Package 'crmPack'

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Maintainer Daniel Sabanes Bove <sabanesd@roche.com>

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Title Object-oriented implementation of CRM designs

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Author Daniel Sabanes Bove <sabanesd@roche.com>

Description Object-oriented implementation of CRM designs

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Imports methods,R2WinBUGS,gridExtra,GenSA,mvtnorm,parallel,BayesLogit,rjags

Suggests ggmcmc,grid

Collate 'Data-class.R' 'Data-methods.R' 'helpers.R' 'Rules-class.R' 'Model-class.R' 'Design-class.R'
'McmcOptions-class.R' 'McmcOptions-methods.R' 'Samples-class.R' 'Model-methods.R'
'Rules-methods.R' 'Samples-methods.R' 'Simulations-class.R' 'Simulations-methods.R'
'crmPack-package.R' 'fromQuantiles.R' 'mcmc.R' 'simulate.R'

R topics documented:

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crmPack-package   *Object-oriented implementation of CRM designs*

Description

Object-oriented implementation of CRM designs

Author(s)

Daniel Sabanes Bove <sabanesd@roche.com>

---

as.list,Data-method   *as.list method for the "Data" class*

Description

as.list method for the "Data" class

Usage

```
## S4 method for signature 'Data'
as.list(x, ...)
```

Arguments

x   the [Data](#) object we want to convert

...   objects, possibly named.

Value

a list of all slots in x

CohortSize-class   *The virtual class for cohort sizes*

Description

The virtual class for cohort sizes

See Also

[CohortSizeMax](#), [CohortSizeMin](#), [CohortSizeRange](#), [CohortSizeDLT](#), [CohortSizeConst](#)

CohortSizeConst-class   *Constant cohort size*

Description

This class is used when the cohort size should be kept constant.

Slots

size the constant integer size

CohortSizeDLT-class   *Cohort size based on number of DLTs*

Description

Cohort size based on number of DLTs

Slots

DLTintervals a vector with the bounds of the relevant DLT intervals of length n

cohortSize an integer vector of length n-1 with the cohort sizes in the DLTintervals

CohortSizeMax-class   *Size based on maximum of multiple cohort size rules*

Description

This class can be used to combine multiple cohort size rules with the MAX operation.

Details

cohortSizeList contains all cohort size rules, which are again objects of class CohortSize. The maximum of these individual cohort sizes is taken to give the final cohort size.

Slots

cohortSizeList list of cohort size rules

CohortSizeMin-class   *Size based on minimum of multiple cohort size rules*

Description

This class can be used to combine multiple cohort size rules with the MIN operation.

Details

cohortSizeList contains all cohort size rules, which are again objects of class CohortSize. The minimum of these individual cohort sizes is taken to give the final cohort size.

Slots

cohortSizeList list of cohort size rules

CohortSizeRange-class   *Cohort size based on dose range*

Description

Cohort size based on dose range

Slots

intervals a vector with the bounds of the relevant dose intervals of length n

cohortSize an integer vector of length n-1 with the cohort sizes in the intervals

---

Data-class   *Class for the data input*

Description

Class for the data input

Slots

x the doses for the patients

y the vector of toxicity events (0 or 1 integers)

ID unique patient IDs (integer vector)

cohort the cohort indices (sorted values from 0, 1, 2, ...)

doseGrid the vector of all possible doses (sorted), i.e. the dose grid

nObs number of observations

nGrid number of gridpoints

xLevel the levels for the doses the patients have been given

DataDual-class   *Class for the dual endpoint data input*

Description

This is a subclass of [Data](#), so contains all slots from [Data](#), and in addition biomarker values.

Slots

w the continuous vector of biomarker values

Design-class   *Class for the CRM design*

Description

Class for the CRM design

Slots

model the model to be used, an object of class [Model](#)

nextBest how to find the next best dose, an object of class [NextBest](#)

stopping stopping rule(s) for the trial, an object of class [Stopping](#)

increments how to control increments between dose levels, an object of class [Increments](#)

cohortSize rules for the cohort sizes, an object of class [CohortSize](#)

data what is the dose grid, any previous data, etc., contained in an object of class [Data](#)

startingDose what is the starting dose? Must lie on the grid in data

---

dose   *Compute the doses for a given probability, given model and samples*

Description

Compute the doses for a given probability, given model and samples

Usage

```
dose(prob, model, samples, ...)
```

Arguments

prob   the probability

model   the [Model](#)

samples   the [Samples](#)

...   unused

```
dose,numeric,Model,Samples-method
```
                            Compute the doses for a given probability, given model and samples

Description

Compute the doses for a given probability, given model and samples

Usage

```
## S4 method for signature 'numeric,Model,Samples'
dose(prob, model, samples, ...)
```

Arguments

prob	the probability
model	the [Model](#)
samples	the [Samples](#)
...	unused

```
DualEndpoint-class        Dual endpoint model
```

Description

todo: describe the model

Slots

mu For the probit toxicity model, mu contains the prior mean vector

Sigma For the probit toxicity model, contains the prior covariance matrix

sigma2betaW For the biomarker model, contains the prior variance factor of the random walk prior. If it is not a single number, it can also contain a vector with elements a and b for the inverse-gamma prior on sigma2betaW.

sigma2W Either a fixed value for the biomarker variance, or a vector with elements a and b for the inverse-gamma prior parameters.

rho Either a fixed value for the correlation (between -1 and 1), or a vector with elements a and b for the Beta prior on the transformation kappa = (rho + 1) / 2, which is in (0, 1). For example, a=1,b=1 leads to a uniform prior on rho.

useRW1 for specifying the random walk prior on the biomarker level: if TRUE, RW1 is used, otherwise RW2.

useFixed a list with logical value for each of the three parameters sigma2betaW, sigma2W and rho indicating whether a fixed value is used or not.

---

extract | *Extract something from an object and produce a data.frame*

Description

Extract something from an object and produce a data.frame

Usage

```
extract(object, ...)
```

Arguments

object   the object

...   unused

Value

the data frame

---

extract,Samples-method
| *Extract certain parameter from Samples object*

Description

Extract certain parameter from Samples object

Usage

```
## S4 method for signature 'Samples'
extract(object, parameter, ...)
```

Arguments

object   the [Samples](#) object

parameter   the name of the parameter

...   unused

Value

the data frame suitable for use with [ggmcmc](#)

`fitted,Samples-method`   *Fit method for the Samples class*

Description

Fit method for the Samples class

Usage

```
## S4 method for signature 'Samples'
fitted(object, model, data, quantiles = c(0.025, 0.975),
  middle = mean, ...)
```

Arguments

object	the [Samples](#) object
model	the [Model](#) object
data	the [Data](#) object
quantiles	the quantiles to be calculated (default: 0.025 and 0.975)
middle	the function for computing the middle point. Default: [mean](#)
...	other arguments.

Value

data frame with dose, middle, lower and upper quantiles

`Increments-class`   *The virtual class for controlling increments*

Description

The virtual class for controlling increments

See Also

[IncrementsRelative](#), [IncrementsRelativeDLT](#)

`IncrementsRelative-class`

                              Increments control based on relative differences in intervals

---

Description

Increments control based on relative differences in intervals

Slots

intervals a vector with the bounds of the relevant intervals of length n

increments a vector of length n-1 with the maximum allowable relative increments in the `intervals`

IncrementsRelativeDLT-class

Increments control based on relative differences in terms of DLTs

Description

Increments control based on relative differences in terms of DLTs

Slots

DLTintervals a vector with the bounds of the relevant DLT intervals of length n

increments a vector of length n-1 with the maximum allowable relative increments in the DLTintervals

initialize,Data-method

Initialization method for the "Data" class

Description

This is the method for initializing a "Data" class object.

