).

Default value is NULL. If this is defined, the "test" argument is ignored.

stopping The stopping rule. The BIC is always used for all methods. If you have linear

regression though you can change this to "adjrsq" and in this case the adjusted

R qaured is used.

tol The difference bewtween two successive values of the stopping rule. By default

this is is set to 2. If for example, the BIC difference between two succesive models is less than 2, the process stops and the last variable, even though significant

does not enter the model.

ncores How many cores to use. This plays an important role if you have tens of thou-

sands of variables or really large sample sizes and tens of thousands of variables and a regression based test which requires numerical optimisation. In other cases it will not make a difference in the overall time (in fact it can be slower). The parallel computation is used in the first step of the algorithm, where univariate associations are examined, those take place in parallel. We have seen a reduction in time of 50% with 4 cores in comparison to 1 core. Note also, that the amount

of reduction is not linear in the number of cores.

## Details

If the current 'test' argument is defined as NULL or "auto" and the user\_test argument is NULL then the algorithm automatically selects the best test based on the type of the data. Particularly:

- if target is a factor, the multinomial or the binary logistic regression is used. If the target has two values only, binary logistic regression will be used.
- if target is a ordered factor, the ordered logit regression is used. Hence, if you want to use multinomial or ordinal logistic regression, make sure your target is factor.
- if target is a numerical vector and the dataset is not a matrix, but a data.frame linear regression is used. If however, the dataset is a matrix, the correlation based forward selection is used. That is, instead of partial F-tests, we do partial correlation tests.
- if target is discrete numerical (counts), the poisson regression conditional independence test is used. If there are only two values, the binary logistic regression is to be used.
- if target is a Surv object, the Survival conditional independence test is used.

#### Value

In the case of test="testIndMMReg" and class(dataset) = matrix, just one matrix is returned with the index of the selected variable(s), the p-value, the test statistic and the BIC value of each model. For all other cases, the output of the algorithm is S3 object including:

runtime	The run time of the algorithm. A numeric vector. The first element is the user time, the second element is the system time and the third element is the elapsed time.
mat	A matrix with the variables and their latest test statistics and <b>logged p-values</b> .
info	A matrix with the selected variables, their <b>logged p-values</b> and test statistics. Each row corresponds to a model which contains the variables up to that line. The BIC in the last column is the BIC of that model.
ci_test	The conditional independence test used.
final	The final regression model.

## Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

### See Also

```
glm.fsreg, lm.fsreg, bic.fsreg, bic.glm.fsreg, CondIndTests, MMPC, SES
```

# **Examples**

```
set.seed(123)
#simulate a dataset with continuous data
dataset <- matrix( runif(500 * 20, 1, 100), ncol = 20 )

#define a simulated class variable
target <- rt(500, 10)

a0 <- fs.reg(target, dataset, threshold = 0.05, stopping = "BIC", tol = 2)

a1 <- fs.reg(target, dataset, threshold = 0.05, test = "testIndRQ", stopping = "BIC",
tol = 2)

require(survival, quietly = TRUE)
y <- survival::Surv(rexp(500), rep(1, 500))
a2 <- fs.reg(y, dataset, threshold = 0.05, test = "censIndWR", stopping = "BIC", tol = 2)
a3 <- MMPC(target, dataset)

target <- factor( rbinom(500, 1, 0.6) )
b2 <- fs.reg(target, dataset, threshold = 0.05, test = NULL, stopping = "BIC", tol = 2)</pre>
```

Forward selection with generalised linear regression models

Variable selection in generalised linear regression models with forward selection

### **Description**

Variable selection in generalised linear regression models with forward selection

## Usage

```
glm.fsreg(target, dataset, ini = NULL, threshold = 0.05, wei = NULL, tol = 2,
ncores = 1)
gammafsreg(target, dataset, ini = NULL, threshold = 0.05, wei = NULL, tol = 2,
ncores = 1)
normlog.fsreg(target, dataset, ini = NULL, threshold = 0.05, wei = NULL, tol = 2,
ncores = 1)
```

## **Arguments**

target	A numerical vector or a factor variable with two levels. The Gamma regression reuqires strictly positive numbers, wehreas the normlog requires positive numbes, zero included.
dataset	The dataset; provide either a data frame or a matrix (columns = variables, rows = samples). In either case, only two cases are available, either all data are continuous, or categorical.
ini	If you have a set of variables already start with this one. Otherwise leave it NULL.
threshold	Threshold (suitable values in $(0, 1)$ ) for assessing the p-values significance. Default value is 0.05.
wei	A vector of weights to be used for weighted regression. An example where weights are used is surveys when stratified sampling has occured.
tol	The difference bewtween two successive values of the stopping rule. By default this is is set to 2. If for example, the BIC difference between two succesive models is less than 2, the process stops and the last variable, even though significant

How many cores to use. This plays an important role if you have tens of thouncores

does not enter the model.

sands of variables or really large sample sizes and tens of thousands of variables and a regression based test which requires numerical optimisation. In other cammmb it will not make a difference in the overall time (in fact it can be slower). The parallel computation is used in the first step of the algorithm, where univariate associations are examined, those take place in parallel. We have seen a reduction in time of 50% with 4 cores in comparison to 1 core. Note also, that

the amount of reduction is not linear in the number of cores.

## Value

The output of the algorithm is S3 object including:

runtime	The run time of the algorithm. A numeric vector. The first element is the user time, the second element is the system time and the third element is the elapsed time.
mat	A matrix with the variables and their latest test statistics and <b>logged p-values</b> . If you have logistic or Poisson regression with continuous predictor variables in a matrix form and no weights, this will not appear. In this case, a C++ code is called and the output is less.
info	A matrix with the selected variables, their <b>logged p-values</b> and test statistics. Each row corresponds to a model which contains the variables up to that line. The BIC in the last column is the BIC of that model.
ci_test	The conditional independence test used.

## Author(s)

final

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

The final regression model.

#### See Also

```
fs.reg, lm.fsreg, bic.fsreg, bic.glm.fsreg, CondIndTests, MMPC, SES
```

## **Examples**

```
set.seed(123)
#simulate a dataset with continuous data
dataset <- matrix( runif(200 * 30, 1, 100), ncol = 30 )

#define a simulated class variable
target <- rpois(200, 10)

a <- glm.fsreg(target, dataset, threshold = 0.05, tol = 2, ncores = 1 )
b <- MMPC(target, dataset, max_k = 3, threshold = 0.05, test = "testIndPois")</pre>
```

Forward selection with linear regression models  $% \left( 1\right) =\left( 1\right) \left( 1\right$ 

Variable selection in linear regression models with forward selection

# Description

Variable selection in linear regression models with forward selection

## Usage

lm.fsreg(target, dataset, ini = NULL, threshold = 0.05, wei = NULL, stopping = "BIC",
tol = 2, ncores = 1)

### **Arguments**

target The class variable. Provide either a string, an integer, a numeric value, a vector,

a factor, an ordered factor or a Surv object. See also Details.

dataset The dataset; provide either a data frame or a matrix (columns = variables, rows

= samples). In either case, only two cases are available, either all data are con-

tinuous, or categorical.

ini If you have a set of variables already start with this one. Currently this can

only be a matrix with continuous variables. In such cases, the dataset must also

contain continuous variables only. Otherwise leave it NULL.

threshold Threshold (suitable values in (0, 1)) for assessing the p-values significance. De-

fault value is 0.05.

wei A vector of weights to be used for weighted regression. The default value is

NULL. An example where weights are used is surveys when stratified sampling

has occured.

stopping The stopping rule. The BIC ("BIC") or the adjusted  $R^2$  ("adjrsq") can be used.

tol The difference bewtween two successive values of the stopping rule. By default

this is is set to 2. If for example, the BIC difference between two succesive models is less than 2, the process stops and the last variable, even though significant does not enter the model. If the adjusted  $R^2$  is used, the tol should be something

like 0.01 or 0.02.

ncores How many cores to use. This plays an important role if you have tens of thou-

sands of variables or really large sample sizes and tens of thousands of variables and a regression based test which requires numerical optimisation. In other cammb it will not make a difference in the overall time (in fact it can be slower). The parallel computation is used in the first step of the algorithm, where univariate associations are examined, those take place in parallel. We have seen a reduction in time of 50% with 4 cores in comparison to 1 core. Note also, that

the amount of reduction is not linear in the number of cores.

#### **Details**

Only linear regression (robust and non robust) is supported from this function.

## Value

The output of the algorithm is S3 object including:

runtime The run time of the algorithm. A numeric vector. The first element is the user

time, the second element is the system time and the third element is the elapsed

time.

mat A matrix with the variables and their latest test statistics and **logged p-values**.

info	A matrix with the selected variables, their <b>logged p-values</b> and test statistics.
	Each row corresponds to a model which contains the variables up to that line.
	The BIC in the last column is the BIC of that model.
models	The regression models, one at each step.
ci_test	The conditional independence test used, "testIndReg".
final	The final regression model.

#### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

## See Also

```
fs.reg, lm.fsreg, bic.fsreg, bic.glm.fsreg. CondIndTests, MMPC, SES
```

#### **Examples**

```
set.seed(123)
#simulate a dataset with continuous data
dataset <- matrix( runif(200 * 20, 1, 100), ncol = 20 )

#define a simulated class variable
target <- 3 * dataset[, 10] + 2 * dataset[, 20] + rnorm(200, 0, 5)
a1 <- lm.fsreg(target, dataset, threshold = 0.05, stopping = "BIC", tol = 2)</pre>
```

```
G-square conditional independence test for discrete data  \textit{G-square conditional independence test for discrete data}
```

## **Description**

The main task of this test is to provide a p-value PVALUE for the null hypothesis: feature 'X' is independent from 'TARGET' given a conditioning set CS. This test is based on the log likelihood ratio test.

## Usage

```
gSquare(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL,
pvalue_hash = NULL)

permgSquare(target, dataset, xIndex, csIndex, wei = NULL,
univariateModels = NULL, hash = FALSE, stat_hash = NULL,
pvalue_hash = NULL, threshold = 0.05, R = 999)
```

#### **Arguments**

target A numeric vector containing the values of the target variable. **The minimum** 

value must be 0.

dataset A numeric matrix containing the variables for performing the test. Rows as

samples and columns as features. The minimum value must be 0.

xIndex The index of the variable whose association with the target we want to test.

csIndex The indices of the variables to condition on.

wei This argument is not used in this test.

univariateModels

Fast alternative to the hash object for univariate tests. List with vectors "pvalues" (p-values), "stats" (statistics) and "flags" (flag = TRUE if the test was successful) representing the univariate association of each variable with the target. Default

value is NULL.

hash A boolean variable which indicates whether (TRUE) or not (FALSE) to use the

hash-based implementation of the statistics of SES. Default value is FALSE. If TRUE you have to specify the stat\_hash argument and the pvalue\_hash argument.

ment.

stat\_hash A hash object which contains the cached generated statistics of a SES run in the

current dataset, using the current test.

pvalue\_hash A hash object which contains the cached generated p-values of a SES run in the

current dataset, using the current test.

threshold Threshold (suitable values in (0, 1)) for assessing p-values significance. Default

value is 0.05. This is actually obsolete here, but has to be in order to have a

concise list of input arguments across the same family of functions.

R The number of permutations to use. The default value is 999.

#### **Details**

If the number of samples is at least 5 times the number of the parameters to be estimated, the test is performed, otherwise, independence is not rejected (see Tsmardinos et al., 2006, pg. 43)

If hash = TRUE, testIndLogistic requires the arguments 'stat\_hash' and 'pvalue\_hash' for the hash-based implementation of the statistical test. These hash Objects are produced or updated by each run of SES (if hash == TRUE) and they can be reused in order to speed up next runs of the current statistic test. If "SESoutput" is the output of a SES run, then these objects can be retrieved by SESoutput@hashObject\$stat\_hash and the SESoutput@hashObject\$pvalue\_hash.

Important: Use these arguments only with the same dataset that was used at initialization.

For all the available conditional independence tests that are currently included on the package, please see "?CondIndTests".

## Value

A list including:

pvalue A numeric value that represents the logarithm of the generated p-value of the

 $G^2$  test (see reference below).

stat	A numeric value that represents the generated statistic of the ${\cal G}^2$ test (see reference below).
stat_hash	The current hash object used for the statistics. See argument stat_hash and details. If argument hash = FALSE this is NULL.
pvalue_hash	The current hash object used for the p-values. See argument stat_hash and details. If argument hash = FALSE this is NULL.

### Author(s)

R implementation and documentation: Giorgos Athineou <athineou@csd.uoc.gr>

#### References

Tsamardinos, Ioannis, Laura E. Brown, and Constantin F. Aliferis. The max-min hill-climbing Bayesian network structure learning algorithm. Machine learning, 2006 65(1): 31–78.

#### See Also

```
SES, testIndFisher, testIndLogistic, censIndCR, CondIndTests
```

## **Examples**

```
#simulate a dataset with binary data
dataset <- matrix(rbinom(500 * 51, 1, 0.6), ncol = 51)
#initialize binary target
target <- dataset[, 51]
#remove target from the dataset
dataset <- dataset[, -51]

#run the gSquare conditional independence test for the binary class variable
results <- gSquare(target, dataset, xIndex = 44, csIndex = c(10,20))
results

#run SES algorithm using the gSquare conditional independence test for the binary class variable
sesObject <- SES(target, dataset, max_k = 3, threshold = 0.05, test = "gSquare");
target <- as.factor(target)
sesObject2 <- SES(target, dataset, max_k = 3, threshold = 0.05, test = "testIndLogistic");</pre>
```

Generalised linear mixed models based on glmm SES and MMPC outputs  $Generalised\ linear\ mixed\ model(s)\ based\ obtained\ from\ glmm\ SES\ or\ MMPC$ 

## Description

One or more regression models obtained from SES or MMPC, are returned.

#### **Usage**

```
mmpc.glmm.model(target, dataset, reps = NULL, group, slopes = FALSE, wei = NULL,
mmpcglmm.Object, test = NULL)

ses.glmm.model(target, dataset, reps = NULL, group, slopes = FALSE, wei = NULL,
sesglmm.Object, nsignat = 1, test = NULL)

mmpc.gee.model(target, dataset, reps = NULL, group, correl = "exchangeable",
se = "jack", wei = NULL, mmpcgee.Object, test = NULL)

ses.gee.model(target, dataset, reps = NULL, group, correl = "exchangeable",
se = "jack", wei = NULL, sesgee.Object, nsignat = 1, test = NULL)
```

### **Arguments**

wei

target The class variable. Provide a vector with continuous (normal), binary (binomial)

or discrete (Poisson) data.

dataset The dataset; provide either a data frame or a matrix (columns = variables, rows

= observations). Currently, only continuous datasets are supported.

reps A numeric vector containing the time points of the subjects. Its length is equal

to the length of the target variable. If you have clustered data, leave this NULL.

group A numeric vector containing the subjects or groups. It must be of the same

legnth as target.

slopes Should random slopes for the ime effect be fitted as well? Default value is

FALSE.

The correlation structure. For the Gaussian, Logistic, Poisson and Gamma regression this can be either "exchangeable" (compound symmetry, suitable for

clustered data) or "ar1" (AR(1) model, suitable for longitudinal data). For the ordinal logistic regression its only the "exchangeable" correlation sturcture.

se The method for estimating standard errors. This is very important and crucial.

The available options for Gaussian, Logistic, Poisson and Gamma regression are: a) 'san.se', the usual robust estimate. b) 'jack': if approximate jackknife variance estimate should be computed. c) 'j1s': if 1-step jackknife variance estimate should be computed and d) 'fij': logical indicating if fully iterated jackknife variance estimate should be computed. If you have many clusters (sets of repeated measurements) "san.se" is fine as it is astmpotically correct, plus jacknife estimates will take longer. If you have a few clusters, then maybe it's better

to use jacknife estimates.

The jackknife variance estimator was suggested by Paik (1988), which is quite suitable for cases when the number of subjects is small (K < 30), as in many biological studies. The simulation studies conducted by Ziegler et al. (2000) and Yan and Fine (2004) showed that the approximate jackknife estimates are in

many cases in good agreement with the fully iterated ones.

A vector of weights to be used for weighted regression. The default value is

NULL.

mmpcglmm.Object

An object with the results of an MMPC.glmm run.

sesglmm.Object An object with the results of a SES.glmm run.
mmpcgee.Object An object with the results of an MMPC.gee run.

sesgee. Object An object with the results of an SES.gee run.

nsignat How many signatures to use. If nsignat = 1 (default value) the first set of vari-

ables will be used for the model. If you want more, then specify the nubmer of signatures you want. If you want the models based on all signatures, specify "all". If you put a number which is higher than the number of signatures, all

models will be returned.

test The conditional independence test to use. Default value is NULL. Currently, the

only available conditional independence test are the testIndGLMMReg, testIndGLMMLogistic,

testIndGLMMPois and testIndLMM which fit linear mixed models.

#### **Details**

This command is useful if you want to see all models and check for example their fitting ability, MSE in linear models for exmaple.

#### Value

A list including:

mod Depending on the number of signatures requested, one or models will be re-

turned.

signature A matrix (or just one vector if one signature only) with the variables of each

signature, along with the BIC of the corresponding regression model.

### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

## References

Tsagris, M., Lagani, V., & Tsamardinos, I. (2018). Feature selection for high-dimensional glmm data. BMC bioinformatics, 19(1), 17.

I. Tsamardinos, M. Tsagris and V. Lagani (2015). Feature selection for longitudinal data. Proceedings of the 10th conference of the Hellenic Society for Computational Biology & Bioinformatics (HSCBB15)

Eugene Demidenko (2013). Mixed Models: Theory and Applications with R, 2nd Edition. New Jersey: Wiley & Sons.

Pinheiro J. and D. Bates. Mixed-effects models in S and S-PLUS. Springer Science & Business Media, 2006.

## See Also

```
SES, MMPC, cv.ses, cv.mmpc
```

### **Examples**

```
## Not run:
require(lme4)
data(sleepstudy)
reaction <- sleepstudy$Reaction
days <- sleepstudy$Days
subject <- sleepstudy$Subject
x <- matrix(rnorm(180 * 50),ncol = 50) ## unrelated predictor variables
m1 <- SES.glmm(reaction, days, subject, x)
m2 <- MMPC.glmm(reaction, days, subject, x)
mod <- mmpc.glmm.model(reaction, dataset = x, reps = days, group = subject, slopes = FALSE,
mmpcglmm.Object = m2)
## End(Not run)</pre>
```

Generalised ordinal regression

Generalised ordinal regression

## **Description**

Generalised ordinal regression.

### Usage

```
ordinal.reg(formula, data)
```

#### **Arguments**

formula An object of class "formula" (or one that can be coerced to that class): a sym-

bolic description of the model to be fitted. This is the usual formula use by many regression models in R and other packages. Type "glm" or "formula" in R for

more information.

data A data.frame object carrying the relevant data.

#### **Details**

Generalised ordinal regression is fitted. This means the instead of having the same coefficient for each predictor variable, they are allowed to vary. The usual, proportional odds, ordinal regression specifies that the lines do not cross. This one does not need the proportional odds assumption. The proportional odds assumption does not always hold in practice and is a rather restrictive model. Be careful though, you may end up qith negative probabilities. We do a tick to fix them, but in that case, you may have not found the optimal model. This is a problematic case unfortunately. Williams (2006) explains in a very nice way how one can fit this model by using many logistic regressions in an incremental way. The number of logistic regression models to be fit is the number of categories of the response variables - 1.

It may be the case that the message says "problematic region". In this case the optimization was not successful and perhaps the deviance is not at the global minimum. For example, with the addition of

one extra variable the deviance might increase. I know, this type of ordinal regression is hard. In these difficult situations other packages return "error". Another difficult I have seen is when "NA" appear in the coefficients. In this case I do not consider these coefficients, not their corresponding variables in the calculation of the deviance.

#### Value

A list including:

message If you hit negative probabilities, the message "problematic region" will be printed.

Otherwise, this is NULL.

be The regression coefficients.

devi The deviance of the model.

#### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

#### References

Williams, R. (2006). Generalized ordered logit/partial proportional odds models for ordinal dependent variables. Stata Journal, 6(1), 58-82

### See Also

```
pc.skel, ridge.reg
```

# Examples

```
y \leftarrow factor( rbinom(100, 3, 0.5) )

x \leftarrow matrix( rnorm(100 * 3), ncol = 3)

ordinal.reg(y \sim x, data = data.frame(x) )

ordinal.reg(y \sim 1, data = data.frame(x) )
```

Generate random folds for cross-validation

Generate random folds for cross-validation

## Description

Random folds for use in a cross validation are generated. There is the option for stratified splitting as well.

