

# Package ‘drc’

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**Title** Analysis of dose-response curves

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**LazyLoad** yes

**LazyData** yes

**Description** Analysis of one or multiple curves with focus on concentration-response, dose-response and time-response curves used, for example in biology, environmental sciences, medicine, pharmacology, toxicology.

**License** GPL-2

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acidiq

*Acifluorfen and diquat tested on Lemna minor.*

---

## Description

Data from an experiment where the chemicals acifluorfen and diquat tested on Lemna minor. The dataset has 7 mixtures used in 8 dilutions with three replicates and 12 common controls, in total 180 observations.

## Usage

```
data(acidiq)
```

## Format

A data frame with 180 observations on the following 3 variables.

dose a numeric vector of dose values

pct a numeric vector denoting the grouping according to the mixtures percentages

rgr a numeric vector of response values (relative growth rates)

## Details

The dataset is analysed in Soerensen et al (2007). Hewlett's symmetric model seems appropriate for this dataset.

## Source

The dataset is kindly provided by Nina Cedergreen, Department of Agricultural Sciences, Royal Veterinary and Agricultural University, Denmark.

## References

Soerensen, H. and Cedergreen, N. and Skovgaard, I. M. and Streibig, J. C. (2007) An isobole-based statistical model and test for synergism/antagonism in binary mixture toxicity experiments, *Environmental and Ecological Statistics*, **14**, 383–397.

## Examples

```
## Fitting the model with freely varying ED50 values
## Oops: Box-Cox transformation is needed
acidiq.free <- drm(rgr ~ dose, pct, data = acidiq, fct = LL.4(),
  pmodels = list(~factor(pct), ~1, ~1, ~factor(pct) - 1))

## Lack-of-fit test
modelFit(acidiq.free)
summary(acidiq.free)
```

```
## Plotting isobole structure
isobole(acidiq.free, xlim = c(0, 400), ylim = c(0, 450))

## Fitting the concentration addition model
acidiq.ca <- mixture(acidiq.free, model = "CA")

## Comparing to model with freely varying e parameter
anova(acidiq.ca, acidiq.free) # rejected

## Plotting isobole based on concentration addition -- poor fit
isobole(acidiq.free, acidiq.ca, xlim = c(0, 420), ylim = c(0, 450)) # poor fit

## Fitting the Hewlett model
acidiq.hew <- mixture(acidiq.free, model = "Hewlett")

## Comparing to model with freely varying e parameter
anova(acidiq.free, acidiq.hew) # accepted
summary(acidiq.hew)

## Plotting isobole based on the Hewlett model
isobole(acidiq.free, acidiq.hew, xlim = c(0, 400), ylim = c(0, 450)) # good fit
```

---

algae	<i>Volume of algae as function of increasing concentrations of a herbicide</i>
-------	--

---

### Description

Dataset from an experiment exploring the effect of increasing concentrations of a herbicide on the volume of the treated algae.

### Usage

```
data(algae)
```

### Format

A data frame with 14 observations on the following 2 variables.

conc a numeric vector of concentrations.

vol a numeric vector of response values, that is relative change in volume.

### Details

This datasets requires a cubic root transformation in order to stabilise the variance.

**Source**

Meister, R. and van den Brink, P. (2000) *The Analysis of Laboratory Toxicity Experiments*, Chapter 4 in *Statistics in Ecotoxicology*, Editor: T. Sparks, New York: John Wiley & Sons, (pp. 114–116).

**Examples**

```
algae.m1 <- drm(vol~conc, data=algae, fct=LL.3())
summary(algae.m1)
```

```
algae.m2 <- boxcox(algae.m1)
summary(algae.m2)
```

---

 anova.drc

---

*ANOVA for dose-response model fits*


---

**Description**

'anova' produces an analysis of variance table for one or two non-linear model fits.

**Usage**

```
## S3 method for class 'drc'
anova(object, ..., details = TRUE, test = NULL)
```

**Arguments**

object	an object of class 'drc'.
...	additional arguments.
details	logical indicating whether or not details on the models compared should be displayed. Default is TRUE (details are displayed).
test	a character string specifying the test statistic to be applied. Use "od" to assess overdispersion for binomial data.

**Details**

Specifying only a single object gives a test for lack-of-fit, comparing the non-linear regression model to a more general one-way or two-way ANOVA model.

If two objects are specified a test for reduction from the larger to the smaller model is given. (This only makes statistical sense if the models are nested, that is: one model is a submodel of the other model.)

**Value**

An object of class 'anova'.

**Author(s)**

Christian Ritz

**References**

Bates, D. M. and Watts, D. G. (1988) *Nonlinear Regression Analysis and Its Applications*, New York: Wiley & Sons (pp. 103–104)

**See Also**

For comparison of nested or non-nested model the function `mselect` can also be used.

The function `anova.lm` for linear models.

**Examples**

```
## Comparing a Gompertz three- and four-parameter models using an F test
ryegrass.m1 <- drm(rootl ~ conc, data = ryegrass, fct = W1.4())
ryegrass.m2 <- drm(rootl ~ conc, data = ryegrass, fct = W1.3())
anova(ryegrass.m2, ryegrass.m1) # reduction to 'W1.3' not possible (highly significant)

anova(ryegrass.m2, ryegrass.m1, details = FALSE) # without details
```

---

 AR

*Asymptotic regression model*


---

**Description**

Providing the mean function and the corresponding self starter function for the asymptotic regression model.

**Usage**

```
AR.2(fixed = c(NA, NA), names = c("d", "e"), ...)
```

```
AR.3(fixed = c(NA, NA, NA), names = c("c", "d", "e"), ...)
```

**Arguments**

<code>fixed</code>	numeric vector. Specifies which parameters are fixed and at what value they are fixed. NAs for parameter that are not fixed.
<code>names</code>	vector of character strings giving the names of the parameters (should not contain ":").
<code>...</code>	additional arguments to be passed from the convenience functions.

**Details**

The asymptotic regression model is a three-parameter model with mean function:

$$f(x) = c + (d - c)(1 - \exp(-x/e))$$

The parameter  $c$  is the lower limit (at  $x = 0$ ), the parameter  $d$  is the upper limit and the parameter  $e > 0$  is determining the steepness of the increase as  $x$ .

**Value**

A list of class `drcMean`, containing the mean function, the self starter function, the parameter names and other components such as derivatives and a function for calculating ED values.

**Note**

The functions are for use with the function `drm`.

**Author(s)**

Christian Ritz

**See Also**

A very similar, but monotonously decreasing model is the exponential decay model: [EXD.2](#) and [EXD.3](#).

**Examples**

```
## First model
met.as.m1<-drm(gain~dose, product, data=methionine, fct=AR.3(),
pmodels = list(~1, ~factor(product), ~factor(product)))
plot(met.as.m1, log = "", ylim=c(1450, 1800))
summary(met.as.m1)

## Calculating bioefficacy: approach 1
coef(met.as.m1)[5] / coef(met.as.m1)[4] * 100

## Calculating bioefficacy: approach 2
SI(met.as.m1, c(50,50))

## Simplified models
met.as.m2<-drm(gain~dose, product, data=methionine, fct=AR.3(),
pmodels = list(~1, ~1, ~factor(product)))
anova(met.as.m2, met.as.m1) # simplification not possible

met.as.m3<-drm(gain~dose, product, data=methionine, fct=AR.3(), pmodels = list(~1, ~factor(product), ~1))
anova(met.as.m3, met.as.m1) # simplification not possible
```

---

auxins	<i>Effect of technical grade and commercially formulated auxin herbicides</i>
--------	---

---

### Description

MCPA, 2,4-D, mecorprop and dichlorprop were applied either as technical grades materials (h = 1, 2, 3, 4) or as commercial formulations (herb = 5, 6, 7, 8). Each experimental unit consisted of five 1-week old seedlings grown together in a pot of nutrient solution during 14 days.

### Usage

```
data(auxins)
```

### Format

A data frame with 150 observations on the following 5 variables.

r a numeric vector

h a numeric vector

w a numeric vector

y a numeric vector

dose a numeric vector

### Details

Data are parts of a larger joint action experiment with various herbicides.

The eight herbicide preparations are naturally grouped into four pairs: (1, 5), (2, 6), (3, 7), and (4, 8), and in each pair of herbicides should have the same active ingredients but different formulation constituents, which were assumed to be biologically inert. The data consist of the 150 observations of dry weights, each observation being the weight of five plants grown in the same pot. All the eight herbicide preparations have essentially the same mode of action in the plant; they all act like the plant auxins, which are plant regulators that affect cell elongation and other essential metabolic pathways. One of the objects of the experiment was to test if the response functions were identical except for a multiplicative factor in the dose. This is a necessary, but not a sufficient, condition for a similar mode of action for the herbicides.

### Source

Streibig, J. C. (1987). Joint action of root-absorbed mixtures of auxin herbicides in *Sinapis alba* L. and barley (*Hordeum vulgare* L.) *Weed Research*, **27**, 337–347.

### References

Rudemo, M., Ruppert, D., and Streibig, J. C. (1989). Random-Effect Models in Nonlinear Regression with Applications to Bioassay. *Biometrics*, **45**, 349–362.

## Examples

```
## Fitting model with varying lower limits
auxins.m1 <- boxcox(drm(y ~ dose, h,
pmodels = data.frame(h, h, 1, h), fct = LL.4(), data = auxins), method = "anova")

## Fitting model with common lower limit
auxins.m2 <- boxcox(drm(y ~ dose, h,
pmodels = data.frame(h, 1, 1, h), fct = LL.4(), data = auxins), method = "anova")

## Comparing the two models
anova(auxins.m2, auxins.m1)
```

---

baro5

*The modified baro5 function*


---

## Description

'baro5' allows specification of the baroreflex 5-parameter dose response function, under various constraints on the parameters.

## Usage

```
baro5(fixed = c(NA, NA, NA, NA, NA), names = c("b1", "b2", "c", "d", "e"),
method = c("1", "2", "3", "4"), ssfct = NULL)
```

## Arguments

fixed	numeric vector. Specifies which parameters are fixed and at what value they are fixed. NAs for parameter that are not fixed.
names	a vector of character strings giving the names of the parameters (should not contain ":"). The order of the parameters is: b1, b2, c, d, e (see under 'Details').
method	character string indicating the self starter function to use.
ssfct	a self starter function to be used.

## Details

The five-parameter function given by the expression

$$y = c + \frac{d - c}{1 + f \exp(b1(\log(x) - \log(e))) + (1 - f) \exp(b2(\log(x) - \log(e)))}$$

$$f = 1 / (1 + \exp((2b1b2 / |b1 + b2|)(\log(x) - \log(e))))$$

If the difference between the parameters b1 and b2 is different from 0 then the function is asymmetric.

**Value**

The value returned is a list containing the nonlinear model function, the self starter function and the parameter names.

**Note**

See the example for the dataset [heartrate](#).

**Author(s)**

Christian Ritz

**References**

Ricketts, J. H. and Head, G. A. (1999) A five-parameter logistic equation for investigating asymmetry of curvature in baroreflex studies. *Am. J. Physiol. (Regulatory Integrative Comp. Physiol. 46)*, **277**, 441–454.

BC.5

*The Brain-Cousens hormesis models***Description**

'BC.4' and 'BC.5' provide the Brain-Cousens modified log-logistic models for describing u-shaped hormesis.

**Usage**

```
BC.5(fixed = c(NA, NA, NA, NA, NA), names = c("b", "c", "d", "e", "f"), ...)
```

```
BC.4(fixed = c(NA, NA, NA, NA), names = c("b", "d", "e", "f"), ...)
```

**Arguments**

fixed	numeric vector specifying which parameters are fixed and at which values they are fixed. NAs designate parameters that are not fixed.
names	a vector of character strings giving the names of the parameters.
...	additional arguments to be passed from the convenience functions.

**Details**

The model function for the Brain-Cousens model (Brain and Cousens, 1989) is

$$f(x, b, c, d, e, f) = c + \frac{d - c + fx}{1 + \exp(b(\log(x) - \log(e)))}$$

,

and it is a five-parameter model, obtained by extending the four-parameter log-logistic model (LL.4) to take into account inverse u-shaped hormesis effects.

The parameters have the following interpretations

- $b$ : Not direct interpretation
- $c$ : Lower horizontal asymptote
- $d$ : Upper horizontal asymptote
- $e$ : Not direct interpretation
- $f$ : Size of the hormesis effect: the larger the value the larger is the hormesis effect.  $f = 0$  corresponds to no hormesis effect and the resulting model is the four-parameter log-logistic model. This parameter should be positive in order for the model to make sense.

Fixing the lower limit at 0 yields the four-parameter model

$$f(x) = 0 + \frac{d - 0 + fx}{1 + \exp(b(\log(x) - \log(e)))}$$

used by van Ewijk and Hoekstra (1993).

### Value

See [braincousens](#).

### Note

This function is for use with the function [drm](#).

### Author(s)

Christian Ritz

### References

Brain, P. and Cousens, R. (1989) An equation to describe dose responses where there is stimulation of growth at low doses, *Weed Research*, **29**, 93–96.

van Ewijk, P. H. and Hoekstra, J. A. (1993) Calculation of the EC50 and its Confidence Interval When Subtoxic Stimulus Is Present, *Ecotoxicology and Environmental Safety*, **25**, 25–32.

### See Also

More details are found for the general model function [braincousens](#).

**Examples**

```
## Fitting the data in van Ewijk and Hoekstra (1993)
lettuce.bcm1 <- drm(weight ~ conc, data = lettuce, fct=BC.5())
modelFit(lettuce.bcm1)
plot(lettuce.bcm1)

lettuce.bcm2 <- drm(weight ~conc, data = lettuce, fct=BC.4())
summary(lettuce.bcm2)
ED(lettuce.bcm2, c(50))
# compare the parameter estimate and
# its estimated standard error
# to the values in the paper by
# van Ewijk and Hoekstra (1993)

## Brain-Cousens model with the constraint b>3
ryegrass.bcm1 <- drm(rootl ~conc, data = ryegrass, fct = BC.5(),
lower = c(3, -Inf, -Inf, -Inf, -Inf), control = drmc(constr=TRUE))

summary(ryegrass.bcm1)

## Brain-Cousens model with the constraint f>0
## (no effect as the estimate of f is positive anyway)
ryegrass.bcm2 <- drm(rootl ~conc, data = ryegrass, fct = BC.5(),
lower = c(-Inf, -Inf, -Inf, -Inf, 0), control = drmc(constr=TRUE))

summary(ryegrass.bcm2)
```

---

beetGrowth

*Example of plant growth curve from Covarelli and Onofri (1998)*


---

**Description**

Crop weight (grams per square meter of dry matter) was recorded at several times after plant emergence

**Usage**

```
data(beetGrowth)
```

**Format**

A data frame with 186 observations on the following 3 variables.

DAE a numeric vector

weightInf a numeric vector

weightFree a numeric vector

**Source**

Covarelli G. and Onofri A., 1998. Effects of timing of weed removal and emergence in sugarbeet. Proceedings 6th EWRS Mediterranean Symposium, Montpellier, 65-72.

**Examples**

```
model <- drm(weightInf ~ DAE, data = beetGrowth, fct=gompGrowth.1())
plot(model, log="")
summary(model)
```

---

 boxcox.drc

*Transform-both-sides Box-Cox transformation*


---

**Description**

Finds the optimal Box-Cox transformation for non-linear regression.

**Usage**

```
boxcox.drc(object, lambda = seq(-2, 2, by = 0.25), plotit = TRUE, bcAdd = 0,
method = c("ml", "anova"), level = 0.95, eps = 1/50,
xlab = expression(lambda), ylab = "log-Likelihood", ...)
```

**Arguments**

object	object of class drc.
lambda	numeric vector of lambda values; the default is (-2, 2) in steps of 0.25.
plotit	logical which controls whether the result should be plotted.
bcAdd	numeric value specifying the constant to be added on both sides prior to Box-Cox transformation. The default is 0.
method	character string specifying the estimation method for lambda: maximum likelihood or ANOVA-based (optimal lambda inherited from more general ANOVA model fit).
eps	numeric value: the tolerance for lambda = 0; defaults to 0.02.
level	numeric value: the confidence level required.
xlab	character string: the label on the x axis, defaults to "lambda".
ylab	character string: the label on the y axis, defaults to "log-likelihood".
...	additional graphical parameters.

**Details**

The optimal lambda value is determined using a profile likelihood approach: For each lambda value the non-linear regression model is fitted and the lambda value resulting in the largest value of the log likelihood function is picked.

**Value**

An object of class `nls` (returned invisibly). If `plotit = TRUE` a plot of `loglik` vs `lambda` is shown indicating a confidence interval (by default 95 the optimal `lambda` value).

**Author(s)**

Christian Ritz

**References**

Carroll, R. J. and Ruppert, D. (1988) *Transformation and Weighting in Regression*, New York: Chapman and Hall (Chapter 4).

**See Also**

For linear regression the analogue is `boxcox`.

**Examples**

```
## Fitting log-logistic model without transformation
m1 <- drm(ryegrass, fct = LL.4())
summary(m1)

## Fitting the same model with optimal Box-Cox transformation
m2 <- boxcox(m1)
summary(m2)
```

---

braincousens

*The Brain-Cousens hormesis models*

---

**Description**

'braincousens' provides a very general way of specifying Brain-Cousens' modified log- logistic model for describing hormesis, under various constraints on the parameters.

**Usage**

```
braincousens(fixed = c(NA, NA, NA, NA, NA),
names = c("b", "c", "d", "e", "f"),
method = c("1", "2", "3", "4"), ssfct = NULL,
fctName, fctText)
```

**Arguments**

fixed	numeric vector. Specifies which parameters are fixed and at what value they are fixed. NAs for parameter that are not fixed.
names	a vector of character strings giving the names of the parameters (should not contain ":"). The default is reasonable (see under 'Usage'). The order of the parameters is: b, c, d, e, f (see under 'Details').
method	character string indicating the self starter function to use.
ssfct	a self starter function to be used.
fctName	optional character string used internally by convenience functions.
fctText	optional character string used internally by convenience functions.

**Details**

The Brain-Cousens model is given by the expression

$$f(x) = c + \frac{d - c + fx}{1 + \exp(b(\log(x) - \log(e)))}$$

which is a five-parameter model.

It is a modification of the four-parameter logistic curve to take hormesis into account proposed by Brain and Cousens (1989).

**Value**

The value returned is a list containing the non-linear function, the self starter function, the parameter names and additional model specific objects.

**Note**

This function is for use with the function [drm](#).

The convenience functions of `braincousens` are [BC.4](#) and [BC.5](#). These functions should be used rather than `braincousens` directly.

**Author(s)**

Christian Ritz

**References**

Brain, P. and Cousens, R. (1989) An equation to describe dose responses where there is stimulation of growth at low doses, *Weed Research*, **29**, 93–96.

---

bread.drc	<i>Bread and meat for the sandwich</i>
-----------	--

---

## Description

Bread and meat for the sandwich estimator of the variance-covariance.

## Usage

```
bread.drc(x, ...)
```

```
estfun.drc(x, ...)
```

## Arguments

x	object of class drc
...	additional arguments. At the moment none are supported.

## Details

More explanations are found in Zeileis (2006).

## Value

The unscaled hessian is returned by `bread.drc`, whereas `estfun.drc` returns the estimating function evaluated at the data and the parameter estimates.

## Author(s)

Christian Ritz

## References

Zeileis, A. (2006) Object-oriented Computation of Sandwich Estimators, *J. Statist. Software*, **16**, Issue 9.

## See Also

For other applications see [sandwich](#).

## Examples

```
## The lines below requires that the packages
## 'lmtest' and 'sandwich' are installed
#library(lmtest)
#library(sandwich)
```

```
#ryegrass.m1<-drm(root1~conc, data=ryegrass, fct=LL.4())

#coefstest(ryegrass.m1)
#coefstest(ryegrass.m1, vcov=sandwich)
```

---

cedergreen

*The Cedergreen-Ritz-Streibig model*


---

## Description

'cedergreen' provides a very general way of specifying then Cedergreen-Ritz-Streibig modified log-logistic model for describing hormesis, under various constraints on the parameters.

[CRS.6](#) is the extension of `link{cedergreen}` with freely varying alpha parameter.

For u-shaped hormesis data 'ucedergreen' provides a very general way of specifying the Cedergreen-Ritz-Streibig modified log-logistic model, under various constraints on the parameters.

## Usage

```
cedergreen(fixed = c(NA, NA, NA, NA, NA),
names = c("b", "c", "d", "e", "f"),
method = c("1", "2", "3", "4"), ssfct = NULL,
alpha)
```

```
CRS.6(fixed = c(NA, NA, NA, NA, NA, NA),
names = c("b", "c", "d", "e", "f", "g"),
method = c("1", "2", "3", "4"), ssfct = NULL)
```

```
ucedergreen(fixed = c(NA, NA, NA, NA, NA),
names = c("b", "c", "d", "e", "f"),
method = c("1", "2", "3", "4"), ssfct = NULL,
alpha)
```

## Arguments

fixed	numeric vector. Specifies which parameters are fixed and at what value they are fixed. NAs for parameter that are not fixed.
names	a vector of character strings giving the names of the parameters (should not contain ":"). The order of the parameters is: b, c, d, e, f (see under 'Details').
method	character string indicating the self starter function to use.
ssfct	a self starter function to be used.
alpha	numeric value between 0 and 1, reflecting the steepness of the hormesis peak. This argument needs to be specified.

**Details**

The model is given by the expression

$$f(x) = c + \frac{d - c + f \exp(-1/x^\alpha)}{1 + \exp(b(\log(x) - \log(e)))}$$

which is a five-parameter model (alpha is fixed or freely varying). Not all features (eg EC/ED calculation) are available for the model with freely varying alpha.

It is a modification of the four-parameter logistic curve to take hormesis into account.

The u-shaped model is given by the expression

$$f(x) = cd - \frac{d - c + f \exp(-1/x^\alpha)}{1 + \exp(b(\log(x) - \log(e)))}$$

**Value**

The value returned is a list containing the non-linear function, the self starter function and the parameter names.

**Note**

The functions are for use with the functions [drm](#).

**Author(s)**

Christian Ritz

**References**

Cedergreen, N. and Ritz, C. and Streibig, J. C. (2005) Improved empirical models describing hormesis, *Environmental Toxicology and Chemistry* **24**, 3166–3172.

**See Also**

For fixed alpha, several special cases are handled by the following convenience functions [CRS.4a](#), [CRS.4b](#), [CRS.4c](#), [CRS.5a](#), [CRS.5b](#), [CRS.5c](#), [UCRS.4a](#), [UCRS.4b](#), [UCRS.4c](#), [UCRS.5a](#), [UCRS.5b](#), [UCRS.5c](#) where a, b and c correspond to the pre-specified alpha values 1, 0.5 and 0.25, respectively.

**Examples**

```
## Estimating CRS model with alpha unknown
lettuce.crsm1 <- drm(weight~conc, data = lettuce, fct = CRS.6())
summary(lettuce.crsm1)
plot(lettuce.crsm1) # oops: not increasing until hormesis peak
```

---

`coef.drc`*Extract Model Coefficients*

---

**Description**

Extract parameter estimates.

**Usage**

```
## S3 method for class 'drc'  
coef(object, ...)
```

**Arguments**

<code>object</code>	an object of class 'drc'.
<code>...</code>	additional arguments.

**Value**

A vector of parameter coefficients which are extracted from the model object 'object'.

**Note**

This function may work even in cases where 'summary' does not, because the parameter estimates are retrieved directly from the model fit object without any additional computations of summary statistics and standard errors.

**Author(s)**

Christian Ritz

**See Also**

A more comprehensive summary is obtained using [summary.drc](#).

**Examples**

```
## Fitting a four-parameter log-logistic model  
ryegrass.m1 <- drm(root1 ~ conc, data = ryegrass, fct = LL.4())  
coef(ryegrass.m1)
```

---

comped	<i>Comparison of effective dose values</i>
--------	--

---

### Description

Comparison of a pair of effective dose values from independent experiments where only the estimates and their standard errors are reported.

