

Package ‘campsis’

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Type Package

Title Generic PK/PD Simulation Platform CAMPSIS

Version 1.4.1

Description A generic, easy-to-use and intuitive pharmacokinetic/pharmacodynamic (PK/PD) simulation platform based on R packages 'rxode2', 'RxODE' and 'mrgsolve'. CAMPSIS provides an abstraction layer over the underlying processes of writing a PK/PD model, assembling a custom dataset and running a simulation. CAMPSIS has a strong dependency to the R package 'campsismod', which allows to read/write a model from/to files and adapt it further on the fly in the R environment. Package 'campsis' allows the user to assemble a dataset in an intuitive manner. Once the user's dataset is ready, the package is in charge of preparing the simulation, calling 'rxode2', 'RxODE' or 'mrgsolve' (at the user's choice) and returning the results, for the given model, dataset and desired simulation settings.

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URL <https://github.com/Calvagone/campsis>, <https://calvagone.github.io/>

BugReports <https://github.com/Calvagone/campsis/issues>

Depends campsismod (>= 1.0.0), R (>= 4.0.0)

Imports assertthat, digest, dplyr, ggplot2, furr, future, MASS, methods, plyr, progressr, purrr, rlang, stats, tibble, tidyr

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Collate 'global.R' 'utilities.R' 'check.R' 'generic.R' 'seed.R' 'distribution.R' 'dataset_config.R' 'time_entry.R' 'occasion.R' 'occasions.R' 'treatment_iov.R' 'treatment_iovs.R' 'dose_adaptation.R' 'dose_adaptations.R' 'treatment_entry.R'

'treatment.R' 'observations.R' 'observations_set.R'
 'covariate.R' 'covariates.R' 'bootstrap.R' 'protocol.R' 'arm.R'
 'arms.R' 'event.R' 'events.R' 'scenario.R' 'scenarios.R'
 'simulation_engine.R' 'dataset.R' 'parameter_uncertainty.R'
 'event_logic.R' 'dataset_summary.R' 'hardware_settings.R'
 'simulation_progress.R' 'solver_settings.R' 'nocb_settings.R'
 'declare_settings.R' 'internal_settings.R'
 'simulation_settings.R' 'plan_setup.R' 'simulate_preprocess.R'
 'simulate.R' 'results_processing.R' 'default_plot.R'

NeedsCompilation no

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applyCompartmentCharacteristics

Apply compartment characteristics from model. In practice, only compartment infusion duration needs to be applied.

Description

Apply compartment characteristics from model. In practice, only compartment infusion duration needs to be applied.

Usage

applyCompartmentCharacteristics(table, properties)

Arguments

| | |
|------------|-----------------------------------|
| table | current dataset |
| properties | compartment properties from model |

Value

updated dataset

| | |
|-----|--------------------------------|
| Arm | <i>Create a treatment arm.</i> |
|-----|--------------------------------|

Description

Create a treatment arm.

Usage

```
Arm(id = as.integer(NA), subjects = 1, label = as.character(NA))
```

Arguments

| | |
|----------|---|
| id | unique identifier for this arm (available through dataset), integer. If NA (default), this identifier is auto-incremented. |
| subjects | number of subjects in arm, integer |
| label | arm label, single character string. If set, this label will be output in the ARM column of CAMPSIS instead of the identifier. |

Value

an arm

| | |
|-----------|-------------------|
| arm-class | <i>Arm class.</i> |
|-----------|-------------------|

Description

Arm class.

Slots

| | |
|------------|------------------------------------|
| id | arm unique ID, integer |
| subjects | number of subjects in arm, integer |
| label | arm label, single character string |
| protocol | protocol |
| covariates | covariates |
| bootstrap | covariates to be bootstrapped |

 arms-class

Arms class.

Description

Arms class.

 Bolus

Create one or several bolus(es).

Description

Create one or several bolus(es).

Usage

```
Bolus(
  time,
  amount,
  compartment = NA,
  f = NULL,
  lag = NULL,
  ii = NULL,
  addl = NULL
)
```

Arguments

| | |
|-------------|---|
| time | treatment time(s), numeric value or vector. First treatment time if used together with ii and addl. |
| amount | amount to give as bolus, single numeric value |
| compartment | compartment index, single integer value |
| f | fraction of dose amount, distribution |
| lag | dose lag time, distribution |
| ii | interdose interval, requires argument 'time' to be a single numeric value |
| addl | number of additional doses, requires argument 'time' to be a single integer value |

Value

a single bolus or a list of boluses

| | |
|-------------|---------------------|
| bolus-class | <i>Bolus class.</i> |
|-------------|---------------------|

Description

Bolus class.

| | |
|-----------|-----------------------------------|
| Bootstrap | <i>Create a bootstrap object.</i> |
|-----------|-----------------------------------|

Description

Create a bootstrap object.

