Package ‘jocre’

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Type Package
Title Joint Confidence Regions
Version 0.3.3
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Description Computing and plotting joint confidence regions and intervals. Regions include classical ellipsoids, minimum-volume or minimum-length regions, and an empirical Bayes region. Intervals include the TOST procedure with ordinary or expanded intervals and a fixed-sequence procedure. Such regions and intervals are useful e.g., for the assessment of multi-parameter (bio-)equivalence. Joint confidence regions for the mean and variance of a normal distribution are available as well.

License GPL-2
Imports boot, KernSmooth, plyr, TSP
Suggests mvtnorm

BugReports https://github.com/PhilipPallmann/jocre/issues
NeedsCompilation no
Author Philip Pallmann [aut, cre]
Maintainer Philip Pallmann <p.pallmann@lancaster.ac.uk>
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**Description**

This package provides functions for computing and plotting joint confidence regions as well as (simultaneous) confidence intervals, with a focus on multivariate normal parameter vectors and parameters of the normal distribution i.e., mean and variance.

**Details**

Package: jocre
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License: GPL-2

cset computes joint confidence regions and (simultaneous) confidence intervals around multivariate normal means. The parameter estimates and interval bounds (in the case of confidence regions their boundaries are projected onto the axes) are displayed with print or summary, and plot generates a graph of the estimate and region or intervals and allows for some fine tuning e.g., shading of an equivalence region.

csetMV computes joint confidence regions for the mean and variance (or standard deviation) of a normal distribution. plot, print, and summary produce the corresponding graphics and summaries. Insights into the conservativeness of the two one-sided test procedure can be obtained with iutsize. Confidence levels of a joint ellipse and marginal intervals can be "translated" back and forth with translate.

**Author(s)**

Philip Pallmann (<p.pallmann@lancaster.ac.uk>)

**References**


**Examples**

```r
## Not run:
data("marzo")
plot(cset(dat=marzo, method="limacon"))

data("wires")
plot(csetMV(dat=wires, method="mood"))
```
Description

Computes boundaries of (simultaneous) confidence regions and intervals around multivariate normal means using different methods.

Usage

cset(dat, method, alpha=0.1, steps=NULL, nboot=1e4, TsengBrownA=1, TsengBrownB=1)

Arguments

dat A matrix or data.frame with independent units in rows and multivariate outcomes in columns.
method A character string specifying the method to be used. See details for available methods.
alpha A numeric value giving the type I error level to be controlled. Default is 0.1.
steps An integer setting the initial number of steps for the search algorithm. Default is NULL, which chooses 300 for two-dimensional and 50 for higher-dimensional problems.
nboot A numeric giving the number of bootstrap replications to be used when method="bootkern" (ignored otherwise). Default is 1e4.
TsengBrownA A numeric giving the parameter A to be used when method="tseng.brown" (ignored otherwise). Default is 1.
TsengBrownB A numeric giving the parameter B to be used when method="tseng.brown" (ignored otherwise). Default is 1.

Details

Available methods for confidence regions are: boot.kern for the nonparametric bootstrap method using kernel density estimation described in Pullmann & Jaki (2017); emp.bayes for the empirical Bayes region described in Casella & Hwang (1983); hotelling for the Hotelling-type region described in Wang et al (1999); limacon.asy for the limacon-shaped mimimum expected volume region described in Brown et al (1995); limacon.fin for the finite-sample variant of the minimum expected volume region described in Berger & Hsu (1996); standard.cor for the standard region incorporating correlation between parameters described in Chew (1966); standard.ind for the standard region ignoring correlation between parameters; tost for the two one-sided test (TOST) intervals described in Schuirmann (1987); tseng for the minimum expected interval length region described in Tseng (2002); tseng.brown for the pseudo-empirical Bayes region described in Tseng & Brown (1997).

Available methods for confidence intervals are: expanded for the two one-sided test (TOST) procedure (Schuirmann 1987) using the expanded intervals described e.g., in Bofinger (1992) and Hsu...
et al. (1994); fixNseq for the fixed sequence intervals described in Maurer et al. (1995) and Hsu & Berger (1999); tost for the two one-sided test (TOST) intervals described in Schuirmann (1987).
See also an overview and comparison of all methods in Pallmann & Jaki (2017).

Value
An object of class JOC.

Note
Warning: please use with care! Some of the functionality has not yet been thoroughly tested.

