

# Package ‘Mulcom’

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**Type** Package

**Title** Calculates Mulcom test

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**Author** Claudio Isella

**Maintainer** Claudio Isella <claudio.isella@ircc.it>

**Depends** R (>= 2.10), fields, Biobase

**Imports** graphics, grDevices, stats, methods

**Description** Identification of differentially expressed genes and false discovery rate (FDR) calculation by Multiple Comparison test

**License** GPL-2

**LazyLoad** yes

**biocViews**

StatisticalMethod, MultipleComparison, Microarray, DifferentialExpression, GeneExpression

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Affy *Affy Dataset*

**Description**

Affy Dataset

**Author(s)**

Claudio Isella, <claudio.isella@ircc.it>

AffyIImn *cross mapping table*

**Description**

cross mapping table

**Author(s)**

Claudio Isella, <claudio.isella@ircc.it>

---

harmonicMean

*MulCom Harmonic Mean*

---

**Description**

Computes harmonic means across groups replicate Should not be called directly

**Usage**

```
harmonicMean(index)
```

**Arguments**

index            a numeric vector with the groups labels of the samples. 0 are the control samples.  
Number must be progressive

**Details**

harmonicMean calculates harmonic means across groups replicate for the estimation of Mulcom Test

**Value**

a numeric vector

**Author(s)**

Claudio Isella, <claudio.isella@ircc.it>

**References**

<claudio.isella@ircc.it>

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Illumina

*Illumina Dataset*

---

**Description**

Illumina Dataset

**Author(s)**

Claudio Isella, <claudio.isella@ircc.it>

Ilnn

*Ilnn Dataset*

---

**Description**

Ilnn Dataset

**Author(s)**

Claudio Isella, &lt;claudio.isella@ircc.it&gt;

---

limmaAffySymbols*significant gene list with limma in Affymetrix*

---

**Description**

significant gene list with limma in Affymetrix

**Author(s)**

Claudio Isella, &lt;claudio.isella@ircc.it&gt;

---

limmaIlnnSymbols*significant gene list with limma in Illumina*

---

**Description**

significant gene list with limma in Illumina

**Author(s)**

Claudio Isella, &lt;claudio.isella@ircc.it&gt;

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mulCalc	<i>MulCom Calculation</i>
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---

**Description**

Calculates MulCom test score for given m and t parameters

**Usage**

```
mulCalc(Mulcom_P, m, t)
```

**Arguments**

Mulcom_P	an object of class MULCOM
m	m: a numeric value corresponding to log 2 ratio correction for MulCom Test
t	t: a numeric value corresponding to T values for MulCom Test

**Details**

mulCalc Calculate the Mulcom Score with m and t defined by the user

Mulcom\_P: an object of class MULCOM\_P

m: a number corresponding to log 2 ratio correction for MulCom Test

t: a number corresponding to T values for MulCom Test

**Author(s)**

Claudio Isella, <claudio.isella@ircc.it>

**Examples**

```
data(benchVign)
mulcom_scores <- mulScores(Affy, Affy$Groups)
mulcom_calc <- mulCalc(mulcom_scores, 0.2, 2)
```

---

mulCAND *Identify the Mulcom candidate feature selection*

---

### Description

Identify the Mulcom candidate feature selection by the m and T defined by the user

### Usage

```
mulCAND(eset, Mulcom_P, m, t, ese = "T")
```

### Arguments

eset	an <a href="#">AffyBatch</a>
Mulcom_P	an object of class MULCOM
m	m: a numeric vector corresponding to log 2 ratio correction
t	t: a numeric vector corresponding to the MulCom T values
ese	True or False

### Details

mulCAND Identify the Mulcom candidate feature selection by the m and T defined by the user

### Author(s)

Claudio Isella, <claudio.isella@ircc.it>

### Examples

```
data(benchVign)
mulcom_perm <- mulPerm(Affy, Affy$Groups, 10,2)
mulcom_cand <- mulCAND(Affy, mulcom_perm, 0.2, 2)
```

---

MULCOM-class *Class MulCom*

---

### Description

This is a class representation MulCom test scores

### Objects from the Class

Objects can be created using the function [mulScores](#) on ExpressionSet.

