Package 'skrmdb'

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Type Package

Title Package to estimate ED50

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Description Package to estimate ED50 by the methods of Spearman-Karber,
Reed-Muench, Dragstedt-Behrens. No endorsement, claim, or warranty is
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pedagogical use only.

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URL https://github.com/ABS-dev/skrmdb/blob/master/README.md

BugReports https://github.com/ABS-dev/skrmdb/issues

LazyLoad true

LazyData true

Depends R (>= 3.5)

Imports data.table,
Formula

Suggests testthat,
knitr,
rmarkdown,
R.rsp

Encoding UTF-8

Roxygen list(markdown = TRUE)

RoxygenNote 7.2.3

Config/build/clean-inst-doc FALSE

VignetteBuilder R.rsp

R topics documented:

1

DragBehr   *skrmdb package*

Description

The skrmdb package provides functionality to compute the median effective dose (ED50) using the Dragstedt-Behrens, Reed-Muench, and Spearman-Kärber estimators.

Usage

```
DragBehr(formula, data, y, n, x, autosort = TRUE, warn.me = TRUE, show = FALSE)

ReedMuench(
  formula,
  data,
  y,
  n,
  x,
  autosort = TRUE,
  warn.me = TRUE,
  show = FALSE
)

SpearKarb(
  formula,
  data,
  y,
  n,
  x,
  autosort = TRUE,
  warn.me = TRUE,
  show = FALSE
)
```

Arguments

formula	a formula of the form y + n ~ x or cbind(y, n) ~ x
data	a data frame
y	an integer vector corresponding to the number responding at each log dilution or dose.
n	an integer vector corresponding to the group size at each log dilution or dose.
x	a vector corresponding to the log dilution or dose for each group.
autosort	Default TRUE. If TRUE will sort the data according to either sort(x) or sort(-x) so that y / n appears to be increasing with the index. This is how the three methods assume the data to be ordered.
warn.me	if TRUE, warnings and messages related to the processing of the data will be displayed.
show	if TRUE, will print the intermediary statistics used to calculate ED50.

Details

The Dragstedt-Behrens and Reed-Muench methods estimate the median effective dose by interpolating between the two doses that bracket the dose producing median response. They accumulate sums in both directions by assuming that those that responded at a lower dose would respond at a higher dose, and those that did not respond at a higher dose would not respond at a lower dose. The Dragstedt-Behrens method estimates ED50 by interpolating on the line that connects the hypothetical fractions of the bracketing doses for ED50, while the Reed-Muench method estimates ED50 as the intersection of the lines connecting the two sets of cumulative sums between bracketing doses.

The Spearman-Karber method gives a non-parametric estimate of the mean of an tolerance distribution from its empirical distribution (EDF). The empirical PMF is derived from the EDF by differencing and the estimator is $\sum x f(x)$. If the EDF does not cover the entire support of x, SpearKarb() extends it by assuming the next lower dilution would produce zero response and the next higher dilution would produce complete response.

Value

An object of class skrmdb-class

Note

These methods assume that the y is monotonic in x, however ED50 will still be computed if this is not the case. These methods also assume that data brackets ED50. If the data does not bracket ED50, a result could still be returned, but the accuracy of this value in estimating ED50 is suspect.

Many microbiology texts mistakenly present the Dragstedt-Behrens method as the Reed-Muench method.

References

Behrens, B. (1929) Zur Auswertung der Digitalisblätter im Froschversuch. *Arkiv für Experimentelle Pathologie und Pharmakologie.* **140: 237-256**.

Dragstedt, C. A., Lang, V. F. (1928). Respiratory Stimulants in Acute Cocaine Poisoning in Rabbits. *J. of Pharmacology and Experimental Therapeutics.* **32: 215–222**.

Kärber, G. (1931). Beitrag zur kollektiven Behandlung Parmakogischer Reihenversuche. *Archiv für Experimentelle Pathologie und Pharmakologie.* **162: 480–483**.

Miller, Rupert G. (1973). Nonparametric Estimators of the Mean Tolerance in Bioassay. *Biometrika.* **60: 535 - 542**.

Reed LJ, Muench H (1938). A Simple Method of Estimating Fifty Percent Endpoints. *American Journal of Hygiene.* **27: 493–497.**

Spearman, C. (1908). The Method of 'Right and Wrong Cases' ('Constant Stimuli') without Gauss's Formulae. *Brit. J. of Psychology.* **2: 227–242.**

