Package ‘mratiost’

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Type Package

Title Ratios of Coefficients in the General Linear Model

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Depends R (>= 2.12.0)

Suggests nlme

Imports mvtnorm, multcomp, survival, survPresmooth, stats

Description
Performs (simultaneous) inferences for ratios of linear combinations of coefficients in the general linear model, linear mixed model, and for quantiles in a one-way layout. Multiple comparisons and simultaneous confidence interval estimations can be performed for ratios of treatment means in the normal one-way layout with homogeneous and heterogeneous treatment variances, according to Dilba et al. (2007) <https://cran.r-project.org/doc/Rnews/Rnews_2007-1.pdf> and Hasler and Hothorn (2008) <doi:10.1002/bimj.200710466>. Confidence interval estimations for ratios of linear combinations of linear model parameters like in (multiple) slope ratio and parallel line assays can be carried out. Moreover, it is possible to calculate the sample sizes required in comparisons with a control based on relative margins. For the simple two-sample problem, functions for a t-test for ratio-formatted hypotheses and the corresponding confidence interval are provided assuming homogeneous or heterogeneous group variances.

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**Description**

With this package, it is possible to perform (simultaneous) inferences for ratios of linear combinations of coefficients in the general linear model. In particular, tests and confidence interval estimations for ratios of treatment means in the normal one-way layout and confidence interval estimations like in (multiple) slope ratio and parallel line assays can be carried out. Moreover, it is possible to calculate the sample sizes required in comparisons with a control based on relative margins. For the simple two-sample problem, functions for a t-test for ratio-formatted hypotheses and Fieller confidence intervals are provided assuming homogeneous or heterogeneous group variances.
Author(s)
Gemechis Dilba Djira, Mario Hasler, Daniel Gerhard, Frank Schaarschmidt
Maintainer: Frank Schaarschmidt <schaarschmidt@biostat.uni-hannover.de>

References


See Also
Multiple comparisons for differences of means: *multcomp*

Examples

```r
library(mratios)

# Two-sample test and confidence interval
# for comparison of means, allowing for heteroscedasticity

data(ASAT)
ASAT
 ttestratio(ASAT~group, data=ASAT, alternative="less", base=1, 
   rho=1.25, var.equal=TRUE)

data(Mutagenicity)
 boxplot(MN~Treatment, data=Mutagenicity)

# It seems to be inappropriate to assume homogeneous variances:

# 1) comparing whether the active control is more effective
# than vehicle control

 ttestratio(MN~Treatment, 
   data=subset(Mutagenicity, Treatment=="Cyclo25"|Treatment=="Vehicle"), 
   alternative="greater", rho=1, var.equal=FALSE)
```
# 2) lowest dose vs. vehicle control

ttestratio(MN~Treatment,
data=subset(Mutagenicity, Treatment=="Hydro30"|Treatment=="Vehicle"),
alternative="greater", rho=1, var.equal=FALSE)

# sci.ratio:
# Calculation of simultaneous confidence intervals for ratios
# of linear combinations of treatment means in a one-way ANOVA model

data(BW)
boxplot(Weight~Dose, data=BW)

# Body weights of a 90-day chronic toxicology study on rats
# with a control (1) and three dose groups (2,3,4).

# Calculate upper confidence limits for the ratio of means
# of the three dose groups vs. the control group:
# Which of the doses lead to not more than 90 percent weight loss
# compared to the control group:

m21 <- sci.ratio(Weight~Dose, data=BW, type="Dunnett",
alternative="greater")

summary(m21)
plot(m21, rho0=0.9)

# simtest.ratio: Simultaneous tests for ratios of means

## Not run:
data(AP)
boxplot(prepost~treatment, data=AP)

# Test whether the differences of doses 50, 100, 150 vs. Placebo
# are non-inferior to the difference Active Control vs. Placebo

NC <- rbind("(D100-D0)" = c(0,-1,1,0,0),
"(D150-D0)" = c(0,-1,0,1,0),
"(D50-D0)" = c(0,-1,0,0,1))

DC <- rbind("(AC-D0)" = c(1,-1,0,0,0),
"(AC-D0)" = c(1,-1,0,0,0),
"(AC-D0)" = c(1,-1,0,0,0))
NC
DC

stAP <- simtest.ratio(prepost ~ treatment, data=AP,
     Num.Contrast=NC, Den.Contrast=DC, Margin.vec=c(0.9,0.9,0.9))
summary(stAP)

## End(Not run)

#####################################################################
# # # sci.ratio.gen:
# Simultaneous confidence intervals for ratios of coefficients
# in the general linear model:
# Slope-ratio assay, data from Jensen(1989), Biometrical Journal 31,
# 841-853.

data(SRAssay)
SRAssay

# In this problem, the interest is in simultaneous estimation
# of the ratios of slopes relative to the slope of the standard
# treatment.

# First it is needed to carefully define the vector of responses
# and the design matrix of the general linear model:
# The design matrix can be constructed using model.matrix,
# and the vector of the response variable can be extracted
# from the dataframe.

X <- model.matrix(Response~Treatment:Dose, data=SRAssay)
Response <- SRAssay[,"Response"]

# The response vector and the design matrix are:

X
Response

# The following coefficients result:

lm(Response~0+X)

# where the last four coefficients are the estimated slopes
# of the control treatment and the three new treatments

# Contrasts for the ratios of the slopes of the three new treatments
# vs. the control are then defined as:

Num.Contrast <- matrix(c(0,0,1,0,
                          0,0,0,1,0,
                          0,0,0,0,1),nrow=3,byrow=TRUE)
The angina data set

**Description**

Dose response study of a drug to treat Angina pectoris. Response variable was the duration of pain-free walking after treatment, relative to the values before treatment. Large values indicate positive effects on patients. Data set taken from Westfall et al. (1999), p. 164.

**Usage**

data(angina)

**Format**

A data frame with 50 observations on the following 2 variables.

- **dose** a factor with levels 0, 1, 2, 3, 4
**response** a numeric vector giving the change from pretreatment as measured in minutes of pain-free walking.

**Details**

See Westfall et al. (1999, p. 164)

**Source**


**References**

angina(multcomp)

**Examples**

```r
library(mratios)
data(angina)
str(angina)
plot(response~dose, data=angina)
```

---

**Description**

A data set is generated (from normal distribution) to imitate the summary statistics in Table II of Bauer et al. (1998). In the experiment, patients with chronic stable angina pectoris were randomized to five treatment arms (placebo, three doses of a new compound, and an active control). The primary endpoint is the difference in the duration of an exercise test before and after treatment.

**Usage**

data(AP)

**Format**

A data frame with 303 observations on the following 2 variables.

- **prepost** a numeric vector, the difference post treatment measurement minus pre treatment measurement
- **treatment** a factor with levels AC (the active control), D0 (the zero dose, placebo), and D50, D100, D150, the three dose groups of the new compound.
Source


Examples

library(mratios)

data(AP)

str(AP)

boxplot(prepost ~ treatment, data=AP)

by(AP,AP$treatment, function(x){mean(x$prepost)})

by(AP,AP$treatment, function(x){sd(x$prepost)})

<table>
<thead>
<tr>
<th>ASAT</th>
<th>ASAT data</th>
</tr>
</thead>
</table>

Description

Data from a toxicity study: ASAT values of the serum of female Wistar rats six months after application

Usage

data(ASAT)

Format

A data frame with 34 observations on the following 2 variables.

group a factor with two levels KON, and TREAT, where KON is the control group consisting of 19 subjects and TREAT is the treatment group consisting of only 15 subjects due to mortality

ASAT a numeric vector containing values of the response variable

Details

The objective is to test that ASAT values of treatment group are not relevantly heightened compared to the control group, where average ASAT value which is more than 25 percent higher than the average of the control group is defined as relevant.

Source

Examples

library(mratios)
data(ASAT)
str(ASAT)
boxplot(ASAT~group, data=ASAT)

bnct

Boron neutron capture therapy (BNCT)

Description

Death times (in days) from a study to determine the efficacy of BNCT in treating therapeutically refractory F98 glioma.

