## Package 'minerva'

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Title Maximal Information-Based Nonparametric Exploration for Variable Analysis

**Depends** R (>= 3.3.0)

Imports parallel, Rcpp, stats, graphics

LinkingTo Rcpp, RcppArmadillo

Suggests testthat

**Description** Wrapper for 'minepy' implementation of Maximal Information-based Nonparametric Exploration statistics (MIC and MINE family). Detailed information of the ANSI C implementation of 'minepy' can be found at <<u>http://minepy.readthedocs.io/en/latest</u>>.

URL https://www.r-project.org, http://minepy.readthedocs.io/en/latest,

http://www.exploredata.net

License GPL-3

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#### Description

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Maximal Information-Based Nonparametric Exploration R Package for Variable Analysis. The package provides the mine function allowing the computation of Maximal Information-based Non-parametric Exploration statistics, firstly introduced in D. Reshef et al. (2011) *Detecting novel associations in large datasets*. Science 334, 6062 (http://www.exploredata.net). In particular, the package is an R wrapper for the C engine *cmine* (http://minepy.readthedocs.io/en/latest/).

#### Details

Summary:

Package:	minerva
Version:	1.4.3
Date:	2014-10-08
Depends:	R >= (2.14.0)
Enshances:	parallel
URL:	http://www.r-project.org,
	http://minepy.readthedocs.io/en/latest/,
	http://www.exploredata.net
License:	GPL-3

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#### cstats

#### Author(s)

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#### References

D. Reshef, Y. Reshef, H. Finucane, S. Grossman, G. McVean, P. Turnbaugh, E. Lander, M. Mitzenmacher, P. Sabeti. (2011) *Detecting novel associations in large datasets*. Science 334, 6062 (http://www.exploredata.net).

D. Albanese, M. Filosi, R. Visintainer, S. Riccadonna, G. Jurman, C. Furlanello. *cmine, minerva & minepy: a C engine for the MINE suite an its R and Python wrappers.* http://minepy.readthedocs.io/en/latest/

*minepy. Maximal Information-based Nonparametric Exploration in C and Python.* (http://minepy.sourceforge.net)

#### cstats

Compute statistics (MIC and normalized TIC) between each pair of the two collections of variables (convenience function). If n and m are the number of variables in X and Y respectively, then the statistic between the (row) i (for X) and j (for Y) is stored in mic[i, j] and tic[i, j].

#### Description

Compute statistics (MIC and normalized TIC) between each pair of the two collections of variables (convenience function). If n and m are the number of variables in X and Y respectively, then the statistic between the (row) i (for X) and j (for Y) is stored in mic[i, j] and tic[i, j].

#### Usage

cstats(x, y, alpha = 0.6, C = 15, est = "mic\_approx")

#### Arguments

х	Numeric Matrix of m-by-n with n variables and m samples.
У	Numeric Matrix of m-by-p with p variables and m samples.
alpha	number (0, 1.0] or >=4 if alpha is in (0,1] then B will be $max(n^{alpha}, 4)$ where n is the number of samples. If alpha is >=4 then alpha defines directly the B parameter. If alpha is higher than the number of samples (n) it will be limited to be n, so B = min(alpha, n).
С	number (> 0) determines how many more clumps there will be than columns in every partition. Default value is 15, meaning that when trying to draw x grid lines on the x-axis, the algorithm will start with at most $15^*x$ clumps.
est	string ("mic_approx", "mic_e") estimator. With est="mic_approx" the original MINE statistics will be computed, with est="mic_e" the equicharacteristic matrix is evaluated and MIC_e and TIC_e are returned.

#### Value

list of two elements: MIC: the MIC statistic matrix (n x p). TIC: the normalized TIC statistic matrix (n x p).