Usage

```
## S4 method for signature 'Data'
initialize(.Object, x = numeric(), y = integer(),
  ID = integer(), cohort = integer(), doseGrid = numeric(), ...)
```

Arguments

.Object	the [Data](#) we want to initialize
x	the doses for the patients
y	the vector of toxicity events (0 or 1 integers)
ID	unique patient IDs (integer vector)
cohort	the cohort indices (sorted values from 0, 1, 2, ...)
doseGrid	the vector of all possible doses
...	data to include in the new object. Named arguments correspond to slots in the class definition. Unnamed arguments must be objects from classes that this class extends.

Details

Note that ID and cohort can be missing, then a warning will be issued and the variables will be filled with default IDs and best guesses, respectively.

---

initialize,DualEndpoint-method

Initialization method for the "DualEndpoint" class

Description

Initialization method for the "DualEndpoint" class

Usage

```
## S4 method for signature 'DualEndpoint'
initialize(.Object, mu, Sigma, sigma2betaW, sigma2W,
  rho, smooth = c("RW1", "RW2"), ...)
```

Arguments

.Object	the [DualEndpoint](#) we want to initialize
mu	see [DualEndpoint](#)
Sigma	see [DualEndpoint](#)
sigma2betaW	see [DualEndpoint](#)
sigma2W	see [DualEndpoint](#)
rho	see [DualEndpoint](#)
smooth	either "RW1" (default) or "RW2", for specifying the random walk prior on the biomarker level.
...	data to include in the new object. Named arguments correspond to slots in the class definition. Unnamed arguments must be objects from classes that this class extends.

---

initialize,LogisticKadane-method

Initialization method for the "LogisticKadane" class

Description

Initialization method for the "LogisticKadane" class

Usage

```
## S4 method for signature 'LogisticKadane'
initialize(.Object, theta, xmin, xmax, ...)
```

Arguments

`.Object`	the [LogisticKadane](#) we want to initialize
`theta`	the target toxicity probability
`xmin`	the minimum of the dose range
`xmax`	the maximum of the dose range
`...`	data to include in the new object. Named arguments correspond to slots in the class definition. Unnamed arguments must be objects from classes that this class extends.

---

initialize,LogisticLogNormal-method

Initialization method for the "LogisticLogNormal" class

Description

Initialization method for the "LogisticLogNormal" class

Usage

```
## S4 method for signature 'LogisticLogNormal'
initialize(.Object, mean, cov, refDose, ...)
```

Arguments

`.Object`	the [LogisticLogNormal](#) we want to initialize
`mean`	the prior mean vector
`cov`	the prior covariance matrix
`refDose`	the reference dose
`...`	data to include in the new object. Named arguments correspond to slots in the class definition. Unnamed arguments must be objects from classes that this class extends.

---

initialize,LogisticNormal-method

Initialization method for the "LogisticNormal" class

Description

Initialization method for the "LogisticNormal" class

Usage

```
## S4 method for signature 'LogisticNormal'
initialize(.Object, mean, cov, refDose, ...)
```

Arguments

`.Object`	the [LogisticNormal](#) we want to initialize
`mean`	the prior mean vector
`cov`	the prior covariance matrix
`refDose`	the reference dose
`...`	data to include in the new object. Named arguments correspond to slots in the class definition. Unnamed arguments must be objects from classes that this class extends.

---

initialize,LogisticNormalMixture-method

Initialization method for the "LogisticNormalMixture" class

Description

Initialization method for the "LogisticNormalMixture" class

Usage

```
## S4 method for signature 'LogisticNormalMixture'
initialize(.Object, comp1, comp2, weightpar,
  refDose, ...)
```

Arguments

`.Object`	the [LogisticNormalMixture](#) we want to initialize
`comp1`	the specifications of the first component: a list with `mean` and `cov` for the first bivariate normal prior
`comp2`	the specifications of the second component
`weightpar`	the beta parameters for the weight of the first component
`refDose`	the reference dose
`...`	data to include in the new object. Named arguments correspond to slots in the class definition. Unnamed arguments must be objects from classes that this class extends.

---

initialize,McmcOptions-method

Initialization method for the "McmcOptions" class

Description

Initialization method for the "McmcOptions" class

Usage

```
## S4 method for signature 'McmcOptions'
initialize(.Object, burnin = 10000L, step = 2L,
  samples = 10000L, ...)
```

Arguments

.Object	the `McmcOptions` we want to initialize
burnin	number of burn-in iterations which are not saved (default: `10,000`)
step	only every step-th iteration is saved after the burn-in (default: `2`)
samples	number of resulting samples (by default `10,000` will result)
...	data to include in the new object. Named arguments correspond to slots in the class definition. Unnamed arguments must be objects from classes that this class extends.

LogisticKadane-class   *Reparametrized logistic model*

Description

This is the logistic model in the parametrization of Kadane et al. (1980).

Details

Let $\rho_0 = p(x_{min})$ be the probability of a DLT and the minimum dose x_{min}, and let γ be the dose with target toxicity probability θ, i.e. $p(\gamma) = \theta$. Then it can easily be shown that the logistic regression model has intercept

$$\frac{\gamma logit(\rho_0) - x_{min} logit(\theta)}{\gamma - x_{min}}$$

and slope

$$\frac{logit(theta) - logit(\rho_0)}{\gamma - x_{min}}$$

The prior is a uniform distribution for γ between x_{min} and x_{max}, and for ρ_0 as well a uniform distribution between 0 and θ.

The slots of this class, required for creating the model, are the target toxicity, as well as the minimum and maximum of the dose range. Note that these can be different from the minimum and maximum of the dose grid in the data later on.

Slots

theta the target toxicity probability θ

xmin the minimum of the dose range x_{min}

xmax the maximum of the dose range x_{max}

`LogisticLogNormal-class`
Standard logistic model with bivariate (log) normal prior

Description

This is the usual logistic regression model with a bivariate normal prior on the intercept and log slope.

Details

The covariate is the natural logarithm of the dose x divided by the reference dose x^*:

$$logit[p(x)] = \alpha + \beta \cdot \log(x/x^*)$$

where $p(x)$ is the probability of observing a DLT for a given dose x.

The prior is

$$(\alpha, \log(\beta)) \sim Normal(\mu, \Sigma)$$

The slots of this class contain the mean vector and the covariance matrix of the bivariate normal distribution, as well as the reference dose.

Slots

mean the prior mean vector μ

cov the prior covariance matrix Σ

refDose the reference dose x^*

`LogisticNormal-class`   *Standard logistic model with bivariate normal prior*

Description

This is the usual logistic regression model with a bivariate normal prior on the intercept and slope.

Details

The covariate is the natural logarithm of the dose x divided by the reference dose x^*:

$$logit[p(x)] = \alpha + \beta \cdot \log(x/x^*)$$

where $p(x)$ is the probability of observing a DLT for a given dose x.

The prior is

$$(\alpha, \beta) \sim Normal(\mu, \Sigma)$$

The slots of this class contain the mean vector, the covariance and precision matrices of the bivariate normal distribution, as well as the reference dose.