### Usage

```
comped(est, se, log = TRUE, interval = TRUE, operator = c("-", "/"), level = 0.95, df = NULL)
```

### Arguments

est	a numeric vector of length 2 containing the two estimated ED values
se	a numeric vector of length 2 containing the two standard errors
log	logical indicating whether or not estimates and standard errors are on log scale
interval	logical indicating whether or not a confidence interval should be returned
operator	character string taking one of the two values "-" (default) or "/" corresponding to a comparison based on the difference or the ratio.
level	numeric value giving the confidence level
df	numeric value specifying the degrees of freedom for the percentile used in the confidence interval (optional)

### Details

The choice "/" for the argument operator and FALSE for log will result in estimation of a so-called relative potency (sometimes also called a selectivity index).

The combination TRUE for log and "/" for operator only influences the confidence interval, that is no ratio is calculated based on logarithm-transformed effective dose values.

By default confidence interval relies on percentiles in the normal distribution.

In case the entire dataset is available the functions [drm](#) and (subsequently) [SI](#) should be used.

### Value

A matrix with the estimated difference or ratio and the associated standard error and the resulting confidence interval (unless not requested).

### Note

The development of the function `comped` is a side effect of the project on statistical analysis of toxicity data funded by the Danish EPA ("Statistisk analyse og biologisk tolkning af toksicitetsdata", MST j.nr. 669-00079).

**Author(s)**

Christian Ritz

**References**

Wheeler, M. W. and Park, R. M. and Bailer, A. J. (2006) Comparing median lethal concentration values using confidence interval overlap or ratio tests, *Environmental Toxicology and Chemistry*, **25**, 1441–1441.

**See Also**

The function [ED.drc](#) calculates arbitrary effective dose values based on a model fit. The function [SI](#) calculates relative potencies based on arbitrary effective dose values.

**Examples**

```
## Fitting the model
S.alba.m1 <- boxcox(drm(DryMatter~Dose, Herbicide, data=S.alba, fct = LL.4(),
pmodels=data.frame(Herbicide,1,1,Herbicide)), method = "anova")

## Displaying estimated ED values
ED(S.alba.m1, c(10, 90))

## Making comparisons of ED50 in two ways and for both differences and ratios
compParm(S.alba.m1, "e", "/")

comped(c(28.396147, 65.573335), c(1.874598, 5.618945), log=FALSE, operator = "/")
# similar result

compParm(S.alba.m1, "e", "-")

comped(c(28.396147, 65.573335), c(1.874598, 5.618945), log=FALSE, operator = "-")
# similar result

## Making comparisons of ED10 and ED90
comped(c(21.173, 44.718), c(11.87, 8.42), log=FALSE, operator = "/")

comped(c(21.173, 44.718), c(11.87, 8.42), log=FALSE, operator = "/", interval = FALSE)

comped(c(21.173, 44.718), c(11.87, 8.42), log=FALSE, operator = "-")
```

---

 compParm

---

*Comparison of parameters*


---

**Description**

Compare parameters from different assays, either by means of ratios or differences.

**Usage**

```
compParm(object, strVal, operator = "/", od = FALSE, pool = TRUE, display = TRUE)
```

**Arguments**

object	an object of class 'drc'.
strVal	a name of parameter to compare.
operator	a character. If equal to "/" (default) parameter ratios are compared. If equal to "-" parameter differences are compared.
od	logical. If TRUE adjustment for over-dispersion is used.
pool	logical. If TRUE curves are pooled. Otherwise they are not. This argument only works for models with independently fitted curves as specified in <a href="#">drm</a> .
display	logical. If TRUE results are displayed. Otherwise they are not (useful in simulations).

**Details**

The function compares actual parameter estimates, and therefore the results depend on the parameterisation used. Probably it is most useful in combination with 'collapse' arguments (in [drm](#)) that are data frames or lists with formulas without intercept (-1).

**Value**

A matrix with columns containing the estimates, estimated standard errors, values of t-statistics and p-values for the null hypothesis that the ratio equals 1 or that the difference equals 0 (depending on the operator argument).

No adjustment for multiplicity is applied. See [p.adjust](#) on how to do adjust p-values.

**Author(s)**

Christian Ritz

**Examples**

```
# Fitting a model with names assigned to the parameters!
spinach.m1 <- drm(SLOPE~DOSE, CURVE, data = spinach,
  fct = LL.4(names = c("b", "lower", "upper", "ed50")))

## Calculating ratios of parameter estimates for the parameter named "ed50"
compParm(spinach.m1, "ed50")

## Calculating differences between parameter estimates for the parameter named "ed50"
compParm(spinach.m1, "ed50", "-")
```

---

`confint.drc`*Confidence Intervals for model parameters*

---

**Description**

Computes confidence intervals for one or more parameters in a model of class 'drc'.

**Usage**

```
## S3 method for class 'drc'  
confint(object, parm, level = 0.95, pool = TRUE, ...)
```

**Arguments**

<code>object</code>	a model object of class 'drc'.
<code>parm</code>	a specification of which parameters are to be given confidence intervals, either a vector of numbers or a vector of names. If missing, all parameters are considered.
<code>level</code>	the confidence level required.
<code>pool</code>	logical. If TRUE curves are pooled. Otherwise they are not. This argument only works for models with independently fitted curves as specified in <a href="#">drm</a> .
<code>...</code>	additional argument(s) for methods. Not used.

**Details**

For binomial data the confidence intervals are based on the normal distribution, whereas  $t$  distributions are used of for continuous/quantitative data.

**Value**

A matrix (or vector) with columns giving lower and upper confidence limits for each parameter. These will be labelled as  $(1-\text{level})/2$  and  $1 - (1-\text{level})/2$  in

**Author(s)**

Christian Ritz

**Examples**

```
## Fitting a four-parameter log-logistic model  
ryegrass.m1 <- drm(root1 ~ conc, data = ryegrass, fct = LL.4())  
  
## Confidence intervals for all parameters  
confint(ryegrass.m1)
```

```
## Confidence interval for a single parameter
confint(ryegrass.m1, "e")
```

---

 CRS.4a

*The Cedergreen-Ritz-Streibig model*


---

### Description

'CRS.4a', 'CRS.4b' and 'CRS.4c' provide the Cedergreen-Ritz-Streibig modified log-logistic model for describing hormesis with the lower limit equal to 0.

'UCRS.4a', 'UCRS.4b' and 'UCRS.4c' provide the Cedergreen-Ritz-Streibig modified log-logistic model for describing u-shaped hormesis with the lower limit equal to 0.

### Usage

```
CRS.4a(names = c("b", "d", "e", "f"), ...)
```

```
UCRS.4a(names = c("b", "d", "e", "f"), ...)
```

### Arguments

names            a vector of character strings giving the names of the parameters. The default is reasonable (see above).

...              additional arguments to be passed from the convenience functions.

### Details

The model is given by the expression

$$f(x) = 0 + \frac{d - 0 + f \exp(-1/x)}{1 + \exp(b(\log(x) - \log(e)))}$$

which is a five-parameter model.

It is a modification of the four-parameter logistic curve to take hormesis into account.

The u-shaped model is given by the expression

$$f(x) = 0 + d - \frac{d - 0 + f \exp(-1/x^\alpha)}{1 + \exp(b(\log(x) - \log(e)))}$$

The a,b,c models are obtained by setting alpha equal to 1, 0.5 and 0.25, respectively.

### Value

See [cedergreen](#).

**Note**

This function is for use with the function [drm](#).

**Author(s)**

Christian Ritz

**References**

See the reference under [cedergreen](#).

**See Also**

Similar functions are [CRS.5a](#) and [UCRS.5a](#), but with an extra parameter for the lower limit.

**Examples**

```
## Fitting modified logistic models
lettuce.crsm1 <- drm(lettuce[,c(2,1)], fct=CRS.4a())
summary(lettuce.crsm1)
ED(lettuce.crsm1, c(50))

## Need to explicitly specify that the upper limit
## is the reference in order to get ED10 and ED90 right
ED(lettuce.crsm1, c(10, 50, 90), reference = "upper")

lettuce.crsm2 <- drm(lettuce[,c(2,1)], fct=CRS.4b())
summary(lettuce.crsm2)
ED(lettuce.crsm2, c(50))

lettuce.crsm3 <- drm(lettuce[,c(2,1)], fct=CRS.4c())
summary(lettuce.crsm3)
ED(lettuce.crsm3, c(50))
```

---

CRS.5a

*Cedergreen-Ritz-Streibig dose-reponse model for describing hormesis*

---

**Description**

'CRS.5a', 'CRS.5b' and 'CRS.5c' provide the Cedergreen-Ritz-Streibig modified log-logistic model for describing (inverse u-shaped or j-shaped) hormesis.

'UCRS.5a', 'UCRS.5b' and 'UCRS.5c' provide the Cedergreen-Ritz-Streibig modified log-logistic model for describing u-shaped hormesis.

**Usage**

CRS.5a(names = c("b", "c", "d", "e", "f"), ...)

UCRS.5a(names = c("b", "c", "d", "e", "f"), ...)

**Arguments**

names            a vector of character strings giving the names of the parameters.  
 ...              additional arguments to be passed from the convenience functions.

**Details**

The model function for inverse u-shaped hormetic patterns is

$$f(x) = c + \frac{d - c + f \exp(-1/x^\alpha)}{1 + \exp(b(\log(x) - \log(e)))}$$

,  
 which is a five-parameter model. It is a modification of the four-parameter log-logistic curve to take hormesis into account.

The parameters have the following interpretations

- *b*: Not direct interpretation
- *c*: Lower horizontal asymptote
- *d*: Upper horizontal asymptote
- *e*: Not direct interpretation
- *f*: Size of the hormesis effect: the larger the value the larger is the hormesis effect.  $f = 0$  corresponds to no hormesis effect and the resulting model is the four-parameter log-logistic model. This parameter should be positive in order for the model to make sense.

The model function for u-shaped hormetic patterns is

$$f(x) = c + d - \frac{d - c + f \exp(-1/x^\alpha)}{1 + \exp(b(\log(x) - \log(e)))}$$

This model also simplifies to the four-parameter log-logistic model in case  $f = 0$  (in a slightly different parameterization as compared to the one used in [LL.4](#)).

The models denoted a,b,c are obtained by fixing the alpha parameter at 1, 0.5 and 0.25, respectively.

**Value**

See [cedergreen](#).

**Note**

This function is for use with the function [drm](#).

**Author(s)**

Christian Ritz

**References**

See the reference under [cedergreen](#).

**See Also**

Similar functions are [CRS.4a](#) and [UCRS.4a](#), but with the lower limit (the parameter  $c$ ) fixed at 0 (one parameter less to be estimated).

**Examples**

```
## Modified logistic model
lettuce.m1 <- drm(lettuce[,c(2,1)], fct=CRS.5a())
summary(lettuce.m1)
ED(lettuce.m1, c(50))

lettuce.m2 <- drm(lettuce[,c(2,1)], fct=CRS.5b())
summary(lettuce.m2)
ED(lettuce.m2, c(50))

lettuce.m3 <- drm(lettuce[,c(2,1)], fct=CRS.5c())
summary(lettuce.m3)
ED(lettuce.m3, c(50))
```

---

daphnids

*Daphnia test*

---

**Description**

The number of immobile daphnids –in contrast to mobile daphnids– out of a total of 20 daphnids was counted for several concentrations of a toxic substance.

**Usage**

```
data(daphnids)
```

**Format**

A data frame with 16 observations on the following 4 variables.

dose a numeric vector

no a numeric vector

total a numeric vector

time a factor with levels 24h 48h

**Details**

The same daphnids were counted at 24h and later again at 48h.

**Source**

Nina Cedergreen, Faculty of Life Sciences, University of Copenhagen, Denmark.

**Examples**

```
## Fitting a model with different parameters
## for different curves
daphnids.m1 <- drm(no/total~dose, time, weights = total,
data = daphnids, fct = LL.2(), type = "binomial")

## Goodness-of-fit test
modelFit(daphnids.m1)

## Summary of the data
summary(daphnids.m1)

## Fitting a model with a common intercept parameter
daphnids.m2 <- drm(no/total~dose, time, weights = total,
data = daphnids, fct = LL.2(), type = "binomial",
pmodels = list(~1, ~time))
```

---

deguelin

*Deguelin applied to chrysanthemum aphis*

---

**Description**

Quantal assay data from an experiment where the insectide deguelin was applied to *Macrosiphoniella sanborni*.

**Usage**

```
data(deguelin)
```

**Format**

A data frame with 6 observations on the following 4 variables.

dose a numeric vector of doses applied

log10dose a numeric vector of logarithm-transformed doses

r a numeric vector contained number of dead insects

n a numeric vector contained the total number of insects

**Details**

The log-logistic model provides an inadequate fit.

The dataset is used in Nottingham and Birch (2000) to illustrate a semiparametric approach to dose-response modelling.

**Source**

Morgan, B. J. T. (1992) *Analysis of Quantal Response Data*, London: Chapman & Hall/CRC (Table 3.9, p. 117).

**References**

Nottingham, Q. J. and Birch, J. B. (2000) A semiparametric approach to analysing dose-response data, *Statist. Med.*, **19**, 389–404.

**Examples**

```
## Log-logistic fit
deguelin.m1 <- drm(r/n~dose, weights=n, data=deguelin, fct=LL.2(), type="binomial")
modelFit(deguelin.m1)
summary(deguelin.m1)

## Loess fit
deguelin.m2 <- loess(r/n~dose, data=deguelin, degree=1)

## Plot of data with fits superimposed
plot(deguelin.m1, ylim=c(0.2,1))
lines(1:60, predict(deguelin.m2, newdata=data.frame(dose=1:60)), col = 2, lty = 2)

lines(1:60, 0.95*predict(deguelin.m2,
newdata=data.frame(dose=1:60))+0.05*predict(deguelin.m1, newdata=data.frame(dose=1:60), se = FALSE),
col = 3, lty=3)
```

---

diagnostics

*Information on estimation*


---

**Description**

Displays information on the convergence of the estimation procedure.

**Usage**

```
diagnostics(object)
```

**Arguments**

object            an object of class 'drc'.

**Details**

The function displays the convergence status and the number of evaluations used.

**Author(s)**

Christian Ritz

**Examples**

```

terbuthylazin.m1 <- drm(rgr~dose, data = terbuthylazin, fct = LL.4())
diagnostics(terbuthylazin.m1)

terbuthylazin.m2 <- drm(rgr~dose, data = terbuthylazin, start=c(1,0.01,0.38,130), fct = LL.4())
diagnostics(terbuthylazin.m2)
## the start values given result in faster convergence

```

---

 drm

*Fitting dose-response models*


---

**Description**

A general model fitting function for concentration/dose/time-response models.

**Usage**

```

drm(formula, curveid, pmodels, weights, data = NULL, subset, fct,
    type = c("continuous", "binomial", "Poisson", "quantal", "event"), bcVal = NULL, bcAdd = 0,
    start, na.action = na.fail, robust = "mean", logDose = NULL,
    control = drmc(), lowerl = NULL, upperl = NULL, separate = FALSE)

```

**Arguments**

formula	a symbolic description of the model to be fit. Either of the form 'response ~ dose' or as a data frame with response values in first column and dose values in second column.
curveid	a numeric vector or factor containing the grouping of the data.
pmodels	a data frame with a many columns as there are parameters in the non-linear function. Or a list containing a formula for each parameter in the non-linear function.
weights	a numeric vector containing weights that are multiplied inside the squared errors (see the details below).
data	an optional data frame containing the variables in the model.
subset	an optional vector specifying a subset of observations to be used in the fitting process.

<code>fct</code>	a list with three or more elements specifying the non-linear function, the accompanying self starter function, the names of the parameter in the non-linear function and, optionally, the first and second derivatives as well as information used for calculation of ED values. Currently available functions include, among others, the four- and five-parameter log-logistic models <a href="#">LL.4</a> , <a href="#">LL.5</a> and the Weibull model <a href="#">W1.4</a> . Use <a href="#">getMeanFunctions</a> for a full list.
<code>bcVal</code>	a numeric value specifying the lambda parameter to be used in the Box-Cox transformation.
<code>bcAdd</code>	a numeric value specifying the constant to be added on both sides prior to Box-Cox transformation. The default is 0.
<code>type</code>	a character string specifying the data type: continuous is the only option currently.
<code>start</code>	an optional numeric vector containing starting values for all mean parameters in the model. Overrides any self starter function.
<code>na.action</code>	a function which indicates what should happen when the data contain 'NA's. The default is <code>na.fail</code> . To omit 'NA's use <code>na.omit</code> .
<code>robust</code>	a character string specifying the rho function for robust estimation. Default is non-robust least squares estimation ("mean"). Available robust methods are: median estimation ("median"), least median of squares ("lms"), least trimmed squares ("lts"), metric trimming ("trimmed"), metric winsorizing ("winsor") and Tukey's biweight ("tukey").
<code>logDose</code>	a numeric value or NULL. If log doses value are provided the base of the logarithm should be specified (exp(1) for the natural logarithm and 10 for 10-logarithm).
<code>control</code>	a list of arguments controlling constrained optimisation (zero as boundary), maximum number of iteration in the optimisation, relative tolerance in the optimisation, warnings issued during the optimisation.
<code>lowerl</code>	a numeric vector of lower limits for all parameters in the model (the default corresponds to minus infinity for all parameters).
<code>upperl</code>	a numeric vector of upper limits for all parameters in the model (the default corresponds to plus infinity for all parameters).
<code>separate</code>	logical value indicating whether curves should be fit separately (independent of each other).

### Details

This function relies on the general multi-purpose optimiser function [optim](#) for the minimisation of the minus log likelihood function. For a quantitative response this reduces to least squares estimation, which is carried out by minimising the following sums of squares

$$\sum_{i=1}^N [w_i (y_i - f_i)]^2$$

where  $y_i$ ,  $f_i$ , and  $w_i$  correspond to the observed value, expected value, and the weight respectively, for the  $i$ th observation (from 1 to  $N$ ).

The control arguments are specified using the function [drc](#).

For robust estimation MAD (median absolute deviance) is used to estimate the residual variance.

Setting `lower1` and/or `upper1` automatically invokes constrained optimisation.

### Value

An object of class 'drc'.

### Note

The `curve` argument is subsequently used for plotting dose-response curves. For large datasets it need not represent the actual curves, but it could represent several curves having the parameters (to avoid too many curves in the plot). The same applies for use with the function [ED.drc](#) and [SI](#).

The columns of a data frame argument to `pmodels` are automatically converted into factors. This does not happen if a list is specified.

### Author(s)

Christian Ritz and Jens C. Streibig

### See Also

Examples using [drc](#) found in the help pages of [secalonic](#), [ryegrass](#), and many other datasets and functions in `drc`.

---

drc

*Sets control arguments*

---

### Description

Set control arguments in the control argument in the function 'drc'.

### Usage

```
drc(constr = FALSE, errorm = TRUE, maxIt = 500, method="BFGS",
noMessage = FALSE, relTol = 1e-07, rmNA=FALSE, useD = FALSE,
trace = FALSE, otrace = FALSE, warnVal = -1)
```

### Arguments

<code>constr</code>	logical. If TRUE optimisation is constrained, only yielding non-negative parameters.
<code>errorm</code>	logical specifying whether failed convergence in <a href="#">drc</a> should result in an error or only a warning.
<code>maxIt</code>	numeric. The maximum number of iterations in the optimisation procedure.

method	character string. The method used in the optimisation procedure. See <code>optim</code> for available methods.
noMessage	logical, specifying whether or not messages should be displayed.
relTol	numeric. The relative tolerance in the optimisation procedure.
rmNA	logical. Should NAs be removed from sum of squares used for estimation? Default is FALSE (not removed).
useD	logical. If TRUE derivatives are used for estimation (if available).
trace	logical. If TRUE the trace from <code>optim</code> is displayed.
otrace	logical. If TRUE the output from <code>optim</code> is displayed.
warnVal	numeric. If equal to 0 then the warnings are stored and displayed at the end. See under 'warn' in <code>options</code> . The default results in suppression of warnings.

**Value**

A list with 8 components, one for each of the above arguments.

**Note**

The use of a non-zero constant `bcAdd` may in some cases make it more difficult to obtain convergence of the estimation procedure.

**Author(s)**

Christian Ritz

**Examples**

```
### Displaying the default settings
drmc()

### Using 'method' argument
model1 <- drm(ryegrass, fct = LL.4())

model2 <- drm(ryegrass, fct = LL.4(),
  control = drmc(method = "Nelder-Mead"))
```

---

earthworms

*Earthworm toxicity test*

---

**Description**

The dataset is obtained from a toxicity test using earthworms, and it contains the number of earthworms remaining in a container that is contaminated with a toxic substance (not disclosed) and not migrating to the neighbouring uncontaminated container).

**Usage**

```
data(earthworms)
```

**Format**

A data frame with 35 observations on the following 3 variables.

dose a numeric vector of dose values

number a numeric vector containing counts of remaining earthworms in the container

total a numeric vector containing total number of earthworms put in the containers

**Details**

At dose 0 around half of the earthworms is expected be in each of the two containers. Thus it is not appropriate to fit an ordinary logistic regression with  $\log(\text{dose})$  as explanatory variable to these data as it implies an upper limit of 1 at dose 0 and in fact this model does not utilise the observations at dose 0 (see the example section below).

**Source**

The dataset is kindly provided by Nina Cedergreen, Faculty of Life Sciences, University of Copenhagen, Denmark.

**Examples**

```
## Fitting a logistic regression model
earthworms.m1 <- drm(number/total~dose, weights = total, data = earthworms,
fct = LL.2(), type = "binomial")
modelFit(earthworms.m1) # a crude goodness-of-fit test

## Fitting an extended logistic regression model
## where the upper limit is estimated
earthworms.m2 <- drm(number/total~dose, weights = total, data = earthworms,
fct = LL.3(), type = "binomial")
modelFit(earthworms.m2) # goodness-of-fit test
# improvement not visible in test!!!

## Comparing model1 and model2
## (Can the first model be reduced to the second model?)
anova(earthworms.m1, earthworms.m2)
```

ED.drc

*Estimating effective doses***Description**

ED estimates effective doses (ECp/EDp/ICp) for given reponse levels.

**Usage**

```
## S3 method for class 'drc'
ED(object, respLev, interval = c("none", "delta", "fls", "tfls"),
    clevel = NULL, level = ifelse(!(interval == "none"), 0.95, NULL),
    reference = c("control", "upper"), type = c("relative", "absolute"), lref, uref,
    bound = TRUE, od = FALSE, display = TRUE, pool = TRUE, logBase = NULL, ...)

## S3 method for class 'mrdrc'
ED(object, respLev, interval = c("none", "approximate", "bootstrap"), level = 0.95,
    method = c("bisection", "grid"), cgridsize = 20, gridsize = 100, display = TRUE, lower, upper,
    intType = c("confidence", "prediction"), minmax = c("response", "dose"), n = 1000, seedVal = 200810311)
```

**Arguments**

object	an object of class 'drc'.
respLev	a numeric vector containing the response levels.
interval	character string specifying the type of confidence intervals to be supplied. The default is "none". Use "delta" for asymptotics-based confidence intervals (using the delta method and the t-distribution). Use "fls" for from logarithm scale based confidence intervals (in case the parameter in the model is log(ED50) as for the <a href="#">llogistic2</a> models). The only alternative for model-robust fits is using inverse regression.
clevel	character string specifying the curve id in case on estimates for a specific curve or compound is requested. By default estimates are shown for all curves.
level	numeric. The level for the confidence intervals. The default is 0.95.
reference	character string. Is the upper limit or the control level the reference?
type	character string. Whether the specified response levels are absolute or relative (default).
lref	numeric value specifying the lower limit to serve reference.
uref	numeric value specifying the upper limit to serve reference (eg. 100%).
bound	logical. If TRUE only ED values between 0 and 100% are allowed. FALSE is useful for hormesis models.
od	logical. If TRUE adjustment for over-dispersion is used.
display	logical. If TRUE results are displayed. Otherwise they are not (useful in simulations).

pool	logical. If TRUE curves are pooled. Otherwise they are not. This argument only works for models with independently fitted curves as specified in <a href="#">drm</a> .
logBase	numeric. The base of the logarithm in case logarithm transformed dose values are used.
method	character string specifying if bisection or grid search should be used to determine ED estimates. Grid search may give better results for ED level close to the boundaries of the dose range or in case of a non-monotonous dose-response curves. The bisection method is faster than the grid search.
cgridsize	numeric specifying the number of grid points in the initial grid used for both bisection and grid search to narrow down the interval where the ED estimate is to be found.
gridsize	numeric specifying the number of grid points in the second finer grid search.
lower	numeric value specifying the lower reference limit.
upper	numeric specifying the upper reference limit.
intType	character string specifying whether confidence or prediction intervals are requested.
minmax	character string indicating if the control level should be based on the the minimum dose or the maximum response. The latter is more suitable for dose-response data showing hormesis.
n	numeric specifying the number of simulations for the bootstrap confidence intervals.
seedVal	numeric giving the seed for the random number generator used for the bootstrap confidence intervals.
...	see the details section below.

