

Package ‘toxtestD’

February 20, 2015

Type Package

Title Experimental design for binary toxicity tests

Version 2.0

Date 2014-11-12

Author Nadia Keddig and Werner Wosniok

Maintainer Nadia Keddig <publication@gmx.net>

Description Calculates sample size and dose allocation for binary toxicity tests, using the Fish Embryo Toxicity Test as example. An optimal test design is obtained by running (i) spoD (calculate the number of individuals to test under control conditions), (ii) setD (estimate the minimal sample size per treatment given the users precision requirements) and (iii) doseD (construct an individual dose scheme).

License GPL-2

NeedsCompilation no

Repository CRAN

Date/Publication 2014-11-13 17:22:05

R topics documented:

toxtestD-package	2
doseD	3
setD	5
spoD	7

Index	10
--------------	-----------

Description

Calculates sample size and dose allocation for binary toxicity tests, using the Fish Embryo Toxicity Test as example. An optimal test design is obtained by running (i) spoD (calculate the number of individuals to test under control conditions), (ii) setD (estimate the minimal sample size per treatment given the users precision requirements) and (iii) doseD (construct an individual dose scheme).

Details

Package: toxtestD
Type: Package
Version: 2.0
Date: 2014-10-27
License: GPL-2

Author(s)

Nadia Keddig & Werner Wosniok

Maintainer: Nadia Keddig <publication@gmx.net>

References

Optimal test design for binary response data: the example of the Fish Embryo Toxicity Test. Submitted.

See Also

None

Examples

```
# == spoD ==  
# determine spontaneous rate  
  
#1a: planning  
spoD(n=600, SL.p=3.5, SLmin=NA, SLmax=NA, bio.sd.p=2.008)  
spoD(n=600, SL.p=NA, SLmin=3, SLmax=4)  
spoD(n=600, SL.p=3.5, SLmin=NA, SLmax=NA, bio.sd.p=2.008, print.result="spoDa.txt")  
spoD(n=600, SL.p=3.5, SLmin=NA, SLmax=NA, bio.sd.p=2.008, print.result=FALSE)
```

```

#1b: analysis
SLdataset <- data.frame(n=rep(60,times=4),bearer=c(1,5,8,3))
spoD(analysis=TRUE,SLdataset=SLdataset)
spoD(analysis=TRUE,SLdataset=SLdataset,print.result="spoDb.txt")
spoD(analysis=TRUE,SLdataset=SLdataset,print.result=FALSE)

# == setD ==
# determine sample size

setD(nmax=350,SL.p=5.5,immunity.p=0,risk.type=2,target.EC=10,
      alpha.p=5,beta.p=20,plot="single")
setD(nmax=350,SL.p=3,target.EC=5,plot="FALSE")
setD(nmax=350,SL.p=3,target.EC=5,plot="FALSE",print.result="setD.txt")
setD(nmax=350,SL.p=3,target.EC=5,plot="FALSE",print.result=FALSE)

# == doseD ==
# dose allocation

DP <- data.frame( name=c("neg.control",rep("substance",times=6)),
                  organisms=c(42,41,42,42,38,42,39),
                  death= c(1,3,40,20,12,40,13),
                  concentration=c(0.0,2.0,3.5,4.0,6.0,8.0,6.0),
                  unit=rep("mg/ml",times=7) )
doseD(DP=DP,immunity.p=4.7,SL.p=9,target.EC.p=c(15,30,40),
      nconc=9,text=TRUE,risk.type=1)
doseD(DP=DP,immunity.p=4.7,SL.p=9,target.EC.p=c(15,30,40),
      nconc=9,text=TRUE,risk.type=2)
doseD(DP=DP,immunity.p=4.7,SL.p=9,target.EC.p=c(15,30,40),
      nconc=9,text=TRUE,risk.type=3)
doseD(DP=DP,immunity.p=4.7,SL.p=9,target.EC.p=c(15,30,40),
      nconc=9,text=TRUE,risk.type=3,print.result="doseD4.txt")
doseD(DP=DP,immunity.p=4.7,SL.p=9,target.EC.p=c(15,30,40),
      nconc=9,text=TRUE,risk.type=3,print.result=FALSE)

```

dosed

doseD: Construction of an individual dose scheme

Description

This function calculates optimal concentration points according to the EC target specification, spontaneous lethality (SL), immunity (IY) and the accepted type I and type II error levels.