Slots

> mean the prior mean vector μ
>
> cov the prior covariance matrix Σ
>
> prec the prior precision matrix Σ^{-1}
>
> refDose the reference dose x^*

LogisticNormalMixture-class
Standard logistic model with mixture of two bivariate normal priors

---

Description

This is stanardard logistic regression model with a mixture of two bivariate normal priors on the intercept and slope parameters. This type of prior is often used with a mixture of a minimal informative and an informative component, in order to make the CRM more robust to data deviations from the informative component.

Details

The covariate is the natural logarithm of the dose x divided by the reference dose x^*:

$$logit[p(x)] = \alpha + \beta \cdot \log(x/x^*)$$

where $p(x)$ is the probability of observing a DLT for a given dose x.

The prior is

$$(\alpha, \beta) \sim w * Normal(\mu_1, \Sigma_1) + (1 - w) * Normal(\mu_2, \Sigma_2)$$

The weight w for the first component is assigned a beta prior B(a, b).

The slots of this class comprise two lists, containing the mean vector, the covariance and precision matrices of the two bivariate normal distributions each, the parameters of the beta prior for the first component weight, as well as the reference dose.

Slots

> comp1 the specifications of the first component: a list with mean, cov and prec for the first bivariate normal prior
>
> comp2 the specifications of the second component
>
> weightpar the beta parameters for the weight of the first component
>
> refDose the reference dose x^*

| logit | *Shorthand for logit function* |

Description

Shorthand for logit function

Usage

```
logit(x)
```

Arguments

x   the function argument

Value

the logit(x)

| maxDose | *Determine the maximum possible next dose* |

Description

Determine the upper limit of the next dose based on the increments rule.

Usage

```
maxDose(increments, data, ...)
```

Arguments

increments	The rule, an object of class Increments
data	The data input, an object of class Data
...	further arguments

Details

This function outputs the maximum possible next dose, based on the corresponding rule increments and the data.

Value

the maximum possible next dose

maxDose,IncrementsRelative,Data-method

Determine the maximum possible next dose based on relative increments

Description

Determine the maximum possible next dose based on relative increments

Usage

```
## S4 method for signature 'IncrementsRelative,Data'
maxDose(increments, data, ...)
```

Arguments

increments	The rule, an object of class [Increments]
data	The data input, an object of class [Data]
...	further arguments

maxDose,IncrementsRelativeDLT,Data-method

Determine the maximum possible next dose based on relative increments determined by DLTs so far

Description

Determine the maximum possible next dose based on relative increments determined by DLTs so far

Usage

```
## S4 method for signature 'IncrementsRelativeDLT,Data'
maxDose(increments, data, ...)
```

Arguments

increments	The rule, an object of class [Increments]
data	The data input, an object of class [Data]
...	further arguments

---

maxSize   *"MAX" combination of cohort size rules*

Description

This function combines cohort size rules by taking the maximum of all sizes.

Usage

```
maxSize(...)
```

Arguments

...   Objects of class [CohortSize](#)

Value

the combination as an object of class [CohortSizeMax](#)

See Also

[minSize](#)

---

maxSize,CohortSize-method
                          The method combining cohort size rules by taking maximum

---

Description

The method combining cohort size rules by taking maximum

Usage

```
## S4 method for signature 'CohortSize'
maxSize(...)
```

Arguments

...   Objects of class [CohortSize](#)

---

mcmc *Obtain posterior samples for all model parameters*

Description

Obtain posterior samples for all model parameters

Usage

```
mcmc(data, model, options, ...)
```

Arguments

data	The data input, an object of class [Data](#)
model	The model input, an object of class [Model](#)
options	MCMC options, an object of class [McmcOptions](#)
...	unused

Details

This is the function to actually run the MCMC machinery to produce posterior samples from all model parameters and required derived values. It is a generic function, so that customized versions may be conveniently defined for specific subclasses of Data, Model, and McmcOptions input.

Value

The posterior samples, an object of class [Samples](#).

---

mcmc,Data,LogisticLogNormal,McmcOptions-method
The fast method for the LogisticLogNormal class

Description

The fast method for the LogisticLogNormal class

Usage

```
## S4 method for signature 'Data,LogisticLogNormal,McmcOptions'
mcmc(data, model, options,
  verbose = FALSE, ...)
```

Arguments

verbose	shall messages be printed? (not default)
data	The data input, an object of class [Data](#)
model	The model input, an object of class [Model](#)
options	MCMC options, an object of class [McmcOptions](#)
...	unused

mcmc,Data,LogisticNormal,McmcOptions-method
                    The fast method for the LogisticNormal class

Description

The fast method for the LogisticNormal class

Usage

```
## S4 method for signature 'Data,LogisticNormal,McmcOptions'
mcmc(data, model, options,
  verbose = FALSE, ...)
```

Arguments

verbose	shall messages be printed? (not default)
data	The data input, an object of class Data
model	The model input, an object of class Model
options	MCMC options, an object of class McmcOptions
...	unused

mcmc,Data,LogisticNormalMixture,McmcOptions-method
                    JAGS for the LogisticNormalMixture method

Description

JAGS for the LogisticNormalMixture method

Usage

```
## S4 method for signature 'Data,LogisticNormalMixture,McmcOptions'
mcmc(data, model, options,
  verbose = FALSE, ...)
```

Arguments

verbose	shall messages be printed? (not default)
data	The data input, an object of class Data
model	The model input, an object of class Model
options	MCMC options, an object of class McmcOptions
...	unused

---

mcmc,Data,Model,McmcOptions-method
Standard method which uses BUGS

Description

Standard method which uses BUGS

Usage

```
## S4 method for signature 'Data,Model,McmcOptions'
mcmc(data, model, options,
  program = "OpenBUGS", verbose = FALSE, ...)
```

Arguments

program	the program which shall be used (see bugs for details)
verbose	shall messages be printed? (not default)
data	The data input, an object of class Data
model	The model input, an object of class Model
options	MCMC options, an object of class McmcOptions
...	unused

McmcOptions-class   *Class for the three canonical MCMC options*

Description

Class for the three canonical MCMC options

Slots

iterations number of MCMC iterations

burnin number of burn-in iterations which are not saved

step only every step-th iteration is saved after the burn-in

MinimalInformative   *Construct a minimally informative prior*

Description

This function constructs a minimally informative prior, which is captured in a [LogisticNormal](#) object.

Usage

```
MinimalInformative(dosegrid, refDose, threshmin = 0.2, threshmax = 0.3, ...)
```

Arguments

dosegrid   the dose grid

refDose   the reference dose

threshmin   Any toxicity probability above this threshold would be very unlikely (5%) at the
               minimum dose (default: 0.2)

threshmax   Any toxicity probability below this threshold would be very unlikely (5%) at the
               maximum dose (default: 0.3)

...   additional arguments for computations, see [Quantiles2LogisticNormal](#)

Details

Based on the proposal by Neuenschwander et al (2008, Statistics in Medicine), a minimally informative prior distribution is constructed. The required key input is the minimum (d_1 in the notation of the Appendix A.1 of that paper) and the maximum value (d_J) of the dose grid supplied to this function. Then threshmin is the probability threshold q_1, such that any probability of DLT larger than q_1 has only 5% probability. Likewise, threshmax is the probability threshold q_J, such that any probability of DLT smaller than q_J has only 5% probability. Subsequently, for all doses supplied in the dosegrid argument, Beta distributions are set up, and [Quantiles2LogisticNormal](#) is used to transform the resulting quantiles into an approximating [LogisticNormal](#) model.