#### Examples

```
x <- matrix(rnorm(2560), ncol=8, nrow=320)
y <- matrix(rnorm(1280), ncol=4, nrow=320)
mictic <- cstats(x, y, alpha=9, C=5, est="mic_e")
head(mictic)</pre>
```

mictools

Function that implements the mictools pipeline. In particular it computes the null and observed distribution of the tic\_e measure

#### Description

Function that implements the mictools pipeline. In particular it computes the null and observed distribution of the tic\_e measure

#### Usage

```
mictools(x, alpha = 9, C = 5, seed = 0, nperm = 2e+05, p.adjust.method = "BH")
```

#### Arguments

x	a numeric matrix with N samples on the rows and M variables on the columns (NxM).
alpha	float (0, 1.0] or >=4 if alpha is in (0,1] then B will be $max(n^alpha, 4)$ where n is the number of samples. If alpha is >=4 then alpha defines directly the B parameter. If alpha is higher than the number of samples (n) it will be limited to be n, so B = min(alpha, n) Default value is 0.6 (see Details).
С	a positive integer number, the C parameter of the mine statistic. See mine func- tion for further details.
seed	seed for random number generation reproducibility
nperm	integer, number of permutation to perform
p.adjust.metho	d
	method for pvalue adjustment, see p.adjust for available methods.

#### Details

This is a function to implement the 'mictools' pipeline. Differently from the python pipeline available on github we consider a data matrix of NxM with N samples by rows and M variables by columns as standard for R.

#### mictools

#### Value

A list of 5 named elements containing the following information of the computed statistic:

- tic This is a vector with the null distribution of tic\_e values based on the permutation.
- nulldist Null distribution of the tic\_e measure. It is a data.frame of 4 columns containing the histogram of the distribution of tic\_e for each bin delimited by BinStart and BinEnd, the count for each bin NullCount and the cumulative distribution of the right tail area NullCumSum
- **obstic** data.frame with the observed tic\_e values, the indexes of the variables between the tic is computed. If the input matrix has column names then the names are reported in the dataframe, otherwise "Var<i>" is added for each variable.
- obsdists data.frame similar to nulldist but with observed values of tic\_e
- **pval** data.frame with the pvalue computed for each comparison. The adjusted pvalue is also reported based on the method chosen with the parameter p.adjust.method

#### References

D. Albanese, S. Riccadonna, C. Donati, P. Franceschi (2018) \_A practical tool for Maximal Information Coefficient Analysis\_ GigaScience, 7, 4, doi: 10.1093/gigascience/giy032

#### See Also

p.adjust, hist, mine

#### Examples

```
data(Spellman)
Spellman <- as.matrix(Spellman)
spellress <- mictools(Spellman[, 10:20], nperm=1000)
```

## Use a different pvalue correction method spellressb <- mictools(Spellman[,10:20], nperm=1000, seed=1234, p.adjust.method="bonferroni")</pre>

```
## Distribution of tic_e null
hist(spellress$tic, breaks=100, main="Tic_e null distribution")
barplot(spellress$nulldist$NullCount)
```

```
## Distribution of the observed tic
hist(spellress$obstic$TIC)
barplot(spellress$obsdist$Count)
```

```
## Distribution of empirical pvalues
hist(spellress$pval$pval, breaks=50)
```

mictools\_null

#### Description

This set of functions are helper function to compute null distribution of the tic\_e and tic\_e observed distribution from a matrix

#### Usage

```
mictools_null(x, alpha = 9, C = 5, nperm = 200000L, seed = 0L)
```

#### Arguments

х	matrix N x M with M variables and N samples
alpha	numeric value representing parameter for the mine statistic see mine
С	c parameter for the mine statistic see mine
nperm	numper of permutation
seed	integer to set the starting seed for random number generation (for reproducibil- ity).

#### Value

It returns a vector of nperm tic\_e values.

#### Functions

• mictools\_null: compute the tic\_e null distribution

#### See Also

mictools

mic\_strength Compute the association strengh

#### Description

This function uses the null distribution of the tic\_e computed with the function mictools. Based on the available pvalue and the permutation null distribution it identifies reliable association between variables.