## Usage

```
generatefolds(target, nfolds = 10, stratified = TRUE, seed = FALSE)
```

### **Arguments**

target A vector with some data, either continuous or categorical.

nfolds The number of folds to produce.

stratified A boolean variable specifying whether stratified random (TRUE) or simple ran-

dom (FALSE) sampling is to be used when producing the folds.

seed A boolean variable. If set to TRUE, the folds will always be the same.

## **Details**

I was inspired by the sam command in the package **TunePareto** in order to do the stratified version.

#### Value

A list with nfolds elements where each elements is a fold containing the indices of the data.

### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

#### See Also

```
cv.ses
```

## **Examples**

```
a <- generatefolds(iris[, 5], nfolds = 5, stratified = TRUE)
table(iris[a[[1]], 5]) ## 10 values from each group</pre>
```

```
Generic orthogonal matching pursuit (gOMP)
```

Generic orthogonal matching pursuit (gOMP)

### **Description**

Generic orthogonal matching pursuit.

## Usage

```
gomp(target, dataset, xstand = TRUE, tol = qchisq(0.95, 1),
test = "testIndLogistic", method = "ar2" )

gomp.path(target, dataset, xstand = TRUE, tol = c(4, 5, 6),
test = "testIndLogistic", method = "ar2" )

boot.gomp(target, dataset, tol = qchisq(0.95, 1),
test = "testIndLogistic", method = "ar2", B = 500, ncores = 1)
```

#### **Arguments**

The response variable, a numeric vector, a matrix or a Surv object.

dataset A matrix with continuous data, where the rows denote the samples and the

columns are the variables.

xstand If this is TRUE the independent variables are standardised.

tol The tolerance value to terminate the algorithm. This is the change in the criterion

value between two successive steps. The default value is the 95% quantile of the  $\chi^2$  distribution with 1 degree of freedom. For test = "testIndFisher" the BIC is

already calculated.

In the case of "gomp.path" this is a vector of values. For each tolerance value

the result of the gOMP is returned. It returns the whole path of solutions.

This denotes the parametric model to be used each time. It depends upon the

nature of the target variable. The possible values are "testIndFisher" (or "testIndReg" for the same purpose), "testIndLogistic", "testIndPois", "testIndQPois", "testIndQbinom", "testIndNormLog", "testIndMVreg", "testIndNB", "testIndBeta", "testIndGamma", "testIndMMReg", "testIndRQ", "testIndOrdinal", "testInd-

Tobit", "censIndCR", "censIndWR", "censIndLLR" and "testIndMultinom".

method This is only for the "testIndFisher". You can either specify, "ar2" for the adjusted

R-square or "sse" for the sum of squares of errors. The tolerance value in both cases must a number between 0 and 1. That will denote a percentage. If the percentage increase or decrease is less than the nubmer the algorithm stops. An alternative is "BIC" for BIC and the tolerance values are like in all other

regression models.

B How many bootstrap samples to generate. The gOMP will be performed for

each of these samples.

ncores How many cores to use. This argument is valid only if you have a multi-threaded

machine.

#### Value

A list including:

runtime The runtime of the algorithm

phi The phi coefficient, returned in the quasi binomial (testIndQBinom), quasi Pois-

 $son \, (testIndQPois), Gamma \, (testIndGamma) \, and \, Gaussian \, with \, log \, link \, (testIndGamma) \,$ 

NormLog). In all other cases this is NULL.

res For the case of "gomp" a matrix with two columns. The selected variable(s)

and the criterion value at every step. For the case of "gomp.path" a matrix with many columns. Every column contains the selected variables for each tolerance calue, starting from the smallest value (which selected most variables). The final column is the deviance of the model at each step. For the "boot.gomp" this is a matrix with two columns. The first one is the selected variables and the second

column is their proportion of selection.

#### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>.

#### References

Pati Y. C., Rezaiifar R. & Krishnaprasad P. S. (1993). Orthogonal matching pursuit: Recursive function approximation with applications to wavelet decomposition. In Signals, Systems and Computers. 1993 Conference Record of The Twenty-Seventh Asilomar Conference on. IEEE.

Davis G. (1994). Adaptive Nonlinear Approximations. PhD thesis. http://www.geoffdavis.net/papers/dissertation.pdf

Mallat S. G. & Zhang Z. (1993). Matching pursuits with time-frequency dictionaries. IEEE Transactions on signal processing, 41(12), 3397-3415. https://www.di.ens.fr/~mallat/papiers/MallatPursuit93.pdf

Gharavi-Alkhansari M., & Huang T. S. (1998, May). A fast orthogonal matching pursuit algorithm. In Acoustics, Speech and Signal Processing, 1998. Proceedings of the 1998 IEEE International Conference on (Vol. 3, pp. 1389-1392). IEEE.

Chen S., Billings S. A., & Luo W. (1989). Orthogonal least squares methods and their application to non-linear system identification. International Journal of control, 50(5), 1873-1896.

Lozano A., Swirszcz G., & Abe N. (2011). Group orthogonal matching pursuit for logistic regression. In Proceedings of the Fourteenth International Conference on Artificial Intelligence and Statistics.

Razavi S. A. Ollila E., & Koivunen V. (2012). Robust greedy algorithms for compressed sensing. In Signal Processing Conference (EUSIPCO), 2012 Proceedings of the 20th European. IEEE.

Mazin Abdulrasool Hameed (2012). Comparative analysis of orthogonal matching pursuit and least angle regression. MSc thesis, Michigan State University. https://www.google.gr/url?sa=t&rct=j&q=&esrc=s&source=web&c

Tsagris M., Papadovasilakis Z., Lakiotaki K. and Tsamardinos I. (2020). The  $\gamma$ -OMP algorithm for feature selection with application to gene expression data. IEEE/ACM Transactions on Computational Biology and Bioinformatics, 19(2), 1214-1224. https://ieeexplore.ieee.org/stamp/stamp.jsp?tp=&arnumber=9219177

#### See Also

```
cor.fbed, cor.fsreg, correls, fs.reg
```

## **Examples**

```
x <- matrix( rnorm(500 * 50), ncol = 50)
y <- rnorm(500)
b <- MXM::gomp(y, x, test = "testIndFisher")</pre>
```

Generic orthogonal matching pursuit(gOMP) for big data

Generic orthogonal matching pursuit(gOMP) for big data

## **Description**

Generic orthogonal matching pursuit(gOMP) for big data.

### Usage

```
big.gomp(target = NULL, dataset, tol = qchisq(0.95, 1) + log(dim(x)[1]),
test = "testIndFisher", method = "ar2")
big.gomp.path(target = NULL, dataset, tol = c(8, 9, 10),
test = "testIndFisher", method = "ar2")
```

#### **Arguments**

test

target The target (response) variable. If NULL, then it must inside the dataset. You

might have the target variable though outside the big data file. This is like in the case of the regular gomp, a Surv object, a factor or a continuous numerical

vector for all other cases. The default value is NULL.

dataset The big.matrix oject. If target is NULL, the first column must be the target, the

response variable and all the others are the predictor variables. In the case of

survival data, the first two columns are used to form the response variable.

The tolerance value to terminate the algorithm. This is the change in the criterion

value between two successive steps. The default value is the 95% quantile of the  $\chi^2$  distribution with 1 degree of freedom. For test = "testIndFisher" the BIC is

already calculated.

In the case of "big.gomp.path" this is a vector of values. For each tolerance

value the result of the gOMP is returned. It returns the whole path of solutions.

This denotes the parametric model to be used each time. It depends upon the nature of the target variable. The possible values are "testIndFisher" (or "testIn-

dReg" for the same purpose), "testIndLogistic", "testIndPois", "testIndQPois", "testIndQbinom", "testIndNormLog", "testIndNB", "testIndGamma", "testInd-

MMReg", "testIndRQ", "testIndOrdinal", "testIndTobit", "censIndCR" and "censIndWR".

method This is only for the "testIndFisher". You can either specify, "ar2" for the adjusted

R-square or "sse" for the sum of squares of errors. The tolerance value in both cases must a number between 0 and 1. That will denote a percentage. If the percentage increase or decrease is less than the nubmer the algorithm stops. An alternative is "BIC" for BIC and the tolerance values are like in all other

regression models.

#### **Details**

The data (matrix) which will be read and compressed into a big.matrix object must be of type "numeric". We tested it and it works with "integer" as well. But, in general, bear in mind that only matrices will be read. We have not tested with data.frame for example. Whatsoever, in the help page of the package "bigmemory" this is mentioned: Any non-numeric entry will be ignored and replaced with NA, so reading something that traditionally would be a data.frame won't cause an error. A warning is issued. In all cases, the object size is always 696 bytes!

### Value

A list including:

runtime The runtime of the algorithm

phi The phi coefficient, returned in the quasi binomial (testIndQBinom), quasi Pois-

son (testIndQPois), Gamma (testIndGamma) and Gaussian with log link (testInd-

NormLog). In all other cases this is NULL.

res For the case of "big.gomp" a matrix with two columns. The selected variable(s)

and the criterion value at every step. For the case of "gomp.path" a matrix with many columns. Every column contains the selected variables for each tolerance value, starting from the smallest value (which selected most variables). The final

column is the deviance of the model at each step.

### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>. For more information see the "bigmemory" package.

### References

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Tsagris M., Papadovasilakis Z., Lakiotaki K. and Tsamardinos I. (2020). The  $\gamma$ -OMP algorithm for feature selection with application to gene expression data. IEEE/ACM Transactions on Computational Biology and Bioinformatics, 19(2), 1214-1224. https://ieeexplore.ieee.org/stamp/stamp.jsp?tp=&arnumber=9219177

### See Also

```
gomp, read.big.data
```

## **Examples**

```
## Not run:
dataset <- matrix( runif(10^6 * 50, 1, 100), ncol = 50 )
write.csv(data, "dataset.csv", sep = ",")
a <- read.big.data("dataset.csv")
mod <- big.gomp(dataset = a, test = "testIndFisher", tol = 0.01)
## End(Not run)</pre>
```

Graph of unconditional associations

Graph of unconditional associations

## **Description**

Calcualtes the graph of unconditional associations. If the correlation (Pearson, Spearman) or the  $G^2$  test of independence, between pairs of continuous or categorical variables respectively is not statistically significant, there is no edge between the two respective nodes.

#### Usage

```
corgraph(dataset, test = "testIndFisher", threshold = 0.01)
```

## **Arguments**

dataset A matrix with the variables. The user must know if they are continuous or if

they are categorical. If you have a matrix with categorical data, i.e. 0, 1, 2, 3 where each number indicates a category, the minimum number for each variable

must be 0.

test The conditional independence test to use. Default value is "testIndFisher". This

procedure allows for "testIndFisher", "testIndSPearman" for continuous vari-

ables and "gSquare" for categorical variables.

threshold Threshold (suitable values in (0, 1)) for assessing p-values significance. Default

value is 0.05.

### Value

A list including:

runtime The run time of the algorithm. A numeric vector. The first element is the user

time, the second element is the system time and the third element is the elapsed

time.

stat A matrix with the test statistics.

pvalue A matrix with the p-values.

G The adjancency matrix. A value of 1 in G[i, j] appears in G[j, i] also, indicating

that i and j have an edge between them.

## Author(s)

Michail Tsagris

R implementation and documentation: Giorgos Athineou <athineou@csd.uoc.gr> and Michail Tsagris <mtsagris@uoc.gr>

### See Also

```
pc.skel, mmhc.skel, corfs.network, bn.skel.utils
```

## **Examples**

```
# simulate a dataset with continuous data
y <- rdag2(500, p = 20, nei = 3)
x <- y$x
a <- mmhc.skel(x, max_k = 5, threshold = 0.01, test = "testIndFisher" )
b <- pc.skel( x, alpha = 0.01 )
d <- corgraph(x, test = "testIndFisher", threshold = 0.01)</pre>
```

IAMB backward selection phase

IAMB backward selection phase

## **Description**

IAMB backward selection phase.

## Usage

```
iamb.bs(target, dataset, threshold = 0.05, wei = NULL, test = NULL, user_test = NULL)
```

#### **Arguments**

target The class variable. Provide either a string, an integer, a numeric value, a vector,

a factor, an ordered factor or a Surv object.

dataset The dataset; provide either a data frame or a matrix (columns = variables, rows

= observations). In either case, only two cases are available, either all data are

continuous, or categorical.

threshold Threshold (suitable values in (0,1)) for assessing p-values significance. Default

value is 0.05.

The regression model to use. Available options are most of the tests for SES and

MMPC. The ones NOT available are "gSquare", "censIndER", "testIndMVreg",

"testIndClogit", "testIndSpearman" and "testIndFisher".

wei A vector of weights to be used for weighted regression. The default value is

NULL. An example where weights are used is surveys when stratified sampling

has occured.

user\_test A user-defined conditional independence test (provide a closure type object).

Default value is NULL. If this is defined, the "test" argument is ignored.

#### **Details**

IAMB stands for Incremental Association Markov Blanket. The algorithm comprises of a forward selection and a modified backward selection process. This functions does the modified backward selection process. In the usual backward selection, among the non singificant variabels, the one with the maximum p-value is dropped. So, one variable is removed at every step. In the IAMB backward phase, at aevery step, all non significant variables are removed. This makes it a lot faster.

### Value

The output of the algorithm is a list of an S3 object including:

runtime The run time of the algorithm. A numeric vector. The first element is the user

time, the second element is the system time and the third element is the elapsed

time.

ci\_test The conditional independence test used.

vars The selected variables.

mat A matrix with the selected variables and their latest test statistic and **logged** 

p-value. If no variable is selected this is NULL.

final The final regression model.

### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

## References

Tsamardinos, I., Aliferis, C. F., Statnikov, A. R., & Statnikov, E. (2003). Algorithms for Large Scale Markov Blanket Discovery. In FLAIRS conference, pp. 376-380.

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### See Also

```
glm.fsreg, lm.fsreg, bic.fsreg, bic.glm.fsreg, CondIndTests, MMPC, SES
```

## **Examples**

```
set.seed(123)
dataset <- matrix( runif(500 * 10, 1, 100), ncol = 10 )
target <- rnorm(500)

a1 <- iamb.bs(target, dataset, threshold = 0.05, test = "testIndRQ")
a2 <- bs.reg(target, dataset, threshold = 0.05, test = "testIndRQ")</pre>
```

IAMB variable selection

IAMB variable selection

# Description

IAMB variable selection.

#### Usage

```
iamb(target, dataset, threshold = 0.05, wei = NULL, test = NULL, user_test = NULL,
stopping = "BIC", tol = 2, ncores = 1, back = "iambbs")
```

## **Arguments**

target	The class variable. Provide either a string, an integer, a numeric value, a vector, a factor, an ordered factor or a Surv object.
dataset	The dataset; provide either a data frame or a matrix (columns = variables, rows = observations). In either case, only two cases are available, either all data are continuous, or categorical.
threshold	Threshold (suitable values in $(0,1)$ ) for assessing p-values significance. Default value is 0.05.
wei	A vector of weights to be used for weighted regression. The default value is NULL. An example where weights are used is surveys when stratified sampling has occured.
test	The regression model to use. Available options are most of the tests for SES and MMPC. The ones NOT available are "gSquare", "censIndER", "testIndMVreg", "testIndClogit", "testIndSpearman" and "testIndFisher" and "testIndIGreg".
user_test	A user-defined conditional independence test (provide a closure type object). Default value is NULL. If this is defined, the "test" argument is ignored.
stopping	The stopping rule. The BIC is always used for all methods. If you have linear regression though you can change this to "adjrsq" and in this case the adjusted R qaured is used.

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tol The difference bewtween two successive values of the stopping rule. By default

this is is set to 2. If for example, the BIC difference between two succesive models is less than 2, the process stops and the last variable, even though significant

does not enter the model.

ncores How many cores to use. This plays an important role if you have tens of thou-

sands of variables or really large sample sizes and tens of thousands of variables and a regression based test which requires numerical optimisation. In other cases it will not make a difference in the overall time (in fact it can be slower). The parallel computation is used in the first step of the algorithm, where univariate associations are examined, those take place in parallel. We have seen a reduction in time of 50% with 4 cores in comparison to 1 core. Note also, that the amount

of reduction is not linear in the number of cores.

back The backward phase. If this "iambbs" (default value) the IAMB backward phase

is performed and hence the IAMB algorithm is completed. If "bs", a simple backward selection phase is performed. This way, the IAMB algorithm is

slightly more general.

#### **Details**

IAMB stands for Incremental Association Markov Blanket. The algorithm comprises of a forward selection and a modified backward selection process. This functions does the modified backward selection process. In the usual backward selection, among the non singificant variables, the one with the maximum p-value is dropped. So, one variable is removed at every step. In the IAMB backward phase, at aevery step, all non significant variables are removed. This makes it a lot faster.

#### Value

The output of the algorithm is a list of an S3 object including:

vars A vector with the selected variables.

mod The output of the backward phase. In the case of no backward procedure this is

the output of the forward phase.

mess If the forward regression returned at most one variable, no backward procedure

takes place and a message appears informing the user about this.

## Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

## References

Tsamardinos, I., Aliferis, C. F., Statnikov, A. R., & Statnikov, E. (2003). Algorithms for Large Scale Markov Blanket Discovery. In FLAIRS conference, pp. 376-380.

## See Also

```
glm.fsreg, lm.fsreg, bic.fsreg, bic.glm.fsreg, CondIndTests, MMPC, SES
```

### **Examples**

```
set.seed(123)
dataset <- matrix( runif(100 * 50, 1, 100), ncol = 50 )

target <- rpois(100, 10)
a1 <- iamb(target, dataset, threshold = 0.05, stopping = "BIC", tol = 0, back = "iambbs")
a2 <- iamb(target, dataset, threshold = 0.05, stopping = "BIC", tol = 0, back = "bs")</pre>
```

Incremental BIC values and final regression model of the FBED algorithm

Incremental BIC values and final regression model of the FBED algorithm

### Description

Incremental BIC values and final regression model of the FBED algorithm.

## Usage

```
fbedreg.bic(target, dataset, wei = NULL, fbedreg.object, test = NULL, graph = TRUE)
```

## **Arguments**

target	A numeric vector containing the values of the target variable. It can also discrete
--------	---

data, binary data (as factor), nominal or ordinal data (as factor). In contrast to SES, no position of the target variable in the dataset is accepted. The target must

be a numerical vector.

dataset A numeric matrix or data frame containing the variables. Rows are samples and

columns are features. If you have categorical variables, this should be a data

frame.

wei A vector of weights to be used for weighted regression. The default value is

NULL. An example where weights are used is surveys when stratified sampling has occured. We suggest not to use weights if you choose "testIndMMReg" as

weights are already being used there.

fbedreg.object An object with the results of an FBED run.

test If you know the test used in SES put it here, otherwise leave it NULL. It will

take this information from the SES object.

graph If you want a graphical representation of the drop in the BIC values set this to

TRUE.

### Details

This function takes the output of the FBED (fbed.reg) and fits succesive models calculating the BIC for each of them. A graph can also be returned.

#### Value

A list including:

res A matrix with the selected variables, their test statistic and p-value (taken from

the fbedreg.object) along with the BIC. Each row contains a BIC, that is the BIC

of the model with the variables up to that row.

mod The final model with all selected variables.

## Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

#### References

Borboudakis G. and Tsamardinos I. (2019). Forward-backward selection with early dropping. Journal of Machine Learning Research, 20(8): 1-39.

#### See Also

```
reg.fit, mmpc.model, SES, MMPC, cv.ses, cv.mmpc
```

## **Examples**

```
dataset <- matrix( runif(100 * 20, 1, 100), ncol = 20 )
#define a simulated class variable
target <- rt(100, 10)
a <- fbed.reg(target, dataset, K = 10, test = "testIndFisher", method = "eBIC")
fbedreg.bic(target, dataset, fbedreg.object = a, test = "testIndFisher")</pre>
```

Interactive plot of an (un)directed graph

Interactive plot of an (un)directed graph

## **Description**

Interactive plot of an (un)directed graph.

