Package 'SimComp'

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Type Package

Title Simultaneous Comparisons for Multiple Endpoints

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Author Mario Hasler, Christof Kluss

Maintainer Mario Hasler <hasler@email.uni-kiel.de>

Imports mvtnorm, multcomp, mratios, graphics, stats

Description Simultaneous tests and confidence intervals are provided for one-way experimental designs with one or many normally distributed, primary response variables (endpoints). Differences (Hasler and Hothorn, 2011 <doi:10.2202/1557-4679.1258>) or ratios (Hasler and Hothorn, 2012 <doi:10.1080/19466315.2011.633868>) of means can be considered. Various contrasts can be chosen, unbalanced sample sizes are allowed as well as heterogeneous variances (Hasler and Hothorn, 2008 <doi:10.1002/bimj.200710466>) or covariance matrices (Hasler, 2014 <doi:10.1515/ijb-2012-0015>).

License GPL

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Contents

`SimComp-package` *Simultaneous Comparisons for Multiple Endpoints*

Description

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Details

The DESCRIPTION file:

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Author:	Mario Hasler, Christof Kluss
Maintainer:	Mario Hasler <hasler@email.uni-kiel.de>
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License:	GPL
LazyLoad:	yes

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                        (1946) for Differences of Means
DfSattRat               Degrees of Freedom Accoding to Satterthwaite
                        (1946) for Ratios of Means
SimCiDiff               Simultaneous Confidence Intervals for General
                        Contrasts (Differences) of Means of Multiple
                        Endpoints
SimCiRat                Simultaneous Confidence Intervals for General
                        Contrasts (Ratios) of Means of Multiple
```

	Endpoints
SimComp-package	Simultaneous Comparisons for Multiple Endpoints
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SimTestRat	Simultaneous Tests for General Contrasts (Ratios) of Means of Multiple Endpoints
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Author(s)

Mario Hasler, Christof Kluss

Maintainer: Mario Hasler <hasler@email.uni-kiel.de>

Thanks to: Frank Schaarschmidt, Gemechis Djira Dilba, Kornelius Rohmeyer

References

Hasler, M. and Hothorn, L.A. (2018): Multi-arm trials with multiple primary endpoints and missing values. *Statistics in Medicine* 37, 710–721, <doi:10.1002/sim.7542>.

Hasler, M. (2014): Multiple contrast tests for multiple endpoints in the presence of heteroscedasticity. *The International Journal of Biostatistics* 10, 17–28, <doi:10.1515/ijb-2012-0015>.

Hasler, M. and Hothorn, L.A. (2012): A multivariate Williams-type trend procedure. *Statistics in Biopharmaceutical Research* 4, 57–65, <doi:10.1080/19466315.2011.633868>.

Hasler, M. and Hothorn, L.A. (2011): A Dunnett-type procedure for multiple endpoints. *The International Journal of Biostatistics* 7, Article 3, <doi:10.2202/1557-4679.1258>.

Hasler, M. and Hothorn, L.A. (2008): Multiple contrast tests in the presence of heteroscedasticity. *Biometrical Journal* 50, 793–800, <doi:10.1002/bimj.200710466>.

Dilba, G. et al. (2006): Simultaneous confidence sets and confidence intervals for multiple ratios. *Journal of Statistical Planning and Inference* 136, 2640–2658, <doi:10.1016/j.jspi.2004.11.009>.

See Also

multcomp, mratios

Examples

```
# Example 1:
# A comparison of the groups B and H against the standard S, for endpoint
```

```
# Thromb.count, assuming unequal variances for the groups. This is an
# extension of the well-known Dunnett-test to the case of heteroscedasticity.

data(coagulation)

comp1 <- SimTestDiff(data=coagulation, grp="Group", resp="Thromb.count",
  type="Dunnett", base=3, alternative="greater", covar.equal=FALSE)
comp1

# Example 2:
# A comparison of the groups B and H against the standard S, simultaneously
# for all endpoints, assuming unequal covariance matrices for the groups. This is
# an extension of the well-known Dunnett-test to the case of heteroscedasticity
# and multiple endpoints.

data(coagulation)

comp2 <- SimTestDiff(data=coagulation, grp="Group", resp=c("Thromb.count","ADP","TRAP"),
  type="Dunnett", base=3, alternative="greater", covar.equal=FALSE)
summary(comp2)
```

`coagulation` *Data from a clinical study of three sets of extracorporeal circulation in heart-lung machines*

Description

Three sets of extracorporeal circulation in heart-lung machines: treatments H and B, and standard S. Twelve (S and H each) and eleven (B) male adult patients have been considered. The analysis is based on a set of laboratory parameters restricted to the blood coagulation system, characterized by three primary endpoints (each as quotient from post- and pre-surgery values). Higher values indicate a better treatment effect. For more details, see Kropf et al. (2000).

Usage

```
data(coagulation)
```

Format

A data frame with 35 observations on the following 5 variables.

`Patient` a numeric vector, the patients' number

`Thromb.count` a numeric vector

`ADP` a numeric vector

`TRAP` a numeric vector

`Group` a factor with levels `B`, `H`, `S` specifying the treatments, where `S` is the standard

Source

Kropf, S. et al. (2000): Multiple comparisons of treatments with stable multivariate tests in a two-stage adaptive design, including a test for non-inferiority. *Biometrical Journal* 42, 951-965.

References

Hasler, M. and Hothorn, L.A. (2011): A Dunnett-type procedure for multiple endpoints. *The International Journal of Biostatistics* 7, Article 3, <doi:10.2202/1557-4679.1258>.

Examples

```
data(coagulation)
str(coagulation)
```

DfSattDiff *Degrees of Freedom Accoding to Satterthwaite (1946) for Differences of Means*

Description

Degrees of freedom accoding to Satterthwaite (1946) for (multivariate) *t*-distributions related to multiple contrast tests or corresponding simultaneous confidence intervals for differences of means. For contrasts representing a two-sample *t*-test, the degree of freedom coincides with the one of Welch (1938).

Usage