#### mic\_strength

#### Usage

mic\_strength(x, pval, alpha = NULL, C = 5, pthr = 0.05, pval.col = NULL)

#### Arguments

x	a numeric matrix with N samples on the rows and M variables on the columns (NxM).
pval	a data.frame with pvalues for each pair of association of the x input matrix. It should contain two colums with the indices of the computed association according to the x input matrix
alpha	float (0, 1.0] or >=4 if alpha is in (0,1] then B will be $max(n^alpha, 4)$ where n is the number of samples. If alpha is >=4 then alpha defines directly the B parameter. If alpha is higher than the number of samples (n) it will be limited to be n, so B = min(alpha, n) Default value is 0.6 (see Details).
С	a positive integer number, the C parameter of the mine statistic. See mine func- tion for further details.
pthr	threshold on pvalue for measure to consider for computing mic_e
pval.col	an integer or character or vector relative to the columns of pval dataframe re- spectively for pvalue, association between variable 1, variable 2 in the x input matrix. See Details for further information.

#### Details

The method implemented here is a wrapper for the original method published by Albanese et al. (2018). The python version is available at https://github.com/minepy/mictools.

This function should be called after the estimation of the null distribution of tic\_e scores based on permutations of the input data.

The mic association is computed only for the variables for which the pvalue in the pval data.frame is less then the threshold set with the pthr input parameter. We assume the first column of the pval data.frame contains the pvalue, this value can be changed using the pval.col[1] parameter.

The pval.col parameter, by default takes the first three columns in the pval data.frame, in particular the first column containing the pvalues of the association between variable in column pval.col[2] and pval.col[3]. If a character vector is provided names in pval.col are matched with the names in pval data.frame. If NULL is passed it is assumed the first column contains pvalue, while the 2 and 3 the index or name of the variable in x. If one value is passed it refers to the pvalue column and the consecutive two columns are assume to contain variable indexes.

#### Value

A dataframe with the tic\_e Pvalue, the mic value and the column identifier regarding the input matrix x of the variables of which the association is computed.

#### See Also

mine, mictools, p.adjust

#### Examples

```
data(Spellman)
mydata <- as.matrix(Spellman[, 10:20])</pre>
ticenull <- mictools(mydata, nperm=1000)</pre>
## Use the nominal pvalue:
ms <- mic_strength(mydata, pval=ticenull$pval, alpha=NULL, pval.col = c(1, 4,5))</pre>
## Use the adjusted pvalue:
ms <- mic_strength(mydata, pval=ticenull$pval, alpha=NULL, pval.col = c(6, 4,5))</pre>
ms
## Not run:
## Use qvalue
require(qvalue)
qobj <- qvalue(ticenull$pval$pval)</pre>
ticenull$pval$qvalue <- qobj$qvalue</pre>
ms <- mic_strength(mydata, pval=ticenull$pval, alpha=NULL, pval.col = c("qvalue", "Var1", "Var2"))</pre>
## Get the data from mictools repository
lnf <- "https://raw.githubusercontent.com/minepy/mictools/master/examples/datasaurus.txt"</pre>
datasaurus <- read.table(lnf, header=TRUE, row.names = 1, stringsAsFactors = FALSE)</pre>
datasaurus <- t(datasaurus)</pre>
ticenull <- mictools(datasaurus, nperm=200000)</pre>
micres <- mic_strength(mydata, ticenull$pval, pval.col=c(6, 4, 5))</pre>
## Plot distribution of pvalues
hist(ticenull$pval, breaks=50, freq=FALSE)
## Plot distribution of tic_e values
hist(ticenull$tic)
## Correct pvalues using qvalue package
require(qvalue)
require(ggplot2)
qobj <- qvalue(ticenull$pval$pval)</pre>
ticenull$pval$qvalue <- qobj$qvalue</pre>
micres <- mic_strength(datasaurus, ticenull$pval, pval.col=c("qvalue", "Var1", "Var2"))</pre>
hist(qobj$qvalue)
df <- data.frame(pi0.labmda=qobj$pi0.lambda, lambda=qobj$lambda, pi0.smooth=qobj$pi0.smooth)
gp0 <- ggplot(df, aes(lambda, pi0.labmda)) + geom_point()</pre>
gp0 <- gp0 + geom_line(aes(lambda, pi0.smooth))</pre>
gp0 <- gp0 + geom_hline(yintercept = qobj$pi0, linetype="dashed", col="red")</pre>
## End(Not run)
```

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mine

mine

MINE family statistics Maximal Information-Based Nonparametric Exploration (MINE) statistics. mine computes the MINE family measures between two variables.