### Details

For hormesis models ([braincousens](#) and [cedergreen](#)), the additional arguments `lower` and `upper` may be supplied. These arguments specify the lower and upper limits of the bisection method used to find the ED values. The lower and upper limits need to be smaller/larger than the ED<sub>x</sub> level to be calculated. The default limits are 0.001 and 1000 for [braincousens](#) and 0.0001 and 10000 for [cedergreen](#) and [ucedergreen](#), but this may need to be modified (for [cedergreen](#) the upper limit may need to be increased and for [ucedergreen](#) the lower limit may need to be increased). Note that the lower limit should not be set to 0 (use instead something like 1e-3, 1e-6, ...).

For model-robust fits the arguments `lower` and `upper` can be used to specify reference values for the lower and upper limits of the dose-response relationship. This only applies for the continuous responses. For quantal responses, the reference values are fixed 0 and 1, respectively.

### Value

A matrix with two or more columns, containing the estimates and the corresponding estimated standard errors and possibly lower and upper confidence limits.

### Author(s)

Christian Ritz

**See Also**

The related function [SI](#). For model-robust fits, examples are found in the help of [mrdrm](#).

**Examples**

```
### How to use 'ED'

## Fitting 4-parameter log-logistic model
ryegrass.m1<-drm(ryegrass, fct = LL.4())

## Calculating EC/ED values
ED(ryegrass.m1, c(10, 50, 90))
## first column: the estimates of ED10, ED50 and ED90
## second column: the estimated standard errors

### How to use the argument 'ci'

## Also displaying 95% confidence intervals
ED(ryegrass.m1, c(10,50,90), interval = "delta")

## Comparing delta method and back-transformed
## confidence intervals for ED values

## Fitting 4-parameter log-logistic
## in different parameterisation (using LL2.4)
ryegrass.m2 <- drm(ryegrass, fct = LL2.4())

ED(ryegrass.m1, c(10,50,90), interval = "fls")
ED(ryegrass.m2, c(10,50,90), interval = "delta")

### How to use the argument 'bound'

## Fitting the Brain-Cousens model
lettuce.m1 <- drm(weight ~ conc,
data = lettuce, fct = BC.4())

### Calculating ED[-10]

# It does not work
#ED(lettuce.m1, -10)

## Now it does work
ED(lettuce.m1, -10, bound = FALSE) # works
ED(lettuce.m1, -20, bound = FALSE) # works

## It does not work for another reason: ED[-30] does not exist
#ED(lettuce.m1, -30, bound = FALSE)
```

---

etmotc

*Effect of erythromycin on mixed sewage microorganisms*

---

### Description

Relative growth rate in biomass of mixed sewage microorganisms (per hour) as a function of increasing concentrations of the antibiotic erythromycin (mg/l).

### Usage

```
data(etmotc)
```

### Format

A data frame with 57 observations on the following 4 variables.

```
cell a numeric vector  
dose1 a numeric vector  
pct1 a numeric vector  
rgr1 a numeric vector
```

### Details

Data stem from an experiment investigating the effect of pharmaceuticals, that are used in human and veterinary medicine and that are being released into the aquatic environment through waste water or through manure used for fertilising agricultural land. The experiment constitutes a typical dose-response situation. The dose is concentration of the antibiotic erythromycin (mg/l), which is an antibiotic that can be used by persons or animals showing allergy to penicillin, and the measured response is the relative growth rate in biomass of mixed sewage microorganisms (per hour), measured as turbidity two hours after exposure by means of a spectrophotometer. The experiment was designed in such a way that eight replicates were assigned to the control (dose 0), but no replicates were assigned to the 7 non-zero doses. Further details are found in Christensen et al (2006).

### Source

Christensen, A. M. and Ingerslev, F. and Baun, A. 2006 Ecotoxicity of mixtures of antibiotics used in aquacultures. *Environmental Toxicology and Chemistry*, **25**, 2208–2215.

### Examples

```
etmotc.m1<-drm(rgr1~dose1, data=etmotc[1:15,], fct=LL.4())  
plot(etmotc.m1)  
modelFit(etmotc.m1)  
summary(etmotc.m1)  
  
etmotc.m2<-drm(rgr1~dose1, data=etmotc[1:15,], fct=W2.4())  
plot(etmotc.m2, add = TRUE)
```

```

modelFit(etmotc.m2)
summary(etmotc.m2)

etmotc.m3<-drm(rgr1~dose1, data=etmotc[1:15,], fct=W2.3())
plot(etmotc.m3, add = TRUE)
modelFit(etmotc.m3)
summary(etmotc.m3)

```

---

EXD

---

*Exponential decay model*


---

### Description

Exponential decay model with or without a nonzero lower limit.

### Usage

```
EXD.2(fixed = c(NA, NA), names = c("d", "e"), ...)
```

```
EXD.3(fixed = c(NA, NA, NA), names = c("c", "d", "e"), ...)
```

### Arguments

<code>fixed</code>	numeric vector. Specifies which parameters are fixed and at what value they are fixed. NAs for parameter that are not fixed.
<code>names</code>	vector of character strings giving the names of the parameters (should not contain ":"). The default parameter names are: <code>init</code> , <code>plateau</code> , <code>k</code> .
<code>...</code>	additional arguments to be passed from the convenience functions.

### Details

The exponential decay model is a three-parameter model with mean function:

$$f(x) = c + (d - c)(\exp(-x/e))$$

The parameter `init` is the upper limit (attained at  $x = 0$ ), the parameter `plateau` is the lower limit reached for  $x$  going to infinity and the parameter  $e > 0$  is determining the steepness of the decay. The curve is monotonously decreasing in  $x$ .

### Value

A list of class `drcMean`, containing the mean function, the self starter function, the parameter names and other components such as derivatives and a function for calculating ED values.

### Author(s)

Christian Ritz

## References

Organisation for Economic Co-operation and Development (OECD) (2006) *Current approaches in the statistical analysis of ecotoxicity data: A guidance to application - annexes*, Paris: OECD (p. 80).

## See Also

Similar models giving exponential increasing curves are [AR. 2](#) and [AR. 3](#).

## Examples

```
## Fitting an exponential decay model
ryegrass.m1<-drm(rootl~conc, data=ryegrass, fct=EXD.3())

plot(ryegrass.m1)

summary(ryegrass.m1)
```

---

finney71

*Example from Finney (1971)*

---

## Description

For each of six concentration of an insecticide the number of insects affected (out of the number of insects) was recorded.

## Usage

```
data(finney71)
```

## Format

A data frame with 6 observations on the following 3 variables.

dose a numeric vector

total a numeric vector

affected a numeric vector

## Source

Finney, D. J. (1971) *Probit Analysis*, Cambridge: Cambridge University Press.

## Examples

```
## Model with ED50 as a parameter
finney71.m1 <- drm(affected/total~dose, weights=total,
data=finney71, fct=LL.2(), type="binomial")

summary(finney71.m1)
plot(finney71.m1, conLevel = 0.1, broken=TRUE, lwd = 2)

ED(finney71.m1, c(10, 20, 50), ci="delta", reference="control")

## Model fitted with 'glm'
#fitl.glm <- glm(cbind(affected, total-affected) ~ log(dose),
#family=binomial(link = logit), data=finney71[finney71$dose != 0, ])
#summary(fitl.glm) # p-value almost agree for the b parameter
#
#xp <- dose.p(fitl.glm, p=c(0.50, 0.90, 0.95)) # from MASS
#xp.ci <- xp + attr(xp, "SE") %*% matrix(qnorm(1 - 0.05/2)*c(-1,1), nrow=1)
#zp.est <- exp(cbind(xp.ci[,1],xp,xp.ci[,2]))
#dimnames(zp.est)[[2]] <- c("zp.lcl","zp","zp.ucl")
#zp.est # not far from above results with 'ED'

## Model with log(ED50) as a parameter
finney71.m2 <- drm(affected/total~dose, weights=total,
data=finney71, fct=LL2.2(), type="binomial")

## Confidence intervals based on back-transformation
## complete agreement with results based on 'glm'
ED(finney71.m2, c(10, 20, 50), ci="fls", reference="control")
```

---

fitted.drc

*Extract fitted values from model*

---

## Description

Extracts fitted values from an object of class 'drc'.

## Usage

```
## S3 method for class 'drc'
fitted(object, ...)
```

## Arguments

object            an object of class 'drc'.  
...                additional arguments.

**Value**

Fitted values extracted from 'object'.

**Author(s)**

Christian Ritz

**Examples**

```
ryegrass.m1 <- drm(root1 ~ conc, data = ryegrass, fct = LL.4())
plot(fitted(ryegrass.m1), residuals(ryegrass.m1)) # a residual plot
```

---

fplogistic

*Fractional polynomial-logistic dose-response models*

---

**Description**

Model function for specifying dose-response models that are a combination of a logistic model and an appropriate class of fractional polynomials.

**Usage**

```
fplogistic(p1, p2, fixed = c(NA, NA, NA, NA), names = c("b", "c", "d", "e"),
method = c("1", "2", "3", "4"), ssfct = NULL, fctName, fctText)
```

```
FPL.4(p1, p2, fixed = c(NA, NA, NA, NA), names = c("b", "c", "d", "e"), ...)
```

**Arguments**

p1	numeric denoting the negative power of $\log(\text{dose}+1)$ in the fractional polynomial.
p2	numeric denoting the positive power of $\log(\text{dose}+1)$ in the fractional polynomial.
fixed	numeric vector. Specifies which parameters are fixed and at what value they are fixed. NAs for parameter that are not fixed.
names	a vector of character strings giving the names of the parameters (should not contain ":"). The default is reasonable (see under 'Usage'). The order of the parameters is: b, c, d, e, f (see under 'Details').
method	character string indicating the self starter function to use.
ssfct	a self starter function to be used.
fctName	optional character string used internally by convenience functions.
fctText	optional character string used internally by convenience functions.
...	Additional arguments (see <a href="#">fplogistic</a> ).

**Details**

The fractional polynomial dose-response models introduced by Namata *et al.* (2008) are implemented using the logistic model as base.

**Value**

The value returned is a list containing the nonlinear function, the self starter function and the parameter names.

**Author(s)**

Christian Ritz

**References**

Namata, Harriet and Aerts, Marc and Faes, Christel and Teunis, Peter (2008) Model Averaging in Microbial Risk Assessment Using Fractional Polynomials, *Risk Analysis* **28**, 891–905.

**See Also**

Examples are found [maED](#).

---

G.aparine

*Herbicide applied to Galium aparine*

---

**Description**

Small plants of *Galium aparine*, growing in pots in a green house, were sprayed with the technical grade phenmidipham herbicide either alone or in mixture with an ester of oleic acid. The plants were allowed to grow in the green house for 14 days after herbicide treatment. Then the dry matter was measured per pot.

**Usage**

data(G.aparine)

**Format**

A data frame with 240 observations on the following 3 variables.

dose a numeric vector of dose value (g/ha)

drymatter a numeric vector of dry matter weights (mg/pot)

treatment a numeric vector giving the grouping: 0: control, 1,2: herbicide formulations

**Source**

Cabanne, F., Gaudry, J. C. and Streibig, J. C. (1999) Influence of alkyl oleates on efficacy of phenmidipham applied as an acetone:water solution on *Galium aparine*, *Weed Research*, **39**, 57–67.

**Examples**

```
## Fitting a model with a common control
c.m1 <- drm(drymatter ~ dose, treatment, data = G.aparine,
pmodels = data.frame(treatment,treatment,1,treatment), fct = LL.4())

## Visual inspection of fit
plot(c.m1, broken = TRUE)

## Lack of fit test
modelFit(c.m1)

## Summary output
summary(c.m1)

## Predicted values with se and confidence intervals
predict(c.m1, interval = "confidence")

## Calculating the relative potency
SI(c.m1, c(50,50))

## Showing the relative potency as a
## function of the response level
relpot(c.m1)
relpot(c.m1, ci = "delta")
# appears constant!

## Response level in percent
relpot(c.m1, scale="percent")

## Fitting a reduced model
c.m2 <- drm(drymatter ~ dose, treatment, data = G.aparine,
pmodels = data.frame(1,treatment,1,treatment), fct = LL.4())

anova(c.m2, c.m1)

## Showing the relative potency
relpot(c.m2)

## Fitting the same model in a different parameterisation
c.m3<-drm(drymatter~dose, treatment, data=G.aparine,
pmodels=data.frame(treatment,treatment,1,treatment),fct=LL2.4())

SI(c.m3, c(50,50), logBase = exp(1))
```

**Description**

Function for showing the starting values of the model parameters used when fitting a dose-response model

**Usage**

```
getInitial(object)
```

**Arguments**

object            object of class 'drc'

**Value**

A vector of starting values for the model parameters used to initialize the estimation procedure.

**Note**

This function is masking the standard function in the stats package.

**Author(s)**

Christian Ritz

---

getMeanFunctions        *Display available dose-response models*

---

**Description**

Display information about available, built-in dose-response models.

**Usage**

```
getMeanFunctions(noParm = NA, fname = NULL, flist = NULL, display =TRUE)
```

**Arguments**

noParm	numeric specifying the number of parameters of the models to be displayed. The default (NA) results in display of all models, regardless of number of parameters.
fname	character string or vector of character strings specifying the short name(s) of the models to be displayed (need to match exactly).
flist	list of built-in functions to be displayed.
display	logical indicating whether or not the requested models should be displayed on the R console.

**Details**

The arguments `noParm` and `fname` can be combined.

**Value**

An invisible list of functions or a list of strings with brief function descriptions is returned.

**Author(s)**

Christian Ritz

**Examples**

```
## Listing all functions
getMeanFunctions()

## Listing all functions with 4 parameters
getMeanFunctions(4)

## Listing all (log-)logistic functions
getMeanFunctions(fname = "L")

## Listing all three-parameter (log-)logistic or Weibull functions
getMeanFunctions(3, fname = c("LL", "W"))

## Listing all four-parameter (log-)logistic or Weibull functions
getMeanFunctions(4, fname = c("LL", "W"))
```

---

glymet

*Glyphosate and metsulfuron-methyl tested on algae.*

---

**Description**

The dataset has 7 mixtures, 8 dilutions, two replicates and 5 common control controls. Four observations are missing, giving a total of 113 observations.

**Usage**

```
data(glymet)
```

**Format**

A data frame with 113 observations on the following 3 variables.

`dose` a numeric vector of dose values

`pct` a numeric vector denoting the grouping according to the mixtures percentages

`rgr` a numeric vector of response values (relative growth rates)

## Details

The dataset is analysed in Soerensen et al (2007). The concentration addition model can be entertained for this dataset.

## Source

The dataset is kindly provided by Nina Cedergreen, Department of Agricultural Sciences, Royal Veterinary and Agricultural University, Denmark.

## References

Soerensen, H. and Cedergreen, N. and Skovgaard, I. M. and Streibig, J. C. (2007) An isobole-based statistical model and test for synergism/antagonism in binary mixture toxicity experiments, *Environmental and Ecological Statistics*, **14**, 383–397.

## Examples

```
## Fitting the model with freely varying ED50 values
glymet.free <- drm(rgr~dose, pct, data = glymet,
fct = LL.3(), pmodels = list(~factor(pct) , ~1, ~factor(pct)))

## Lack-of-fit test
modelFit(glymet.free) # acceptable
summary(glymet.free)

## Plotting isobole structure
isobole(glymet.free, exchange=0.01)

## Fitting the concentration addition model
glymet.ca <- mixture(glymet.free, model = "CA")

## Comparing to model with freely varying e parameter
anova(glymet.ca, glymet.free) # borderline accepted

## Plotting isobole based on concentration addition
isobole(glymet.free, glymet.ca, exchange = 0.01) # acceptable fit

## Fitting the Hewlett model
glymet.hew <- mixture(glymet.free, model = "Hewlett")

### Comparing to model with freely varying e parameter
anova(glymet.ca, glymet.hew)
# borderline accepted
# the Hewlett model offers no improvement over concentration addition

## Plotting isobole based on the Hewlett model
isobole(glymet.free, glymet.hew, exchange = 0.01)
# no improvement over concentration addition
```

gompertz

*Mean function for the Gompertz dose-response or growth curve***Description**

This function provides a very general way of specifying the mean function of the decreasing or increasing Gompertz dose-response or growth curve models.

**Usage**

```
gompertz(fixed = c(NA, NA, NA, NA), names = c("b", "c", "d", "e"),
method = c("1", "2", "3", "4"), ssfct = NULL,
fctName, fctText)
```

**Arguments**

<code>fixed</code>	numeric vector. Specifies which parameters are fixed and at what value they are fixed. NAs for parameter that are not fixed.
<code>names</code>	vector of character strings giving the names of the parameters (should not contain ":"). The order of the parameters is: b, c, d, e (see under 'Details' for the precise meaning of each parameter).
<code>method</code>	character string indicating the self starter function to use.
<code>ssfct</code>	a self starter function to be used.
<code>fctName</code>	character string used internally by convenience functions (optional).
<code>fctText</code>	character string used internally by convenience functions (optional).

**Details**

The Gompertz model is given by the mean function

$$f(x) = c + (d - c)(\exp(-\exp(b(x - e))))$$

and it is a dose-response/growth curve on the entire real axis, that is it is not limited to non-negative values even though this is the range for most dose-response and growth data. One consequence is that the curve needs not reach the lower asymptote at dose 0.

If

$$b < 0$$

the mean function is increasing and it is decreasing for

$$b > 0$$

. The decreasing Gompertz model is not a well-defined dose-response model and other dose-response models such as the Weibull models should be used instead.

Various re-parameterisations of the model are used in practice.

**Value**

The value returned is a list containing the non-linear function, the self starter function and the parameter names.

**Note**

The function is for use with the function `drm`, but typically the convenience functions [G.2](#), [G.3](#), [G.3u](#), and [G.4](#) should be used.

**Author(s)**

Christian Ritz

**References**

Seber, G. A. F. and Wild, C. J. (1989) *Nonlinear Regression*, New York: Wiley & Sons (p. 331).

**See Also**

The Weibull model [weibull2](#) is closely related to the Gompertz model.

**Examples**

```
bg.m1 <- drm(weightInf~DAE, data = beetGrowth, fct = G.3())
summary(bg.m1)
plot(bg.m1)
```

---

gompertzd

*The derivative of the Gompertz function*

---

**Description**

'gompertzd' provides a way of specifying the derivative of the Gompertz function as a dose-response model.

**Usage**

```
gompertzd(fixed = c(NA, NA), names = c("a", "b"))
```

**Arguments**

fixed	numeric vector. Specifies which parameters are fixed and at what value they are fixed. NAs for parameter that are not fixed.
names	a vector of character strings giving the names of the parameters (should not contain ":"). The default is (notice the order): a, b.

**Details**

The derivative of the Gompertz function is defined as

$$f(x) = a \exp(bx - a/b(\exp(bx) - 1))$$

For  $a > 0$  and  $b$  not 0, the function is decreasing, equaling  $a$  at  $x = 0$  and approaching 0 at plus infinity.

**Value**

The value returned is a list containing the model function, the self starter function and the parameter names.

**Note**

This function is for use with the function `drm`.

**Author(s)**

Christian Ritz

---

gompGrowth

*Gompertz growth models*


---

**Description**

Gompertz growth model, with biologically meaningful parameters. Different parameterisations have been included for specific cases and needs.

**Usage**

```
gompGrowth.1(fixed = c(NA, NA, NA), names = c("c", "m", "plateau"))
gompGrowth.2(fixed = c(NA, NA, NA), names = c("c", "d", "plateau"))
gompGrowth.3(fixed = c(NA, NA, NA), names = c("b", "c", "plateau"))
```

**Arguments**

`fixed` numeric vector. Specifies which parameters are fixed and at what value they are fixed. NAs for parameter that are not fixed.

`names` vector of character strings giving the names of the parameters (should not contain ":"). The default parameter names are: init, m, plateau.

**Details**

The Gompertz growth model is a Gompertz curve, that has been reparameterised to include some biologically meaningful parameters. The mean function for `gompGrowth.1()` is:

$$f(x) = plateau * \exp(-(m/c) * \exp(-c * x))$$

The parameter `plateau` is the final plant weight, reached for  $x$  going to infinity the parameter  $c$  is relative growth rate at inflection point and the parameter  $m$  is the initial relative growth rate (when  $x=0$ ). Thus the curve is monotonously increasing in  $x$ . The mean function for `gompGrowth.2()` is:

$$f(x) = plateau * \exp(-\exp(c * (d - x)))$$

where the parameter  $c$  is the relative growth rate at inflection point and the parameter  $d$  is the abscissa of the inflection point. The mean function for `gompGrowth.3()` is the classical Gompertz function:

$$f(x) = plateau * \exp(-b * \exp(-c * x))$$

where  $b$  is proportional to the initial relative growth rate ( $m = b * c$ ).

**Value**

A list of class `drcMean`, containing the mean function, the self starter function, the parameter names.

**Note**

Growth functions are generally fitted on log-transformed weight data, which equals to setting `bc` parameter to 0

**Author(s)**

Andrea Onofri

**References**

Roderick Hunt, 1982. Plant Growth Curves. Edward Arnold Publisher, Great Britain, 248 pp

**Examples**

```
## Fitting a Gompertz growth curve

beet.model <- drm(weightInf ~ DAE, data = beetGrowth, fct=gompGrowth.1())
plot(beet.model, log = "")
summary(beet.model)
```

---

H.virescens	<i>Mortality of tobacco budworms</i>
-------------	--------------------------------------

---

### Description

For three days, moths of the tobacco budworm (*Heliothis virescens*) were exposed to doses of the pyrethroid trans-cypermethrin.

### Usage

```
data(H.virescens)
```

### Format

A data frame with 12 observations on the following 4 variables.

dose a numeric vector of dose values ( $\mu g$ )

numdead a numeric vector of dead or knocked-down moths

total a numeric vector of total number of moths

sex a factor with levels F M denoting a grouping according to sex

### Details

In Venables and Ripley (2002), these data are analysed using a logistic regression with base-2 logarithm of dose as explanatory variable.

### Source

Venables, W. N. and Ripley, B. D (2002) *Modern Applied Statistics with S*, New York: Springer (fourth edition).

### Examples

```
## Fitting dose-response model (log-logistic with common slope)
Hv.m1 <- drm(numdead/total~dose, sex, weights = total, data = H.virescens, fct = LL.2(),
pmodels = list(~1,~sex), type = "binomial")
summary(Hv.m1)

## Fitting the same model as in Venables and Riply (2002)
Hv.m2 <- glm(cbind(numdead, total-numdead)~sex+I(log2(dose))-1, data = H.virescens, family = binomial)

## Comparing the fits
logLik(Hv.m1)
logLik(Hv.m2)

## Estimated ED values (matching those given in MASS)
ED(Hv.m1, c(25, 50, 75))
```

---

heartrate

*Heart rate baroreflexes for rabbits*

---

### Description

The dataset contains measurements of mean arterial pressure (mmHG) and heart rate (b/min) for a baroreflex curve.

### Usage

```
data(heartrate)
```

### Format

A data frame with 18 observations on the following 2 variables.

pressure a numeric vector containing measurements of arterial pressure.

rate a numeric vector containing measurements of heart rate.