Usage

```
doseD(DP, immunity.p = 0, SL.p = 0, target.EC.p = 10,
```

```
nconc = 8, text = TRUE, risk.type = 2,
print.result = "03.dosestrategy.txt")
```

Arguments

DP	The results from pretests should be given as a data.frame with the columns "name", "organisms", "death", "concentration" and "unit", which will be needed for the calculations of the dose scheme
immunity.p	Immunity in percent (see also explanation in "spoD")
SL.p	Spontaneous level in percent, calculated from the users experimental data by the function "spoD"
target.EC.p	Effect of special interest in percent. More than one target may be given for one calculation. Example: if EC5 and EC10 are of special interest, then use target.EC=c(5,10). Corresponding dose points will be allocated around both targets with distances derived from the confidence interval width.
nconc	Number of different concentrations the user is willing to test in the experiment.
text	text=TRUE adds extended information in the plot.
risk.type	Choose one of (1,2,3) to select a risk type (see reference for more detail): 1: Total risk (TR): The total risk is the total response expressed as percentage of affected biological units among all treated units. Spontaneous lethality and immunity are ignored. 2: Added risk (AR): The reference frame is restricted below and above by spontaneous lethality (SL) and immunity (IY). Only the response above the SL is considered as an effect. Using AR, the total response associated with a target effect of size xx and a spontaneous lethality SL is $xx + SL$. 3: Extra risk (ER): The reference frame is the interval from SL to (100%-IY). Using ER, the total response associated with a target effect of size xx is $SL + 0.01 * xx * (100\% - SL - IY)$.
print.result	If empty, the result is written to "03.dosestrategy.txt" in the calling directory, if a file name is given, the result is written to that file, if FALSE, nothing is written

Value

A matrix with the recommended dose scheme is returned. It has nconc rows and contains columns c("concentration", "unit", "effect") describing the concentrations in units "unit" for the effect in "effect".

Author(s)

Nadia Keddig & Werner Wosniok

References

Optimal test design for binary response data: the example of the Fish Embryo Toxicity Test. Submitted.

Examples

```
# calculation of an optimal dose scheme
# pretest results as dataframe (DP)
DP <- data.frame( name=c("neg.control",rep("substance",times=6)),
                  organisms=c(42,41,42,42,38,42,39),
                  death= c(1,3,40,20,12,40,13),
                  concentration=c(0.0,2.0,3.5,4.0,6.0,8.0,6.0),
                  unit=rep("mg/ml",times=7) )

# test design
doseD(DP=DP,immunity.p=4.7,SL.p=9,target.EC.p=c(15,30,40),
      nconc=9,text=TRUE,risk.type=1)
doseD(DP=DP,immunity.p=4.7,SL.p=9,target.EC.p=c(15,30,40),
      nconc=9,text=TRUE,risk.type=2)
doseD(DP=DP,immunity.p=4.7,SL.p=9,target.EC.p=c(15,30,40),
      nconc=9,text=TRUE,risk.type=3)
doseD(DP=DP,immunity.p=4.7,SL.p=9,target.EC.p=c(15,30,40),
      nconc=9,text=TRUE,risk.type=3,print.result="dose4.txt")
doseD(DP=DP,immunity.p=4.7,SL.p=9,target.EC.p=c(15,30,40),
      nconc=9,text=TRUE,risk.type=3,print.result=FALSE)
```

 setD

setD: Determining the optimal number of objects per treatment

Description

"setD" estimates the minimal sample size given the users precision requirements including the accepted errors of the first and second type.