```
DfSattDiff(n, sd, type = "Dunnett", base = 1, ContrastMat = NULL)
```

Arguments

n	a vector of numbers of observations
sd	a vector of standard deviations
type	a character string, defining the type of contrast, with the following options: • "Dunnett": many-to-one comparisons • "Tukey": all-pair comparisons • "Sequen": comparisons of consecutive groups • "AVE": comparison of each group with average of all others • "GrandMean": comparison of each group with grand mean of all groups • "Changepoint": differences of averages of groups of higher order to averages of groups of lower order • "Marcus": Marcus contrasts • "McDermott": McDermott contrasts • "Williams": Williams trend tests • "UmbrellaWilliams": Umbrella-protected Williams trend tests

	note that `type` is ignored if `ContrastMat` is specified by the user (see below)
`base`	a single integer specifying the control group for Dunnett contrasts, ignored otherwise
`ContrastMat`	a contrast matrix, where columns correspond to groups and rows correspond to contrasts

Details

The calculation of critical values or (adjusted) *p*-values related to multiple contrast tests or corresponding simultaneous confidence intervals is based on a multivariate *t*-distribution. For homoscedastic data, the respective degree of freedom only depends on the total sample size and the number of groups. A simple and well-known special case is the usual *t*-test. If the data are heteroscedastic, however, the degree of freedom of a *t*-test must be decreased according to Welch (1938) to come to an approximate solution. Degrees of freedom according to Satterthwaite (1946) refer to any linear combinations (contrasts) of normal means. They are applied, for example, when doing multiple contrast tests for heteroscedastic data according to Hasler and Hothorn (2008) <doi:10.1002/bimj.200710466> or Hasler (2014) <doi:10.1515/ijb-2012-0015>. Like Welch (1938), Satterthwaite (1946) approximated the degree of freedom by matching first and second moments. The resulting degree of freedom then depends on the contrast and on the sample sizes and sample variances per group.

Value

A vector of degrees of freedom.

Note

The commands `SimTestDiff()` and `SimCiDiff()` use these degrees of freedom automatically if `covar.equal=FALSE` (default). You don't need to apply `DfSattDiff()` additionally.

Author(s)

Mario Hasler

References

Hasler, M. (2014): Multiple contrast tests for multiple endpoints in the presence of heteroscedasticity. *The International Journal of Biostatistics* 10, 17–28, <doi:10.1515/ijb-2012-0015>.

Hasler, M. and Hothorn, L.A. (2008): Multiple contrast tests in the presence of heteroscedasticity. *Biometrical Journal* 50, 793–800, <doi:10.1002/bimj.200710466>.

Satterthwaite, F.E. (1946): An approximate distribution of estimates of variance components. *Biometrics* 2, 110–114.

Welch, B.L. (1938): The significance of the difference between two means when the population variances are unequal. *Biometrika* 29, 350–362.

See Also

`DfSattRat`

Examples

```
# Example 1:
# Degrees of freedom for a comparison of group two and three against group one, assuming
# unequal standard deviations for the groups. This is an extension for the well-known
# Dunnett-test to the case of heteroscedasticity.

# Either by specifying the type of contrast:
DfSattDiff(n=c(10,6,6), sd=c(1,3,6), type="Dunnett", base=1)

# Or by specifying the contrast matrix:
DfSattDiff(n=c(10,6,6), sd=c(1,3,6), ContrastMat=rbind(c(-1,1,0),c(-1,0,1)))

# Example 2:
# Degrees of freedom for an all-pair comparison of the groups B, H and S on endpoint ADP,
# assuming unequal standard deviations for the groups. This is an extension for the well-
# known Tukey-test to the case of heteroscedasticity. The same degrees of freedom are
# used automatically by command \code{SimTestDiff()}.

data(coagulation)

DfSattDiff(n=tapply(X=coagulation$ADP, INDEX=coagulation$Group, FUN=length),
  sd=tapply(X=coagulation$ADP, INDEX=coagulation$Group, FUN=sd),
  type="Tukey")
```

`DfSattRat` *Degrees of Freedom Accoding to Satterthwaite (1946) for Ratios of Means*

Description

Degrees of freedom accoding to Satterthwaite (1946) for (multivariate) *t*-distributions related to multiple contrast tests or corresponding simultaneous confidence intervals for ratios of means. For contrasts representing a two-sample *t*-test, the degree of freedom coincides with the one of Welch (1938).

Usage

```
DfSattRat(n, sd, type = "Dunnett", base = 1, Num.Contrast = NULL, Den.Contrast = NULL,
          Margin = 1)
```

Arguments

`n`	a vector of numbers of observations
`sd`	a vector of standard deviations
`type`	a character string, defining the type of contrast, with the following options: • "Dunnett": many-to-one comparisons • "Tukey": all-pair comparisons

- "Sequen": comparisons of consecutive groups
- "AVE": comparison of each group with average of all others
- "GrandMean": comparison of each group with grand mean of all groups
- "Changepoint": differences of averages of groups of higher order to averages of groups of lower order
- "Marcus": Marcus contrasts
- "McDermott": McDermott contrasts
- "Williams": Williams trend tests
- "UmbrellaWilliams": Umbrella-protected Williams trend tests

note that `type` is ignored if `Num.Contrast` or `Den.Contrast` is specified by the user (see below)

`base` a single integer specifying the control group for Dunnett contrasts, ignored otherwise

`Num.Contrast` a numerator contrast matrix, where columns correspond to groups and rows correspond to contrasts

`Den.Contrast` a denominator contrast matrix, where columns correspond to groups and rows correspond to contrasts

`Margin` a single numeric value, or a numeric vector with length equal to the number of contrasts, default is 1

Details

The calculation of critical values or (adjusted) *p*-values related to multiple contrast tests or corresponding simultaneous confidence intervals is based on a multivariate *t*-distribution. For homoscedastic data, the respective degree of freedom only depends on the total sample size and the number of groups. A simple and well-known special case is the usual *t*-test. If the data are heteroscedastic, however, the degree of freedom of a *t*-test must be decreased according to Welch (1938) to come to an approximate solution. Degrees of freedom according to Satterthwaite (1946) refer to any linear combinations (contrasts) of normal means. They are applied, for example, when doing multiple contrast tests for heteroscedastic data according to Hasler and Hothorn (2008) <doi:10.1002/bimj.200710466> or Hasler (2014) <doi:10.1515/ijb-2012-0015>. Like Welch (1938), Satterthwaite (1946) approximated the degree of freedom by matching first and second moments. The resulting degree of freedom then depends on the numerator contrast, the denominator contrast, the (relative) margin to test against, and on the sample sizes and sample variances per group. If `Margin=1` or `Margin=NULL` (default), the result coincides with the result of `DfSattDiff()`.

Value

A vector of degrees of freedom.

Note

The commands `SimTestRat()` and `SimCiRat()` use these degrees of freedom automatically if `covar.equal=FALSE` (default). You don't need to apply `DfSattRat()` additionally.

Author(s)

Mario Hasler

References

Hasler, M. (2014): Multiple contrast tests for multiple endpoints in the presence of heteroscedasticity. *The International Journal of Biostatistics* 10, 17–28, <doi:10.1515/ijb-2012-0015>.

Hasler, M. and Hothorn, L.A. (2008): Multiple contrast tests in the presence of heteroscedasticity. *Biometrical Journal* 50, 793–800, <doi:10.1002/bimj.200710466>.

Satterthwaite, F.E. (1946): An approximate distribution of estimates of variance components. *Biometrics* 2, 110–114.

Welch, B.L. (1938): The significance of the difference between two means when the population variances are unequal. *Biometrika* 29, 350–362.

See Also

DfSattDiff

Examples

```
# Example 1:
# Degrees of freedom for a non-inferiority test of group two and three against group one,
# assuming unequal standard deviations for the groups. This is an extension for the well-
# known Dunnett-test to the case of heteroscedasticity and in terms of ratios of means
# instead of differences.