### Details

The dataset is an example of an asymmetric dose-response curve, that is not easily handled using the log-logistic or Weibull models ([LL.4](#), [LL.5](#), [W1.4](#) and [W2.4](#)), whereas the `baro5` model provides a nice fit.

### Source

Ricketts, J. H. and Head, G. A. (1999) A five-parameter logistic equation for investigating asymmetry of curvature in baroreflex studies, *Am. J. Physiol. (Regulatory Integrative Comp. Physiol. 46)*, **277**, 441–454.

### Examples

```
## Fitting the baro5 model
heartrate.m1 <- drm(rate~pressure, data=heartrate, fct=baro5())
plot(heartrate.m1)
```

---

isobole	<i>Creating isobolograms</i>
---------	------------------------------

---

## Description

'isobole' displays isobole based on EC/ED50 estimates from a log-logistic model. Additionally isoboles determined by the concentration addition model, Hewlett's model and Voelund's model can be added to the plot.

## Usage

```
isobole(object1, object2, exchange = 1, cifactor = 2, ename = "e", xaxis = "100", xlab, ylab, xlim, ylim,
```

## Arguments

object1	object of class 'drc' where EC/ED50 parameters vary freely.
object2	object of class 'drc' where EC/ED50 parameters vary according to Hewlett's model.
ename	character string. The name of the EC/ED50 variable.
xaxis	character string. Is the mixture "0:100" or "100:0" on the x axis?
exchange	numeric. The exchange rate between the two substances.
cifactor	numeric. The factor to be used in the confidence intervals. Default is 2, but 1 has been used in publications.
xlab	an optional label for the x axis.
ylab	an optional label for the y axis.
xlim	a numeric vector of length two, containing the lower and upper limit for the x axis.
ylim	a numeric vector of length two, containing the lower and upper limit for the y axis.
...	Additional graphical parameters.

## Details

The model fits to be supplied as first and optionally second argument are obtained using [mixture](#) and [drm](#).

## Value

No value is returned. Only used for the side effect: the isobologram shown.

## Author(s)

Christian Ritz

**See Also**

The examples in [acidiq](#), [glymet](#) and [mecter](#).

---

leaflength	<i>Leaf length of barley</i>
------------	------------------------------

---

**Description**

In an experiment barley was grown in a hydroponic solution with a herbicide.

**Usage**

```
data(leaflength)
```

**Format**

A data frame with 42 observations on the following 2 variables.

Dose a numeric vector

DW a numeric vector

**Details**

The dataset exhibits a large hormetical effect.

**Source**

Nina Cedergreen, Royal Veterinary and Agricultural University, Denmark.

**Examples**

```
## Fitting a hormesis model
leaflength.crs4c1 <- drm(DW ~ Dose, data = leaflength, fct = CRS.4c())
plot(fitted(leaflength.crs4c1), residuals(leaflength.crs4c1))

leaflength.crs4c2 <- boxcox(drm(DW ~ Dose, data = leaflength, fct = CRS.4c()), method = "anova", plotit = FALSE)
summary(leaflength.crs4c2)

## Plottinf fitted curve and original data
plot(leaflength.crs4c2, broken = TRUE, conLevel = 0.001, type = "all", legend = FALSE,
     ylab = "Produced leaf length (cm)", xlab = "Metsulfuron-methyl (mg/l)",
     main = "Hormesis: leaf length of barley")
```

---

lepidium	<i>Dose-response profile of degradation of agrochemical using lepidium</i>
----------	--

---

**Description**

Estimation of the degradation profile of an agrochemical based on soil samples at depth 0-10cm from a calibration experiment.

**Usage**

```
data(lepidium)
```

**Format**

A data frame with 42 observations on the following 2 variables.

conc a numeric vector of concentrations (g/ha)

weight a numeric vector of plant weight (g) after 3 weeks' growth

**Details**

It is an experiment with seven concentrations and six replicates per concentration. *Lepidium* is rather robust as it only responds to high concentrations.

**Source**

Racine-Poon, A. (1988) A Bayesian Approach to Nonlinear Calibration Problems, *J. Am. Statist. Ass.*, **83**, 650–656.

**Examples**

```
lepidium.m1 <- drm(weight~conc, data=lepidium, fct = LL.4())  
modelFit(lepidium.m1)  
plot(lepidium.m1, type = "all", log = "")
```

---

lettuce

*Isobutylalcohol in nutrient solution in which lettuce plants were grown*

---

### Description

Data are from an experiment where isobutylalcohol was dissolved in a nutrient solution in which lettuce (*Lactuca sativa*) plants were grown. The plant biomass of the shoot was determined af 21 days.

### Usage

```
data(lettuce)
```

### Format

A data frame with 14 observations on the following 2 variables.

**conc** a numeric vector of concentrations of isobutylalcohol (mg/l)

**weight** a numeric vector of biomass of shoot (g)

### Details

The data set illustrates hormesis, presence of a subtoxic stimulus at low concentrations.

### Source

van Ewijk, P. H. and Hoekstra, J. A. (1993) Calculation of the EC50 and its Confidence Interval When Subtoxic Stimulus Is Present, *ECOTOXICOLOGY AND ENVIRONMENTAL SAFETY*, **25**, 25–32.

### References

van Ewijk, P. H. and Hoekstra, J. A. (1994) Curvature Measures and Confidence Intervals for the Linear Logistic Model, *Appl. Statist.*, **43**, 477–487.

### Examples

```
## Look at data
lettuce

## Monotonous dose-response model
lettuce.m1 <- drm(weight~conc, data=lettuce, fct=LL.3())

plot(lettuce.m1, broken = TRUE)

## Model fit in van Ewijk and Hoekstra (1994)
lettuce.m2 <- drm(weight~conc, data=lettuce, fct=BC.4())
modelFit(lettuce.m2)
```

```

plot(lettuce.m2, add = TRUE, broken = TRUE, type = "none", lty = 2)

## Hormesis effect only slightly significant
summary(lettuce.m2)

## Hormesis effect highly significant
## compare with t-test
anova(lettuce.m1, lettuce.m2)

```

---

lin.test

*Lack-of-fit test for the mean structure based on cumulated residuals*


---

### Description

The function provides a lack-of-fit test for the mean structure based on cumulated residuals from the model fit.

### Usage

```
lin.test(object, nokSim = 20, seed = 20070325, plotit = TRUE, log = "", bp = 0.01, xlab, ylab, ylim, ..
```

### Arguments

object	object of class 'drc'.
nokSim	numeric specifying the number of simulations used to obtain the p-value.
seed	numeric specifying the seed value for the random number generator.
plotit	logical indicating whether or not the observed cumulated residual process should be plotted. Default is to plot the process.
log	character string which should contains "x" if the x axis is to be logarithmic, "y" if the y axis is to be logarithmic and "xy" or "yx" if both axes are to be logarithmic. The default is "x". The empty string "" yields the original axes.
bp	numeric value specifying the break point below which the dose is zero (the amount of stretching on the dose axis above zero in order to create the visual illusion of a logarithmic scale <i>including</i> 0).
xlab	string character specifying an optional label for the x axis.
ylab	character string specifying an optional label for the y axis.
ylim	numeric vector of length two, containing the lower and upper limit for the y axis.
...	additional arguments to be passed further to the basic <a href="#">plot</a> method.

### Details

The function provides a graphical model checking of the mean structure in a dose-response model. The graphical display is supplemented by a p-value based on a supremum-type test.

The test is applicable even in cases where data are non-normal or exhibit variance heterogeneity.

**Value**

A p-value for test of the null hypothesis that the mean structure is appropriate. Ritz and Martinussen (2009) provide the details.

**Author(s)**

Christian Ritz

**References**

Ritz, C and Martinussen, T. (2009) Lack-of-fit tests for assessing mean structures for continuous dose-response data, *Submitted manuscript*

**See Also**

Other available lack-of-fit tests are the Neill test ([neill.test](#)) and ANOVA-based test ([modelFit](#)).

**Examples**

```
## Fitting a log-logistic model to the dataset 'etmotc'
etmotc.m1<-drm(rgr1~dose1, data=etmotc[1:15,], fct=LL.4())

## Test based on umulated residuals
lin.test(etmotc.m1, 1000)
#lin.test(etmotc.m1, 10000, plotit = FALSE) # more precise

## Fitting an exponential model to the dataset 'O.mykiss'
O.mykiss.m1<-drm(weight~conc, data=O.mykiss, fct=EXD.2(), na.action=na.omit)

## ANOVA-based test
modelFit(O.mykiss.m1)

## Test based on umulated residuals
lin.test(O.mykiss.m1, log = "", cl = 0.2, xlab = "Dose (mg/l)", main = "B", ylim = c(-0.6, 0.6))
#lin.test(O.mykiss.m1, nokSim = 10000, plotit = FALSE) # more precise
```

**Description**

'LL.2' and 'LL2.2' provide the two-parameter log-logistic function where the lower limit is fixed at 0 and the upper limit is fixed at 1, mostly suitable for binomial/quantal responses.

**Usage**

```
LL.2(upper = 1, fixed = c(NA, NA), names = c("b", "e"), ...)
```

```
l2(upper = 1, fixed = c(NA, NA), names = c("b", "e"), ...)
```

```
LL2.2(upper = 1, fixed = c(NA, NA), names = c("b", "e"), ...)
```

**Arguments**

upper	numeric value. The fixed, upper limit in the model. Default is 1.
fixed	numeric vector. Specifies which parameters are fixed and at what value they are fixed. NAs for parameter that are not fixed.
names	a vector of character strings giving the names of the parameters. The default is reasonable.
...	Additional arguments (see <a href="#">llogistic</a> ).

**Details**

The two-parameter logistic function is given by the expression

$$f(x) = \frac{1}{1 + \exp(b(\log(x) - \log(e)))}$$

or in another parameterisation

$$f(x) = \frac{1}{1 + \exp(b(\log(x) - e))}$$

The function is symmetric about the inflection point ( $e$ ).

**Value**

See [llogistic](#).

**Note**

This function is for use with the function [drm](#).

**Author(s)**

Christian Ritz

**See Also**

Related functions are [LL.3](#), [LL.4](#), [LL.5](#) and the more general [llogistic](#).

## Examples

```
## Fitting a two-parameter logistic model
## to binomial responses (a logit model)
earthworms.m1 <- drm(number/total~dose, weights=total,
  data = earthworms, fct = LL.2(), type = "binomial")

plot(earthworms.m1) # not fitting at the upper limit!
```

---

 LL.3

*The three-parameter log-logistic function*


---

## Description

'LL.3' and 'LL2.3' provide the three-parameter log-logistic function where the lower limit is equal to 0.

'LL.3u' and 'LL2.3u' provide three-parameter logistic function where the upper limit is equal to 1, mainly for use with binomial/quantal response.

## Usage

```
LL.3(fixed = c(NA, NA, NA), names = c("b", "d", "e"), ...)
```

```
LL.3u(upper = 1, fixed = c(NA, NA, NA), names = c("b", "c", "e"), ...)
```

```
l3(fixed = c(NA, NA, NA), names = c("b", "d", "e"), ...)
```

```
l3u(upper = 1, fixed = c(NA, NA, NA), names = c("b", "c", "e"), ...)
```

```
LL2.3(fixed = c(NA, NA, NA), names = c("b", "d", "e"), ...)
```

```
LL2.3u(upper = 1, fixed = c(NA, NA, NA), names = c("b", "c", "e"), ...)
```

## Arguments

upper	numeric value. The fixed, upper limit in the model. Default is 1.
fixed	numeric vector. Specifies which parameters are fixed and at what value they are fixed. NAs for parameter that are not fixed.
names	a vector of character strings giving the names of the parameters. The default is reasonable.
...	Additional arguments (see <a href="#">llogistic</a> ).

**Details**

The three-parameter logistic function with lower limit 0 is

$$f(x) = 0 + \frac{d - 0}{1 + \exp(b(\log(x) - \log(e)))}$$

or in another parameterisation

$$f(x) = 0 + \frac{d - 0}{1 + \exp(b(\log(x) - e))}$$

The three-parameter logistic function with upper limit 1 is

$$f(x) = c + \frac{1 - c}{1 + \exp(b(\log(x) - \log(e)))}$$

or in another parameterisation

$$f(x) = c + \frac{1 - c}{1 + \exp(b(\log(x) - e))}$$

Both functions are symmetric about the inflection point ( $e$ ).

**Value**

See [llogistic](#).

**Note**

This function is for use with the function [drm](#).

**Author(s)**

Christian Ritz

**References**

Finney, D. J. (1971) *Probit Analysis*, Cambridge: Cambridge University Press.

**See Also**

Related functions are [LL.2](#), [LL.4](#), [LL.5](#) and the more general [llogistic](#).

**Examples**

```
## Fitting model with lower limit equal 0
ryegrass.model1 <- drm(root1 ~ conc, data = ryegrass, fct = LL.3())
summary(ryegrass.model1)

## Fitting binomial response
```

```
## with non-zero control response

## Example dataset from Finney (1971) - example 19
logdose <- c(2.17, 2, 1.68, 1.08, -Inf, 1.79, 1.66, 1.49, 1.17, 0.57)
n <- c(142, 127, 128, 126, 129, 125, 117, 127, 51, 132)
r <- c(142, 126, 115, 58, 21, 125, 115, 114, 40, 37)
treatment <- factor(c("w213", "w213", "w213", "w213",
"control", "w214", "w214", "w214", "w214", "w214"))
finney.ex19 <- data.frame(logdose, n, r, treatment)

## Fitting model where the lower limit is estimated
fe19.model1 <- drm(r/n~logdose, treatment, weights = n, data = finney.ex19,
logDose = 10, fct = LL.3u(), type="binomial",
pmodels = data.frame(treatment, 1, treatment))

summary(fe19.model1)
modelFit(fe19.model1)
plot(fe19.model1, ylim = c(0, 1.1), bp = -1, broken = TRUE, legendPos = c(0, 1))
abline(h = 1, lty = 2)
```

---

LL.4

*The four-parameter log-logistic function*


---

### Description

'LL.4' and 'LL2.4' provide the four-parameter log-logistic function, self starter function, names of the parameters and, optionally, first and second derivatives for a faster estimation.

### Usage

```
LL.4(fixed = c(NA, NA, NA, NA), names = c("b", "c", "d", "e"), ...)
```

```
l4(fixed = c(NA, NA, NA, NA), names = c("b", "c", "d", "e"), ...)
```

```
LL2.4(fixed = c(NA, NA, NA, NA), names = c("b", "c", "d", "e"), ...)
```

### Arguments

fixed	numeric vector. Specifies which parameters are fixed and at what value they are fixed. NAs for parameter that are not fixed.
names	a vector of character strings giving the names of the parameters. The default is reasonable.
...	Additional arguments (see <a href="#">llogistic</a> ).

**Details**

The four-parameter log-logistic function is given by the expression

$$f(x) = c + \frac{d - c}{1 + \exp(b(\log(x) - \log(e)))}$$

or in another parameterisation (converting the term  $\log(e)$  into a parameter)

$$f(x) = c + \frac{d - c}{1 + \exp(b(\log(x) - \bar{e}))}$$

The function is symmetric about the inflection point ( $e$ ).

**Value**

See [llogistic](#).

**Note**

This function is for use with the function [drm](#).

**Author(s)**

Christian Ritz and Jens C. Streibig

**References**

Seber, G. A. F. and Wild, C. J (1989) *Nonlinear Regression*, New York: Wiley & Sons (p. 330).

**See Also**

Setting  $c = 0$  yields [LL.3](#). See also [LL.5](#).

**Examples**

```
spinach.m1 <- drm(SLOPE~DOSE, CURVE, data = spinach, fct = LL.4())
spinach.m1

rm(model1)
```

LL.5

*The five-parameter log-logistic function***Description**

'LL.5' and 'LL2.5' provide the five-parameter log-logistic function, self starter function and names of the parameters.

**Usage**

```
LL.5(fixed = c(NA, NA, NA, NA, NA), names = c("b", "c", "d", "e", "f"), ...)
```

```
l5(fixed = c(NA, NA, NA, NA, NA), names = c("b", "c", "d", "e", "f"), ...)
```

```
LL2.5(fixed = c(NA, NA, NA, NA, NA), names = c("b", "c", "d", "e", "f"), ...)
```

**Arguments**

<code>fixed</code>	numeric vector. Specifies which parameters are fixed and at what value they are fixed. NAs for parameter that are not fixed.
<code>names</code>	a vector of character strings giving the names of the parameters. The default is reasonable.
<code>...</code>	Additional arguments (see <a href="#">llogistic</a> ).

**Details**

The five-parameter logistic function is given by the expression

$$f(x) = c + \frac{d - c}{(1 + \exp(b(\log(x) - \log(e))))^f}$$

or in another parameterisation

$$f(x) = c + \frac{d - c}{(1 + \exp(b(\log(x) - e)))^f}$$

The function is asymmetric for  $f$  different from 1.

**Value**

See [llogistic](#).

**Note**

This function is for use with the function [drm](#).

**Author(s)**

Christian Ritz

**References**

Finney, D. J. (1979) Bioassay and the Practise of Statistical Inference, *Int. Statist. Rev.*, **47**, 1–12.

**See Also**

Related functions are [LL.4](#) and [LL.3](#).

**Examples**

```
ryegrass.m1 <- drm(root1 ~ conc, data = ryegrass, fct = LL.5())
summary(ryegrass.m1)
```

---

llogistic

*The log-logistic function*


---

**Description**

'llogistic' provides a very general way of specifying log-logistic models, under various constraints on the parameters.

**Usage**

```
llogistic(fixed = c(NA, NA, NA, NA, NA),
names = c("b", "c", "d", "e", "f"),
method = c("1", "2", "3", "4"), ssfct = NULL,
fctName, fctText)
```

```
llogistic2(fixed = c(NA, NA, NA, NA, NA),
names = c("b", "c", "d", "e", "f"),
ss = c("1", "2", "3"), ssfct = NULL,
fctName, fctText)
```

**Arguments**

fixed	numeric vector. Specifies which parameters are fixed and at what value they are fixed. NAs for parameter that are not fixed.
names	a vector of character strings giving the names of the parameters (should not contain ":"). The default is reasonable (see under 'Usage'). The order of the parameters is: b, c, d, e, f (see under 'Details').
method	character string indicating the self starter function to use.
ss	character string indicating the self starter function to use.
ssfct	a self starter function to be used.
fctName	optional character string used internally by convenience functions.
fctText	optional character string used internally by convenience functions.

**Details**

The default arguments yields the five-parameter log-logistic function given by the expression

$$f(x) = c + \frac{d - c}{(1 + \exp(b(\log(x) - \log(e))))^f}$$

If the parameter  $f$  differs from 1 then the function is asymmetric; otherwise it is symmetric (on log scale). This function is fitted using [llogistic](#).

The log-logistic function with  $\log(e)$  rather than  $e$  as a parameter, that is using the parameterisation

$$f(x) = c + \frac{d - c}{(1 + \exp(b(\log(x) - e)))^f}$$

is fitted using [llogistic2](#).

Sometimes the log-logistic models are also called Hill models.

**Value**

The value returned is a list containing the nonlinear function, the self starter function and the parameter names.

**Note**

The functions are for use with the function [drm](#).

**Author(s)**

Christian Ritz

**References**

- Finney, D. J. (1979) Bioassay and the Practise of Statistical Inference, *Int. Statist. Rev.*, **47**, 1–12.  
 Seber, G. A. F. and Wild, C. J. (1989) *Nonlinear Regression*, New York: Wiley & Sons (p. 330).

**See Also**

For convenience several special cases are available: [LL.2](#), [LL.3](#), [LL.4](#) and [LL.5](#). Examples are provided in the help pages for these functions.

---

Inormal	<i>Log-normal dose-response model</i>
---------	---------------------------------------

---

### Description

Inormal and the accompanying convenience functions provide a general framework for specifying the mean function of the decreasing or increasing log-normal dose-response model.

### Usage

```
Inormal(fixed = c(NA, NA, NA, NA), names = c("b", "c", "d", "e"),
method = c("1", "2", "3", "4"), ssfct = NULL,
fctName, fctText, loge = FALSE)
```

```
LN.2(upper = 1, fixed = c(NA, NA), names = c("b", "e"), ...)
```

```
LN.3(fixed = c(NA, NA, NA), names = c("b", "d", "e"), ...)
```

```
LN.3u(upper = 1, fixed = c(NA, NA, NA), names = c("b", "c", "e"), ...)
```

```
LN.4(fixed = c(NA, NA, NA, NA), names = c("b", "c", "d", "e"), ...)
```

### Arguments

fixed	numeric vector. Specifies which parameters are fixed and at what value they are fixed. NAs for parameter that are not fixed.
names	vector of character strings giving the names of the parameters (should not contain ":"). The default is reasonable (see under 'Usage'). The order of the parameters is: b, c, d, e, f (see under 'Details' for the precise meaning of each parameter).
method	character string indicating the self starter function to use.
ssfct	a self starter function to be used.
fctName	character string used internally by convenience functions (optional).
fctText	character string used internally by convenience functions (optional).
loge	logical indicating whether or not ED50 or log(ED50) should be a parameter in the model. By default ED50 is a model parameter.
upper	numeric specifying the upper horizontal asymptote in the convenience function. The default is 1.
...	additional arguments to be passed from the convenience functions to Inormal.

**Details**

For the case where  $\log(\text{ED50})$ , denoted  $e$  in the equation below, is a parameter in the model, the mean function is:

$$f(x) = c + (d - c)(\Phi(b(\log(x) - e)))$$

and the mean function is:

$$f(x) = c + (d - c)(\Phi(b(\log(x) - \log(e))))$$

in case ED50, which is also denoted  $e$ , is a parameter in the model. If the former model is fitted any estimated ED values will need to be back-transformed subsequently in order to obtain effective doses on the original scale.

The mean functions above yield the same models as those described by Bruce and Versteeg (1992), but in a different parameterisations (among other things the natural logarithm is used).

For the case  $c = 0$  and  $d = 1$ , the log-normal model reduces the classic probit model (Finney, 1971) with log dose as explanatory variable (mostly used for quantal data). This special case is available through the convenience function LN. 2.

The case  $c = 0$  is available as the function LN. 3, whereas the LN. 3u corresponds to the special case where the upper horizontal asymptote is fixed (default is 1). The full four-parameter model is available through LN. 4.

**Value**

The value returned is a list containing the non-linear function, the self starter function and the parameter names.

**Note**

The function is for use with the function `drm`, but typically the convenience functions `link{LN. 2}`, `link{LN. 3}`, `link{LN. 3u}`, and `link{LN. 4}` should be used.

**Author(s)**

Christian Ritz

**References**

- Finney, D. J. (1971) *Probit analysis*, London: Cambridge University Press.
- Bruce, R. D. and Versteeg, D. J. (1992) A statistical procedure for modeling continuous toxicity data, *Environ. Toxicol. Chem.*, **11**, 1485–1494.

**See Also**

The log-logistic model (`llogistic`) is very similar to the log-normal model at least in the middle, but they may differ in the tails and thus provide different estimates of low effect concentrations EC/ED.

Examples are provided in the help pages of the datasets [S.capricornutum](#), [P.promelas](#), and [M.bahia](#).

logistic

*The logistic model***Description**

The general asymmetric five-parameter logistic model for describing dose-response relationships.

**Usage**

```
logistic(fixed = c(NA, NA, NA, NA, NA), names = c("b", "c", "d", "e", "f"),
method = c("1", "2", "3", "4"), ssfct = NULL,
fctName, fctText)
```

```
L.3(fixed = c(NA, NA, NA), names = c("b", "d", "e"), ...)
```

```
L.4(fixed = c(NA, NA, NA, NA), names = c("b", "c", "d", "e"), ...)
```

```
L.5(fixed = c(NA, NA, NA, NA, NA), names = c("b", "c", "d", "e", "f"), ...)
```

**Arguments**

fixed	numeric vector. Specifies which parameters are fixed and at what value they are fixed. NAs for parameter that are not fixed.
names	a vector of character strings giving the names of the parameters (should not contain ":"). The order of the parameters is: b, c, d, e, f (see under 'Details').
method	character string indicating the self starter function to use.
ssfct	a self starter function to be used.
fctName	optional character string used internally by convenience functions.
fctText	optional character string used internally by convenience functions.
...	Additional arguments (see <a href="#">llogistic</a> ).