Examples

```
# All examples are with \code{SpearKarb}, however, the usage for
# \code{DragBehr} and \code{ReedMuench} is identical.

## Monotonically increasing data
# The three calls are equivalent.
dead <- c(0, 3, 5, 8, 10, 10)
total <- rep(10, 6)
dil <- 1:6
data <- data.frame(y = dead, n = total, x = dil)
SpearKarb(dead + total ~ dil)
```

```
SpearKarb(y + n ~ x, data)
SpearKarb(y = dead, n = total, x = dil)  # depreciated

## Decreasing data
# The function will reverse the order of the data
# and two calls are equivalent.
dead <- c(10, 10, 8, 5, 3, 0)
total <- rep(10, 6)
dil <- 1:6
SpearKarb(dead + total ~ dil)
SpearKarb(rev(dead) + rev(total) ~ rev(dil))

## Unordered data
# Observe that the data is not monotonic after being sorted by dil.
dead <- c(10, 8,5, 3, 0)
total <- rep(10, 5)
dil <- c(1, 3, 2, 4, 5)
SpearKarb(dead + total ~ dil)
```

---

getdata   *Accessor to retrieve the the data used in the call to create an skrmdb*
                                 object

Description

This is an accessor function for retrieving the data used to compute the effective median dose from
a skrmdb-class object object generated by ReedMuench, SpearKarb, or DragBehr.

Usage

```
getdata(x)
```

Arguments

x   class skrmdb.

Value

a dataframe containing the sorted data.

Examples

```
temp <- DragBehr(y=c(0, 3,5, 8, 10, 10), n=rep(10, 6), x=1:6)
getdata(temp)
```

---

getED   *Accessor to retrieve the numeric median effective dose from a skrmdb*
                                        object

Description

This is an accessor function for retrieving the numeric value of the effective median dose from a
skrmdb-class object object generated by ReedMuench, SpearKarb, or DragBehr.

Usage

```
getED(x)
```

Arguments

x   class skrmdb.

Value

the estimated ED50.

Examples

```
temp <- DragBehr(y=c(0, 3,5, 8, 10, 10), n=rep(10, 6), x=1:6)
getED(temp)
```

---

getvar   *Accessor to retrieve the variance from a skrmdb object*

Description

This is an accessor function for retrieving the numeric value of the variance from a skrmdb-class
object object generated by ReedMuench, SpearKarb, or DragBehr.

Usage

```
getvar(x)
```

Arguments

x   class skrmdb.

Value

the estimated variance.

Examples

```
temp <- DragBehr(y=c(0, 3,5, 8, 10, 10), n=rep(10, 6), x=1:6)
getvar(temp)
```

---

skrmdb-class   *Class definition for skrmdb object*

Description

The skrmdb object holds output from functions in the skrmdb package. A valid skrmdb object is a list whicn contains the followling components:

Arguments

eval	Evaluation method. One of 'ReedMuench', 'SpearKarb', or 'DragBehr'. character string.
ed	Median effective dose by eval method. numeric.
var	Variance (for Spearman-Kärber method only). numeric.
data	The data used to compute the effective median dose. data.frame, numeric.
message	Messages and warnings generated durning the calculation. character string.

---

skrmdb.all   *Function to run all three methods for determining ED50.*

Description

This function is used primarily by the CVB statistics section to run all three methods included in the [skrmdb](#) package for determining ED50.

Usage

```
skrmdb.all(formula, data, autosort = TRUE)
```

Arguments

formula	A formula of the form y + n ~ x or y + n ~ x	v1 + ... + vK. y is the number responding at each dilution level, n is the number tested at each dilution level, and x is the dilution levels. v1, ..., vK are the grouping variables. y, n, x, v1, ..., vK must all be distenct.
data	A data.frame containting the titration data. Formatted as specified in the CVB Data Guide.
autosort	Default TRUE. If TRUE will sort the data according to either sort(x) or sort(-x) so that y / n appears to be increasing with the index. This is how the three methods assume the data to be ordered.

Value

A [data.frame](#) containing columns for each of the subset variables, the ED50 as computed by DragBehr, ReedMuench, the ED50 and variance as computed by SpearKarb, and columns of logical values which indicate if the data are increasing or decreasing with log_dil, has an even dilution scheme, are monotonic, and brackets the midpoint.

Examples

```
data(titration)
titration$log_dil = -log10(titration$dil)
skrmdb.all(positive + total ~ log_dil | Vial + Operator, titration)

titration$dil = NULL
skrmdb.all(positive + total ~ log_dil | ., titration)
```

---

titration   *Example titration data.*

Description

A dataset that illustrates the dichotomous data format for titration data as found in the CVB DATA Guide. The data is purposely incomplete and not- monotonic.

Usage

```
titration
```

Format

A data.frame with 67 rows and 9 columns

testID Mandatory. A test identifier that is unique in the table. Every test must have a test identifier.

PrepID Mandatory. The identifier of the preparation used. This will usually be a lot or serial number of a vaccine.

PrepRole Mandatory. The role of the preparation. This must be reference, test, or other.

Date Optional. The Date the test was performed.

Vial Optional. The vial number tested.

Operator Optional. The operator who performed the test.

dil Mandatory. The dilution used in a well.

positive Mandatory. Total number of positive readings (tubes or wells) affected by challenge.

total Mandatory. The total number of tubes or wells in a group (treatment group or at a specified dilution).

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