#### Description

MINE family statistics Maximal Information-Based Nonparametric Exploration (MINE) statistics. mine computes the MINE family measures between two variables.

#### Usage

```
mine(
    x,
    y = NULL,
    master = NULL,
    alpha = 0.6,
    C = 15,
    n.cores = 1,
    var.thr = 1e-05,
    eps = NULL,
    est = "mic_approx",
    na.rm = FALSE,
    use = "all.obs",
    normalization = FALSE,
    ...
)
```

#### Arguments

х	a numeric vector (of size <i>n</i> ), matrix or data frame (which is coerced to matrix).
У	NULL (default) or a numeric vector of size <i>n</i> ( <i>i.e.</i> , with compatible dimensions to x).
master	an optional vector of indices (numeric or character) to be given when y is not set, otherwise master is ignored. It can be either one column index to be used as reference for the comparison (versus all other columns) or a vector of column indices to be used for computing all mutual statistics.
alpha	float (0, 1.0] or >=4 if alpha is in (0,1] then B will be $max(n^{alpha}, 4)$ where n is the number of samples. If alpha is >=4 then alpha defines directly the B parameter. If alpha is higher than the number of samples (n) it will be limited to be n, so B = min(alpha, n) Default value is 0.6 (see Details).
С	an optional number determining the starting point of the <i>X-by-Y</i> search-grid. When trying to partition the <i>x</i> -axis into <i>X</i> columns, the algorithm will start with at most CX <i>clumps</i> . Default value is 15 (see Details).

n.cores	ooptional number of cores to be used in the computations, when master is specified. It requires the <b>parallel</b> package, which provides support for parallel computing, released with $R \ge 2.14.0$ . Defaults is 1 ( <i>i.e.</i> , not performing parallel computing).
var.thr	minimum value allowed for the variance of the input variables, since mine can not be computed in case of variance close to 0. Default value is 1e-5. Information about failed check are reported in <i>var_thr.log</i> file.
eps	integer in [0,1]. If 'NULL' (default) it is set to 1-MIC. It can be set to zero for noiseless functions, but the default choice is the most appropriate parametrization for general cases (as stated in Reshef et al. SOM). It provides robustness.
est	Default value is "mic_approx". With est="mic_approx" the original MINE statis- tics will be computed, with est="mic_e" the equicharacteristic matrix is is eval- uated and the mic() and tic() methods will return MIC_e and TIC_e values re- spectively.
na.rm	boolean. This variable is passed directly to the cor-based functions. See cor for further details.
use	Default value is "all.obs". This variable is passed directly to the cor-based functions. See cor for further details.
normalization	logical whether to use normalization when computing tic measure. Ignored for other measures. Default to FALSE.
	currently ignored

#### Details

mine is an R wrapper for the C engine *cmine* (http://minepy.readthedocs.io/en/latest/), an implementation of Maximal Information-Based Nonparametric Exploration (MINE) statistics. The MINE statistics were firstly detailed in D. Reshef et al. (2011) *Detecting novel associations in large datasets*. Science 334, 6062 (http://www.exploredata.net).

Here we recall the main concepts of the MINE family statistics. Let D = (x, y) be the set of *n* ordered pairs of elements of x and y. The data space is partitioned in an *X-by-Y* grid, grouping the x and y values in X and Y bins respectively.

#### The Maximal Information Coefficient (MIC) is defined as

$$MIC(D) = \max_{XY < B(n)} M(D)_{X,Y} = \max_{XY < B(n)} \frac{I^*(D, X, Y)}{log(\min X, Y)},$$

where  $B(n) = n^{\alpha}$  is the search-grid size,  $I^*(D, X, Y)$  is the maximum mutual information over all grids *X-by-Y*, of the distribution induced by D on a grid having X and Y bins (where the probability mass on a cell of the grid is the fraction of points of D falling in that cell). The other statistics of the MINE family are derived from the mutual information matrix achieved by an *X-by-Y* grid on D.

