Package 'LW1949'

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Title An Automated Approach to Evaluating Dose-Effect Experiments Following Litchfield and Wilcoxon (1949)

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Depends R (>= 3.1.0)

Imports mgcv

Description LW1949 takes the manual approach to evaluating dose-effect experiments (Litchfield and Wilcoxon 1949) and automates the steps so that the computer can do the work.

License GPL

LazyData TRUE

URL https://github.com/JVAdams/LW1949

R topics documented:

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assessfit   *Assess Fit of Dose Response Curve*

Description

Assess the fit of a dose response curve using the chi-squared statistic. The curve is described by two lethal concentrations, and is represented by a straight line in the log dose vs. probit effect scale.

Usage

```
assessfit(LCs, DEdata, fit, simple = TRUE)
```

Arguments

LCs   A numeric vector of estimated lethal concentrations on the log10 scale. The first element is the LC50%, the second is the LC99.9%. These two points define the dose response curve.

DEdata   A data frame of dose-effect data (typically, the output from `dataprep` containing at least these four variables: dose, ntot, pdead, mcateg.

fit   A model object that can be used to predict the corrected values (as proportions) from `distexpprop5`, the distance from the expected values (as proportions) and 0.5. Typically the output from `gamtable1()`.

simple   A logical scalar indicating if the output should be restricted just the P value, default TRUE.

Details

This function is used as part of a routine that attempts to find the dose response curve that maximizes the P value from the chi-squared statistic measuring the distance between the observed and expected values. Following Litchfield and Wilcoxon (1949, steps B1 and B2), records for any 0% or 100% dose with expected values < 0.01% or > 99.99% are deleted, and expected values are corrected using the `correctval` function.

Value

If `simple=FALSE`, a vector of length three: chistat, a numeric scalar, the chi-squared statistic; pval, a numeric scalar, its associated P value; and df, an integer, the degrees of freedom of `chistat`. If `simple=TRUE`, a numeric scalar, the P value of the chi-squared statistic (see details).

References

J. T. Litchfield, Jr. and F. Wilcoxon. 1949. A simplified method of evaluating dose-effect experiments[1]. Journal of Pharmacology and Experimental Therapeutics 99(2):99-113.

See Also

`chi2` and `chisq.test`.

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[1]http://jpet.aspetjournals.org/content/96/2/99.short

Examples

```
conc <- c(0.0625, 0.125, 0.25, 0.5, 1)
numtested <- rep(8, 5)
nmort <- c(1, 4, 4, 7, 8)
mydat <- dataprep(dose=conc, ntot=numtested, ndead=nmort)
gamfit <- gamtable1()
assessfit(log10(c(0.125, 0.5)), mydat, gamfit, simple=FALSE)
```

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chi2   *Chi-Squared Statistic*

Description

Calculate the chi-squared statistic from observed and expected counts.

Usage

```
chi2(obsn, expn)
```

Arguments

obsn   A numeric vector of observed counts.

expn   A numeric vector of expected counts.

Value

A numeric vector of length three: chistat, the chi-squared statistic; pval, its associated P value; and df, the degrees of freedom of `chistat`.

See Also

`chisq.test`.

Examples

```
chi2(c(10, 8, 3), c(7, 7, 7))
```

---

constrain   *Constrain Data to a Specified Range*

Description

Constrain data to a specified range, assigning values from the specified range to those outside the range, typically for graphing purposes.

Usage

```
constrain(x, xrange)
```

Arguments

x	A numeric vector of values to constrain.
xrange	A numeric vector of length two specifying the constraints, the minimum and maximum value for x.

Value

A numeric vector, the same length as x, in which the minimum constraint is assigned to values of x less than the minimum, and the maximum constraint is assigned to values of x greater than the maximum.

Examples

```
constrain(1:20, c(3, 19))
```

---

correctval	*Predict the corrected proportion using a model fit of Table 1 of Litchfield and Wilcoxon (1949)*

Description

Given an expected proportion, calculate the corrected proportion using a model fit of Table 1 of Litchfield and Wilcoxon (1949).