Author(s)
Philip Pallmann (<p.pallmann@lancaster.ac.uk>)

References
csetMV


# bootkern not included so far

See Also

csetMV for (simultaneous) confidence regions for normal mean and variance.

Examples

## Not run:

# Example 1: simultaneous 90% confidence intervals for trivariate data
tivar <- mvtnorm::rmvnorm(n=20, mean=rep(0.05, 3), sigma=toeplitz(c(0.05, 0.04, 0.03)))
colnames(tivar) <- c("AUCinf", "AUCT", "Cmax")
tost <- cset(dat=tivar, method="tost", alpha=0.1)
summary(tost)

# Example 2: simultaneous 90% confidence regions for bivariate data
bivar <- mvtnorm::rmvnorm(n=20, mean=rep(0.05, 2), sigma=toeplitz(c(0.05, 0.04)))
colnames(bivar) <- c("AUC", "Cmax")
hotelling <- cset(dat=bivar, method="hotelling", alpha=0.1)
summary(hotelling)
plot(hotelling, main="90% Hotelling Region")
limacon <- cset(dat=bivar, method="limacon.asy", alpha=0.1)
summary(limacon)
plot(limacon, main="90% Limacon Region")
tseng <- cset(dat=bivar, method="tseng", alpha=0.1)
summary(tseng)
plot(tseng, main="90% Tseng Region")

## End(Not run)

---

csetMV

Confidence regions and intervals for a normal mean and variance

Description

Computes boundaries of (simultaneous) confidence regions for the mean and variance of a normal distribution using different methods.

Usage

csetMV(dat, n, method, alpha=0.1, scale="var", steps=500)
Arguments

dat  A vector of numeric values assumed to follow a normal distribution. Not required for method="cheng.iles" or "min.area".
n  A numeric value giving the sample size. Only required for method="cheng.iles" or "min.area".
method  A character string specifying the method to be used. See details for available methods.
alpha  A numeric value giving the type I error level to be controlled. Default is 0.1.
scale  A character string specifying whether the variance (var) or standard deviation (sd) is to be plotted on the y axis. Not required for method="cheng.iles" or "min.area".
steps  An integer setting the initial number of steps for the search algorithm. Default is 800.

Details

Available methods are: mood for the classical region described in Mood (1950); large for the large-sample approximation region described in section 4.1 of Arnold & Shavelle (1998); plugin for a plug-in variant of the large-sample approximation region described in section 4.2 of Arnold & Shavelle (1998); pluginf for the plug-in variant of the large-sample approximation region described in section 4.3 of Arnold & Shavelle (1998) using an asymptotic F distribution as in Douglas (1993); lrt for the likelihood ratio test region described in section 4.4 of Arnold & Shavelle (1998); cheng.iles for the region described in Cheng & Iles (1983); min.area for the minimum-area region described in Frey et al. (2009).

Value

An object of class JOCMV.

Note

Warning: please use with care! Some of the functionality has not yet been thoroughly tested.

Author(s)

Philip Pallmann (<p.pallmann@lancaster.ac.uk>)

References


See Also
cset for (simultaneous) confidence regions and intervals around multivariate normal means.

Examples
## Not run:
# Simultaneous 90% confidence regions for the mean and variance or sd of univariate normal data
univar <- rnorm(n=50)
moodvar <- csetMV(dat=univar, method="mood", alpha=0.1, scale="var")
summary(moodvar)
plot(moodvar)
moodsd <- csetMV(dat=univar, method="mood", alpha=0.1, scale="sd")
summary(moodsd)
plot(moodsd)
## End(Not run)

Description
Generic functions for summarising and plotting objects of class JOC or JOCMV.

Usage
## S3 method for class 'JOC'
plot(x, equi=log(c(0.8, 1.25)), axnames=NULL, main=NULL, xlim=log(c(0.77, 1.3)), ylim=log(c(0.77, 1.3)), col="black", convexify=FALSE, ...)

