

Package ‘maxstat’

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Title Maximally Selected Rank Statistics

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Author Torsten Hothorn

Maintainer Torsten Hothorn <Torsten.Hothorn@R-project.org>

Description Maximally selected rank statistics with several p-value approximations.

Depends R (>= 1.7.0), exactRankTests(>= 0.8-0), mvtnorm(>= 0.5-10),survival

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R topics documented:

corrmsrs	2
DLBCL	3
hohnloser	6
maxstat.test	8
pexactgauss	11
pLausen92	12
pLausen94	13
plot.maxtest	14
pmaxstat	15
sphase	16
treepipit	17

Index	19
--------------	-----------

`corrmsrs`*Correlation Matrix*

Description

Correlation matrix of maximally selected rank statistics.

Usage

```
corrmsrs(X, minprop=0.1, maxprop=0.9)
```

Arguments

<code>X</code>	the vector, matrix or data.frame of prognostic factors under test.
<code>minprop</code>	at least <code>minprop*100%</code> of the observations in the first group.
<code>maxprop</code>	not more than <code>minprop*100%</code> of the observations in the first group.

Details

The correlations between all two-sample rank statistics induced by all possible cutpoints in `X` are computed.

Value

The correlation matrix with dimension depending on ties in `X` is returned.

Author(s)

Torsten Hothorn <Torsten.Hothorn@rzmail.uni-erlangen.de>

References

Hothorn, T. and Lausen, B. (2003). On the Exact Distribution of Maximally Selected Rank Statistics. *Computational Statistics & Data Analysis*, **43**, 121–137.

Lausen, B., Hothorn, T., Bretz, F. and Schmacher, M. (2002). Assessment of Optimally Selected Prognostic Factors. *submitted*. Preprint available from <http://www.mathpreprints.com/math/Preprint/blausen/20021007/1/>

Examples

```
# matrix of hypothetical prognostic factors
X <- matrix(rnorm(30), ncol=3)
# this function
print(system.time(a <- corrmsrs(X, minprop=0, maxprop=0.999)))
```

```

# coded by just typing the definition of the correlation

testcorr <- function(X) {
  wh <- function(cut, x)
    which(x <= cut)
  index <- function(x) {
    ux <- unique(x)
    ux <- ux[ux < max(ux)]
    lapply(ux, wh, x = x)
  }
  a <- unlist(test <- apply(X, 2, index), recursive=FALSE)
  cnull <- rep(0, nrow(X))
  mycorr <- diag(length(a))
  for (i in 1:(length(a)-1)) {
    for (j in (i+1):length(a)) {
      cone <- cnull
      cone[a[[i]]] <- 1
      ctwo <- cnull
      ctwo[a[[j]]] <- 1
      sone <- sqrt(sum((cone - mean(cone))^2))
      stwo <- sqrt(sum((ctwo - mean(ctwo))^2))
      tcorr <- sum((cone - mean(cone))*(ctwo - mean(ctwo)))
      tcorr <- tcorr/(sone * stwo)
      mycorr[i,j] <- tcorr
    }
  }
  mycorr
}

print(system.time(tc <- testcorr(X)))
tc <- tc + t(tc)
diag(tc) <- 1
stopifnot(all.equal(tc, a))

```

DLBCL

Diffuse large B-cell lymphoma

Description

A data frame with gene expression data from DLBCL (diffuse large B-cell lymphoma) patients.

Usage

```
data(DLBCL)
```

Format

DLCLid DLBCL identifier
 GEG Gene Expression Group
 time survival time in month
 cens censoring: 0 censored, 1 dead
 IPI International Prognostic Index
 MGE Mean Gene Expression

Source

Except of MGE, the data is published at <http://llmpp.nih.gov/lymphoma/data.shtml>. MGE is the mean of the gene expression.

