Package 'ed50'

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Type Package

Title Estimate ED50 and Its Confidence Interval

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Description Functions of five estimation method for ED50 (50 percent effective dose) are provided, and they are respectively
Dixon-Mood method (1948) <doi:10.2307/2280071>, Choi's original turning point method (1990) <doi:10.2307/2531453> and it's modified version given by us, as well as logistic regression and isotonic regression. Besides, the package also supports comparison between two estimation results.

Imports stats, boot, utils

License GPL-3

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R topics documented:

`bootBC.ci` *Estimate Confidence Interval of ED50 Using Isotonic Regression*

Description

Estimate confidence interval of ED50 using isotonic regression based on bootstrap method.

Usage

```
bootBC.ci(tObserved, tBoot, conf = 0.95)
```

Arguments

`tObserved`	the vector of observed statistics.
`tBoot`	The matrix with R rows each of which is a bootstrap replicate of the statistics.
`conf`	Confidence level.

Examples

```
library(ed50)
library(boot)
pavaData <- preparePava(groupS)
bootResult <- boot(data = groupS,
              statistic = bootIsotonicRegression,
                      R = 10,
                    sim = 'parametric',
                ran.gen = bootIsotonicResample,
                    mle = list(baselinePava = pavaData,
                               firstDose = 2.5,
                          PROBABILITY.GAMMA = 0.5),
           baselinePava = pavaData,
      PROBABILITY.GAMMA = 0.5)
bootBC.ci(tObserved = bootResult$t0[3],
              tBoot = bootResult$t[, 3],
               conf = 0.95)
```

`bootIsotonicRegression`
Isotonic Regression Function

Description

Function of isotonic regression.

Usage

```
bootIsotonicRegression(data, PROBABILITY.GAMMA = 0.5, baselinePava)
```

Arguments

data	the same dataframe called by the boot function.
PROBABILITY.GAMMA	the target effect probability in the BCD experiment; default = 0.5 and need not be specified.
baselinePava	the dataframe prepared by the function preparePava.

Examples

```
library(ed50)
pavaData <- preparePava(groupS)
bootIsotonicRegression(data = groupS, PROBABILITY.GAMMA = 0.5, baselinePava = pavaData)
```

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bootIsotonicResample *The resample function of isotonic regression*

Description

The function is designed as an argument for the boot function of the Canty Bootstrap package.

Usage

```
bootIsotonicResample(data, mle)
```

Arguments

data	Original experiment data.
mle	A list of additional arguments to be used by bootIsotonicResample.

Examples

```
library(ed50)
pavaData <- preparePava(groupS)
bootIsotonicResample(data = groupS,
                     mle = list(baselinePava = pavaData,
                                firstDose = 2.5,
                           PROBABILITY.GAMMA = 0.5))
```

compare *Compare ED50 Estimation of Independent Two-sample Case*

Description

Test the statistical difference of two independent estimation results of ED50.

Usage

```
compare(group1, group2, alpha = 0.05)
```

Arguments

group1	A list object of ED50 estimation.
group2	Another list object of ED50 estimation to be compared with.
alpha	The significant level of test. 0.05 is the defaut value.

Value

The difference between two groups of ED50 estimation in terms of statistical significance.

References

Noguchi, K., & Marmolejo-Ramos, F. (2016). Assessing equality of means using the overlap of range-preserving confidence intervals. American Statistician, 70(4), 325-334.

Examples

```
library(ed50)
ans1 <- estimate(groupS$doseSequence, groupS$responseSequence, method = 'ModTurPoint')
ans2 <- estimate(groupSN$doseSequence, groupSN$responseSequence, method = 'Dixon-Mood')
compare(ans1, ans2)
```

estimate *Estimate ED50*

Description

Estimate 50 percent effective dose using different methods.

Usage

```
estimate(doseSequence, doseResponse, confidence = 0.95,
  method = c("Dixon-Mood", "Choi", "ModTurPoint", "Logistic",
  "Isotonic"), tpCiScale = 2.4/qnorm(0.975), boot.n = 10000)
```

Arguments

doseSequence	A sequence of doses given in order
doseResponse	A sequence of response results shown in order
confidence	The confidence level of interval estimate
method	The method used to estimate ED50, there are five methods here, respectively Dixon-Mood, Choi (Choi's Original Turning Point), ModTurPoint (Modified Turning Point), Logistic (Logistic Regression) and Isotonic (Isotonic Regression). The defaut is Dixon-Mood.
tpCiScale	The scale level to enlarge the confidence interval estimated by Modified Turning Point Method. The default value is `2.4/qnorm(0.975)`.
boot.n	The number of boot process if Logistic method is chosen to estimate ED50.