Usage

```
Bootstrap(
  data,
  id = "BS_ID",
  replacement = FALSE,
  random = FALSE,
  export_id = FALSE
)
```

Arguments

| | |
|-------------|--|
| data | data frame to be bootstrapped. It must have a unique identifier column named according to the specified argument 'id' (default value is 'BS_ID'). Other columns are covariates to bootstrap. They must all be numeric. Whatever the configuration of the bootstrap, these covariates are always read row by row and belong to a same individual. |
| id | unique identifier column name in data |
| replacement | values can be reused or not when drawn, logical |
| random | values are drawn randomly, logical |
| export_id | tell CAMPSIS if the identifier 'BS_ID' must be output or not, logical |

Value

a bootstrap object

| | |
|-----------------|-------------------------|
| bootstrap-class | <i>Bootstrap class.</i> |
|-----------------|-------------------------|

Description

Bootstrap class.

Slots

data data frame to be bootstrapped. Column 'BS_ID' is mandatory and corresponds to the original row ID from the bootstrap. It must be numeric and unique. Other columns are covariates to be bootstrapped (row by row).

replacement values can be reused or not, logical

random values are drawn randomly, logical

export_id tell CAMPSIS if 'BS_ID' must be exported into the dataset, logical

| | |
|-----------------------|---|
| BootstrapDistribution | <i>Create a bootstrap distribution. During function sampling, CAMPSIS will generate values depending on the given data and arguments.</i> |
|-----------------------|---|

Description

Create a bootstrap distribution. During function sampling, CAMPSIS will generate values depending on the given data and arguments.

Usage

```
BootstrapDistribution(data, replacement = FALSE, random = FALSE)
```

Arguments

data values to draw, numeric vector

replacement values can be reused or not, logical

random values are drawn randomly, logical

Value

a bootstrap distribution

bootstrap_distribution-class
Bootstrap distribution class.

Description

Bootstrap distribution class.

Slots

data values to draw, numeric vector
replacement values can be reused or not, logical
random values are drawn randomly, logical

campsis_handler *Suggested Campsis handler for showing the progress bar.*

Description

Suggested Campsis handler for showing the progress bar.

Usage

campsis_handler()

Value

a progressr handler list

ConstantDistribution *Create a constant distribution. Its value will be constant across all generated samples.*

Description

Create a constant distribution. Its value will be constant across all generated samples.

Usage

ConstantDistribution(value)

Arguments

value covariate value, single numeric value

Value

a constant distribution (same value for all samples)

constant_distribution-class
Constant distribution class.

Description

Constant distribution class.

Slots

value covariate value, single numeric value

Covariate *Create a non time-varying (fixed) covariate.*

Description

Create a non time-varying (fixed) covariate.

Usage

Covariate(name, distribution)

Arguments

name covariate name, single character value
distribution covariate distribution

Value

a fixed covariate

covariate-class *Covariate class.*

Description

Covariate class.

Slots

name covariate name, single character value
distribution covariate distribution

| | |
|------------------|--------------------------|
| covariates-class | <i>Covariates class.</i> |
|------------------|--------------------------|

Description

Covariates class.

| | |
|---------|--------------------------|
| Dataset | <i>Create a dataset.</i> |
|---------|--------------------------|

Description

Create a dataset.

Usage

```
Dataset(subjects = NULL)
```

Arguments

subjects number of subjects in the default arm

Value

a dataset

| | |
|---------------|-----------------------|
| dataset-class | <i>Dataset class.</i> |
|---------------|-----------------------|

Description

Dataset class.

Slots

arms a list of treatment arms

config dataset configuration for export

iiv data frame containing the inter-individual variability (all ETAS) for the export

| | |
|---------------|---|
| DatasetConfig | <i>Create a dataset configuration. This configuration allows CAMPSIS to know which are the default depot and observed compartments.</i> |
|---------------|---|

Description

Create a dataset configuration. This configuration allows CAMPSIS to know which are the default depot and observed compartments.

Usage

```
DatasetConfig(
  defDepotCmt = 1,
  defObsCmt = 1,
  exportTSLD = FALSE,
  exportTDOS = FALSE
)
```

Arguments

| | |
|-------------|--|
| defDepotCmt | default depot compartment, integer |
| defObsCmt | default observation compartment, integer |
| exportTSLD | export column TSLD (time since last dose), logical |
| exportTDOS | export column TDOS (time of last dose), logical |

Value

a dataset configuration

| | |
|----------------------|-------------------------------------|
| dataset_config-class | <i>Dataset configuration class.</i> |
|----------------------|-------------------------------------|

Description

Dataset configuration class.

Slots

| | |
|---------------|--|
| def_depot_cmt | default depot compartment, integer |
| def_obs_cmt | default observation compartment, integer |
| export_tsld | export column TSLD, logical |
| export_tdos | export column TDOS, logical |

Declare *Create declare settings.*

Description

Create declare settings.

Usage

Declare(variables = character(0))

Arguments

variables uninitialized variables to be declared, only needed with mrgsolve

Value

Declare settings

declare_settings-class *Declare settings class.*

Description

Declare settings class.

Slots

variables uninitialized variables to be declared, only needed with mrgsolve

DiscreteDistribution *Discrete distribution.*

Description

Discrete distribution.

Usage

DiscreteDistribution(x, prob, replace = TRUE)

Arguments

| | |
|---------|--|
| x | vector of one or more integers from which to choose |
| prob | a vector of probability weights for obtaining the elements of the vector being sampled |
| replace | should sampling be with replacement, default is TRUE |

Value

a discrete distribution

distribution-class *Distribution class. See this class as an interface.*

Description

Distribution class. See this class as an interface.

