

# Package ‘ctgt’

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**Type** Package

**Title** Closed Testing with Globaltest for Pathway Analysis

**Version** 1.0

**Date** 2020-02-21

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**Description** A shortcut procedure is proposed to implement closed testing for large-scale multiple testings, especially with the global test. This shortcut is asymptotically equivalent to closed testing and post hoc. Users could detect any possible sets of features or pathways with family-wise error rate controlled. The global test is powerful to detect associations between a group of features and an outcome of interest.

**License** GPL (>= 2)

**Imports** Rcpp (>= 1.0.3)

**LinkingTo** Rcpp, BH

**SystemRequirements** C++11

**NeedsCompilation** yes

**Repository** CRAN

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ctgt-package

*'Closed Testing with Globaltest for Pathway Analysis'*

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### Description

A shortcut procedure for closed testing with the global test is presented.

### Details

See examples in `actgt` function.

### Author(s)

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### References

Ningning Xu, Aldo solari, Jelle Goeman, Cloed testing with global test, with applications on metabolomics data, arXiv:2001.01541, <https://arxiv.org/abs/2001.01541> Jelle J. Goeman, Sara A. van de Geer, Floor de Kort, Hans C. van Houwelingen, A global test for groups of genes: testing association with a clinical outcome, *Bioinformatics*, Volume 20, Issue 1, 1 January 2004, Pages 93-99, <https://doi.org/10.1093/bioinformatics/btg382>

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1-alpha quantile

*The 1-alpha quantile of globaltest*

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### Description

Robbins and Pitman Algorithm to calculate the criticalvalue given eigenvalue vector and alpha level.

### Usage

```
criticalvalue(lam, alpha = 0.05)
```

### Arguments

lam            The numeric vector with eigenvalues as elements.  
alpha         The type I error rate allowed. The default is 0.05.

### Value

Returns a real number.

**Author(s)**

Ningning Xu

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**References**

Ningning Xu, Aldo solari, Jelle Goeman, Clsoed testing with global test, with applications on metabolomics data, arXiv:2001.01541, <https://arxiv.org/abs/2001.01541>

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closed testing with globaltest

*Approximated Closed Testing with Global Test*

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**Description**

To detect the significance of the set of features after correcting for multiple global tests, with family-wise error rate controlled.

**Usage**

```
actgt (y, X, xs, hyps, maxit = 0, alpha = 0.05)
```

**Arguments**

y	The response vector (numeric vector).
X	The full design matrix, whose columns are named by the covariates.
xs	The name vector of all covariates (character vector).
hyps	The name vector of the covariates in the pathway of interest (character vector).
maxit	An optional integer to denote the maximal iterations for branch and bound method. The default value 0 means the single-step shortcut without branch and bound method. Note that larger value is more time-consuming.
alpha	The type I error rate allowed. The default is 0.05.

**Value**

Returns a list of rejection indicator and the number of iterations.

**Author(s)**

Ningning Xu

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**References**

Ningning Xu, Aldo solari, Jelle Goeman, Clsoed testing with global test, with applications on metabolomics data, arXiv:2001.01541, <https://arxiv.org/abs/2001.01541>

**Examples**

```

#Generate the design matrix and response vector for logistic regression models
n= 100
m = 5
X = matrix(0, n, m,byrow = TRUE )
for ( i in 1:n){
  set.seed(1234+i)
  X[i,] = as.vector(arima.sim(model = list(order = c(1, 0, 0), ar = 0.2), n = m) )
}

y = rbinom(n,1,0.6)
X[which(y==1),1:3] = X[which(y==1),1:3] + 0.8

xs = paste("x",seq(1,m,1),sep="")
colnames(X) = xs

hyps=xs[1]

#The sinle-step ctgt procedure
actgt(y,X,xs,hyps)
#Result Iterations
#"unsure"      "0"

# The iterative ctgt procedure with more iterations
actgt(y,X,xs,hyps,maxit=10)
#Result Iterations
#"reject"      "2"
#which means that x1 is rejected by closed testing within two more iterations of the shortcut

# For a group of feature sets
mysets = list(xs[1:5], xs[c(1,4)], xs[c(1,4,5)])
sapply(mysets, function(i) actgt(y,X,xs,i))
#Result      "reject" "unsure" "reject"
#Iterations "0"      "0"      "0"

mysets = list(xs[1:5], xs[c(1,4)], xs[c(1,4,5)])
sapply(mysets, function(i) actgt(y,X,xs,i,maxit=10))
#Result      "reject" "reject" "reject"
#Iterations "0"      "2"      "0"

```

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internalfunctions      *'Internal Functions (ctgt)'*

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**Description**

Internal functions of ctgt.