Usage

data("bnct")

Format

A data frame with 30 observations on the following 3 variables.

trt  a numeric vector: Treatment (1=untreated, 2=radiated, 3=radiated + BPA)
time  a numeric vector: Death time or on-study time, days
dead  a numeric vector: Death indicator (1=dead, 0=alive)

Details

A right censored data from a study performed to determine the efficacy of boron neutron capture therapy (BNCT) in treating the therapeutically refractory F98 glioma, using boronophenylalanine (BPA) as the capture agent. F98 glioma cells were implanted into the brains of rats. Three groups of rats each with 10 rats were studied. One group went untreated, another was treated only with radiation, and the third group received radiation plus an appropriate concentration of BPA.

Source

Examples

```r
data(bnct)
str(bnct)

with(bnct, mcpqdc(y = time, f = trt, event = death, TRUE))
with(bnct, mcpqrc(y = time, f = trt, event = death, TRUE))
```

---

**BW**

*Body weights measured in a toxicological study*

Description

Body weights of a 90-day chronic toxicological study on rats with a control and three dose groups.

Usage

```r
data(BW)
```

Format

A data frame with 60 observations on the following 2 variables.

- **Weight** a numeric vector containing the bodyweights of rats
- **Dose** a factor with levels 1, 2, 3, 4, specifying the dose groups, where 1 is the control group

Source


Examples

```r
library(mratios)
data(BW)
str(BW)
boxplot(Weight~Dose, data=BW)
```
contrMatRatio

Creates numerator and denominator contrast matrices for ratio-based hypotheses for common multiple comparison and trend test problems.

Description

Creates numerator and denominator contrast matrices for some common multiple comparison and trend test problems. These matrices are internally used by the sci.ratio and simtest.ratio functions. The contrMatRatio function is a modification of the function contrMat (multcomp).

Whether the given definitions of contrast matrices for trend test problems in terms of ratios make sense and how they are to be interpreted is to be discussed.

Usage


Arguments

n integer vector of sample sizes
type the type of multiple contrasts
• "Dunnett": many to one comparisons, with the control group in the denominator
• "Tukey": all-pair comparisons
• "Sequen": comparison of consecutive groups, where the groups of lower order is the denominator
• "AVE": comparison of each group with average of all others, where the average is taken as denominator
• "GrandMean": comparison of each group with grand mean of all groups, where the grand mean is taken as denominator
• "Changepoint": ratio of averages of groups of higher order divided by averages of groups of lower order
• "Marcus": Marcus contrasts defined for ratios
• "McDermott": McDermott contrasts for ratios
• "Williams": Williams contrasts for ratios
• "UmbrellaWilliams": Umbrella-protected Williams contrasts for ratios, i.e., a sequence of Williams-type contrasts with groups of higher order step-wise omitted
base a single integer specifying the control (i.e., denominator) group for "Dunnett"-type contrasts for calculating the ratios to the control

Details

This is a simple adaption of the contrMat function in the package multcomp for ratio hypotheses.
Value

A list containing:

- `numC`: the (named) numerator contrast where rows correspond to contrasts
- `denC`: the (named) denominator contrast where rows correspond to contrasts
- `rnames`: a character vector with names of the contrasts

and the type of contrast as attr.

Author(s)

Frank Schaarschmidt and Daniel Gerhard by modifying the code of `contrMat(multcomp)`

See Also

`contrMat(multcomp)`

Examples

```r
library(mratios)
n=c(A=10,B=20,Z=10,D=10)
contrMatRatio(n=n, type="Dunnett", base=1)
contrMatRatio(n=n, type="Dunnett", base=3)
contrMatRatio(n=n, type="Tukey")
contrMatRatio(n=n, type="Sequen")
contrMatRatio(n=n, type="AVE")
contrMatRatio(n=n, type="GrandMean")
contrMatRatio(n=n, type="Williams")
contrMatRatio(n=n, type="UmbrellaWilliams")
```

---

### DiabeticMice

<table>
<thead>
<tr>
<th>Serum albumin of diabetic mice</th>
</tr>
</thead>
</table>

**Description**

The amounts of nitrogen-bound bovine serum albumen produced by three groups of diabetic mice

**Usage**

data("DiabeticMice")
Format

A data frame with 57 observations on the following 2 variables.

- group: a factor with levels alloxan insulin normal
- response: Amounts of nitrogen-bound bovine serum albumen produced by the mice

Details

The 57 observations of the amounts of nitrogen-bound bovine serum albumen produced by three groups of diabetic mice, these being normal, alloxan diabetic and alloxan diabetic treated with insulin.

Source


Examples

```r
data(DiabeticMice)
str(DiabeticMice)
boxplot(response~group, data = DiabeticMice)

y <- DiabeticMice$response
f <- DiabeticMice$group
mcpqdc(y, f)
mcpqrc(y, f)
```

---

### gsci.ratio

Simultaneous confidence intervals for ratios of linear combinations of parameters.

**Description**

This function calculates simultaneous confidence intervals for ratios of user-defined linear combinations, given a vector parameter estimates and a corresponding variance-covariance matrix. Besides unadjusted intervals, multiplicity adjustments are available using quantiles of a multivariate Normal- or t-distribution. The function provides a more general, but less user-friendly function to calculate ratios of mean parameters from linear (mixed models).

**Usage**

```r
gsci.ratio(est, vmat, Num.Contrast, Den.Contrast,
    degfree = NULL, conf.level = 0.95, alternative = "two.sided",
    adjusted = TRUE)
```
Arguments

- **est**: A numeric vector of parameter estimates, for example coefficients of a linear model.
- **vcmat**: The corresponding variance-covariance matrix (Number of rows and columns should be the same as the length of the parameter vector).
- **Num.Contrast**: Numerator contrast matrix, where the number of columns must be the same as the length of the parameter vector, and each row represents one contrast.
- **Den.Contrast**: Denominator contrast matrix, where the number of columns must be the same as the length of the parameter vector, and each row represents one contrast.
- **degfree**: Degrees of freedom used for calculating quantiles of a (multivariate) t-distribution. If NULL, Normal approximations are used.
- **conf.level**: Simultaneous confidence level in case of adjusted == TRUE, and comparison-wise confidence level in case of adjusted == FALSE.
- **alternative**: A character string: "two.sided" for two-sided intervals, "less" for upper confidence limits, "greater" for lower confidence limits.
- **adjusted**: If TRUE, the simultaneous confidence level is controlled, otherwise the comparisonwise confidence level is used.

Details

Given a parameter vector and its corresponding covariance matrix from a linear model fit, approximate simultaneous confidence intervals for several ratios of linear combinations of these parameters are calculated. For simultaneous confidence intervals (adjusted=TRUE) the plug-in method is used (plugging the maximum likelihood estimates of the ratios to obtain the correlation matrix for calculating quantiles of a multivariate t or normal distribution).

Linear combinations can be defined by providing matrices for the nominator and the denominator; some pre-defined contrasts can be constructed by the function contrMatRatio. (These may be weighted for different sample sizes.)

Value

An object of class "sci.ratio" and "gsci.ratio", containing a list with elements:

- **estimate**: point estimates of the ratios
- **CorrMat.est**: estimate of the correlation matrix
- **Num.Contrast**: matrix of contrasts used for the numerator of ratios
- **Den.Contrast**: matrix of contrasts used for the denominator of ratios
- **conf.int**: confidence interval estimates of the ratios

And some further elements to be passed to print and summary functions.