DoseAdaptation *Create a dose adaptation.*

Description

Create a dose adaptation.

Usage

```
DoseAdaptation(formula, compartments = integer(0))
```

Arguments

| | |
|--------------|--|
| formula | formula to apply, single character string, e.g. "AMT*WT" |
| compartments | compartment numbers where the formula needs to be applied, integer vector. Default is integer(0) (formula applied on all compartments) |

Value

a fixed covariate

dose_adaptation-class *Dose adaptation class.*

Description

Dose adaptation class.

Slots

formula formula to apply, single character string, e.g. "AMT*WT"

compartments compartment numbers where the formula needs to be applied

dose_adaptations-class
Dose adaptations class.

Description

Dose adaptations class.

dosingOnly *Filter CAMPSIS output on dosing rows.*

Description

Filter CAMPSIS output on dosing rows.

Usage

dosingOnly(x)

Arguments

x data frame, CAMPSIS output

Value

a data frame with the dosing rows

| | |
|-----------------|---|
| EtaDistribution | <i>Create an ETA distribution. The resulting distribution is a normal distribution, with mean=0 and sd=sqrt(OMEGA).</i> |
|-----------------|---|

Description

Create an ETA distribution. The resulting distribution is a normal distribution, with mean=0 and sd=sqrt(OMEGA).

Usage

```
EtaDistribution(model, omega)
```

Arguments

| | |
|-------|-------------------------------------|
| model | model |
| omega | corresponding THETA name, character |

Value

an ETA distribution

| | |
|-------|--------------------------------------|
| Event | <i>Create an interruption event.</i> |
|-------|--------------------------------------|

Description

Create an interruption event.

Usage

```
Event(name = NULL, times, fun, debug = FALSE)
```

Arguments

| | |
|-------|---|
| name | event name, character value |
| times | interruption times, numeric vector |
| fun | event function to apply at each interruption |
| debug | output the variables that were changed through this event |

Value

an event definition

| | |
|-------------|---------------------|
| event-class | <i>Event class.</i> |
|-------------|---------------------|

Description

Event class.

Slots

name event name, character value
 times interruption times, numeric vector
 fun event function to apply at each interruption
 debug output the variables that were changed through this event

| | |
|----------------|--|
| EventCovariate | <i>Create an event covariate. These covariates can be modified further in interruption events.</i> |
|----------------|--|

Description

Create an event covariate. These covariates can be modified further in interruption events.

Usage

```
EventCovariate(name, distribution)
```

Arguments

name covariate name, character
 distribution covariate distribution at time 0

Value

a time-varying covariate

| | |
|--------|--|
| Events | <i>Create a list of interruption events.</i> |
|--------|--|

Description

Create a list of interruption events.

Usage

Events()

Value

a events object

| | |
|--------------|----------------------|
| events-class | <i>Events class.</i> |
|--------------|----------------------|

Description

Events class.

| | |
|-----------------------|-------------------------------|
| event_covariate-class | <i>Event covariate class.</i> |
|-----------------------|-------------------------------|

Description

Event covariate class.

| | |
|-------------------|---|
| FixedDistribution | <i>Create a fixed distribution. Each sample will be assigned a fixed value coming from vector 'values'.</i> |
|-------------------|---|

Description

Create a fixed distribution. Each sample will be assigned a fixed value coming from vector 'values'.

Usage

```
FixedDistribution(values)
```

Arguments

values covariate values, numeric vector (1 value per sample)

Value

a fixed distribution (1 value per sample)

fixed_covariate-class *Fixed covariate class.*

Description

Fixed covariate class.

fixed_distribution-class
Fixed distribution class.

Description

Fixed distribution class.

Slots

values covariate values, numeric vector (1 value per sample)

FunctionDistribution *Create a function distribution. During distribution sampling, the provided function will be responsible for generating values for each sample. If first argument of this function is not the size (n), please tell which argument corresponds to the size 'n' (e.g. list(size="n")).*

Description

Create a function distribution. During distribution sampling, the provided function will be responsible for generating values for each sample. If first argument of this function is not the size (n), please tell which argument corresponds to the size 'n' (e.g. list(size="n")).

Usage

```
FunctionDistribution(fun, args)
```

Arguments

fun function name, character (e.g. 'rnorm')
args list of arguments (e.g list(mean=70, sd=10))

Value

a function distribution

function_distribution-class
Function distribution class.

Description

Function distribution class.

Slots

fun function name, character (e.g. 'rnorm')
args list of arguments (e.g list(mean=70, sd=10))

| | |
|-------------|---|
| generateIIV | <i>Generate IIV matrix for the given Campsis model.</i> |
|-------------|---|

Description

Generate IIV matrix for the given Campsis model.

Usage

```
generateIIV(model, n, offset = 0)
```

Arguments

| | |
|--------|--|
| model | Campsis model |
| n | number of subjects |
| offset | if specified, resulting ID will be ID + offset |

Value

IIV data frame with ID column

| | |
|--------------|--|
| generateIIV_ | <i>Generate IIV matrix for the given OMEGA matrix.</i> |
|--------------|--|

Description

Generate IIV matrix for the given OMEGA matrix.