# Either by specifying the type of contrast:
DfSattRat(n=c(10,6,6), sd=c(1,3,6), type="Dunnett", base=1, Margin=0.8)

# Or by specifying the contrast matrices:
DfSattRat(n=c(10,6,6), sd=c(1,3,6), Num.Contrast=rbind(c(0,1,0),c(0,0,1)),
  Den.Contrast=rbind(c(1,0,0),c(1,0,0)), Margin=0.8)

# Example 2:
# Degrees of freedom for an all-pair comparison of the groups B, H and S on endpoint ADP,
# assuming unequal standard deviations for the groups. This is an extension for the well-
# known Tukey-test to the case of heteroscedasticity and in terms of ratios of means
# instead of differences. The same degrees of freedom are used automatically by command
# \code{SimTestRat()}.

data(coagulation)

DfSattRat(n=tapply(X=coagulation$ADP, INDEX=coagulation$Group, FUN=length),
  sd=tapply(X=coagulation$ADP, INDEX=coagulation$Group, FUN=sd),
  type="Tukey")
```

ermvnorm *Multivariate Normal Random Numbers with Exact Parameters*

Description

Random numbers of the multivariate normal distribution with EXACT mean vector, EXACT variance vector and approximate correlation matrix. This function is based on the function `rmvnorm` of the package **mvtnorm**.

Usage

```
ermvnorm(n, mean, sd, corr = diag(rep(1, length(mean))), mnt = 10000)
```

Arguments

`n`	a number of observations
`mean`	a mean vector
`sd`	a vector of standard deviations
`corr`	a correlation matrix
`mnt`	a maximum number of tries for the computation

Details

Unfortunately, it's very common to present only summary statistics in the literature when evaluating real data. This makes it hard to retrace or to verify the related statistical evaluation. Also, the use of such data as an example for other statistical tests is hardly possible. For that reason, `ermvnorm` allows to reproduce data by simulation. In contrast to `rmvnorm` of the package mvtnorm, the function `ermvnorm` produces random numbers which have EXACTLY the same paramer values as specified by `mean` and `sd`. The correlation matrix `corr` is met only approximately.

The simple idea behind `ermvnorm` is to apply `rmvnorm` of the package mvtnorm, but only for the first n-2 random numbers. The remaining 2 numbers are obtained by solving a quadratic equation to achieve the specified values for the mean vector and for the vector of standard deviations. Depending on the n-2 random numbers, the underlying quadratic equation can possibly have no solution. In this case, `ermvnorm` creates a new set of n-2 random numbers until a valid data set is obtained, or until the maximum number of tries `mnt` is reached.

Value

A matrix of random numbers with dimension n * length(mean).

Note

This function is to be used only with caution. Usually, random numbers with exact mean and standard deviation are not intended to be used. For example, simulations concerning type I error or power of statistical tests cannot be based on `ermvnorm`.

Author(s)

Gemechis Djira Dilba and Mario Hasler

References

Hothorn, T. et al. (2001): On Multivariate *t* and Gauss Probabilities in R. *R News* 1, 27–29.

See Also

rmvnorm, rcm

Examples

```
# Example 1:
# A dataset representing one endpoint.

set.seed(1234)
dataset1 <- ermvnorm(n=10,mean=100,sd=10)
dataset1
mean(dataset1)
sd(dataset1)

# Example 2:
# A dataset representing two correlated endpoints.

set.seed(5678)
dataset2 <- ermvnorm(n=10,mean=c(10,120),sd=c(1,10),corr=rbind(c(1,0.7),c(0.7,1)))
dataset2
mean(dataset2[,1]); mean(dataset2[,2])
sd(dataset2[,1]); sd(dataset2[,2])
round(cor(dataset2),3)
pairs(dataset2)

# Example 3:
# A dataset representing three uncorrelated endpoints.

set.seed(9101)
dataset3 <- ermvnorm(n=20,mean=c(1,12,150),sd=c(0.5,2,20))
dataset3
mean(dataset3[,1]); mean(dataset3[,2]); mean(dataset3[,3])
sd(dataset3[,1]); sd(dataset3[,2]); sd(dataset3[,3])
pairs(dataset3)

# Example 4:
# A dataset representing four randomly correlated endpoints.

set.seed(1121)
dataset4 <- ermvnorm(n=10,mean=c(2,10,50,120),sd=c(1,4,8,10),corr=rcm(ncol=4))
dataset4
mean(dataset4[,1]); mean(dataset4[,2]); mean(dataset4[,3]); mean(dataset4[,4])
sd(dataset4[,1]); sd(dataset4[,2]); sd(dataset4[,3]); sd(dataset4[,4])
round(cor(dataset4),3)
```

```
pairs(dataset4)
```

`plot.SimCi` *Plot function for SimCi-objects*

Description

A plot of the results of `SimCiDiff` and `SimCiRat`, respectively.

Usage

```
## S3 method for class 'SimCi'
plot(x, xlim, xlab, ylim, ...)
```

Arguments

`x`	an object of class "SimCi" as obtained by calling `SimCiDiff` or `SimCiRat`
`xlim`	a numeric vector of length 2, giving the x coordinate range
`xlab`	a title for the x axis
`ylim`	a numeric vector of length 2, giving the y coordinate range
`...`	arguments to be passed to `plot`

Value

A plot of the confidence intervals of a "SimCi" object.

Author(s)

Christof Kluss and Mario Hasler

See Also

`SimCiDiff`, `SimCiRat`

Examples

```
# Example 1:
# Simultaneous confidence intervals related to a comparison of the groups
# B and H against the standard S, on endpoint Thromb.count, assuming unequal
# variances for the groups. This is an extension of the well-known Dunnett-
# intervals to the case of heteroscedasticity.

data(coagulation)

interv1 <- SimCiDiff(data=coagulation, grp="Group", resp="Thromb.count",
  type="Dunnett", base=3, alternative="greater", covar.equal=FALSE)
interv1
plot(interv1)
```

```
# Example 2:
# Simultaneous confidence intervals related to a comparisons of the groups
# B and H against the standard S, simultaneously on all endpoints, assuming
# unequal covariance matrices for the groups. This is an extension of the well-
# known Dunnett-intervals to the case of heteroscedasticity and multiple
# endpoints.

data(coagulation)

interv2 <- SimCiDiff(data=coagulation, grp="Group", resp=c("Thromb.count","ADP","TRAP"),
  type="Dunnett", base=3, alternative="greater", covar.equal=FALSE)
summary(interv2)
par(mfrow=c(1,3)); plot(interv2)
```

`print.SimCi` *Print function for SimCi-objects*

Description

A short print out of the results of `SimCiDiff` and `SimCiRat`, respectively.

Usage