#### The Maximum Asymmetry Score (MAS) is defined as

$$MAS(D) = \max_{XY < B(n)} |M(D)_{X,Y} - M(D)_{Y,X}|.$$

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$$MEV(D) = \max_{XY < B(n)} \{ M(D)_{X,Y} : X = 2 \text{ or } Y = 2 \}.$$

The Minimum Cell Number (MCN) is defined as

$$\mathrm{MCN}(D,\epsilon) = \min_{XY < B(n)} \{ \log(XY) : M(D)_{X,Y} \ge (1-\epsilon)MIC(D) \}.$$

More details are provided in the supplementary material (SOM) of the original paper.

The MINE statistics can be computed for two numeric vectors x and y. Otherwise a matrix (or data frame) can be provided and two options are available according to the value of master. If master is a column identifier, then the MINE statistics are computed for the *master* variable versus the other matrix columns. If master is a set of column identifiers, then all mutual MINE statistics are computed among the column subset. master, alpha, and C refers respectively to the *style, exp*, and c parameters of the original *java* code. In the original article, the authors state that the default value  $\alpha = 0.6$  (which is the exponent of the search-grid size  $B(n) = n^{\alpha}$ ) has been empirically chosen. It is worthwhile noting that alpha and C are defined to obtain an heuristic approximation in a reasonable amount of time. In case of small sample size (n) it is preferable to increase alpha to 1 to obtain a solution closer to the theoretical one.

#### Value

The Maximal Information-Based Nonparametric Exploration (MINE) statistics provide quantitative evaluations of different aspects of the relationship between two variables. In particular mine returns a list of 5 statistics:

MIC	Maximal Information Coefficient.
	It is related to the relationship strenght and it can be interpreted as a correlation
	measure. It is symmetric and it ranges in [0,1], where it tends to 0 for statisti-
	cally independent data and it approaches 1 in probability for noiseless functional
	relationships (more details can ben found in the original paper).
MAS	Maximum Asymmetry Score.
	It captures the deviation from monotonicity. Note that $MAS < MIC$ .
	Note: it can be useful for detecting periodic relationships (unknown frequen-
	cies).
MEV	Maximum Edge Value.
	It measures the closeness to being a function. Note that MEV $\leq$ MIC.
MCN	Minimum Cell Number.
	It is a complexity measure.
MIC-R2	It is the difference between the MIC value and the Pearson correlation coeffi-
	cient.

When computing mine between two numeric vectors x and y, the output is a list of 5 numeric values. When master is provided, mine returns a list of 5 matrices having ncol equal to m. In particular, if master is a single value, then mine returns a list of 5 matrices having 1 column, whose rows correspond to the MINE measures between the *master* column versus all. Instead if master is a vector of m indices, then mine output is a list of 5 m-by-m matrices, whose element i, j corresponds to the MINE statistics computed between the i and j columns of x.

#### Author(s)

Michele Filosi and Roberto Visintainer

#### References

D. Reshef, Y. Reshef, H. Finucane, S. Grossman, G. McVean, P. Turnbaugh, E. Lander, M. Mitzenmacher, P. Sabeti. (2011) *Detecting novel associations in large datasets*. Science 334, 6062 http://www.exploredata.net

(SOM: Supplementary Online Material at https://science.sciencemag.org/content/suppl/ 2011/12/14/334.6062.1518.DC1)

D. Albanese, M. Filosi, R. Visintainer, S. Riccadonna, G. Jurman, C. Furlanello. *minerva and minepy: a C engine for the MINE suite and its R, Python and MATLAB wrappers*. Bioinformatics (2013) 29(3): 407-408, doi: 10.1093/bioinformatics/bts707.