**Usage**

```
## iterative shortcut with branch and bound
actgt_it(y,Tmatrix, Cmatrix,fxs, sxs,Tf,Lamf,Cf,Ts,Lams,Cs,count=1,maxIt=1,a = 0.05)

## to check whether tmin is above cmax
tacmax(tmins,levels,tw, cf,lf,ls,alp )

## to check whether tmin is above ctrue
tactrue(tmins,hyxs,cfull,Wmatrix,alp )
```

**Arguments**

y	The response vector (numeric vector).
Tmatrix	The matrix used to calculate the test statistics.
Cmatrix	The matrix used to calculate the critical values.
fxs	The name vector of upper model (character vector).
sxs	The name vector of lower model (character vector).
Tf,Lamf,Cf	Test statistic, eigenvalues, and critical value of fxs.
Ts,Lams,Cs	Test statistic, eigenvalues, and critical value of sxs.
count	count the branches, default is 1.
maxIt	maximal number of branches chosen by user, default is 1.
a, alp	alpha level.
tmins	Minimum test statistics.
levels	levels
tw, cf,lf,ls	sorted weights, critical values and level for fxs and sxs.
hyxs	The name vector of the covariates of interest (character vector).
cfull	critical value of full model.
Wmatrix	matrix to calculate majorizing vector.

**Author(s)**

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majorizing vector      *The majorizing vector*

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**Description**

To get the majorizing vector at a specific level, given the upbound and lowbound.

**Usage**

```
getL (ub, lb, level)
```

**Arguments**

ub	upper bound.
lb	lower bound.
level	level of interest.

**Value**

Returns a numeric vector with the same length as ub and lb.

**Author(s)**

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**References**

Ningning Xu, Aldo solari, Jelle Goeman, Clsoed testing with global test, with applications on metabolomics data, arXiv:2001.01541, <https://arxiv.org/abs/2001.01541>

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non-standardized globaltest  
*'Non-standardized globaltest'*

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**Description**

This is the sencond version of the globaltest, the non-standardized globaltest

**Usage**

```
## a powerful variant of globaltest  
gt2 (y, X, hys, alpha = 0.05)
```

**Arguments**

y	The response vector (numeric vector).
X	The full design matrix, whose columns are named by the covariates.
hyps	The name vector of the covariates in the pathway of interest (character vector).
alpha	The type I error rate allowed. The default is 0.05.

**Value**

Returns the p-value, the observed and expected test statistics and the number of covariates.

**Author(s)**

Ningning Xu

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**References**

Ningning Xu, Aldo solari, Jelle Goeman, Clsoed testing with global test, with applications on metabolomics data, arXiv:2001.01541, <https://arxiv.org/abs/2001.01541>

**Examples**

```
#Generate the design matrix and response vector for logistic regression models
n= 100
m = 5
X = matrix(0, n, m,byrow = TRUE )
for ( i in 1:n){
  set.seed(1234+i)
  X[i,] = as.vector(arima.sim(model = list(order = c(1, 0, 0), ar = 0.2), n = m) )
}

y = rbinom(n,1,0.6)
X[which(y==1),1:3] = X[which(y==1),1:3] + 0.8

xs = paste("x",seq(1,m,1),sep="")
colnames(X) = xs

hyps=xs[1]

#The raw p-values of globaltest
gt2(y,X,hyps)
#p-value Statistic Expected      #Cov
#7.64e-03  2.30e+02  1.24e+02  1.00e+00
```

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p-value	<i>p-value of globaltest</i>
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**Description**

Robbins and Pitman Algorithm to calculate the p-value given the observed value and the eigenvalue vector.

**Usage**

```
pv(x, lam)
```

**Arguments**

x	The observed value that is used to calculate the corresponding the p-value.
lam	The numeric vector with eigenvalues as elements.

**Value**

Returns a value between 0 and 1.

**Author(s)**

Ningning Xu

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**References**

Ningning Xu, Aldo solari, Jelle Goeman, Clsoed testing with global test, with applications on metabolomics data, arXiv:2001.01541, <https://arxiv.org/abs/2001.01541>

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true discoveries	<i>True discoveries</i>
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**Description**

To count the number of true discoveries within a given pathway or feature set of interest.

**Usage**

```
discoveries (y, X, xs, hyps, maxit = 0, alpha = 0.05)
```



**Arguments**

y	The response vector (numeric vector).
X	The full design matrix, whose columns are named by the covariates.
xs	The name vector of all covariates (character vector).
hyps	The name vector of the covariates in the pathway of interest (character vector).
maxit	An optional integer to denote the maximal iterations for branch and bound method. The default value 0 means the single-step shortcut without branch and bound method. Note that larger value is more time-consuming.
alpha	The type I error rate allowed. The default is 0.05.

**Value**

Returns a non-negative interger.

**Author(s)**

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**References**

Ningning Xu, Aldo solari, Jelle Goeman, Clsoed testing with global test, with applications on metabolomics data, arXiv:2001.01541, <https://arxiv.org/abs/2001.01541>

**Examples**

```
#Generate the design matrix and response vector for logistic regression models
n= 100
m = 5
X = matrix(0, n, m,byrow = TRUE )
for ( i in 1:n){
  set.seed(1234+i)
  X[i,] = as.vector(arima.sim(model = list(order = c(1, 0, 0), ar = 0.2), n = m) )
}

y = rbinom(n,1,0.6)
X[which(y==1),1:3] = X[which(y==1),1:3] + 0.8

xs = paste("x",seq(1,m,1),sep="")
colnames(X) = xs

# For standardized data
X = scale(X,center = FALSE,scale = TRUE)/sqrt(n-1)
interest = xs

discoveries(y,X,xs,hyps = interest)
#2
discoveries(y,X,xs,hyps = interest,maxit=10)
#2
```

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