```
## S3 method for class 'SimCi'
print(x, digits = 4, ...)
```

Arguments

`x`	an object of class "SimCi" as obtained by calling `SimCiDiff` or `SimCiRat`
`digits`	digits for rounding the results
`...`	arguments to be passed to `print`

Value

A print out containing the estimates, degrees of freedom, raw and simultaneous confidence intervals computed by `SimCiDiff` or `SimCiRat`, respectively.

Author(s)

Mario Hasler

See Also

`print.SimTest`

print.SimTest *Print function for SimTest-objects*

Description

A short print out of the results of SimTestDiff and SimTestRat, respectively.

Usage

```
## S3 method for class 'SimTest'
print(x, digits = 4, ...)
```

Arguments

x	an object of class "SimTest" as obtained by calling SimTestDiff or SimTestRat
digits	digits for rounding the results
...	arguments to be passed to print

Value

A print out containing the margins, estimates, test statistics, degrees of freedom, raw and adjusted *p*-values computed by SimTestDiff or SimTestRat, respectively.

Author(s)

Mario Hasler

See Also

print.SimCi

rcm *Random Correlation Matrices*

Description

Correlation matrices with random off-diagonal elements.

Usage

```
rcm(nrow = NULL, ncol = NULL)
```

Arguments

nrow	the desired number of rows
ncol	the desired number of columns

Details

As a correlation matrix is symmetric, only one of `nrow` or `ncol` needs to be specified.

Value

A symmetric correlation matrix with random elements.

Author(s)

Kornelius Rohmeyer and Mario Hasler

References

Holmes, R.B. (1991): On random correlation matrices. *Siam Journal on Matrix Analysis and Applications* 12, 239–272.

See Also

`ermvnorm`

Examples

```
# Example 1:
# A correlation matrix representing three randomly correlated endpoints.

set.seed(1234)
rcm(nrow=3)

# Example 2:
# A correlation matrix representing five randomly correlated endpoints.

set.seed(5678)
rcm(ncol=5)
```

`SimCiDiff` *Simultaneous Confidence Intervals for General Contrasts (Differences) of Means of Multiple Endpoints*

Description

Simultaneous confidence intervals for general contrasts (linear functions) of normal means (e.g., "Dunnett", "Tukey", "Williams" ect.), and for single or multiple endpoints (primary response variables) simultaneously. The procedure of Hasler and Hothorn (2011) <doi:10.2202/1557-4679.1258> is applied for differences of means of normally distributed data. The variances/ covariance matrices of the treatment groups (containing the covariances between the endpoints) may be assumed to be equal or possibly unequal for the different groups (Hasler, 2014 <doi:10.1515/ijb-2012-0015>). For the case of only a single endpoint and unequal covariance matrices (variances), the procedure coincides with the PI procedure of Hasler and Hothorn (2008) <doi:10.1002/bimj.200710466>.

Usage

```
## Default S3 method:
SimCiDiff(data, grp, resp = NULL, na.action = "na.error", type = "Dunnett",
  base = 1, ContrastMat = NULL, alternative = "two.sided", covar.equal = FALSE,
  conf.level = 0.95, CorrMatDat = NULL, ...)
## S3 method for class 'formula'
SimCiDiff(formula, ...)
```

Arguments

`data`	a data frame containing a grouping variable and the endpoints as columns
`grp`	a character string with the name of the grouping variable
`resp`	a vector of character strings with the names of the endpoints; if `resp=NULL` (default), all column names of the data frame without the grouping variable are chosen automatically
`formula`	a formula specifying a numerical response and a grouping factor (e.g. `response ~ treatment`)
`na.action`	a character string indicating what should happen when the data contain `NA`s; if `na.action="na.error"` (default) the procedure stops with an error message; if `na.action="multi.df"` a new experimental version is used (details will follow soon)
`type`	a character string, defining the type of contrast, with the following options: • "Dunnett": many-to-one comparisons • "Tukey": all-pair comparisons • "Sequen": comparisons of consecutive groups • "AVE": comparison of each group with average of all others • "GrandMean": comparison of each group with grand mean of all groups • "Changepoint": differences of averages of groups of higher order to averages of groups of lower order • "Marcus": Marcus contrasts • "McDermott": McDermott contrasts • "Williams": Williams trend tests • "UmbrellaWilliams": Umbrella-protected Williams trend tests note that `type` is ignored if `ContrastMat` is specified by the user (see below)
`base`	a single integer specifying the control group for Dunnett contrasts, ignored otherwise
`ContrastMat`	a contrast matrix, where columns correspond to groups and rows correspond to contrasts
`alternative`	a character string specifying the alternative hypothesis, must be one of `"two.sided"` (default), `"greater"` or `"less"`
`covar.equal`	a logical variable indicating whether to treat the variances/ covariance matrices of the treatment groups (containing the covariances between the endpoints) as being equal; if `TRUE` then the pooled variance/ covariance matrix is used, otherwise the Satterthwaite approximation to the degrees of freedom is used

conf.level	a numeric value defining the simultaneous confidence level
CorrMatDat	a correlation matrix of the endpoints, if NULL (default) it is estimated from the data
...	arguments to be passed to SimCiDiff.default

Details

The interest is in simultaneous confidence intervals for several linear combinations (contrasts) of treatment means in a one-way ANOVA model, and for single or multiple endpoints simultaneously. For example, corresponding intervals for the all- pair comparison of Tukey (1953) and the many-to-one comparison of Dunnett (1955) are implemented, but allowing for heteroscedasticity and multiple endpoints. The user is also free to create other interesting problem-specific contrasts. Approximate multivariate *t*-distributions are used to calculate lower and upper limits (Hasler and Hothorn, 2011 <doi:10.2202/1557-4679.1258>). Simultaneous tests based on these intervals control the familywise error rate in admissible ranges and in the strong sense. The variances/ covariance matrices of the treatment groups (containing the covariances between the endpoints) can be assumed to be equal (covar.equal=TRUE) or unequal (covar.equal=FALSE). If being equal, the pooled variance/ covariance matrix is used, otherwise approximations to the degrees of freedom (Satterthwaite, 1946) are used (Hasler, 2014 <doi:10.1515/ijb-2012-0015>; Hasler and Hothorn, 2008 <doi:10.1002/bimj.200710466>). Unequal covariance matrices occure if variances or correlations of some endpoints differ depending on the treatment groups.

Value

An object of class SimCi containing:

estimate	a matrix of estimated differences
lower.raw	a matrix of raw (unadjusted) lower limits
upper.raw	a matrix of raw (unadjusted) upper limits
lower	a matrix of lower limits adjusted for multiplicity
upper	a matrix of upper limits adjusted for multiplicity
CorrMatDat	if not prespecified by CorrMatDat, either the estimated common correlation matrix of the endpoints (covar.equal=TRUE) or a list of different (one for each treatment) estimated correlation matrices of the endpoints (covar.equal=FALSE)
CorrMatComp	the estimated correlation matrix of the comparisons
degr.fr	a matrix of degrees of freedom

Note

By default (na.action="na.error"), the procedure stops if there are missing values. A new experimental version for missing values is used if na.action="multi.df". If covar.equal=TRUE, the number of endpoints must not be greater than the total sample size minus the number of treatment groups. If covar.equal=FALSE, the number of endpoints must not be greater than the minimal sample size minus 1. Otherwise the procedure stops.

All intervals have the same direction for all comparisons and endpoints (alternative="..."). In case of doubt, use "two.sided".

Author(s)

Mario Hasler

References

Hasler, M. (2014): Multiple contrast tests for multiple endpoints in the presence of heteroscedasticity. *The International Journal of Biostatistics* 10, 17–28, <doi:10.1515/ijb-2012-0015>.

Hasler, M. and Hothorn, L.A. (2011): A Dunnett-type procedure for multiple endpoints. *The International Journal of Biostatistics* 7, Article 3, <doi:10.2202/1557-4679.1258>.

Hasler, M. and Hothorn, L.A. (2008): Multiple contrast tests in the presence of heteroscedasticity. *Biometrical Journal* 50, 793–800, <doi:10.1002/bimj.200710466>.

See Also

SimTestDiff, SimTestRat, SimCiRat

Examples