Value

see [Quantiles2LogisticNormal](#)

---

minSize   *"MIN" combination of cohort size rules*

Description

This function combines cohort size rules by taking the minimum of all sizes.

Usage

```
minSize(...)
```

Arguments

... Objects of class CohortSize

Value

the combination as an object of class CohortSizeMin

See Also

maxSize

---

minSize,CohortSize-method
The method combining cohort size rules by taking minimum

Description

The method combining cohort size rules by taking minimum

Usage

```
## S4 method for signature 'CohortSize'
minSize(...)
```

Arguments

... Objects of class CohortSize

Model-class *Class for the model input*

Description

This is the general model class, from which all other specific models inherit.

Details

The datamodel must obey the convention that the data input is called exactly as in the Data class. All prior distributions for parameters should be contained in the model function priormodel. The background is that this can be used to simulate from the prior distribution, before obtaining any data.

The dose function has as first argument prob, a scalar toxicity probability which is targeted. Additional arguments are model parameters. Then it computes, using model parameter(s) (samples), the resulting dose. Note that the model parameters are called exactly as in the model and must be included in the sample vector. The vectors of all samples for these parameters will then be supplied to the function. So your function must be able to process vectors of the model parameters, i.e. it must vectorize over them.

The `prob` function has as first argument dose, which is a scalar dose. Additional arguments are model parameters. Then it computes, using model parameter(s) (samples), the resulting probability of toxicity at that dose. Again here, the function must vectorize over the model parameters.

If you work with multivariate parameters, then please assume that your the two functions receive either one parameter value as a row vector, or a samples matrix where the rows correspond to the sampling index, i.e. the layout is then nSamples x dimParameter.

Note that `dose` and `prob` are the inverse functions of each other.

Slots

datamodel a function representing the BUGS data model specification (see the details above)

priormodel a function representing the BUGS prior specification (see the details above)

datanames The names of all [Data](#) slots that are used in the `datamodel` and/or `priormodel` definition. Note that you cannot specify more variables than those that are really used in the model!

modelspecs a function computing the list of the data model and prior model specifications that are required for fully specifying them (e.g. prior parameters, reference dose, etc.), based on the [Data](#) slots that are then required as arguments of this function. This will then be passed to BUGS for the computations.

dose a function computing the dose reaching a specific target probability, based on the model parameters and additional prior settings (see the details above)

prob a function computing the probability of toxicity for a specific dose, based on the model parameters and additional prior settings (see the details above)

init a function computing the list of starting values for parameters required to be initialized in the MCMC sampler, based on the [Data](#) slots that are then required as arguments of this function

sample names of all parameters from which you would like to save the MCMC samples. These must include the ones required by the `dose` and `prob` functions.

See Also

[LogisticNormal](#), [LogisticLogNormal](#), [LogisticKadane](#), [DualEndpoint](#)

---

nextBest   *Find the next best dose*

Description

Compute the recommended next best dose.

Usage

```
nextBest(nextBest, doselimit, samples, model, data, ...)
```

Arguments

nextBest	The rule, an object of class [NextBest](#)
doselimit	The maximum allowed next dose
samples	the [Samples](#) object
model	The model input, an object of class [Model](#)
data	The data input, an object of class [Data](#)
...	possible additional arguments without method dispatch

Details

This function outputs the next best dose recommendation based on the corresponding rule `nextBest`, the posterior `samples` from the `model` and the underlying `data`.

Value

a list with the next best dose (element `value`) on the grid defined in `data`, and a plot depicting this recommendation (element `plot`)

---

nextBest,NextBestDualEndpoint,numeric,Samples,DualEndpoint,Data-method
Find the next best dose based on the dual endpoint model

Description

Find the next best dose based on the dual endpoint model

Usage

```
   ## S4 method for signature
## 'NextBestDualEndpoint,numeric,Samples,DualEndpoint,Data'
nextBest(nextBest,
  doselimit, samples, model, data, ...)
```

Arguments

nextBest	The rule, an object of class [NextBest](#)
doselimit	The maximum allowed next dose
samples	the [Samples](#) object
model	The model input, an object of class [Model](#)
data	The data input, an object of class [Data](#)
...	possible additional arguments without method dispatch

---

nextBest,NextBestMTD,numeric,Samples,Model,Data-method
Find the next best dose based on the MTD rule

Description

Find the next best dose based on the MTD rule

Usage

```
## S4 method for signature 'NextBestMTD,numeric,Samples,Model,Data'
nextBest(nextBest, doselimit,
  samples, model, data, ...)
```

Arguments

nextBest	The rule, an object of class [NextBest](#)
doselimit	The maximum allowed next dose
samples	the [Samples](#) object
model	The model input, an object of class [Model](#)
data	The data input, an object of class [Data](#)
...	possible additional arguments without method dispatch

---

nextBest,NextBestNCRM,numeric,Samples,Model,Data-method

Find the next best dose based on the NCRM method

Description

Find the next best dose based on the NCRM method

Usage

```
## S4 method for signature 'NextBestNCRM,numeric,Samples,Model,Data'
nextBest(nextBest,
  doselimit, samples, model, data, ...)
```

Arguments

nextBest	The rule, an object of class [NextBest](#)
doselimit	The maximum allowed next dose
samples	the [Samples](#) object
model	The model input, an object of class [Model](#)
data	The data input, an object of class [Data](#)
...	possible additional arguments without method dispatch

NextBest-class   *The virtual class for finding next best dose*

Description

The virtual class for finding next best dose

See Also

[NextBestMTD](#), [NextBestNCRM](#), [NextBestDualEndpoint](#)

NextBestDualEndpoint-class

The class with the input for finding the next dose based on the dual endpoint model

---

Description

The class with the input for finding the next dose based on the dual endpoint model

Slots

target the biomarker level, relative to the maximum, that needs to be reached. For example, 0.9 means that a dose with 90 of the maximum biomarker level is considered as having reached sufficient biomarker level.

overdose the overdose toxicity interval

maxOverdoseProb maximum overdose probability that is allowed

NextBestMTD-class *The class with the input for finding the next best MTD estimate*

Description

The class with the input for finding the next best MTD estimate

Slots

target the target toxicity probability

derive the function which derives from the input, a vector of posterior MTD samples called mtdSamples, the final next best MTD estimate.

NextBestNCRM-class *The class with the input for finding the next dose in target interval*

Description

The class with the input for finding the next dose in target interval

Slots

target the target toxicity interval

overdose the overdose toxicity interval

maxOverdoseProb maximum overdose probability that is allowed

or-Stopping-Stopping   *The method combining two atomic stopping rules*

Description

The method combining two atomic stopping rules

Usage

```
## S4 method for signature 'Stopping,Stopping'
e1 | e2
```

Arguments

e1   First [Stopping](#) object

e2   Second [Stopping](#) object

Value

The [StoppingAny](#) object

---

or-Stopping-StoppingAny

The method combining a stopping list and an atomic

Description

The method combining a stopping list and an atomic

Usage

```
## S4 method for signature 'StoppingAny,Stopping'
e1 | e2
```

Arguments

e1   [StoppingAny](#) object

e2   [Stopping](#) object

Value

The modified [StoppingAny](#) object

`or-StoppingAny-Stopping`
The method combining an atomic and a stopping list

Description

The method combining an atomic and a stopping list

Usage

```
## S4 method for signature 'Stopping,StoppingAny'
e1 | e2
```

Arguments

e1	[Stopping](#) object
e2	[StoppingAny](#) object

Value

The modified [StoppingAny](#) object

`plot,Data,missing-method`
Plot method for the "Data" class

Description

Plot method for the "Data" class

Usage

```
## S4 method for signature 'Data,missing'
plot(x, y, ...)
```

Arguments

x	the [Data](#) object we want to plot
y	the y coordinates of points in the plot, *optional* if x is an appropriate structure.
...	Arguments to be passed to methods, such as [graphical parameters](#) (see [par](#)). Many methods will accept the following arguments:

    type what type of plot should be drawn. Possible types are

- `"p"` for **p**oints,
- `"l"` for **l**ines,
- `"b"` for **b**oth,
- `"c"` for the lines part alone of `"b"`,
- `"o"` for both '**o**verplotted',

- "h" for '**h**istogram' like (or 'high-density') vertical lines,
- "s" for stair **s**teps,
- "S" for other **s**teps, see 'Details' below,
- "n" for no plotting.