**Slots**

- FC:** Object of class `numeric` representing difference between all experimental groups and the reference groups
- HM:** Object of class `numeric` representing the harmonic means in all subgroups
- MSE\_Corrected:** Object of class `numeric` representing the MulCom test estimation of mean square error as described in the formula of the Dunnett's t-test

**Author(s)**

Claudio Isella

**Examples**

```
data(benchVign)
mulcom_scores <- mulScores(Affy, Affy$Groups)
```

---

`mulcomGeneListIlmn`      *significant gene list with limma in Illumina*

---

**Description**

significant gene list with limma in Illumina

**Author(s)**

Claudio Isella, <claudio.isella@ircc.it>

---

`MULCOM_P-class`      *Class MulCom Permutation*

---

**Description**

This is a class representation MulCom test scores permutation

**Objects from the Class**

Objects can be created using the function `mulScores` on `ExpressionSet`.

**Slots**

- FC:** Object of class `numeric` representing delta between all experimental groups and the reference groups
- MSE\_Corrected:** Object of class `numeric` representing the MulCom test estimation of mean square error as described in the formula of the Dunnett's t-test
- FCp:** Object of class `numeric` representing delta between all experimental groups and the reference groups in permuted data
- MSE\_Correctedp:** Object of class `numeric` representing the MulCom test estimation of mean square error as described in the formula of the Dunnett's t-test in permuted data

**Author(s)**

Claudio Isella

**Examples**

```
data(benchVign)
mulcom_scores <- mulScores(Affy, Affy$Groups)
```

---

mulDELTA

*MulCom Delta*

---

**Description**

Computes Delta for all the experimental points in the datasets in respect to control Should not be called directly

**Usage**

```
mulDELTA(vector, index)
```

**Arguments**

vector	vector: numeric vector with data measurements
index	a numeric vector with the labels of the samples. 0 are the control samples. number must be progressive

**Details**

mulDELTA An internal function that should not be called directly. It calculates differential expression in the groups defined in the index class vector, in respect to the 0 groups

**Value**

vector	a numeric vector with data measurements
index	a numeric vector with the labels of the samples. 0 are the control samples. number must be progressive

**Author(s)**

Claudio Isella, <claudio.isella@ircc.it>

**Examples**

```
data(benchVign)
mulcom_delta <- mulDELTA(exprs(Affy[1,]), Affy$Groups)
```



---

`mulDiff`*MulCom Test Differential analysis*

---

**Description**

Identify the differentially expressed features for a specific comparison with given m and t value

**Usage**

```
mulDiff(eset, Mulcom_P, m, t, ind)
```

**Arguments**

<code>eset</code>	An ExpressionSet object from package affy
<code>Mulcom_P</code>	An object of class Mulcom_P
<code>m</code>	the m values for the analysis
<code>t</code>	the t values for the analysis
<code>ind</code>	and index refeing to te comparison, should be numeric

**Value**

<code>eset</code>	An ExpressionSet object from package affy
<code>Mulcom_P</code>	An object of class Mulcom_P
<code>m</code>	the m values for the analysis
<code>t</code>	the t values for the analysis
<code>ind</code>	and index refeing to te comparison, should be numeric

**Author(s)**

Claudio Isella, <claudio.isella@ircc.it>

**Examples**

```
data(benchVign)
mulcom_perm <- mulPerm(Affy, Affy$Groups, 10, 7)
mulcom_diff <- mulDiff(Affy, mulcom_perm, 0.2, 2)
```

mulFSG

*MulCom False Significant Genes*

---

**Description**

Calculate the False Significant Genes for m and t defined by the user

**Usage**

```
mulFSG(Mulcom_P, m, t)
```

**Arguments**

Mulcom_P	an object of class MULCOM
m	m: a numeric value corresponding to log 2 ratio correction for MulCom Test
t	t: a numeric value corresponding to t values for MulCom Test