```
# Example 1:
# Simultaneous confidence intervals related to a comparison of the groups
# B and H against the standard S, for endpoint Thromb.count, assuming unequal
# variances for the groups. This is an extension of the well-known Dunnett-
# intervals to the case of heteroscedasticity.

data(coagulation)

interv1 <- SimCiDiff(data=coagulation, grp="Group", resp="Thromb.count",
  type="Dunnett", base=3, alternative="greater", covar.equal=FALSE)
interv1
plot(interv1)

# Example 2:
# Simultaneous confidence intervals related to a comparisons of the groups
# B and H against the standard S, simultaneously for all endpoints, assuming
# unequal covariance matrices for the groups. This is an extension of the well-
# known Dunnett-intervals to the case of heteroscedasticity and multiple
# endpoints.

data(coagulation)

interv2 <- SimCiDiff(data=coagulation, grp="Group", resp=c("Thromb.count","ADP","TRAP"),
  type="Dunnett", base=3, alternative="greater", covar.equal=FALSE)
summary(interv2)
plot(interv2)
```

SimCiRat *Simultaneous Confidence Intervals for General Contrasts (Ratios) of Means of Multiple Endpoints*

Description

Simultaneous confidence intervals for general contrasts (linear functions) of normal means (e.g., "Dunnett", "Tukey", "Williams" ect.), and for single or multiple endpoints (primary response variables) simultaneously. The procedure of Hasler and Hothorn (2012) <doi:10.1080/19466315.2011.633868> is applied for ratios of means of normally distributed data. The variances/ covariance matrices of the treatment groups (containing the covariances between the endpoints) may be assumed to be equal or possibly unequal for the different groups (Hasler, 2014 <doi:10.1515/ijb-2012-0015>). For the case of only a single endpoint and unequal covariance matrices (variances), the procedure coincides with the PI procedure of Hasler and Hothorn (2008) <doi:10.1002/bimj.200710466>.

Usage

```
## Default S3 method:
SimCiRat(data, grp, resp = NULL, na.action = "na.error", type = "Dunnett",
  base = 1, Num.Contrast = NULL, Den.Contrast = NULL, alternative = "two.sided",
  covar.equal = FALSE, conf.level = 0.95, CorrMatDat = NULL, ...)
## S3 method for class 'formula'
SimCiRat(formula, ...)
```

Arguments

`data`	a data frame containing a grouping variable and the endpoints as columns
`grp`	a character string with the name of the grouping variable
`resp`	a vector of character strings with the names of the endpoints; if `resp=NULL` (default), all column names of the data frame without the grouping variable are chosen automatically
`formula`	a formula specifying a numerical response and a grouping factor (e.g. `response ~ treatment`)
`na.action`	a character string indicating what should happen when the data contain `NA`s; if `na.action="na.error"` (default) the procedure stops with an error message; if `na.action="multi.df"` a new experimental version is used (details will follow soon)
`type`	a character string, defining the type of contrast, with the following options: • "Dunnett": many-to-one comparisons • "Tukey": all-pair comparisons • "Sequen": comparisons of consecutive groups • "AVE": comparison of each group with average of all others • "GrandMean": comparison of each group with grand mean of all groups • "Changepoint": differences of averages of groups of higher order to averages of groups of lower order

- "Marcus": Marcus contrasts
- "McDermott": McDermott contrasts
- "Williams": Williams trend tests
- "UmbrellaWilliams": Umbrella-protected Williams trend tests

note that `type` is ignored if `Num.Contrast` or `Den.Contrast` is specified by the user (see below)

`base`	a single integer specifying the control group for Dunnett contrasts, ignored otherwise
`Num.Contrast`	a numerator contrast matrix, where columns correspond to groups and rows correspond to contrasts
`Den.Contrast`	a denominator contrast matrix, where columns correspond to groups and rows correspond to contrasts
`alternative`	a character string specifying the alternative hypothesis, must be one of `"two.sided"` (default), `"greater"` or `"less"`
`covar.equal`	a logical variable indicating whether to treat the variances/ covariance matrices of the treatment groups (containing the covariances between the endpoints) as being equal; if `TRUE` then the pooled variance/ covariance matrix is used, otherwise the Satterthwaite approximation to the degrees of freedom is used
`conf.level`	a numeric value defining the simultaneous confidence level
`CorrMatDat`	a correlation matrix of the endpoints, if `NULL` (default) it is estimated from the data
`...`	arguments to be passed to SimCiRat.default

Details

The interest is in simultaneous confidence intervals for several linear combinations (contrasts) of treatment means in a one-way ANOVA model, and for single or multiple endpoints simultaneously. For example, corresponding intervals for the all- pair comparison of Tukey (1953) and the many-to-one comparison of Dunnett (1955) are implemented, but allowing for heteroscedasticity and multiple endpoints, and in terms of ratios of means. The user is also free to create other interesting problem-specific contrasts. Approximate multivariate *t*-distributions are used to calculate lower and upper limits (Hasler and Hothorn, 2012 <doi:10.1080/19466315.2011.633868>). Simultaneous tests based on these intervals control the familywise error rate in admissible ranges and in the strong sense. The variances/ covariance matrices of the treatment groups (containing the covariances between the endpoints) can be assumed to be equal (`covar.equal=TRUE`) or unequal (`covar.equal=FALSE`). If being equal, the pooled variance/ covariance matrix is used, otherwise approximations to the degrees of freedom (Satterthwaite, 1946) are used (Hasler, 2014 <doi:10.1515/ijb-2012-0015>; Hasler and Hothorn, 2008 <doi:10.1002/bimj.200710466>). Unequal covariance matrices occure if variances or correlations of some endpoints differ depending on the treatment groups.

Value

An object of class SimCi containing:

`estimate`	a matrix of estimated ratios

lower.raw	a matrix of raw (unadjusted) lower limits
upper.raw	a matrix of raw (unadjusted) upper limits
lower	a matrix of lower limits adjusted for multiplicity
upper	a matrix of upper limits adjusted for multiplicity
CorrMatDat	if not prespecified by CorrMatDat, either the estimated common correlation matrix of the endpoints (covar.equal=TRUE) or a list of different (one for each treatment) estimated correlation matrices of the endpoints (covar.equal=FALSE)
CorrMatComp	the estimated correlation matrix of the comparisons
degr.fr	a matrix of degrees of freedom

Note

By default (na.action="na.error"), the procedure stops if there are missing values. A new experimental version for missing values is used if na.action="multi.df". If covar.equal=TRUE, the number of endpoints must not be greater than the total sample size minus the number of treatment groups. If covar.equal=FALSE, the number of endpoints must not be greater than the minimal sample size minus 1. Otherwise the procedure stops.

All intervals have the same direction for all comparisons and endpoints (alternative="..."). In case of doubt, use "two.sided".

The correlation matrix for the multivariate *t*-distribution also depends on the unknown ratios. The same problem also arises for the degrees of freedom if the covariance matrices for the different groups are assumed to be unequal (covar.equal=FALSE). Both problems are handled by a plug-in approach, see the references therefore.

Author(s)

Mario Hasler

References

Hasler, M. (2014): Multiple contrast tests for multiple endpoints in the presence of heteroscedasticity. *The International Journal of Biostatistics* 10, 17–28, <doi:10.1515/ijb-2012-0015>.

Hasler, M. and Hothorn, L.A. (2012): A multivariate Williams-type trend procedure. *Statistics in Biopharmaceutical Research* 4, 57–65, <doi:10.1080/19466315.2011.633868>.

Hasler, M. and Hothorn, L.A. (2008): Multiple contrast tests in the presence of heteroscedasticity. *Biometrical Journal* 50, 793–800, <doi:10.1002/bimj.200710466>.

Dilba, G. et al. (2006): Simultaneous confidence sets and confidence intervals for multiple ratios. *Journal of Statistical Planning and Inference* 136, 2640–2658, <DOI:10.1016/j.jspi.2004.11.009>.

See Also

SimTestRat, SimTestDiff, SimCiDiff

Examples