Usage

```
generateIIV_(omega, n)
```

Arguments

| | |
|-------|--------------------|
| omega | omega matrix |
| n | number of subjects |

Value

IIV data frame

| | |
|---------------|--|
| getCovariates | <i>Get all covariates (fixed / time-varying / event covariates).</i> |
|---------------|--|

Description

Get all covariates (fixed / time-varying / event covariates).

Usage

```
getCovariates(object)

## S4 method for signature 'covariates'
getCovariates(object)

## S4 method for signature 'arm'
getCovariates(object)

## S4 method for signature 'arms'
getCovariates(object)

## S4 method for signature 'dataset'
getCovariates(object)
```

Arguments

object any object

Value

all covariates from object

| | |
|--------------------|--|
| getEventCovariates | <i>Get all event-related covariates.</i> |
|--------------------|--|

Description

Get all event-related covariates.

Usage

```
getEventCovariates(object)

## S4 method for signature 'covariates'
getEventCovariates(object)

## S4 method for signature 'arm'
```

```
getEventCovariates(object)

## S4 method for signature 'arms'
getEventCovariates(object)

## S4 method for signature 'dataset'
getEventCovariates(object)
```

Arguments

object any object

Value

all event-related covariates from object

getFixedCovariates *Get all fixed covariates.*

Description

Get all fixed covariates.

Usage

```
getFixedCovariates(object)

## S4 method for signature 'covariates'
getFixedCovariates(object)

## S4 method for signature 'arm'
getFixedCovariates(object)

## S4 method for signature 'arms'
getFixedCovariates(object)

## S4 method for signature 'dataset'
getFixedCovariates(object)
```

Arguments

object any object

Value

all fixed covariates from object

| | |
|---------|-----------------------------|
| getIOVs | <i>Get all IOV objects.</i> |
|---------|-----------------------------|

Description

Get all IOV objects.

Usage

```
getIOVs(object)

## S4 method for signature 'arm'
getIOVs(object)

## S4 method for signature 'arms'
getIOVs(object)

## S4 method for signature 'dataset'
getIOVs(object)
```

Arguments

object any object

Value

all IOV's from object

| | |
|--------------|---------------------------|
| getOccasions | <i>Get all occasions.</i> |
|--------------|---------------------------|

Description

Get all occasions.

Usage

```
getOccasions(object)

## S4 method for signature 'arm'
getOccasions(object)

## S4 method for signature 'arms'
getOccasions(object)

## S4 method for signature 'dataset'
getOccasions(object)
```


Arguments

object any object

Value

all occasions from object

getSeedForDatasetExport *Get seed for dataset export.*

Description

Get seed for dataset export.

Usage

getSeedForDatasetExport(seed, progress)

Arguments

seed original seed
progress simulation progress

Value

the seed value used to export the dataset

getSeedForIteration *Get seed for iteration.*

Description

Get seed for iteration.

Usage

getSeedForIteration(seed, progress)

Arguments

seed original seed
progress simulation progress

Value

the seed value to be used for the given replicate number and iteration

getSeedForParametersSampling

Get seed for parameter uncertainty sampling.

Description

Get seed for parameter uncertainty sampling.

Usage

```
getSeedForParametersSampling(seed)
```

Arguments

| | |
|------|---------------|
| seed | original seed |
|------|---------------|

Value

the seed value used to sample parameter uncertainty

getSplittingConfiguration

Get splitting configuration for parallel export.

Description

Get splitting configuration for parallel export.

Usage

```
getSplittingConfiguration(dataset, hardware)
```

Arguments

| | |
|----------|---------------------------|
| dataset | Campsis dataset to export |
| hardware | hardware configuration |

Value

splitting configuration list (if 'parallel_dataset' is enabled) or NA (if 'parallel_dataset' disabled or if the length of the dataset is less than the dataset export slice size)

| | |
|----------|---|
| getTimes | <i>Get all distinct times for the specified object.</i> |
|----------|---|

Description

Get all distinct times for the specified object.

Usage

```
getTimes(object)

## S4 method for signature 'observations_set'
getTimes(object)

## S4 method for signature 'arm'
getTimes(object)

## S4 method for signature 'arms'
getTimes(object)

## S4 method for signature 'events'
getTimes(object)

## S4 method for signature 'dataset'
getTimes(object)
```

Arguments

object any object

Value

numeric vector with all unique times, sorted

| | |
|--------------------------|---|
| getTimeVaryingCovariates | <i>Get all time-varying covariates.</i> |
|--------------------------|---|

Description

Get all time-varying covariates.

Usage

```
getTimeVaryingCovariates(object)

## S4 method for signature 'covariates'
getTimeVaryingCovariates(object)

## S4 method for signature 'arm'
getTimeVaryingCovariates(object)

## S4 method for signature 'arms'
getTimeVaryingCovariates(object)

## S4 method for signature 'dataset'
getTimeVaryingCovariates(object)
```

Arguments

object any object

Value

all time-varying covariates from object

Hardware

Create hardware settings.