**Details**

mulFDR evaluate the False Significant genes on the Mulcom\_P object according to specific m and t parameters. For each permutation it is calculated the number of positive genes. An estimation of the false called genes is evaluated with the median for each experimental subgroups

**Author(s)**

Claudio Isella, <claudio.isella@ircc.it>

**Examples**

```
data(benchVign)
mulcom_perm <- mulPerm(Affy, Affy$Groups, 10, 7)
mulcom_fsg <- mulFSG(mulcom_perm, 0.2, 2)
```

---

mulIndex*Mulcom Index for Monte Carlo Simlation*

---

**Description**

Random assebly of the groups indices for Monte Carlo Simulation

**Usage**

```
mulIndex(index, np, seed)
```

**Arguments**

index	the vector with the groups of analysis, must be numeric and 0 correspond to the reference.
np	number of permutation in the simulation
seed	seed for permtations

**Details**

'mulIndex' generates random index for the function mulPerm. it is not directly called by the user.

**Value**

A matrix with all indices permutations

**Author(s)**

Claudio Isella, <claudio.isella@ircc.it>

**Examples**

```
data(benchVign)
mulcom_scores <- mulIndex(Affy$Groups, 5, 7)
```

---

mulInt *generates a consensus matrix from list of genes*

---

**Description**

generates a consensus matrix from list of genes

**Usage**

```
mulInt(...)
```

**Arguments**

... the function requires vector files as inputs

**Details**

mulCAND generates a consensus matrix from list of genes

**Author(s)**

Claudio Isella, <claudio.isella@ircc.it>

**Examples**

```

data(benchVign)
mulcom_perm <- mulPerm(Affy, Affy$Groups, 10,2)
mulcom_opt <- mulOpt(mulcom_perm, vm = seq(0,0.5, 0.1), vt = seq(1,3, 0.1))

h1_opt <- mulParOpt(mulcom_perm, mulcom_opt, ind = 1, th = 0.05)
h2_opt <- mulParOpt(mulcom_perm, mulcom_opt, ind = 1, th = 0.05)

int <- mulInt(h1_opt, h2_opt)

```

---

mulMSE

*MulCom Mean Square Error*


---

**Description**

Computes Mean Square Error for all the experimental points in the datasets in respect to control  
Should not be called directly

**Usage**

```
mulMSE(vector, index, tmp = vector())
```

**Arguments**

vector	a numeric vector with data measurements
index	a numeric vector with the labels of the samples. 0 are the control samples. number must be progressive
tmp	a vector

**Details**

mulMSE An internal function that should not be called directly. It calculates within group means square error for the values defined in the x vector according to the index class vector

**Value**

vector	a numeric vector with data measurements
index	a numeric vector with the labels of the samples. 0 are the control samples. number must be progressive
tmp	a vector

**Author(s)**

Claudio Isella, <claudio.isella@ircc.it>

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mulOpt	<i>MulCom optimization</i>
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---

**Description**

The function systematically performs the calculation of significant genes and corresponding FDR for all the combination of given list of m and t values.

**Usage**

```
mulOpt(Mulcom_P, vm, vt)
```

**Arguments**

Mulcom_P	an object of class Mulcom_P
vm	a vector of m values to test
vt	a vector of t values to test

**Details**

mulOpt The function systematically performs the calculation of significant genes and corresponding FDR for all the combination of given list of m and t values.

