

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>

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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(params, DEdata, fit, simple = TRUE)
```

Arguments

params	A numeric vector of length two, with the estimated intercept and slope of the dose-effect relation on the log10 and probit scale. These parameters define the dose response curve.
DEdata	A data frame of dose-effect data (typically, the output from <code>dataprep</code> containing at least these four variables: dose, ntot, pfx, fxcateg).
fit	A model object that can be used to predict the corrected values (as proportions) from <code>distexpprop5</code> , the distance from the expected values (as proportions) and 0.5. Typically the output from <code>gamtable1()</code> .
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 minimizes the chi-squared statistic measuring the distance between the observed and expected values of the proportion affected. 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 list of length two. The first element, `chi`, is a numeric vector of length three: `chistat`, the chi-squared statistic; `df`, the degrees of freedom of `chistat`; and `pval`, their associated P value. The second element, `stepB`, is a matrix of three numeric vectors the same length as `obsn`, `exp`, expected effects; `expcorr`, expected effects corrected; and `contrib`, contributions to the chi-squared. If `simple=TRUE`, a numeric scalar, the chi-squared statistic (see details).

References

J. T. Litchfield, Jr. and F. Wilcoxon. 1949. A simplified method of evaluating dose-effect experiments¹. *Journal of Pharmacology and Experimental Therapeutics* 99(2):99-113.

See Also

`chi2` and `chisq.test`.

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)
nalive <- c(1, 4, 4, 7, 8)
mydat <- dataprep(dose=conc, ntot=numtested, nfx=nalive)
gamfit <- gamtable1()
assessfit(log10(c(0.125, 0.5)), mydat, gamfit, simple=FALSE)

```

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 list of length two. The first element is a numeric vector of length three: `chistat`, the chi-squared statistic; `df`, the degrees of freedom of `chistat`; and `pval`, their associated P value. The second element is a numeric vector the same length as `obsn`, contributions to the chi-squared.

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

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

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))
```

<code>correctval</code>	<i>Predict the corrected proportion using a model fit of Table 1 of Litchfield and Wilcoxon (1949)</i>
-------------------------	--

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

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

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, nfx)
```

Arguments

dose	A numeric vector of chemical concentrations.
ntot	A numeric vector of the number of individuals that were tested at each dose.
nfx	A numeric vector of the number of individuals that were affected at each dose.

Value

A data frame with eight columns (ordered by dose and proportion affected), seven numeric vectors and one logical vector: dose - chemical concentrations. ntot - the number of individuals that were tested at each dose. nfx - the number of individuals that were affected at each dose. pfx - the proportion of individuals that were affected at each dose. logdose - log transformed dose, `log10(dose)`. bitpfx - probit transformed proportional affected, `probit(pfx)`. fxcateg - effects category: 0 for none affected, 100 for all affected, and 50 for other proportions affected. 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 experiments². *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)
nalive <- c(1, 4, 4, 7, 8)
dataprep(dose=conc, ntot=numtested, nfx=nalive)
```

²<http://jpet.aspetjournals.org/content/96/2/99.abstract>

DEcoef	<i>Determine Linear Regression Coefficients from Dose-Effect Data</i>
--------	---

Description

Determine coefficients (intercept and slope) from dose-effect data using simple linear regression on the log10 dose vs. probit effect scale.

Usage

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

Arguments

DEdata	A data frame of dose-effect data (typically, the output from <code>dataprep</code> containing eight variables: <code>dose</code> , <code>ntot</code> , <code>nfx</code> , <code>pfx</code> , <code>logdose</code> , <code>bitpfx</code> , <code>fxcateg</code> , and <code>LWkeep</code>).
fit	A model object that can be used to predict the corrected values (as proportions) from <code>distexpprop5</code> , the distance from the expected values (as proportions) and 0.5. Typically the output from <code>gamtable1()</code> .
constr	A numeric vector of length two, indicating the constraints (see <code>constrain</code>) applied to the proportional effects, default <code>c(0.0001, 0.9999)</code> .

Value

A numeric vector of length two, the estimated intercept and slope.

Examples

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

estimable	<i>Determine if Lethal Concentrations are Estimable</i>
-----------	---

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 <code>dataprep</code> containing at least two variables: <code>dose</code> , a numeric vector of chemical concentrations, and <code>pfx</code> , a numeric vector of proportional effects 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 effects.

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)
nalive <- c(1, 4, 4, 7, 8)
mydat <- dataprep(dose=conc, ntot=numtested, nfx=nalive)
estimable(mydat)
nalive2 <- rep(4, 5)
mydat2 <- dataprep(dose=conc, ntot=numtested, nfx=nalive2)
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)
```

fxcat

*Define Effect Category***Description**

Define three effect categories, 0 for none affected, 100 for all affected, and 50 for other proportions affected.

Usage

```
fxcat(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 nfx (the number of affected 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),
  nfx = c(0, 4, 6, 8))
cbind(test, fxcat(test))
```

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(quant)
```

Arguments

`quant` A numeric vector of probit quantiles.

Details

Simply calls `pnorm(quant)`.

Value

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

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

<code>orderedx</code>	A numeric vector.
<code>extremes</code>	A numeric vector of length two, boundary limits of numeric vector, default <code>c(0, 100)</code> .
<code>nconsec</code>	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 percent effect.

Usage

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

Arguments

<code>pct</code>	A numeric vector of effects (in percents) for which to estimate the lethal concentration.
<code>b0</code>	A numeric vector (more commonly a scalar) giving the intercept of the dose-response curve.
<code>b1</code>	A numeric vector (more commonly a scalar) giving the slope of the dose-response curve. <code>x</code> = dose (the concentration of the applied chemical on the log10 scale), and <code>y</code> , the proportion of affected 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 Center³, 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 GitHub⁴, <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 experiments⁵. *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`, `nfx`, `pfx`, `logdose`, `bitpfx`, `fxcateg`, and `LWkeep`).

³<http://www.glsc.usgs.gov/>

⁴<https://github.com/JVAdams/LW1949>

⁵<http://jpet.aspetjournals.org/content/96/2/99.abstract>

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

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

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))
```