

Analysis of a single dose-response curve

Binary/binomial data

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Example 1

Dose-response data from a acute inhalation toxicity test where 20 animals were exposed to 4 doses (mg/ml of an unknown substance), 5 animals per dose:

```
library(drc)

library(devtools)
install_github("DoseResponse/drcData")
library(drcData)
```

```
acute.inh
```

##	dose	total	num.dead
## 1	422	5	0
## 2	744	5	1
## 3	948	5	3
## 4	2069	5	5

Fitting the model

The proportions of dead animals (`num.dead/total`), which is the response, are specified on the left hand side of the tilde (`~`), and the dose (`dose`) on the right hand side. The totals (`total`) are provided through the argument `weights`

We fit a two-parameter log-logistic model:

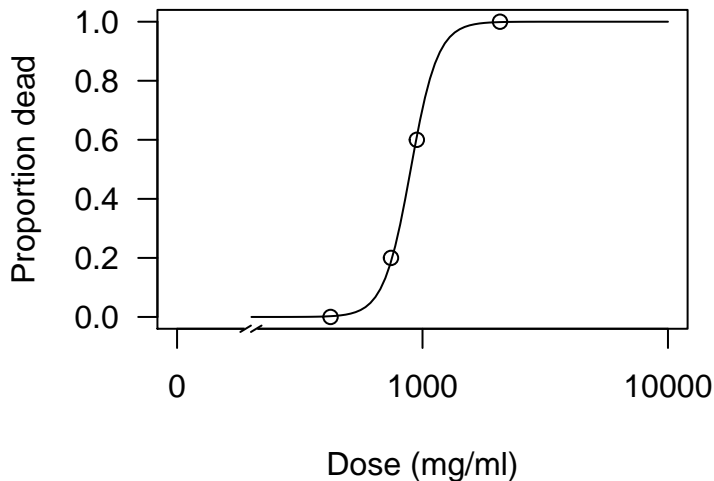
```
acute.inh.LL.2 <- drm(num.dead/total ~ dose,  
                     weights = total,  
                     data = acute.inh,  
                     fct = LL.2(),  
                     type = "binomial")
```

Fitted dose-response curve (1)

Using plot() again:

```
plot(acute.inh.LL.2, broken = TRUE,  
     xlim = c(0, 10000), ylim = c(0, 1),  
     ylab = "Proportion dead",  
     xlab = "Dose (mg/ml)")
```

Fitted dose-response curve (2)



Summary of the model fit

Showing parameter estimates:

```
summary(acute.inh.LL.2)
```

```
##  
## Model fitted: Log-logistic (ED50 as parameter) with lower limit at 0 and upper 1  
##  
## Parameter estimates:  
##  
##           Estimate Std. Error t-value p-value  
## b:(Intercept)  -7.9301      5.0812 -1.5607  0.1186  
## e:(Intercept)  895.2982     83.5547 10.7151  <2e-16 ***  
## ---  
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Getting confidence intervals:

```
confint(acute.inh.LL.2)
```

```
##           2.5 %      97.5 %  
## b:(Intercept) -17.88909    2.028992  
## e:(Intercept) 731.53397 1059.062485
```

Example 2

Data are from an earthworm toxicity test with 6 concentrations of the herbicide chloracetamide. For each concentration, 40 earthworms were exposed to the herbicide and subsequently the number of dead earthworms was counted. The control or natural mortality was $3/40 = 7.5\%$.

```
chlorac
```

##	conc	total	num.dead
## 1	0	40	3
## 2	10	40	5
## 3	20	40	6
## 4	40	40	38
## 5	80	40	40
## 6	160	40	40

Fitting the model

Natural mortality incorporated using a three-parameter dose-response model where there is an additional model parameter describing the proportion of natural mortality

We fit a three-parameter log-normal model including a parameter for the lower limit (corresponding to the natural mortality), but fixing the upper limit at 1 as was also the case for the two-parameter models in the previous example:

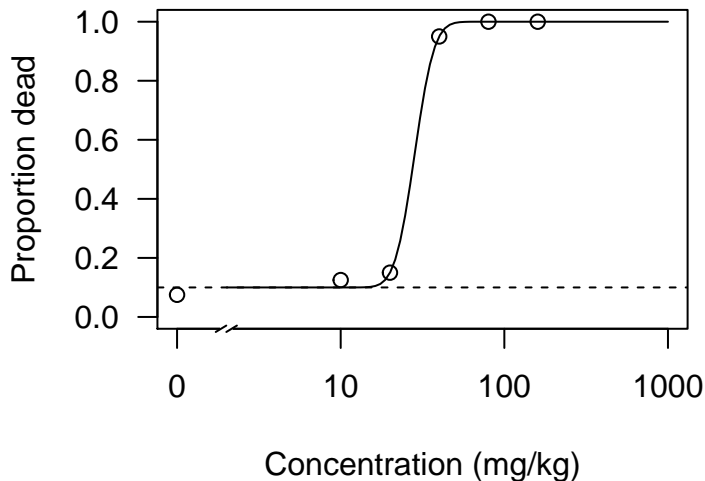
```
chlorac.LN.3u <- drm(num.dead/total ~ conc,  
                    weights = total,  
                    data = chlorac,  
                    fct = LN.3u(),  
                    type = "binomial")
```


Fitted dose-response curve (1)

Using the plot function once more:

```
plot(chlorac.LN.3u, broken = TRUE,  
     xlim = c(0, 1000), ylim = c(0, 1),  
     ylab = "Proportion dead",  
     xlab = "Concentration (mg/kg)")  
  
abline(a = coef(chlorac.LN.3u)[2], b = 0, lty = 2)
```

Fitted dose-response curve (2)



Summary of the model fit

```
summary(chlorac.LN.3u)
```

```
##
## Model fitted: Log-normal with upper limit at 1 (3 parms)
##
## Parameter estimates:
##
##           Estimate Std. Error t-value   p-value
## b:(Intercept)  4.603773   1.043813  4.4105 1.031e-05 ***
## c:(Intercept)  0.099988   0.033573  2.9783 0.002899 **
## e:(Intercept) 28.291922   2.271962 12.4526 < 2.2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
confint(chlorac.LN.3u)
```

```
##           2.5 %      97.5 %
## b:(Intercept)  2.55793762  6.6496084
## c:(Intercept)  0.03418668  0.1657886
## e:(Intercept) 23.83895875 32.7448861
```

Estimating EC values

We can estimate the concentration resulting in a total mortality of 50%, which is an EC value that is defined in absolute terms based on the probability scale and not relative to limits partly or fully estimated from the data:

```
ED(chlorac.LN.3u, 50 / 100, type = "absolute", interval = "delta")
```

```
##  
## Estimated effective doses  
##  
##      Estimate Std. Error   Lower   Upper  
## e:1:0.5  27.4464      2.3155 22.9080 31.9847
```

If instead a two-parameter model had been fitted then the estimated EC50 would become smaller, biased downwards, with a more narrow 95% confidence intervals: a less accurate but more precise estimate of EC50 would be the result (bias-variance tradeoff)