**Author(s)**

Claudio Isella, <claudio.isella@ircc.it>

**Examples**

```
data(benchVign)
mulcom_perm <- mulPerm(Affy, Affy$Groups, 10, 7)
mulcom_opt <- mulOpt(mulcom_perm, seq(0.1, 0.5, 0.1), seq(1, 3, 0.1))
```

---

mulOptPars	<i>MulCom Parameter Optimization</i>
------------	--------------------------------------

---

**Description**

Function to optimize Mulcom parameter for maximum number of genes with a user defined FDR

**Usage**

```
mulOptPars(opt, ind, ths)
```

**Arguments**

opt            an MulCom optimization object  
ind            index corresponding to the comparison  
ths            a threshold for the FDR optimization, default is 0.05

**Details**

mulOptPars MulCom optimization function to identify best parameters

**Author(s)**

Claudio Isella, <claudio.isella@ircc.it>

**Examples**

```
data(benchVign)
mulcom_perm <- mulPerm(Affy, Affy$Groups, 10, 7)
#mulcom_opt <- mulOpt(mulcom_perm, seq(0.1, 0.5, 0.1), seq(1, 3, 0.1))
#optThs <- mulOptPars(mulcom_opt, 1, 0.05)
```

---

mulOptPlot

*MulCom optimization Plot*


---

**Description**

MulCom optimization Plot to identify best configuration paramters

**Usage**

```
mulOptPlot(M.Opt, ind, th, smooth = "NO")
```

**Arguments**

M.Opt            an MulCom optimization object  
ind            index corresponding to the comparison to plot  
th            a threshold for the FDR plot  
smooth           indicates whether the FDR plot will show a significant threshold or will be continuous.

**Details**

mulOptPlot MulCom optimization Plot

**Value**

a numeric vector

**Author(s)**

Claudio Isella, <claudio.isella@ircc.it>

**Examples**

```
data(benchVign)
mulcom_perm <- mulPerm(Affy, Affy$Groups, 10,2)
mulcom_opt <- mulOpt(mulcom_perm, vm=seq(0.1, 0.5, 0.1), vt=seq(1, 3,1))
mulOptPlot(mulcom_opt, 1, 0.05)
```

---

mulParOpt

*MulCom Parameters Optimization*


---

**Description**

MulCom parameter optimization function to identify best combination of t and m providing maximum number of genes at a given FDR

**Usage**

```
mulParOpt(perm, M.Opt, ind, th, image = "T")
```

**Arguments**

perm	a object with permuted MulCom Scores
M.Opt	an MulCom optimization object
ind	index corresponding to the comparison to plot
th	a threshold for the FDR plot
image	default = "T", indicates is print the MulCom optimization plot

**Details**

mulParOpt The function mulParOpt is designed to identify the optimal m and t values combination leading to the maximum number of differentially regulated genes satisfying an user define FDR threshold. In case of equal number of genes, the combination of m and t with the lower FDR will be prioritized. In case of both identical number of genes and FDR, the function will chose the highest t. The function optionally will define a graphical output to visually inspect the performance of the test at given m and t parameters for a certain comparison.

**Author(s)**

Claudio Isella, <claudio.isella@ircc.it>

**Examples**

```
data(benchVign)
mulcom_perm <- mulPerm(Affy, Affy$Groups, 10,2)
mulcom_opt <- mulOpt(mulcom_perm, vm=seq(0.1, 0.5, 0.1), vt=seq(1, 3,1))
mulParOpt(mulcom_perm, mulcom_opt, 1, 0.05)
```

---

mulPerm	<i>MulCom Permutation</i>
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---

### Description

Reiterate MulCom Test on permuted data to perform Montecarlo simulation

### Usage

```
mulPerm(eset, index, np, seed, segm = "F")
```

### Arguments

eset	An an <a href="#">AffyBatch</a> object, each row of must correspond to a variable and each column to a sample.
index	a numeric vector of length ncol(data) with the labels of the samples. 0 are the reference samples.
np	a numeric values indicating the number of permutation to perform. It is set as default to 10
seed	set the seed of the permutaton, default is 1
segm	a default set to F. This parametheres requires to be setted to avoid segmentation fault of C subroutin in the case of very large datasets.