Usage

```
correctval(val, fit)
```

Arguments

val	A numeric vector of expected values (as proportions).
fit	A model object that can be used to predict the corrected values (as proportions) from distexpprop5, the distance from the expected values (as proportions) and 0.5. Typically the output from gamtable1().

Value

A numeric vector of corrected values (as proportions), the same length as val.

Examples

```
gamfit <- gamtable1()
correctval(c(0.37, 0.5, 0.63), gamfit)
```

---

dataprep *Prepare Data*

Description

Prepare dose-effect data for evaluation.

Usage

```
dataprep(dose, ntot, ndead)
```

Arguments

dose   A numeric vector of chemical concentrations.

ntot   A numeric vector of the number of individuals that were tested at each dose.

ndead   A numeric vector of the number of individuals that died at each dose.

Value

A data frame with eight columns (ordered by dose and pdead), seven numeric vectors and one logical vector: dose - chemical concentrations. ntot - the number of individuals that were tested at each dose. ndead - the number of individuals that died at each dose. pdead - the proportion of individuals that died at each dose. logdose - log transformed dose, `log10(dose)`. bitpdead - probit transformed proportional mortality, `probit(pdead)`. mcateg - mortality category: 0 for none dead, 100 for all dead, and 50 for any proportional mortality. LWkeep - logical vector identifying records to keep for Litchfield and Wilcoxon (1949, step A1) method.

References

Litchfield, JT Jr. and F Wilcoxon. 1949. A simplified method of evaluating dose-effect experiments[2]. Journal of Pharmacology and Experimental Therapeutics 99(2):99-113.

Examples

```
conc <- c(0.0625, 0.125, 0.25, 0.5, 1)
numtested <- rep(8, 5)
nmort <- c(1, 4, 4, 7, 8)
dataprep(dose=conc, ntot=numtested, ndead=nmort)
```

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[2]http://jpet.aspetjournals.org/content/96/2/99.abstract

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estimable   *Determine if Lethal Concentrations are Estimable*

Description

Determine if lethal concentrations are estimable based on available dose-effect data.

Usage

```
estimable(DEdata)
```

Arguments

DEdata   A data frame of dose-effect data (typically, the output from `dataprep` containing at least two variables: dose, a numeric vector of chemical concentrations, and pdead, a numeric vector of proportional mortality at each dose.

Details

Lethal concentrations are defined to be estimable (with error) if and only if there are at least three test records and there is some (non-zero) variability in both the doses and the proportional mortalities.

Value

A logical scalar indicating if lethal concentrations are estimable. If FALSE, a warning is generated.

Examples

```
conc <- c(0.0625, 0.125, 0.25, 0.5, 1)
numtested <- rep(8, 5)
nmort <- c(1, 4, 4, 7, 8)
mydat <- dataprep(dose=conc, ntot=numtested, ndead=nmort)
estimable(mydat)
nmort2 <- rep(4, 5)
mydat2 <- dataprep(dose=conc, ntot=numtested, ndead=nmort2)
estimable(mydat2)
```

---

fill   *Fill in Missing Values*

Description

Fill in missing values in a vector, using the last recorded value.

Usage

```
fill(x)
```

Arguments

x   A vector, can be character, numeric, or logical.

Details

Similar to `na.locf` in the `zoo` package, but works for "" in character vectors as well.

Value

A vector the same length as `x`, with all NAs or ""s replace by the last value for the vector. Note that and missing values at the beginning of the vector will not be replaced.

Examples

```
numvec <- c(NA, 1:5, NA, NA, NA, 10:12, NA)
fill(numvec)

charvec <- c("", letters[1:5], "", "", "", letters[10:12], "")
fill(charvec)
```

---

gamtable1   *Fit a smooth GAM to Table 1 of Litchfield and Wilcoxon (1949)*

Description

Fit a smooth GAM function to replace looking up values in Table 1 of Litchfield and Wilcoxon (1949).