References

Ash A. Alizadeh et. al (2000), Distinct types of diffuse large B-cell lymphoma identified by gene expression profiling. *Nature*, **403**, 504–509

Examples

```
data(DLBCL)

# compute the cutpoint and plot the empirical process

mod <- maxstat.test(Surv(time, cens) ~ MGE, data=DLBCL, smethod="LogRank")

print(mod)

## Not run:
# postscript("statDLBCL.ps", horizontal=F, width=8, height=8)
# pdf("statDLBCL.pdf", width=8, height=8)

## End(Not run)
par(mai=c(1.0196235, 1.0196235, 0.8196973, 0.4198450))
plot(mod, cex.lab=1.6, cex.axis=1.6, xlab="Mean gene expression", lwd=2)
## Not run:
# dev.off()

## End(Not run)

# significance of the cutpoint
# limiting distribution

maxstat.test(Surv(time, cens) ~ MGE, data=DLBCL,
             smethod="LogRank", pmethod="Lau92", iscores=TRUE)

# improved Bonferroni inequality, plot with significance bound

maxstat.test(Surv(time, cens) ~ MGE, data=DLBCL,
```

```

smethod="LogRank", pmethod="Lau94", iscores=TRUE)

mod <- maxstat.test(Surv(time, cens) ~ MGE, data=DLBCL, smethod="LogRank",
                  pmethod="Lau94", alpha=0.05)
plot(mod, xlab="Mean gene expression")

## Not run:
# postscript(file="RNewsStat.ps",horizontal=F, width=8, height=8)
# pdf("RNewsStat.pdf", width=8, height=8)

## End(Not run)
par(mai=c(1.0196235, 1.0196235, 0.8196973, 0.4198450))
plot(mod, xlab="Mean gene expression", cex.lab=1.6, cex.axis=1.6)
## Not run:
dev.off()

## End(Not run)

# small sample solution Hothorn & Lausen

maxstat.test(Surv(time, cens) ~ MGE, data=DLBCL,
             smethod="LogRank", pmethod="HL")

# normal approximation

maxstat.test(Surv(time, cens) ~ MGE, data=DLBCL,
             smethod="LogRank", pmethod="exactGauss", iscores=TRUE,
             abseps=0.01)

# conditional Monte-Carlo

maxstat.test(Surv(time, cens) ~ MGE, data=DLBCL,
             smethod="LogRank", pmethod="condMC", B = 9999)

# survival analysis and plotting like in Alizadeh et al. (2000)
if(require(survival, quietly = TRUE)) {

  splitGEG <- rep(1, nrow(DLBCL))
  DLBCL <- cbind(DLBCL, splitGEG)
  DLBCL$splitGEG[DLBCL$GEG == "Activated B-like"] <- 0

  plot(survfit(Surv(time, cens) ~ splitGEG, data=DLBCL),
       xlab="Survival time in month", ylab="Probability")

  text(90, 0.7, "GC B-like")
  text(60, 0.3, "Activated B-like")

  splitIPI <- rep(1, nrow(DLBCL))
  DLBCL <- cbind(DLBCL, splitIPI)
  DLBCL$splitIPI[DLBCL$IPI <= 2] <- 0

```

```

plot(survfit(Surv(time, cens) ~ splitIPI, data=DLBCL),
     xlab="Survival time in month", ylab="Probability")

text(90, 0.7, "Low clinical risk")
text(60, 0.25, "High clinical risk")

# survival analysis using the cutpoint

splitMGE <- rep(1, nrow(DLBCL))
DLBCL <- cbind(DLBCL, splitMGE)
DLBCL$splitMGE[DLBCL$MGE <= mod$estimate] <- 0

## Not run:
# postscript("survDLBCL.ps",horizontal=F, width=8, height=8)
pdf("survDLBCL.pdf", width=8, height=8)

## End(Not run)
par(mai=c(1.0196235, 1.0196235, 0.8196973, 0.4198450))

plot(survfit(Surv(time, cens) ~ splitMGE, data=DLBCL),
     xlab = "Survival time in month",
     ylab="Probability", cex.lab=1.6, cex.axis=1.6, lwd=2)

text(90, 0.9, expression("Mean gene expression" > 0.186), cex=1.6)
text(90, 0.45, expression("Mean gene expression" <= 0.186 ), cex=1.6)

## Not run:
dev.off()

## End(Not run)
}

```

hohnloser

Left ventricular ejection fraction of patients with malignant ventricular tachyarrhythmias.