### Usage

```
plotnetwork(G, titlos)
```

## **Arguments**

G The adjacency matrix as produced from mmhc.skel, pc.skel, pc.con or any

other algorithm. This can correspond to an undirected, partially directed or a

completely directed graph.

titlos A character argument specifying the title of the graph, for example "PC net-

work".

### **Details**

This visualises the directed graph.

#### Value

The plot of the directed graph. This is interactive, in the sense that the user can "play" with it. Move the nodes, zoom it, strectch it etc.

### Author(s)

Michail Tsagris

R implementation and documentation: Giorgos Athineou <athineou@csd.uoc.gr> and Michail Tsagris <mtsagris@uoc.gr>

#### See Also

```
mmhc.skel, nei, pc.skel, mb
```

## **Examples**

```
## Not run:
# simulate a dataset with continuous data
dataset <- matrix( runif(200 * 20, 1, 100), nrow = 200 )</pre>
a <- mmhc.skel(dataset, max_k = 3, threshold = 0.05, test = "testIndFisher",
nc = 1
plotnetwork(a$G)
plotnetwork(a$G, titlos = "DAG skeleton")
## End(Not run)
```

Lower limit of the confidence of an edge Lower limit of the confidence of an edge

## **Description**

Lower limit of the confidence of an edge.

## Usage

```
conf.edge.lower(p)
```

# **Arguments** р

A numerical vector with the proportion of times an edge was found in the bootstrapped PC algorithm or the confidence of the edge returned by bn. skel.utils2. mammpc.output-class 171

### **Details**

After having performed PC algorithm many times in the bootstrap samples (using pc.skel.boot for example) you get a symmetric matrix with the proportion of times an edge was discovered. Take the lower (or upper) triangular elements of that matrix and pass them as input in this function. This will tell you the minimum proportion required to be confident that an edge is trully significant.

#### Value

The estimated cutoff limit above which an edge can be deemed significant.

### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

### References

Scutari M. and Nagarajan R. (2013). Identifying significant edges in graphical models of molecular networks. Artifficial Intelligence in Medicine, 57: 207-217.

### See Also

```
pc.skel.boot
```

#### **Examples**

```
y <- rdag2(200, p = 40, nei = 3)
x <- y$x
g <- pc.skel.boot(x, R = 199)$Gboot
a <- g[ lower.tri(g) ]
conf.edge.lower(a)</pre>
```

```
mammpc.output-class
```

Class "mammpc.output"

## Description

mammpc. output object class.

## **Objects from the Class**

Objects can be created by calls of the form new("mammpc.output", ...).

## **Slots**

```
selectedVars: Object of class "numeric"
selectedVarsOrder: Object of class "numeric"
hashObject: Object of class "list"
pvalues: Object of class "numeric"
stats: Object of class "numeric"
univ: Object of class "list"
max_k: Object of class "numeric"
threshold: Object of class "numeric"
test: Object of class "character"
runtime: Object of class "proc_time"
```

#### Methods

```
plot plot(x = "mammpc.output", mode = "all"): Generic function for plotting the generated pval-
ues of the MMPCoutput object. Argument mode = "all" for plotting all the pvalues or mode="partial"
for partial plotting the first 500 pvalues
```

## Author(s)

Giorgos Athineou <athineou@csd.uoc.gr>

#### See Also

```
ma.mmpc, ma.ses
```

### **Examples**

```
showClass("mammpc.output")
```

```
Many approximate simple logistic regressions

Many approximate simple logistic regressions.
```

## **Description**

Many approximate simple logistic regressions.

## Usage

```
sp.logiregs(target, dataset, logged = FALSE)
```

## Arguments

target	The dependent variable.	a numerical vector with 0s or 1s.
cai gc c	The dependent variable,	a numerical vector with ob or 15.

dataset A matrix with the indendent variables.

logged Should the p-values be returned (FALSE) or their logarithm (TRUE)?

#### **Details**

Many simple approximate logistic regressions are performed and hypothesis testing for the singificance of each coefficient is returned. The code is available in the paper by Sikorska et al. (2013). We simply took the code and made some minor modifications. The explanation and the motivation can be found in their paper. They call it semi-parallel logistic regressions, hence we named the function sp.logiregs.

#### Value

A two-column matrix with the test statistics (Wald statistic) and their associated p-values (or their loggarithm).

## Author(s)

Initial author Karolina Sikorska in the above reference paper. Modifications by Michail Tsagris.

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

#### References

Karolina Sikorska, Emmanuel Lesaffre, Patrick FJ Groenen and Paul HC Eilers (2013), 14:166. GWAS on your notebook: fast semi-parallel linear and logistic regression for genome-wide association studies. https://bmcbioinformatics.biomedcentral.com/track/pdf/10.1186/1471-2105-14-166.pdf

### See Also

```
logiquant.regs, bic.regs
```

# **Examples**

```
y <- rbinom(200, 1, 0.5)
x <- matrix( rnorm(200 * 30), ncol = 30 )
a <- MXM::sp.logiregs(y, x)</pre>
```

Many simple beta regressions

Many simple beta regressions.

## **Description**

Many simple beta regressions.

## Usage

```
beta.regs(target, dataset, wei = NULL, check = FALSE, logged = FALSE, ncores = 1)
perm.betaregs(target, dataset, wei = NULL, check = FALSE, logged = FALSE,
threshold = 0.05, R = 999, ncores = 1)
wald.betaregs(target, dataset, wei = NULL, check = FALSE, logged = FALSE, ncores = 1)
```

# Arguments

target	The target (dependent) variable. It must be a numerical vector with integers.
dataset	The indendent variable(s). It can be a vector, a matrix or a dataframe with continuous only variables, a data frame with mixed or only categorical variables.
wei	A vector of weights to be used for weighted regression. The default value is NULL. An example where weights are used is surveys when stratified sampling has occured.
check	A boolean variable indicating whether to check for variables with identical values. The default is FALSE.
logged	A boolean variable; it will return the logarithm of the p-value if set to TRUE.
threshold	Threshold (suitable values in $(0, 1)$ ) for assessing p-values significance. Default value is 0.05.
R	The number of permutations, set to 999 by default. There is a trick to avoind doing all permutations. As soon as the number of times the permuted test statistic is more than the observed test statistic is more than 50 (in this example case), the p-value has exceeded the signifiance level (threshold value) and hence the predictor variable is not significant. There is no need to continue do the extra permutations, as a decision has already been made.
ncores	The number of cores to use. The default value is 1.

## **Details**

Many simple beta regressions are fitted.

## Value

A matrix with the test statistic values, their relevant (logged) p-values and the BIC values.

### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

#### References

Ferrari S.L.P. and Cribari-Neto F. (2004). Beta Regression for Modelling Rates and Proportions. Journal of Applied Statistics, 31(7): 799-815.

### See Also

```
beta.mod, testIndBeta, reg.fit, ridge.reg
```

## **Examples**

```
y <- rbeta(80, 5, 3)
x <- matrix( rnorm(80 * 7), ncol = 7)
a1 <- beta.regs(y, x)
a2 <- perm.betaregs(y, x[, 1:4], R = 299)</pre>
```

Many simple quantile regressions using logistic regressions

Many simple quantile regressions using logistic regressions.

### **Description**

Many simple quantile regressions using logistic regressions.

## Usage

```
logiquant.regs(target, dataset, logged = FALSE)
```

#### **Arguments**

target The dependent variable, a numerical vector.

dataset A matrix with the indendent variables.

logged Should the p-values be returned (FALSE) or their logarithm (TRUE)?

### **Details**

Instead of fitting quantile regression models, one for each predictor variable and trying to assess its significance, Redden et al. (2004) proposed a simple singificance test based on logistic regression. Create an indicator variable I where 1 indicates a response value above its median and 0 elsewhere. Since I is binary, perform logistic regression for the predictor and assess its significance using the likelihood ratio test. We perform many logistic regression models since we have many predictors whose univariate association with the response variable we want to test.

### Value

A two-column matrix with the test statistics (likelihood ratio test statistic) and their associated p-values (or their loggarithm).

#### Author(s)

Author: Michail Tsagris.

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

#### References

David T. Redden, Jose R. Fernandez and David B. Allison (2004). A simple significance test for quantile regression. Statistics in Medicine, 23(16): 2587-2597

### See Also

```
bic.regs, sp.logiregs
```

## **Examples**

```
y <- rcauchy(100, 3, 2)
x <- matrix( rnorm(100 * 50), ncol = 50 )
a <- MXM::logiquant.regs(y, x)</pre>
```

Many simple zero inflated Poisson regressions

Many simple zero inflated Poisson regressions.

### **Description**

Many simple zero inflated Poisson regressions.

## Usage

```
zip.regs(target, dataset, wei = NULL, check = FALSE, logged = FALSE, ncores = 1)
perm.zipregs(target, dataset, wei = NULL, check = FALSE, logged = FALSE, R = 999,
threshold = 0.05, ncores = 1)
wald.zipregs(target, dataset, wei = NULL, check = FALSE, logged = FALSE, ncores = 1)
```

### **Arguments**

target	The target (dependent) variable. It must be a numerical vector with integers.
dataset	The indendent variable(s). It can be a vector, a matrix or a dataframe with continuous only variables, a data frame with mixed or only categorical variables.
wei	A vector of weights to be used for weighted regression. The default value is NULL. An example where weights are used is surveys when stratified sampling has occured.
check	A boolean variable indicating whether to cheke for variables with identical values. The defauls is FALSE.
logged	A boolean variable; it will return the logarithm of the pvalue if set to TRUE.
R	The number of permutations, set to 999 by default. There is a trick to avoind doing all permutations. As soon as the number of times the permuted test statistic is more than the observed test statistic is more than 50 (in this example case), the p-value has exceeded the significance level (threshold value) and hence the predictor variable is not significant. There is no need to continue do the extra permutations, as a decision has already been made.
threshold	Threshold (suitable values in $(0, 1)$ ) for assessing p-values significance. Default value is $0.05$ .
ncores	The number of cores to use. The default value is 1.

## **Details**

Many simple zero inflated Poisson regressions are fitted. The permutations based approach may cause some errors sometimes, and this is due to the nature of the distribution and its maximisation process. "nlm" and "optim" are used internally.

## Value

A matrix with the test statistic values, their relevant (logged) p-values and the BIC values.

## Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

## References

Lambert D. (1992). Zero-inflated Poisson regression, with an application to defects in manufacturing. Technometrics, 34(1):1-14.

### See Also

```
zip.mod, testIndZIP, reg.fit, ridge.reg
```

### **Examples**

```
y <- rpois(50, 3)
x <- matrix( rnorm(50 * 7), ncol = 7)
y[1:10] <- 0
a1 <- zip.regs(y, x)
a2 <- perm.zipregs(y, x[, 1:3], R = 299)</pre>
```

## **Description**

Many Wald based tests for logistic and Poisson regressions with continuous predictors.

## Usage

```
wald.logisticregs(y, x, tol = 1e-09, wei = NULL, check = FALSE, logged = FALSE,
ncores = 1)
wald.poissonregs(y, x, tol = 1e-09, wei = NULL, check = FALSE, logged = FALSE,
ncores = 1)
```

### **Arguments**

У	A vector with either 0s and 1 (logistic regression) or discrete data, counts (Poisson regression).
x	A data frame, the predictor variables. If you have no categorical variables, the fucntion will still work but it's better to use the score.glms because it is faster.
tol	The tolerance value to stop the Newton-Raphson iterations. It is set to 1e-09 by default.
wei	A vector of weights to be used for weighted regression. The default value is NULL. An example where weights are used is surveys when stratified sampling has occured.
check	A boolean variable indicating whether to cheke for variables with identical values. The defauls is FALSE.
logged	A boolean variable; it will return the logarithm of the pvalue if set to TRUE.
ncores	How many to cores to useq the default value is 1.

### **Details**

Instead of using R built-in function glm we implemented the newton-Raphson in order to avoid unnecessary calculations. The functions are much faster.

## Value

A matrix with three columns, the test statistic, its associated (**logged**) p-value and the BIC of each model.

### Author(s)

Michail Tsagris

#### References

Draper, N.R. and Smith H. (1988). Applied regression analysis. New York, Wiley, 3rd edition. McCullagh, Peter, and John A. Nelder. Generalized linear models. CRC press, USA, 2nd edition, 1989.

### See Also

```
univregs, perm.univregs
```

## **Examples**

```
## 20 variables, hence 20 univariate regressions are to be fitted
x <- matrix( rnorm(200 * 20), ncol = 20 )
y <- rpois(200, 4)
a <- wald.poissonregs(y, x)
b <- univregs(y, x, test = testIndPois)
cor(exp(a[, 2]), exp(b$pvalue) )</pre>
```

Markov Blanket of a node in a directed graph

Returns the Markov blanket of a node (or variable)

## Description

Returns the Markov blanket of a node (or variable).

### Usage

```
mb(G, node)
```

## **Arguments**

node

G The graph matrix as produced from pc.or or any other algorithm which pro-

duces directed graphs.

A vector with one or more numbers indicating the seleted node(s) (or vari-

able(s)).

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#### **Details**

This is a way to see the network for some given nodes. It is useful if you have many nodes and the whole network is a bit difficult to see clearly. Bear in mind that the values can be extracted with the \$ symbol, i.e. this is an S3 class output.

#### Value

parents The parents of the node of interest.

children The children of the node of interest.

spouses The spouses of the node of interest. These are the other parents of the children

of the node of interest.

relatives Nodes which are connected with the node of interest, but it is not known whether

they are parents or children. The edge between them is undirected.

markov.blanket The Markov blanket of the node of interest. The collection of all the previous.

### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

#### See Also

```
plotnetwork, nei, pc.or
```

## **Examples**

```
# simulate a dataset with continuous data
# simulate a dataset with continuous data
y <- rdag(1000, 10, 0.3)
tru <- y$G
x <- y$x
mod <- pc.con(x)
G <- pc.or(mod)$G
plotnetwork(G)
dev.new()
mb(G, 8)</pre>
```

mases.output-class

Class "mases.output"

## **Description**

Meta analytic SES output object class.

## **Objects from the Class**

Objects can be created by calls of the form new("mases.output", ...).

# **Slots**

```
selectedVars: Object of class "numeric"
selectedVarsOrder: Object of class "numeric"
queues: Object of class "list"
signatures: Object of class "matrix"
hashObject: Object of class "list"
pvalues: Object of class "numeric"
stats: Object of class "numeric"
univ: Object of class "list"
max_k: Object of class "numeric"
threshold: Object of class "numeric"
runtime: Object of class "proc_time"
test: Object of class "character"
```

#### Methods

plot plot(x = "mases.output", mode = "all"): Generic function for plotting the generated pvalues of the mases.output object. Argument mode = "all" for plotting all the pvalues or mode="partial" for partial plotting the first 500 pvalues

# Author(s)

Giorgos Athineou <athineou@csd.uoc.gr>

## See Also

```
ma.ses, ma.mmpc
```

## **Examples**

```
showClass("mases.output")
```

MMPC solution paths for many combinations of hyper-parameters  $MMPC \ solution \ paths \ for \ many \ combinations \ of \ hyper-parameters$ 

# Description

MMPC solution paths for many combinations of hyper-parameters.

### Usage

```
mmpc.path(target, dataset, wei = NULL, max_ks = NULL, alphas = NULL, test = NULL,
user_test = NULL, ncores = 1)
wald.mmpc.path(target, dataset, wei = NULL, max_ks = NULL, alphas = NULL, test = NULL,
user_test = NULL, ncores = 1)
perm.mmpc.path(target, dataset, wei = NULL, max_ks = NULL, alphas = NULL, test = NULL,
user_test = NULL, R = 999, ncores = 1)
```

#### **Arguments**

target The class variable. Provide either a string, an integer, a numeric value, a vector,

a factor, an ordered factor or a Surv object. See also Details.

dataset The dataset; provide either a data frame or a matrix (columns = variables, rows

= samples). Alternatively, provide an ExpressionSet (in which case rows are

samples and columns are features, see bioconductor for details).

wei A vector of weights to be used for weighted regression. The default value is

NULL. An example where weights are used is surveys when stratified sampling

has occured.

max\_ks A vector of possible max\_k values. Can be a number as well, but this does not

really make sense to do. If nothing is given, the values  $\max_{k} = (4,3,2)$  are used

by default.

alphas A vector of possible threshold values. Can be a number as well, but this does

not really make sense to do. If nothing is given, the values (0.1, 0.05, 0.01) are

used by default.

test The conditional independence test to use. Default value is NULL. See also

CondIndTests.

user\_test A user-defined conditional independence test (provide a closure type object).

Default value is NULL. If this is defined, the "test" argument is ignored.

R The number of permutations, set to 999 by default. There is a trick to avoind do-

ing all permutations. As soon as the number of times the permuted test statistic is more than the observed test statistic is more than 50 (if threshold = 0.05 and R = 999), the p-value has exceeded the significance level (threshold value) and hence the predictor variable is not significant. There is no need to continue do

the extra permutations, as a decision has already been made.

ncores How many cores to use. This plays an important role if you have tens of thou-

sands of variables or really large sample sizes and tens of thousands of variables and a regression based test which requires numerical optimisation. In other cases it will not make a difference in the overall time (in fact it can be slower). The parallel computation is used in the first step of the algorithm, where univariate associations are examined, those take place in parallel. We have seen a reduction in time of 50% with 4 cores in comparison to 1 core. Note also, that the amount of reduction is not linear in the number of cores. This argument is used only in the first run of MMPC and for the univariate associations only and the results are stored (hashed). In the enxt runs of MMPC the results are used (cashed) and

so the process is faster.

# **Details**

For different combinations of the hyper-parameters, max\_k and the significance level (threshold or alpha) the MMPC algorith is run.

#### Value

The output of the algorithm is an object of the class 'SESoutput' for SES or 'MMPCoutput' for MMPC including:

bic	A matrix with the BIC values of the final fitted model based on the selected variables identified by each configuration, combination of the hyper-parameters.
size	A matrix with the legnth of the selected variables identified by each configuration of MMPC.
variables	A list containing the variables from each configuration of MMPC
runtime	The run time of the algorithm. A numeric vector. The first element is the user time, the second element is the system time and the third element is the elapsed time.

# Author(s)

Ioannis Tsamardinos, Vincenzo Lagani

R implementation and documentation: Giorgos Athineou <athineou@csd.uoc.gr> Vincenzo Lagani <vlagani@csd.uoc.gr>

# References

Tsamardinos, Brown and Aliferis (2006). The max-min hill-climbing Bayesian network structure learning algorithm. Machine learning, 65(1): 31-78.

# See Also

```
CondIndTests, cv.ses
```

```
set.seed(123)
# simulate a dataset with continuous data
dataset <- matrix(runif(500 * 51, 1, 100), nrow = 500 )
#the target feature is the last column of the dataset as a vector
target <- dataset[, 51]
dataset <- dataset[, -51]

a <- mmpc.path(target, dataset, max_ks = NULL, alphas = NULL, test = NULL,
user_test = NULL, ncores = 1)</pre>
```

```
MMPC.gee.output-class Class "MMPC.gee.output"
```

# **Description**

MMPC.glmm output object class.

# **Objects from the Class**

Objects can be created by calls of the form new("MMPC.gee.output", ...).

## **Slots**

```
selectedVars: Object of class "numeric"
selectedVarsOrder: Object of class "numeric"
hashObject: Object of class "list"
pvalues: Object of class "numeric"
stats: Object of class "numeric"
univ: Object of class "list"
max_k: Object of class "numeric"
threshold: Object of class "numeric"
n.tests: Object of class "numeric"
runtime: Object of class "proc_time"
test: Object of class "character"
se: Object of class "character"
```

## Methods

```
plot plot(x = "MMPC.gee.output", mode = "all"): Generic function for plotting the generated
    pvalues of the MMPC.glmm.output object. Argument mode = "all" for plotting all the pvalues
    or mode="partial" for partial plotting the first 500 pvalues
```

# Author(s)

Giorgos Athineou and Michail Tsagris <mtsagris@uoc.gr>

## See Also

```
MMPC.gee, SES.gee
```

```
showClass("MMPC.gee.output")
```

```
\begin{tabular}{ll} MMPC.glmm.output-class \\ & \textit{Class} \ "MMPC.glmm.output" \\ \end{tabular}
```

# **Description**

MMPC.glmm output object class.

# **Objects from the Class**

Objects can be created by calls of the form new("MMPC.glmm.output", ...).