Author(s)

Daniel Gerhard & Frank Schaarschmidt adapting code of Gemechis Dilba Djira
References

The general methodology of constructing inference for ratios of linear model parameters can be found in:


However, when adjusted=TRUE, the quantiles are not obtained as described in Zerbe(1978) or Young et al. (1997), but by adapting the 'plug-in' method described for the completely randomized one-way layout in


A simulation study of the performance of these methods in linear mixed models:


See Also

`glht(multcomp)` for simultaneous CI of differences of means, and function `sci.ratio.gen(mratios)`

Examples

```r
library(mratios)

# A 90-days chronic toxicity assay:
# Which of the doses (groups 2,3,4) do not show a decrease in
# bodyweight more pronounced than 90 percent of the bodyweight
# in the control group?

data(BW)
boxplot(Weight~Dose,data=BW)

lmfit <- lm(Weight~Dose-1, data=BW)
est <- coefficients(lmfit)
vc <- vcov(lmfit)
CMAT <- contrMatRatio(table(BW$Dose), type="Dunnett")

BWnoninf <- gsci.ratio(est, vc, CMAT$numC, CMAT$denC, alternative="greater", degfree=lmfit$df.residual)
```
Plot

```r
plot(BWnoninf, rho0=0.9)
```

### Mixed Model Example

```r
library("nlme")
data(Milk)

# Fit a linear mixed model (maybe there are nicer models available!)

lmefit <- lme(protein ~ Diet-1, data=Milk,
              random=~Time|Cow, correlation=corAR1(form=~Time|Cow))

# Extract the parameter estimates and the corresponding
# variance-covariance matrix

estm <- fixef(lmefit)
vcm <- vcov(lmefit)

# Define the matrices defining the ratios of interest for
# all-pair comparisons: CM is the numerator matrix and
# DM is the denominator matrix.

CM <- rbind(c(1,0,0),
            c(1,0,0),
            c(0,1,0))
DM <- rbind(c(0,1,0),
            c(0,0,1),
            c(0,0,1))

# Add some row names (This is optional!)
rownames(CM) <- c("b/b+l", "b/l", "b+l/l")

# Calculate and plot simultaneous confidence intervals:

gscimix <- gsci.ratio(estm, vcm, CM, DM, degfree=anova(lmefit)[,2])
plot(gscimix)
```

---

**mcpqest**

Point and variance estimation for quantiles of independent groups of samples
mcpqest

Description

Computes the pth quantile and variances for groups of given samples in one-way anova layout. It has option for right censored data.

Usage

mcpqest(y, f, event = NULL, Right.Censored = FALSE, p = 0.5, ...)

Arguments

y a numeric vector, the response variable. If Right.Censored = True, y is non-negative follow up time for right censored in survival data.

f a factor variable of the same length as y, assigning the observations in y into k groups.

event a binary variable indicating status for right censored data. Usually, 1 if event of interest has occurred (death = 1) and 0 otherwise (alive = 0).

Right.Censored a logical expression indicating right-censored data is being used for constructing simultaneous confidence interval.

p a single numeric value between 0 and 1 indicating the level of quantile for the contrasts. The default is p = 0.5 (the median).

... further arguments to be passed to the internal methods, in particular: bw.selec is a single character string specifying the method of bandwidth selection when using right censored survival data; bw.selec= "plug-in".

Details

Mainly for internal use.

Value

a list with elements:

quantileEST a numeric vector, the point estimates of quantiles for each factor level.

varEST a numeric vector, the variance estimates for each factor level.

n a numeric vector, the sample size of each factor level

Author(s)

Lawrence S. Segbehoe, Gemechis Dilba Djira, Frank Schaarschmidt (package inclusion)
Simultaneous confidence intervals for contrasts of quantiles

**Description**

The following functions construct simultaneous confidence intervals for multiple contrasts of quantiles (for ratios and differences) in a one-way layout. The "mcpqrci" is for ratios and "mcpqdci" is for differences of quantiles. Both functions have also options for right censored data.

**Usage**

```r
mcpqrci(y, f, event = NULL, Right.Censored = FALSE, p = 0.5, conf.level = 0.95, type = "Dunnett", base = 1, Num.cmat = NULL, Den.cmat = NULL, method = c("Wald", "Fieller"), ...)
```

```r
mcpqdci(y, f, event = NULL, Right.Censored = FALSE, p = 0.5, conf.level = 0.95, type = "Dunnett", base = 1, cmat = NULL,...)
```

**Arguments**

- `y`: a numeric vector, the response variable. If `Right.Censored = TRUE`, y is non-negative follow up time for right censored in survival data.
- `f`: a factor variable of the same length as y, assigning the observations in y into k groups.
- `event`: a binary variable indicating status for right censored data. Usually, 1 if event of interest has occurred (death = 1) and 0 otherwise (alive = 0); (optional: only if y is survival data).
- `Right.Censored`: a logical expression indicating right-censored data is being used for constructing simultaneous confidence intervals, (optional: only if y is survival data).
- `p`: a single numeric value between 0 and 1 indicating the level of quantile for the contrasts. The default is `p = 0.5` (the median).
- `conf.level`: a single numeric value between 0 and 1 indicating the level of confidence interval.
- `type`: a single character string, naming a contrast type, see `contrMat` and `contrMatRatio`, for the options; this argument is ignored if a contrast matrix is specified in `cmat` or `Num.cmat` and `Den.cmat`.
- `base`: a positive integer specifying the control group for the Dunnett contrasts, ignored otherwise. When base is not given the first group in terms of an alphanumeric order is taken as the control group.
- `cmat`: (optional) a matrix with numeric entries, containing contrast coefficients defining differences of quantiles in function `mcpqdci`; if there are k levels in f, the matrix should have k columns. type is ignored if cmat is specified.
Details

The interest is to construct simultaneous confidence intervals for several contrast of quantiles in a one-way layout. An asymptotic approach is used in estimating the variance of estimated quantiles. The `mcpqrci` handles ratios of multiple contrasts of quantiles and `mcpqdc1` handles differences of multiple contrast of quantiles.

If `event` argument is provided and `Right.Censored = TRUE`, the functions computes simultaneous confidence intervals for right censored data in `y`. The type argument defines the type of contrast matrix to use. Users can also define a preferred contrast matrix, `cmat`.

Value

a list with elements

- `cmat` Matrix of contrast used for contrast differences.
- `Num.Contrast` Matrix of contrast used for the numerator of ratios.
- `Den.Contrast` Matrix of contrast used for the denominator of ratios.
- `conf.level` A numeric value, as input.
- `estimate` a column vector, containing the point estimates of the contrasts.
- `std.err` a column vector, containing the standard error of the contrast estimates.
- `conf.int` a Mx2 matrix of confidence bounds, if M comparisons among the K samples are invoked.

Author(s)

Lawrence S. Segbehoe, Gemechis Dilba Djira, and Frank schaarschmidt (inclusion in the package)

See Also

sciratio for simultaneous confidence intervals for ratios of linear combinations of means
Examples

data("DiabeticMice")
response <- DiabeticMice$response
group <- DiabeticMice$group
## Example 1
Num.cmat <- matrix(c(1,1,0,0,0,0,1,0,0,0),3)
Den.cmat <- matrix(c(0,0,1,0,0,0,1,0,0,1),3)
mcpqdci(y = response, f = group, cmat = (Num.cmat + -1*Den.cmat))
mcpqdci(y = response, f = group, cmat = (Num.cmat + -1*Den.cmat)[-1,])
mcpqrci(y = response, f = group, Num.cmat = Num.cmat, Den.cmat = Den.cmat )
mcpqrci(y = response, f = group, Num.cmat = Num.cmat[-1,], Den.cmat = Den.cmat[-1,] )

## Example 2

data("bnct")
mcpqrci(y = bnct$time, f = bnct$trt, event = bnct$death, Right.Censored=TRUE)

## Sampled data:
y <- c(rnorm(20),rnorm(16,3),rnorm(24,7,2))
f <- rep(paste0("group", 1:3), c(20,16, 24))
event <- rbinom(60,1,0.8)
mcpqdci(y=y, f=f, method = "Fieller", base = 3)
mcpqrci(y=abs(y), f=f, event=event, Right.Censored=TRUE, Num.cmat = cbind(c(1,1), 0*diag(2)),
Den.cmat = cbind(c(0,0), diag(2)))
cmat <- cbind(-c(1,1),diag(2))
mcpqdci(y=y, f=f, method = "Fieller", cmat = cmat)

Mutagenicity

Mutagenicity assay

Description

Mutagenicity assay for 4 doses of a compound (hydroquinone) against a negative (vehicle) control and a positive (active) control (cyclophosphamide). Hydroquinone was applied in doses of 30, 50, 70, 100 mg/kg, positive control was applied with 25mg/kg. Counts of micronuclei in polychromatic erythrocytes after 24h are taken as a measure for the potency to induce chromosome damage. Data of male mice are presented (Hauschke et al., 2005).

Usage

data(Mutagenicity)
**Format**

A data frame with 31 observations on the following 2 variables.

- **Treatment**: a factor with levels Cyclo25, Hydro100, Hydro30, Hydro50, Hydro75, Vehicle
- **MN**: a numeric vector, giving the counts of micronuclei after 24h

**Source**

*Adler, ID, and Kliesch, U (1990).* Comparison of single and multiple treatment regiments in the mouse bone marrow micronucleus assay for hydroquinone and cyclophosphamide. *Mutation Research* 234, 115-123.

