Package 'LW1949'

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Following Litchfield and Wilcoxon (1949)
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Depends R (>= $3.1.0$)
Imports mgcv, tcltk, MASS
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
IIRI https://github.com/JVAdams/IW1949

${\sf R}$ 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 the intercept and slope of 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 dataprep) 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 $\texttt{distexpprop5}$, the distance from the expected values (as proportions) and 0.5. Typically the output from $\texttt{gamtable1}$ ().
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 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).

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References

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

See Also

```
chi2 and chisq.test.
```

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.
```

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

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

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coefprobit

Calculate the Coefficients of a Probit Regression Fit

Description

Calculate the coefficients from a fitted probit regression model.

Usage

```
coefprobit (pfit)
```

Arguments

pfit

An object of class glm representing a probit regression fit to dose-effect data, typically the result of a call to fitprobit.

Value

A numeric vector of length three, the intercept and slope of the dose-response curve, each with 95% confidence limits.

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)
myfit <- fitprobit(mydat)
coefprobit(myfit)</pre>
```

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.

correctval 5

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 distemprop5, 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.

References

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

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

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

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.1	
data	prep

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.
- rec = the record number corresponding to the input vectors dose, ntot, nfx.
- pfx = the proportion of individuals that were affected at each dose.
- log10dose = 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 experiments. Journal of Pharmacology and Experimental Therapeutics 99(2):99-113. [link]³.

```
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)</pre>
```

³http://jpet.aspetjournals.org/content/96/2/99.abstract

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estimable

Determine if a Dose-Effect Relation is Estimable

Description

Determine if a dose-effect relation is estimable based on available 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 pfx, a numeric vector of proportional effects at each dose.

Details

A dose-effect relation is defined to be estimable if and only if there are at least two test records and there is some (non-zero) variability in both the doses and the proportional effects.

Value

A logical scalar indicating if a dose-effect relation is 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)</pre>
```

fill

Fill in Missing Values

Description

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

Usage

```
fill(x)
```

Arguments

Х

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

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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)</pre>
```

fitlinear

Determine Linear Regression Coefficients from Dose-Effect Data

Description

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

Usage

```
fitlinear (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, nfx, pfx, log10dose, bitpfx, fxcateg, and LWkeep.
fit	A model object that can be used to predict the corrected values (as proportions) from $\texttt{distexpprop5}$, the distance from the expected values (as proportions) and 0.5. Typically the output from $\texttt{gamtable1}()$.
constr	A numeric vector of length two, indicating the constraints (see constrain) applied to the proportional effects, default c(0.0001, 0.9999).

Value

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

```
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()
fitlinear(mydat, gamfit)</pre>
```

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fitLW

Apply Litchfield and Wilcoxon Evaluation of Dose-Effect Experiments

Description

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

Usage

```
fitLW(DEdata)
```

Arguments

DEdata

A data frame of dose-effect data (typically, the output from dataprep) containing at least eight variables: dose, ntot, nfx, pfx, log10dose, bitpfx, fxcateg, and LWkeep.

Value

A list of length three:

- chi = the chi-squared statistic with associated P value and degrees of freedom,
- params = the estimated intercept and slope of the dose-response curve on the log10 probit scale,
- LWest = the Litchfield Wilcoxon estimates of ED50 with 95% confidence intervals and other metrics used in their step-by-step approach (ED16, ED84, S, N', and fED50).

References

Litchfield, JT Jr. and F Wilcoxon. 1949. A simplified method of evaluating dose-effect experiments. Journal of Pharmacology and Experimental Therapeutics 99(2):99-113. [link]⁴.

```
dose <- c(0.0625, 0.125, 0.25, 0.5, 1)

ntested <- rep(8, 5)

nalive <- c(1, 4, 4, 7, 8)

mydat <- dataprep(dose=dose, ntot=ntested, nfx=nalive)

mydat

fitLW(mydat)
```

⁴http://jpet.aspetjournals.org/content/96/2/99.abstract

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fitprobit

Fit a Probit Regression to Dose-Effect Data

Description

Fit a probit regression to dose-effect data, using the log10 of the dose, the binomial family, and the probit link.

Usage

```
fitprobit (DEdata)
```

Arguments

DEdata

A data frame of dose-effect data (typically, the output from dataprep) containing eight variables: dose, ntot, nfx, pfx, log10dose, bitpfx, fxcateg, and LWkeep.

Value

A an object of class glm.

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)
fitprobit(mydat)</pre>
```

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.