#### **Slots**

```
selectedVars: Object of class "numeric"
hashObject: Object of class "list"
pvalues: Object of class "numeric"
stats: Object of class "numeric"
univ: Object of class "list"
max_k: Object of class "numeric"
threshold: Object of class "numeric"
n.tests: Object of class "numeric"
runtime: Object of class "proc_time"
test: Object of class "character"
slope: Object of class "logical"
```

### Methods

```
plot plot(x = "MMPC.glmm.output", mode = "all"): Generic function for plotting the generated
    pvalues of the MMPC.glmm.output object. Argument mode = "all" for plotting all the pvalues
    or mode="partial" for partial plotting the first 500 pvalues
```

# Author(s)

Giorgos Athineou <athineou@csd.uoc.gr>

#### See Also

```
MMPC.glmm, SES.glmm
```

```
showClass("MMPC.glmm.output")
```

186 MMPCoutput-class

MMPCoutput-class

Class "MMPCoutput"

# **Description**

MMPC output object class.

# **Objects from the Class**

Objects can be created by calls of the form new("MMPCoutput", ...).

#### **Slots**

```
selectedVars: Object of class "numeric"
selectedVarsOrder: Object of class "numeric"
hashObject: Object of class "list"
pvalues: Object of class "numeric"
stats: Object of class "numeric"
univ: Object of class "list"
max_k: Object of class "numeric"
threshold: Object of class "numeric"
n.tests: Object of class "numeric"
runtime: Object of class "proc_time"
test: Object of class "character"
```

## Methods

```
plot plot(x = "MMPCoutput", mode = "all"): Generic function for plotting the generated pval-
ues of the MMPCoutput object. Argument mode = "all" for plotting all the pvalues or mode="partial"
for partial plotting the first 500 pvalues
```

# Author(s)

Giorgos Athineou <athineou@csd.uoc.gr>

## See Also

```
MMPC, SES
```

```
showClass("MMPCoutput")
```

MXM-internal

Internal MXM Functions

# **Description**

Internal functions of Package MXM

# **Details**

These functions are only for internal usage of the MXM package - NOT to be called by the user.

## **Functions**

```
• InternalSES( ... )
```

- InternalMMPC( ... )
- Internalmases( ... )
- Internalmammpc( ... )
- IdentifyEquivalence( ... )
- IdentifyEquivalence.ma( ... )
- apply\_ideq( ... )
- apply\_ideq.ma( ... )
- compare\_p\_values( ... )
- identifyTheEquivalent( ... )
- identifyTheEquivalent.ma( ... )
- max\_min\_assoc( ... )
- max\_min\_assoc.ma( ... )
- min\_assoc( ... )
- min\_assoc.ma( ... )
- univariateScore( ... )
- univariateScore.ma( ... )
- condi.perm( ... )
- InternalSES.glmm( ... )
- InternalMMPC.glmm( ... )
- IdentifyEquivalence.glmm( ... )
- $\bullet \ apply\_ideq.glmm(\ ...\ )$
- identifyTheEquivalent.glmm( ... )
- max\_min\_assoc.glmm( ... )
- min\_assoc.glmm( ... )
- univariateScore.glmm( ... )

```
• is.sepset( ... )
• lm.fsreg_2( ... )
• glm.fsreg_2( ... )
• dag_to_eg( ... )
• nchoosek( ... )
• R0( ... )
• R1(...)
• R2( ... )
• R3(...)
• is.sepset( ... )
• regbeta( ... )
• regbetawei( ... )
• betamle.wei( ... )
• regzip( ... )
• regzipawei( ... )
• zipmle.wei( ... )
• zipwei( ... )
• bic.betafsreg( ... )
• bic.zipfsreg( ... )
• beta.fsreg( ... )
• zip.fsreg( ... )
• beta.bsreg( ... )
• zip.bsreg( ... )
• iamb.betabs( ... )
• iamb.zipbs( ... )
• iamb.glmbs( ... )
• internaliamb.binombs( ... )
• internaliamb.poisbs( ... )
• internaliamb.lmbs( ... )
• InternalMMPC.glmm( ... )
• InternalSES.glmm( ... )
• InternalSES( ... )
• InternalMMPC( ... )
```

univariateScore( ... )
perm.univariateScore( ... )
max\_min\_assoc( ... )
min\_assoc( ... )

```
• nchoosek( ... )
• Internalmases( ... )
• compare_p_values( ... )
• perm.Internalmmpc
• wald.Internalmmpc
· wald.Internalses
• perm.IdentifyEquivalence( ... )
• perm.identifyTheEquivalent( ... )
• perm.apply_ideq( ... )
• IdentifyEquivalence( ... )
• apply_ideq( ... )
• identifyTheEquivalent( ... )
• cvses.par( ... )
• cvmmpc.par( ... )
• cvwaldses.par( ... )
• cvwaldmmpc.par( ... )
• cvpermses.par( ... )
• cvpermmpc.par( ... )
• wald.univariateScore( ... )
• univariateScore.ma( ... )
• IdentifyEquivalence.ma( ... )
• identifyTheEquivalent.ma( ... )
• apply_ideq.ma( ... )
• max_min_assoc.ma( ... )
• min_assoc.ma( ... )
• fs.reg_2( ... )
• gammafsreg_2( ... )
• beta.fsreg_2( ... )
• zip.fsreg_2( ... )
• internaliamb.zipbs( ... )
• internaliamb.betabs( ... )
• iamb.gammabs( ... )
• iamb.normlogbs( ... )
• internaliamb.gammabs( ... )
```

• internaliamb.normlogbs( ... )

bic.tobit.fsreg( ... )iamb.tobitbs( ... )

```
• ebic.fbed.beta( ... )
• ebic.fbed.cr( ... )
• ebic.fbed.glm( ... )
• ebic.fbed.lm( ... )
• ebic.fbed.mmreg( ... )
• ebic.fbed.multinom( ... )
• ebic.fbed.nb( ... )
• ebic.fbed.ordinal( ... )
• ebic.fbed.tobit( ... )
• ebic.fbed.wr( ... )
• ebic.fbed.zip( ... )
• ebic.beta.bsreg( ... )
• ebic.cr.bsreg( ... )
• ebic.glm.bsreg( ... )
• ebic.lm.bsreg( ... )
• ebic.mm.bsreg( ... )
• ebic.multinom.bsreg( ... )
• ebic.ordinal.bsreg( ... )
• ebic.tobit.bsreg( ... )
• ebic.wr.bsreg( ... )
• ebic.zip.bsreg( ... )
• cat_condis( ... )
• pearson_condis( ... )
• pearson_condis.rob( ... )
• disctor_condis( ... )
• comb_condis( ... )
• fbed.glmm( ... )
• fbed.lmm( ... )
• ebic.fbed.glmm( ... )
• ebic.fbed.lmm( ... )
• lmm.bsreg( ... )
• clogit.fsreg( ... )
• clogit.fsreg_2( ... )
• bic.clogit.fsreg( ... )
• quasibinom.fsreg( ... )
```

• quasipois.fsreg( ... )

• internaliamb.tobitbs( ... )

- quasibinom.fsreg\_2( ... )
- quasipois.fsreg\_2( ... )
- fbed.geeglm( ... )
- fbed.geeglm.reps( ... )
- fbed.ordgee( ... )
- internaliamb.mmbs( ... )
- iamb.gammabs( ... )
- iamb.normlogbs( ... )
- internaliamb.gammabs( ... )
- internaliamb.normlogbs( ... )
- bic.wr.fsreg( ... )
- wr.fsreg( ... )
- wr.fsreg\_2( ... )
- ebicScore( ... )
- fbed.glmm.reps( ... )
- fbed.lmm.reps( ... )
- ebic.fbed.lmm.reps( ... )
- ebic.fbed.glmm.reps( ... )
- ebic.glmm.reps.bsreg( ... )
- fbed.ordgee.reps( ... )
- fbed.geelm( ... )
- fbed.geelm.reps( ... )
- univariateScore.gee( ... )
- InternalMMPC.gee( .. )
- InternalSES.gee( .. )
- max\_min\_assoc.gee( ... )
- min\_assoc.gee( ... )
- IdentifyEquivalence.gee( ... )
- identifyTheEquivalent.gee( ... )
- univariateScore.timeclass( ... )
- InternalMMPC.timeclass( ... )
- gomp2( ... )
- kfbed.reg( ... )
- kfbed.glmm.reg( ... )
- kfbed.gee.reg( ... )
- bs.g2( ... )
- fbed.g2( ... )

```
\bullet \ \ fbed.glmm.ordinal(\ ...\ )
```

- fbed.glmm.ordinal.reps( ... )
- ebic.fbed.glmm.ordinal( ... )
- ebic.fbed.glmm.ordinal.reps( ... )
- glmm.ordinal.bsreg( ... )
- glmm.ordinal.reps.bsreg( ... )
- ebic.glmm.reps.bsreg( ... )
- ebic.glmm.ordinal.reps.bsreg( ... )
- big.model( ... )
- big.fbed.g2( ... )
- big.bs.g2( ... )
- clogit.cv.ses( ... )
- bsreg.big( ... )
- fbed.glmm.cr( ... )
- ebic.fbed.glmm.cr( ... )
- glmm.cr.bsreg( ... )
- ebic.glmm.cr.bsreg( ... )
- test.maker( ... )
- ebic.model( ... )
- fbed.lr( ... )
- fbed.ebic( ... )
- spml.bsreg( ... )
- bic.llr.fsreg( ... )
- ebic.llr.bsreg( ... )
- llr.bsreg( ... )
- beta.reg( ... )
- ebic.spml.bsreg( ... )
- regzinb( ... )
- zinb.mle( ... )
- fbed.glmm.nb( ... )
- fbed.glmm.nb.reps( ... )
- glmm.nb.bsreg( ... )
- glmm.nb.reps.bsreg( ... )

Neighbours of nodes in an undirected graph

Returns the node(s) and their neighbour(s), if there are any.

# **Description**

Returns the node(s) and their neighbour(s) of one or more nodes (if there are any).

## Usage

```
nei(G, node)
```

# **Arguments**

G The adjacency matrix of an undirected graph as produced by mmhc.skel, pc.skel

or any other algorithm.

node A vector with one or more numbers indicating the seleted node(s) (or vari-

able(s)).

## **Details**

This is a way to see the network for some given nodes. It is useful if you have many nodes and the whole network is a bit difficult to see clearly.

#### Value

A list object called "geit" containing the neighbours of the node(s). If there are no neighbours a message appears and no plot is presented. If the "graph" argument is set to TRUE and there are neighbours, a plot will appear.

Bear in mind that the values can be extracted with the \$ symbol, i.e. this is an S3 class output.

# Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

#### See Also

```
mmhc.skel, SES, MMPC
```

```
# simulate a dataset with continuous data
set.seed(1234)
dataset <- matrix(runif(500 * 20, 1, 100), nrow = 500 )
G <- pc.con(dataset)$G
plotnetwork(G)</pre>
```

```
dev.new()
nei( G, c(3, 4) )
nei( G, c(1, 3) )
```

Network construction using the partial correlation based forward regression or FBED Network construction using the partial correlation based forward regression of FBED

# Description

Network construction using the partial correlation based forward regression or FBED.

# Usage

```
corfs.network(x, threshold = 0.05, tolb = 2, tolr = 0.02, stopping = "BIC",
symmetry = TRUE, nc = 1)
corfbed.network(x, threshold = 0.05, symmetry = TRUE, nc = 1)
```

# **Arguments**

iguments	
X	A matrix with continuous data.
threshold	Threshold (suitable values in $(0, 1)$ ) for assessing p-values significance. Default value is 0.05.
tolb	The difference in the BIC bewtween two successive values. By default this is is set to 2. If for example, the BIC difference between two succesive models is less than 2, the process stops and the last variable, even though significant does not enter the model.
tolr	The difference in the adjusted $R^2$ bewtween two successive values. By default this is set to 0.02. If for example, the difference between the adjusted $R^2$ of two succesive models is less than 0.02, the process stops and the last variable, even though significant does not enter the model.
stopping	The stopping rule. The "BIC" is the default value, but can change to "ar2" and in this case the adjusted $\mathbb{R}^2$ is used. If you want both of these criteria to be satisified, type "BICR2".
symmetry	In order for an edge to be added, a statistical relationship must have been found from both directions. If you want this symmetry correction to take place, leave this boolean variable to TRUE. If you set it to FALSE, then if a relationship between Y and X is detected but not between X and Y, the edge is still added.
nc	How many cores to use. This plays an important role if you have many variables, say thousands or so. You can try with nc = 1 and with nc = 4 for example to see the differences. If you have a multicore machine, this is a must option. There was an extra argument for plotting the skeleton but it does not work with the current visualisation packages, hence we removed the argument. Use plotnetwork to plot the skeleton.

#### **Details**

In the MMHC algorithm (see mmhc.skel), the MMPC or SES algorithms are run for every variable. Hence, one can use forward regression for each variable and this is what we are doing here. Partial correlation forward regression is very efficient, since only correlations are being calculated.

#### Value

# A list including:

runtime	The run time of the algorithm. A numeric vector. The first element is the user time, the second element is the system time and the third element is the elapsed time.
density	The number of edges divided by the total possible number of edges, that is $\#edges / n(n-1)/2$ , where $n$ is the number of variables.
info	Some summary statistics about the edges, minimum, maximum, mean, median number of edges.
ntests	The number of tests MMPC (or SES) performed at each variable.
G	The adjancency matrix. A value of 1 in $G[i, j]$ appears in $G[j, i]$ also, indicating that i and j have an edge between them.

Bear in mind that the values can be extracted with the \$ symbol, i.e. this is an S3 class output.

#### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

#### References

Sanford Weisberg (2014). Applied Linear Regression. Hoboken NJ: John Wiley, 4th edition.

Draper N.R. and Smith H. (1988). Applied regression analysis. New York, Wiley, 3rd edition.

Tsamardinos, Brown and Aliferis (2006). The max-min hill-climbing Bayesian network structure learning algorithm. Machine learning, 65(1), 31-78.

Borboudakis G. and Tsamardinos I. (2019). Forward-backward selection with early dropping. Journal of Machine Learning Research, 20(8): 1-39.

# See Also

```
mmhc.skel, pc.skel
```

```
# simulate a dataset with continuous data
dataset <- matrix(runif(400 * 20, 1, 100), ncol = 20 )
a1 <- mmhc.skel(dataset, max_k = 3, threshold = 0.05, test = "testIndFisher",
nc = 1)
a2 <- corfs.network(dataset, threshold = 0.05, tolb = 2, tolr = 0.02, stopping = "BIC",
symmetry = TRUE, nc = 1)</pre>
```

a1\$runtime a2\$runtime

Orientation rules for the PC algorithm

The orientations part of the PC algorithm.

# **Description**

The function takes the outcome of the PC algorithm, as produced by pc.skel or pc.con and performes the 4 orientation rules. A graph is also possible to visualize.

# Usage

pc.or(mod)

#### **Arguments**

mod

An object with the results of the PC algorithm, as produced by pc.skel or pc.con. There was an extra argument for plotting the skeleton but it does not work with the current visualisation packages, hence we removed the argument. Use plotnetwork to plot the skeleton.

# **Details**

After having calculated the skeleton of the PC algorithm one may wants to perform orientations, leading to causal relationships. The rules as stated in Spirtes, Glymour and Scheines (2001) are

- 1. **Rule 0**. For each triple of vertices X, Y, Z such that the pair X, Y and the pair Y, Z are each adjacent in C but the pair X, Z are not adjacent in C, orient X Y Z as X -> Y <- Z if and only if Y is not in Sepset(X, Z).
- 2. **Rule 1**. If A -> B, B and C are adjacent, A and C are not adjacent, and there is no arrowhead at B, then orient B C as B -> C.
- 3. **Rule 2**. If there is a directed path from A to B, and an edge between A and B, then orient A B as A -> B.
- 4. **Rule 3**. If A -> B <- C, A D C, A and C are not adjacent, and D B, then orient D B as D -> B.

The first rule is applied once. Rules 2-4 are applied repeatedly until no more edges can be oriented. If when a rule is applied and a cycle is detected, the rule is cancelled. Also, when applying Rules 1-3 we try to avoid the creation of new v-structures  $(X \rightarrow Y \leftarrow Z)$ .

#### Value

A list including:

Gini The initial adjacency matrix, no orientations. This is the matrix produced by

pc.skel or pc.con.

G The final adjaceny matrix with the orientations. If G[i, j] = 2 then G[j, i] = 3.

This means that there is an arrow from node i to node j. If G[i, j] = G[j, i] = 0; there is no edge between nodes i and j. If G[i, j] = G[j, i] = 1; there is an

(undirected) edge between nodes i and j.

runtime The run time of the algorithm. A numeric vector. The first element is the user

time, the second element is the system time and the third element is the elapsed

time.

#### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

#### References

Spirtes P., Glymour C. and Scheines R. (2001). Causation, Prediction, and Search. The MIT Press, Cambridge, MA, USA, 3nd edition.

Zhang, Jiji. (2008). On the completeness of orientation rules for causal discovery in the presence of latent confounders and selection bias. Artificial Intelligence 172(16): 1873–1896.

Tsagris M. (2019). Bayesian network learning with the PC algorithm: an improved and correct variation. Applied Artificial Intelligence 33(2): 101-123.

#### See Also

```
pc.con, pc.skel, mmhc.skel, is.dag, mb
```

```
# simulate a dataset with continuous data
y <- rdag2(2000, p = 20, nei = 3)
ind <- sample(1:20, 20)
tru <- y$G[ind, ind]
x <- y$x[, ind]
mod <- pc.con(x)
mod$runtime

plotnetwork(tru)
b <- pc.or(mod)
plotnetwork( dag2eg(tru) ) ## essential graph
plotnetwork(b$G)</pre>
```

Partial correlation between two variables

Partial correlation

# **Description**

Partial correlation between two variables when a correlation matrix is given.

# Usage

```
partialcor(R, indx, indy, indz, n)
```

# **Arguments**

R	A correlation matrix.
indx	The index of the first variable whose conditional correlation is to estimated.
indy	The index of the second variable whose conditional correlation is to estimated.
indz	The index of the conditioning variables.
n	The sample size of the data from which the correlation matrix was computed.

## **Details**

Given a correlation matrix the function will calculate the partial correlation between variables indx and indy conditioning on variable(s) indz. The logarithm of the p-value is also returned.

## Value

The partial correlation coefficient and the logged p-value for the test of no association.

# Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

## See Also

```
testIndFisher,\ testIndSpearman,\ permcor,\ pc.\ con
```

```
r <- cor( iris[, 1:4] )
partialcor(r, 1, 2, 0, 150)
r[1, 2] ## the same as above

y <- as.vector( iris[, 1] )
x <- as.vector( iris[, 2] )
z <- as.vector( iris[, 3] )</pre>
```

```
e1 <- resid( lm(y ~ z) )
e2 <- resid( lm(x ~ z) )
cor(e1, e2)
partialcor(r, 1, 2, 3, 150)
```

Permutation based p-value for the Pearson correlation coefficient Permutation based p-value for the Pearson correlation coefficient

## **Description**

The main task of this test is to provide a p-value PVALUE for the null hypothesis: feature 'X' is independent from 'TARGET' given a conditioning set CS.

## Usage

```
permcor(x1, x2, R = 999)
permcorrels(y, x, R = 999)
```

## Arguments

x1	A numerical vector.
x2	A numerical vector of the same size as x1.
у	A vector whose length is equal to the number of rows of x.
X	This is a matrix with many variables.
R	The number of permutations to be conducted; set to 999 by default.

#### **Details**

This is a computational non parametric (permutation based) correlation coefficient test and is advised to be used when a small sample size is available. If you want to use the Spearman correlation instead, simply provide the ranks of x or of y and x.

#### Value

For the case of "permcor" a vector consisting of two values, the Pearson correlation and the permutation based p-value. For the "permcorrels" a vector with three values, the Pearson correlation, the test statistic value and the permutation based logged p-value.

## Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

# References

Legendre Pierre (2000). Comparison of permutation methods for the partial correlation and partial Mantel tests. Journal of Statistical Computation and Simulation 67(1):37-73.

## See Also

```
pc.skel, testIndSpearman, testIndFisher, SES, CondIndTests
```

# **Examples**

```
MXM::permcor(iris[, 1], iris[, 2], R = 999)
x <- matrix( rnorm(50 * 100), ncol = 100)
a <- permcorrels(iris[1:50, 1], x)</pre>
```

```
Plot of longitudinal data
```

Plot of longitudinal data

# Description

Plot of longitudinal data.