*minepy. Maximal Information-based Nonparametric Exploration in C and Python.* http://minepy.sourceforge.net

#### Examples

```
A <- matrix(runif(50),nrow=5)</pre>
mine(x=A, master=1)
mine(x=A, master=c(1,3,5,7,8:10))
x <- runif(10); y <- 3*x+2; plot(x,y,type="l")</pre>
mine(x,y)
\# MIC = 1
# MAS = 0
\# MEV = 1
\# MCN = 2
\# MIC-R2 = 0
set.seed(100); x <- runif(10); y <- 3*x+2+rnorm(10,mean=2,sd=5); plot(x,y)</pre>
mine(x,y)
# rounded values of MINE statistics
\# MIC = 0.61
# MAS = 0
\# MEV = 0.61
\# MCN = 2
# MIC-R2 = 0.13
t <-seq(-2*pi,2*pi,0.2); y1 <- sin(2*t); plot(t,y1,type="l")</pre>
mine(t,y1)
# rounded values of MINE statistics
\# MIC = 0.66
\# MAS = 0.37
# MEV = 0.66
\# MCN = 3.58
\# MIC-R2 = 0.62
y2 <- sin(4*t); plot(t,y2,type="1")</pre>
```

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```
mine(t,y2)
# rounded values of MINE statistics
\# MIC = 0.32
\# MAS = 0.18
# MEV = 0.32
# MCN = 3.58
# MIC-R2 = 0.31
# Note that for small n it is better to increase alpha
mine(t,y1,alpha=1)
# rounded values of MINE statistics
\# MIC = 1
\# MAS = 0.59
# MEV = 1
\# MCN = 5.67
# MIC-R2 = 0.96
mine(t,y2,alpha=1)
# rounded values of MINE statistics
\# MIC = 1
\# MAS = 0.59
# MEV = 1
# MCN = 5
# MIC-R2 = 0.99
# Some examples from SOM
x <- runif(n=1000, min=0, max=1)</pre>
# Linear relationship
y1 <- x; plot(x,y1,type="1"); mine(x,y1)</pre>
\# MIC = 1
# MAS = 0
# MEV = 1
\# MCN = 4
# MIC-R2 = 0
# Parabolic relationship
y2 <- 4*(x-0.5)^2; plot(sort(x),y2[order(x)],type="1"); mine(x,y2)</pre>
# rounded values of MINE statistics
\# MIC = 1
\# MAS = 0.68
# MEV = 1
\# MCN = 5.5
\# MIC-R2 = 1
# Sinusoidal relationship (varying frequency)
y3 <- sin(6*pi*x*(1+x)); plot(sort(x),y3[order(x)],type="1"); mine(x,y3)</pre>
# rounded values of MINE statistics
\# MIC = 1
\# MAS = 0.85
# MEV = 1
\# MCN = 4.6
# MIC-R2 = 0.96
```

```
# Circle relationship
t <- seq(from=0,to=2*pi,length.out=1000)
x4 <- cos(t); y4 <- sin(t); plot(x4, y4, type="l",asp=1)
mine(x4,y4)
# rounded values of MINE statistics
# MIC = 0.68
# MAS = 0.01
# MEV = 0.32
# MCN = 5.98
# MIC-R2 = 0.68
data(Spellman)
res <- mine(Spellman,master=1,n.cores=1)
## Not run: ## example of multicore computation
res <- mine(Spellman,master=1,n.cores=parallel::detectCores()-1)
## End(Not run)
```

```
mine_stat
```

This is an helper function to compute one mine statistic. It take two vectors of the same dimension as an input.

#### Description

This is an helper function to compute one mine statistic. It take two vectors of the same dimension as an input.

#### Usage

```
mine_stat(
    x,
    y,
    alpha = 0.6,
    C = 15,
    est = "mic_approx",
    measure = "mic",
    eps = NA_real_,
    p = -1,
    norm = FALSE
)
```

#### Arguments

х	Numeric Vector of size n
у	Numeric Vector of size n
alpha	numeric value representing parameter for the mine statistic see mine
С	c parameter for the mine statistic see mine

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#### pstats

est	character estimation parameter for the mine statistic. Possible values are "mic_approx" or "mic_e"
measure	integer indicating which measure to return available measures are: mic, mas, mev, mcn, tic, gmic. The string could be also uppercase. For measure mic-r2 see details.
eps	eps value for MCN statistic should be in (0,1). If NA (default) is passed then the normal MCN statistic is returned.
р	probability for the generalized mic
norm	boolean if require normalization between 0 and 1 for the tic statistic

#### Details

This is a wrapper function to compute the mine statistic between two variables. for more details on the available measure and the meaning of the other parameters see also the documentation for the mine function.

For measure mic-r2 use the Pearson R coefficient score cor and the measure mic. See the example below.

#### See Also

mine

#### Examples