```
# Example 1:
# Simultaneous confidence intervals related to a comparison of the groups
# B and H against the standard S, for endpoint Thromb.count, assuming unequal
# variances for the groups. This is an extension of the well-known Dunnett-
# intervals to the case of heteroscedasticity and in terms of ratios of means
# instead of differences.

data(coagulation)

interv1 <- SimCiRat(data=coagulation, grp="Group", resp="Thromb.count",
  type="Dunnett", base=3, alternative="greater", covar.equal=FALSE)
interv1
plot(interv1)

# Example 2:
# Simultaneous confidence intervals related to a comparisons of the groups
# B and H against the standard S, simultaneously for all endpoints, assuming
# unequal covariance matrices for the groups. This is an extension of the well-
# known Dunnett-intervals to the case of heteroscedasticity and multiple
# endpoints and in terms of ratios of means instead of differences.

data(coagulation)

interv2 <- SimCiRat(data=coagulation, grp="Group", resp=c("Thromb.count","ADP","TRAP"),
  type="Dunnett", base=3, alternative="greater", covar.equal=FALSE)
summary(interv2)
plot(interv2)
```

`SimTestDiff` *Simultaneous Tests for General Contrasts (Differences) of Means of Multiple Endpoints*

Description

Simultaneous tests for general contrasts (linear functions) of normal means (e.g., "Dunnett", "Tukey", "Williams" ect.), and for single or multiple endpoints (primary response variables) simultaneously. The procedure of Hasler and Hothorn (2011) <doi:10.2202/1557-4679.1258> is applied for differences of means of normally distributed data. The variances/ covariance matrices of the treatment groups (containing the covariances between the endpoints) may be assumed to be equal or possibly unequal for the different groups (Hasler, 2014 <doi:10.1515/ijb-2012-0015>). For the case of only a single endpoint and unequal covariance matrices (variances), the procedure coincides with the PI procedure of Hasler and Hothorn (2008) <doi:10.1002/bimj.200710466>.

Usage

```
## Default S3 method:
SimTestDiff(data, grp, resp = NULL, na.action = "na.error", type = "Dunnett",
  base = 1, ContrastMat = NULL, alternative = "two.sided", Margin = 0,
```