**Details**

The default arguments yields the five-parameter logistic mean function given by the expression

$$f(x) = c + \frac{d - c}{(1 + \exp(b(x - e)))^f}$$

The model is different from the log-logistic models [llogistic](#) and [llogistic2](#) where the term

$$\log(x)$$

is used instead of

$$x$$

.

The model is sometimes referred to as the Boltzmann model.

### Value

The value returned is a list containing the nonlinear function, the self starter function and the parameter names.

### Author(s)

Christian Ritz

### Examples

```
## Fitting the four-parameter logistic model
ryegrass.m1 <- drm(root1 ~ conc, data = ryegrass, fct = L.4())
summary(ryegrass.m1)

## Fitting an asymmetric logistic model
## requires installing the package 'NISTnls'
# Ratkowsky3.m1 <- drm(y~x, data = Ratkowsky3,
# fct = L.5(fixed = c(NA, 0, NA, NA, NA)))
# plot(Ratkowsky3.m1)
# summary(Ratkowsky3.m1)
## okay agreement with NIST values
## for the two parameters that are the same
```

---

logLik.drc

*Extracting the log likelihood*

---

### Description

logLik extracts the value of the log likelihood function evaluated at the parameter estimates.

### Usage

```
## S3 method for class 'drc'
logLik(object, ...)
```

### Arguments

object            an object of class 'drc'.  
 ...                additional arguments.

**Value**

The evaluated log likelihood as a numeric value and the corresponding degrees of freedom as well as the number of observations as attributes.

**Note**

The value of the log likelihood could be used to compare model fits of the same data based on different dose-response models or based on the same model but fitted different algorithms, software programmes, or starting values. For comparisons: Larger is better.

**Author(s)**

Christian Ritz

**Examples**

```
## Fitting a four-parameter log-logistic model
ryegrass.m1 <- drm(root1 ~conc, data = ryegrass, fct = LL.4())
logLik(ryegrass.m1)
```

---

M.bahia

*Effect of an effluent on the growth of mysid shrimp*

---

**Description**

Juvenile mysid shrimp (*Mysidopsis bahia*) were exposed to up to 32% effluent in a 7-day survival and growth test. The average weight per treatment replicate of surviving organisms was measured.

**Usage**

```
data(M.bahia)
```

**Format**

A data frame with 40 observations on the following 2 variables.

conc a numeric vector of effluent concentrations (%)

dryweight a numeric vector of average dry weights (mg)

**Details**

The data are analysed in Bruce and Versteeg (1992) using a log-normal dose-response model (using the logarithm with base 10).

At 32% there was complete mortality, and this justifies using a model where a lower asymptote of 0 is assumed.

**Source**

Bruce, R. D. and Versteeg, D. J. (1992) A statistical procedure for modeling continuous toxicity data, *Environ. Toxicol. Chem.*, **11**, 1485–1494.

**Examples**

```
M.bahia.m1 <- drm(dryweight~conc, data=M.bahia, fct=LN.3())

## Variation increasing
plot(fitted(M.bahia.m1), residuals(M.bahia.m1))

## Using transform-both-sides approach
M.bahia.m2 <- boxcox(M.bahia.m1, method = "anova")
summary(M.bahia.m2) # logarithm transformation

## Variation roughly constant, but still not a great fit
plot(fitted(M.bahia.m2), residuals(M.bahia.m2))

## Visual comparison of fits
plot(M.bahia.m1, type="all", broken=TRUE)
plot(M.bahia.m2, add=TRUE, type="none", broken=TRUE, lty=2)

ED(M.bahia.m2, c(10,20,50), ci="fls")

## A better fit
M.bahia.m3 <- boxcox(update(M.bahia.m1, fct = LN.4()), method = "anova")
#plot(fitted(M.bahia.m3), residuals(M.bahia.m3))
plot(M.bahia.m3, add=TRUE, type="none", broken=TRUE, lty=3, col=2)
ED(M.bahia.m3, c(10,20,50), ci="fls")
```

---

maED

*Estimation of ED values using model-averaging*


---

**Description**

Estimates and confidence intervals for ED values are estimated using model-averaging.

**Usage**

```
maED(object, fctList = NULL, respLev, interval = c("none", "buckland", "kang"), linreg = FALSE,
      clevel = NULL, level = 0.95, type = c("relative", "absolute"), display = TRUE, na.rm = FALSE, extended =
```

**Arguments**

**object**            an object of class 'drc'.  
**fctList**            a list of non-linear functions to be compared.

respLev	a numeric vector containing the response levels.
interval	character string specifying the type of confidence intervals to be supplied. The default is "none". The choices "buckland" and "kang" are explained in the Details section.
linreg	logical indicating whether or not additionally a simple linear regression model should be fitted.
clevel	character string specifying the curve id in case on estimates for a specific curve or compound is requested. By default estimates are shown for all curves.
level	numeric. The level for the confidence intervals. The default is 0.95.
type	character string. Whether the specified response levels are absolute or relative (default).
display	logical. If TRUE results are displayed. Otherwise they are not (useful in simulations).
na.rm	logical indicating whether or not NA occurring during model fitting should be left out of subsequent calculations.
extended	logical specifying whether or not an extended output (including fit summaries) should be returned.

### Details

Model-averaging of individual estimates is carried out as described by Buckland *et al.* (1997) and Kang *et al.* (2000) using AIC-based weights. The two approaches differ w.r.t. the calculation of confidence intervals: Buckland *et al.* (1997) provide an approximate variance formula under the assumption of perfectly correlated estimates (so, confidence intervals will tend to be too wide), whereas Kang *et al.* (2000) use the model weights to calculate confidence limits as weighted means of the confidence limits for the individual fits.

### Value

A matrix with two or more columns, containing the estimates and the corresponding estimated standard errors and possibly lower and upper confidence limits.

### Author(s)

Christian Ritz

### References

- Buckland, S. T. and Burnham, K. P. and Augustin, N. H. (1997) Model Selection: An Integral Part of Inference, *Biometrics* **53**, 603–618.
- Kang, Seung-Ho and Kodell, Ralph L. and Chen, James J. (2000) Incorporating Model Uncertainties along with Data Uncertainties in Microbial Risk Assessment, *Regulatory Toxicology and Pharmacology* **32**, 68–72.

### See Also

The function `mselect` provides a summary of fit statistics for several models fitted to the same data.

**Examples**

```

## Fitting an example dose-response model
ryegrass.m1 <- drm(root1~conc, data = ryegrass, fct = LL.4())

## Comparing models (showing the AIC values)
mselect(ryegrass.m1, list(LL.5(), LN.4(), W1.4(), W2.4(), FPL.4(-1,1), FPL.4(-2,3), FPL.4(-0.5,0.5)))

## Doing the actual model-averaging
maED(ryegrass.m1, list(LL.5(), LN.4(), W1.4(), W2.4(), FPL.4(-1,1), FPL.4(-2,3), FPL.4(-0.5,0.5)),
c(10, 50, 90))

## With confidence intervals according to Buckland et al. (1997)
maED(ryegrass.m1, list(LL.5(), LN.4(), W1.4(), W2.4(), FPL.4(-1,1), FPL.4(-2,3), FPL.4(-0.5,0.5)),
c(10, 50, 90), "buckland")

## With confidence intervals according to Kang et al. (2000)
maED(ryegrass.m1, list(LL.5(), LN.4(), W1.4(), W2.4(), FPL.4(-1,1), FPL.4(-2,3), FPL.4(-0.5,0.5)),
c(10, 50, 90), "kang")

## Comparing to model-averaged ED values with simple linear regression included
maED(ryegrass.m1, list(LL.5(), LN.4(), W1.4(), W2.4(), FPL.4(-1,1), FPL.4(-2,3), FPL.4(-0.5,0.5)),
c(10, 50, 90), interval = "buckland", linreg = TRUE)

## Example with a model fit involving two compounds/curves
S.alba.m1 <- drm(DryMatter~Dose, Herbicide, data=S.alba, fct = LL.4(),
pmodels=data.frame(Herbicide,1,1,Herbicide))

## Model-averaged ED50 for both compounds
maED(S.alba.m1, list(LL.3(), LN.4()), 50)

## Model-averaged ED50 only for one compound (glyphosate)
maED(S.alba.m1, list(LL.3(), LN.4()), 50, clevel="Glyphosate")

## With confidence intervals
maED(S.alba.m1, list(LL.3(), LN.4()), 50, interval="buckland")

## For comparison model-specific confidence intervals
ED(S.alba.m1, 50, interval="delta") # wider!

```

---

MAX

*Maximum mean response*


---

**Description**

MAX estimates the maximum mean response and the dose at which it occurs.

**Usage**

```
MAX(object, lower = 1e-3, upper = 1000, pool = TRUE)
```

**Arguments**

object	an object of class 'drc'.
lower	numeric. Lower limit for bisection method. Need to be smaller than EDx level to be calculated.
upper	numeric. Upper limit for bisection method. Need to be larger than EDx level to be calculated.
pool	logical. If TRUE curves are pooled. Otherwise they are not. This argument only works for models with independently fitted curves as specified in <a href="#">drm</a> .

**Details**

This function is only implemented for the built-in functions of class [braincousens](#) and [cedergreen](#).

This function was used for obtaining the results on hormesis effect size reported in Cedergreen et al. (2005).

**Value**

A matrix with one row per curve in the data set and two columns: one containing the dose at which the maximum occurs and one containing the corresponding maximum response.

**Author(s)**

Christian Ritz

**References**

Cedergreen, N. and Ritz, C. and Streibig, J. C. (2005) Improved empirical models describing hormesis, *Environmental Toxicology and Chemistry* **24**, 3166–3172.

**Examples**

```
## Fitting a Cedergreen-Ritz-Streibig model
lettuce.m1 <- drm(weight~conc, data = lettuce, fct = CRS.4c())

## Finding maximum average response and the corresponding dose
MAX(lettuce.m1)
```

---

mecter

*Mechlorprop and terbythylazine tested on Lemna minor*


---

### Description

Data consist of 5 mixture, 6 dilutions, three replicates, and 12 common controls; in total 102 observations.

### Usage

```
data(mecter)
```

### Format

A data frame with 102 observations on the following 3 variables.

dose a numeric vector of dose values

pct a numeric vector denoting the grouping according to the mixtures percentages

rgr a numeric vector of response values (relative growth rates)

### Details

The dataset is analysed in Soerensen et al (2007). The asymmetric Voelund model is appropriate, whereas the symmetric Hewlett model is not.

### Source

The dataset is kindly provided by Nina Cedergreen, Department of Agricultural Sciences, Royal Veterinary and Agricultural University, Denmark.

### References

Soerensen, H. and Cedergreen, N. and Skovgaard, I. M. and Streibig, J. C. (2007) An isobole-based statistical model and test for synergism/antagonism in binary mixture toxicity experiments, *Environmental and Ecological Statistics*, **14**, 383–397.

### Examples

```
## Fitting the model with freely varying ED50 values
mecter.free <- drm(rgr ~ dose, pct, data = mecter,
  fct = LL.4(), pmodels = list(~1, ~1, ~1, ~factor(pct) - 1))

## Lack-of-fit test
modelFit(mecter.free) # not really acceptable
summary(mecter.free)

## Plotting isobole structure
```

```
isobole(mecter.free, exchange = 0.02)

## Fitting the concentration addition model
mecter.ca <- mixture(mecter.free, model = "CA")

## Comparing to model with freely varying e parameter
anova(mecter.ca, mecter.free) # rejected

## Plotting isobole based on concentration addition
isobole(mecter.free, mecter.ca, exchange = 0.02) # poor fit

## Fitting the Hewlett model
mecter.hew <- mixture(mecter.free, model = "Hewlett")

## Comparing to model with freely varying e parameter
anova(mecter.hew, mecter.free) # rejected

## Plotting isobole based on the Hewlett model
isobole(mecter.free, mecter.hew, exchange = 0.02) # poor fit

## Fitting the Voelund model
mecter.voe<-mixture(mecter.free, model = "Voelund")

## Comparing to model with freely varying e parameter
anova(mecter.voe, mecter.free) # accepted

## Plotting isobole based on the Voelund model
isobole(mecter.free, mecter.voe, exchange = 0.02) # good fit
```

---

methionine

*Weight gain for different methionine sources*

---

### **Description**

Data consist of average body weight gain of chickens being treated with one of the two methionine sources DLM and HMTBA.

### **Usage**

```
data(methionine)
```

### **Format**

A data frame with 9 observations on the following 3 variables:

product a factor with levels control, DLM and MHA denoting the treatments

dose a numeric vector of methionine dose

gain a numeric vector of average body weight gain

**Details**

The dataset contains a common control measurement for the two treatments. More examples using this dataset are found under [AR. 2](#) and [MM. 2](#).

**Source**

Kratzer. D. D. and Littell, R. C. (2006) Appropriate Statistical Methods to Compare Dose Responses of Methionine Sources, *Poultry Science*, **85**, 947–954.

**Examples**

```
## Fitting model with constraint on one parameter
met.ar.m1 <- drm(gain~dose, product, data = methionine,
fct = AR.3(), pmodels = list(~1, ~factor(product), ~factor(product)),
upper1 = c(Inf, Inf, 1700, Inf, Inf))

plot(met.ar.m1, xlim=c(0,0.3), ylim=c(1450, 1800))
abline(h=1700, lty=1)

summary(met.ar.m1)
```

---

mixture

*Fitting mixture models*


---

**Description**

'mixture' fits a concentration addition, Hewlett or Voelund model to data from mixture toxicity experiments.

**Usage**

```
mixture(object, model = c("CA", "Hewlett", "Voelund"), start, startm, control = drmc())
```

**Arguments**

object	object of class 'drc' corresponding to the model with freely varying EC50 values.
model	character string. It can be "CA", "Hewlett" or "Voelund".
start	optional numeric vector supplying starting values for all parameters in the mixture model.
startm	optional numeric vector supplying the lambda parameter in the Hewlett model or the eta parameters (two parameters) in the Voelund model.
control	list of arguments controlling constrained optimisation (zero as boundary), maximum number of iteration in the optimisation, relative tolerance in the optimisation, warnings issued during the optimisation.

**Details**

The function is a wrapper to [drm](#), implementing the models described in Soerensen et al. (2007). See the paper for a discussion of the merits of the different models.

Currently only the log-logistic models are available. Application of Box-Cox transformation is not yet available.

**Value**

An object of class 'drc' with a few additional components.

**Author(s)**

Christian Ritz

**References**

Soerensen, H. and Cedergreen, N. and Skovgaard, I. M. and Streibig, J. C. (2007) An isobole-based statistical model and test for synergism/antagonism in binary mixture toxicity experiments, *Environmental and Ecological Statistics*, **14**, 383–397.

**See Also**

The examples in [acidiq](#) (the Hewlett model), [glymet](#) (concentration addition) and [mecter](#) (the Voelund model).

---

MM

*Michaelis-Menten model*


---

**Description**

The functions can be used to fit (shifted) Michaelis-Menten models that are used for modeling enzyme kinetics, weed densities etc.

**Usage**

```
MM.2(fixed = c(NA, NA), names = c("d", "e"), ...)
```

```
MM.3(fixed = c(NA, NA, NA), names = c("c", "d", "e"), ...)
```

**Arguments**

fixed	numeric vector. Specifies which parameters are fixed and at what value they are fixed. NAs for parameter that are not fixed.
names	a vector of character strings giving the names of the parameters (should not contain ":").
...	additional arguments from convenience functions to <a href="#">llogistic</a> .

**Details**

The model is defined by the three-parameter model function

$$f(x, (c, d, e)) = c + \frac{d - c}{1 + (e/x)}$$

It is an increasing as a function of the dose  $x$ , attaining the lower limit  $c$  at dose 0 ( $x = 0$ ) and the upper limit  $d$  for infinitely large doses. The parameter  $e$  corresponds to the dose yielding a response halfway between  $c$  and  $d$ .

The common two-parameter Michaelis-Menten model (MM.2) is obtained by setting  $e$  equal to 0.

**Value**

A list of class `drcMean`, containing the mean function, the self starter function, the parameter names and other components such as derivatives and a function for calculating ED values.

**Note**

At the moment the implementation cannot deal with infinite concentrations.

**Author(s)**

Christian Ritz

**See Also**

Related models are the asymptotic regression models [AR.2](#) and [AR.3](#).

**Examples**

```
## Fitting Michaelis-Menten model
met.mm.m1 <- drm(gain~dose, product, data=methionine, fct=MM.3(),
  pmodels = list(~1, ~factor(product), ~factor(product)))
plot(met.mm.m1, log = "", ylim=c(1450, 1800))
summary(met.mm.m1)
ED(met.mm.m1, c(10, 50))

## Calculating bioefficacy: approach 1
coef(met.mm.m1)[4] / coef(met.mm.m1)[5] * 100

## Calculating bioefficacy: approach 2
SI(met.mm.m1, c(50,50))

## Simplified models
met.mm.m2a <- drm(gain~dose, product, data=methionine, fct=MM.3(), pmodels = list(~1, ~factor(product), ~1))
anova(met.mm.m2a, met.mm.m1) # model reduction not possible

met.mm.m2b <- drm(gain~dose, product, data=methionine, fct=MM.3(), pmodels = list(~1, ~1, ~factor(product)))
anova(met.mm.m2b, met.mm.m1) # model reduction not possible
```

---

modelFit	<i>Checking the model fit</i>
----------	-------------------------------

---

**Description**

Checking the fit of dose-response model by means of formal lack-of-fit tests or graphical procedures.

**Usage**

```
modelFit(object, test = NULL, method = c("gof", "cum"))
```

**Arguments**

object	object of class 'drc'
test	character string defining the test method to apply
method	character string specifying the method to be used for assessing the model fit

**Details**

Currently two methods are available. For continuous data the classical lack-of-fit test is applied (Bates and Watts, 1988). The test compares the dose-response model to a more general ANOVA model using an approximate F-test. For quantal data the crude goodness-of-fit test based on Pearson's statistic is used. None of these tests are very powerful. A significant test result is more alarming than a non-significant one.

More methods will become available in the future.

**Value**

An object of class 'anova' which will be displayed in much the same way as an ordinary ANOVA table.

**Author(s)**

Christian Ritz

**References**

Bates, D. M. and Watts, D. G. (1988) *Nonlinear Regression Analysis and Its Applications*, New York: Wiley & Sons (pp. 103–104).

## Examples

```
## Comparing the four-parameter log-logistic model to a one-way ANOVA model using an approximate F test
## in other words applying a lack-of-fit test
ryegrass.m1 <- drm(root1 ~ conc, data = ryegrass, fct = W1.4())
modelFit(ryegrass.m1)
```

---

mr.test

*Mizon-Richard test for dose-response models*

---

## Description

The function provides a lack-of-fit test for the mean structure based on the Mizon-Richard test as compared to a specific alternative model.

## Usage

```
mr.test(object1, object2, object, x, var.equal = TRUE, component = 1)
```

## Arguments

object1	object of class 'drc' (null model).
object2	object of class 'drc' (alternative model).
object	object of class 'drc' (fitted model under alternative).
x	numeric vector of dose values.
var.equal	logical indicating whether or not equal variances can be assumed across doses.
component	numeric vector specifying the component(s) in the parameter vector to use in the test.

## Details

The function provides a p-value indicating whether or not the mean structure is appropriate.

The test is applicable even in cases where data are non-normal or exhibit variance heterogeneity.

## Value

A p-value for test of the null hypothesis that the chosen mean structure is appropriate as compared to the alternative mean structure provided. Ritz and Martinussen (2009) provide the details.

## Note

This functionality is still under development. Currently, the null and alternative models are hard-coded! In near future the function will be working for null and alternative models specified by the user.

**Author(s)**

Christian Ritz

**References**

Ritz, C and Martinussen, T. (2009) Lack-of-fit tests for assessing mean structures for continuous dose-response data, *Submitted manuscript*

**See Also**

See also [modelFit](#) for details on the lack-of-fit test against an ANOVA model.

**Examples**

```
## Fitting log-logistic and Weibull models
## The Weibull model is the alternative
etmotc.m1<-drm(rgr1~dose1, data=etmotc[1:15,], fct=LL.4())
etmotc.m2 <- update(etmotc.m1, fct=W1.4())

## Fitting the fitted model (using the alternative model)
etmotc.m3 <- drm(fitted(etmotc.m1)~dose1, data=etmotc[1:15,], fct=W1.4())

## Handling missing values
xVec <- etmotc[1:15,]$dose1
xVec[1:8] <- 1e-10 # avoiding 0's

## Obtaining the Mizon-Richard test
mr.test(etmotc.m1, etmotc.m2, etmotc.m3, xVec, var.equal = FALSE)
```

---

 mrdrm

---

*Model-robust dose-response modelling*


---

**Description**

Model-robust dose-response modelling is based on an optimal linear convex combination of two model fits, a parametric and a non-parametric model fit. The current implementation relies on local linear regression (loess) for the non-parametric part.

**Usage**

```
mrdrm(object1, object2, lambda = (0:10)/10, criterion = c("gcv", "lcv"), critFct = c("ls", "ll"),
ls.weights = c("nonpar", "ad hoc", "none", "par", "response"), fixedEnd = FALSE, unitScale = FALSE)
```

**Arguments**

object1	object of class 'drc' (the parametric fit).
object2	object of class 'loess' (the non-parametric fit).
lambda	numeric vector of potential mixing values (between 0 and 1).
criterion	character string specifying the criterion to use in the PRESS* procedure.
critFct	character string specifying the criterion function to use in the PRESS* procedure.
ls.weights	character string specifying the type weights to use in the PRESS* criterion.
fixedEnd	logical indicating whether or not the leave-one-out predictions of the non-parametric fit should be equal to the average response at the boundary dose values. If not, no such predictions are obtained at all.
unitScale	logical indicating if the dose values should be transformed to the unit interval in order to improve the local regression fit.

**Details**

The PRESS\* leave-one-out criterion is used to determine the optimal mixing of the parametric and non-parametric model fits (Nottingham and Birch, 2000)).

**Value**

A list of components from the fit.

**Note**

Currently, there is no check ensuring that the parametric and non-parametric fits are based on the same data!

**Author(s)**

Christian Ritz

**References**

Nottingham, Q. J. and Birch, J. B. (2000) A semiparametric approach to analysing dose-response data, *Statist. Med.*, **19**, 389–404.