Description

A data frame with the left ventricular ejection fraction of patients with malignant ventricular tachyarrhythmias including recurrence-free month and censoring.

Usage

```
data(hohnloser)
```

Format

EF left ventricular ejection in percent

month recurrence-free month

cens censoring: 0 censored, 1 not censored

The data used here is published in Table 1 of Lausen and Schumacher (1992).

Source

The data was first published by Hohnloser et al. (1987), the data used here is published in Table 1 of Lausen and Schumacher (1992).

References

Hohnloser, S.H., Raeder, E.A., Podrid, P.J., Graboys, T.B. and Lown, B. (1987), Predictors of antiarrhythmic drug efficacy in patients with malignant ventricular tachyarrhythmias. *American Heart Journal* **114**, 1–7

Lausen, B. and Schumacher, M. (1992), Maximally Selected Rank Statistics. *Biometrics* **48**, 73–85

Examples

```
data(hohnloser)

# limiting distribution

maxstat.test(Surv(month, cens) ~ EF, data=hohnloser,
smethod="LogRank", pmethod="Lau92")

# with integer valued scores for comparison

maxstat.test(Surv(month, cens) ~ EF, data=hohnloser,
smethod="LogRank", pmethod="Lau92", iscores=TRUE)

# improved Bonferroni inequality

maxstat.test(Surv(month, cens) ~ EF, data=hohnloser,
smethod="LogRank", pmethod="Lau94")

maxstat.test(Surv(month, cens) ~ EF, data=hohnloser,
smethod="LogRank", pmethod="Lau94", iscores=TRUE)

# small sample solution by Hothorn & Lausen

maxstat.test(Surv(month, cens) ~ EF, data=hohnloser,
smethod="LogRank", pmethod="HL")

# normal approximation

maxstat.test(Surv(month, cens) ~ EF, data=hohnloser,
```

```

smethod="LogRank", pmethod="exactGauss")

maxstat.test(Surv(month, cens) ~ EF, data=hohnloser,
smethod="LogRank", pmethod="exactGauss", iscores=TRUE)

# conditional Monte-Carlo

maxstat.test(Surv(month, cens) ~ EF, data=hohnloser,
smethod="LogRank", pmethod="condMC", B = 9999)

```

maxstat.test

Maximally Selected Rank and Statistics

Description

Performs a test of independence of a response and one or more covariables using maximally selected rank statistics.

Usage

```

## S3 method for class 'data.frame'
maxstat.test(formula, data, subset, na.action, ...)
maxstat(y, x=NULL, weights = NULL, smethod=c("Wilcoxon", "Median",
      "NormalQuantil", "LogRank", "Data"), pmethod=c("none", "Lau92",
      "Lau94", "exactGauss", "HL", "condMC", "min"), iscores=(pmethod=="HL"),
      minprop = 0.1, maxprop=0.9, alpha = NULL, keepxy=TRUE, ...)