Value

A list of estimation result consisting of method of estimation, ED50 estimate, standard error of ED50 estimate, confidence level and estimate of confidence interval.

References

Dixon, W. J., & Mood, A. M. (1948). A method for obtaining and analyzing sensitivity data. Publications of the American Statistical Association, 43(241), 109-126. Choi, S. C. (1990). Interval estimation of the ld50based on an up-and-down experiment. Biometrics, 46(2), 485-492. Pace, N. L., & Stylianou, M. P. (2007). Advances in and limitations of up-and-down methodology: a precis of clinical use, study design, and dose estimation in anesthesia research. Anesthesiology, 107(1), 144-52.

Examples

```
library(ed50)
estimate(groupS$doseSequence, groupS$responseSequence, method = 'Dixon-Mood')
estimate(groupS$doseSequence, groupS$responseSequence, method = 'Logistic', boot.n = 1000)
```

---

generateData *Generate Simulation Data of Up-and-Down Experiment*

Description

The function is used to generate simulation data of up-and-down experiment, and provide three cases that tolerance distribution obeys normal, triangle or chi-square distribution.

Usage

```
generateData(number, useTurPoint = FALSE, start, doseStep = 1,
  distribution = c("Normal", "Triangle", "Chi-square"), normalMean = 0,
  normalStd = 1, triMean = 0, triWidth = 2, chiDegree = 1)
```

Arguments

number	The number of experiments in a trail.
useTurPoint	A logical value indicating whether the parameter number refers to the amount of turning points. The default value is FALSE.
start	The first dose level given in this trail.
doseStep	A fix value that represents the difference between two adjacent dose levels.
distribution	The tolerance distribution, including normal, triangle and chi-square distribution, and the default distribution is N(0, 1).
normalMean	Parameter mean of normal distribution, the default value is 0.
normalStd	Parameter std of normal distribution, the default value is 1.
triMean	Parameter mean of triangle distribution, the default value is 0.
triWidth	Parameter width of triangle distribution, the default value is 2.
chiDegree	Parameter degree of freedom of chi-square distribution, the default value is 1.

Value

A data frame.

Examples

```
library(ed50)
generateData(number = 20, start = 2, doseStep = 0.2, distribution = 'Normal')
generateData(number = 40, start = 2, doseStep = 0.2, distribution = 'Chi-square')
```

---

groupS *A Real Experiment Dose Data*

Description

A group of real experiment data based on up-and-down method.

Usage

```
groupS
```

Format

A data of 36 samples and 2 variables:

responseSequence A value of 0 or 1 indicating the experiment outcome. 0 refers to a failure outcome while 1 refers to a success.

doseSequence The dose given in each experiment.

Source

The data is from the article in the references below.

References

Niu B, Xiao JY, Fang Y, et al. Sevoflurane-induced isoelectric EEG and burst suppression: differential and antagonistic effect of added nitrous oxide. Anaesthesia 2017; 72: 570-9.

`groupSN` *A Real Experiment Dose Data*

Description

A group of real experiment data based on up-and-down method.

Usage

```
groupSN
```

Format

A data of 38 samples and 2 variables:

responseSequence A value of 0 or 1 indicating the experiment outcome. 0 refers to a failure outcome while 1 refers to a success.

doseSequence The dose given in each experiment.

Source

The data is from the article in the references below.

References

Niu B, Xiao JY, Fang Y, et al. Sevoflurane-induced isoelectric EEG and burst suppression: differential and antagonistic effect of added nitrous oxide. Anaesthesia 2017; 72: 570-9.

gTableOrigin *G Table*

Description

A table containing parameter G used in Dixon-Mood method.

Usage

```
gTableOrigin
```

Format

A data table containing 3 columns:

Ratio The ratio of dose step and estimate standard error

G1 The value of parameter G when the estimate of ED50 falls on a dose level

G2 The value of parameter G when the estimate of ED50 falls between two dose levels

Source

The table is obtained from Figure 2 in the reference below

References

Dixon, W. J., & Mood, A. M. (1948). A method for obtaining and analyzing sensitivity data. Publications of the American Statistical Association, 43(241), 109-126.

preparePava *Covert Data Using PAVA Algorithm*

Description

Covert data using PAVA algorithm, the result is uesd for isotonic regression estimation.

Usage

```
preparePava(data)
```

Arguments

data	A data frame of dose experiments.

Examples

```
library(ed50)
preparePava(groupS)
preparePava(groupSN)
```

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