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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))</pre>
```

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

References

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

```
fit <- gamtable1()
summary(fit)
plot(fit)</pre>
```

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

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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(x, extremes = c(0, 100), nconsec = 2)
```

Arguments

x 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.

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Examples

```
vec <- c(0, 0, 0, 4, 4, 4, 100, 100, 100, 100)
vec[keeponly(vec)]
# the original vector need not be ordered
vec <- c(100, 4, 100, 4, 0, 100, 0, 4, 0, 100)
vec[keeponly(vec)]</pre>
```

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

An example of how to use the functions in LW1949 is given in this vignette [link]⁶. Use dataprep to create a data frame with the results of a dose-effect experiment. Use fitLW and fitprobit to fit dose-effect relations. And use plotDE to plot the results.

U.S. Geological Survey (USGS) Computer Program **LW1949** version 2015-01. Written by Jean V. Adams, USGS - Great Lakes Science Center glsc.usgs.gov⁷, 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, github.com/JVAdams/LW1949⁸, *jvadams* (at) usgs (dot) 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. Journal of Pharmacology and Experimental Therapeutics 99(2):99-113. [link]⁹.

 $^{^6}$ https://github.com/JVAdams/LW1949/blob/master/Vignette.md

⁷http://www.glsc.usgs.gov/

⁸https://github.com/JVAdams/LW1949

⁹http://jpet.aspetjournals.org/content/96/2/99.abstract

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LWP	User Friendly Evaluation of Dose-Effect Experiments using Litchfield-
	Wilcoxon and Probit Methods

Description

User friendly evaluation of dose-effect experiments using automated Litchfield Wilcoxon (1949) and probit estimation methods. This function has been tailored for non-R users with input data set up in a particular way (see Details).

Usage

```
LWP(rawfile = NULL, descroolz = 4, saveplots = TRUE, showplots = FALSE, saveresults = TRUE, showresults = TRUE, returnresults = FALSE)
```

Arguments

rawfile	A character scalar specifying the path of the input data as a csv file. If NULL, default, the user will be prompted to browse to a file using a menu.						
descrcolz	A numeric scalar, the number of columns to use as the description of the test, from 1 to descreolz, default 4.						
saveplots	A logical scalar indicating if plots should be saved to a pdf file, default TRUE.						
showplots	A logical scalar indicating if plots should be shown on screen, default FALSE.						
saveresults	A logical scalar indicating if results should be saved to a csv file, default TRUE. The csv file is given the same name (plus the suffix "Smry") and is placed in the same directory as the input file.						
showresults	A logical scalar indicating if results should be printed to the console, default TRUE. These results include the chi-squared statistic, degrees of freedom, and p-value for the Litchfield Wilcoxon method.						
returnresult	returnresults						
	A logical scalar indicating if results should be returned by the function, default						

FALSE.

Details

The input data must include at least these seven columns, with these names in the header row:

- Test ID = A character or numeric vector, the unique identifier for each test
- Source = A character vector, the source of the chemical
- Batch = A character or numeric vector, the batch of the chemical
- Species = A character vector, the species tested
- TFM Conc. (mg/L) = A numeric vector, the concentration of TFM in mg/L
- No. Tested = A numeric vector, the number of animals tested
- No. Dead = A numeric vector, the number of animals dead

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Value

If returnresults=TRUE, a data frame with 11 rows per test and 2 more columns than the input data. Three columns from the input data are not included (TFM Conc. (mg/L), No. Tested, and No. Dead). Five columns are added: the parameter (param), the method used (method), the estimate (estimate), and the 95% confidence interval of the estimate (lower95ci and upper95ci)

References

Litchfield, JT Jr. and F Wilcoxon. 1949. A simplified method of evaluating dose-effect experiments. Journal of Pharmacology and Experimental Therapeutics 99(2):99-113. [link]¹⁰.

Examples

```
## Not run:
LWP()
## End(Not run)
```

plotDE

Plot Dose-Effect Experiments

Description

Plot the results of dose-effect experiments.

Usage

```
plotDE(DEdata, xlab = "Dose", ylab = "Affected (%)", ylim = c(0.1, 99.9), \ldots)
```

Arguments

DEdata	A data frame of dose-effect data (typically, the output from dataprep) containing at least five variables: dose, pfx, log10dose, bitpfx, fxcateg.
xlab	A character scalar, the title for the dose (x) axis, default "Dose".
ylab	A character scalar, the title for the affects (y) axis, default "Affected (%)".
ylim	A numeric vector of length two giving the y coordinate range for affects (%), default c(0.1, 99.9). Observed effects beyond this range will be plotted at the limits of this range using an open symbol.
	Additional arguments to plot.