**References**


**Examples**

```r
data(Mutagenicity)
str(Mutagenicity)
boxplot(MN~Treatment, data=Mutagenicity)
```

---

**n.ratio**

*Sample size computation in simultaneous tests for ratios of means*

**Description**

Computes the sample sizes required in simultaneous tests for non-inferiority (or superiority) based on relative margins in multiple comparisons with a control.

**Usage**

```r
n.ratio(m, rho, Power, CV0, rho.star, alpha, Min.power = TRUE)
```

**Arguments**

- **m**: number of comparisons with a control group
- **rho**: relative non-inferiority (or superiority) margin
- **Power**: given power (1-beta)
- **CV0**: coefficient of variation of the control group
- **rho.star**: the percentage (of the mean of the control group) to be detected
- **alpha**: familywise error rate
- **Min.power**: if set to TRUE (by default), the minimal power will be controlled, otherwise complete power
Details

The sample sizes are computed at the least favourable configurations, based on the assumption of no prior information regarding the true configuration of the ratios under the alternative hypotheses. The formula is

\[
n = \frac{(C_1 + C_2)^2(1 + \rho^2)/((\rho - \rho^*)^2)CV_0^2}{(\rho - \rho^*)^2}.
\]

where \(C_1\) is the lower \(1 - \alpha\) equi-coordinate percentage point of an \(m\)-variate normal distribution and \(C_2\) is the quantile of univariate (multivariate) normal distribution depending on the type of power controlled. In tests for non-inferiority (or superiority) with large response values indicating better treatment benefit, \(\rho < \rho^*\), where \(\rho < 1\) for non-inferiority and \(\rho > 1\) for superiority testing. Whereas, if small response values indicate better treatment benefit, \(\rho^* < \rho\), where \(\rho > 1\) for non-inferiority and \(\rho < 1\) for superiority testing.

Author(s)

Gemechis Dilba Djira

References


Examples

```r
# Example 1: Sample size calculation in tests for non-inferiority
# (two-sample case)(Laster and Johnson (2003),
# Statistics in Medicine 22:187-200)

n.ratio(m=1, rho=0.8, Power=0.8, CV0=0.75, rho.star=1,
alpha=0.05)

# Example 2: Sample size calculation in simultaneous tests for
# non-inferiority
# (Dilba et al. (2006), Statistics in Medicine 25:1131-1147)

n.ratio(m=3, rho=0.7, Power=0.8, CV0=0.5, rho.star=0.95,
alpha=0.05)

# Example 3: Controlling complete power

n.ratio(m=5, rho=1.2, Power=0.8, CV0=0.2, rho.star=1.40,
alpha=0.05, Min.power=FALSE)
```
Comparing 6 strains with respect to production of antibiotics

Description
The production of antibiotics of 6 strains (mutants of the same micro organism) was compared. MO were put to holes in agar infected with Bacteria. The diameter of Bacteria-free areas around the colonies of the MO was recorded. Each strain was repeated 8 times.

Usage
data(Penicillin)

Format
A data frame with 48 observations on the following 2 variables.

strain a numeric vector, the number identifying the strains
diameter a numeric vector, size of the diameter of Bacteria-free area around each colony

Source

Examples
library(mratios)
data(Penicillin)
str(Penicillin)
boxplot(diameter ~ strain, data=Penicillin)
plot.sci.ratio

Plot output for sci.ratio and sci.ratio.gen

Description

Plot the intervals returned by sci.ratio

Usage

## S3 method for class 'sci.ratio'
plot(x, rho0 = 1, rho0lty=2, rho0lwd=1, rho0col="black", 
CIvert = FALSE, CIlty = 1, CIlwd = 1, CIcex = 1, CIpch=16, 
main = NULL, ylab = NULL, xlab = NULL, sub = NULL, length=NULL, 
sortby=NULL, decreasing=NULL, ...)

Arguments

x an object of class "sci.ratio" as can be obtained by calling the function sci.ratio
rho0 a single numeric value or vector of values defining the hypothesized ratio
rho0lty integer values to specify the line type for the rho0 line(s)
rho0lwd integer values to specify the line width for the rho0 line(s)
rho0col character vector to specify the colour for the rho0 line(s)
CIvert logical, CI are plotted horizontal if CIvert=FALSE and vertical otherwise
CIlty numeric value, giving the line type of the plotted confidence interval, see argument lty in ?par
CIlwd numeric value, giving the line width of the plotted confidence interval, see argument lwd in ?par
CIcex a single numeric value: by which amount the symbols in the CI shall be scaled relative to the default (see argument cex in ?par)
CIpch the symbol to be used for the point estimate, see pch in ?points
main character string to be plotted as main title of the plot
ylab character string, label of the y axis (ignored if CIvert=TRUE)
xlab character string, label of the x axis (ignored if CIvert=FALSE)
sub as in plot
length a numeric value, specifying the length/2 of the bars at the ends of the confidence intervals in inches
sortby a character string, one of "estimate", "lower, or "upper"; if specified, the results are ordered by magnitude of estimates, lower or upper limits
decreasing logical, to be passed to order, if sortby is specified, ignored otherwise
...

further arguments to be passed to axis()
Details
Too long names of the contrasts/comparisons should be avoided, otherwise use par() to change plot parameters.

Value
A plot of the confidence intervals in the sci.ratio object.

Author(s)
Frank Schaarschmidt

References
plot.hmtest(multcomp)

Examples

library(mratios)
data(angina)
aCI<-sci.ratio(response~dose, data=angina, type="Dunnett", alternative="greater")

# Visualize testing for superiority
plot(aCI, rho0=1.25, rho0lty=3)

print.sci.ratio
Print function for sci.ratio objects

Description
A short print out of the value of a sci.ratio object.

Usage
## S3 method for class 'sci.ratio'
print(x, digits=4, ...)

Arguments
x an object of class "sci.ratio" as can be obtained by calling the function sci.ratio
digits digits for rounding the output
... arguments to be passed to print
Value
A print out of the confidence intervals computed by sci.ratio.

See Also
plot.sci.ratio, summary.sci.ratio

print.simtest.ratio   \hspace{1cm}  \textit{Print out the results of simtest.ratio}

Description
A short print out of the results of simtest.ratio

Usage
## S3 method for class 'simtest.ratio'
print(x, digits = 4, ...)

Arguments
x  \hspace{1cm}  An object of class "simtest.ratio" as obtained by calling simtest.ratio
digits  \hspace{1cm}  digits for rounding of the results
...  \hspace{1cm}  arguments to be passed to print

Value
A print out, containing the margins, estimates, teststatistics, and p.values computed by simtest.ratio.

rat.weight   \hspace{1cm}  \textit{Body weight of rats in a toxicity study}

Description
Body weights of male rats were compared between a control group and a group which had received a high dose of a chemical in a toxicity study after a period of recovery

Usage
data(rat.weight)
Format

A data frame with 20 observations on the following 2 variables.

**group** a factor with two levels, Dosis and Kon, where Dosis is the high dose group, consisting of ten individuals and Kon is the control group, consisting of ten individuals

**weight** a numeric vector containing the values of response variable, final body weight in gramm

Details

Aim was to test that application of the chemical does not lead to a relevantly lowered or heightened body weight after a time of recovery. 0.8 and 1.25 were defined as relevance boundaries compared to the mean of control group

Source


Examples

```r
library(mratios)
data(rat.weight)
boxplot(weight~group, data=rat.weight)
```

---

**sci.ratio**  
*Simultaneous confidence intervals for ratios of linear combinations of means*

Description

This function constructs simultaneous confidence intervals for ratios of linear combinations of normal means in a one-way ANOVA model. Different methods are available for multiplicity adjustment.