**Examples**

```
## deguelin data from Nottingham and Birch (2000)
deguelin.m1 <- drm(r/n~dose, weights=n, data=deguelin, fct=LL.2(), type="binomial")
deguelin.m2 <- loess(r/n~dose, data=deguelin, degree=1) # local linear regression

deguelin.mr <- mrdrm(deguelin.m1, deguelin.m2)
deguelin.mr

predict(deguelin.mr, interval = "confidence")
```

```

ED(deguelin.mr, c(10, 20, 50, 80, 90), interval = "approximate")
ED(deguelin.m1, c(10, 20, 50, 80, 90), ci = "delta")

plot(deguelin.m1, ylim=c(0,1))
plot(deguelin.mr, add = TRUE, lty = 2)

## The same results (loess fit automatically supplied)
deguelin.mr2 <- mrdrm(deguelin.m1)
ED(deguelin.mr2, c(10, 20, 50, 80, 90), interval = "approximate")

## With fixed lambda
deguelin.mr3 <- mrdrm(deguelin.m1, deguelin.m2, lambda = 0.8)
plot(deguelin.mr3, add = TRUE, lty = 3)

## Purely non-parametric fit
deguelin.mr4 <- mrdrm(deguelin.m1, deguelin.m2, lambda = 1)
plot(deguelin.mr4, add = TRUE, lty = 4)

## On log scale (completely different results)
deguelin.m2b <- loess(r/n ~ log(dose), data = deguelin, degree = 1)
deguelin.mr2b1 <- mrdrm(deguelin.m1, deguelin.m2b, critFct = "l1")
deguelin.mr2b1

deguelin.mr2b2 <- mrdrm(deguelin.m1, deguelin.m2b, critFct = "ls")
deguelin.mr2b2

deguelin.mr2b3 <- mrdrm(deguelin.m1, deguelin.m2b, critFct = "ls", fixedEnd = TRUE)
deguelin.mr2b3

## daphnids dataset at 24 hours
daphnids1.m1<-drm(no/total~dose, weights = total, data = daphnids[1:8,], fct = LL.2(), type = "binomial")
daphnids1.m2<-loess(no/total~dose, data = daphnids[1:8,], degree = 1)

daphnids1.mr<-mrdrm(daphnids1.m1, daphnids1.m2)
daphnids1.mr

plot(daphnids1.m1)
plot(daphnids1.mr, add=TRUE, type="none", lty=2)

## daphnids dataset at 48 hours
daphnids2.m1<-drm(no/total~dose, weights = total, data = daphnids[9:16,], fct = LL.2(), type = "binomial")
daphnids2.m2<-loess(no/total~dose, data = daphnids[9:16,], degree = 1)

daphnids2.mr<-mrdrm(daphnids2.m1, daphnids2.m2)
daphnids2.mr

plot(daphnids2.m1)
plot(daphnids2.mr, add=TRUE, type="none", lty=2)

## fly dataset from Nottingham & Birch (1996)
fly<-data.frame(

```

```

conc = c(0.1,0.15,0.2,0.3,0.5,0.7,0.95),
total = c(47,53,55,52,46,54,52),
killed = c(8,14,24,32,38,50,50))

fly.m1 <- drm(killed/total~conc, weights = total, data = fly, fct = LL.2(), type = "binomial")
fly.m2 <- loess(killed/total~conc, data = fly, degree = 1)

fly.mr1 <- mrdrm(fly.m1, fly.m2)
fly.mr2 <- mrdrm(fly.m1, fly.m2, criterion="lcv")

plot(fly.m1, ylim = c(0,1))
plot(fly.mr1, add = TRUE, type = "none", lty = 3)
plot(fly.mr2, add = TRUE, type = "none", lty = 2)

fly.mr1
fly.mr2
AIC(fly.m1)

## ryegrass dataset (continuous response)
ryegrass.m1 <- drm(rootl~conc, data=ryegrass, fct=LL.4())
ryegrass.m2 <- loess(rootl~conc, data=ryegrass, degree=1)
ryegrass.mr <- mrdrm(ryegrass.m1, ryegrass.m2)
ryegrass.mr

predict(ryegrass.mr)
ED(ryegrass.mr, c(10, 50, 90), interval = "approximate")

## lettuce dataset (continuous response)
lettuce.m1 <- drm(weight~conc, data = lettuce, fct = LL.3())
lettuce.m2 <- loess(weight~conc, data = lettuce, degree = 1, span = 0.5)
lettuce.mr <- mrdrm(lettuce.m1, lettuce.m2)
lettuce.mr

plot(lettuce.mr, type = "all")

## Obtaining ED values (not working with bisection method)
ED(lettuce.mr, c(10,50), interval = "approximate", method = "grid",
upper = predict(lettuce.mr, data.frame(conc=0)))

```

---

mselect

*Model selection*


---

### Description

Model selection by comparison of different models using the maximum log likelihood value, Akaike's information criterion (AIC), the estimated residual variance and the p-value from a lack-of-fit test as criteria.

**Usage**

```
mselect(object, fctList = NULL, nested = FALSE, sorted = c("IC", "Res var", "Lack of fit", "no"), linreg
```

**Arguments**

object	an object of class 'drc'.
fctList	a list of dose-response functions to be compared.
nested	logical. TRUE results in F tests between adjacent models (in 'fctList'). Only sensible for nested models.
sorted	character string determining according to which criterion the model fits are ranked.
linreg	logical indicating whether or not additionally polynomial regression models (linear, quadratic, and cubic models) should be fitted (they could be useful for a kind of informal lack-of-test consideration for the models specified, capturing unexpected departures).
icfct	function for supplying the information criterion to be used. <a href="#">AIC</a> and <a href="#">BIC</a> are two options.

**Details**

The maximum likelihood cannot be used for comparison unless the models are nested.

For Akaike's information criterion and the residual variance: the smaller the better and for lack-of-fit test: the larger the better. Note that the residual variance is only available for continuous dose-response data.

**Value**

A matrix with one row for each model and one column for each criterion.

**Author(s)**

Christian Ritz

**Examples**

```
### Example with continuous data
## Fitting initial four-parameter log-logistic model
ryegrass.m1 <- drm(rootl ~ conc, data = ryegrass, fct = LL.4())

## Model selection
mselect(ryegrass.m1, list(LL.3(), LL.5(), W1.3(), W1.4(), W2.4(), baro5()))

## Model selection including linear, quadratic, and cubic regression models
mselect(ryegrass.m1, list(LL.3(), LL.5(), W1.3(), W1.4(), W2.4(), baro5()), linreg = TRUE)

## Comparing nested models
mselect(ryegrass.m1, list(LL.5()), nested = TRUE)
```

```

### Example with quantal data
## Fitting initial two-parameter log-logistic model
earthworms.m1 <- drm(number/total~dose, weights=total,
data = earthworms, fct = LL.2(), type = "binomial")

## Comparing 4 models
mselect(earthworms.m1, list(W1.2(), W2.2(), LL.3()))
# model selection based AIC or p value not working in this example!!!

```

---

nasturtium	<i>Dose-response profile of degradation of agrochemical using nasturtium</i>
------------	--

---

### Description

Estimation of the degradation profile of an agrochemical based on soil samples at depth 0-10cm from a calibration experiment.

### Usage

```
data(nasturtium)
```

### Format

A data frame with 42 observations on the following 2 variables.

conc a numeric vector of concentrations (g/ha)

weight a numeric vector of plant weight (mg) after 3 weeks' growth

### Details

It is an experiment with seven concentrations and six replicates per concentration. *Nasturtium* is sensitive and its weight reduces noticeable at low concentrations.

Racine-Poon (1988) suggests using a three-parameter log-logistic model.

### Source

Racine-Poon, A. (1988) A Bayesian Approach to Nonlinear Calibration Problems, *J. Am. Statist. Ass.*, **83**, 650–656.

### Examples

```

nasturtium.m1 <- drm(weight~conc, data=nasturtium, fct = LL.3())

modelFit(nasturtium.m1)

plot(nasturtium.m1, type = "all", log = "", xlab = "Concentration (g/ha)", ylab = "Weight (mg)")

```

---

NEC *Dose-response model for estimation of no effect concentration (NEC).*

---

### Description

The no effect concentration has been proposed as an alternative to both the classical no observed effect concentration (NOEC) and the regression-based EC/ED approach. The NEC model is a dose-response model with a threshold below which the response is assumed constant and equal to the control response.

### Usage

```
NEC(fixed = c(NA, NA, NA, NA), names = c("b", "c", "d", "e"), fctName, fctText)
```

```
NEC.2(upper = 1, fixed = c(NA, NA), names = c("b", "e"), ...)
```

```
NEC.3(fixed = c(NA, NA, NA), names = c("b", "d", "e"), ...)
```

```
NEC.4(fixed = c(NA, NA, NA, NA), names = c("b", "c", "d", "e"), ...)
```

### Arguments

<code>fixed</code>	numeric vector specifying which parameters are fixed and at what value they are fixed. NAs are used for parameters that are not fixed.
<code>names</code>	a vector of character strings giving the names of the parameters (should not contain ":"). The default is reasonable (see under 'Usage').
<code>fctName</code>	optional character string used internally by convenience functions.
<code>fctText</code>	optional character string used internally by convenience functions.
<code>upper</code>	numeric value. The fixed, upper limit in the model. Default is 1.
<code>...</code>	additional arguments in <a href="#">NEC</a>

### Details

The NEC model function proposed by Pires *et al* (2002) is defined as follows

$$f(x) = c + (d - c) \exp(-b(x - e)I(x - e)) + \frac{d2}{1 + \exp(b2(\log(x) - \log(e2)))}$$

where  $I(x - e)$  is the indicator function. It is equal to 0 for  $x \leq e$  and equal 1 for  $x > e$ .

In other words: The parameter  $e$  in NEC in "drc" corresponds to the parameter  $c'$  in Pires *et al* (2002), the parameter  $b$  in NEC in "drc" corresponds to the parameter  $m'$  in Pires *et al* (2002), the parameter  $d$  in NEC in "drc" corresponds to the parameter  $l'$  in Pires *et al* (2002), and finally the parameter  $c$  in NEC in "drc" (the lower horizontal limit) is (implicitly) fixed at 0 in Pires *et al* (2002)

**Value**

The value returned is a list containing the nonlinear function, the self starter function and the parameter names.

**Author(s)**

Christian Ritz

**References**

Pires, A. M., Branco, J. A., Picado, A., Mendonca, E. (2002) Models for the estimation of a 'no effect concentration', *Environmetrics*, **13**, 15–27.

**Examples**

```
nec.m1 <- drm(root1~conc, data=ryegrass, fct=NEC.4())
summary(nec.m1)
plot(nec.m1)
```

---

neill.test

*Neill's lack-of-fit test for dose-response models*


---

**Description**

'neill.test' provides a lack-of-fit test for non-linear regression models. It is applicable both in cases where there are replicates (in which case it reduces to the standard lack-of-fit test against an ANOVA model) and in cases where there are no replicates, though then a grouping has to be provided.

**Usage**

```
neill.test(object, grouping, method = c("c-finest", "finest", "percentiles"), breakp = NULL, display =
```

**Arguments**

object	object of class 'drc' or 'nls'.
grouping	character or numeric vector that provides the grouping of the dose values.
method	character string specifying the method to be used to generate a grouping of the dose values.
breakp	numeric vector of break points for generating dose intervals that form a grouping.
display	logical. If TRUE results are displayed. Otherwise they are not (useful in simulations).

## Details

The functions used the methods `df.residual` and `residuals` and the 'data' component of object (only for determining the number of observations).

## Value

The function returns an object of class `anova` which is displayed using `print.anova`.

## Note

A clustering technique could be employed to determine the grouping to be used in cases where there are no replicates. There should at most be  $\text{ceiling}(n/2)$  clusters as otherwise some observations will not be used in the test. At the other end there need to be more clusters than parameters in the model.

## Author(s)

Christian Ritz

## References

Neill, J. W. (1988) Testing for lack of fit in nonlinear regression, *Ann. Statist.*, **16**, 733–740

## See Also

See also `modelFit` for details on the lack-of-fit test against an ANOVA model.

## Examples

```
### Example with 'drc' object

## Lack-of-fit test against ANOVA
ryegrass.m1 <- drm(rootl~conc, data = ryegrass, fct = LL.4())
modelFit(ryegrass.m1)

## The same test using 'neill.test'
neill.test(ryegrass.m1, ryegrass$conc)

## Generating a grouping
neill.test(ryegrass.m1, method="c-finest")
neill.test(ryegrass.m1, method="finest")
neill.test(ryegrass.m1, method="perc")
```

---

 0.mykiss

*Test data from a 21 day fish test*


---

**Description**

Test data from a 21 day fish test following the guidelines OECD GL204, using the test organism Rainbow trout *Oncorhynchus mykiss*.

**Usage**

```
data(0.mykiss)
```

**Format**

A data frame with 70 observations on the following 2 variables.

conc a numeric vector of concentrations (mg/l)

weight a numeric vector of wet weights (g)

**Details**

Weights are measured after 28 days.

**Source**

Organisation for Economic Co-operation and Development (OECD) (2006) *CURRENT APPROACHES IN THE STATISTICAL ANALYSIS OF ECOTOXICITY DATA: A GUIDANCE TO APPLICATION - ANNEXES*, Paris (p. 65).

**References**

Organisation for Economic Co-operation and Development (OECD) (2006) *CURRENT APPROACHES IN THE STATISTICAL ANALYSIS OF ECOTOXICITY DATA: A GUIDANCE TO APPLICATION - ANNEXES*, Paris (pp. 80–85).

**Examples**

```
head(0.mykiss)

## Fitting exponential model
0.mykiss.m1 <- drm(weight ~ conc, data = 0.mykiss, fct = EXD.2(), na.action = na.omit)
modelFit(0.mykiss.m1)
summary(0.mykiss.m1)

## Fitting same model with transform-both-sides approach
0.mykiss.m2 <- boxcox(0.mykiss.m1 , method = "anova")
summary(0.mykiss.m2)
# no need for a transformation
```

```
## Plotting the fit
plot(O.mykiss.m1, type = "all", xlim = c(0, 500), ylim = c(0,4),
     xlab = "Concentration (mg/l)", ylab = "Weight (g)", broken = TRUE)
```

---

P.promelas

*Effect of sodium pentachlorophenate on growth of fathead minnow*


---

### Description

Fathead minnows (*Pimephales promelas*) were exposed to sodium pentachlorophenate concentrations ranging from 32 to 512 micro g/L in a 7-day larval survival and growth test. The average dry weight was measured.

### Usage

```
data(P.promelas)
```

### Format

A data frame with 24 observations on the following 2 variables.

conc a numeric vector of sodium pentachlorophenate concentrations (micro g/L).

dryweight a numeric vector dry weights (mg)

### Details

The data are analysed in Bruce and Versteeg (1992) using a log-normal dose-response model (using the logarithm with base 10).

### Source

Bruce, R. D. and Versteeg, D. J. (1992) A statistical procedure for modeling continuous toxicity data, *Environ. Toxicol. Chem.*, **11**, 1485–1494.

### Examples

```
## Model with ED50 on log scale as parameter
p.prom.m1<-drm(dryweight~conc, data=P.promelas, fct=LN.3())

plot(fitted(p.prom.m1), residuals(p.prom.m1))

plot(p.prom.m1, type="all", broken=TRUE, xlim=c(0,1000))
summary(p.prom.m1)
ED(p.prom.m1, c(10,20,50), interval="delta")

## Model with ED50 as parameter
```

```
p.prom.m2<-drm(dryweight~conc, data=P.promelas, fct=LN.3(log=TRUE))
summary(p.prom.m2)
ED(p.prom.m2, c(10,20,50), interval="f1s")
```

---

plot.drc

*Plotting fitted curves for a 'drc' or 'mrdrc' object*


---

## Description

plot displays fitted curves and observations in the same plot window, distinguishing between curves by different plot symbols and line types.

## Usage

```
## S3 method for class 'drc'
plot(x, ..., add = FALSE, level = NULL, type = c("average", "all", "bars", "none", "obs"),
      broken = FALSE, bp, bcontrol = NULL, conName = NULL, axes = TRUE, gridsize = 100,
      log = "x", xtsty, xtrim = TRUE, xt = NULL, xtlab = NULL, xlab, xlim,
      yt = NULL, ytlab = NULL, ylab, ylim,
      cex, cex.axis = 1, col = FALSE, lty, pch,
      legend, legendText, legendPos, cex.legend = 1)

## S3 method for class 'mrdrc'
plot(x, ..., pava = FALSE)
```

## Arguments

x	an object of class 'drc'.
...	additional graphical arguments. For instance, use lwd=2 or lwd=3 to increase the width of plot symbols.
add	logical. If TRUE then add to already existing plot.
level	vector of character strings. To plot only the curves specified by their names.
type	a character string specifying how to plot the data. There are currently 5 options: "average" (averages and fitted curve(s); default), "none" (only the fitted curve(s)), "obs" (only the data points), "all" (all data points and fitted curve(s)) and "bars" (averages and fitted curve(s) with model-based error ).
broken	logical. If TRUE the x axis is broken provided this axis is logarithmic (using functionality in the CRAN package 'plotrix').
bp	numeric value specifying the break point below which the dose is zero (the amount of stretching on the dose axis above zero in order to create the visual illusion of a logarithmic scale <i>including</i> 0). The default is the base-10 value corresponding to the rounded value of the minimum of the log10 values of all positive dose values. This argument is only working for logarithmic dose axes.

bcontrol	a list with components factor, style and width. Controlling the appearance of the break (in case broken is TRUE). The component factor is the distance from the control to the break as a multiple of the value of bp (default is 2). The component style can take the values: gap, slash or zigzag. The component width is the width of the break symbol (default is 0.02).
conName	character string. Name on x axis for dose zero. Default is ""0"".
axes	logical indicating whether both axes should be drawn on the plot.
gridsize	numeric. Number of points in the grid used for plotting the fitted curves.
log	a character string which contains "x" if the x axis is to be logarithmic, "y" if the y axis is to be logarithmic and "xy" or "yx" if both axes are to be logarithmic. The default is "x". The empty string "" yields the original axes.
xtsty	a character string specifying the dose axis style for arrangement of tick marks. By default ("base10") For a logarithmic axis by default only base 10 tick marks are shown ("base10"). Otherwise sensible equidistantly located tick marks are shown ("standard"), relying on <a href="#">axTicks</a> .
xttrim	logical specifying if the number of tick marks should be trimmed in case too many tick marks are initially determined.
xt	a numeric vector containing the positions of the tick marks on the x axis.
xtlab	a vector containing the tick marks on the x axis.
xlab	an optional label for the x axis.
xlim	a numeric vector of length two, containing the lower and upper limit for the x axis.
yt	a numeric vector, containing the positions of the tick marks on the y axis.
ytlab	a vector containing the tick marks on the y axis.
ylab	an optional label for the y axis.
ylim	a numeric vector of length two, containing the lower and upper limit for the y axis.
cex	numeric or numeric vector specifying the size of plotting symbols and text (see <a href="#">par</a> for details).
cex.axis	numeric value specifying the magnification to be used for axis annotation relative to the current setting of cex.
col	either logical or a vector of colours. If TRUE default colours are used. If FALSE (default) no colours are used.
legend	logical. If TRUE a legend is displayed.
legendText	a character string or vector of character strings specifying the legend text (the position of the upper right corner of the legend box).
legendPos	numeric vector of length 2 giving the position of the legend.
cex.legend	numeric specifying the legend text size.
lty	a numeric vector specifying the line types.
pch	a vector of plotting characters or symbols (see <a href="#">points</a> ).
pava	logical. If TRUE the fit is monotonised using pool adjacent violators algorithm.

## Details

`plot.mrdrc` takes the same arguments as `plot.drc`.

Suitable labels are automatically provided.

The use of `xlim` allows changing the range of the x axis, extrapolating the fitted dose-response curves. Note that changing the range on the x axis may also entail a change of the range on the y axis. Sometimes it may be useful to extend the upper limit on the y axis (using `ylim`) in order to fit a legend into the plot.

See [colors](#) for the available colours.

The arguments `broken` and `bcontrol` rely on the function `link{axis.break}` with arguments `style` and `brw` in the package `plotrix`.

## Value

An invisible data frame with the values used for plotting the fitted curves. The first column contains the dose values, and the following columns (one for each curve) contain the fitted response values.

## Author(s)

Christian Ritz and Jens C. Streibig Contributions from Xiaoyan Wang

## Examples

```
## Fitting models to be plotted below
ryegrass.m1 <- drm(rootl~conc, data = ryegrass, fct = LL.4())
ryegrass.m2 <- drm(rootl~conc, data = ryegrass, fct = LL.3()) # lower limit fixed at 0

## Plotting observations and fitted curve for the first model
plot(ryegrass.m1, broken = TRUE)

## Adding fitted curve for the second model (not much difference)
plot(ryegrass.m2, broken = TRUE, add = TRUE, type = "none", col = 2, lty = 2)

## Finetuning the axis break
plot(ryegrass.m1, broken = TRUE, bcontrol = list(style = "gap"))
plot(ryegrass.m1, broken = TRUE, bcontrol = list(style = "slash"))
plot(ryegrass.m1, broken = TRUE, bcontrol = list(style = "zigzag"))

## Plot without axes
plot(ryegrass.m1, axes = FALSE)

## Fitting model to be plotted below
spinach.m1 <- drm(SLOPE~DOSE, CURVE, data = spinach, fct = LL.4())

## Plot with no colours
plot(spinach.m1, main = "Different line types (default)")

## Plot with default colours
plot(spinach.m1, col = TRUE, main = "Default colours")
```

```

## Plot with specified colours
plot(spinach.m1, col = c(2,6,3,23,56), main = "User-specified colours")

## Plot of curves 1 and 2 only
plot(spinach.m1, level = c(1,2), main = "User-specified curves")

## Plot with symbol of different sizes
plot(spinach.m1, cex = c(1,2,3,4,5), main = "User-specified symbil sizes")

## Fitting another model to be plotted below
lettuce.m1 <- drm(weight~conc, data = lettuce, fct = LL.4())

## Using the argument 'bp'. Compare the plots!
par(mfrow = c(2, 2))
plot(lettuce.m1, main = "bp = default") # using the default
plot(lettuce.m1, bp = 1e-4, main = "bp = 1e-4")
plot(lettuce.m1, bp = 1e-6, main = "bp = 1e-6")
plot(lettuce.m1, bp = 1e-8, main = "bp = 1e-8")
par(mfrow = c(1,1))

## User-specified position of legend
S.alba.m1 <- drm(DryMatter~Dose, Herbicide, data = S.alba, fct = LL.4())

plot(S.alba.m1)
plot(S.alba.m1, legendPos = c(0.3, 4.8))

```

---

PR

*Expected or predicted response*


---

## Description

The function returns the expected or predicted response for specified dose values.

## Usage

```
PR(object, xVec, ...)
```

## Arguments

object	object of class <code>drc</code> obtaining fitting a dose-response model.
xVec	numeric vector of dose values.
...	additional arguments to be supplied to <a href="#">predict.drc</a> . No effect at the moment.

## Details

This function is a convenience function for easy access to predicted values.

**Value**

A numeric vector of predicted values or possibly a matrix of predicted values and corresponding standard errors.

**Author(s)**

Christian Ritz after a suggestion from Andrew Kniss.

**See Also**

Predictions can also be obtained using [predict.drc](#).

**Examples**

```
ryegrass.m1 <- drm(ryegrass, fct = LL.4())
PR(ryegrass.m1, c(5, 10))

ryegrass.m2 <- drm(ryegrass, fct = LL2.4())
PR(ryegrass.m2, c(5, 10))

spinach.m1 <- drm(SLOPE~DOSE, CURVE, data=spinach, fct = LL.4())
PR(spinach.m1, c(5, 10))
```

---

predict.drc

*Prediction*

---

**Description**

Predicted values for models of class 'drc' or class 'mrdrc'.

**Usage**

```
## S3 method for class 'drc'
predict(object, newdata, se.fit = FALSE, interval = c("none", "confidence", "prediction"),
  level = 0.95, na.action = na.pass, od = FALSE, ...)

## S3 method for class 'mrdrc'
predict(object, newdata, se.fit = FALSE, interval = c("none", "confidence", "prediction"),
  level = 0.95, pava = FALSE, ...)
```

**Arguments**

object	an object of class 'drc'.
newdata	An optional data frame in which to look for variables with which to predict. If omitted, the fitted values are used.
se.fit	logical. If TRUE standard errors are required.
interval	character string. Type of interval calculation: "none", "confidence" or "prediction".
level	Tolerance/confidence level.
na.action	function determining what should be done with missing values in 'newdata'. The default is to predict 'NA'.
od	logical. If TRUE adjustment for over-dispersion is used.
pava	logical. If TRUE the fit is monotonised using pool adjacent violators algorithm.
...	further arguments passed to or from other methods.

**Details**

For the built-in log-logistics and Weibull-type models standard errors and confidence/prediction intervals can be calculated. At the moment it only works for the situations where all observations are assumed to have a common variance.

**Value**

A matrix with as many rows as there are dose values provided in 'newdata' or in the original dataset (in case 'newdata' is not specified) and columns with fitted, standard errors, lower and upper limits of confidence intervals.

**Author(s)**

Christian Ritz

**See Also**

For details are found in the help page for [predict.lm](#).