### Details

mulPerm

### Author(s)

Claudio Isella, <claudio.isella@ircc.it>

### Examples

```
data(benchVign)
mulcom_perm <- mulPerm(Affy, Affy$Groups, 10,2)
```



---

`mulPermC`*MulCom Permutation*

---

**Description**

R pipe to C function not called directly by user that reiterate MulCom Test on permuted data to perform Monte Carlo simulation

**Usage**

```
mulPermC(eset, index, means, mse, n, m, nump, ngroups, reference)
```

**Arguments**

<code>eset</code>	An an <a href="#">AffyBatch</a> object, each row of must correspond to a variable and each column to a sample.
<code>index</code>	a numeric vector of length <code>ncol(data)</code> with the labels of the samples. 0 are the reference samples.
<code>means</code>	entry for the means output.
<code>mse</code>	entry for the mean square errors output
<code>n</code>	number of rows in obext of class <code>eset</code>
<code>m</code>	number of columns
<code>nump</code>	number of permutation to perform
<code>ngroups</code>	a number corresponding to the number of groups in the analysis.
<code>reference</code>	reference for the comparisons. typically it is 0

**Details**`mulPerm`**Author(s)**

Claudio Isella, <[claudio.isella@ircc.it](mailto:claudio.isella@ircc.it)>

**Examples**

```
data(benchVign)
```

---

`mulScores`*MulCom Score Calculation*

---

**Description**

Computes the scores for the MulCom test. The function calculates the numerator and the denominator of the test without the parameters `m` and `t`

**Usage**

```
mulScores(eset, index)
```

**Arguments**

<code>eset</code>	An an <a href="#">AffyBatch</a> object, each row of must correspond to a variable and each column to a sample.
<code>index</code>	a numeric vector of length <code>ncol(data)</code> with the labels of the samples. 0 are the reference samples.

**Details**

'mulScore' computes the scores for the MulCom test for multiple point profile. The Mulcom test is designed to compare each experimental mean with the control mean and it is derived from the "Dunnett's test". Dunnett's test controls the Experiment-wise Error Rate and is more powerful than tests designed to compare each mean with each other mean. The test is conducted by computing a modified t-test between each experimental group and the control group.

**Value**

An Object of class MULCOM from Mulcom package

**Author(s)**

Claudio Isella, <claudio.isella@ircc.it>

**Examples**

```
data(benchVign)
mulcom_scores <- mulScores(Affy, Affy$Groups)
```

---

mulSSE	<i>MulCom Sum of Square Error</i>
--------	-----------------------------------

---

**Description**

Computes sum of square errors for all the experimental points in the datasets Should not be called directly

**Usage**

```
mulSSE(vec, index)
```

**Arguments**

vec	a numeric vector with data measurements
index	a numeric vector with the labels of the samples. 0 are the control samples. number should be progressive

**Details**

mulSSE An internal function that should not be called directly. It calculates sum of square error in the groups defined in the index class vector.

**Value**

vec	a numeric vector with data measurements
index	a numeric vector with the labels of the samples. 0 are the control samples. number must be progressive

**Author(s)**

Claudio Isella, <claudio.isella@ircc.it>

---

samAffySymbols	<i>significant gene list with SAM in Affymetrix</i>
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**Description**

significant gene list with SAM in Affymetrix

**Author(s)**

Claudio Isella, <claudio.isella@ircc.it>

---

samI1mnSymbols	<i>significant gene list with SAM in Illumina</i>
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---

**Description**

significant gene list with SAM in Illumina

**Author(s)**

Claudio Isella, <claudio.isella@ircc.it>

---

samOptPars	<i>sam Parameter Optimization</i>
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---

**Description**

Function to optimize Sam parameter for maximim nuber of genes with a user defined FDR

**Usage**

```
samOptPars(opt, ths)
```

**Arguments**

opt	an Sam optimization object
ths	a threshold for the FDR optimization

**Value**

a numeric vector

**Author(s)**

Claudio Isella, <claudio.isella@ircc.it>

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