Description

Create hardware settings.

Usage

```
Hardware(
  cpu = 1,
  replicate_parallel = FALSE,
  scenario_parallel = FALSE,
  slice_parallel = FALSE,
  slice_size = NULL,
  dataset_parallel = FALSE,
  dataset_slice_size = 500,
  auto_setup_plan = NULL
)
```

Arguments

| | |
|--------------------|--|
| cpu | number of CPU cores to use, default is 1 |
| replicate_parallel | enable parallel computing for replicates, default is FALSE |
| scenario_parallel | enable parallel computing for scenarios, default is FALSE |
| slice_parallel | enable parallel computing for slices, default is FALSE |
| slice_size | number of subjects per simulated slice, default is NULL (auto-configured by Campsis depending on the specified engine) |
| dataset_parallel | enable parallelisation when exporting dataset into a table, default is FALSE |
| dataset_slice_size | dataset slice size when exporting subjects to a table, default is 500. Only applicable if 'dataset_parallel' is enabled. |
| auto_setup_plan | auto-setup plan with the library future, if not set (i.e. =NULL), plan will be setup automatically if the number of CPU's > 1. |

Value

hardware settings

hardware_settings-class

Hardware settings class.

Description

Hardware settings class.

Slots

| | |
|--------------------|--|
| cpu | number of CPU cores to use, default is 1 |
| replicate_parallel | enable parallel computing for replicates, default is FALSE |
| scenario_parallel | enable parallel computing for scenarios, default is FALSE |
| slice_parallel | enable parallel computing for slices, default is FALSE |
| slice_size | number of subjects per simulated slice, default is NULL (auto-configured by Campsis depending on the specified engine) |
| dataset_parallel | enable parallelisation when exporting dataset into a table, default is FALSE |
| dataset_slice_size | dataset slice size when exporting subjects to a table, default is 500. Only applicable if 'dataset_parallel' is enabled. |
| auto_setup_plan | auto-setup plan with the library future, default is FALSE |

Infusion *Create one or several infusion(s).*

Description

Create one or several infusion(s).

Usage

```
Infusion(
  time,
  amount,
  compartment = NA,
  f = NULL,
  lag = NULL,
  duration = NULL,
  rate = NULL,
  ii = NULL,
  addl = NULL
)
```

Arguments

| | |
|-------------|---|
| time | treatment time(s), numeric value or vector. First treatment time if used together with ii and addl. |
| amount | total amount to infuse, numeric |
| compartment | compartment index, integer |
| f | fraction of infusion amount, distribution |
| lag | infusion lag time, distribution |
| duration | infusion duration, distribution |
| rate | infusion rate, distribution |
| ii | interdose interval, requires argument 'time' to be a single numeric value |
| addl | number of additional doses, requires argument 'time' to be a single integer value |

Value

a single infusion or a list of infusions.

| | |
|----------------|------------------------|
| infusion-class | <i>Infusion class.</i> |
|----------------|------------------------|

Description

Infusion class.

Slots

duration infusion duration, distribution
 rate infusion rate, distribution

| | |
|-------------------------|---|
| internal_settings-class | <i>Internal settings class (transient object from the simulation settings).</i> |
|-------------------------|---|

Description

Internal settings class (transient object from the simulation settings).

Slots

dataset_summary dataset summary
 progress simulation progress
 iterations list of event iterations

| | |
|-----|--|
| IOV | <i>Define inter-occasion variability (IOV) into the dataset. A new variable of name 'colname' will be output into the dataset and will vary at each dose number according to the given distribution.</i> |
|-----|--|

Description

Define inter-occasion variability (IOV) into the dataset. A new variable of name 'colname' will be output into the dataset and will vary at each dose number according to the given distribution.

Usage

IOV(colname, distribution, doseNumbers = NULL)

Arguments

| | |
|---------------------------|--|
| <code>colname</code> | name of the column that will be output in dataset |
| <code>distribution</code> | distribution |
| <code>doseNumbers</code> | dose numbers, if provided, IOV is generated at these doses only. By default, IOV is generated for all doses. |

Value

an IOV object

| | |
|--------------------------|------------------------------|
| <code>leftJoinIIV</code> | <i>Left-join IIV matrix.</i> |
|--------------------------|------------------------------|

Description

Left-join IIV matrix.

Usage

```
leftJoinIIV(table, iiv)
```

Arguments

| | |
|--------------------|-----------------------|
| <code>table</code> | dataset, tabular form |
| <code>iiv</code> | IIV matrix |

Value

updated table with IIV matrix

| | |
|--------------------------------|---|
| <code>length,arm-method</code> | <i>Return the number of subjects contained in this arm.</i> |
|--------------------------------|---|

Description

Return the number of subjects contained in this arm.

Usage

```
## S4 method for signature 'arm'
length(x)
```

Arguments

| | |
|----------------|-----|
| <code>x</code> | arm |
|----------------|-----|

Value

a number

length,dataset-method *Return the number of subjects contained in this dataset.*

Description

Return the number of subjects contained in this dataset.

Usage

```
## S4 method for signature 'dataset'  
length(x)
```

Arguments

x dataset

Value

a number

LogNormalDistribution *Create a log normal distribution.*

Description

Create a log normal distribution.