All other types give a warning or an error; using, e.g., type = "punkte" being equivalent to type = "p" for S compatibility. Note that some methods, e.g. plot.factor, do not accept this.

main an overall title for the plot: see title.

sub a sub title for the plot: see title.

xlab a title for the x axis: see title.

ylab a title for the y axis: see title.

asp the y/x aspect ratio, see plot.window.

Value

the ggplot object

---

plot,DataDual,missing-method
                        Plot method for the "DataDual" class

Description

Plot method for the "DataDual" class

Usage

```
## S4 method for signature 'DataDual,missing'
plot(x, y, ...)
```

Arguments

x   the DataDual object we want to plot

y   the y coordinates of points in the plot, *optional* if x is an appropriate structure.

...   Arguments to be passed to methods, such as graphical parameters (see par). Many methods will accept the following arguments:

                type what type of plot should be drawn. Possible types are

- "p" for **p**oints,
- "l" for **l**ines,
- "b" for **b**oth,
- "c" for the lines part alone of "b",
- "o" for both '**o**verplotted',
- "h" for '**h**istogram' like (or 'high-density') vertical lines,
- "s" for stair **s**teps,
- "S" for other **s**teps, see 'Details' below,
- "n" for no plotting.

All other `types` give a warning or an error; using, e.g., `type = "punkte"` being equivalent to `type = "p"` for S compatibility. Note that some methods, e.g. `plot.factor`, do not accept this.

main an overall title for the plot: see `title`.

sub a sub title for the plot: see `title`.

xlab a title for the x axis: see `title`.

ylab a title for the y axis: see `title`.

asp the y/x aspect ratio, see `plot.window`.

Value

the `ggplot` object

`plot,Samples,DualEndpoint-method`

Plot method for the "Samples" object, when we have the dual endpoint model

---

Description

Plot method for the "Samples" object, when we have the dual endpoint model

Usage

```
## S4 method for signature 'Samples,DualEndpoint'
plot(x, y, data, extrapolate = TRUE, ...)
```

Arguments

x	the `Samples` object
y	the `DualEndpoint` object
data	the `DataDual` object
extrapolate	should the biomarker fit be extrapolated to the whole dose grid? (default)
...	Arguments to be passed to methods, such as graphical parameters (see `par`). Many methods will accept the following arguments:

type what type of plot should be drawn. Possible types are

- `"p"` for **p**oints,
- `"l"` for **l**ines,
- `"b"` for **b**oth,
- `"c"` for the lines part alone of `"b"`,
- `"o"` for both '**o**verplotted',
- `"h"` for '**h**istogram' like (or 'high-density') vertical lines,
- `"s"` for stair **s**teps,
- `"S"` for other **s**teps, see 'Details' below,
- `"n"` for no plotting.

All other `types` give a warning or an error; using, e.g., `type = "punkte"` being equivalent to `type = "p"` for S compatibility. Note that some methods, e.g. `plot.factor`, do not accept this.

main an overall title for the plot: see `title`.

sub a sub title for the plot: see `title`.

xlab a title for the x axis: see `title`.

ylab a title for the y axis: see `title`.

asp the y/x aspect ratio, see `plot.window`.

Value

the `ggplot` object

---

plot,Samples,Model-method

Plot method for the "Samples" and "Model" object

Description

Plot method for the "Samples" and "Model" object

Usage

```
## S4 method for signature 'Samples,Model'
plot(x, y, data, ...)
```

Arguments

x	the `Samples` object
y	the `Model` object
data	the `Data` object
...	Arguments to be passed to methods, such as graphical parameters (see `par`). Many methods will accept the following arguments:

type what type of plot should be drawn. Possible types are

- `"p"` for **p**oints,
- `"l"` for **l**ines,
- `"b"` for **b**oth,
- `"c"` for the lines part alone of `"b"`,
- `"o"` for both '**o**verplotted',
- `"h"` for '**h**istogram' like (or 'high-density') vertical lines,
- `"s"` for stair **s**teps,
- `"S"` for other **s**teps, see 'Details' below,
- `"n"` for no plotting.

All other `type`s give a warning or an error; using, e.g., type = `"punkte"` being equivalent to type = `"p"` for S compatibility. Note that some methods, e.g. `plot.factor`, do not accept this.

main an overall title for the plot: see `title`.

sub a sub title for the plot: see `title`.

xlab a title for the x axis: see `title`.

ylab a title for the y axis: see `title`.

asp the y/x aspect ratio, see `plot.window`.

Value

the [ggplot](#) object

---

plot,Simulations,missing-method
Plot simulations

Description

Summarize the simulations with plots

Usage

```
## S4 method for signature 'Simulations,missing'
plot(x, y, type = c("trajectory",
  "dosesTried"), ...)
```

Arguments

x	the [Simulations](#) object we want to plot from
type	the type of plots you want to obtain.
y	the y coordinates of points in the plot, *optional* if x is an appropriate structure.
...	Arguments to be passed to methods, such as [graphical parameters](#) (see [par](#)). Many methods will accept the following arguments:

type what type of plot should be drawn. Possible types are

- "p" for **p**oints,
- "l" for **l**ines,
- "b" for **b**oth,
- "c" for the lines part alone of "b",
- "o" for both '**o**verplotted',
- "h" for '**h**istogram' like (or 'high-density') vertical lines,
- "s" for stair **s**teps,
- "S" for other **s**teps, see 'Details' below,
- "n" for no plotting.

All other types give a warning or an error; using, e.g., type = "punkte" being equivalent to type = "p" for S compatibility. Note that some methods, e.g. [plot.factor](#), do not accept this.

main an overall title for the plot: see [title](#).

sub a sub title for the plot: see [title](#).

xlab a title for the x axis: see [title](#).

ylab a title for the y axis: see [title](#).

asp the y/x aspect ratio, see [plot.window](#).

Details

This plot method can be applied to [Simulations](#) objects in order to summarize them graphically. Possible types of plots at the moment are:

trajectory Summary of the trajectory of the simulated trials

dosesTried Average proportions of the doses tested in patients

You can specify one or both of these in the type argument.

Value

A single [ggplot2](#) object if a single plot is asked for, otherwise a [gridExtra](#){gTree} object. The first can be plotted with the print command, the latter with the [grid.draw](#) command.