```

Arguments

y	numeric vector of data values, dependent variable.
x	numeric vector of data values, independent variable.
weights	an optional numeric vector of non-negative weights, summing to the number of observations.
smethod	kind of statistic to be computed, i.e. defines the scores to be used for computing the statistic.
pmethod	kind of p-value approximation to be used.
iscores	logical: should the scores be mapped into integers 1:length(x)? This is TRUE by default for pmethod=="HL" and FALSE otherwise.
minprop	at least minprop*100% of the observations in the first group.
maxprop	not more than minprop*100% of the observations in the first group.
alpha	significance niveau, the appropriate quantile is computed if alpha is specified. Used for plotting within <code>plot.maxtest</code> .
keepxy	logical: return y and x as elements of the maxtest object.

formula	a formula describing the model to be tested of the form $lhs \sim rhs$ where lhs is the response variable. For survival problems, i.e. using the log-rank statistic, the formula is of the form $Surv(time, event) \sim rhs$, see above.
data	an data frame containing the variables in the model formula. data is required.
subset	an optional vector specifying a subset of observations to be used.
na.action	a function which indicates what should happen when the data contain NAs. Defaults to <code>getOption("na.action")</code> .
...	additional parameters to be passed to <code>pmvnorm</code> or <code>B</code> , an integer defining the number of Monte-Carlo replications.

Details

The assessment of the predictive power of a variable x for a dependent variable y can be determined by a maximally selected rank statistic.

`smethod` determines the kind of statistic to be used. `Wilcoxon` and `Median` denote maximally selected Wilcoxon and Median statistics. `NormalQuantile` and `LogRank` denote v.d. Waerden and log-rank scores.

`pmethod` specifies which kind of approximation of the p-value should be used. `Lau92` is the limiting distribution by a Brownian bridge (see Lausen and Schumacher, 1992, and [pLausen92](#)), `Lau94` the approximation based on an improved Bonferroni inequality (see Lausen, Sauerbrei and Schumacher, 1994, and [pLausen94](#)).

`exactGauss` returns the exact p-value for a maximally selected Gauss statistic, see Hothorn and Lausen (2003).

`HL` is a small sample approximation based on the Streitberg-Röhmel algorithm (see [pperm](#)) introduced by Hothorn and Lausen (2003). This requires integer valued scores. For v. d. Waerden and Log-rank scores we try to find integer valued scores having the same shape. This results in slightly different scores (and a different test), the procedure is described in Hothorn (2001) and Hothorn and Lausen (2003).

All the approximations are known to be conservative, so `min` gives the minimum p-value of all procedures.

`condMC` simulates the distribution via conditional Monte-Carlo.

For survival problems, i.e. using a maximally selected log-rank statistic, the interface is similar to [survfit](#). The depended variable is a survival object `Surv(time, event)`. The argument `event` may be a numeric vector of 0 (alive) and 1 (dead) or a vector of logicals with `TRUE` indicating death.

If more than one covariable is specified in the right hand side of `formula` (or if x is a matrix or data frame), the variable with smallest p-value is selected and the p-value for the global test problem of independence of y and every variable on the right hand side is returned (see Lausen et al., 2002).

Value

An object of class `maxtest` or `mmaxtest` (if more than one covariable was specified) containing the following components is returned:

<code>statistic</code>	the value of the test statistic.
<code>p.value</code>	the p-value for the test.

smethod	the type of test applied.
pmethod	the type of p-value approximation applied.
estimate	the estimated cutpoint (of x) which separates y best.
maxstats	a list of maxtest objects, one for each covariable.
whichmin	an integer specifying the element of maxstats with smallest p-value.
p.value	the p-value of the global test.
univp.values	the p-values for each of the variables under test.
cm	the correlation matrix the p-value is based on.

`plot.maxtest` and `print.maxtest` can be used for plotting and printing. If `keepxy = TRUE`, there are elements `y` and `x` giving the response and independent variable.

