Package 'bmd'

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Title Benchmark dose analysis for dose-response data

LazyLoad yes

LazyData yes

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Author Christian Ritz <ritz@life.ku.dk>

Maintainer Christian Ritz <ritz@life.ku.dk>

Description Benchmark dose analysis for continuous and quantal dose-response data.

License GPL (>= 2)

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R topics documented:

bmd *Calculation of benchmark doses*

Description

Calculation of benchmark doses based on continuous or qunatal dose-response data.

Usage

```
bmd(object, bmr, backg = 0, def = c("excess", "additional", "relative", "hybrid"),
interval = c("delta"), ma = FALSE, maList = NULL, display = FALSE)
```

Arguments

object	object of class drc
bmr	numeric vector of bench mark response levels for which to calculate benchmark doses (should be between 0 and 1)
backg	numeric value specifying the background level (defaults to 0)
def	character string specifiying the definition of the benchmark dose to use in the calculations. "excess" and "additional" are for binomial response whereas "relative" and "hybrid" (additive hybrid) are for continuous response
interval	character string specifying the type of confidence interval to use
ma	logical value switching on/off model averaging using a default list of model functions
maList	list of model functions to include in the model averaging
display	logical. If TRUE results are displayed; otherwise they are not

Details

This package project just started and is still under development. The aim to provide an R package calculating the benchmark dose (BMD) and the lower limit of the corresponding 95% confidence interval (BMDL) for continuous and quantal dose-response data for a range of dose-response model based on the available definitions of the benchmark dose concepts.

Details on the implemented definitions and methods can be found in Crump (2002).

Value

A matrix with two column, one containing BMD and the other containing BMDL.

Author(s)

Christian Ritz

References

Budtz-Jorgensen, E., Keiding, N., and Grandjean, P. (2001) Benchmark Dose Calculation from Epidemiological Data, *Biometrics* **57**, 698–706.

Crump, K. (2002) Critical Issues in Benchmark Calculations from Continuous Data, *Critical Reviews in Toxicology* **32**, 133–153.

Examples

```
## Fitting log-logistic two-parameter model to binomial data
deguelin.m1 <- drm(r/n~dose, weights=n, data=deguelin, fct=LL.2(), type="binomial")

## Estimated EC values for comparison
ED(deguelin.m1, c(5, 10, 50), interval = "delta")

## Excess risk with BMR=5% and background 0
bmd(deguelin.m1, 0.05)

## Additional risk BMR=5% and with background 0
bmd(deguelin.m1, 0.05, def = "additional")

## Excess risk with BMR=5% and known background
bmd(deguelin.m1, 0.05, backg = 0.05)

## Additional risk with BMR=5% and known background
## similar but not identical to excess risk
bmd(deguelin.m1, 0.05, backg = 0.05, def = "additional", display = TRUE)

## Model-average BMD using additional risk
bmd(deguelin.m1, 0.05, backg = 0.05, def = "additional", ma = TRUE, display = TRUE)


## Benchmark doses for a continuous response
ryegrass.m1 <- drm(rootl ~ conc, data = ryegrass, fct = LL.4())

## Standard single-model BMD using relative values (background level cannot be incorporated)
bmd(ryegrass.m1, 0.05, def = "relative", display = TRUE)

## Standard single-model BMD using the hybrid method (background level can be incorporated)
bmd(ryegrass.m1, 0.05, backg = 0.05, def = "hybrid", display = TRUE)

## Model avaraged BMD using relative values (background level cannot be incorporated)
bmd(ryegrass.m1, 0.05, def = "relative", ma = TRUE, display = TRUE)

## Model avaraged BMD using the "hybrid" method
bmd(ryegrass.m1, 0.05, backg = 0.05, def = "hybrid", ma = TRUE, display = TRUE)


## Example from p. 41 in: EFSA (2009). Guidance of the Scientific Committee on a request from EFSA
##  on the use of the benchmark dose approach in risk assessment
##  The EFSA Journal, 1150, 1-72
```

```
efsa2009p41 <- data.frame(dose=c(0,3,12,30), number=c(6,6,34,42), total=rep(50,4))
efsa2009p41.LL2 <- drm(number/total~dose, weights=total, data=efsa2009p41, type="binomial", fct=LL.2())
plot(efsa2009p41.LL2)  # no great fit close to the control group

efsa2009p41.LL3u <- drm(number/total~dose, weights=total, data=efsa2009p41, type="binomial", fct=LL.3u())
plot(efsa2009p41.LL3u)
modelFit(efsa2009p41.LL3u)
summary(efsa2009p41.LL3u)  # background level is 0.096477

bmd(efsa2009p41.LL3u, 0.1, backg = coef(efsa2009p41.LL3u)[2])
# using a background level of 0.096477
# not far from the estimates reported by EFSA: BMD=3.23, BMDL=1.9


## Example from Hwang et al. (2009)
hwang2009 <- data.frame(dose = c(0, 2.68, 10.34, 37.03), number = c(1,0,2,9), total = c(50,50,50,50))
hwang2009.LN2 <- drm(number/total ~ dose, weights = total, data = hwang2009, type = "binomial", fct = LN.2())

plot(hwang2009.LN2)
summary(hwang2009.LN2)

bmd(hwang2009.LN2, 0.1)  # BMR=0.1
# BMD=21.94894, BMDL=13.34339 (smaller than the estimates reported by Piegorsch (2010))
#  but the models also differ as here log-transformed dose is implicitly used
# additional and extra risks are identical for this model (because the background p0 is 0)

hwang2009.N2 <- glm(number/total~dose, weights=total, data=hwang2009, family=binomial("probit"))
summary(hwang2009.N2)  # same estimates as in Piegorsch (2010)
# a model implicitly assuming a non-zero background p0=pnorm(-2.252)=0.012
```

`cleft.palate` *Dose-response data on cleft palate*

Description

Developmental dose-response data on cleft palate for two compounds believed to operate via similar mechanisms of action.

Usage

```
data(cleft.palate)
```

Format

A data frame with 9 observations on the following 4 variables.

`dose` a numeric vector

`affected` a numeric vector

`total` a numeric vector

`compound` a factor with levels `2,3,7,8-TCDD1` `2,3,7,8-TCDD2`

Details

The data are part of a larger collection of datasets reported in Sand et al. (2002).

Source

Sand, S., Falk Fillipsson, A. and Victorin, K. (2002) Evaluation of the Benchmark Dose Method for Dichotomous Data: Model Dependence and Model Selection, *Regulatory Toxicology and Pharmacology*, **36**, 184–197.

Examples

```
cleft.palate
```

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