# Usage

# **Arguments**

target	A numerical vector with the longitudinal data.
tp	The time points. It can either be a vector with length either equal to the number of time points or equal to the legnth of the target.
id	A numerical vector specifying the subjects. It can either be a vector with length either equal to the number of subjects or equal to the legnth of the target.
type	This is a graphical parameter. You can have lines "l" everywhere or lines with points at each time point "p".
ylab	This is a graphical parameter. The label on the y axis.
xlab	This is a graphical parameter. The label on the x axis.
col	This is a graphical parameter. The color of the lines.
lwd	This is a graphical parameter. The thickness of the lines.
lty	This is a graphical parameter. The type of line, e.g. dashed, dotted, etc.
pch	This is a graphical parameter. If the type is "b", then you can specify if you want different signs, for example circles, crosses, diamonds etc.
main	This is a graphical parameter. The title of the graph.

## **Details**

The data must be longitudinal (the same subject measured multiple times at different time points) and for one variable only. For the graphical parameters see plot or par.

## Value

A plot with the longitudinal data over time.

#### Author(s)

Michail Tsagris

R implementation and documentation: Giorgos Athineou <athineou@csd.uoc.gr> Michail Tsagris <mtsagris@uoc.gr>

#### References

Tsamardinos I., Aliferis C. F. and Statnikov, A. (2003). Time and sample efficient discovery of Markov blankets and direct causal relations. In Proceedings of the 9th ACM SIGKDD international conference on Knowledge discovery and data mining (pp. 673-678).

## See Also

```
testIndGLMMReg, SES.glmm
```

# **Examples**

```
y <- rnorm(70)
Days <- rep(1:7, each = 10)
id <- rep(1:10, 7)
tc.plot(y, Days, id)
tc.plot(y, Days, id, type = "b")</pre>
```

Probability residual of ordinal logistic regreession

Probability residual of ordinal logistic regreession

## **Description**

Probability residual of ordinal logistic regreession.

## Usage

```
ord.resid(y, est)
```

## **Arguments**

y An ordered factor variable or a numerical vector.

est A matrix with the fitted values of an ordinal logistic regression model.

## **Details**

The probability residual of an ordinal logistic regression model is calculated (Li and Shepherd, 2012). It is a vector, irrespective of how many categories there are.

## Value

A vector with the probability residuals.

## Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

# References

Li C., & Shepherd B. E. (2012). A new residual for ordinal outcomes. Biometrika, 99(2): 473-480.

## See Also

```
testIndOrdinal, ordinal.reg
```

# **Examples**

```
library(MASS)
y <- factor( rbinom(400, 3, 0.6), ordered = TRUE )
x <- rnorm(400)
mod <- MASS::polr(y ~ x)
res <- ord.resid(y, mod$fitted.values)</pre>
```

```
Read big data or a big.matrix object
```

Read big data or a big.matrix object

# **Description**

Read big data or a big.matrix object.

## Usage

```
read.big.data(path, sep = ",", header = FALSE)
```

# Arguments

path The path where the big.matrix object is.

sep A field delimiter, for example " " (tab separated) or "," (comma separated).

header If there are column names, then this should be TRUE.

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#### **Details**

The data (matrix) which will be read and compressed into a big.matrix object must be of type "numeric". We tested it and it works with "integer" as well. But, in general, bear in mind that only matrices will be read. We have not tested with data.frame for example. Woever, in the help page of "bigmemory" this is mentioned: Any non-numeric entry will be ignored and replaced with NA, so reading something that traditionally would be a data.frame won't cause an error. A warning is issued. In all cases, the object size is always 696 bytes!

#### Value

A big.matrix object.

# Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>. For more information see the "bigmemory" package.

#### See Also

```
big.gomp
```

# **Examples**

```
## Not run:
dataset <- matrix( runif(100 * 50, 1, 100), ncol = 50 )
write.csv(dataset, "dataset.csv", sep = ",")
a <- read.big.data("dataset.csv", header = TRUE)
## End(Not run)</pre>
```

Regression modeler

Generic regression modelling function

# **Description**

Generic regression modelling function.

## Usage

```
modeler(target, dataset = NULL, test = "testIndFisher")
```

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#### **Arguments**

The target (dependent) variable. It can be a numerical variable, factor, ordinal

factor, percentages, or time to event.

dataset The predictor variable(s). It can be a vector, a matrix with continuous only

variables. If there are no predictor variables leave this NULL.

test Unlike reg.fit this accepts the test. The test argument is exactly like in all

feature selection methods. This function accepts the following: "testIndReg", "testIndPois", "testIndNB", "testIndLogistic", "testIndMMReg", "testIndRQ",

"testIndBinom", "censIndCR", "censIndWR", "censIndLLR", "testIndBeta", "testIndGamma,

"testIndNormLog", "testIndTobit", "testIndQPois", "testIndQBinom", "testInd-

Fisher", "testIndMultinom" and "testIndOrdinal".

#### **Details**

This is a generic regression function designed for continuous predictor variables only. It was useful for me so I decided to epxort it.

#### Value

# A list including:

mod The fitted model.

dev The deviance. For some models though ("testIndMMReg", "testIndRQ", "censIndCR",

"censIndWR", "testIndTobit", "testIndBeta", "testIndNB", ""testIndQPois", "testIndQBi-

nom") this contains twice the log-likelihood.

bic The BIC of the model. This is NA for the "testIndQPois" and "testIndQBinom"

because they are quasi likhelidood models and hence have no BIC.

res The residuals of the fitted model.

## Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

#### References

Almost the same as in CondIndTests.

# See Also

```
reg.fit, fbedreg.bic, mmpc.model, ridge.reg
```

```
#simulate a dataset with continuous data
dataset <- matrix(runif(100 * 5, 1, 100), nrow = 100 )
#the target feature is the last column of the dataset as a vector
target <- dataset[, 1]</pre>
```

```
dataset <- dataset[, -1]
a <- modeler(target, dataset)</pre>
```

Regression models based on SES and MMPC outputs

Regression model(s) obtained from SES or MMPC

# **Description**

One or more regression models obtained from SES or MMPC, are returned.

# Usage

```
ses.model(target, dataset, wei = NULL, sesObject, nsignat = 1, test = NULL)
mmpc.model(target, dataset, wei = NULL, mmpcObject, test = NULL)
waldses.model(target, dataset, wei = NULL, wald.sesObject, nsignat = 1, test = NULL)
waldmmpc.model(target, dataset, wei = NULL, wald.mmpcObject, test = NULL)
```

## **Arguments**

target A numeric vector containing the values of the target variable. If the values are

proportions or percentages, i.e. strictly within 0 and 1 they are mapped into R using log(target/(1 - target)). It can also discrete data, binary data (as factor), nominal or ordinal data (as factor). In contrast to SES, no position of the target variable in the detaset is accepted. The target must be a numerical vector.

variable in the dataset is accepted. The target must be a numerical vector.

dataset A numeric matrix or data frame containing the variables. Rows are samples and

columns are features. If you have categorical variables, this should be a data

frame.

wei A vector of weights to be used for weighted regression. The default value is

NULL. An example where weights are used is surveys when stratified sampling

has occured.

sesObject An object with the results of a SES run.

mmpcObject An object with the results of an MMPC run.

wald.sesObject An object with the results of a wald.ses run.

wald.mmpcObject

An object with the results of an wald.mmpc run.

nsignat How many signatures to use. If nsignat = 1 (default value) the first set of vari-

ables will be used for the model. If you want more, then specify the nubmer of signatures you want. If you want the models based on all signatures, specify "all". If you put a number which is higher than the number of signatures, all

models will be returned.

test If you know the test used in SES put it here, otherwise leave it NULL. It will

take this information from the SEs object. If you used a robust version of a test

(wherever possible), robust model(s) will be created.

#### **Details**

This command is useful if you want to see all models and check for example their fitting ability, MSE in linear models for example.

#### Value

A list including:

mod Depending on the number of signatures requested, one or models will be re-

turned.

signature A matrix (or just one vector if one signature only) with the variables of each

signature, along with the BIC of the corresponding regression model.

#### Author(s)

Michail Tsagris

R implementation and documentation: Giorgos Athineou <athineou@csd.uoc.gr> and Michail Tsagris <mtsagris@uoc.gr>

#### References

Aitchison J. (1986). The Statistical Analysis of Compositional Data, Chapman & Hall; reprinted in 2003, with additional material, by The Blackburn Press.

Cox D.R. (1972). Regression models and life-tables. J. R. Stat. Soc., 34, 187-220.

Draper, N.R. and Smith H. (1988). Applied regression analysis. New York, Wiley, 3rd edition.

Ferrari S.L.P. and Cribari-Neto F. (2004). Beta Regression for Modelling Rates and Proportions. Journal of Applied Statistics, 31(7): 799-815.

Gutenbrunner C., Jureckova J., Koenker R. and Portnoy S. (1993). Tests of Linear Hypothesis based on Regression Rank Scores, Journal of NonParametric Statistics 2, 307-331.

Joseph M.H. (2011). Negative Binomial Regression. Cambridge University Press, 2nd edition.

Koenker R.W. (2005). Quantile Regression, Cambridge University Press.

Lagani V., Kortas G. and Tsamardinos I. (2013). Biomarker signature identification in "omics" with multiclass outcome. Computational and Structural Biotechnology Journal, 6(7): 1-7.

Lagani V. and Tsamardinos I. (2010). Structure-based variable selection for survival data. Bioinformatics Journal 16(15): 1887-1894.

Lambert, Diane (1992). Zero-inflated Poisson regression, with an application to defects in manufacturing. Technometrics 34(1)1: 1-14.

Mardia K.V., Kent J.T. and Bibby J.M. (1979). Multivariate Analysis, Academic Press, New York, USA.

Maronna R.D. Yohai M.V. (2006). Robust Statistics, Theory and Methods. Wiley.

McCullagh P., and Nelder J.A. (1989). Generalized linear models. CRC press, USA, 2nd edition.

# See Also

```
SES, MMPC, cv.ses, cv.mmpc
```

## **Examples**

```
# simulate a dataset with continuous data
dataset <- matrix( runif(500 * 20, 1, 20), nrow = 500 )
#the target feature is the last column of the dataset as a vector
target <- dataset[, 20]
dataset <- dataset[, -20]
sesObject <- SES(target , dataset , max_k=3 , threshold = 0.05)
ses.model(target, dataset, sesObject = sesObject, nsignat = 1, test = NULL)
ses.model(target, dataset, sesObject = sesObject, nsignat = 40, test = NULL)
mmpcObject <- MMPC(target, dataset, max_k=3, threshold = 0.05)
mmpc.model(target, dataset, mmpcObject = mmpcObject, test = NULL)</pre>
```

Regression models based on SES.timeclass and MMPC.timeclass outputs  $Regression \ model(s) \ obtained \ from \ SES.timeclass \ or \ MMPC.timeclass$ 

# Description

One or more regression models obtained from SES.timeclass or MMPC.timeclass, are returned.

## Usage

```
mmpc.timeclass.model(target, dataset, id, reps, wei = NULL, mmpctimeclass.Object)
ses.timeclass.model(target, dataset, id, reps, wei = NULL, sestimeclass.Object,
nsignat = 1)
```

# Arguments

sestimeclass.Object

target	The class variable. Provide a vector or a factor with discrete numbers indicating the class. Its length is equal to the number of rows of the dataset.
dataset	The dataset; provide a matrix. Currently, only continuous datasets are supported. The dataset contains longitudinal data, where each column is a variable. The repeated measurements are the samples.
id	A numeric vector containing the subjects or groups. Its length is equal to the number of rows of the dataset.
reps	A numeric vector containing the time points of the subjects. Its length is equal to the number of rows of the dataset.
wei	A vector of weights to be used for weighted regression. The default value is NULL.
mmpctimeclass.Object	
	An object with the results of an MMPC.timeclass run.

An object with the results of a SES.timeclass run.

nsignat How many signatures to use. If nsignat = 1 (defa

How many signatures to use. If nsignat = 1 (default value) the first set of variables will be used for the model. If you want more, then specify the nubmer of signatures you want. If you want the models based on all signatures, specify "all". If you put a number which is higher than the number of signatures, all models will be returned.

#### **Details**

This command is useful if you want to see all models and check for example their fitting ability.

#### Value

A list including:

mod Depending on the number of signatures requested, one or models will be re-

turned.

signature A matrix (or just one vector if one signature only) with the variables of each

signature, along with the BIC of the corresponding regression model.

# Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

#### References

Tsagris, M., Lagani, V., & Tsamardinos, I. (2018). Feature selection for high-dimensional glmm data. BMC bioinformatics, 19(1), 17.

McCullagh P., and Nelder J.A. (1989). Generalized linear models. CRC press, USA, 2nd edition.

## See Also

```
MMPC.timeclass
```

# **Examples**

```
## assume these are longitudinal data, each column is a variable (or feature)
dataset <- matrix( rnorm(400 * 50), ncol = 50 )
id <- rep(1:80, each = 5)  ## 80 subjects
reps <- rep( seq(4, 12, by = 2), 80)  ## 5 time points for each subject
## dataset contains are the regression coefficients of each subject's values on the
## reps (which is assumed to be time in this example)
target <- rep(0:1, each = 200)
a <- MMPC.timeclass(target, reps, id, dataset)
mmpc.timeclass.model(target, dataset, id, reps, mmpctimeclass.Object = a)</pre>
```

Regression models fitting

Regression modelling

# Description

Generic regression modelling function.

### Usage

```
reg.fit(y, dataset, event = NULL, reps = NULL, group = NULL, slopes = FALSE,
reml = FALSE, model = NULL, wei = NULL, xnew = NULL)
```

# **Arguments** y

dataset

The target (dependent) variable. It can be a numerical variable, factor, ordinal factor, percentages, matrix, or time to event. If the values are proportions or percentages, i.e. strictly within 0 and 1 they are mapped into R using log( target/(1 - target)). If they are compositional data the additive log-ratio (multivariate logit) transformation is aplied beforehand. If the model is "clogit" this must be a matrix with two columns. The first column must be 0 and 1, standing for 0 = control and 1 = case. The second column is the id of the patients. A numerical variable, for example c(1,2,3,4,5,6,7,1,2,3,4,5,6,7).

The indendent variable(s). It can be a vector, a matrix or a dataframe with con-

tinuous only variables, a data frame with mixed or only categorical variables.

event This is NULL unless you have time to event data (survival regression).

This is NULL unless you have time measurements (longitudinal data).

group This is NULL unless you have grouped (or clustered) data or longitudinal data

(is the latter case the arugment reps is required).

slopes This is for the longitudinal data only, TRUE or FALSE. Should random slopes

e added or not?

reml This is for the longitudinal or grouped data only, TRUE or FALSE. If TRUE,

REML will be used, otherwise ML will be used.

model The type of model you want to use. It can be specified by the user or left

NULL, if other correct arguments have been passed. Poissible values (apart from NULL) are: "gaussian" (default), "binary", "binomial", "multinomial", "poisson", "ordinal", "gamma", "normlog", "tobit", "cox", "weibull", "exponential", "zip", "beta", "median", "negbin", "longitudinal", "grouped", "qpois" and "qbinom". The "zip" means that the zero part is constant, the variables are not associated with the excessive zeros. The value "grouped" refers to grouped data, but this does not have to be given if the argument "group" is given, but not the argument "reps. The "binomial" is when you have the number of successes and also the number of trials. "MM" stands for robust regression using MM estima-

tion and "clogit" stands for conditional logistic regression.

wei A vector of weights to be used for weighted regression. The default value is

NULL. An example where weights are used is surveys when stratified sampling

has occured.

xnew If you have new data whose target values you want to predict put it here, other-

wise leave it blank.

#### **Details**

This is a generic regression function, which offers prediction as well. It is important that you pass the arguments with their names, for example if you have time to event data, write "event = ..." and not just put your event variable. This will avoid confusion. For the mixed models you need to specify the relevant arguments, "slopes", "reps", "reml" and "group"

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## Value

A list including:

mod The fitted model.

pred If you have new data the predicted values of the target (dependent) variable.

# Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

## References

Almost the same as in CondIndTests.

## See Also

```
modeler, fbedreg.bic, mmpc.model, ridge.reg
```

# **Examples**

```
#simulate a dataset with continuous data
dataset <- matrix(runif(100 * 5, 1, 100), nrow = 100 )
#the target feature is the last column of the dataset as a vector
target <- dataset[, 1]
dataset <- dataset[, -1]
a <- reg.fit(target, dataset)</pre>
```

Ridge regression

Ridge regression

# **Description**

Regularisation via ridge regression is performed.

## Usage

```
ridge.reg(target, dataset, lambda, B = 1, newdata = NULL)
```

# **Arguments**

target A numeric vector containing the values of the target variable. If the values are

proportions or percentages, i.e. strictly within 0 and 1 they are mapped into R

using log( target/(1 - target) ).

dataset A numeric matrix containing the variables. Rows are samples and columns are

features.

lambda The value of the regularisation parameter  $\lambda$ .

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В	Number of bootstraps. If $B = 1$ no bootstrap is performed and no standard error

for the regression coefficients is returned.

otherwise, leave it NULL.

# **Details**

There is also the lm.ridge command in MASS library if you are interested in ridge regression.

## Value

# A list including:

beta	The regression coefficients if no bootstrap is performed. If bootstrap is performed their standard error appears as well.
seb	The standard error of the regression coefficients. If bootstrap is performed their bootstrap estimated standard error appears.
est	The fitted values if no new data are available. If you have used new data these will be the predicted target values.

## Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

## References

Hoerl A.E. and R.W. Kennard (1970). Ridge regression: Biased estimation for nonorthogonal problems. Technometrics, 12(1): 55-67.

Brown P. J. (1994). Measurement, Regression and Calibration. Oxford Science Publications.

#### See Also

```
ridgereg.cv
```

```
#simulate a dataset with continuous data
dataset <- matrix(runif(100 * 30, 1, 100), nrow = 100 )
#the target feature is the last column of the dataset as a vector
target <- dataset[, 10]
dataset <- dataset[, -10]
a1 <- ridge.reg(target, dataset, lambda = 0.5, B = 1, newdata = NULL)
a2 <- ridge.reg(target, dataset, lambda = 0.5, B = 100, newdata = NULL)</pre>
```

Ridge regression coefficients plot Ridge regression

# Description

A plot of the regularised parameters is shown.

## Usage

```
ridge.plot(target, dataset, lambda = seq(0, 5, by = 0.1))
```

# **Arguments**

target A numeric vector containing the values of the target variable. If the values are

proportions or percentages, i.e. strictly within 0 and 1 they are mapped into R

using log( target/(1 - target) ). In any case, they must be continuous only.

dataset A numeric matrix containing the continuous variables. Rows are samples and

columns are features.

lambda A grid of values of the regularisation parameter  $\lambda$ .

## **Details**

For every value of  $\lambda$  the coefficients are obtained. They are plotted versus the  $\lambda$  values.

# Value

A plot with the values of the coefficients as a function of  $\lambda$ .

# Author(s)

Michail Tsagris

R implementation and documentation: Giorgos Athineou <athineou@csd.uoc.gr>, Vincenzo Lagani <vlagani@csd.uoc.gr> and Michail Tsagris <mtsagris@uoc.gr>

#### References

Hoerl A.E. and R.W. Kennard (1970). Ridge regression: Biased estimation for nonorthogonal problems. Technometrics, 12(1): 55-67.

Brown P. J. (1994). Measurement, Regression and Calibration. Oxford Science Publications.

#### See Also

```
ridge.reg, ridgereg.cv
```

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# **Examples**

```
#simulate a dataset with continuous data
dataset <- matrix( runif(300 * 20, 1, 20), nrow = 300 )
#the target feature is the last column of the dataset as a vector
target <- dataset[, 20]
dataset <- dataset[, -20]
ridge.plot(target, dataset)</pre>
```

ROC and AUC

ROC and AUC

## **Description**

Receiver operating curve and area under the curve.

# Usage

```
auc(group, preds, roc = FALSE, cutoffs = NULL)
```

# **Arguments**

group A numerical vector with the predicted values of each group as 0 and 1.

preds The predicted values of each group.

roc If you want the ROC to appear set it to TRUE.

cutoffs If you provide a vector with decreasing numbers from 1 to 0 that will be used

for the ROC, otherwise, the values from 1 to 0 with a step equal to -0.01 will be

used.