References

- Hothorn, T. and Lausen, B. (2003). On the Exact Distribution of Maximally Selected Rank Statistics. *Computational Statistics & Data Analysis*, **43**, 121–137.
- Lausen, B. and Schumacher, M. (1992). Maximally Selected Rank Statistics. *Biometrics*, **48**, 73–85
- Lausen, B., Sauerbrei, W. and Schumacher, M. (1994). Classification and Regression Trees (CART) used for the exploration of prognostic factors measured on different scales. in: P. Dirschedl and R. Ostermann (Eds), *Computational Statistics*, Heidelberg, Physica-Verlag, 483–496
- Hothorn, T. (2001). On Exact Rank Tests in R. *R News*, **1**, 11–12
- Lausen, B., Hothorn, T., Bretz, F. and Schmacher, M. (2002). Assessment of Optimally Selected Prognostic Factors. *submitted*. Preprint available from <http://www.mathpreprints.com/math/Preprint/blausen/20021007/1/>

Examples

```
x <- sort(runif(20))
y <- c(rnorm(10), rnorm(10, 2))
mydata <- data.frame(cbind(x,y))

mod <- maxstat.test(y ~ x, data=mydata, smethod="Wilcoxon", pmethod="HL",
                    minprop=0.25, maxprop=0.75, alpha=0.05)

print(mod)
plot(mod)

# adjusted for more than one prognostic factor.

data(DLBCL)

mstat <- maxstat.test(Surv(time, cens) ~ IPI + MGE, data=DLBCL,
                      smethod="LogRank", pmethod="exactGauss",
                      abseps=0.01)

plot(mstat)
```

Description

Computes the exact probability that a maximally selected gauss statistic is greater or equal to b.

Usage

```
pexactgauss(b, x, minprop=0.1, maxprop=0.9, ...)  
qexactgauss(p, x, minprop=0.1, maxprop=0.9, ...)
```

Arguments

b	quantile.
p	probability.
x	the prognostic factor(s) under test.
minprop	at least minprop*100% of the observations in the first group.
maxprop	not more than minprop*100% of the observations in the first group.
...	additional parameters to be passed to pmvnorm .

Details

This is the exact distribution of a maximally selected Gauss statistic and the asymptotic distribution for maximally selected rank statistics. Normal probabilities are derived from the procedures by Genz/Bretz (see [pmvnorm](#) for details).

Value

The probability that, under the hypothesis of independence, a maximally selected gauss statistic greater equal b is observed.

References

- Genz, A. (1992). Numerical computation of multivariate normal probabilities. *Journal of Computational and Graphical Statistics*, **1**, 141–150
- Genz, A. (1993). Comparison of methods for the computation of multivariate normal probabilities. *Computing Science and Statistics*, **25**, 400–405

Examples

```
x <- rnorm(20)  
  
pexact <- pexactgauss(2.5, x, abseps=0.01)
```

pLausen92

*Approximating Maximally Selected Statistics***Description**

Approximates the probability that a maximally selected rank statistic is greater or equal to b .

Usage

```
pLausen92(b, minprop=0.1, maxprop=0.9)
qLausen92(p, minprop=0.1, maxprop=0.9)
```

Arguments

<code>b</code>	quantile.
<code>p</code>	probability.
<code>minprop</code>	at least <code>minprop*100%</code> of the observations in the first group.
<code>maxprop</code>	not more than <code>minprop*100%</code> of the observations in the first group.

Details

Large sample approximation by Miller and Siegmund (1982) based on a Brownian bridge, cf. Lausen and Schumacher (1992).

Value

The probability that, under the hypothesis of independence, a maximally selected statistic greater equal b is observed.

References

Miller, R. and Siegmund, D. (1982), Maximally Selected Chi Square Statistics. *Biometrics*, **38**, 1011–1016

Lausen, B. and Schumacher, M. (1992), Maximally Selected Rank Statistics. *Biometrics*, **48**, 73–85

Examples

```
# Compute quantiles. Should be equal to Table 2 in Lausen and Schumacher

load(file.path(system.file(package = "maxstat"), "results", "LausenTab2.rda"))

a <- rev(c(0.01, 0.025, 0.05, 0.1))
prop <- rbind(c(0.25, 0.75), c(0.4, 0.6), c(0.1, 0.9), c(0.4, 0.9))
Quant <- matrix(rep(0, length(a)*nrow(prop)), nrow=length(a))

for (i in 1:length(a)) {
```

```

    for (j in 1:nrow(prop)) {
      Quant[i,j] <- qLausen92(a[i], minprop=prop[j,1], maxprop=prop[j,2])
    }
  }

Quant <- round(Quant, 3)
rownames(Quant) <- a
colnames(Quant) <- c("A2575", "A46", "A19", "A49")
Quant <- as.data.frame(Quant)
rownames(LausenTab2) <- a

Quant

LausenTab2

if(!all.equal(LausenTab2, Quant)) stop("error checking pLausen92")