---

plot,Simulations-summary,missing-method
                        Plot summaries of the simulations

Description

Graphical display of the simulation summary

Usage

```
## S4 method for signature 'Simulations-summary,missing'
plot(x, y, type = c("nObs",
  "doseSelected", "propDLTs", "nAboveTarget", "meanFit"), ...)
```

Arguments

x	the [Simulations-summary](#) object we want to plot from
type	the types of plots you want to obtain.
y	the y coordinates of points in the plot, *optional* if x is an appropriate structure.
...	Arguments to be passed to methods, such as [graphical parameters](#) (see [par](#)). Many methods will accept the following arguments:

type what type of plot should be drawn. Possible types are

- "p" for **p**oints,
- "l" for **l**ines,
- "b" for **b**oth,
- "c" for the lines part alone of "b",
- "o" for both '**o**verplotted',
- "h" for '**h**istogram' like (or 'high-density') vertical lines,
- "s" for stair **s**teps,
- "S" for other **s**teps, see 'Details' below,
- "n" for no plotting.

All other types give a warning or an error; using, e.g., type = "punkte" being equivalent to type = "p" for S compatibility. Note that some methods, e.g. [plot.factor](#), do not accept this.

main an overall title for the plot: see `title`.

sub a sub title for the plot: see `title`.

xlab a title for the x axis: see `title`.

ylab a title for the y axis: see `title`.

asp the y/x aspect ratio, see `plot.window`.

Details

This plot method can be applied to `Simulations` objects in order to summarize them graphically. Possible `types` of plots at the moment are:

nObs Distribution of the number of patients in the simulated trials

doseSelected Distribution of the final selected doses in the trials. Note that this can include zero entries, meaning that the trial was stopped because all doses in the dose grid appeared too toxic.

propDLTs Distribution of the proportion of patients with DLTs in the trials

nAboveTarget Distribution of the number of patients treated at doses which are above the target toxicity interval (as specified by the `truth` and `target` arguments to `summary,Simulations-method`)

meanFit Plot showing the average fitted dose-toxicity curve across the trials, together with 95% credible intervals, and comparison with the assumed truth (as specified by the `truth` argument to `summary,Simulations-method`)

You can specify any subset of these in the `type` argument.

Value

A single `ggplot2` object if a single plot is asked for, otherwise a `gridExtra`{gTree} object. The first can be plotted with the `print` command, the latter with the `grid.draw` command.

---

prob   *Compute the probability for a given dose, given model and samples*

Description

Compute the probability for a given dose, given model and samples

Usage

```
prob(dose, model, samples, ...)
```

Arguments

dose   the dose

model   the `Model`

samples   the `Samples`

...   unused

`prob,numeric,Model,Samples-method`

Compute the probability for a given dose, given model and samples

---

Description

Compute the probability for a given dose, given model and samples

Usage

```
## S4 method for signature 'numeric,Model,Samples'
prob(dose, model, samples, ...)
```

Arguments

dose	the dose
model	the [Model](#)
samples	the [Samples](#)
...	unused

`Quantiles2LogisticNormal`

Convert prior quantiles (lower, median, upper) to logistic (log) normal model

---

Description

This function uses generalised simulated annealing to optimise a [LogisticNormal](#) model to be as close as possible to the given prior quantiles.

Usage

```
Quantiles2LogisticNormal(dosegrid, refDose, lower, median, upper,
  level = 0.95, logNormal = FALSE, parstart = NULL, parlower = c(-10,
  -10, 0, 0, -0.95), parupper = c(10, 10, 10, 10, 0.95),
  control = list(threshold.stop = 0.01, maxit = 50000, temperature = 50000,
  max.time = 600, verbose = TRUE))
```

Arguments

dosegrid	the dose grid
refDose	the reference dose
lower	the lower quantiles
median	the medians
upper	the upper quantiles
level	the credible level of the (lower, upper) intervals (default: 0.95)

logNormal	use the log-normal prior? (not default) otherwise, the normal prior for the logistic regression coefficients is used
parstart	starting values for the parameters. By default, these are determined from the medians supplied.
parlower	lower bounds on the parameters (intercept alpha and the slope beta, the corresponding standard deviations and the correlation.)
parupper	upper bounds on the parameters
control	additional options for the optimisation routine, see [GenSA](#) for more details

Value

a list with the best approximating model ([LogisticNormal](#) or [LogisticLogNormal](#)), the resulting quantiles, the required quantiles and the distance to the required quantiles, as well as the final parameters (which could be used for running the algorithm a second time)

Samples-class   *Class for the MCMC output*

Description

Class for the MCMC output

Slots

data a list where each entry contains the samples of a (vector-valued) parameter in a vector/matrix in the format (number of samples) x (dimension of the parameter).

options the [McmcOptions](#) which have been used

---

sampleSize   *Compute the number of samples for a given MCMC options triple*

Description

Compute the number of samples for a given MCMC options triple

Usage

```
sampleSize(mcmcOptions)
```

Arguments

mcmcOptions   the [McmcOptions](#) object

Value

the resulting sample size

---

show,Simulations-summary-method

Show the summary of the simulations

Description

Show the summary of the simulations

Usage

```
## S4 method for signature 'Simulations-summary'
show(object)
```

Arguments

object   the Simulations-summary object we want to print

Value

invisibly returns a data frame of the results with one row and appropriate column names

---

simulate,Design-method

Simulate outcomes from a CRM design

Description

Simulate outcomes from a CRM design

Usage

```
## S4 method for signature 'Design'
simulate(object, truth, args = NULL,
  firstSeparate = FALSE, nsim = 1L, mcmcOptions = new("McmcOptions"),
  seed = NULL, parallel = FALSE, ...)
```

Arguments

object   the Design object we want to simulate data from

truth   a function which takes as input a dose (vector) and returns the true probability
                (vector) for toxicity. Additional arguments can be supplied in `args`.

args   data frame with arguments for the `truth` function. The column names corre-
                spond to the argument names, the rows to the values of the arguments. The
                rows are appropriately recycled in the `nsim` simulations. In order to produce
                outcomes from the posterior predictive distribution, e.g, pass an `object` that
                contains the data observed so far, `truth` contains the `prob` function from the
                model in `object`, and `args` contains posterior samples from the model.

firstSeparate   enroll the first patient separately from the rest of the cohort? (not default) If yes,
                the cohort will be closed if a DLT occurs in this patient.

nsim	the number of simulations (default: 1)
mcmcOptions	object of class [McmcOptions](#), giving the MCMC options for each evaluation in the trial. By default, the standard options are used
seed	an object specifying if and how the random number generator should be initialized ("seeded"). Either NULL (default) or an integer that will be used in a call to [set.seed](#) before simulating the response vectors. If set, the value is saved as the seed slot of the returned object. The default, NULL will not change the random generator state, and .Random.seed will be saved.
parallel	should the simulation runs be parallelized across the clusters of the computer? (not default)
...	additional optional arguments.

Value

an object of class [Simulations](#)

Simulations-class *Class for the simulations output*

Description

This class captures the trial simulations.

Details

Here also the random generator state before starting the simulation is saved, in order to be able to reproduce the outcome. For this just use [set.seed](#) with the seed as argument before running [simulate,Design-method](#).