# **Details**

The ara under the curve is returned. The user has the option of getting the receiver operating curve as well.

# Value

A list including:

cutoffs The cutoff values.

sensitivity The sensitivity values for each cutoff value. specificity The specificity value for each cutoff value.

youden The pair of of 1- specificity and sensitivity where the Youden's J appears on the

graph and the Youden index which is defined as the maximum value of sensitiv-

ity - specificity + 1.

auc The area under the curve, plus a circle with the point where Youden's J is located.

If "roc" is set to FALSE, this is the only item in the list to be returned.

## Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

#### See Also

```
bbc, testIndLogistic
```

## **Examples**

```
g <- rbinom(150, 1, 0.6)
f <- rnorm(150)
auc(g, f, roc = FALSE)</pre>
```

Search for triangles in an undirected graph

Search for triangles in an undirected graph

# **Description**

Search for triangles in an undirected graph.

## Usage

```
triangles.search(G)
```

# Arguments

G

The adjacency matrix of an undirected graph. G[i, j] = G[j, i] = 1 means there is an edge between modes i and j. Zero values indicate the absence of edges.

# **Details**

The functions searches for triangles, that is for tripletes of nodes (or variables) for which X-Y, Y-Z and X-Z.

# Value

A matrix with thre columns. If there are no triangles, the matrix is empty. If there is at least one triangle, then each row contains three numbers, one for each node. See the examples below.

## Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

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## See Also

```
plotnetwork, pc.skel, mmhc.skel
```

#### **Examples**

```
set.seed(123)
x <- rdag2(1000, p = 20, nei = 4)$x
a <- pc.skel(x, alpha = 0.05)
plotnetwork(a$G)
triangles.search(a$G)</pre>
```

```
SES.gee.output-class Class "SES.gee.output"
```

# **Description**

SES.gee output object class.

# **Objects from the Class**

Objects can be created by calls of the form new("SES.glmm.output", ...).

#### Slots

```
selectedVars: Object of class "numeric"
selectedVarsOrder: Object of class "numeric"
queues: Object of class "list"
signatures: Object of class "matrix"
hashObject: Object of class "list"
pvalues: Object of class "numeric"
stats: Object of class "numeric"
univ: Object of class "list"
max_k: Object of class "numeric"
threshold: Object of class "numeric"
n.tests: Object of class "numeric"
runtime: Object of class "proc_time"
test: Object of class "character"
se: Object of class "character"
```

# Methods

```
plot plot(x = "SES.gee.output", mode = "all"): Generic function for plotting the generated
    pvalues of the SES.glmm.output object. Argument mode = "all" for plotting all the pvalues or
    mode="partial" for partial plotting the first 500 pvalues
```

## Author(s)

Giorgos Athineou <athineou@csd.uoc.gr>

#### See Also

```
MMPC.gee, SES.gee
```

## **Examples**

```
showClass("SES.glmm.output")
```

```
SES.glmm.output-class Class "SES.glmm.output"
```

# Description

SES.glmm output object class.

## **Objects from the Class**

Objects can be created by calls of the form new("SES.glmm.output", ...).

#### **Slots**

```
selectedVars: Object of class "numeric"
selectedVarsOrder: Object of class "numeric"
queues: Object of class "list"
signatures: Object of class "matrix"
hashObject: Object of class "list"
pvalues: Object of class "numeric"
stats: Object of class "numeric"
univ: Object of class "list"
max_k: Object of class "numeric"
threshold: Object of class "numeric"
n.tests: Object of class "numeric"
runtime: Object of class "proc_time"
test: Object of class "character"
slope: Object of class "logical"
```

# Methods

plot plot(x = "SES.glmm.output", mode = "all"): Generic function for plotting the generated
 pvalues of the SES.glmm.output object. Argument mode = "all" for plotting all the pvalues or
 mode="partial" for partial plotting the first 500 pvalues

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### Author(s)

Giorgos Athineou <athineou@csd.uoc.gr>

#### See Also

```
MMPC.glmm, SES.glmm
```

# **Examples**

```
showClass("SES.glmm.output")
```

SESoutput-class

Class "SESoutput"

# **Description**

SES output object class.

# **Objects from the Class**

Objects can be created by calls of the form new("SESoutput", ...).

### **Slots**

```
selectedVars: Object of class "numeric"
selectedVarsOrder: Object of class "numeric"
queues: Object of class "list"
signatures: Object of class "matrix"
hashObject: Object of class "list"
pvalues: Object of class "numeric"
stats: Object of class "numeric"
univ: Object of class "list"
max_k: Object of class "numeric"
threshold: Object of class "numeric"
n.tests: Object of class "numeric"
runtime: Object of class "proc_time"
test: Object of class "character"
```

### Methods

```
plot plot(x = "SESoutput", mode = "all"): Generic function for plotting the generated pvalues
    of the SESoutput object. Argument mode = "all" for plotting all the pvalues or mode="partial"
    for partial plotting the first 500 pvalues
```

#### Author(s)

Giorgos Athineou <athineou@csd.uoc.gr>

#### See Also

**SES** 

#### **Examples**

showClass("SESoutput")

Skeleton (local) around a node of the max-min hill-climbing (MMHC) algorithm

Skeleton (local) around a node of the MMHC algorithm

# **Description**

The local skeleton of a Bayesian network around a node produced by MMHC. No orientations are involved.

### Usage

local.mmhc.skel(dataset, node, max\_k = 3, threshold = 0.05, test = "testIndFisher")

# **Arguments**

dataset A matrix with the variables. The user must know if they are continuous or if

they are categorical. If you have a matrix with categorical data, i.e. 0, 1, 2, 3 where each number indicates a category, the minimum number for each variable must be 0. data.frame is also supported, as the dataset in this case is converted

into a matrix.

node A number between 1 and the number of columns of the dataset. The local net-

work (edges only) will be built around this node. At first the parents and children of this node are identified and then their parents and children. No inconsistencies correction whastsoever is attempted. A variable detected by the node, but

the node was not detected by that variable.

max\_k The maximum conditioning set to use in the conditional indepedence test (see

Details of SES or MMPC).

threshold Threshold (suitable values in (0, 1)) for assessing p-values significance. Default

value is 0.05.

test The conditional independence test to use. Default value is "testIndFisher". This

procedure allows for "testIndFisher", "testIndSPearman" for continuous variables and "gSquare" for categorical variables. Or in general, if the dataset is a data.frame with different types of data, leave this NULL. See also link{MMPC}

for the automatic choice of tests.

#### **Details**

The MMPC is run on the user specific variable. The backward phase (see Tsamardinos et al., 2006) takes place automatically. Then, the MMPC is run on the parents and children of that variable. If the node variable is not detected by a variable, this variable is not removed though.

#### Value

### A list including:

runtime The run time of the algorithm. A numeric vector. The first element is the user

time, the second element is the system time and the third element is the elapsed

time.

ntests The number of tests MMPC (or SES) performed at each variable.

res A list with the parents and children of each variable. The first element is the

parents and children of the node variable.

Gloc The local adjancency matrix. A value of 1 in G[i, j] may not appear appear

in  $G[j,\,i]$  also, indicating that variable j was discovered as a possible parent or child of node i, but not the covnerse. The usual MMHC (mmhc.skel) removes

the edge between them as this is an inconsistency.

#### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

# References

Tsamardinos, Brown and Aliferis (2006). The max-min hill-climbing Bayesian network structure learning algorithm. Machine learning, 65(1), 31-78.

### See Also

```
mmhc.skel, pc.skel, pc.or, corfs.network
```

### **Examples**

```
# simulate a dataset with continuous data
dataset <- matrix(runif(500 * 30, 1, 100), nrow = 500 )
a1 <- mmhc.skel(dataset, max_k = 3, threshold = 0.05, test = "testIndFisher")
a2 <- local.mmhc.skel(dataset, 4)
a1$runtime
a2$runtime

dataset <- rdag2(500, p = 20, nei = 3)$x
a1 <- mmhc.skel(dataset, max_k = 3, threshold = 0.05, test = "testIndFisher")
a2 <- local.mmhc.skel(dataset, 5)
a1$runtime
a2$runtime</pre>
```

```
Skeleton of the max-min hill-climbing (MMHC) algorithm

The skeleton of a Bayesian network as produced by MMHC
```

# **Description**

The skeleton of a Bayesian network produced by MMHC. No orientations are involved.

#### Usage

```
mmhc.skel(dataset, max_k = 3, threshold = 0.05, test = "testIndFisher", type = "MMPC",
hash = FALSE, backward = TRUE, symmetry = TRUE, nc = 1, ini.pvalue = NULL)

glmm.mmhc.skel(dataset, group, max_k = 3, threshold = 0.05, test = "testIndLMM",
type = "MMPC.glmm", hash = FALSE, symmetry = TRUE, nc = 1, ini.pvalue = NULL)

gee.mmhc.skel(dataset, group, max_k = 3, threshold = 0.05, test = "testIndGEEReg",
type = "MMPC.gee", se = "jack", hash = FALSE, symmetry = TRUE, nc = 1,
ini.pvalue = NULL)
```

### **Arguments**

dataset	A matrix with the variables. The user must know if they are continuous or if they are categorical. If you have a matrix with categorical data, i.e. 0, 1, 2, 3 where each number indicates a category, the minimum number for each variable must be 0. For the "glmm.mmhc.skel" this must be only a matrix.
group	This is to be used in the "glmm.mmhc.skel" and "gee.mmhc.skel" only. It is a vector for identifying the grouped data, the correlated observations, the subjects.
max_k	The maximum conditioning set to use in the conditional indepedence test (see Details of SES or MMPC).
threshold	Threshold (suitable values in $(0, 1)$ ) for assessing p-values significance. Default value is 0.05.
test	The conditional independence test to use. Default value is "testIndFisher". This procedure allows for "testIndFisher", "testIndSPearman" for continuous variables and "gSquare" for categorical variables. In case the dataset is a data.frame with mixed types of data leave this NULL and an appropriate test will be selected. See MMPC for the automatic choice of tests.
	For the "glmm.mmhc.skel" the available tests in MMPC.glmm.
type	The type of variable selection to take place for each variable (or node). The default (and standard) is "MMPC" and "MMPC.glmm". You can also choose to run it via "SES" and "SES.glmm" and thus allow for multiple signatures of variables to be connected to a variable.
se	The method for estimating standard errors. This is very important and crucial. The available options for Gaussian, Logistic, Poisson and Gamma regression

are: a) 'san.se': the usual robust estimate. b) 'jack': approximate jackknife variance estimate. c) 'j1s': if 1-step jackknife variance estimate and d) 'fij': fully iterated jackknife variance estimate. If you have many clusters (sets of repeated measurements) "san.se" is fine as it is asympotically correct, plus jacknife estimates will take longer. If you have a few clusters, then maybe it's better to use jacknife estimates.

The jackknife variance estimator was suggested by Paik (1988), which is quite suitable for cases when the number of subjects is small (K < 30), as in many biological studies. The simulation studies conducted by Ziegler et al. (2000) and Yan and Fine (2004) showed that the approximate jackknife estimates are in many cases in good agreement with the fully iterated ones.

hash

A boolean variable which indicates whether (TRUE) or not (FALSE). Default value is FALSE. If TRUE a hashObject is produced and hence more memory is required. If you want to know the number of tests executed for each variable

then make it TRUE.

If TRUE, the backward (or symmetry correction) phase will be implemented. This removes any falsely included variables in the parents and children set of the target variable. It call the mmpcbackphase for this purpose. For perm.ses

and wald.ses this is not yet applicable.

In order for an edge to be added, a statistical relationship must have been found symmetry

> from both directions. If you want this symmetry correction to take place, leave this boolean variable to TRUE. If you set it to FALSE, then if a relationship between Y and X is detected but not between X and Y, the edge is still added.

How many cores to use. This plays an important role if you have many variables, say thousands or so. You can try with nc = 1 and with nc = 4 for example to see the differences. If you have a multicore machine, this is a must option. There was an extra argument for plotting the skeleton but it does not work with the current visualisation packages, hence we removed the argument. Use plotnetwork

to plot the skeleton.

ini.pvalue This is a list with the matrix of the univariate p-values. If you want to run

mmhc.skel again, the univariate associations need not be calculated again.

# **Details**

The MMPC is run on every variable. The backward phase (see Tsamardinos et al., 2006) takes place automatically. After all variables have been used, the matrix is checked for inconsistencies and they are corrected.

A trick mentioned in that paper to make the procedure faster is the following. In the k-th variable, the algorithm checks how many previously scanned variables have an edge with the this variable and keeps them (it discards the other variables with no edge) along with the next (unscanned) variables.

This trick reduces time, but can lead to different results. For example, if the i-th variable is removed, the k-th node might not remove an edge between the j-th variable, simply because the i-th variable that could d-sepate them is missing.

The user is given this option via the argument "fast", which can be either TRUE or FALSE. Parallel computation is also available.

backward

nc

#### Value

A list including:

runtime The run time of the algorithm. A numeric vector. The first element is the user

time, the second element is the system time and the third element is the elapsed

time.

density The number of edges divided by the total possible number of edges, that is

#edges / n(n-1)/2, where n is the number of variables.

info Some summary statistics about the edges, minimum, maximum, mean, median

number of edges.

ms If you run "MMPC" for each variable this is NULL. If you run "SES" is a vector

denoting which variables had more than one signature, i.e. more than one set of

variables associated with them.

ntests The number of tests MMPC (or SES) performed at each variable.

ini.pvalue A matrix with the p-values of all pairwise univariate assocations.

pvalue A matrix with the final p-values. These are the maximum p-values calculated

during the process. When the process finishes, the matrix is not symmetric. It becomes symmetric though by keeping the maximum between any two off-diagonal elements. These p-values now can be used to sort the strength of the edges. If you know the true adjacency matrix you can use them and create a

ROC curve (see bn. skel.utils for more information).

G The adjancency matrix. A value of 1 in G[i, j] appears in G[j, i] also, indicating

that i and j have an edge between them.

Bear in mind that the values can be extracted with the \$ symbol, i.e. this is an S3 class output.

#### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

### References

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#### See Also

```
pc.skel, pc.or, corfs.network, bn.skel.utils
```

### **Examples**

```
# simulate a dataset with continuous data y \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow y$x a \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow p$x b \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(500, p = 20, nei = 3) x \leftarrow rdag2(
```

Skeleton of the PC algorithm

The skeleton of a Bayesian network produced by the PC algorithm

# **Description**

The skeleton of a Bayesian network produced by the PC algorithm. No orientations are involved. The pc.con is for continuous data only and it calls the same C++ as pc.skel. Hence, you are advised to use pc.skel.

# Usage

```
pc.skel(dataset, method = "pearson", alpha = 0.01, rob = FALSE, R = 1, stat = NULL,
ini.pvalue = NULL)

pc.con(dataset, method = "pearson", alpha = 0.01)

pc.skel.boot(dataset, method = "pearson", alpha = 0.01, R = 199, ncores = 1)

glmm.pc.skel(dataset, group, method = "comb.mm", alpha = 0.01, stat = NULL,
ini.pvalue = NULL)

gee.pc.skel(dataset, group, se = "jack", method = "comb.mm", alpha = 0.01, stat = NULL,
ini.pvalue = NULL)
```

#### **Arguments**

dataset

A matrix with the variables. The user must know if they are continuous or if they are categorical. If you have categorical data though, the user must transform the data.frame into a matrix. In addition, the numerical matrix must have values starting from 0. For example, 0, 1, 2, instead of "A", "B" and "C". In the case of mixed variables, continuous, binary and ordinal this must a data.frame and the non continuous variables must be ordered factors, even the binary variables.

For the pc.con, pc.skel.boot and glmm.pc.skel, the dataset can only be a matrix.

method

If you have continuous data, you can choose either "pearson", "spearman" or "distcor". The latter uses the distance correlation and should not be used with lots of observations as it is by default really slow. If you have categorical data, this must be "cat". If you have a mix of continuous, binary and ordinal data (we will expand the available dataset in the future) then choose "comb.fast" or "comb.mm". These two methods perform the symmetric test for mixed data (Tsagris et al., 2018). See details for more information on this. For the mixed models PC algorithm, this is the same argument, but currently only "comb.mm" is accepted.

group

This is to be used in the "glmm.pc.skel" and "gee.pc.skel" only. It is a vector for identifying the grouped data, the correlated observations, the subjects.

se

The method for estimating standard errors. This is very important and crucial. The available options for Gaussian, Logistic, Poisson and Gamma regression are: a) 'san.se': the usual robust estimate. b) 'jack': approximate jackknife variance estimate. c) 'j1s': if 1-step jackknife variance estimate and d) 'fij': fully iterated jackknife variance estimate. If you have many clusters (sets of repeated measurements) "san.se" is fine as it is asympotically correct, plus jacknife estimates will take longer. If you have a few clusters, then maybe it's better to use jacknife estimates.

The jackknife variance estimator was suggested by Paik (1988), which is quite suitable for cases when the number of subjects is small (K < 30), as in many biological studies. The simulation studies conducted by Ziegler et al. (2000) and Yan and Fine (2004) showed that the approximate jackknife estimates are in many cases in good agreement with the fully iterated ones.

alpha

The significance level (suitable values in (0, 1)) for assessing the p-values. Default value is 0.01.

rob

This is for robust estimation of the Pearson correlation coefficient. Default value is FALSE.

R

The number of permutations to be conducted. This is taken into consideration for the "pc.skel" only. The Pearson correlation coefficient is calculated and the p-value is assessed via permutations. There was an extra argument for plotting the skeleton but it does not work with the current visualisation packages, hence we removed the argument. Use plotnetwork to plot the skeleton.

In the pc.skel.boot this is the number of bootstrap resamples to draw. The PC algorithm is performed in each bootstrap sample. In the end, the adjacency matrix on the observed data is returned, along with another adjacency matrix

produced by the bootstrap. The latter one contains values from 0 to 1 indicating

the proportion of times an edge between two nodes was present.

ncores The number of cores to use. By default this is set to 1.

stat If you have the initial test statistics (univariate associations) values supply them

here.

ini.pvalue If you have the initial p-values of the univariate associations supply them here.

#### **Details**

The PC algorithm as proposed by Spirtes et al. (2000) is implemented. The variables must be either continuous or categorical, only. The skeleton of the PC algorithm is order independent, since we are using the third heuristic (Spirte et al., 2000, pg. 90). At every ste of the alogirithm use the pairs which are least statistically associated. The conditioning set consists of variables which are most statistically associated with each either of the pair of variables.

For example, for the pair (X, Y) there can be two coniditoning sets for example (Z1, Z2) and (W1, W2). All p-values and test statistics and degrees of freedom have been computed at the first step of the algorithm. Take the p-values between (Z1, Z2) and (X, Y) and between (Z1, Z2) and (X, Y). The conditioning set with the minimum p-value is used first. If the minimum p-values are the same, use the second lowest p-value. In the event of 2 or more p-values being the same (with permutations for example), the test statistic divided by the degrees of freedom is used as a means of choosing which conditioning set is to be used first. If two or more p-values are below the machine epsilon (.Machine\$double.eps which is equal to 2.220446e-16), all of them are set to 0. To make the comparison or the ordering feasible we use the logarithm of the p-value. Hence, the logarithm of the p-values is always calculated and used.

In the case of the  $G^2$  test of independence (for categorical data) we have incorporated a rule of thumb. I the number of samples is at least 5 times the number of the parameters to be estimated, the test is performed, otherwise, independence is not rejected (see Tsamardinos et al., 2006).

The "comb.fast" and "comb.mm" methods are used with mixed variables, continuous, binary and ordinal. The "comb.mm" performs two log-likelihood ratio tests. For every pair of variables each of the two variables is treated as response and the suitable regression model is fitted. Then, two likelihood ratio tests are performed and the 2 p-values are combined in a meta-analytic way. In the case of "comb.fast" one regression model is fitted, the easiest (between the two) to implement. The ordering of the "easiness" is as follows: linear regression > logistic regression > ordinal regression.

The "pc.con" is a faster implementation of the PC algorithm but for continuous data only, without the robust option, unlike pc.skel which is more general and even for the continuous datasets slower. pc.con accepts only "pearson" and "spearman" as correlations.

If there are missing values they are placed by their median in case of continuous data and by their mode (most frequent value) if they are categorical.