## S3 method for class 'JOC'
print(x, digits=max(3,getOption("digits") - 4), ...)

## S3 method for class 'JOC'
summary(object, digits=max(3,getOption("digits") - 4), ...)

## S3 method for class 'JOCMV'
plot(x, axnames=NULL, main=NULL, xlim=NULL, ylim=NULL, col="black", ...)

## S3 method for class 'JOCMV'
print(x, digits=max(3,getOption("digits") - 4), ...)

## S3 method for class 'JOCMV'
summary(object, digits=max(3,getOption("digits") - 4), ...)
**Arguments**

- `x` An output object of class JOC or JOCMV.
- `object` An output object of class JOC or JOCMV.
- `digits` A numeric value giving the number of significant digits to be printed.
- `equi` A numeric vector of length 2 specifying the equivalence region (lower and upper equivalence threshold) to be shaded in grey. When set to NULL no equivalence region is drawn. Default is \( \log(c(0.8, 1.25)) \).
- `axnames` A vector of two character strings giving the x and y axis labels. For `plot.JOC`, when set to NULL the column names of `dat` are used as axis labels. Default is NULL.
- `main` A character string giving the plot title. Default is NULL.
- `xlim` A numeric vector of length two specifying the plotting range on the x-axis. Default is \( \log(c(0.77, 1.3)) \) for `plot.JOC` and NULL for `plot.JOCMV`.
- `ylim` A numeric vector of length two specifying the plotting range on the y-axis. Default is \( \log(c(0.77, 1.3)) \) for `plot.JOC` and NULL for `plot.JOCMV`.
- `col` A character string specifying the colour of the plotted region or intervals.
- `convexify` A logical specifying whether the convex hull around a non-convex region should be plotted instead of the region itself. Ignored unless method="limacon.fin" or method="limacon.asy" for the JOC object. Default is FALSE.
- ... Further plotting arguments to be passed to methods. Type ?plot for details.

**Details**

print and summary summarise the estimates and confidence set boundaries of an object of class JOC or JOCMV that was created with cset or csetMV, respectively. plot displays a (simultaneous) confidence region or intervals when applied to an object of class JOC or JOCMV.

**Value**

An on-screen summary or graphical display.

**Note**

Warning: please use with care! Some of the functionality has not yet been thoroughly tested.

**Author(s)**

Philip Pallmann (<p.pallmann@lancaster.ac.uk>)

**References**


**See Also**

cset and csetMV for computing (simultaneous) confidence regions and intervals.
Examples

## Not run:

# Example 1: simultaneous 90% confidence region for bivariate data

```r
bivar <- mvtnorm::rmvnorm(n=100, mean=rep(0.05, 2), sigma=diag(2) * 0.05)

hotelling <- cset(dat=bivar, method="hotelling", alpha=0.1)
summary(hotelling)
plot(hotelling, main="90% Hotelling Region")
```

# Example 2: simultaneous 90% confidence region for the mean and variance of univariate normal data

```r
univar <- rnorm(n=50)

moodvar <- csetMV(dat=univar, method="mood", alpha=0.1, scale="var")
summary(moodvar)
plot(moodvar, main="90% Mood Region")
```

## End(Not run)

---

**iutsize**

Size of intersection union tests derived from confidence sets

Description

Computes the actual size of a intersection union test procedure that corresponds to a (1 – alpha) confidence set.

Usage

```r
iutsize(p, n, alpha=0.1, sim=1e6)
```

Arguments

- `p`: An integer giving the number of dimensions.
- `n`: An integer giving the sample size.
- `alpha`: A numeric value specifying the type I error level to be controlled. Default is 0.1.
- `sim`: An integer giving the number of simulations to be carried out. Default is 1 million.

Details

A (1 – alpha) confidence set can be used to derive a two one-sided tests (TOST) procedure (Schuirmann 1987) whereby type I error rate control is ensured at level alpha due to the intersection union principle (Berger 1982). The actual test size, however, is often substantially lower than alpha i.e., the approach is conservative. It is well known for the one-dimensional case that the TOST corresponding to a (1 – alpha) confidence interval has size (1 – alpha/2). This function computes the achieved test size with dimension p and n according to the formula on p. 399 of Wang et al (1999).
Value

A numeric value giving the actual size of the test.

Author(s)

Philip Pallmann (<p.pallmann@lancaster.ac.uk>)

References


Examples

# For p=1 we get the well-known result that the 90% CI corresponds to the TOST at 5%:

iutsize(p=1, n=20)

# With increasing dimension the test gets conservative:

iutsize(p=2, n=20)
iutsize(p=3, n=20)

# For p>1 the conservativeness also depends on sample size:

iutsize(p=2, n=10)
iutsize(p=2, n=1000)

---

Bioequivalence study of ticlopidine hydrochloride

Description

Pharmacokinetic data from a study on the bioequivalence of a test and a reference formulation of ticlopidine hydrochloride in 24 healthy male volunteers, using a randomised crossover design (Marzo et al. 2002).