Usage

```
gamtable1()
```

Details

Note that for an expected value of 37 Table 1 gives a corrected value of 9.4, but for an expected value of 63 it gives a corrected value of 90.5. To ensure that both values add to 100, I used corrected values of 9.45 and 90.55. The expected and corrected values from Table 1 are then used to build a GAM model, which is used as input to the `correctval` function.

Value

A `gamObject` that can be used to predict the corrected values (as proportions) from `distexpprop5`, the distance from the expected values (as proportions) and 0.5

Examples

```
fit <- gamtable1()
summary(fit)
plot(fit)
```

---

invprobit	*Convert Probit Scale to Proportions*

Description

Convert values on the probit scale to their proportions on the 0 to 1 scale.

Usage

```
invprobit(quan)
```

Arguments

quan   A numeric vector of probit quantiles.

Details

Simply calls `pnorm(quan)`.

Value

A numeric vector of proportions the same length as `quan`.

Examples

```
invprobit(c(-3, -1, 0, 1, 3))
```

---

keeponly	*Eliminate Consecutive Extreme Values*

Description

Generate the index for eliminating values beyond a given maximum number of consecutive extremes allowed.

Usage

```
keeponly(orderedx, extremes = c(0, 100), nconsec = 2)
```

Arguments

orderedx   A numeric vector.

extremes   A numeric vector of length two, boundary limits of numeric vector, default c(0, 100).

nconsec   An integer scalar, the maximum number of consecutive extreme values allowed, default 2.

Value

A logical vector for selecting all elements of `orderedx` without exceeding `nconsec` consecutive extreme values.

Examples

```
vec <- c(0, 0, 0, 4, 4, 4, 100, 100, 100, 100)
vec[keeponly(vec)]
```

LC	*Determine the Lethal Concentration*

Description

Determine the lethal concentration for a specified level of mortality.

Usage

```
LC(pct, b0, b1)
```

Arguments

pct   A numeric vector of mortalities (in percents) for which to estimate the lethal concentration.

b0   A numeric vector (more commonly a scalar) giving the intercept of the dose-response curve.

b1   A numeric vector (more commonly a scalar) giving the slope of the dose-response curve. x = dose (the concentration of the applied chemical on the log10 scale), and y, the proportion of dead individuals (on the probit scale, with 0s converted to 0.1% and 1s converted to 99.9%).

Value

A list with two elements: sv, a numeric vector of length two giving the starting values for the LC50% and LC99.9%, and p, a numeric scalar giving the P value of the associated chi-squared statistic.

Examples

```
LC(c(16, 50, 84, 99.9), 1.700875, 2.199559)
```

LW1949	*Automated Litchfield and Wilcoxon (1949) Evaluation of Dose-Effect Experiments*

Description

LW1949 is an automated approach to Litchfield and Wilcoxon's (1949) evaluation of dose-effect experiments. **LW1949** was first introduced by Adams et al. (*in preparation*).

Details

U.S. Geological Survey (USGS) Computer Program **LW1949** version 2014-10. Written by Jean V. Adams, USGS - Great Lakes Science Center[3], Ann Arbor, Michigan, USA. Written in programming language R (R Core Team, 2014, www.R-project.org), version 3.1.1 (2014-07-10). Run on a PC with Intel(R) Core(TM) I7-4600m CPU, 2.90 GHz processor, 16.0 GB RAM, and Microsoft Windows 7 Enterprise operating system 2009 Service Pack 1. Source code is available from Jean V. Adams on GitHub[4], <jvadams@usgs.gov>.

Disclaimer: Although this program has been used by the USGS, no warranty, expressed or implied, is made by the USGS or the United States Government as to the accuracy and functioning of the program and related program material nor shall the fact of distribution constitute any such warranty, and no responsibility is assumed by the USGS in connection therewith.