**Examples**

```
## Fitting a model
spinach.model1 <- drm(SLOPE~DOSE, CURVE, data = spinach, fct = LL.4())

## Predicting values a dose=2 (with standard errors)
predict(spinach.model1, data.frame(dose=2, CURVE=c("1", "2", "3")), se.fit = TRUE)

## Getting confidence intervals
predict(spinach.model1, data.frame(dose=2, CURVE=c("1", "2", "3")),
interval = "confidence")

## Getting prediction intervals
```

```
predict(spinach.model1, data.frame(dose=2, CURVE=c("1", "2", "3")),
interval = "prediction")
```

---

print.drc

*Printing key features*

---

## Description

'print' displays brief information on an object of class 'drc'.

## Usage

```
## S3 method for class 'drc'
print(x, ..., digits = max(3, getOption("digits") - 3))

## S3 method for class 'mrdrc'
print(x, ...)
```

## Arguments

x	an object of class 'drc'.
...	additional arguments.
digits	an integer giving the number of digits of the parameter coefficients. Default is 3.

## Author(s)

Christian Ritz

## Examples

```
## Fitting a four-parameter log-logistic model
ryegrass.m1 <- drm(root1 ~conc, data = ryegrass, fct = LL.4())

## Displaying the model fit
print(ryegrass.m1)
ryegrass.m1 # gives the same output as the previous line
```

---

print.summary.drc      *Printing summary of non-linear model fits*

---

**Description**

This method produces formatted output of the summary statistics: parameter estimates, estimated standard errors, z-test statistics and corresponding p-values.

**Usage**

```
## S3 method for class 'summary.drc'  
print(x, ...)
```

**Arguments**

x                    an object of class 'drc'.  
...                   additional arguments.

**Value**

The object (argument x) is returned invisibly.

**Author(s)**

Christian Ritz

**Examples**

```
ryegrass.m1 <- drm(root1~conc, data=ryegrass, fct= LL.4())  
  
summary(ryegrass.m1)
```

---

rdrm                    *Simulating a dose-response curve*

---

**Description**

Simulation of a dose-response curve with user-specified dose values and error distribution.

**Usage**

```
rdrm(nosim, fct, mpar, xerror, xpar = 1, yerror = "rnorm", ypar = c(0, 1),  
onlyY = FALSE)
```

**Arguments**

<code>nosim</code>	numeric. The number of simulated curves to be returned.
<code>fct</code>	list. Any built-in function in the package <i>drc</i> or a list with similar components.
<code>mpar</code>	numeric. The model parameters to be supplied to <code>fct</code> .
<code>xerror</code>	numeric or character. The distribution for the dose values.
<code>xpar</code>	numeric vector supplying the parameter values defining the distribution for the dose values. If <code>xerror</code> is a distribution then remember that the number of dose values also is part of this argument (the first argument).
<code>yerror</code>	numeric or character. The error distribution for the response values.
<code>ypar</code>	numeric vector supplying the parameter values defining the error distribution for the response values.
<code>onlyY</code>	logical. If TRUE then only the response values are returned (useful in simulations). Otherwise both dose values and response values (and for binomial data also the weights) are returned.

**Details**

The distribution for the dose values can either be a fixed set of dose values (a numeric vector) used repeatedly for creating all curves or be a distribution specified as a character string resulting in varying dose values from curve to curve.

The error distribution for the response values can be any continuous distribution like [rnorm](#) or [rgamma](#). Alternatively it can be the binomial distribution [rbinom](#).

**Value**

A list with up to 3 components (depending on the value of the `onlyY` argument).

**Author(s)**

Christian Ritz

**References**

~put references to the literature/web site here ~

**Examples**

```
## Simulating normally distributed dose-response data

## Model fit to simulate from
ryegrass.m1 <- drm(root1~conc, data = ryegrass, fct = LL.4())

## 10 random dose-response curves based on the model fit
sim10a <- rdrm(10, LL.4(), coef(ryegrass.m1), xerror = ryegrass$conc)
sim10a
```

```
## Simulating binomial dose-response data

## Model fit to simulate from
deguelin.m1 <- drm(r/n~dose, weights=n, data=deguelin, fct=LL.2(), type="binomial")

## 10 random dose-response curves
sim10b <- rdrm(10, LL.2(), coef(deguelin.m1), deguelin$dose, yerror="rbinom", ypar=deguelin$n)
sim10b
```

---

residuals.drc                      *Extracting residuals from model*

---

## Description

'residuals' extracts residuals from an object of class 'drc'.

## Usage

```
## S3 method for class 'drc'
residuals(object, typeRes = c("working", "standardised", "studentised"), ...)
```

## Arguments

object	an object of class 'drc'.
typeRes	character string specifying the type of residual to be returned: raw/working residuals, residuals standardised using the estimated residual standard error, or studentised residuals based on the H matrix of partial derivatives of the model function.
...	additional arguments.

## Details

Standardised residuals are the raw residuals divided by a scale estimate (if available).

Studentised residuals are obtained by dividing by a scale estimate and in addition a correction factor (square root of 1 minus h with h is a diagonal element in the hat matrix).

## Value

The raw (also called working) residuals or some kind of scaled residuals extracted from 'object'.

## Note

The 'standardised' residuals are available for least squares estimation with or without Box-Cox transformation or variance as a power of the mean.

**Author(s)**

Christian Ritz

**Examples**

```
## Fitting a four-parameter log-logistic model
ryegrass.m1 <- drm(root1 ~conc, data = ryegrass, fct = LL.4())

## Displaying the residual plot (raw residuals)
plot(fitted(ryegrass.m1), residuals(ryegrass.m1))

## Using the standardised residuals
plot(fitted(ryegrass.m1), residuals(ryegrass.m1, typeRes = "standard"))

## Overlaying the studentised residuals ... not much of a difference
points(fitted(ryegrass.m1), residuals(ryegrass.m1, typeRes = "student"), col = 2)
```

---

RScpetition

*Competition between two biotypes*

---

**Description**

To assess the competitive ability between two biotypes of *Lolium rigidum*, one resistant to glyphosate and the other a sensitive wild type, the density of resistant and sensitive biotypes was counted after germination.

**Usage**

```
data(RScpetition)
```

**Format**

A data frame with 49 observations on the following 3 variables.

z a numeric vector with densities of the resistant biotype (plants/m<sup>2</sup>)

x a numeric vector with densities of the sensitive biotype (plants/m<sup>2</sup>)

biomass a numeric vector of biomass weight (g/plant)

**Details**

A hyperbolic model (Jensen, 1993) is describing the data reasonably well.

**Source**

The dataset is from Pedersen et al (2007).

## References

- Jensen, J. E. (1993) Fitness of herbicide-resistant weed biotypes described by competition models, *Proceedings of the 8th EWRS Symposium, 14-16 June, Braunschweig, Germany*, **1**, 25–32.
- Pedersen, B. P. and Neve, P. and Andreasen, C. and Powles, S. (2007) Ecological fitness of a glyphosate resistant *Lolium rigidum* population: Growth and seed production along a competition gradient, *Basic and Applied Ecology*, **8**, 258–268.

---

 ryegrass
 

---

*Effect of ferulic acid on growth of ryegrass*


---

## Description

A single dose-response curve.

## Usage

```
data(ryegrass)
```

## Format

A data frame with 24 observations on the following 2 variables.

**rootl** a numeric vector of root lengths

**conc** a numeric vector of concentrations of ferulic acid

## Details

The data are part of a study to investigate the joint action of phenolic acids on root growth inhibition of perennial ryegrass (*Lolium perenne* L).

conc is the concentration of ferulic acid in mM, and rootl is the root length of perennial ryegrass measured in cm.

## Source

Inderjit and J. C. Streibig, and M. Olofsson (2002) Joint action of phenolic acid mixtures and its significance in allelopathy research, *Physiologia Plantarum*, **114**, 422–428, 2002.

## Examples

```
## Displaying the data set
ryegrass

## Fitting a four-parameter Weibull model (type 2)
ryegrass.m1 <- drm(rootl ~ conc, data = ryegrass, fct = W2.4())

## Displaying a summary of the model fit
```

```

summary(ryegrass.m1)

## Plotting the fitted curve together with the original data
plot(ryegrass.m1)

## Fitting a four-parameter Weibull model (type 1)
ryegrass.m2 <- drm(rootl ~ conc, data = ryegrass, fct = W1.4())
plot(ryegrass.m2)

## Fitting a four-parameter log-logistic model
## with user-defined parameter names
ryegrass.m3 <- drm(rootl ~ conc, data = ryegrass,
fct = LL.4(names = c("Slope", "Lower Limit", "Upper Limit", "ED50")))
summary(ryegrass.m3)

## Comparing log-logistic and Weibull models
## (Figure 2 in Ritz (2009))
ryegrass.m0 <- drm(rootl ~ conc, data = ryegrass, fct = LL.4())
ryegrass.m1 <- drm(rootl ~ conc, data = ryegrass, fct = W1.4())
ryegrass.m2 <- drm(rootl ~ conc, data = ryegrass, fct = W2.4())

plot(ryegrass.m0, broken=TRUE, xlab="Dose (mM)", ylab="Root length (cm)", lwd=2,
cex=1.2, cex.axis=1.2, cex.lab=1.2)
plot(ryegrass.m1, add=TRUE, broken=TRUE, lty=2, lwd=2)
plot(ryegrass.m2, add=TRUE, broken=TRUE, lty=3, lwd=2)

arrows(3, 7.5, 1.4, 7.5, 0.15, lwd=2)
text(3,7.5, "Weibull-2", pos=4, cex=1.2)

arrows(2.5, 0.9, 5.7, 0.9, 0.15, lwd=2)
text(3,0.9, "Weibull-1", pos=2, cex=1.2)

```

---

S.alba

*Potency of two herbicides*


---

### Description

Data are from an experiment, comparing the potency of the two herbicides glyphosate and benta-zone in white mustard *Sinapis alba*.

### Usage

```
data(S.alba)
```

### Format

A data frame with 68 observations on the following 3 variables.

Dose a numeric vector containing the dose in g/ha.

Herbicide a factor with levels Bentazone Glyphosate (the two herbicides applied).

DryMatter a numeric vector containing the response (dry matter in g/pot).

### Details

The lower and upper limits for the two herbicides can be assumed identical, whereas slopes and ED50 values are different (in the log-logistic model).

### Source

Christensen, M. G. and Teicher, H. B., and Streibig, J. C. (2003) Linking fluorescence induction curve and biomass in herbicide screening, *Pest Management Science*, **59**, 1303–1310.

### See Also

See the examples in the examples sections in [drm](#) and [SI](#).

### Examples

```
## Fitting a log-logistic model with
## common lower and upper limits
S.alba.m1 <- drm(DryMatter~Dose, Herbicide, data=S.alba, fct = LL.4(),
pmodels=data.frame(Herbicide,1,1,Herbicide))

## Applying the optimal transform-both-sides Box-Cox transformation
S.alba.m2 <- boxcox(S.alba.m1, method = "anova")

## Plotting fitted regression curves together with the data
plot(S.alba.m2)
```

---

S.capricornutum	<i>Effect of cadmium on growth of green alga</i>
-----------------	--

---

### Description

Green alga (*Selenastrum capricornutum*) was exposed to cadmium chloride concentrations ranging from 5 to 80 micro g/L in geometric progression in 4-day population growth test.

### Usage

```
data(S.capricornutum)
```

**Format**

A data frame with 18 observations on the following 2 variables.

conc a numeric vector of cadmium chloride concentrations (micro g/L)

count a numeric vector of algal counts (10000 x cells /ml)

**Details**

The data are analysed in Bruce and Versteeg (1992) using a log-normal dose-response model (using the logarithm with base 10).

**Source**

Bruce, R. D. and Versteeg, D. J. (1992) A statistical procedure for modeling continuous toxicity data, *Environ. Toxicol. Chem.*, **11**, 1485–1494.

**Examples**

```
## Fitting 3-parameter log-normal model
s.cap.m1 <- drm(count ~ conc, data = S.capricornutum, fct = LN.3())

## Residual plot
plot(fitted(s.cap.m1), residuals(s.cap.m1))

## Fitting model with transform-both-sides approach
s.cap.m2 <- boxcox(s.cap.m1, method = "anova")
summary(s.cap.m2)

## Residual plot after transformation (looks better)
plot(fitted(s.cap.m2), residuals(s.cap.m2))

## Calculating ED values on log scale
ED(s.cap.m2, c(10, 20, 50), interval="delta")

## Fitting model with ED50 as parameter
## (for comparison)
s.cap.m3 <- drm(count ~ conc, data = S.capricornutum, fct = LN.3(log=TRUE))
s.cap.m4 <- boxcox(s.cap.m3, method = "anova")
summary(s.cap.m4)
ED(s.cap.m4, c(10, 20, 50), interval = "fls")
```

**Description**

'searchdrc' provides a facility for searching through a range of parameter values (one-dimensional) in order to obtain convergence of the estimation procedure.

**Usage**

```
searchdrc(object, which, range, len = 50)
```

**Arguments**

object	an object of class 'drc'. The object can be from a model that could not fitted.
which	a character string containing the parameter name
range	a numeric vector of length 2 specifying the interval endpoints for the range.
len	numeric. The number of points in the interval.

**Details**

The function goes through the range with increments such that in total at most len sets of parameter values are used as initial values for the estimation procedure. You would need to identify the parameter which is most likely to cause problems for the estimation procedure.

**Value**

An object of class 'drc'.

**Author(s)**

Christian Ritz

**Examples**

```
## No example yet
```

---

secalonic

*Root length measurements*

---

**Description**

Data stem from an experiment assessing the inhibitory effect of secalonic acids on plant growth.

**Usage**

```
data(secalonic)
```

**Format**

A data frame with 7 observations on the following 2 variables:

dose a numeric vector containing dose values (mM)

rootl a numeric vector containing root lengths (cm)

**Details**

For each dose the root length is an average three measurements.

**Source**

Gong, X. and Zeng, R. and Luo, S. and Yong, C. and Zheng, Q. (2004) Two new secalonic acids from *Aspergillus Japonicus* and their allelopathic effects on higher plants, *Proceedings of International Symposium on Allelopathy Research and Application, 27-29 April, Shanshui, Guangdong, China* (Editors: R. Zeng and S. Luo), 209–217.

Ritz, C (2009) Towards a unified approach to dose-response modeling in ecotoxicology *To appear in Environ Toxicol Chem.*

**Examples**

```
## Fitting a four-parameter log-logistic model
secalonic.m1 <- drm(rootl ~ dose, data = secalonic, fct = LL.4())
summary(secalonic.m1)

## Fitting a three-parameter log-logistic model
## lower limit fixed at 0
secalonic.m2 <- drm(rootl ~ dose, data = secalonic, fct = LL.3())
summary(secalonic.m1)

## Comparing logistic and log-logistic models
## (Figure 1 in Ritz (2009))
secalonic.LL4 <- drm(rootl ~ dose, data = secalonic, fct = LL.4())
secalonic.L4 <- drm(rootl ~ dose, data = secalonic, fct = L.4())

plot(secalonic.LL4, broken=TRUE, ylim=c(0,7), xlab="Dose (mM)", ylab="Root length (cm)",
     cex=1.2, cex.axis=1.2, cex.lab=1.2, lwd=2)

plot(secalonic.L4, broken=TRUE, ylim=c(0,7), add=TRUE, type="none", lty=2, lwd=2)

abline(h=coef(secalonic.L4)[3], lty=3, lwd=2)
```

---

 SI *Comparing selectivity indices across curves*


---

**Description**

'SI' compares selectivity indices for arbitrary dosage across curves. The selectivity is the ratio between effective dosages from different curves.

**Usage**

```
SI(object, percVec, compMatch = NULL, od = FALSE, reverse = FALSE,
   interval = c("none", "delta", "fieller", "fls"),
   level = ifelse(!(interval == "none"), 0.95, NULL),
   reference = c("control", "upper"),
   type = c("relative", "absolute"),
   display = TRUE, pool = TRUE, logBase = NULL, ...)
```

```
relpot(object, plotit = TRUE, compMatch = NULL, percVec = NULL, interval = "none",
   type = c("relative", "absolute"), scale = c("original", "percent", "unconstrained"), ...)
```

**Arguments**

object	an object of class 'drc'.
percVec	a numeric vector of dosage values.
compMatch	an optional character vector of names of assays to be compared. If not specified all comparisons are supplied.
od	logical. If TRUE adjustment for over-dispersion is used. This argument only makes a difference for binomial data.
reverse	logical. If TRUE the order of comparison of two curves is reversed.
interval	character string specifying the type of confidence intervals to be supplied. The default is "none". Use "delta" for asymptotics-based confidence intervals (using the delta method and the t-distribution). Use "fieller" for confidence intervals based on Fieller's theorem (with help from the delta method). Use "fls" for from-logarithm-scale-based confidence intervals (in case the parameter in the model fit is $\log(\text{ED}_{50})$ as is the case for the <a href="#">logistic</a> or <a href="#">llogistic2</a> models); currently the argument logBase then also needs to be specified.
level	numeric. The level for the confidence intervals. Default is 0.95.
reference	character string. Is the upper limit or the control level the reference?
type	character string specifying whether absolute or relative response levels are supplied.
logBase	numeric. The base of the logarithm in case logarithm transformed dose values are used.
display	logical. If TRUE results are displayed. Otherwise they are not (useful in simulations).

pool	logical. If TRUE curves are pooled. Otherwise they are not. This argument only works for models with independently fitted curves as specified in <a href="#">drm</a> .
...	In SI: additional arguments to the function doing the calculations. For instance the upper limit for the bisection method needs to be larger than the ED values used in the required relative potency. In relpot: additional graphical parameters.
plotit	logical. If TRUE the relative potencies are plotted as a function of the response level.
scale	character string indicating the scale to be used on the x axis: original or percent response level (only having an effect for type="relative").

### Details

The function `relpot` is a convenience function, which is useful for assessing how the relative potency changes as a function of the response level (eg for plotting as outlined in Ritz *et al* (2006)).

Fieller's theorem is incorporated using the formulas Kotz and Johnson (1983) and Finney (1978).

For objects of class 'braincousens' or 'mlogistic' the additional argument may be the 'upper' argument or the 'interval' argument. The 'upper' argument specifies the upper limit of the bisection method. The upper limit needs to be larger than the EDx level to be calculated. The default limit is 1000. The 'interval' argument should specify a rough interval in which the dose yielding the maximum hormetical response lies. The default interval is 'c(0.001, 1000)'. Notice that the lower limit should not be set to 0 (use something like 1e-3, 1e-6, ...).

### Value

A matrix with columns containing the estimates, estimated standard errors, t-statistics for testing indices equal to 1 and the corresponding p-values.

### Note

This function is only implemented for the following built-in functions available in the package *drm*: [braincousens](#), [cedergreen](#), [ucedergreen](#), [llogistic](#) and [weibull1](#).

### Author(s)

Christian Ritz

### References

- Finney, D. J. (1978) *Statistical method in Biological Assay*, London: Charles Griffin House, 3rd edition (pp. 80–82).
- Kotz, S. and Johnson, N. L. (1983) *Encyclopedia of Statistical Sciences Volume 3*, New York: Wiley & Sons (pp. 86–87).
- Ritz, C. and Cedergreen, N. and Jensen, J. E. and Streibig, J. C. (2006) Relative potency in nonsimilar dose-response curves, *Weed Science*, **54**, 407–412.

**See Also**

A related functions [ED.drc](#) (for calculating effective doses) and [relpot](#) (for displaying relative potencies).

**Examples**

```
m1 <- drm(SLOPE~DOSE, CURVE, data = spinach, fct = LL.4())

SI(m1, c(50,50))
SI(m1, c(10,50))
SI(m1, c(10,50), reverse = TRUE)

## Relative potency of two herbicides
m2 <- drm(DryMatter~Dose, Herbicide,
data = S.alba, fct = LL.3())

SI(m2, c(50, 50))
SI(m2, c(50, 50), ci = "delta")
SI(m2, c(50, 50), ci = "fieller")

## Comparison based on absolute
## response level

m3 <- drm(SLOPE~DOSE, CURVE,
data = spinach, fct = LL.4())

SI(m3, c(0.5,0.5), c(2,4), type="a", ci="fieller")

SI(m3, c(55,80), c(2,4))
# same comparison using a relative response level

## Relative potency transformed from log scale
m4 <- drm(drymatter~log(dose), treatment, data=G.aparine[-c(1:40), ],
pmodels = data.frame(treatment,treatment,1,treatment), fct = LL2.4())

SI(m4, c(50,50), ci="fls", logBase=exp(1))
```

**Description**

Simulating ED values for a given model and given dose values.

**Usage**

```
simDR(mpar, sigma, fct, noSim = 1000, conc, edVec = c(10, 50), seedVal = 20070723)
```

**Arguments**

<code>mpar</code>	numeric vector of model parameters
<code>sigma</code>	numeric specifying the residual standard deviation
<code>fct</code>	list supplying the chosen mean function
<code>conc</code>	numeric vector of concentration/dose values
<code>edVec</code>	numeric vector of ED values to estimate in each simulation
<code>noSim</code>	numeric giving the number of simulations
<code>seedVal</code>	numeric giving the seed used to initiate the random number generator

**Details**

The arguments `mpar` and `sigma` are typically obtained from a previous model fit.

Only dose-response models assuming normally distributed errors can be used.

**Value**

A list of matrices with as many components as there are chosen ED values. The entries in the matrices are empirical standard deviations of the estimated ED values. Row-wise from top to bottom more and more concentration/dose values are included in the simulations; top row starting with 5 concentrations. The number of replicates increases column by column from left to right.

The list is returned invisibly as the matrices also are displayed.

**Author(s)**

Christian Ritz

**Examples**

```
ryegrass.m1 <- drm(ryegrass, fct=LL.4())
```

```
simDR(coef(ryegrass.m1), sqrt(summary(ryegrass.m1)$resVar), LL.4(), 2,  
c(1.88, 3.75, 7.50, 0.94, 15, 0.47, 30, 0.23, 60), seedVal = 200710291)
```

---

spinach

*Inhibition of photosynthesis*

---

### Description

Data from an experiment investigating the inhibition of photosynthesis in response to two synthetic photosystem II inhibitors, the herbicides diuron and bentazon. More specifically, the effect of oxygen consumption of thylakoid membranes (chloroplasts) from spinach was measured after incubation with the synthetic inhibitors in 5 assays, resulting in 5 dose-response curves.

### Usage

```
data(spinach)
```

### Format

A data frame with 105 observations on the following four variables:

**CURVE** a numeric vector specifying the assay or curve (a total of 5 independent assays where used in this experiment).

**HERBICIDE** a character vector specifying the herbicide applied: bentazon or diuron.

**DOSE** a numeric vector giving the herbicide concentration in  $\mu\text{Mol}$ .

**SLOPE** a numeric vector with the measured response: oxygen consumption of thylakoid membranes.

### Details

The experiment is described in more details by Streibig (1998).

### Source

Streibig, J. C. (1998) Joint action of natural and synthetic photosystem II inhibitors, *Pesticide Science*, **55**, 137–146.

### Examples

```
## Displaying the first rows in the dataset  
head(spinach) # displaying first 6 rows in the data set
```

---

summary.drc

*Summarising non-linear model fits*


---

**Description**

'summary' compiles a comprehensive summary for objects of class 'drc'.

**Usage**

```
## S3 method for class 'drc'
summary(object, od = FALSE, pool = TRUE, ...)
```

**Arguments**

object	an object of class 'drc'.
od	logical. If TRUE adjustment for over-dispersion is used.
pool	logical. If TRUE curves are pooled. Otherwise they are not. This argument only works for models with independently fitted curves as specified in <a href="#">drm</a> .
...	additional arguments.

**Value**

A list of summary statistics that includes parameter estimates and estimated standard errors.

**Note**

Examples on usage are for instance found in the help pages of [ryegrass](#) and [secalonic](#).

**Author(s)**

Christian Ritz

---

terbuthylazin

*The effect of terbuthylazin on growth rate*


---

**Description**

Test on the effect of terbuthylazin on *Lemna minor*, performed on an aseptic culture according to the OECD-guidelines.

**Usage**

```
data(terbuthylazin)
```

**Format**

A data frame with 30 observations on the following 2 variables.

**dose** a numeric vector of dose values.

**rgr** a numeric vector of relative growth rates.

**Details**

Dose is

$$\mu l^{-1}$$

and rgr is the relative growth rate of *Lemna*.