Usage

data("marzo")
**Format**

A data frame with 24 observations on the following 8 variables.

- **Volunteer** A numeric vector giving the volunteer ID.
- **Sequence** A factor with levels `RT` and `TR` specifying the sequence a volunteer was randomised to (R=reference, T=test).
- **Cmax_T** A numeric vector of the maximum concentration (Cmax) with the test product.
- **Cmax_R** A numeric vector of the maximum concentration (Cmax) with the reference product.
- **AUC_T** A numeric vector of the area under the concentration-time curve (AUC) from zero to the last observed time point with the test product.
- **AUC_R** A numeric vector of the area under the concentration-time curve (AUC) from zero to the last observed time point with the reference product.
- **AUCinf_T** A numeric vector of the area under the concentration-time curve (AUC) from zero to infinity with the test product.
- **AUCinf_R** A numeric vector of the area under the concentration-time curve (AUC) from zero to infinity with the reference product.

**Details**

The pharmacokinetic parameters (Cmax and AUC) were calculated using a non-compartmental approach. The data were taken from Tables I and II of Marzo et al. (2002).

**Source**


**References**


**Examples**

data(marzo)

```r
## An example analysis of Cmax assuming log-normality

diff <- log(marzo$Cmax_T) - log(marzo$Cmax_R)

mean(diff) / sqrt(nrow(marzo))

t.test(x=diff, alternative="less", mu=log(1.25))$p.value
```
translate

Conversion of confidence levels between intervals and ellipses

Description

Translates the confidence level of a joint 100(1 – alpha)% confidence ellipse into that of the corresponding marginal confidence interval when projecting the ellipse’s boundary onto the axes. Also does the "inverse operation" i.e., calculates the confidence level of a joint confidence ellipse so that its perpendicular shadows onto the axes are 100(1 – alpha)% confidence intervals.

Usage

translate(level=0.95, ddf, direction)

Arguments

level A numeric value giving the confidence level.
ddf An integer specifying the denominator degrees of freedom. Setting this to 0 enforces an asymptotic computation.
direction A character string indicating what is to be computed. Choose either ci2cr or cr2ci (see details).

Details

Setting direction="ci2cr" calculates the confidence level of a confidence interval generating ellipse (CIGE) whose perpendicular shadows onto the axes are 100(1 – alpha)% confidence intervals with a marginal confidence level (1 – alpha) as specified in level; see p. 205 of Fox (2008).

On the other hand, setting direction="cr2ci" computes the marginal confidence level of the intervals obtained by projecting a joint 100(1 – alpha)% confidence ellipse with (1 – alpha) as specified in level; see p. 254 of Monette (1990). These marginal intervals can be viewed as including a Scheffe penalty (Scheffe 1953).

For ddf=0 the F-distribution used for calculating the confidence levels is replaced with an asymptotic chi-square distribution.

Value

A numeric value giving the calculated confidence level.

Author(s)

Philip Pallmann (<p.pallmann@lancaster.ac.uk>)

t.test(x=marzo$deltalogCmax, alternative="greater", mu=log(0.80))$p.value

# 90% TOST confidence interval
t.test(x=marzo$deltalogCmax, conf.level=0.9)$conf.int[1:2]
References


Examples

# Get CIGE level
translate(0.95, ddf=1, "ci2cr")
translate(0.95, ddf=9999, "ci2cr")
translate(0.95, ddf=0, "ci2cr")

# Get Scheffe CI level
translate(0.95, ddf=1, "cr2ci")
translate(0.95, ddf=9999, "cr2ci")
translate(0.95, ddf=0, "cr2ci")

<table>
<thead>
<tr>
<th>wires</th>
<th>Quality control study of wire connections</th>
</tr>
</thead>
</table>

Description

Data from a study in quality control assessing the breaking strengths of 20 wire connections between a semiconductor wafer and a terminal post (King 1971).

Usage

data("wires")

Format

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

Strength  A numeric vector giving the strength at which the connection failed.

Failure  A factor with levels b and w specifying whether the bond or wire failed.

Details

The data were taken from Table 4.1 of Nelson (1982).

Source

References


Examples

```r
## Not run:
data(wires)

# Simultaneous 90% confidence regions for the mean and variance
plot(csetMV(wires$Strength, method="mood"), main="Mood")
plot(csetMV(wires$Strength, method="lrt"), main="LRT")

## End(Not run)
```
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