Usage

```
sci.ratio(formula, data, type = "Dunnett", base = 1,
method = "Plug", Num.Contrast = NULL, Den.Contrast = NULL,
alternative = "two.sided", conf.level = 0.95, names=TRUE)
```
Arguments

formula A formula specifying a numerical response and a grouping factor as e.g. response ~ treatment

data A dataframe containing the response and group variable
type type of contrast, with the following options:
  - "Dunnett": many-to-one comparisons, with the control group in the denominator
  - "Tukey": all-pair comparisons
  - "Sequen": comparison of consecutive groups, where the group with lower order is the denominator
  - "AVE": comparison of each group with average of all others, where the average is taken as denominator
  - "GrandMean": comparison of each group with grand mean of all groups, where the grand mean is taken as denominator
  - "Changepoint": ratio of averages of groups of higher order divided by averages of groups of lower order
  - "Marcus": Marcus contrasts as ratios
  - "McDermott": McDermott contrasts as ratios
  - "Williams": Williams contrasts as ratios
  - "UmbrellaWilliams": Umbrella-protected Williams contrasts as ratios

Note: type is ignored, if Num.Contrast and Den.Contrast are specified by the user (See below).

base a single integer specifying the control (i.e. denominator) group for the Dunnett contrasts, ignored otherwise

method character string specifying the method to be used for confidence interval construction:
  - "Plug": Plug-in of ratio estimates in the correlation matrix of the multivariate t distribution. This method is the default.
  - "Bonf": Simple Bonferroni-adjustment of Fieller confidence intervals for the ratios
  - "MtI": Sidak or Slepian- adjustment for two-sided and one-sided confidence intervals, respectively
  - "Unadj": Unadjusted Fieller confidence intervals for the ratios (i.e. with comparisonwise confidence level = conf.level)

Num.Contrast Numerator contrast matrix, where columns correspond to groups and rows correspond to contrasts

Den.Contrast Denominator contrast matrix, where columns correspond to groups and rows correspond to contrasts

alternative a character string: "two.sided" for two-sided intervals, "less" for upper confidence limits, "greater" for lower confidence limits

conf.level simultaneous confidence level in case of method="Plug", "Bonf", or "MtI", and comparisonwise confidence level in case of method="Unadj"

names logical, indicating whether rownames of the contrast matrices shall be retained in the output
Details

Given a one-way ANOVA model, the interest is in simultaneous confidence intervals for several ratios of linear combinations of the treatment means. It is assumed that the responses are normally distributed with homogeneous variances. Unlike in multiple testing for ratios, the joint distribution of the likelihood ratio statistics has a multivariate t-distribution the correlation matrix of which depends on the unknown ratios. This means that the critical point needed for CI calculations also depends on the ratios. There are various methods of dealing with this problem (for example, see Dilba et al., 2006). The methods include (i) the unadjusted intervals (Fieller confidence intervals without multiplicity adjustments), (ii) Bonferroni (Fieller intervals with simple Bonferroni adjustments), (iii) MtI (a method based on Sidak and Slepian inequalities for two- and one-sided confidence intervals, respectively), and (iv) plug-in (plugging the maximum likelihood estimates of the ratios in the unknown correlation matrix). The latter method is known to have good simultaneous coverage probabilities. The MtI method consists of replacing the unknown correlation matrix of the multivariate t by an identity matrix of the same dimension.

See the examples for the usage of Numerator and Denominator contrasts. Note that the argument names Num.Contrast and Den.Contrast need to be specified. If numerator and denominator contrasts are plugged in without their argument names, they will not be recognized.

Value

An object of class "sci.ratio", containing a list with elements:

- estimate: point estimates of the ratios
- CorrMat.est: estimate of the correlation matrix (for the plug-in approach)
- Num.Contrast: matrix of contrasts used for the numerator of ratios
- Den.Contrast: matrix of contrasts used for the denominator of ratios
- conf.int: confidence interval estimates of the ratios

And some further elements to be passed to print and summary functions.

Author(s)

Gemechis Dilba Djira

References


See Also

glht(multcomp) for simultaneous CI of differences of means, plot.sci.ratio for a plotting function of the intervals
Examples

```r
# A 90-days chronic toxicity assay:
# Which of the doses (groups 2,3,4) do not show a decrease in
# bodyweight more pronounced than 90 percent of the bodyweight
# in the control group?

data(BW)
boxplot(Weight~Dose, data=BW)

BWnoninf <- sci.ratio(Weight~Dose, data=BW, type="Dunnett",
alternative="greater")

plot(BWnoninf, rho0=0.9)

## Not run:

# Antibiotic activity of 8 different strains of a micro organisms.
# (Horn and Vollandt, 1995):

data(Penicillin)
boxplot(diameter~strain, data=Penicillin)

allpairs<-sci.ratio(diameter~strain, data=Penicillin, type="Tukey")
plot(allpairs)
summary(allpairs)

## End(Not run)
```

sci.ratio.gen

Simultaneous confidence intervals for ratios of coefficients in the general linear model

Description

Constructs simultaneous confidence intervals for multiple ratios of linear combinations of coefficients in the general linear model.

Usage

```r
sci.ratio.gen(Y, X, Num.Contrast, Den.Contrast,
alternative = "two.sided", conf.level = 0.95,
method="Plug")
```
Arguments

Y: A numerical vector, containing the values of the response variable
X: A design matrix for the linear model, defining the parameters to be estimated, must have same number of rows as Y
Num.Contrast: Numerator contrast matrix
Den.Contrast: Denominator contrast matrix
alternative: one of "two.sided", "less", or "greater"
conf.level: simultaneous confidence levels
method: character string, specifying the method for confidence interval calculation:
  • "Plug": Plug-in of ratio estimates in the correlation matrix of the multivariate t distribution. This method is the default.
  • "Bonf": Simple Bonferroni-adjustment of Fieller confidence intervals for the ratios
  • "MtI": Sidak or Slepian- adjustment for two-sided and one-sided confidence intervals, respectively
  • "Unadj": Unadjusted Fieller confidence intervals for the ratios (i.e. with comparisonwise confidence level = conf.level)

Details

Given a general linear model, the interest is in simultaneous confidence intervals for several ratios of linear combinations of the coefficients in the model. It is assumed that the responses are normally distributed with homogeneous variances. In this problem, the joint distribution of the likelihood ratio statistics has a multivariate t-distribution the correlation matrix of which depends on the unknown ratios. This means that the critical point needed for CI calculations also depends on the ratios. There are various methods of dealing with this problem (for example, see Dilba et al., 2006). The methods include (i) the unadjusted intervals (Fieller confidence intervals without multiplicity adjustments), (ii) Bonferroni (Fieller intervals with simple Bonferroni adjustments), (iii) MtI (a method based on Sidak and Slepian inequalities for two- and one-sided confidence intervals, respectively), and (iv) plug-in (plugging the maximum likelihood estimates of the ratios in the unknown correlation matrix). The MtI method consists of replacing the unknown correlation matrix by an identity matrix of the same dimension.

Applications include relative potency estimations in multiple parallel line or slope-ratio assays. Users need to define the design matrix of the linear model and the corresponding contrast matrices in an appropriate way.

Value

A list containing

estimate: point estimates for the ratios
CorrMat.est: estimates of the correlation matrix (for the plug-in approach)
Num.Contrast: matrix of contrasts used for the numerator of ratios
Den.Contrast: matrix of contrasts used for the denominator of ratios
conf.int: confidence interval estimates of the ratios
Y       response vector
X       design matrix
fit     the model fit, an object of class "lm"

and some further input arguments, to be passed to print and summary functions.

Author(s)
Gemechis Dilba Djira

References

See Also
glht(multcomp) for multiple comparisons of parameters from lm, glm,..., sci.ratio for confidence intervals for ratios of means in a one-way-layout, simtest.ratio for simultaneous tests for ratios of means in a one-way-layout, plot.sci.ratio for plotting the confidence intervals.