Slots

data list of produced [Data](#) objects

doses the vector of final dose recommendations

fit list with the final fits

stopReasons list of stopping reasons for each simulation run

seed random generator state before starting the simulation

Simulations-summary-class
                        Class for the summary of simulations output

---

Description

Class for the summary of simulations output

Slots

target target toxicity interval

targetDoseInterval corresponding target dose interval

nsim number of simulations

propDLTs proportions of DLTs in the trials

meanToxRisk mean toxicity risks for the patients

doseSelected doses selected as MTD

toxAtDosesSelected true toxicity at doses selected

propAtTarget Proportion of trials selecting target MTD

doseMostSelected dose most often selected as MTD

obsToxRateAtDoseMostSelected observed toxicity rate at dose most often selected

fitAtDoseMostSelected fitted toxicity rate at dose most often selected

meanFit list with the average, lower (2.5 quantiles of the mean fitted toxicity at each dose level

nObs number of patients overall

nAboveTarget number of patients treated above target tox interval

doseGrid the dose grid that has been used

---

size   *Determine the size of the next cohort*

Description

This function determines the size of the next cohort.

Usage

```
size(cohortSize, dose, data, ...)
```

Arguments

cohortSize   The rule, an object of class [CohortSize](#)

dose   the next dose

data   The data input, an object of class [Data](#)

...   additional arguments

Value

the size as integer value

size,CohortSizeConst,ANY,Data-method
Constant cohort size

Description

Constant cohort size

Usage

```
## S4 method for signature 'CohortSizeConst,ANY,Data'
size(cohortSize, dose, data, ...)
```

Arguments

cohortSize	The rule, an object of class [CohortSize](#)
dose	the next dose
data	The data input, an object of class [Data](#)
...	additional arguments

size,CohortSizeDLT,ANY,Data-method
Determine the cohort size based on the number of DLTs so far

Description

Determine the cohort size based on the number of DLTs so far

Usage

```
## S4 method for signature 'CohortSizeDLT,ANY,Data'
size(cohortSize, dose, data, ...)
```

Arguments

cohortSize	The rule, an object of class [CohortSize](#)
dose	the next dose
data	The data input, an object of class [Data](#)
...	additional arguments

size,CohortSizeMax,ANY,Data-method
Size based on maximum of multiple cohort size rules

Description

Size based on maximum of multiple cohort size rules

Usage

```
## S4 method for signature 'CohortSizeMax,ANY,Data'
size(cohortSize, dose, data, ...)
```

Arguments

cohortSize	The rule, an object of class [CohortSize]
dose	the next dose
data	The data input, an object of class [Data]
...	additional arguments

size,CohortSizeMin,ANY,Data-method
Size based on minimum of multiple cohort size rules

Description

Size based on minimum of multiple cohort size rules

Usage

```
## S4 method for signature 'CohortSizeMin,ANY,Data'
size(cohortSize, dose, data, ...)
```

Arguments

cohortSize	The rule, an object of class [CohortSize]
dose	the next dose
data	The data input, an object of class [Data]
...	additional arguments

size,CohortSizeRange,ANY,Data-method
: *Determine the cohort size based on the range into which the next dose falls into*

Description

Determine the cohort size based on the range into which the next dose falls into

Usage

```
## S4 method for signature 'CohortSizeRange,ANY,Data'
size(cohortSize, dose, data, ...)
```

Arguments

cohortSize	The rule, an object of class [CohortSize]
dose	the next dose
data	The data input, an object of class [Data]
...	additional arguments

Stopping-class
: *The virtual class for stopping rules*

Description

The virtual class for stopping rules

See Also

[StoppingList], [StoppingMaxPatients], [StoppingCohortsNearDose], [StoppingPatientsNearDose], [StoppingMinCohorts], [StoppingMinPatients], [StoppingTargetProb] [StoppingMTDdistribution], [StoppingTargetBiomarker]

StoppingAll-class
: *Stop based on fullfillment of all multiple stopping rules*

Description

This class can be used to combine multiple stopping rules with an AND operator.

Details

stopList contains all stopping rules, which are again objects of class [Stopping]. All stopping rules must be fulfilled in order that the result of this rule is to stop.

Slots

stopList list of stopping rules of the stopping rules into a single result

StoppingAny-class   *Stop based on fullfillment of any stopping rule*

Description

This class can be used to combine multiple stopping rules with an OR operator.

Details

stopList contains all stopping rules, which are again objects of class [Stopping](). Any of these rules must be fulfilled in order that the result of this rule is to stop.

Slots

stopList list of stopping rules of the stopping rules into a single result

StoppingCohortsNearDose-class
                           Stop based on number of cohorts near to next best dose

Description

Stop based on number of cohorts near to next best dose

Slots

nCohorts number of required cohorts

percentage percentage (between 0 and 100) within the next best dose the cohorts must lie

StoppingList-class   *Stop based on multiple stopping rules*

Description

This class can be used to combine multiple stopping rules.

Details

stopList contains all stopping rules, which are again objects of class [Stopping](), and the summary is a function taking a logical vector of the size of stopList and returning a single logical value. For example, if the function all is given as summary function, then this means that all stopping rules must be fulfilled in order that the result of this rule is to stop.

Slots

stopList list of stopping rules

summary the summary function to combine the results of the stopping rules into a single result

StoppingMaxPatients-class

Stop based on maximum number of patients

Description

Stop based on maximum number of patients

Slots

nPatients maximum allowed number of patients

StoppingMinCohorts-class

Stop based on minimum number of cohorts

Description

Stop based on minimum number of cohorts

Slots

nCohorts minimum required number of cohorts

StoppingMinPatients-class

Stop based on minimum number of patients

Description

Stop based on minimum number of patients

Slots

nPatients minimum required number of patients

StoppingMTDdistribution-class

Stop based on MTD distribution

Description

Has 90% probability above a threshold of 50% of the current MTD been reached? This class is used for this question.

Slots

target the target toxicity probability (e.g. 0.33) defining the MTD

thresh the threshold relative to the MTD (e.g. 0.5)

prob required probability (e.g. 0.9)

`StoppingPatientsNearDose-class`
Stop based on number of patients near to next best dose

Description

Stop based on number of patients near to next best dose

Slots

`nPatients` number of required patients

`percentage` percentage (between 0 and 100) within the next best dose the patients must lie

---

`StoppingTargetBiomarker-class`
Stop based on probability of target biomarker

Description

Stop based on probability of target biomarker

Slots

`target` the biomarker level, relative to the maximum, that needs to be reached

`prob` required target probability for reaching sufficient precision

---

`StoppingTargetProb-class`
Stop based on probability of target tox interval

Description

Stop based on probability of target tox interval

Slots

`target` the target toxicity interval

`prob` required target toxicity probability for reaching sufficient precision

---

stopTrial *Stop the trial?*

Description

This function returns whether to stop the trial.

Usage

```
stopTrial(stopping, dose, samples, model, data, ...)
```

Arguments

stopping	The rule, an object of class [Stopping](#)
dose	the recommended next best dose
samples	the [Samples](#) object
model	The model input, an object of class [Model](#)
data	The data input, an object of class [Data](#)
...	additional arguments

Value

logical value: TRUE if the trial can be stopped, FALSE otherwise. It should have an attribute message which gives the reason for the decision.