The "glmm.pc.skel" and "gee.pc.skel" are designed for clustered or grouped data. It uses linear mixed models and works in the same way as the PC with mixed data. For each variable, a random intercepts model is fitted and the significance of the other variable is assessed. The two p-values are meta-analytically combined.

For all cases, we return the maximum logged p-value of the conditional independence tests between the pairs. This can be used to order the strength of association between pairs of variables. In addition, one can use it to estimate the AUC. See the example in bn.skel.utils.

If you want to use the GEE methodology, make sure you load the library geepack first.

#### Value

A list including:

The test statistics of the univariate associations.

ini.pvalue

The initival univariate associations p-values.

pvalue The logarithm of the maximum p-values from every conditional independence

test. Note also, that if there is a log p-value smaller that the log of the threshold value that means there is an edge. This can be used to estimate the FDR (Tsamardinos and Brown, 2008). See details for more information. This is also an estimate of the strength of the association between pairs of variables.

At the moment this is not possible for method = c("pearson", "spearman", "cat") with R = 1, or R > 1 because these cases are handled in C++. We will add those

cases in the future.

info Some summary statistics about the edges, minimum, maximum, mean, median

number of edges.

runtime The run time of the algorithm. A numeric vector. The first element is the user

time, the second element is the system time and the third element is the elapsed

time.

kappa The maximum value of k, the maximum cardinality of the conditioning set at

which the algorithm stopped.

density The number of edges divided by the total possible number of edges, that is

#edges / n(n-1)/2, where n is the number of variables.

info Some summary statistics about the edges, minimum, maximum, mean, median

number of edges.

G The adjancency matrix. A value of 1 in G[i, j] appears in G[j, i] also, indicating

that i and j have an edge between them.

sepset A list with the separating sets for every value of k.

title The name of the dataset.

Bear in mind that the values can be extracted with the \$ symbol, i.e. this is an S3 class output.

#### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>.

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Paik M.C. (1988). Repeated measurement analysis for nonnormal data in small samples. Communications in Statistics-Simulation and Computation, 17(4): 1155-1171.

Ziegler A., Kastner C., Brunner D. and Blettner M. (2000). Familial associations of lipid profiles: A generalised estimating equations approach. Statistics in Medicine, 19(24): 3345-3357

Yan J. and Fine J. (2004). Estimating equations for association structures. Statistics in Medicine, 23(6): 859-874.

Liang K.Y. and Zeger S.L. (1986). Longitudinal data analysis using generalized linear models. Biometrika, 73(1): 13-22.

Eugene Demidenko (2013). Mixed Models: Theory and Applications with R, 2nd Edition. New Jersey: Wiley \& Sons.

#### See Also

```
bn.skel.utils, mmhc.skel, corfs.network, local.mmhc.skel
```

# **Examples**

```
# simulate a dataset with continuous data
y <- rdag2(300, p = 20, nei = 3)
ind <- sample(1:20, 20)
x <- y$x[, ind]
a <- mmhc.skel(x, max_k = 3, threshold = 0.05, test = "testIndFisher" )
b <- pc.skel( x, method = "pearson", alpha = 0.05 )
a$runtime
b$runtime</pre>
```

Structural Hamming distance between two partially oriented DAGs

Structural Hamming distance between two partially oriented DAGs

### **Description**

Structural Hamming distance between two partially oriented DAGs.

### Usage

```
shd(est, true)
```

# **Arguments**

est The first (partially oriented) DAG. This could also be the estimated DAG.

true The second (partially oriented) DAG. This could also be the equivalence class

of the true DAG.

#### **Details**

The structural Hamming distance as proposed by Tsamardinos et al. (2006) is calculated and returned. The cases are listed below

True	<b>Estimated</b>	Penalty
-		1
	-	1
->		1
	<-	1
->	-	1
-	<-	1
->	<-	1

#### Value

A list including

mat A table with the agreements and disagreements between the two DAGs.

shd The structural Hamming distance.

### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

# References

Tsamardinos, Brown and Aliferis (2006). The max-min hill-climbing Bayesian network structure learning algorithm. Machine learning, 65(1), 31-78.

#### See Also

```
pc.skel, pc.or, mmhc.skel, plotnetwork
```

# **Examples**

```
y <- rdag(1000, 20, 0.2)
tru <- y$G
mod <- pc.skel(y$x)
a <- pc.or(mod)
shd( a$G, dag2eg(tru) )</pre>
```

Supervised PCA 229

# **Description**

Supervised PCA.

# Usage

```
supervised.pca(target, dataset, indices, center = TRUE, scale = TRUE,
colours = NULL, graph = TRUE)
```

# **Arguments**

target	A numerical vector or a factor denoting the class of each sample, the response variable.
dataset	A matrix with numerical data (the predictor variables).
indices	A vector with indices denoting wheih variables have been selected.
center	In the calculation of the PCA, should the data be centered? Default value is TRUE.
scale	In the calculation of the PCA, should the data be scaled to unity variance? Default value is TRUE.
colours	Should the colour of the points be defined by the target variable or do you want to pass your own colours? This must be a vector whose length is equal to the length of the target.
graph	Should two graphs be returned? The scores of the frist two principal components based on all the data and based on the selected variables.

# **Details**

This is not exactly the standard supervised PCA as suggested by Bair et al (2006). What we do here essentially is the following: PCA on all variables and on the variables selected by a variable selection algorithm.

# Value

A list including:

mod.all The output returned by prcomp applied to all variables.

mode.sel The output returned by prcomp applied to the selected variables.

var.percent The percentage of variance explained by the selected variables.

# Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

#### References

Bair E., Hastie T., Debashis P. and Tibshirani R. (2006). Prediction by supervised principal components. Journal of the American Statistical Association 101(473): 119–137.

#### See Also

```
gomp, fbed.reg, MMPC
```

### **Examples**

```
x <- as.matrix(iris[, 1:4])
target <- iris[, 5]
supervised.pca(target, x, indices = 1:2)</pre>
```

Symmetric conditional independence test with clustered data

Symmetric conditional independence test with clustered data

# Description

Symmetric conditional independence test with clustered data.

#### Usage

```
glmm.ci.mm(ind1, ind2, cs = NULL, dat, group)
gee.ci.mm(ind1, ind2, cs = NULL, dat, group, se = "jack")
```

#### **Arguments**

ind1	The index of the one variable to be considered.	
ind2	The index of the other variable to be considered.	
cs	The index or indices of the conditioning set of variable(s). If you have no variables set this equal to 0.	
dat	A numerical matrix with data.	
group	This is a numerical vector denoting the groups or the subjects.	
se	The method for estimating standard errors. This is very important and cru-	

The method for estimating standard errors. This is very important and crucial. The available options for Gaussian, Logistic and Poisson regression are: a) 'san.se': the usual robust estimate. b) 'jack': approximate jackknife variance estimate. c) 'j1s': if 1-step jackknife variance estimate and d) 'fij': fully iterated jackknife variance estimate. If you have many clusters (sets of repeated measurements) "san.se" is fine as it is asympotically correct, plus jacknife estimates will take longer. If you have a few clusters, then maybe it's better to use jacknife estimates.

The jackknife variance estimator was suggested by Paik (1988), which is quite suitable for cases when the number of subjects is small (K < 30), as in many biological studies. The simulation studies conducted by Ziegler et al. (2000) and Yan and Fine (2004) showed that the approximate jackknife estimates are in many cases in good agreement with the fully iterated ones.

#### **Details**

Two linear random intercept models are fitted, one for each variable and the p-value of the hypothesis test that the other variable is significant is calculated. These two p-values are combined in a meta-analytic way. The models fitted are either linear, logistic and Poisson regression.

#### Value

A vector including the test statistic, it's associated p-value and the relevant degrees of freedom.

# Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

#### References

Tsagris M. (2019). Bayesian network learning with the PC algorithm: an improved and correct variation. Applied Artificial Intelligence, 33(2): 101-123.

Tsagris M., Borboudakis G., Lagani V. and Tsamardinos I. (2018). Constraint-based Causal Discovery with Mixed Data. International Journal of Data Science and Analytics.

Paik M.C. (1988). Repeated measurement analysis for nonnormal data in small samples. Communications in Statistics-Simulation and Computation, 17(4): 1155-1171.

Ziegler A., Kastner C., Brunner D. and Blettner M. (2000). Familial associations of lipid profiles: A generalised estimating equations approach. Statistics in medicine, 19(24): 3345-3357

Yan J. and Fine J. (2004). Estimating equations for association structures. Statistics in medicine, 23(6): 859-874.

Eugene Demidenko (2013). Mixed Models: Theory and Applications with R, 2nd Edition. New Jersey: Wiley \& Sons.

#### See Also

```
pc.skel, condi, testIndGLMMReg
```

### **Examples**

```
## we generate two independent vectors of clustered data
s1 <- matrix(1.5, 4, 4)
diag(s1) <- 2.5
s2 <- matrix(1.5, 4, 4)
diag(s2) <- 2
x1 <- MASS::mvrnorm(10, rnorm(4), s1)
x1 <- as.vector( t(x1) )
x2 <- MASS::mvrnorm(10, rnorm(4), s2)
x2 <- as.vector( t(x2) )
id <- rep(1:10, each = 4)
glmm.ci.mm(1, 2, dat = cbind(x1,x2), group = id)
gee.ci.mm(1, 2, dat = cbind(x1,x2), group = id)</pre>
```

Symmetric conditional independence test with mixed data

Symmetric conditional independence test with mixed data

# **Description**

Symmetric conditional independence test with mixed data.

# Usage

```
ci.mm(ind1, ind2, cs = NULL, dat, type, rob = FALSE, R = 1)
ci.fast(ind1, ind2, cs = NULL, dat, type, rob = FALSE, R = 1)
ci.mm2(ind1, ind2, cs = NULL, suffStat)
ci.fast2(ind1, ind2, cs = NULL, suffStat)
```

### **Arguments**

ind1	The index of the one variable to be considered.
ind2	The index of the other variable to be considered.
cs	The index or indices of the conditioning set of variable(s). If you have no variables set this equal to $0$ .
dat	A data frame with numerical, binary, nominal and ordinal variables only.
type	This is obsolete basically, but we need it here, so that the functions ci.mm and ci.fast have the same signatures as in cat.ci, condi and dist.condi.
rob	This is obsolete basically, but we need it here, so that the functions ci.mm and ci.fast have the same signatures as in cat.ci, condi and dist.condi.
R	This is obsolete basically, but we need it here, so that the functions ci.mm and ci.fast have the same signatures as in cat.ci, condi and dist.condi.
suffStat	This is a list with only the dataset and the name must be "dataset". A data.frame with numerical, binary, nominal and ordinal variables only.

#### **Details**

The functions "ci.mm" and "ci.fast" are general functions to be used anywhere. The functions "ci.mm2" and "ci.fast2" are designed to be accepted by the command "pc" in the package "pcalg". The functions "ci.mm2" and "ci.fast2" can be fed in the "pc" function of the "pcalg" package in order to produce a PDAG with mixed data using the PC algorithm. For more information see the relevant paper in the references.

The "ci.mm" and "ci.fast" work with linear, logistic, multinomial and ordinal regression, whereas the "ci.mm2" and "ci.fast2" work with linear, logistic and ordinal regression only.

### Value

A vector including the test statistic, it's associated p-value and the relevant degrees of freedom.

#### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

#### References

Tsagris M. (2019). Bayesian network learning with the PC algorithm: an improved and correct variation. Applied Artificial Intelligence, 33(2): 101-123.

Tsagris M., Borboudakis G., Lagani V. and Tsamardinos I. (2018). Constraint-based Causal Discovery with Mixed Data. International Journal of Data Science and Analytics.

Spirtes P., Glymour C. and Scheines R. (2001). Causation, Prediction, and Search. The MIT Press, Cambridge, MA, USA, 3nd edition.

Sedgewick, A. J., Ramsey, J. D., Spirtes, P., Glymour, C., & Benos, P. V. (2017). Mixed Graphical Models for Causal Analysis of Multi-modal Variables. arXiv preprint arXiv:1704.02621.

#### See Also

```
pc.skel, mmhc.skel, cat.ci, condi
```

### **Examples**

```
ci.mm(1, 2, dat = iris)

ci.mm(1, 5, dat = iris)

ci.fast(1, 5, dat = iris)

x \leftarrow iris

x[, 5] \leftarrow as.numeric(x[, 5]) ## Caution:: this will be treated as ordered variable.

x[, 5] \leftarrow factor(x[, 5], ordered = TRUE)

## ci.mm2 and ci.fast2 do not perform multinomial regression.

ci.mm2(1, 5, suffStat = list(dataset = x))

ci.fast2(1, 5, suffStat = list(dataset = x))
```

The max-min Markov blanket algorithm

Max-min Markov blanket algorithm

### **Description**

The MMMB algorithm follows a forward-backward filter approach for feature selection in order to provide a minimal, highly-predictive, feature subset of a high dimensional dataset. See also Details.

# Usage

```
mmmb(target , dataset , max_k = 3 , threshold = 0.05 , test = "testIndFisher", user_test = NULL, ncores = 1)
```

#### **Arguments**

target The class variable. Provide either a string, an integer, a numeric value, a vector,

a factor, an ordered factor or a Surv object. See also Details.

dataset The dataset; provide either a data frame or a matrix (columns = variables, rows

= samples). In either case, only two cases are available, either all data are con-

tinuous, or categorical.

max\_k The maximum conditioning set to use in the conditional indepedence test (see

Details). Integer, default value is 3.

threshold Threshold (suitable values in (0, 1)) for assessing the p-values. Default value is

0.05.

test The conditional independence test to use. Default value is "testIndFisher". See

also link{CondIndTests}.

user\_test A user-defined conditional independence test (provide a closure type object).

Default value is NULL. If this is defined, the "test" argument is ignored.

ncores How many cores to use. This plays an important role if you have tens of thou-

sands of variables or really large sample sizes and tens of thousands of variables and a regression based test which requires numerical optimisation. In other cammub it will not make a difference in the overall time (in fact it can be slower). The parallel computation is used in the first step of the algorithm, where univariate associations are examined, those take place in parallel. We have seen a reduction in time of 50% with 4 cores in comparison to 1 core. Note also, that

the amount of reduction is not linear in the number of cores.

#### Details

The idea is to run the MMPC algorithm at first and identify the parents and children (PC) of the target variable. As a second step, the MMPC algorithm is run on the discovered variables to return PC. The parents of the children of the target are the spouses of the target. Every variable in PCi is checked to see if it is a spouse of the target. If yes, it is included in the Markov Blanket of the target, otherwise it is thrown. If the data are continous, the Fisher correlation test is used or the Spearman correlation (more robust). If the data are categorical, the  $G^2$  test is used.

#### Value

The output of the algorithm is an S3 object including:

mb The Markov Blanket of the target variable. The parents and children of the

target variable, along with the spouses of the target, which are the parents of the

children of the target variable.

runtime The run time of the algorithm. A numeric vector. The first element is the user

time, the second element is the system time and the third element is the elapsed

time.

# Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

### References

Tsamardinos I., Aliferis C. F. and Statnikov, A. (2003). Time and sample efficient discovery of Markov blankets and direct causal relations. In Proceedings of the 9th ACM SIGKDD international conference on Knowledge discovery and data mining, pp. 673-678.

### See Also

```
CondIndTests, MMPC, SES
```

# **Examples**

```
set.seed(123)
#simulate a dataset with continuous data
dataset <- matrix( runif(200 * 50, 1, 100), ncol = 50 )
#define a simulated class variable
target <- 3 * dataset[, 10] + 2 * dataset[, 50] + 3 * dataset[, 20] + rnorm(200, 0, 5)
a1 <- mmmb(target , dataset , max_k = 3 , threshold = 0.05, test= "testIndFisher",
ncores = 1,)
a2 <- MMPC(target, dataset, test="testIndFisher")</pre>
```

```
Topological sort of a DAG
```

Topological sort of a DAG

### **Description**

Topological sort of a DAG.

# Usage

```
topological_sort(dag)
```

### **Arguments**

dag

A square matrix representing a directed graph which contains 0s and 1s. If G[i, j] = 1 it means there is an arrow from node i to node j. When there is no edge between nodes i and j if G[i, j] = 0.

#### **Details**

The function is an R translation from an old matlab code.

# Value

A vector with numbers indicating the sorting. If the matrix does not correspond to a DAG, NA will be returned.

### Author(s)

Ioannis Tsamardinos and Michail Tsagris

R implementation and documentation: Ioannis Tsamardinos <tsamard@csd.uoc.gr> and Michail Tsagris <mtsagris@uoc.gr>

#### References

Chickering, D.M. (1995). A transformational characterization of equivalent Bayesian network structures. Proceedings of the 11th Conference on Uncertainty in Artificial Intelligence, Montreal, Canada, 87-98.

#### See Also

```
plotnetwork, nei, pc.or
```

# **Examples**

```
# simulate a dataset with continuous data
# simulate a dataset with continuous data
G = rdag(100, 10, 0.3)$G
G[G == 2] <- 1
G[G == 3] <- 0
topological_sort(G)</pre>
```

Total causal effect of a node on another node

Total causal effect of a node on another node

### **Description**

Total causal effect of a node on another node.

# Usage

```
ida(x, y, G, dataset)
```

# **Arguments**

X	A number between 1 and the number of variables (nodes) indicating the node
	whose total causal effect we want to estimate. This is the independent variable.
	See details for more on this.

y A number between 1 and the number of variables (nodes) indicating the node who is the dependent variable. The goal is to estimate the total causal effect of x on y.

A square matrix representing a (partially) directed graph which contains 0s and 1s. If G[i, j] = 2 it means there is an arrow from node i to node j. If G[i, j] = 1, there is an undirected edge between nodes i and j and there is no edge between nodes i and j if G[i, j] = 0.

dataset The dataset. This is a numerical matrix with data.

#### **Details**

The total causal effect defined in Pearl's do-calculus is E(Y|do(X=z+1)) - E(Y|do(X=z)). As Pearl described it, he used linear regression, hence this function works for continuous data which are assumed to be Gaussian.

We estimate a set of possible total causal effects using linear regression. if y is a parent, or a descendant, of x in G, the estimated causal effect of x on y is zero. If y is not a parent of x, we take the regression coefficient of x in the regression  $lm(y \sim x + pa(x))$ , where pa(x) denotes the parents of x. This is repeated using all parents of x (including the empty set) and all possible parents values of x and their combinations.

One restriction to bear in mind. If a collider is created that combination of nodes is not used in the regression.

### Value

A lis tincluding:

tc A matrix with 4 elements. The first columns one is the estimated beta coefficient,

the second is its standard error, its t-value and the p-value for testing whether this

is equal to 0.

mess If the x node has no parents a message about this appears. Otherwise this is

NULL.

### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

# References

M.H. Maathuis, M. Kalisch and P. Buehlmann (2009). Estimating high-dimensional intervention effects from observational data. Annals of Statistics 37, 3133-3164.

Pearl (2005). Causality. Models, reasoning and inference. Cambridge University Press, New York.

#### See Also

```
plotnetwork, nei, pc.or
```

### **Examples**

```
dataset <- rdag2(1000, p = 20, nei = 3)$x
mod <- pc.skel(dataset ,alpha = 0.01)
G <- pc.or(mod)$G
ida(10, 15, G, dataset)</pre>
```

Transformation of a DAG into an essential graph

Transforms a DAG into an essential graph

# **Description**

Transforms a DAG into an essential graph.

### Usage

```
dag2eg(dag, type = NULL)
```

#### **Arguments**

dag The graph matrix as produced from pc.or or any other algorithm which pro-

duces directed graphs. A DAG in general.

type This can be either NULL or 1 or 2. type = 1 means that the matrix contains 0, 1, 2, 3 where G[i, j] = g[j, i] = 0, means there is no edge between nodes i and

i, j, j = g[j, i] = 0, means there is no edge between nodes i and j and G[i, j] = 2 and G[j, i] = 3 means that there is an arrow from node i to node j. If type 2, the matrix contains 0 for no edge and 1 for a directed edge. In this case, G[i,j]=1 and G[j,i]=0 means that there is an arrow from node i to node j. If you are not sure of what you have, just leave it NULL, the function will check to which case

your matrix belongs.

#### **Details**

The function is an R translation from an old matlab code.

# Value

The matrix of the essential graph.