Examples

```
# Slope-ratio assay on data from Jensen(1989),
# Biometrical Journal 31, 841-853.

# Definition of the vector of responses and
# the design matrix can be done directly as
# follows:

Y0 <- c(1.3, 1.7, 2.4, 2.7, 3.6, 3.6, 4.7, 5.0, 6.1, 6.3)
Y1 <- c(2.8, 2.9, 4.1, 3.7, 5.5, 5.5, 6.4, 6.7)
Y2 <- c(2.2, 2.1, 3.2, 3.2, 3.8, 3.9, 4.7, 4.9)
Y3 <- c(2.3, 2.3, 3.2, 3.0, 4.2, 4.2, 4.6, 5.1)
Y  <- c(Y0,Y1,Y2,Y3) # the response vector
xi <- rep(1,34)
x0 <- c(0,0, gl(4,2),rep(0,8*3))
x1 <- c(rep(0,10),gl(4,2), rep(0,8*2))
x2 <- c(rep(0,18),gl(4,2), rep(0,8))
x3 <- c(rep(0,26),gl(4,2))
X  <- cbind(xi,x0,x1,x2,x3) # the design matrix

# Have a look at the response vector:
Y

# and the design matrix:
```
X

# Internally in sci.ratio.gen, the following model is fitted

Fiti <- lm(Y ~ X - 1)
Fiti
summary(Fiti)

# In this problem, interest is simultaneous estimation of
# the ratios of slopes relative to the slope of the standard
# treatment. Therefore, the appropriate contrast matrices are:

Num.Contrast <- matrix(c(0,0,1,0,
                         0,0,0,1,
                         0,0,0,0),nrow=3,byrow=TRUE)
Den.Contrast <- matrix(c(0,1,0,0,
                         0,1,0,0,
                         0,1,0,0),nrow=3,byrow=TRUE)

SlopeRatioCI <- sci.ratio.gen(Y=Y, X=X,
SlopeRatioCI

# Further details of the fitted model and the contrasts used:

summary(SlopeRatioCI)
plot(SlopeRatioCI)

############################################################
## Not run:
# If one starts with a dataframe, the function model.matrix
# can be used to create the design matrix:

data(SRAssay)
SRAssay

# Create the design matrix using model.matrix

X <- model.matrix(Response~Treatment:Dose, data=SRAssay)
Response <- SRAssay[,"Response"]

# The response vector and the design matrix are now:

X
Response
The following coefficients result from fitting this model:

lm(Response ~ 0 + X)

The same contrasts as above are used:

Num.Contrast <- matrix(c(0,0,1,0, 0,0,1,0, 0,0,0,1), nrow=3, byrow=TRUE)
Den.Contrast <- matrix(c(0,1,0,0, 0,1,0,0, 0,1,0,0), nrow=3, byrow=TRUE)

summary(sci.ratio.gen(Y=Response, X=X, Num.Contrast, Den.Contrast))

## End(Not run)

---

sci.ratioVH

**Approximate simultaneous confidence intervals for ratios of means when variances are heterogeneous**

**Description**

This function constructs simultaneous confidence intervals for ratios of linear combinations of normal means in a one-way model, allowing that the variances differ among groups. Different methods are available for multiplicity adjustment.

**Usage**

sci.ratioVH(formula, data, 
    type = "Dunnett", base = 1, method = "Plug", 
    Num.Contrast = NULL, Den.Contrast = NULL, 
    alternative = "two.sided", conf.level = 0.95, 
    names = TRUE)

**Arguments**

- **formula** A formula specifying a numerical response and a grouping factor as e.g. response ~ treatment
- **data** A dataframe containing the response and group variable
- **type** type of contrast, with the following options:
  - "Dunnett": many-to-one comparisons, with control in the denominator
  - "Tukey": all-pair comparisons
  - "Sequen": comparison of consecutive groups, where the group with lower order is the denominator
• "AVE": comparison of each group with average of all others, where the average is taken as denominator
• "Changepoint": ratio of averages of groups of higher order divided by averages of groups of lower order
• "Marcus": Marcus contrasts as ratios
• "McDermott": McDermott contrasts as ratios
• "Williams": Williams contrasts as ratios

Note: type is ignored, if Num.Contrast and Den.Contrast are specified by the user (See below).

base
a single integer specifying the control (i.e. denominator) group for the Dunnett contrasts, ignored otherwise

method
a character string, specifying the method to be used for confidence interval construction:

• "Plug": Plug-in of ratio estimates to obtain the correlation matrix of contrasts (default)
• "Bonf": Simple Bonferroni-adjustment of Fieller confidence intervals for the ratios
• "MtI": Sidak- or Slepian- adjustment for two-sided and one-sided confidence intervals, respectively
• "Unadj": Unadjusted Fieller confidence intervals for the ratios (i.e. with comparisonwise confidence level = conf.level)

Num.Contrast
Numerator contrast matrix, where columns correspond to groups and rows correspond to contrasts

Den.Contrast
Denominator contrast matrix, where columns correspond to groups and rows correspond to contrasts

alternative
a character string

• "two.sided": for two-sided intervals
• "less": for upper confidence limits
• "greater": for lower confidence limits

conf.level
simultaneous confidence level in case of method="Plug","Bonf", or "MtI", and comparisonwise confidence level in case of method="Unadj"

names
logical, indicating whether rownames of the contrast matrices shall be retained in the output

Details

Given a one-way ANOVA model, the interest is in simultaneous confidence intervals for several ratios of linear combinations of the treatment means. It is assumed that the responses are normally distributed with possibly heterogeneous variances. Multivariate t-distributions are applied with a correlation matrix depending on the unknown ratios and sample variances and degrees of freedom according to Satterthwaite (1946).

Using method="Unadj" results in the methods described in Hasler, Vonk and Hothorn (2007).
Value

An object of class "sci.ratio", containing a list with elements:

- `estimate` the point estimates of the ratios
- `CorrMat.est` the estimated correlation matrix
- `Num.Contrast` matrix of contrasts used for the numerator of ratios
- `Den.Contrast` matrix of contrasts used for the denominator of ratios
- `conf.int` the estimated confidence intervals
- `NSD` a logical indicating whether any denominator occurred, which were not significantly different from 0

and some of the input arguments.

Author(s)

Mario Hasler

References

Simultaneous confidence intervals:


Marginal (unadjusted) confidence intervals:


See Also

- `plot.sci.ratio` for plots of confidence intervals and `simtest.ratioVH` for raw and multiplicity-adjusted p-values

Examples

data(Mutagenicity, package="mratios")

boxplot(MN~Treatment, data=Mutagenicity)

# Unless it is hard to assume Gaussian distribution
# in this example this is an attempt to take
# heterogeneous variances into account.

# Comparisons to the vehicle control,
# Proof of Hazard, using multiplicity adjusted
# confidence intervals:
## Not run:

```r
sci.ratioVH(MN~Treatment, data=Mutagenicity,
           type="Dunnett", base=6, method="Plug")
```

# Unadjusted confidence intervals for an
# intersection union test to proof safety
# for all doses of the compound.
```r
sci.ratioVH(MN~Treatment, data=Mutagenicity,
           type="Dunnett", base=6, method="Unadj", alternative="less")
```

```r
# User-defined contrasts:
# Mutagenicity of the doses of the new compound,
# expressed as ratio (DoseX-Vehicle)/(Cyclo25-Vehicle):

# Check the order of the factor levels:
levels(Mutagenicity$Treatment)

# numerators:
NC<-rbind(
  "Hydro30-Vehicle"=c(0,0,1,0,0,-1),
  "Hydro50-Vehicle"=c(0,0,0,1,0,-1),
  "Hydro75-Vehicle"=c(0,0,0,0,1,-1),
  "Hydro100-Vehicle"=c(0,1,0,0,0,-1)
)

DC<-rbind(
  "Cyclo25-Vehicle"=c(1,0,0,0,0,-1),
  "Cyclo25-Vehicle"=c(1,0,0,0,0,-1),
  "Cyclo25-Vehicle"=c(1,0,0,0,0,-1),
  "Cyclo25-Vehicle"=c(1,0,0,0,0,-1)
)

colnames(NC)<-colnames(DC)<-levels(Mutagenicity$Treatment)

NC

DC

CIs<-sci.ratioVH(MN~Treatment, data=Mutagenicity,
                 Num.Contrast=NC,
                 Den.Contrast=DC)
# Unadjusted confidence intervals for multiple ratios
# of means assuming heterogeneous group variances.
# The following code produces the results given in Table V of Hasler, Vonk and Hothorn (2007).
# The upper confidence limits in Table V can produced
# by calling:

```r
sci.ratioVH(formula=MN~Treatment, data=Mutagenicity,
            Num.Contrast=NC, Den.Contrast=DC,
            method="Unadj", alternative="less", conf.level=0.95)
```

## End(Not run)

---

**simtest.ratio**

*Simultaneous tests for ratios of normal means*

### Description

Performs simultaneous tests for several ratios of linear combinations of treatment means in the normal one-way ANOVA model with homogeneous variances.

### Usage