 $^{^{10} \}texttt{http://jpet.aspetjournals.org/content/96/2/99.abstract}$

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Examples

```
dose <- c(0.0625, 0.125, 0.25, 0.5, 1)
ntested <- rep(8, 5)
nalive <- c(1, 4, 4, 7, 8)
mydat <- dataprep(dose=dose, ntot=ntested, nfx=nalive)
# just plot the raw data
plotDE(mydat)
# plot the raw data and some fitted lines
fLW <- fitLW(mydat)
fp <- fitprobit(mydat)
plotDE(mydat)
abline(fp$coef, lty=2)
abline(fLW$params)
legend("topleft", c("Litchfield-Wilcoxon", "Probit"), lty=c(1, 2), bg="white")</pre>
```

predlinear

Determine the Effective Dose from a Linear Regression Fit

Description

Determine the effective dose for a specified percent effect from the intercept and slope of a linear regression.

Usage

```
predlinear(pct, LWmod, simple = FALSE)
```

Arguments

A numeric vector of effects (in percents) for which to estimate the effective

dose(s).

LWmod If simple=TRUE, a numeric vector of length two giving the intercept and

slope of the linear relation between the dose (x, the concentration of the applied chemical on the log10 scale), and the proportion of affected individuals (y, on the probit scale, with 0s converted to 0.1% and 1s converted to 99.9%). If simple=FALSE, a list with the results of fitting a Litchfield and Wilcoxon

model to dose-effect data, the output from fitLW.

simple A logical scalar indicating whether to carry out a simple estimation of effec-

tive doses from the intercept and slope (TRUE), or an estimation of effective doses with confidence intervals from the Litchfield and Wilcoxon model (de-

fault, FALSE).

Details

Follows methods outlined in Litchfield and Wilcoxon (1949). Specifically, for the 95% confidence intervals, see page 105, and equation 13 in the Appendix (corresponding to Nomograph 4).

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Value

A numeric vector the same length as pct giving the estimated dose at the specified percent effect.

If simple=TRUE, a numeric vector the same length as pct with the estimated effective doses. If simple=FALSE, an n*4 numeric matrix with the given effects (pct), the effective doses (ED), and Litchfield and Wilcoxon's (1949) 95% confidence intervals for the effective doses (lower and upper). The number of rows of the matrix, n, is the length of pct.

References

Litchfield, JT Jr. and F Wilcoxon. 1949. A simplified method of evaluating dose-effect experiments. Journal of Pharmacology and Experimental Therapeutics 99(2):99-113. [link]¹¹.

Examples

```
predlinear(c(16, 50, 84, 99.9), c(1.700875, 2.199559), simple=TRUE)

dose <- c(0.0625, 0.125, 0.25, 0.5, 1)

ntested <- rep(8, 5)

nalive <- c(1, 4, 4, 7, 8)

mydat <- dataprep(dose=dose, ntot=ntested, nfx=nalive)
fLW <- fitLW(mydat)
predlinear(c(25, 50, 99.9), fLW)</pre>
```

predprobit

Determine the Effective Dose from a Probit Regression Fit

Description

Determine the effective dose for a specified percent effect from a fitted probit regression model.

Usage

```
predprobit(pct, pfit)
```

Arguments

pct	A numeric scalar of the effect (as a percent) for which to estimate the effective dose.
pfit	An object of class glm representing a probit regression fit to dose-effect data, typically the result of a call to fitprobit.

Value

A numeric vector of length three, the effective dose and the lower and upper 95% confidence limits.

 $^{^{11} \}verb|http://jpet.aspetjournals.org/content/96/2/99.abstract|\\$

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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)
myfit <- fitprobit(mydat)
predprobit(50, myfit)</pre>
```

prettylog

Pretty Breakpoints on Log Scale

Description

Compute a sequence of "round" values which cover the range of \boldsymbol{x} on the log scale.

Usage

```
prettylog(x, lead = c(1, 5), extra = 5)
```

Arguments

X	A numeric vector.
lead	An integer vector giving the desired lead digits of pretty values on the log scale, default $c(1, 5)$.
extra	An integer scalar giving the desired number of additional non-log scale values to include, default 5.

Value

A numeric vector of pretty values covering the range of x on the log scale.

```
vals <- rlnorm(100, 6)
summary(vals)
prettylog(vals, 1, 0)
prettylog(vals, 1)
prettylog(vals, c(1, 2, 5))</pre>
```

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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.

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