#### Author(s)

Ioannis Tsamardinos and Michail Tsagris

R implementation and documentation: Ioannis Tsamardinos <tsamard@csd.uoc.gr> and and Michail Tsagris <mtsagris@uoc.gr>

### References

Chickering, D.M. (1995). A transformational characterization of equivalent Bayesian network structures. Proceedings of the 11th Conference on Uncertainty in Artificial Intelligence, Montreal, Canada, 87-98.

### See Also

```
plotnetwork, is.dag, topological_sort
```

### **Examples**

```
# simulate a dataset with continuous data
y <- rdag(1000, 10, 0.3)
tru <- y$G
eg <- dag2eg(tru)
par( mfrow = c(1, 2) )
plotnetwork(tru)
plotnetwork(eg)</pre>
```

Transitive closure of an adjacency matrix

\*Returns the transitive closure of an adjacency matrix\*

# **Description**

Returns the transitive closure of an adjacency matrix.

# Usage

```
transitiveClosure(amat)
```

### **Arguments**

amat

The adjacency matrix of a graph.

#### **Details**

A function that computes the transitive closure of a graph. The transitive closure C(G) of a graph is a graph which contains an edge between nodes u and v whenever there is a directed path from u to v (Skiena 1990, p. 203). http://mathworld.wolfram.com/TransitiveClosure.html

# Value

closure

The transititve closure of the adjacency matrix representing a graph.

### Author(s)

Anna Roumpelaki

R implementation and documentation: Anna Roumpelaki <anna.roumpelaki@gmail.com>

### References

Skiena S. (1990). Implementing Discrete Mathematics: Combinatorics and Graph Theory with Mathematica. Reading, MA: Addison-Wesley

### **Examples**

```
# example adjacency matrix
# simulate a dataset with continuous data
dataset <- matrix( runif(300 * 20, 1, 100), nrow = 300 )
test <- pc.con( dataset, method = "pearson", alpha = 0.05 )$G
transitiveClosure(test)</pre>
```

Undirected path(s) between two nodes

*Undirected path(s) between two nodes* 

# **Description**

Undirected path(s) between two nodes.

### Usage

```
undir.path(G, y, x)
```

### **Arguments**

G	An adjacency matrix where $G[i,j] = G[j,i] = 1$ means there is an edge between nodes i and j. If $G[i,j] = G[j,i] = 0$ there is no edge between them.
у	A numerical value indicating the first node, it has to be a number between 1 and the maximum number of variables.
X	A numerical value indicating the second node, it has to be a number between 1 and the maximum number of variables. The order of the nodes does not make a difference.

# **Details**

The algorithm finds all the nodes between the two nodes. It finds all paths between the two chosen nodes.

# Value

A vector with the two nodes and all nodes between them in the case of connecting nodes. Otherwise, a matrix with the neighbours of each node.

# Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

# References

Tsamardinos, Brown and Aliferis (2006). The max-min hill-climbing Bayesian network structure learning algorithm. Machine learning, 65(1), 31-78.

### See Also

```
SES, MMPC, pc.skel
```

### **Examples**

```
# simulate a dataset with continuous data
set.seed(1234)
dataset <- matrix(runif(1000 * 10, 1, 100), nrow = 1000 )
G <- pc.con(dataset)$G
plotnetwork(G)
undir.path(G, 3, 4)
undir.path(G, 1, 3)</pre>
```

Univariate regression based tests

Univariate regression based tests

# **Description**

Univariate regression based tests.

### Usage

```
univregs(target, dataset, targetID = -1, test = NULL, user_test = NULL,
wei = NULL, ncores = 1)

ebic.univregs(target, dataset, targetID = -1, test = NULL, user_test = NULL,
wei = NULL, ncores = 1, gam = NULL)

wald.univregs(target, dataset, targetID = -1, test = NULL, user_test = NULL,
wei = NULL, ncores = 1)

perm.univregs(target, dataset, targetID = -1, test = NULL, user_test = NULL,
wei = NULL, threshold = 0.05, R = 999, ncores = 1)

score.univregs(target, dataset, test)

big.score.univregs(target = NULL, dataset, test)

rint.regs(target, dataset, targetID = -1, id, reps = NULL, tol = 1e-07)

glmm.univregs(target, reps = NULL, id, dataset, targetID = -1, test, wei = NULL,
slopes = FALSE, ncores = 1)

gee.univregs(target, reps = NULL, id, dataset, targetID = -1, test, wei = NULL,
correl = "echangeable", se = "jack", ncores = 1)
```

#### **Arguments**

target

The target (dependent) variable. It must be a numerical vector. In the case of "big.score.univregs" this can also be NULL if it is included in the first column of the dataset.

dataset

The indendent variable(s). For the "univregs" this can be a matrix or a dataframe with continuous only variables, a data frame with mixed or only categorical variables. For the "wald.univregs", "perm.univregs", "score.univregs" and "rint.regs" this can only by a numerical matrix. For the "big.score.univregs" this is a big.matrix object with continuous data only.

targetID

This is by default -1. If the target is not a variable but is in included in the dataset, you can specify the column of dataset playing the role of the target.

test

For the "univregs" this can only be one of the following: testIndFisher, testInd-Spearman, gSquare, testIndBeta, testIndReg, testIndLogistic, testIndMultinom, testIndOrdinal, testIndPois, testIndZIP, testIndNB, testIndClogit, testIndBinom, testIndIGreg, censIndCR, censIndWR, censIndER, censIndLLR, testIndTobit, testIndGamma, testIndNormLog or testIndSPML for a circular target. For the testIndSpearman the user must supply the ranked target and ranked dataset. The reason for this, is because this function is called internally by SES and MMPC, the ranks have already been applied and there is no reason to re-rank the data.

For the "ebic.univregs" this can only be one of the following: testIndFisher, testIndBeta, testIndReg, testIndLogistic, testIndMultinom, testIndOrdinal, testIndPois, testIndZIP, testIndNB, testIndClogit, testIndBinom, censIndCR, censIndWR, censIndER, censIndLLR, testIndTobit, testIndGamma, testIndNormLog or testIndSPML for a circular target.

For the "wald.univregs" this can only be one of the following: waldBeta, waldCR, waldWR, waldER, waldLLR, waldTobit, waldClogit, waldLogistic, wald-Pois, waldNB, waldBinom, waldZIP, waldMMReg, waldIGreg, waldOrdinal, waldGamma or waldNormLog.

For the "perm.univregs" this can only be one of the following: **permFisher**, **permReg**, **permRQ**, **permBeta**, **permCR**, **permWR**, **permER**, **permLLR**, **permTobit**, **permClogit**, **permLogistic**, **permPois**, **permNB**, **permBinom**, **permgSquare**, **permZIP**, **permMVreg**, **permIGreg**, **permGamma** or **permNormLog**.

For the "score.univregs" and "big.score.univregs" this can only be one of the following: **testIndBeta**, **testIndLogistic**, **testIndMultinom**, **testIndPois**, **testIndNB**, **testIndGamma** or **censIndWR** but with no censored values and simply the vector, not a Surv object. Ordinal regression is not supported.

For the "glmm.univregs" this can only be one of the following: testIndGLMM-Reg, testIndLMM, testIndGLMMLogistic, testIndGLMMOrdinal, testIndGLMMN-Pois, testIndGLMMNB, testIndGLMMGamma, testIndGLMMNormLog or testIndGLMMCR.

For the "gee.univregs" this can only be one of the following: **testIndGLMM-Reg**, **testIndGLMMLogistic**, **testIndGLMMOrdinal**, **testIndGLMMPois**, **testIndGLMMNormLog**.

Note that in all cases you must give the name of the test, without " ".

wei

R

se

user\_test A user-defined conditional independence test (provide a closure type object).

Default value is NULL. If this is defined, the "test" argument is ignored.

A vector of weights to be used for weighted regression. The default value is NULL. An example where weights are used is surveys when stratified sampling

has occured.

This is for ebic.univregs only and it refers to the *gamma* value of the eBIC. If it is NULL, the default value is calculated and if gam is zero, the usual BIC is

returned. see Chen and Chen (2008) for more information.

threshold (suitable values in (0, 1)) for assessing p-values significance. Default

value is 0.05. The reason for this is to speed up the computations. The permutation p-value is calculated as the proportion of times the permuted test statistic is higher than the observed test statistic. When running the permutations, if the proportion is more than 0.05, the process stops. A decision must be made fast, and if the non rejection decision has been made, there is no need to perform the

rest permutations; the decision cannot change.

This is for the permutations based regression models. It is the number of permutations to apply. Note, that not all the number of permutations need be performed. If the number of times the test statistic is greater than the observed test

been made.

ncores How many cores to use. This plays an important role if you have tens of thou-

sands of variables or really large sample sizes and tens of thousands of variables and a regression based test which requires numerical optimisation. In other cases it will not make a difference in the overall time (in fact it can be slower). The parallel computation is used in the first step of the algorithm, where univariate associations are examined, those take place in parallel. We have seen a reduction in time of 50% with 4 cores in comparison to 1 core. Note also, that the amount

statistic is more than threshold \* R, the iterations stop, as a decision has already

of reduction is not linear in the number of cores.

A numerical vector of the same length as target with integer valued numbers, such as 1, 2, 3,... (zeros, negative values and factors are not allowed) specifying

the clusters or subjects. This argument is for the rint.regs (see details for more

information).

reps If you have measurements over time (lognitudinal data) you can put the time here

(the length must be equal to the length of the target) or set it equal to NULL.

(see details for more information).

tol The tolerance value to terminate the Newton-Raphson algorithm in the random

effects models.

slopes Should random slopes for the ime effect be fitted as well? Default value is

FALSE.

correl The correlation structure. For the Gaussian, Logistic, Poisson and Gamma re-

gression this can be either "exchangeable" (compound symmetry, suitable for clustered data) or "ar1" (AR(1) model, suitable for longitudinal data). For the ordinal logistic regression its only the "exchangeable" correlation sturcture.

The method for estimating standard errors. This is very important and crucial. The available options for Gaussian, Logistic, Poisson and Gamma regression

are: a) 'san.se', the usual robust estimate. b) 'jack': if approximate jackknife variance estimate should be computed. c) 'j1s': if 1-step jackknife variance estimate should be computed and d) 'fij': logical indicating if fully iterated jackknife variance estimate should be computed. If you have many clusters (sets of repeated measurements) "san.se" is fine as it is astmpotically correct, plus jacknife estimates will take longer. If you have a few clusters, then maybe it's better to use jacknife estimates.

The jackknife variance estimator was suggested by Paik (1988), which is quite suitable for cases when the number of subjects is small (K < 30), as in many biological studies. The simulation studies conducted by Ziegler et al. (2000) and Yan and Fine (2004) showed that the approximate jackknife estimates are in many cases in good agreement with the fully iterated ones. This is obsolete for "testIndGEEOrdinal", but is here for compatibility reasons.

### **Details**

This function is more as a help function for SES and MMPC, but it can also be called directly by the user. In some, one should specify the regression model to use and the function will perform all simple regressions, i.e. all regression models between the target and each of the variables in the dataset.

For the score.univregs, score based tests are used which are extremely fast.

For the rint.regs, we perform linear mixed models (weights are not allowed) with random intercepts only (no ranodm slopes). This function works for clustered or longitudinal data. The covariance structure we impose is compound symmetry, hence for longitudinal data, this may not be the best option, yet it will work.

If you want to use the GEE methodology, make sure you load the library geepack first.

### Value

ebic

In the case of "ebic.univregs" a list with one element

had zero variance. It had the same value everywhere.

For all other cases a list including:

stat The value of the test statistic. If the i-th value is zero (0) it means that the i-th

variable had zero variance. It had the same value everywhere.

pvalue The **logarithm of the p-value** of the test. If the i-th value is zero (0) it means

that the i-th variable had zero variance. It had the same value everywhere.

The eBIc of every model. If the i-th value is "Inf" it means that the i-th variable

# Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

### References

Chen J. and Chen Z. (2008). Extended Bayesian information criteria for model selection with large model spaces. Biometrika, 95(3): 759-771.

Eugene Demidenko (2013). Mixed Models: Theory and Applications with R, 2nd Edition. New Jersey: Wiley \& Sons.

McCullagh, Peter, and John A. Nelder. Generalized linear models. CRC press, USA, 2nd edition, 1989.

Presnell Brett, Morrison Scott P. and Littell Ramon C. (1998). Projected multivariate linear models for directional data. Journal of the American Statistical Association, 93(443): 1068-1077.

#### See Also

```
cond.regs, SES, MMPC, CondIndTests, reg.fit, ridge.reg
```

# **Examples**

```
y <- rpois(50, 15)
x <- matrix( rnorm(50 * 7), ncol = 7)
a1 <- univregs(y, x, test = testIndPois)
a2 <- perm.univregs(y, x, test = permPois)
a3 <- wald.univregs(y, x, test = waldPois)</pre>
```

```
Utilities for the skeleton of a (Bayesian) Network

Utilities for the skeleton of a (Bayesian) Network
```

# Description

Utilities for the skeleton of a (Bayesian) Network

# Usage

```
bn.skel.utils(mod, G = NULL, roc = TRUE, alpha = 0.01)
bn.skel.utils2(mod, G = NULL, roc = TRUE, alpha = 0.01)
```

# **Arguments**

mod	An object as retured by pc.skel, glmm.pc.skel or mmhc.skel.
G	The true adjacency matrix with 1 indicating an edge and zero its absence. Symmetric or not is not important. If this is not available, leave it NULL.
roc	Do you want a graph with the ROC curve be returned? Default value is TRUE.
alpha	The significance level ( suitable values in $(0, 1)$ ) for assessing the p-values. Default value is $0.01$ .

#### **Details**

Given the true adjaceny matrix one can evaluate the estimated adjacency matrix, skeleton, of the PC or the MMHC algorithm.

The bn.skels.utils give you the area under the curve, false discovery rate and sorting of the edges based on their p-values.

The bn.skel.utils2 estimates the confidence of each edge. The estimated proportion of null p-values is estimated the algorithm by Storey and Tibshirani (2003).

#### Value

For the "bn.skel.utils" a list including:

fdr The false discovery rate as estimated using the Benjamini-Hochberg correction.

area This is a list with the elements of the auc function. The area under the curve,

the sensitivy and specificity for a range of values, the Youden index, etc.

sig.pvalues A matrix with the row and column of each significant p-value sorted in asending

order. As we move down the matrix, the p-values increase and hence the strength

of the associations decreases.

For the "bn.skel.utils2" a list including:

area This is a list with the elements of the auc function. The area under the curve,

the sensitivy and specificity for a range of values, the Youden index, etc.

pxy A matrix with the row and column of the confidence of each p-value sorted in

asending order. As we move down the matrix, the confidences decrease.

The lower confidence limit of an edge as estimated by conf.edge.lower.

# Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

#### References

Tsamardinos I. and Brown L.E. Bounding the False Discovery Rate in Local Bayesian Network Learning. AAAI, 2008.

Triantafillou S., Tsamardinos I. and Roumpelaki A. (2014). Learning neighborhoods of high confidence in constraint-based causal discovery. In European Workshop on Probabilistic Graphical Models, pp. 487-502.

Storey J.D. and Tibshirani R. (2003). Statistical significance for genome-wide experiments. Proceedings of the National Academy of Sciences, 100: 9440-9445.

Benjamini Y. and Hochberg Y. (1995). Controlling the false discovery rate: a practical and powerful approach to multiple testing. Journal of the Royal Statistical Society Series B, 57(1), 289-300.

Spirtes P., Glymour C. and Scheines R. (2001). Causation, Prediction, and Search. The MIT Press, Cambridge, MA, USA, 3nd edition.

### See Also

```
pc.skel, mmhc.skel, corfs.network, local.mmhc.skel, conf.edge.lower
```

### **Examples**

```
## simulate a dataset with continuous data
y <- rdag2(500, p = 25, nei = 3)
ind <- sample(1:25, 25)
x <- y$x[, ind]
mod <- pc.skel( x, method = "comb.fast", alpha = 0.01 )
G <- y$G[ind, ind]
G <- G + t(G)
bn.skel.utils(mod, G, roc = FALSE, alpha = 0.01)
bn.skel.utils2(mod, G, roc = FALSE, alpha = 0.01)</pre>
```

Variable selection using the PC-simple algorithm

Variable selection using the PC-simple algorithm

# **Description**

Variable selection using the PC-simple algorithm.

### Usage

```
pc.sel(target, dataset, threshold = 0.05)
```

### **Arguments**

target A numerical vector with continuous data.

dataset A matrix with numerical data; the independent variables, of which some will

probably be selected.

threshold The significance level.

# **Details**

Variable selection for continuous data only is performed using the PC-simple algorithm (Buhlmann, Kalisch and Maathuis, 2010). The PC algorithm used to infer the skeleton of a Bayesian Network has been adopted in the context of variable selection. In other words, the PC algorithm is used for a single node.

### Value

A list including:

vars A vector with the selected variables.

n.tests The number of tests performed.

runtime The runtime of the algorithm.

#### Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

#### References

Buhlmann P., Kalisch M. and Maathuis M. H. (2010). Variable selection in high-dimensional linear models: partially faithful distributions and the PC-simple algorithm. Biometrika, 97(2), 261-278. https://arxiv.org/pdf/0906.3204.pdf

#### See Also

```
pc.skel, omp
```

### **Examples**

```
y <- rnorm(100)
x <- matrix( rnorm(100 * 30), ncol = 30)
a <- MXM::pc.sel(y, x)
b <- MMPC(y, x)</pre>
```

Zero inflated Poisson and negative binomial regression

Zero inflated Poisson and negative binomial regression

# Description

Zero inflated Poisson and negative binomial regression.

# Usage

```
zip.mod(target, dataset, wei = NULL, xnew = NULL)
zip.reg(target, dataset, wei = NULL, lgy = NULL)
zinb.mod(target, dataset, xnew = NULL)
zinb.reg(target, dataset, lgy = NULL)
```

### **Arguments**

target The target (dependent) variable. It must be a numerical vector with integers.

dataset The indendent variable(s). It can be a vector, a matrix or a dataframe with con-

tinuous only variables, a data frame with mixed or only categorical variables. If this is NULL, a zero inflated Poisson distribution is fitted, no covariates are

present.

wei A vector of weights to be used for weighted regression. The default value is

NULL. An example where weights are used is surveys when stratified sampling has occured. This is applicable only in the zero inflated Poisson distribution.

xnew	If you have nev	v values for the pre	dictor variables	(dataset) whose target v	variable
------	-----------------	----------------------	------------------	--------------------------	----------

you want to predict insert them here. If you put the "dataset" or leave it NULL

it will calculate the regression fitted values.

lgy If you have already calculated the constant term of the ZIP regression plug it

here. This is the sum of the logarithm of the factorial of the values.

#### **Details**

The zero inflated Poisson regression as suggested by Lambert (1992) is fitted. Unless you have a sufficient number of zeros, there is no reason to use this model. The "zip.reg" is an internal wrapper function and is used for speed up purposes. It is not to be called directly by the user unless they know what they are doing. The zero inflated negative binomial regression does not accept weights though.

#### Value

A list including:

be The estimated coefficients of the model and for the zip.mod and zinb.mod the

standard errors, Wald test statistics and p-values are included.

prop The estimated proportion of zeros.

loglik The log-likelihood of the regression model.

est The estimated values if "xnew" is not NULL.

# Author(s)

Michail Tsagris

R implementation and documentation: Michail Tsagris <mtsagris@uoc.gr>

#### References

Lambert D. (1992). Zero-inflated Poisson regression, with an application to defects in manufacturing. Technometrics, 34(1):1-14.

Rui Fang (2013). Zero-inflated neagative binomial (ZINB) regression model for over-dispersed count data with excess zeros and repeated measures, an application to human microbiota sequence data. MSc thesis, University of Colorado. https://mountainscholar.org/bitstream/handle/10968/244/FANG\_ucdenveramc\_16.

### See Also

```
testIndZIP, zip.regs, reg.fit, ridge.reg
```

### **Examples**

```
y <- rpois(100, 2)
x <- matrix( rnorm(100 * 2), ncol = 2)
a1 <- glm(y ~ x, poisson)
a2 <- zip.mod(y, x)
summary(a1)
logLik(a1)</pre>
```

```
a2 ## a ZIP is not really necessary
y[1:20] <- 0
a1 <- glm(y ~ x, poisson)
a2 <- zip.mod(y, x)
summary(a1)
logLik(a1)
a2 ## a ZIP is probably more necessary</pre>
```

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