Usage

```
LogNormalDistribution(meanlog, sdlog)
```

Arguments

meanlog mean value of distribution in log domain
sdlog standard deviation of distribution in log domain

Value

a log normal distribution

mrgsolve_engine-class *mrgsolve engine class.*

Description

mrgsolve engine class.

NOCB *Create NOCB settings.*

Description

Create NOCB settings.

Usage

```
NOCB(enable = NULL, variables = character(0))
```

Arguments

| | |
|-----------|---|
| enable | enable/disable next-observation carried backward mode (NOCB), default value is TRUE for mrgsolve, FALSE for RxODE |
| variables | variable names subject to NOCB behavior (see vignette for more info) |

Value

NOCB settings

nocb_settings-class *NOCB settings class.*

Description

NOCB settings class.

Slots

| | |
|-----------|---|
| enable | enable/disable next-observation carried backward mode (NOCB), default value is TRUE for mrgsolve, FALSE for RxODE |
| variables | variable names subject to NOCB behavior (see vignette for more info) |

NormalDistribution *Create a normal distribution.*

Description

Create a normal distribution.

Usage

```
NormalDistribution(mean, sd)
```

Arguments

| | |
|------|------------------------------------|
| mean | mean value of distribution |
| sd | standard deviation of distribution |

Value

a normal distribution

Observations *Create an observations list. Please note that the provided 'times' will automatically be sorted. Duplicated times will be removed.*

Description

Create an observations list. Please note that the provided 'times' will automatically be sorted. Duplicated times will be removed.

Usage

```
Observations(times, compartment = NA)
```

Arguments

| | |
|-------------|-----------------------------------|
| times | observation times, numeric vector |
| compartment | compartment index, integer |

Value

an observations list

observations-class *Observations class.*

Description

Observations class.

Slots

times observation times, numeric vector

compartment compartment index, integer

dv observed values, numeric vector (FOR EXTERNAL USE)

observations_set-class
 Observations set class.

Description

Observations set class.

obsOnly *Filter CAMPSIS output on observation rows.*

Description

Filter CAMPSIS output on observation rows.

Usage

obsOnly(x)

Arguments

x data frame, CAMPSIS output

Value

a data frame with the observation rows

| | |
|----------|---|
| Occasion | <i>Define a new occasion. Occasions are defined by mapping occasion values to dose numbers. A new column will automatically be created in the exported dataset.</i> |
|----------|---|

Description

Define a new occasion. Occasions are defined by mapping occasion values to dose numbers. A new column will automatically be created in the exported dataset.

Usage

```
Occasion(colname, values, doseNumbers)
```

Arguments

| | |
|-------------|---|
| colname | name of the column that will be output in dataset |
| values | the occasion numbers, any integer vector |
| doseNumbers | the related dose numbers, any integer vector of same length as 'values' |

Value

occasion object

| | |
|----------------|------------------------|
| occasion-class | <i>Occasion class.</i> |
|----------------|------------------------|

Description

Occasion class.

Slots

| | |
|--------------|--|
| colname | single character value representing the column name related to this occasion |
| values | occasion values, integer vector, same length as dose_numbers |
| dose_numbers | associated dose numbers, integer vector, same length as values |

| | |
|-----------------|-------------------------|
| occasions-class | <i>Occasions class.</i> |
|-----------------|-------------------------|

Description

Occasions class.

`ParameterDistribution` *Create a parameter distribution. The resulting distribution is a log-normal distribution, with $\text{meanlog}=\log(\text{THETA})$ and $\text{sdlog}=\sqrt{\text{OMEGA}}$.*

Description

Create a parameter distribution. The resulting distribution is a log-normal distribution, with $\text{meanlog}=\log(\text{THETA})$ and $\text{sdlog}=\sqrt{\text{OMEGA}}$.

Usage

```
ParameterDistribution(model, theta, omega = NULL)
```

Arguments

| | |
|--------------------|--|
| <code>model</code> | model |
| <code>theta</code> | corresponding THETA name, character |
| <code>omega</code> | corresponding OMEGA name, character, NULL if not defined |

Value

a parameter distribution

PI *Compute the prediction interval summary over time.*

Description

Compute the prediction interval summary over time.

Usage

```
PI(x, output, scenarios = NULL, level = 0.9, gather = TRUE)
```

Arguments

| | |
|------------------------|---|
| <code>x</code> | data frame |
| <code>output</code> | variable to show, character value |
| <code>scenarios</code> | scenarios, character vector, NULL is default |
| <code>level</code> | PI level, default is 0.9 (90% PI) |
| <code>gather</code> | FALSE: med, low & up columns, TRUE: metric column |

Value

a summary table

| | |
|----------------|------------------------|
| protocol-class | <i>Protocol class.</i> |
|----------------|------------------------|

Description

Protocol class.

| | |
|------------------------|--|
| retrieveParameterValue | <i>Retrieve the parameter value (standardized) for the specified parameter name.</i> |
|------------------------|--|

Description

Retrieve the parameter value (standardized) for the specified parameter name.