```

pLausen94

Approximating Maximally Selected Statistics

Description

Approximates the probability that a maximally selected rank statistic is greater or equal to b.

Usage

```

pLausen94(b, N, minprop=0.1, maxprop=0.9, m=NULL)
qLausen94(p, N, minprop=0.1, maxprop=0.9, m=NULL)

```

Arguments

b	quantile.
p	probability.
N	number of observations.
minprop	at least minprop*100% of the observations in the first group.
maxprop	not more than minprop*100% of the observations in the first group.
m	a integer vector containing the sample sizes in the first groups for each cutpoint considered. If is.null(m) a continuous predictor is assumed.

Details

Approximation based on an improved Bonferroni inequality.

Value

The probability that, under the hypothesis of independence, a maximally selected statistic greater equal b is observed.

References

- Worsley, K.J. (1982), An Improved Bonferroni Inequality and Applications. *Biometrika*, **69**, 297–302
- Lausen, B. (1990), Maximal Selektierte Rangstatistiken. Dissertation. Universität Dortmund
- Lausen, B., Sauerbrei, W. & Schumacher, M. (1994). Classification and Regression Trees (CART) used for the exploration of prognostic factors measured on different scales. in: P. Dirschedl & R. Ostermann (Eds), *Computational Statistics*, Heidelberg, Physica-Verlag, 483–496

Examples

```
p <- pLausen94(2.5, 20, 0.25, 0.75)

# Lausen 94, page 489

if (round(p, 3) != 0.073) stop("error checking pLausen94")

# the same

p2 <- pLausen94(2.5, 200, 0.25, 0.75, m=seq(from=50, to=150, by=10))

stopifnot(all.equal(round(p,3), round(p2,3)))
```

plot.maxtest

Print and Plot Standardized Statistics

Description

Printing and plotting method of objects of class maxtest

Usage

```
## S3 method for class 'maxtest'
plot(x, xlab=NULL, ylab=NULL, ...)
## S3 method for class 'maxtest'
print(x, digits = 4, ...)
## S3 method for class 'mmaxtest'
plot(x, xlab=NULL, ylab=NULL, nrow=2, ...)
## S3 method for class 'mmaxtest'
print(x, digits = 4, ...)
```

Arguments

x	an object of class maxtest or mmaxtest.
xlab	label of x-axis.
ylab	label of y-axis.

nrow number of rows for multiple plots at one page.
 digits number of significant digits to be printed.
 ... additional arguments to plot or print.htest.

Details

The standardized statistics are plotted. If alpha was given in `maxstat.test` the appropriate significance bound is plotted as a red line. `print.maxtest` is just a wrapper to `print.htest`.

Examples

```
x <- sort(runif(20))
y <- rbinom(20, 1, 0.5)
mydata <- data.frame(c(x,y))

mod <- maxstat.test(y ~ x, data=mydata, smethod="Median",
                   pmethod="HL", alpha=0.05)

print(mod)
plot(mod)
```

pmaxstat

Approximating Maximally Selected Statistics

Description

Approximates the probability that a maximally selected rank statistic is greater or equal to b.

Usage

```
pmaxstat(b, scores, msample, quant=FALSE)
qmaxstat(p, scores, msample)
```

Arguments

b quantile.
 p propability.
 scores integer valued scores assigned to the observations.
 msample all possible splitpoints.
 quant logical. Returns the results of SR instead of P-values. Only to be used in qmaxstat.