References

Adams, JV, KS Slaght, and MA Boogaard. *In preparation.* An automated approach to Litchfield and Wilcoxon's evaluation of dose-effect experiments.

Litchfield, JT Jr. and F Wilcoxon. 1949. A simplified method of evaluating dose-effect experiments[5]. Journal of Pharmacology and Experimental Therapeutics 99(2):99-113.

LWauto	*Apply Litchfield and Wilcoxon Evaluation of Dose-Effect Experiments*

Description

Automatically apply Litchfield and Wilcoxon's (1949) evaluation of dose-effect experiments.

Usage

```
LWauto(DEdata)
```

Arguments

DEdata   A data frame of dose-effect data (typically, the output from dataprep containing at eight variables: dose, ntot, ndead, pdead, logdose, bitpdead, mcateg, and LWkeep.

Value

A list of length three: chi = the chi-squared statistic with associated P value and degrees of freedom, params = the estimated LC50 and LC99.9 on the log10 scale used to describe the dose-response curve, LWest = the Litchfield Wilcoxon estimates of LC50 with 95 (LC16, LC84, S, and slope).

Examples

```
conc <- c(0.0625, 0.125, 0.25, 0.5, 1)
numtested <- rep(8, 5)
nmort <- c(1, 4, 4, 7, 8)
mydat <- dataprep(dose=conc, ntot=numtested, ndead=nmort)
LWauto(mydat)
```

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[3]http://www.glsc.usgs.gov/
[4]https://github.com/JVAdams/LW1949
[5]http://jpet.aspetjournals.org/content/96/2/99.abstract

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mcat *Define Mortality Category*

Description

Define three mortality categories, 0 for none dead, 100 for all dead, and 50 for anything in between, partial mortality.

Usage

```
mcat(dat)
```

Arguments

dat   A data frame of raw toxicity data, including these three variables: dose (the concentration of the applied chemical), ntot (the number of individuals tested), and ndead (the number of dead individuals).

Value

A numeric vector the same length as `prob` with quantiles on the probit scale.

Examples

```
test <- data.frame(
dose=c(0.0625, 0.125, 0.25, 0.5),
ntot=rep(8, 4),
ndead = c(0, 4, 6, 8))
cbind(test, mcat(test))
```

---

probit *Convert Proportions to the Probit Scale*

Description

Convert proportions to the probit scale.

Usage

```
probit(prob)
```

Arguments

prob   A numeric vector of proportions.

Details

Simply calls `qnorm(prob)`.

Value

A numeric vector the same length as `prob` with quantiles on the probit scale.

Examples

```
probit(c(0.001, 0.01, 0.1, 0.5, 0.9, 0.99, 0.999))
```

---

startvals   *Determine Starting Values for LC50% and LC99.9%*

Description

Determine starting values for the LC50% and LC99.9% (both on the log10 scale) using simple linear regression on the log10 dose vs. probit effect scale.

Usage

```
startvals(DEdata, fit, constr = c(0.0001, 0.9999))
```

Arguments

DEdata   A data frame of dose-effect data (typically, the output from `dataprep` containing eight variables: dose, ntot, ndead, pdead, logdose, bitpdead, mcateg, and LWkeep.

fit   A model object that can be used to predict the corrected values (as proportions) from `distexpprop5`, the distance from the expected values (as proportions) and 0.5. Typically the output from `gamtable1()`.

constr   A numeric vector of length two, indicating the constraints (see `constrain`) applied to the proportional mortalities, default c(0.0001, 0.9999).

Value

A list with two elements: sv, a numeric vector of length two giving the starting values for the LC50% and LC99.9%, and p, a numeric scalar giving the P value of the associated chi-squared statistic.

Examples

```
conc <- c(0.0625, 0.125, 0.25, 0.5, 1)
numtested <- rep(8, 5)
nmort <- c(1, 4, 4, 7, 8)
mydat <- dataprep(dose=conc, ntot=numtested, ndead=nmort)
gamfit <- gamtable1()
startvals(mydat, gamfit)
```