Usage

```
retrieveParameterValue(model, paramName, default = NULL, mandatory = FALSE)
```

Arguments

| | |
|-----------|----------------------------|
| model | model |
| paramName | parameter name |
| default | default value if not found |
| mandatory | must be in model or not |

Value

the standardized parameter value or the given default value if not found

| | |
|--------------------|-----------------------------------|
| rxode_engine-class | <i>RxODE/rxode2 engine class.</i> |
|--------------------|-----------------------------------|

Description

RxODE/rxode2 engine class.

Slots

rxode2 logical field to indicate if CAMPSIS should use rxode2 (field set to TRUE) or RxODE (field set to FALSE). Default is TRUE.

sample

Sample generic object.

Description

Sample generic object.

Usage

```
sample(object, n, ...)
```

```
## S4 method for signature 'constant_distribution,integer'  
sample(object, n)
```

```
## S4 method for signature 'fixed_distribution,integer'  
sample(object, n)
```

```
## S4 method for signature 'function_distribution,integer'  
sample(object, n)
```

```
## S4 method for signature 'bootstrap_distribution,integer'  
sample(object, n)
```

```
## S4 method for signature 'bolus,integer'  
sample(object, n, ...)
```

```
## S4 method for signature 'infusion,integer'  
sample(object, n, ...)
```

```
## S4 method for signature 'observations,integer'  
sample(object, n, ...)
```

```
## S4 method for signature 'covariate,integer'  
sample(object, n)
```

```
## S4 method for signature 'bootstrap,integer'  
sample(object, n)
```

```
## S4 method for signature 'campsis_model,integer'  
sample(object, n)
```

Arguments

| | |
|--------|----------------------------|
| object | generic object |
| n | number of samples required |
| ... | extra arguments |

Value

sampling result

| | |
|-------------|---------------------------------------|
| scatterPlot | <i>Scatter plot (or X vs Y plot).</i> |
|-------------|---------------------------------------|

Description

Scatter plot (or X vs Y plot).

Usage

```
scatterPlot(x, output, scenarios = NULL, time = NULL)
```

Arguments

| | |
|-----------|--|
| x | data frame |
| output | the 2 variables to show, character vector |
| scenarios | scenarios |
| time | the time to look at those 2 variables, if NULL, min time is used (usually 0) |

Value

a ggplot object

| | |
|----------|----------------------------|
| Scenario | <i>Create an scenario.</i> |
|----------|----------------------------|

Description

Create an scenario.

Usage

```
Scenario(name = NULL, model = NULL, dataset = NULL)
```

Arguments

| | |
|---------|--|
| name | scenario name, single character string |
| model | either a CAMPSIS model, a function or lambda-style formula |
| dataset | either a CAMPSIS dataset, a function or lambda-style formula |

Value

a new scenario

| | |
|----------------|------------------------|
| scenario-class | <i>Scenario class.</i> |
|----------------|------------------------|

Description

Scenario class.

Slots

name scenario name, single character string

model either a CAMPSIS model, a function or lambda-style formula

dataset either a CAMPSIS dataset, a function or lambda-style formula

| | |
|-----------|------------------------------------|
| Scenarios | <i>Create a list of scenarios.</i> |
|-----------|------------------------------------|

Description

Create a list of scenarios.

Usage

Scenarios()

Value

a scenarios object

| | |
|-----------------|-------------------------|
| scenarios-class | <i>Scenarios class.</i> |
|-----------------|-------------------------|

Description

Scenarios class.

| | |
|----------|-----------------------|
| setLabel | <i>Set the label.</i> |
|----------|-----------------------|

Description

Set the label.

Usage

```
setLabel(object, x)
```

```
## S4 method for signature 'arm,character'  
setLabel(object, x)
```

Arguments

| | |
|--------|-----------------------------|
| object | any object that has a label |
| x | the new label |

Value

the updated object

| | |
|-------------|------------------------------------|
| setSubjects | <i>Set the number of subjects.</i> |
|-------------|------------------------------------|

Description

Set the number of subjects.

Usage

```
setSubjects(object, x)
```

```
## S4 method for signature 'arm,integer'  
setSubjects(object, x)
```

```
## S4 method for signature 'dataset,integer'  
setSubjects(object, x)
```

Arguments

| | |
|--------|----------------------------|
| object | any object |
| x | the new number of subjects |

Value

the updated object

Settings

Create advanced simulation settings.

Description

Create advanced simulation settings.

Usage

Settings(...)

Arguments

... any user-required settings: see ?Hardware, ?Solver, ?NOCB or ?Declare settings

Value

advanced simulation settings

setupPlanDefault

Setup default plan for the given simulation or hardware settings. This plan will prioritise the ditribution of workers in the following order: 1) Replicates (if 'replicate_parallel' is enabled) 2) Scenarios (if 'scenario_parallel' is enabled) 3) Dataset export / slices (if 'dataset_export' or 'slice_parallel' is enabled)

Description

Setup default plan for the given simulation or hardware settings. This plan will prioritise the ditribution of workers in the following order: 1) Replicates (if 'replicate_parallel' is enabled) 2) Scenarios (if 'scenario_parallel' is enabled) 3) Dataset export / slices (if 'dataset_export' or 'slice_parallel' is enabled)

Usage

setupPlanDefault(object)

Arguments

object simulation or hardware settings

Value

nothing

setupPlanSequential *Setup plan as sequential (i.e. no parallelisation).*

Description

Setup plan as sequential (i.e. no parallelisation).