Details

Small sample approximation by Hothorn and Lausen (2003).

Value

An upper limit for the probability that, under the hypothesis of independence, a maximally selected statistic greater equal b is observed. `qmaxstat` needs optimization.

References

Hothorn, T. and Lausen, B. (2003). On the Exact Distribution of Maximally Selected Rank Statistics. *Computational Statistics & Data Analysis*, **43**, 121–137.

Examples

```
pmaxstat(2.5, 1:20, 5:15)
```

sphase

S-phase fraction of tumor cells

Description

S-phase fraction of tumor cells in breast cancer patients.

Usage

```
data(sphase)
```

Format

This data frame contains the following columns:

SPF S-phase fraction

RFS recurrence free survival

cens censoring indicator (1 event)

Details

The data have been used to address the question whether a simple cutpoint in S-phase fraction can be used to discriminate between patients with good and bad prognosis (for example in Hothorn & Lausen, 2003).

Source

J. Pfisterer, F. Kommoss, W. Sauerbrei, D. Menzel, M. Kiechle, E. Giese, M. Hilgarth & A. Pfeilerer (1995). DNA flow cytometry in node positive breast cancer: Prognostic value and correlation to morphological and clinical factors. *Analytical and Quantitative Cytology and Histology* **7**(6), 406–412.

References

Torsten Hothorn & Berthold Lausen (2003). On the Exact Distribution of Maximally Selected Rank Statistics. *Computational Statistics & Data Analysis* **43**, 121–137.

Examples

```
data(sphase)
maxstat.test(Surv(RFS, cens) ~ SPF, data=sphase, smethod="LogRank",
pmethod="Lau94")
maxstat.test(Surv(RFS, cens) ~ SPF, data=sphase, smethod="LogRank",
pmethod="Lau94", iscores=TRUE)
maxstat.test(Surv(RFS, cens) ~ SPF, data=sphase, smethod="LogRank",
pmethod="HL")
maxstat.test(Surv(RFS, cens) ~ SPF, data=sphase, smethod="LogRank",
pmethod="condMC", B = 9999)
plot(maxstat.test(Surv(RFS, cens) ~ SPF, data=sphase, smethod="LogRank"))
```

treepipit

Tree Pipit Data

Description

Counts of tree pipits at 86 raster points in oak forests.

Usage

```
data(treepipit)
```

Format

A data frame with 86 observations on the following 2 variables.

counts number of tree pipits counted.

coverstorey canopy overstorey in percent.

Details

The influence of canopy overstorey on the number of bird individuals is of special interest.

Source

Data collected and kindly provided by Joerg Mueller <mue@lwf.uni-muenchen.de>.

References

Mueller J. and Hothorn T. (2003), On the Identification and Assessment of Habitat Patterns with Impact in Breeding Bird Communities in Oak Forests. *submitted manuscript*.

Index

*Topic **datasets**

DLBCL, 3
hohnloser, 6
sphase, 16
treepipit, 17

*Topic **distribution**

pexactgauss, 11
pLausen92, 12
pLausen94, 13
pmaxstat, 15

*Topic **htest**

maxstat.test, 8
plot.maxtest, 14

*Topic **misc**

corrmsrs, 2

corrmsrs, 2

DLBCL, 3

hohnloser, 6

maxstat (maxstat.test), 8

maxstat.test, 8, 15

pexactgauss, 11

pLausen92, 9, 12

pLausen94, 9, 13

plot.maxtest, 8, 10, 14

plot.mmaxtest (plot.maxtest), 14

pmaxstat, 15

pmvnorm, 9, 11

pperm, 9

print.maxtest, 10

print.maxtest (plot.maxtest), 14

print.mmaxtest (plot.maxtest), 14

qexactgauss (pexactgauss), 11

qLausen92 (pLausen92), 12

qLausen94 (pLausen94), 13

qmaxstat (pmaxstat), 15

sphase, 16

survfit, 9

treepipit, 17