```
  covar.equal = FALSE, CorrMatDat = NULL, ...)
## S3 method for class 'formula'
SimTestDiff(formula, ...)
```

Arguments

data	a data frame containing a grouping variable and the endpoints as columns
grp	a character string with the name of the grouping variable
resp	a vector of character strings with the names of the endpoints; if resp=NULL (default), all column names of the data frame without the grouping variable are chosen automatically
formula	a formula specifying a numerical response and a grouping factor (e.g. response ~ treatment)
na.action	a character string indicating what should happen when the data contain NAs; if na.action="na.error" (default) the procedure stops with an error message; if na.action="multi.df" multiple marginal degrees of freedom are used to adjust for the missing values problem
type	a character string, defining the type of contrast, with the following options: • "Dunnett": many-to-one comparisons • "Tukey": all-pair comparisons • "Sequen": comparisons of consecutive groups • "AVE": comparison of each group with average of all others • "GrandMean": comparison of each group with grand mean of all groups • "Changepoint": differences of averages of groups of higher order to averages of groups of lower order • "Marcus": Marcus contrasts • "McDermott": McDermott contrasts • "Williams": Williams trend tests • "UmbrellaWilliams": Umbrella-protected Williams trend tests note that type is ignored if ContrastMatis specified by the user (see below)
base	a single integer specifying the control group for Dunnett contrasts, ignored otherwise
ContrastMat	a contrast matrix, where columns correspond to groups and rows correspond to contrasts
alternative	a character string specifying the alternative hypothesis, must be one of "two.sided" (default), "greater" or "less"
Margin	a single numeric value, or a numeric vector corresponding to endpoints, or a matrix where columns correspond to endpoints and rows correspond to contrasts
covar.equal	a logical variable indicating whether to treat the variances/ covariance matrices of the treatment groups (containing the covariances between the endpoints) as being equal; if TRUE then the pooled variance/ covariance matrix is used, otherwise the Satterthwaite approximation to the degrees of freedom is used
CorrMatDat	a correlation matrix of the endpoints, if NULL (default) it is estimated from the data
...	arguments to be passed to SimTestDiff.default

Details

The interest is in simultaneous tests for several linear combinations (contrasts) of treatment means in a one-way ANOVA model, and for single or multiple endpoints simultaneously. For example, the all-pair comparison of Tukey (1953) and the many- to-one comparison of Dunnett (1955) are implemented, but allowing for heteroscedasticity and multiple endpoints. The user is also free to create other interesting problem-specific contrasts. Approximate multivariate *t*- distributions are used to calculate (adjusted) *p*-values (Hasler and Hothorn, 2011 <doi:10.2202/1557-4679.1258>). This approach controls the familywise error rate in admissible ranges and in the strong sense. The variances/ covariance matrices of the treatment groups (containing the covariances between the endpoints) can be assumed to be equal (`covar.equal=TRUE`) or unequal (`covar.equal=FALSE`). If being equal, the pooled variance/ covariance matrix is used, otherwise approximations to the degrees of freedom (Satterthwaite, 1946) are used (Hasler, 2014 <doi:10.1515/ijb-2012-0015>; Hasler and Hothorn, 2008 <doi:10.1002/bimj.200710466>). Unequal covariance matrices occure if variances or correlations of some endpoints differ depending on the treatment groups.

Value

An object of class SimTest containing:

`estimate`	a matrix of estimated differences
`statistic`	a matrix of the calculated test statistics
`p.val.raw`	a matrix of raw *p*-values
`p.val.adj`	a matrix of *p*-values adjusted for multiplicity
`CorrMatDat`	if not prespecified by `CorrMatDat`, either the estimated common correlation matrix of the endpoints (`covar.equal=TRUE`) or a list of different (one for each treatment) estimated correlation matrices of the endpoints (`covar.equal=FALSE`)
`CorrMatComp`	the estimated correlation matrix of the comparisons
`degr.fr`	a matrix of degrees of freedom

Note

By default (`na.action="na.error"`), the procedure stops if there are missing values. A new experimental version for missing values is used if `na.action="multi.df"`. If `covar.equal=TRUE`, the number of endpoints must not be greater than the total sample size minus the number of treatment groups. If `covar.equal=FALSE`, the number of endpoints must not be greater than the minimal sample size minus 1. Otherwise the procedure stops.

All hypotheses are tested with the same test direction for all comparisons and endpoints (`alternative="..."`). In case of doubt, use `"two.sided"`.

If `Margin` is a single numeric value or a numeric vector, then the same value(s) are used for the remaining comparisons or endpoints.

Author(s)

Mario Hasler

References

Hasler, M. and Hothorn, L.A. (2018): Multi-arm trials with multiple primary endpoints and missing values. *Statistics in Medicine* 37, 710–721, <doi:10.1002/sim.7542>.

Hasler, M. (2014): Multiple contrast tests for multiple endpoints in the presence of heteroscedasticity. *The International Journal of Biostatistics* 10, 17–28, <doi:10.1515/ijb-2012-0015>.

Hasler, M. and Hothorn, L.A. (2011): A Dunnett-type procedure for multiple endpoints. *The International Journal of Biostatistics* 7, Article 3, <doi:10.2202/1557-4679.1258>.

Hasler, M. and Hothorn, L.A. (2008): Multiple contrast tests in the presence of heteroscedasticity. *Biometrical Journal* 50, 793–800, <doi:10.1002/bimj.200710466>.

See Also

SimCiDiff, SimTestRat, SimCiRat

Examples

```
# Example 1:
# A comparison of the groups B and H against the standard S, for endpoint
# Thromb.count, assuming unequal variances for the groups. This is an
# extension of the well-known Dunnett-test to the case of heteroscedasticity.

data(coagulation)

comp1 <- SimTestDiff(data=coagulation, grp="Group", resp="Thromb.count",
  type="Dunnett", base=3, alternative="greater", covar.equal=FALSE)
comp1

# Example 2:
# A comparison of the groups B and H against the standard S, simultaneously
# for all endpoints, assuming unequal covariance matrices for the groups. This is
# an extension of the well-known Dunnett-test to the case of heteroscedasticity
# and multiple endpoints.

data(coagulation)

comp2 <- SimTestDiff(data=coagulation, grp="Group", resp=c("Thromb.count","ADP","TRAP"),
  type="Dunnett", base=3, alternative="greater", covar.equal=FALSE)
summary(comp2)
```

SimTestRat *Simultaneous Tests for General Contrasts (Ratios) of Means of Multiple Endpoints*

Description

Simultaneous tests for general contrasts (linear functions) of normal means (e.g., "Dunnett", "Tukey", "Williams" ect.), and for single or multiple endpoints (primary response variables) simultaneously. The procedure of Hasler and Hothorn (2012) <doi:10.1080/19466315.2011.633868> is applied for ratios of means of normally distributed data. The variances/ covariance matrices of the treatment groups (containing the covariances between the endpoints) may be assumed to be equal or possibly unequal for the different groups (Hasler, 2014 <doi:10.1515/ijb-2012-0015>). For the case of only a single endpoint and unequal covariance matrices (variances), the procedure coincides with the PI procedure of Hasler and Hothorn (2008) <doi:10.1002/bimj.200710466>.

Usage