```r
simtest.ratio(formula, data, type = "Dunnett", base = 1,
               alternative = "two.sided", Margin.vec = NULL, FWER = 0.05,
               Num.Contrast = NULL, Den.Contrast = NULL, names = TRUE)
```

### Arguments

- **formula**: A formula specifying a numerical response and a grouping factor (e.g., response ~ treatment)
- **data**: A dataframe containing the response and group variable
- **type**: type of contrast, with the following options:
  - "Dunnett": many-to-one comparisons, with control in the denominator
  - "Tukey": all-pair comparisons
  - "Sequen": comparison of consecutive groups, where the group with lower order is the denominator
  - "AVE": comparison of each group with average of all others, where the average is taken as denominator
  - "GrandMean": comparison of each group with grand mean of all groups, where the grand mean is taken as denominator
  - "Changepoint": ratio of averages of groups of higher order divided by averages of groups of lower order
• "Marcus": Marcus contrasts as ratios
• "McDermott": McDermott contrasts as ratios
• "Williams": Williams contrasts as ratios
• "UmbrellaWilliams": Umbrella-protected Williams contrasts as ratios

Note: type is ignored if Num.Contrast and Den.Contrast are specified by the user (See below).

base
a single integer specifying the control (i.e. denominator) group for the Dunnett contrasts, ignored otherwise

alternative
a character string:
• "two.sided": for two-sided tests
• "less": for lower tail tests
• "greater": for upper tail tests

Margin.vec
a single numerical value or vector of Margins under the null hypotheses, default is 1

FWER
a single numeric value specifying the family-wise error rate to be controlled

Num.Contrast
Numerator contrast matrix, where columns correspond to groups and rows correspond to contrasts

Den.Contrast
Denominator contrast matrix, where columns correspond to groups and rows correspond to contrasts

names
a logical value: if TRUE, the output will be named according to names of user defined contrast or factor levels

Details

Given a one-way ANOVA model, the interest is in simultaneous tests for several ratios of linear combinations of the treatment means. Let us denote the ratios by \( \gamma_i, i = 1, \ldots, r \), and let \( \psi_i, i = 1, \ldots, r \), denote the relative margins against which we compare the ratios. For example, upper-tail simultaneous tests for the ratios are stated as

\[
H_0^i : \gamma_i \leq \psi_i
\]

versus

\[
H_{1i} : \gamma_i > \psi_i, i = 1, \ldots, r
\]

The associated likelihood ratio test statistic \( T_i \) has a t-distribution. For multiplicity adjustments, we use the joint distribution of the \( T_i, i = 1, \ldots, r \), which under the null hypotheses follows a central \( r \)-variate t-distribution. Adjusted p-values can be calculated by adapting the results of Westfall et al. (1999) for ratio formatted hypotheses.
Value

An object of class simtest.ratio containing:

- `estimate` a (named) vector of estimated ratios
- `teststat` a (named) vector of the calculated test statistics
- `Num.Contrast` the numerator contrast matrix
- `Den.Contrast` the denominator contrast matrix
- `CorrMat` the correlation matrix of the multivariate t-distribution calculated under the null hypotheses
- `critical.pt` the equicoordinate critical value of the multi-variate t-distribution for a specified FWER
- `p.value.raw` a (named) vector of unadjusted p-values
- `p.value.adj` a (named) vector of p-values adjusted for multiplicity
- `Margin.vec` the vector of margins under the null hypotheses

and some other input arguments.

Author(s)

Gemechis Dilba Djira

References


See Also

While `print.simtest.ratio` produces a small default print-out of the results, `summary.simtest.ratio` can be used to produce a more detailed print-out, which is recommended if user-defined contrasts are used, `sci.ratio` for constructing simultaneous confidence intervals for ratios in oneway layout

See `summary.glht(multcomp)` for multiple tests for parameters of lm, glm.

Examples

```r
library(mratios)

# User-defined contrasts for comparisons
# between Active control, Placebo and three dosage groups:
```
data(AP)
AP
boxplot(prepost~treatment, data=AP)

# Test whether the differences of doses 50, 100, 150 vs. Placebo
# are non-inferior to the difference of Active control vs. Placebo

# User-defined contrasts:

# Numerator Contrasts:
NC <- rbind(
  "(D100-D0)" = c(0,-1,1,0,0),
  "(D150-D0)" = c(0,-1,0,1,0),
  "(D50-D0)" = c(0,-1,0,0,1))

# Denominator Contrasts:
DC <- rbind(
  "(AC-D0)" = c(1,-1,0,0,0),
  "(AC-D0)" = c(1,-1,0,0,0),
  "(AC-D0)" = c(1,-1,0,0,0))

NC
DC

noninf <- simtest.ratio(prepost ~ treatment, data=AP,
  Num.Contrast=NC, Den.Contrast=DC, Margin.vec=c(0.9,0.9,0.9),
  alternative="greater")

summary( noninf )

=-=-=-=-=-=-=-=-=-=-=-=-=-=-=-=-=-=-=-=-=-=-=-=-=-=-=-=-=-=-=-=-=-=-=-=-=-=-

## Not run:

# Some more examples on standard multiple comparison procedures
# stated in terms of ratio hypotheses:

# Comparisons vs. Control:

many21 <- simtest.ratio(prepost ~ treatment, data=AP,
  type="Dunnett")

summary(many21)

# Let the Placebo be the control group, which is the second level
# in alpha-numeric order. A simultaneous test for superiority of
# the three doses and the Active control vs. Placebo could be
# done as:

many21P <- simtest.ratio(prepost ~ treatment, data=AP,
simtest.ratioVH

Approximate simultaneous tests for ratios of normal means with heterogeneous variances

Description

Performs simultaneous tests for several ratios of linear combinations of treatment means in a normal one-way layout, assuming normal distribution of the data allowing heterogeneous variances.

Usage

simtest.ratioVH(formula, data,
    type = "Dunnett", base = 1, alternative = "two.sided",
    Margin.vec = NULL, FWER = 0.05,
    Num.Contrast = NULL, Den.Contrast = NULL,
    names = TRUE)

Arguments

formula A formula specifying a numerical response and a grouping factor (e.g., response ~ treatment)

data A dataframe containing the response and group variable
type type of contrast, with the following options:
• "Dunnett": many-to-one comparisons, with control in the denominator
• "Tukey": all-pair comparisons
• "Sequen": comparison of consecutive groups, where the group with lower order is the denominator
• "AVE": comparison of each group with average of all others, where the average is taken as denominator
• "Changepoint": ratio of averages of groups of higher order divided by averages of groups of lower order
• "Marcus": Marcus contrasts as ratios
• "McDermott": McDermott contrasts as ratios
• "Williams": Williams contrasts as ratios

Note: type is ignored if Num.Contrast and Den.Contrast are specified by the user (See below).

base
a single integer specifying the control (i.e. denominator) group for the Dunnett contrasts, ignored otherwise

alternative
a character string:
• "two.sided": for two-sided tests
• "less": for lower tail tests
• "greater": for upper tail tests

Margin.vec
a single numerical value or vector of Margins under the null hypotheses, default is 1

FWER
a single numeric value specifying the family-wise error rate to be controlled

Num.Contrast
Numerator contrast matrix, where columns correspond to groups and rows correspond to contrasts

Den.Contrast
Denominator contrast matrix, where columns correspond to groups and rows correspond to contrasts

names
a logical value: if TRUE, the output will be named according to names of user defined contrast or factor levels

Details
The associated ratio test statistic $T[i]$ has a t-distribution. Multiplicity adjustment is achieved by using quantiles of $r r$-variate t-distributions, which differ in the degree of freedom and share the correlation structure. The comparison-specific degrees of freedom are derived using the approximation according to Satterthwaite (1946).

Value
An object of class simtest.ratio containing:

estimate
a (named) vector of estimated ratios
teststat
a (named) vector of the calculated test statistics
Num.Contrast
the numerator contrast matrix
Den.Contrast
the denominator contrast matrix
CorrMat: the correlation matrix of the multivariate t-distribution calculated under the null hypotheses.

critical.pt: the equicoordinate critical value of the multi-variate t-distribution for a specified FWER.
p.value.raw: a (named) vector of unadjusted p-values.
p.value.adj: a (named) vector of p-values adjusted for multiplicity.
Margin.vec: the vector of margins under the null hypotheses.

and some other input arguments.

Author(s)

Mario Hasler

References

Simultaneous tests (adjusted p-values)


Unadjusted tests (raw p-values)


See Also

sci.ratioVH for corresponding confidence intervals

Examples

# Unadjusted confidence intervals for multiple ratios
# of means assuming heterogeneous group variances.
# The following code produces the results given in Table
# V of Hasler, Vonk and Hothorn (2007).
# The upper confidence limits in Table V can produced
# by calling:

# Mutagenicity of the doses of the new compound,
# expressed as ratio (DoseX-Vehicle)/(Cyclo25-Vehicle):

# Check the order of the factor levels:
levels(Mutagenicity$Treatment)

# numerators:
NC<-rbind(
  "Hydro30-Vehicle"=c(0,0,1,0,0,-1),
  "Hydro50-Vehicle"=c(0,0,0,1,0,-1),
  "Hydro75-Vehicle"=c(0,0,0,0,1,-1),
  "Hydro100-Vehicle"=c(0,1,0,0,0,-1)
)

DC<-rbind(
  "Cyclo25-Vehicle"=c(1,0,0,0,0,-1),
  "Cyclo25-Vehicle"=c(1,0,0,0,0,-1),
  "Cyclo25-Vehicle"=c(1,0,0,0,0,-1),
  "Cyclo25-Vehicle"=c(1,0,0,0,0,-1)
)

colnames(NC)<-colnames(DC)<-levels(Mutagenicity$Treatment)
NC
DC

# The raw p-values are those presented in Table V:

simtest.ratioVH(formula=MN~Treatment, data=Mutagenicity,
  Num.Contrast=NC, Den.Contrast=DC,
  alternative="less", Margin.vec=0.5, FWER=0.05)

## End(Not run)

---

**SRAssay**

*Slope ratio assay of panthotenic acid contents in plant tissues*

---

**Description**

Content of panthotenic acid in a standard and three unknown samples were measured. The response variable is the titer of a sample to pH 6.8.
Summary:sci.ratio

Usage

data(SRAssay)

Format

A data frame with 34 observations on the following 3 variables.

Response  a numeric vector, containing the response variable (titer to pH 6.8)
Treatment a factor with levels St, U1, U2 and U3, specifying the standard and 3 unknown samples, respectively
Dose  a numeric vector

Source


References


Examples

library(mratios)
data(SRAssay)
str(SRAssay)
plot(Response~Dose, data=SRAssay)

# library(lattice)
# xyplot(Response~Dose|Treatment, data=SRAssay)
# see ?sci.ratio.gen for the analysis of this dataset

---

summary.sci.ratio  Summary function for sci.ratio

Description

Detailed print out for sci.ratio objects.

Usage

## S3 method for class 'sci.ratio'
summary(object, digits=4, ...)

A detailed print out of the results of simtest.ratio

Usage

## S3 method for class 'simtest.ratio'
summary(object, digits = 4, ...)

Arguments

object An object of class "simtest.ratio" as obtained by calling simtest.ratio
digits digits for rounding of the results
... arguments to be passed to print

Value

A print out, containing the numerator and denominator contrast matrices, the correlation under the null-hypothesis, margins, estimates, teststatistics, and p.values computed by simtest.ratio.
### ttestratio

**t-test for the ratio of two means**

#### Description

Performs t-test for the ratio of means of two independent samples from two gaussian distributions. In case of heterogeneous variances a Satterthwaite approximation of the degrees of freedom is used (Tamhane & Logan, 2004).

#### Usage