Usage

```
setD(nmax, SL.p, immunity.p = 0, risk.type = 2,
     target.EC.p = 10, plot = FALSE, alpha.p = 5,
     beta.p = 20, print.result = "02.sample size.txt")
```

Arguments

nmax	maximum available number of organisms that can be tested per treatment. The calculation of the optimal number will only be done if this number is high enough to generate the response of at least one organism under control conditions ($nmax * SL.p > 1$). Otherwise a warning message is issued.
SL.p	spontaneous lethality in percent. The function "spoD" can be used to calculate SL.p from own experimental data.
immunity.p	Immunity in percent. A population of biological objects might contain a subpopulation which shows no reaction at all (is immune). immunity.p gives the size of the subpopulation in percent of total population size. The concentration-response curve always has [100% - IY] as maximum. EC values are affected by immunity.p only if risktype=3 is used.

risk.type	<p>Choose one of (1,2,3) to select a risk type (see reference for more detail):</p> <p>1: Total risk (TR): The total risk is the total response expressed as percentage of affected biological units among all treated units. Spontaneous lethality and immunity are ignored.</p> <p>2: Added risk (AR): The reference frame is restricted below and above by spontaneous lethality (SL) and immunity (IY). Only the response above the SL is considered as an effect. Using AR, the total response associated with a target effect of size xx and a spontaneous lethality SL is $xx + SL$.</p> <p>3: Extra risk (ER): The reference frame is the interval from SL to $(100\% - IY)$. Using ER, the total response associated with a target effect of size xx is $SL + 0.01 * xx * (100\% - SL - IY)$.</p>
target.EC.p	The target response in percent (e.g. 10% to calculate EC10). Only a single value is allowed. Note that the interpretation of target.EC depends on the risktype setting.
plot	<p>There are three possibilities:</p> <p>plot = FALSE: no plots.</p> <p>plot = "single": Creates one plot showing the distributions under no treatment and under treated conditions with the optimal number of cases. Additionally, the actual rates of the type I and type II error are given.</p> <p>plot = "all": In addition to the "single" plot this option provides a sample size estimation for all possible target values. This gives an impression which possibilities of detection exist under the chosen conditions. This option may need a lot of computer capacity and time. It should not be activated in general.</p>
alpha.p	alpha & beta: size of the type I and type II in percent. The default global settings for alpha and beta are alpha = 5 percent and beta = 20 percent. Increasing the default error rates is not recommended. The accepted error rates are global parameters and affect all calculations.
beta.p	see alpha.p
print.result	If omitted, the result is written to "02.sample size.txt" in the calling directory, if a file name is given, the result is written to that file, if FALSE, nothing is written

Value

number.organisms	sample size per treatment, substance and run
spontaneous.lethality	assumed spontaneous lethality in %
immunity	assumed immunity in %
delta.to.zero	total response (= target.EC + spontaneous.lethality)
risk.type	risk type, see arguments
target.EC	the target response in percent
exact.alpha	exact alpha error when testing H0: $p(\text{response}) = \text{spontaneous.lethality}$, given the parameters assumed and number of organisms = number.organisms
exact.beta	exact beta error, given the parameters assumed and number of organisms = number.organisms

Author(s)

Nadia Keddig & Werner Wosniok

References

Optimal test design for binary response data: the example of the Fish Embryo Toxicity Test. Submitted.

Examples

```
# sample size calculation per treatment and experimental run
setD(nmax=350,SL.p=5.5,immunity.p=0,risk.type=2,target.EC=10,
     alpha.p=5,beta.p=20,plot="single")
setD(nmax=350,SL.p=3,target.EC=5,plot="FALSE")
setD(nmax=350,SL.p=3,target.EC=5,plot="FALSE",print.result="setD.txt")
setD(nmax=350,SL.p=3,target.EC=5,plot="FALSE",print.result=FALSE)
```

spoD

spoD: Determine spontaneous response level or the optimal sample size

Description

The function "spoD" offers two services. In the planning process the number of individuals to test under control conditions is calculated, together with a proposal for partitioning the total data set into subgroups in order to identify the amount of biological variation between experiments. In the analysis process, the spontaneous lethality together with its 95% confidence interval and the biological variation are computed from the users data.