```
## Default S3 method:
SimTestRat(data, grp, resp = NULL, na.action = "na.error", type = "Dunnett",
  base = 1, Num.Contrast = NULL, Den.Contrast = NULL, alternative = "two.sided",
  Margin = 1, covar.equal = FALSE, CorrMatDat = NULL, ...)
## S3 method for class 'formula'
SimTestRat(formula, ...)
```

Arguments

`data`	a data frame containing a grouping variable and the endpoints as columns
`grp`	a character string with the name of the grouping variable
`resp`	a vector of character strings with the names of the endpoints; if `resp=NULL` (default), all column names of the data frame without the grouping variable are chosen automatically
`formula`	a formula specifying a numerical response and a grouping factor (e.g. `response ~ treatment`)
`na.action`	a character string indicating what should happen when the data contain `NA`s; if `na.action="na.error"` (default) the procedure stops with an error message; if `na.action="multi.df"` a new experimental version is used (details will follow soon)
`type`	a character string, defining the type of contrast, with the following options: • "Dunnett": many-to-one comparisons • "Tukey": all-pair comparisons • "Sequen": comparisons of consecutive groups • "AVE": comparison of each group with average of all others • "GrandMean": comparison of each group with grand mean of all groups • "Changepoint": differences of averages of groups of higher order to averages of groups of lower order • "Marcus": Marcus contrasts • "McDermott": McDermott contrasts • "Williams": Williams trend tests • "UmbrellaWilliams": Umbrella-protected Williams trend tests

	note that type is ignored if Num.Contrast or Den.Contrast is specified by the user (see below)
base	a single integer specifying the control group for Dunnett contrasts, ignored otherwise
Num.Contrast	a numerator contrast matrix, where columns correspond to groups and rows correspond to contrasts
Den.Contrast	a denominator contrast matrix, where columns correspond to groups and rows correspond to contrasts
alternative	a character string specifying the alternative hypothesis, must be one of "two.sided" (default), "greater" or "less"
Margin	a single numeric value, or a numeric vector corresponding to endpoints, or a matrix where columns correspond to endpoints and rows correspond to contrasts
covar.equal	a logical variable indicating whether to treat the variances/ covariance matrices of the treatment groups (containing the covariances between the endpoints) as being equal; if TRUE then the pooled variance/ covariance matrix is used, otherwise the Satterthwaite approximation to the degrees of freedom is used
CorrMatDat	a correlation matrix of the endpoints, if NULL (default) it is estimated from the data
...	arguments to be passed to SimTestRat.default

Details

The interest is in simultaneous tests for several linear combinations (contrasts) of treatment means in a one-way ANOVA model, and for single or multiple endpoints simultaneously. For example, the all-pair comparison of Tukey (1953) and the many- to-one comparison of Dunnett (1955) are implemented, but allowing for heteroscedasticity and multiple endpoints, and in terms of ratios of means. The user is also free to create other interesting problem-specific contrasts. Approximate multivariate *t*-distributions are used to calculate (adjusted) *p*-values (Hasler and Hothorn, 2012 <doi:10.1080/19466315.2011.633868>). This approach controls the familywise error rate in admissible ranges and in the strong sense. The variances/ covariance matrices of the treatment groups (containing the covariances between the endpoints) can be assumed to be equal (covar.equal=TRUE) or unequal (covar.equal=FALSE). If being equal, the pooled variance/ covariance matrix is used, otherwise approximations to the degrees of freedom (Satterthwaite, 1946) are used (Hasler, 2014 <doi:10.1515/ijb-2012-0015>; Hasler and Hothorn, 2008 <doi:10.1002/bimj.200710466>). Unequal covariance matrices occure if variances or correlations of some endpoints differ depending on the treatment groups.

Value

An object of class SimTest containing:

estimate	a matrix of estimated differences
statistic	a matrix of the calculated test statistics
p.val.raw	a matrix of raw *p*-values
p.val.adj	a matrix of *p*-values adjusted for multiplicity

CorrMatDat	if not prespecified by CorrMatDat, either the estimated common correlation matrix of the endpoints (covar.equal=TRUE) or a list of different (one for each treatment) estimated correlation matrices of the endpoints (covar.equal=FALSE)
CorrMatComp	the estimated correlation matrix of the comparisons
degr.fr	a matrix of degrees of freedom

Note

By default (na.action="na.error"), the procedure stops if there are missing values. A new experimental version for missing values is used if na.action="multi.df". If covar.equal=TRUE, the number of endpoints must not be greater than the total sample size minus the number of treatment groups. If covar.equal=FALSE, the number of endpoints must not be greater than the minimal sample size minus 1. Otherwise the procedure stops.

All hypotheses are tested with the same test direction for all comparisons and endpoints (alternative="..."). In case of doubt, use "two.sided".

If Margin is a single numeric value or a numeric vector, then the same value(s) are used for the remaining comparisons or endpoints.

Author(s)

Mario Hasler

References

Hasler, M. (2014): Multiple contrast tests for multiple endpoints in the presence of heteroscedasticity. *The International Journal of Biostatistics* 10, 17–28, <doi:10.1515/ijb-2012-0015>.

Hasler, M. and Hothorn, L.A. (2012): A multivariate Williams-type trend procedure. *Statistics in Biopharmaceutical Research* 4, 57–65, <doi:10.1080/19466315.2011.633868>.

Hasler, M. and Hothorn, L.A. (2008): Multiple contrast tests in the presence of heteroscedasticity. *Biometrical Journal* 50, 793–800, <doi:10.1002/bimj.200710466>.

Dilba, G. et al. (2006): Simultaneous confidence sets and confidence intervals for multiple ratios. *Journal of Statistical Planning and Inference* 136, 2640–2658, <doi:10.1016/j.jspi.2004.11.009>.

See Also

SimCiRat, SimTestDiff, SimCiDiff

Examples

```
# Example 1:
# A comparison of the groups B and H against the standard S, for endpoint
# Thromb.count, assuming unequal variances for the groups. This is an
# extension of the well-known Dunnett-test to the case of heteroscedasticity
# and in terms of ratios of means instead of differences.

data(coagulation)

comp1 <- SimTestRat(data=coagulation, grp="Group", resp="Thromb.count",
```

```
  type="Dunnett", base=3, alternative="greater", covar.equal=FALSE)
comp1

# Example 2:
# A comparison of the groups B and H against the standard S, simultaneously
# for all endpoints, assuming unequal covariance matrices for the groups. This is
# an extension of the well-known Dunnett-test to the case of heteroscedasticity
# and multiple endpoints and in terms of ratios of means instead of differences.

data(coagulation)

comp2 <- SimTestDiff(data=coagulation, grp="Group", resp=c("Thromb.count","ADP","TRAP"),
  type="Dunnett", base=3, alternative="greater", covar.equal=FALSE)
summary(comp2)
```

`summary.SimCi` *Summary function for SimCi-objects*

Description

A detailed print out of the results of `SimCiDiff` and `SimCiRat`, respectively.

Usage

```
## S3 method for class 'SimCi'
summary(object, digits = 4, ...)
```

Arguments

`object`	an object of class "SimCi" as obtained by calling `SimCiDiff` or `SimCiRat`
`digits`	digits for rounding the results
`...`	arguments to be passed to `print`

Value

A print out containing the estimates, degrees of freedom, raw and simultaneous confidence intervals, estimated covariance and correlation matrices of the data and of the comparisons computed by `SimCiDiff` or `SimCiRat`, respectively.

Author(s)

Mario Hasler

See Also

`summary.SimTest`

summary.SimTest *Summary function for SimTest-objects*

Description

A detailed print out of the results of SimTestDiff and SimTestRat, respectively.

Usage

```
## S3 method for class 'SimTest'
summary(object, digits = 4, ...)
```

Arguments

object	an object of class "SimTest" as obtained by calling SimTestDiff or SimTestRat
digits	digits for rounding the results
...	arguments to be passed to print

Value

A print out containing the estimates, test statistics, degrees of freedom, raw and adjusted p-values, estimated covariance correlation matrices of the data and of the comparisons computed by SimTestDiff or SimTestRat, respectively.

Author(s)

Mario Hasler

See Also

summary.SimCi

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