---

stopTrial,StoppingAll,ANY,ANY,ANY,ANY-method
Stop based on fulfillment of all multiple stopping rules

Description

Stop based on fulfillment of all multiple stopping rules

Usage

```
## S4 method for signature 'StoppingAll,ANY,ANY,ANY,ANY'
stopTrial(stopping, dose, samples,
  model, data, ...)
```

Arguments

stopping	The rule, an object of class [Stopping](#)
dose	the recommended next best dose
samples	the [Samples](#) object
model	The model input, an object of class [Model](#)
data	The data input, an object of class [Data](#)
...	additional arguments

stopTrial,StoppingAny,ANY,ANY,ANY,ANY-method
                          Stop based on fulfillment of any stopping rule

Description

Stop based on fulfillment of any stopping rule

Usage

```
## S4 method for signature 'StoppingAny,ANY,ANY,ANY,ANY'
stopTrial(stopping, dose, samples,
  model, data, ...)
```

Arguments

stopping	The rule, an object of class Stopping
dose	the recommended next best dose
samples	the Samples object
model	The model input, an object of class Model
data	The data input, an object of class Data
...	additional arguments

stopTrial,StoppingCohortsNearDose,numeric,ANY,ANY,Data-method
                          Stop based on number of cohorts near to next best dose

Description

Stop based on number of cohorts near to next best dose

Usage

```
## S4 method for signature 'StoppingCohortsNearDose,numeric,ANY,ANY,Data'
stopTrial(stopping,
  dose, samples, model, data, ...)
```

Arguments

stopping	The rule, an object of class Stopping
dose	the recommended next best dose
samples	the Samples object
model	The model input, an object of class Model
data	The data input, an object of class Data
...	additional arguments

stopTrial,StoppingList,ANY,ANY,ANY,ANY-method
Stop based on multiple stopping rules

Description

Stop based on multiple stopping rules

Usage

```
## S4 method for signature 'StoppingList,ANY,ANY,ANY,ANY'
stopTrial(stopping, dose, samples,
  model, data, ...)
```

Arguments

stopping	The rule, an object of class Stopping
dose	the recommended next best dose
samples	the Samples object
model	The model input, an object of class Model
data	The data input, an object of class Data
...	additional arguments

stopTrial,StoppingMaxPatients,ANY,ANY,ANY,Data-method
Stop based on maximum number of patients

Description

Stop based on maximum number of patients

Usage

```
## S4 method for signature 'StoppingMaxPatients,ANY,ANY,ANY,Data'
stopTrial(stopping, dose,
  samples, model, data, ...)
```

Arguments

stopping	The rule, an object of class Stopping
dose	the recommended next best dose
samples	the Samples object
model	The model input, an object of class Model
data	The data input, an object of class Data
...	additional arguments

stopTrial,StoppingMinCohorts,ANY,ANY,ANY,Data-method
                    Stop based on minimum number of cohorts

Description

Stop based on minimum number of cohorts

Usage

```
## S4 method for signature 'StoppingMinCohorts,ANY,ANY,ANY,Data'
stopTrial(stopping, dose,
  samples, model, data, ...)
```

Arguments

stopping	The rule, an object of class Stopping
dose	the recommended next best dose
samples	the Samples object
model	The model input, an object of class Model
data	The data input, an object of class Data
...	additional arguments

stopTrial,StoppingMinPatients,ANY,ANY,ANY,Data-method
                    Stop based on minimum number of patients

Description

Stop based on minimum number of patients

Usage

```
## S4 method for signature 'StoppingMinPatients,ANY,ANY,ANY,Data'
stopTrial(stopping, dose,
  samples, model, data, ...)
```

Arguments

stopping	The rule, an object of class Stopping
dose	the recommended next best dose
samples	the Samples object
model	The model input, an object of class Model
data	The data input, an object of class Data
...	additional arguments

stopTrial,StoppingMTDdistribution,numeric,Samples,Model,ANY-method
Stop based on MTD distribution

Description

Stop based on MTD distribution

Usage

```
   ## S4 method for signature 'StoppingMTDdistribution,numeric,Samples,Model,ANY'
stopTrial(stopping,
  dose, samples, model, data, ...)
```

Arguments

stopping	The rule, an object of class [Stopping](#)
dose	the recommended next best dose
samples	the [Samples](#) object
model	The model input, an object of class [Model](#)
data	The data input, an object of class [Data](#)
...	additional arguments

stopTrial,StoppingPatientsNearDose,numeric,ANY,ANY,Data-method
Stop based on number of patients near to next best dose

Description

Stop based on number of patients near to next best dose

Usage

```
## S4 method for signature 'StoppingPatientsNearDose,numeric,ANY,ANY,Data'
stopTrial(stopping,
  dose, samples, model, data, ...)
```

Arguments

stopping	The rule, an object of class [Stopping](#)
dose	the recommended next best dose
samples	the [Samples](#) object
model	The model input, an object of class [Model](#)
data	The data input, an object of class [Data](#)
...	additional arguments

stopTrial,StoppingTargetBiomarker,numeric,Samples,DualEndpoint,ANY-method
Stop based on probability of targeting biomarker

Description

Stop based on probability of targeting biomarker

Usage

```
   ## S4 method for signature
## 'StoppingTargetBiomarker,numeric,Samples,DualEndpoint,ANY'
stopTrial(stopping,
  dose, samples, model, data, ...)
```

Arguments

stopping	The rule, an object of class [Stopping]
dose	the recommended next best dose
samples	the [Samples] object
model	The model input, an object of class [Model]
data	The data input, an object of class [Data]
...	additional arguments

stopTrial,StoppingTargetProb,numeric,Samples,Model,ANY-method
Stop based on probability of target tox interval

Description

Stop based on probability of target tox interval

Usage

```
## S4 method for signature 'StoppingTargetProb,numeric,Samples,Model,ANY'
stopTrial(stopping,
  dose, samples, model, data, ...)
```

Arguments

stopping	The rule, an object of class [Stopping]
dose	the recommended next best dose
samples	the [Samples] object
model	The model input, an object of class [Model]
data	The data input, an object of class [Data]
...	additional arguments

summary,Simulations-method
Summarize the simulations, relative to a given truth

Description

Summarize the simulations, relative to a given truth

Usage

```
## S4 method for signature 'Simulations'
summary(object, truth, target = c(0.2, 0.35), ...)
```

Arguments

object	the [Simulations](#) object we want to summarize
truth	a function which takes as input a dose (vector) and returns the true probability (vector) for toxicity. Additional arguments can be supplied via . . . .
target	the target toxicity interval (default: 20-35%) used for the computations
...	additional arguments affecting the summary produced.

Value

an object of class [Simulations-summary](#)

---

update,Data-method   *Update method for the "Data" class*

Description

Add new data to the [Data](#) object

Usage

```
## S4 method for signature 'Data'
update(object, x, y, ID, ...)
```

Arguments

object	the old [Data](#) object
x	the dose level (one level only!)
y	the DLT vector (0/1 vector), for all patients in this cohort
ID	the patient IDs
...	Additional arguments to the call, or arguments with changed values. Use name = NULL to remove the argument name.

Value

the new [Data](#) object

`&,Stopping,Stopping-method`

The method combining two atomic stopping rules

Description

The method combining two atomic stopping rules

Usage

```
## S4 method for signature 'Stopping,Stopping'
e1 & e2
```

Arguments

e1	First [Stopping](#) object
e2	Second [Stopping](#) object

Value

The [StoppingAll](#) object

`&,Stopping,StoppingAll-method`

The method combining an atomic and a stopping list

Description

The method combining an atomic and a stopping list

Usage

```
## S4 method for signature 'Stopping,StoppingAll'
e1 & e2
```

Arguments

e1	[Stopping](#) object
e2	[StoppingAll](#) object

Value

The modified [StoppingAll](#) object

&,StoppingAll,Stopping-method

The method combining a stopping list and an atomic

Description

The method combining a stopping list and an atomic

Usage

```
## S4 method for signature 'StoppingAll,Stopping'
e1 & e2
```

Arguments

e1   [StoppingAll](#) object

e2   [Stopping](#) object

Value

The modified [StoppingAll](#) object

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