```
x <- runif(10); y <- 3*x+2;
mine_stat(x,y, measure="mic")
## Measure mic-r2
x <- matrix(rnorm(20), ncol=2, nrow=10)
mmic <- mine_stat(x[,1], x[,2], measure="mic")
r2 <- cor(x[,1], x[,2])
mmic - r2**2
```

pstats

*Compute pairwise statistics (MIC and normalized TIC) between variables (convenience function).* 

#### Description

For each statistic, the upper triangle of the matrix is stored by row (condensed matrix). If m is the number of variables, then for i < j < m, the statistic between (col) i and j is stored in k = m\*i - i\*(i+1)/2 - i - 1 + j. The length of the vectors is n = m\*(m-1)/2.

#### Usage

pstats(x, alpha = 0.6, C = 15, est = "mic\_approx")

#### Arguments

x	Numeric Matrix of m-by-n with n variables and m samples.
alpha	number (0, 1.0] or >=4 if alpha is in (0,1] then B will be $max(n^alpha, 4)$ where n is the number of samples. If alpha is >=4 then alpha defines directly the B parameter. If alpha is higher than the number of samples (n) it will be limited to be n, so B = min(alpha, n).
С	number (> 0) determines how many more clumps there will be than columns in every partition. Default value is 15, meaning that when trying to draw x grid lines on the x-axis, the algorithm will start with at most $15*x$ clumps.
est	string ("mic_approx", "mic_e") estimator. With est="mic_approx" the original MINE statistics will be computed, with est="mic_e" the equicharacteristic matrix is is evaluated and MIC_e and TIC_e are returned.

#### Value

A matrix of  $(n \times (n-1)/2)$  rows and 4 columns. The first and second column are the indexes relative to the columns in the input matrix x for which the statistic is computed for. Column 3 contains the MIC statistic, while column 4 contains the normalized TIC statistic.

#### Examples

```
## Create a matrix of random numbers
## 10 variables x 100 samples
x <- matrix(rnorm(1000), ncol=10)
res <- pstats(x)</pre>
```

head(res)

Spellman

CDC15 Yeast Gene Expression Dataset

#### Description

The Spellman dataset provides the gene expression data measured (on a custom platform) in *Saccharomyces cerevisiae* cell cultures that have been synchronized at different points of the cell cycle by using a temperature-sensitive mutation (*cdc15-2*), which arrestes cells late in mitosis at the restrictive temperature (it can cause heat-shock).

#### Usage

Spellman

#### Format

23 rows x 4382 columns: 4381 transcripts (columns 2:4382) measured at 23 timepoints (column 1).

#### Spellman

#### Source

The original data were published by Spellman and colleagues in Mol. Biol. Cell (1998) as the Botstein dataset. Here we include the version of the dataset as processed by Reshef and colleagues for the MINE statistics original article published in Science (2011) (details are provided in the supplementary material).

#### References

D. Reshef, Y. Reshef, H. Finucane, S. Grossman, G. McVean, P. Turnbaugh, E. Lander, M. Mitzenmacher, P. Sabeti. (2011) *Detecting novel associations in large datasets*. Science 334, 6062 (http://www.exploredata.net).

P. T. Spellman, G. Sherlock, M. Q. Zhang, V. R. Iyer, K. Anders, M. B. Eisen, P. O. Brown, D. Botstein, B. Futcher. (1998) *Comprehensive Identification of Cell Cycle–regulated Genes of the Yeast Saccharomyces cerevisiae by Microarray Hybridization*. Mol. Biol. Cell, 9:12 3273–3297.

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