Usage

```
spoD(n = 500, SL.p = 5, SLmin = NA, SLmax = NA,
     bio.sd.p = 2.008, maxCI = 2.5,
     analysis = FALSE, SLdataset = NA,
     print.result = "01_spontaneous lethality.txt")
```

Arguments

n	maximally possible number (integer) of test organisms. Limiting this number is necessary to avoid non-essential calculations and thereby save computing time. The program will invite the user to increase the number if the number is not high enough to estimate the SL with the specified precision.
SL.p	A rough guess of the spontaneous lethality (SL) in %. It is possible to specify SL.p either as single number or as an interval between 0-100% by using SLmin and SLmax. At least SL.p or (SLmin,SLmax) must be specified.
SLmin	see SL.p
SLmax	see SL.p

bio.sd.p	(optional): an assumption about the biological contribution the standard deviation of the estimated SL. The default of 2.008% holds for the Fish Embryo Toxicity test. The optimal number of partitions of the sample under control conditions will be determined using the bio.sd.p specified.
maxCI	the maximally accepted absolute difference in percent between mean SL and its confidence limits. Default: 2.5%.
analysis	defaults to FALSE, indicating that the function does planning. To analyze an SLdataset as described below, choose analysis=TRUE.
SLdataset	the data frame containing the spontaneous data to analyze. It has columns titled "n" and "bearer". Column "n" contains the total number of observations, column "bearer" contains the number of organisms which are carriers (in the case of FET the counts of dead or lethal malformed eggs). Each row contains the outcome from one experimental run.
print.result	If omitted, the result is written to "01_spontaneous lethality.txt" in the calling directory, if a file name is given, the result is written to that file, if FALSE, nothing is written

Value

if analyse=FALSE:

targetSL	assumed spontaneous lethality in %, typically close or identical to SL.p
ntarget	total number of organisms to test, based on the point estimate SL.p
optnum	optimal number of separate sub-tests, based on SL.p
nopt	number of organisms per sub-test, based on SL.p
maxSL	spontaneous lethality associated with maxn
Intmin	lower limit of interval for assumed spontaneous lethality
Intmax	upper limit of interval for assumed spontaneous lethality
maxn	maximal number of organisms to test, if an interval was given for the assumed spontaneous lethality
optmax	optimal number of separate sub-tests, based on Int.min, Int.max
noptmax	number of organisms per sub-test, based on Int.min, Int.max

with analyse=TRUE:

SL	estimated spontaneous lethality in %
CIlo	lower limit of 95% confidence interval for SL
CIup	upper limit of 95% confidence interval for SL
sdSL	standard deviation of SL

Author(s)

Nadia Keddig & Werner Wosniok

References

Optimal test design for binary response data: the example of the Fish Embryo Toxicity Test. Submitted.

Examples

```
#spontaneous lethality

#1a: planning
spoD(n=600, SL.p=3.5, SLmin=NA, SLmax=NA, bio.sd.p=2.008)
spoD(n=600, SL.p=NA, SLmin=3, SLmax=4)
spoD(n=600, SL.p=3.5, SLmin=NA, SLmax=NA, bio.sd.p=2.008, print.result="spoDa.txt")
spoD(n=600, SL.p=3.5, SLmin=NA, SLmax=NA, bio.sd.p=2.008, print.result=FALSE)

#1b: analysis
SLdataset <- data.frame(n=rep(60, times=4), bearer=c(1,5,8,3))
spoD(analysis=TRUE, SLdataset=SLdataset)
spoD(analysis=TRUE, SLdataset=SLdataset, print.result="spoDb.txt")
spoD(analysis=TRUE, SLdataset=SLdataset, print.result=FALSE)
```

Index

*Topic **design**

doseD, [3](#)

setD, [5](#)

spoD, [7](#)

toxtestD-package, [2](#)

*Topic **package**

toxtestD-package, [2](#)

doseD, [3](#)

setD, [5](#)

spoD, [7](#)

toxtestD (toxtestD-package), [2](#)

toxtestD-package, [2](#)