```r
## Default S3 method:
ttestratio(x, y, alternative = "two.sided",
          rho = 1, var.equal = FALSE, conf.level = 0.95,
          iterativeCI=FALSE, ul=1e+10, ll=-1e+10, ...)
## S3 method for class 'formula'
ttestratio(formula, data, base=2, ...)
```

#### Arguments

- **x**
  A numeric vector (group in the numerator of the ratio)
- **y**
  A numeric vector (group in the denominator of the ratio)
- **formula**
  A two-sided formula specifying a numeric response variable and a factor with two levels
- **data**
  A dataframe containing the variables specified in formula. Note: the first group in alpha-numeric order will appear in the denominator of the ratio
- **alternative**
  character string defining the alternative hypothesis, one of "two.sided", "less" or "greater"
- **rho**
  a single numeric value: the margin or ratio under the null hypothesis
- **var.equal**
  logical, if set TRUE, a ratio-t-test assuming equal group variances is performed, otherwise (default) unequal variances are assumed
- **conf.level**
  confidence level of Fieller's interval for the ratio of two means
- **base**
  if formula is used: a single numeric value specifying whether the first or second group (according to alpha-numeric order) is to be used as denominator
- **iterativeCI**
  a single logical, indicating whether the confidence limits shall be found with based on Fiellers formula (default) or by iteratively inverting the test (if TRUE); ignored when var.equal=FALSE
- **ul**
  a single numeric, defining the upper limit for searching the upper confidence bound in uniroot, if iterativeCI=TRUE and var.equal=FALSE, ignored otherwise
- **ll**
  a single numeric, defining the lower limit for searching the lower confidence bound in uniroot, if iterativeCI=TRUE and var.equal=FALSE, ignored otherwise
- **...**
  arguments to be passed to ttestratio.default
Details

This function implements the t-test for the ratio of two means and Fieller's confidence interval for the ratio of two means assuming mutually independent Gaussian errors with homogeneous variances, e.g. in Hauschke, Kieser, Hothorn (1999), when the argument `var.equal=TRUE`. With the argument `var.equal=FALSE` (default), the t-test for the ratio of two means assuming mutually independent Gaussian errors and possibly heterogeneous group variances (Tamhane and Logan, 2004) is implemented. When `iterativeCI = FALSE` (default) the corresponding confidence limits are obtained by using Fieller's formula with plug-in of the Satterthwaites degree of freedom calculated with the sample estimates for ratio and variances (not published). These bounds perform quite well but do not necessarily exactly coincide with the test decision. Setting `iterativeCI = TRUE` invokes iteratively searching for the confidence limits by inverting Tamhane and Logan's test using the function `uniroot`. If the confidence set is unbounded or gives irregular upper and/or lower bounds, a warning and NAs for the confidence limits are returned.

Note that when the mean of the denominator of the ratio is close to zero, confidence intervals might be degenerated and are not returned.

Value

An object of class "htest"

Author(s)

Frank Schaarschmidt

References


Examples

```r
library(mratios)

# ASAT values of female rats in a toxicity study
# (Hauschke, 1999).

data(ASAT)
ASAT

ttestratio(ASAT~group, data=ASAT, alternative="less",
base=1, rho=1.25, var.equal=TRUE)

# Bodyweights of male rats in a toxicity study.
```
# Objective was to show equivalence between the high dose group (Dosis) and the control group (Kon).
# Equivalence margins are set to 0.8 and 1.25. The type-I-error to show equivalence is set to alpha=0.05.

data(rat.weight)

# two one-sided tests:
ttestratio(weight~group, data=rat.weight, alternative="less", rho=1.25, var.equal=TRUE)
ttestratio(weight~group, data=rat.weight, alternative="greater", rho=0.8, var.equal=TRUE)

# For rho=1, ttestratio corresponds to a simple t.test with the difference of means under the null set to zero (i.e. mu=0).

ttestratio(ASAT~group, data=ASAT, alternative="less", rho=1, var.equal=TRUE)
t.test(ASAT~group, data=ASAT, alternative="less", mu=0, var.equal=TRUE)

# Ratio of means between negative and positive control in the mutagenicity data set, allowing heterogeneous variances:
data(Mutagenicity)
DM<-subset(Mutagenicity, Treatment=="Vehicle"|Treatment=="Cyclo25")

# 95%-CI using the Fieller formula, Satterthwaite df with plug-in of ratio estimate

ttestratio(MN~Treatment, data=DM, alternative="two.sided", var.equal=FALSE, iterativeCI=FALSE)

# 95%-CI based on directly inverting Tamhane and Logans test (Satterthwaite df, avoiding simple plug-in of the ratio estimate)

ttestratio(MN~Treatment, data=DM, alternative="two.sided", var.equal=FALSE, iterativeCI=TRUE)
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