**Source**

Cedergreen N. (2004). Unpublished bioassay data.

**Examples**

```
## displaying first 6 rows of the data set
head(terbuthylazin)

## Fitting log-logistic model
terbuthylazin.m1 <- drm(rgr~dose, data = terbuthylazin, fct = LL.4())
summary(terbuthylazin.m1)

## Fitting log-logistic model
## with Box-Cox transformation
terbuthylazin.m2 <- boxcox(terbuthylazin.m1, method = "anova")
summary(terbuthylazin.m2)
```

---

twophase

*Two-phase dose-response model*


---

**Description**

The two-phase dose-response model is a combination of log-logistic models that should be useful for describing more complex dose-response patterns.

**Usage**

```
twophase(fixed = c(NA, NA, NA, NA, NA, NA, NA),
names = c("b1", "c1", "d1", "e1", "b2", "d2", "e2"), fctName, fctText)
```

**Arguments**

fixed	numeric vector specifying which parameters are fixed and at what value they are fixed. NAs are used for parameters that are not fixed.
names	a vector of character strings giving the names of the parameters (should not contain ":"). The default is reasonable (see under 'Usage').
fctName	optional character string used internally by convenience functions.
fctText	optional character string used internally by convenience functions.

**Details**

Following Groot *et al* (1996) the two-phase model function is defined as follows

$$f(x) = c + \frac{d1 - c}{1 + \exp(b1(\log(x) - \log(e1)))} + \frac{d2}{1 + \exp(b2(\log(x) - \log(e2)))}$$

For each of the two phases, the parameters have the same interpretation as in the ordinary log-logistic model.

**Value**

The value returned is a list containing the nonlinear function, the self starter function and the parameter names.

**Author(s)**

Christian Ritz

**References**

Groot, J. C. J., Cone, J. W., Williams, B. A., Debersaques, F. M. A., Lantinga, E. A. (1996) Multi-phasic analysis of gas production kinetics for in vitro fermentation of ruminant feeds, *Animal Feed Science Technology*, **64**, 77–89.

**See Also**

The basic component in the two-phase model is the log-logistic model [llogistic](#).

---

update.drc

*Updating and re-fitting a model*

---

**Description**

'update' updates and re-fits a model on the basis of an object of class 'drc'.

**Usage**

```
## S3 method for class 'drc'  
update(object, ..., evaluate = TRUE)
```

**Arguments**

`object` an object of class 'drc'.  
`...` arguments to alter in object.  
`evaluate` logical. If TRUE model is re-fit; otherwise an unevaluated call is returned.

**Value**

An object of class 'drc'.

**Author(s)**

Christian Ritz

**Examples**

```
## Fitting a four-parameter Weibull model  
model1 <- drm(ryegrass, fct = W1.4())  
  
## Updating 'model1' by fitting a three-parameter Weibull model instead  
model2 <- update(model1, fct = W1.3())  
anova(model2, model1)
```

---

ursa

*Model function for the universal response surface approach (URSA)  
for the quantitative assessment of drug interaction*

---

**Description**

URSA provides a parametric approach for modelling the joint action of several agents. The model allows quantification of synergistic effects through a single parameter.

**Usage**

```
ursa(fixed = rep(NA, 7), names = c("b1", "b2", "c", "d", "e1", "e1", "f"), ssfct = NULL)
```

```
genursa(fixed = rep(NA, 13), names = c("b1", "b2", "c1", "c2", "d", "e1", "e2", "f1", "f2", "e3", "f3", "
```

```
actimL(fixed = rep(NA, 14), names = c("b1", "b2", "c1", "c2", "d", "e1", "e2", "f1", "f2", "e3", "f3", "
```

```
genLoewe(fixed = rep(NA, 8), names = c("b1", "b2", "c", "d", "e1", "e2", "f1", "f2"), ssfct = NULL)
```

```
genLoewe2(fixed = rep(NA, 9), names = c("b1", "b2", "c1", "c2", "d", "e1", "e2", "f1", "f2"), ssfct = NU
```

```
iceLoewe.1(fixed = rep(NA, 7), names = c("b1", "b2", "c", "d", "e1", "e2", "f"), ssfct = NULL)
```

```
iceLoewe2.1(fixed = rep(NA, 8), names = c("b1", "b2", "c1", "c2", "d", "e1", "e2", "f"), ssfct = NULL)
```

```
genBliss(fixed = rep(NA, 8), names = c("b1", "b2", "c", "d", "e1", "e2", "f1", "f2"), ssfct = NULL)
```

```
genBliss2(fixed = rep(NA, 9), names = c("b1", "b2", "c1", "c2", "d", "e1", "e2", "f1", "f2"), ssfct = NU
```

**Arguments**

<code>fixed</code>	numeric vector. Specifies which parameters are fixed and at what value they are fixed. NAs for parameter that are not fixed.
<code>names</code>	a vector of character strings giving the names of the parameters. The default is reasonable.
<code>ssfct</code>	a self starter function to be used (optional).

**Details**

The model function is defined implicitly through an appropriate equation. The details are found in Syracuse and Greco (1986), Greco et al (1990, 1995).

**Value**

A list containing the nonlinear function, the self starter function, and the parameter names.

**Author(s)**

Christian Ritz after an idea by Hugo Ceulemans

**References**

Finney, D. J. (1979) Bioassay and the Practise of Statistical Inference, *Int. Statist. Rev.*, **47**, 1–12.

Syracuse, K. C. and Greco, W. R. (1986) Comparison between the method of Chou and Talalay and a new method for the assessment of the combined effects of drugs: A Monte-Carlo simulation study, *Proceedings of the Biopharmaceutical Section of the American Statistical Association*, 127–132.



```

#greco.m0d <- drm(effect~d1, data=greco, fct=genLoewe2(fixed=c(NA,NA,NA,NA,NA,NA,NA,NA,NA,NA)), pmodels=list(~1,~1,
greco.m0d <- drm(effect~d1+d2, data=greco, fct=genLoewe2(fixed=c(NA,NA,NA,NA,NA,NA,NA,NA,1,1)))
summary(greco.m0d)

## Checking the model fit
#plot(fitted(greco.m0d), residuals(greco.m0d))

## Looking at the summary output
#summary(greco.m0d) # suboptimal fit!

## Fitting the URSA model
#greco.m1 <- drm(effect~d1+d2, data=greco, fct=ursa(fixed=c(NA,NA,0,NA,NA,NA,NA)))
#plot(fitted(greco.m1), residuals(greco.m1))
#summary(greco.m1)

## Fitting the URSA model using values from Greco et al (1995) (p. 364)
#greco.m2 <- drm(effect~d1+d2, data=greco, fct=ursa(fixed=c(NA,NA,0,NA,NA,NA,NA)), start=c(-1.05, -2.04,95.1,11.
# same fit as above

## Fitting with weights
#greco.m2b <- drm(effect~d1, data=greco, fct=ursa(fixed=c(NA,NA,0,NA,NA,NA,NA)), pmodels=list(~1,~1,~1,~I(1/d1)-
#summary(greco.m2b)

## Adjusting for variance heterogeneity
#greco.m3 <- boxcox(greco.m2, method = "anova")

#plot(fitted(greco.m3), residuals(greco.m3)) # improved, not great
#summary(greco.m3)

## Getting closer to Greco's estimates
#greco.m4<-drm(effect~d1, data=greco, fct=ursa(fixed=c(NA,NA,0,NA,NA,NA,NA)), pmodels=list(~1,~1,~1,~I(1/d1)-1,
#greco.m4 <- drm(effect~d1, data=greco, fct=ursa(fixed=c(NA,NA,0,NA,NA,NA,NA)), pmodels=list(~1,~1,~1,~I(1/d1)-1
#start=coef(greco.m3))

#plot(fitted(greco.m4), residuals(greco.m4)) # better!

#summary(greco.m4)

## Fitting the Bliss independence model (with common baseline and maximal response)
greco.bliss.m0 <- drm(effect~d1+d2, data=greco, fct=genBliss(fixed = c(rep(NA, 6),1,1)))
summary(greco.bliss.m0)

## Fitting the generalized Bliss independence model (with common baseline and maximal response)
#greco.bliss.m1 <- drm(effect~d1+d2, data=greco, fct=genBliss())
#summary(greco.bliss.m1)
# huge estimated f parameters!
# huge standard errors on e parameter!

# Likelihood ratio test comparing the two Bliss models
#anova(greco.bliss.m1, greco.bliss.m0)

```

```

# No need to assume that the f parameters are different from 1

## Fitting the generalized Bliss independence model (with different maximal responses)
#greco.bliss.m2 <- drm(effect~d1+d2, data=greco, fct=genBliss2())
#summary(greco.bliss.m2)
# huge estimated f parameters!
# huge standard errors on e parameter!

#greco.bliss.m3 <- drm(effect~d1+d2, data=greco, fct=genBliss2(fixed=c(rep(NA, 7),1,1)))
#summary(greco.bliss.m3)
# much more realistic estimated e parameters

# Likelihood ratio test comparing the two generalized Bliss models
#anova(greco.bliss.m3, greco.bliss.m2)
# No need to assume that the f parameters are different from 1

## Fitting the actimL model (needs some tweaking with the starting values)
#greco.actimL.m1 <- drm(effect~d1+d2, data=greco, fct=actimL(fixed=c(rep(NA,7),1,1,NA,1,rep(NA,3))))
# now works (July 19 2011)

#greco.actimL.m2 <- drm(effect~d1+d2, data=greco, fct=actimL(fixed=c(rep(NA,7),1,1,NA,1,rep(NA,3))), start=coef(
## perhaps some more tweaking with the starting values is needed to get the standard errors

#summary(greco.actimL.m2)

```

---

vcov.drc

---

*Calculating variance-covariance matrix for objects of class 'drc'*


---

## Description

'vcov' returns the estimated variance-covariance matrix for the parameters in the non-linear function.

## Usage

```

## S3 method for class 'drc'
vcov(object, ..., corr = FALSE, od = FALSE, pool = TRUE, unscaled = FALSE)

```

## Arguments

object	an object of class 'drc'.
...	additional arguments.
corr	logical. If TRUE a correlation matrix is returned.
od	logical. If TRUE adjustment for over-dispersion is used. This argument only makes a difference for binomial data.

pool	logical. If TRUE curves are pooled. Otherwise they are not. This argument only works for models with independently fitted curves as specified in <a href="#">drm</a> .
unscaled	logical. If TRUE the unscaled variance-covariance is returned. This argument only makes a difference for continuous data.

**Value**

A matrix of estimated variances and covariances.

**Author(s)**

Christian Ritz

**Examples**

```
## Fitting a four-parameter log-logistic model
ryegrass.m1 <- drm(root1 ~ conc, data = ryegrass, fct = LL.4())
vcov(ryegrass.m1)
vcov(ryegrass.m1, corr = TRUE)
```

---

vinclozolin

*Vinclozolin from AR in vitro assay*


---

**Description**

Dose-response experiment with vinclozolin in an AR reporter gene assay

**Usage**

```
data(vinclozolin)
```

**Format**

A data frame with 53 observations on the following 3 variables.

exper a factor with levels 10509 10821 10828 10904 11023 11106

conc a numeric vector of concentrations of vinclozolin

effect a numeric vector of luminescence effects

**Details**

The basic dose-response experiment was repeated 6 times on different days. Chinese Hamster Ovary cells were exposed to various concentrations of vinclozolin for 22 hours and the resulting luminescence effects were recorded.

Data are part of mixture experiment reported in Nellemann *et al* (2003).

**Source**

Nellemann C., Dalgaard M., Lam H.R. and Vinggaard A.M. (2003) The combined effects of vinclozolin and procymidone do not deviate from expected additivity *in vitro* and *in vivo*, *Toxicological Sciences*, **71**, 251–262.

**Examples**

```
vinclozolin.m1 <- drm(effect~conc, exper, data=vinclozolin, fct = LL.3())
plot(vinclozolin.m1, xlim=c(0,50), ylim=c(0,2800), conLevel=1e-4)

vinclozolin.m2 <- drm(effect~conc, data=vinclozolin, fct = LL.3())
plot(vinclozolin.m2, xlim=c(0,50), conLevel=1e-4, add=TRUE, type="none", col="red")

## Are the ED50 values indetical across experiments?
vinclozolin.m3 <- update(vinclozolin.m1, pmodels=data.frame(exper, exper, 1))
anova(vinclozolin.m3, vinclozolin.m1) # No!
```

W1.2

*The two-parameter Weibull functions***Description**

'W1.2' is the two-parameter Weibull function where the lower limit is fixed at 0 and the upper limit is fixed at 1, mostly suitable for binomial/quantal responses.

**Usage**

```
W1.2(upper = 1, fixed = c(NA, NA), names = c("b", "e"), ...)
```

```
W2.2(upper = 1, fixed = c(NA, NA), names = c("b", "e"), ...)
```

**Arguments**

upper	numeric value. The fixed, upper limit in the model. Default is 1.
fixed	numeric vector. Specifies which parameters are fixed and at what value they are fixed. NAs for parameter that are not fixed.
names	a vector of character strings giving the names of the parameters. The default is reasonable.
...	additional arguments to be passed from the convenience functions.

**Details**

The two-parameter Weibull model is given by the expression

$$f(x) = \exp(-\exp(b(\log(x) - e))).$$

The function is asymmetric about the inflection point, that is the parameter  $\exp(e)$ .

**Value**

See [weibull1](#).

**Note**

This function is for use with the function [drm](#).

**Author(s)**

Christian Ritz

**See Also**

Related functions are [W1.3](#), [W1.4](#), [weibull1](#) and [weibull2](#).

**Examples**

```
## Fitting a two-parameter Weibull model
earthworms.m1 <- drm(number/total~dose, weights = total,
  data = earthworms, fct = W1.2(), type = "binomial")

summary(earthworms.m1)
```

---

W1.3

*The three-parameter Weibull functions*


---

**Description**

'W1.3' and W2.3 provide the three-parameter Weibull function, self starter function and names of the parameters.

'W1.3u' and 'W2.3u' provide three-parameter Weibull function where the upper limit is equal to 1, mainly for use with binomial/quantal response.

**Usage**

```
W1.3(fixed = c(NA, NA, NA), names = c("b", "d", "e"), ...)
```

```
W2.3(fixed = c(NA, NA, NA), names = c("b", "d", "e"), ...)
```

```
W2x.3(fixed = c(NA, NA, NA), names = c("d", "e", "t0"), ...)
```

```
W1.3u(upper = 1, fixed = c(NA, NA, NA), names = c("b", "c", "e"), ...)
```

```
W2.3u(upper = 1, fixed = c(NA, NA, NA), names = c("b", "c", "e"), ...)
```

**Arguments**

upper	numeric value. The fixed, upper limit in the model. Default is 1.
fixed	numeric vector. Specifies which parameters are fixed and at what value they are fixed. NAs for parameter that are not fixed.
names	a vector of character strings giving the names of the parameters. The default is reasonable.
...	additional arguments to be passed from the convenience functions.

**Details**

The three-parameter Weibull model is given by the expression

$$f(x) = 0 + (d - 0) \exp(-\exp(b(\log(x) - e))).$$

The function is asymmetric about the inflection point, that is the parameter  $\exp(e)$ .

The three-parameter Weibull model with upper limit 1 is given by the expression

$$f(x) = 0 + (1 - 0) \exp(-\exp(b(\log(x) - e))).$$

**Value**

See [weibull1](#).

**Note**

This function is for use with the function [drm](#).

**Author(s)**

Christian Ritz

**See Also**

Related functions are [W1.4](#) and [weibull1](#).

**Examples**

```
## Fitting a three-parameter Weibull model
ryegrass.m1 <- drm(root1 ~ conc, data = ryegrass, fct = W1.3())
ryegrass.m1
```

**Description**

'W1.4' and 'W2.4' provide the four-parameter Weibull functions, self starter function and names of the parameters.

**Usage**

```
W1.4(fixed = c(NA, NA, NA, NA), names = c("b", "c", "d", "e"), ...)
```

```
W2.4(fixed = c(NA, NA, NA, NA), names = c("b", "c", "d", "e"), ...)
```

**Arguments**

fixed	numeric vector. Specifies which parameters are fixed and at what value they are fixed. NAs for parameter that are not fixed.
names	a vector of character strings giving the names of the parameters. The default is reasonable.
...	additional arguments to be passed from the convenience functions.

**Details**

The equations for the mean functions are given at [weibull1](#).

**Value**

See [weibull1](#).

**Note**

This function is for use with the model fitting function [drm](#).

**Author(s)**

Christian Ritz

**References**

Seber, G. A. F. and Wild, C. J (1989) *Nonlinear Regression*, New York: Wiley & Sons (pp. 330–331).

Ritz, C (2009) Towards a unified approach to dose-response modeling in ecotoxicology *To appear in Environ Toxicol Chem*.

**See Also**

Setting  $c = 0$  yields [W1.3](#). A more flexible function, allowing fixing or constraining parameters, is available through [weibull1](#).

**Examples**

```
## Fitting a four-parameter Weibull (type 1) model
terbuthylazin.m1 <- drm(rgr~dose, data = terbuthylazin, fct = W1.4())
summary(terbuthylazin.m1)

## Fitting a first-order multistage model
## to data from BMDS by EPA
## (Figure 3 in Ritz (2009))
bmds.ex1 <- data.frame(ad.dose=c(0,50,100), dose=c(0, 2.83, 5.67), num=c(6,10,19), total=c(50,49,50))

bmds.ex1.m1<-drm(num/total~dose, weights=total, data=bmds.ex1, fct=W2.4(fixed=c(1,NA,1,NA)), type="binomial")

modelFit(bmds.ex1.m1) # same as in BMDS

summary(bmds.ex1.m1) # same background estimate as in BMDS

logLik(bmds.ex1.m1)

## BMD estimate identical to BMDS result
## BMDL estimate differs from BMDS result (different method)
ED(bmds.ex1.m1, 10, ci="delta")

## Better fit

bmds.ex1.m2<-drm(num/total~dose, weights=total, data=bmds.ex1, fct=W1.4(fixed=c(-1,NA,1,NA)), type="binomial")
modelFit(bmds.ex1.m2)
summary(bmds.ex1.m2)

ED(bmds.ex1.m2, 50, ci = "delta")

## Creating Figure 3 in Ritz (2009)
bmds.ex1.m3 <- drm(num/total~dose, weights=total, data=bmds.ex1, fct=LL.4(fixed=c(-1,NA,1,NA)), type="binomial")

plot(bmds.ex1.m1, ylim = c(0.05, 0.4), log = "", lty = 3, lwd = 2, xlab = "Dose (mg/kg/day)", ylab = "",
cex=1.2, cex.axis=1.2, cex.lab=1.2)

mtext("Tumor incidence", 2, line=4, cex=1.2) # tailored y axis label

plot(bmds.ex1.m2, ylim = c(0.05, 0.4), log = "", add = TRUE, lty = 2, lwd = 2)

plot(bmds.ex1.m3, ylim = c(0.05, 0.4), log = "", add = TRUE, lty = 1, lwd = 2)

arrows(2.6 , 0.14, 2, 0.14, 0.15, lwd=2)
text(2.5, 0.14, "Weibull-1", pos=4, cex=1.2)
```

weibull1

*Weibull model functions***Description**

'weibull' and 'weibull2' provide a very general way of specifying Weibull dose response functions, under various constraints on the parameters.

**Usage**

```
weibull1(fixed = c(NA, NA, NA, NA),
         names = c("b", "c", "d", "e"),
         method = c("1", "2", "3", "4"),
         ssfct = NULL,
         fctName, fctText)

weibull2(fixed = c(NA, NA, NA, NA),
         names = c("b", "c", "d", "e"),
         method = c("1", "2", "3", "4"),
         ssfct = NULL,
         fctName, fctText)

weibull2x(fixed = rep(NA, 5),
          names = c("b", "c", "d", "e", "t0"),
          method = c("1", "2", "3", "4"),
          ssfct = NULL,
          fctName, fctText)
```

**Arguments**

fixed	numeric vector. Specifies which parameters are fixed and at what value they are fixed. NAs for parameter that are not fixed.
names	a vector of character strings giving the names of the parameters (should not contain ":"). The default is reasonable (see under 'Usage'). The order of the parameters is: b, c, d, e (see under 'Details').
method	character string indicating the self starter function to use.
ssfct	a self starter function to be used.
fctName	optional character string used internally by convenience functions.
fctText	optional character string used internally by convenience functions.

**Details**

As pointed out in Seber and Wild (1989), there exist two different parameterisations of the Weibull model. They do not yield the same fitted curve for a given dataset (see under Examples).

One four-parameter Weibull model ('weibull1') is

$$f(x) = c + (d - c) \exp(-\exp(b(\log(x) - \log(e))))).$$

Another four-parameter Weibull model ('weibull2') is

$$f(x) = c + (d - c)(1 - \exp(-\exp(b(\log(x) - \log(e))))).$$

Both four-parameter functions are asymmetric with inflection point at the dose  $e$ .

### Value

The value returned is a list containing the non-linear function, the self starter function and the parameter names.

### Note

The functions are for use with the function [drm](#).

### Author(s)

Christian Ritz

### References

Seber, G. A. F. and Wild, C. J (1989) *Nonlinear Regression*, New York: Wiley & Sons (pp. 338–339).

### See Also

For convenience several special cases of the function 'weibull1' are available: [W1.2](#), [W1.3](#) and [W1.4](#).

Special cases of 'weibull2' are: [W2.2](#), [W2.3](#) and [W2.4](#).

These convenience functions should be used rather than the underlying functions weibull1 and weibull2.

### Examples

```
## Fitting two different Weibull models
ryegrass.m1 <- drm(ryegrass, fct = W1.4())
plot(ryegrass.m1, conLevel=0.5)

ryegrass.m2 <- drm(ryegrass, fct = W2.4())
plot(ryegrass.m2, conLevel=0.5, add = TRUE, type = "none", col = 2)
# you could also look at the ED values to see the difference

## A four-parameter Weibull model with b fixed at 1
ryegrass.m3 <- drm(ryegrass, fct = W1.4(fixed = c(1, NA, NA, NA)))
summary(ryegrass.m3)

## A four-parameter Weibull model with the constraint b>3
```

```
ryegrass.m4 <- drm(ryegrass, fct = W1.4(), lower1 = c(3, -Inf, -Inf, -Inf),
control = drmc(constr=TRUE))
summary(ryegrass.m4)
```

---

yieldLoss

*Calculating yield loss parameters*


---

### Description

Calculation of parameters in the re-parameterization of the Michaelis-Menten model that is commonly used to assess yield loss (the rectangular hyperbola model)

### Usage

```
yieldLoss(object, interval = c("none", "as"), level = 0.95, display = TRUE)
```

### Arguments

object	object of class 'drm'
interval	character string specifying the type of confidence intervals to be supplied. The default is "none". Use "as" for asymptotically-based confidence intervals.
level	numeric. The level for the confidence intervals. The default is 0.95.
display	logical. If TRUE results are displayed. Otherwise they are not (useful in simulations).

### Details

The rectangular hyperbola model is a reparameterization of the Michaelis-Menten in terms of parameters  $A$  and  $I$

$$Y_L = \frac{Id}{1 + Id/A}$$

where  $d$  denotes the weed density and  $Y_L$  the resulting yield loss.

### Value

For each of the two parameters, a matrix with two or more columns, containing the estimates and the corresponding estimated standard errors and possibly lower and upper confidence limits.

### Note

This function is only for use with model fits based on Michaelis-Menten models.

### Author(s)

Christian Ritz

**References**

Cousens, R. (1985). A simple model relating yield loss to weed density, *Ann. Appl. Biol.*, **107**, 239–252.

**Examples**

```
## Fitting Michaelis-Menten model
met.mm.m1 <- drm(gain~dose, product, data = methionine, fct = MM.3(),
pmodels = list(~1, ~factor(product), ~factor(product)))

## Yield loss parameters with standard errors
yieldLoss(met.mm.m1)

## Also showing confidence intervals
yieldLoss(met.mm.m1, "as")
```

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