Usage

```
setupPlanSequential()
```

Value

nothing

shadedPlot *Shaded plot (or prediction interval plot).*

Description

Shaded plot (or prediction interval plot).

Usage

```
shadedPlot(x, output, scenarios = NULL, level = 0.9, alpha = 0.25)
```

Arguments

| | |
|-----------|---|
| x | data frame |
| output | variable to show |
| scenarios | scenarios |
| level | PI level, default is 0.9 (90% PI) |
| alpha | alpha parameter (transparency) given to geom_ribbon |

Value

a ggplot object

| | |
|----------|---------------------------|
| simulate | <i>Simulate function.</i> |
|----------|---------------------------|

Description

Simulate function.

Usage

```
simulate(  
  model,  
  dataset,  
  dest = NULL,  
  events = NULL,  
  scenarios = NULL,  
  tablefun = NULL,  
  outvars = NULL,  
  outfun = NULL,  
  seed = NULL,  
  replicates = 1,  
  dosing = FALSE,  
  settings = NULL  
)  
  
## S4 method for signature  
## 'campsis_model,  
## dataset,  
## character,  
## events,  
## scenarios,  
## `function`,  
## character,  
## `function`,  
## integer,  
## integer,  
## logical,  
## simulation_settings'  
simulate(  
  model,  
  dataset,  
  dest = NULL,  
  events = NULL,  
  scenarios = NULL,  
  tablefun = NULL,  
  outvars = NULL,  
  outfun = NULL,  
  seed = NULL,
```

```
    replicates = 1,
    dosing = FALSE,
    settings = NULL
)

## S4 method for signature
## 'campsis_model,
## tbl_df,
## character,
## events,
## scenarios,
## `function`,
## character,
## `function`,
## integer,
## integer,
## logical,
## simulation_settings'
simulate(
  model,
  dataset,
  dest = NULL,
  events = NULL,
  scenarios = NULL,
  tablefun = NULL,
  outvars = NULL,
  outfun = NULL,
  seed = NULL,
  replicates = 1,
  dosing = FALSE,
  settings = NULL
)

## S4 method for signature
## 'campsis_model,
## data.frame,
## character,
## events,
## scenarios,
## `function`,
## character,
## `function`,
## integer,
## integer,
## logical,
## simulation_settings'
simulate(
  model,
```

```
dataset,
dest = NULL,
events = NULL,
scenarios = NULL,
tablefun = NULL,
outvars = NULL,
outfun = NULL,
seed = NULL,
replicates = 1,
dosing = FALSE,
settings = NULL
)

## S4 method for signature
## 'campsis_model,
## tbl_df,
## rxode_engine,
## events,
## scenarios,
## `function`,
## character,
## `function`,
## integer,
## integer,
## logical,
## simulation_settings'
simulate(
  model,
  dataset,
  dest = NULL,
  events = NULL,
  scenarios = NULL,
  tablefun = NULL,
  outvars = NULL,
  outfun = NULL,
  seed = NULL,
  replicates = 1,
  dosing = FALSE,
  settings = NULL
)

## S4 method for signature
## 'campsis_model,
## tbl_df,
## mrgsolve_engine,
## events,
## scenarios,
## `function`,
```



```
## character,  
## `function`,  
## integer,  
## integer,  
## logical,  
## simulation_settings'  
simulate(  
  model,  
  dataset,  
  dest = NULL,  
  events = NULL,  
  scenarios = NULL,  
  tablefun = NULL,  
  outvars = NULL,  
  outfun = NULL,  
  seed = NULL,  
  replicates = 1,  
  dosing = FALSE,  
  settings = NULL  
)
```

Arguments

| | |
|------------|---|
| model | generic CAMPSIS model |
| dataset | CAMPSIS dataset or 2-dimensional table |
| dest | destination simulation engine, default is 'RxODE' |
| events | interruption events |
| scenarios | list of scenarios to be simulated |
| tablefun | function or lambda formula to apply on exported 2-dimensional dataset |
| outvars | variables to output in resulting dataframe |
| outfun | function or lambda formula to apply on resulting dataframe after each replicate |
| seed | seed value |
| replicates | number of replicates, default is 1 |
| dosing | output dosing information, default is FALSE |
| settings | advanced simulation settings |

Value

dataframe with all results

SimulationProgress *Create a simulation progress object.*

Description

Create a simulation progress object.

Usage

```
SimulationProgress(  
    replicates = 1,  
    scenarios = 1,  
    progressor = NULL,  
    hardware = NULL  
)
```

Arguments

| | |
|------------|--|
| replicates | total number of replicates to simulate |
| scenarios | total number of scenarios to simulate |
| progressor | progressor |
| hardware | hardware settings |

Value

a progress bar

simulation_engine-class
Simulation engine class.

Description

Simulation engine class.

simulation_progress-class
Simulation progress class.

Description

Simulation progress class.

Arguments

| | |
|------------|--|
| replicates | total number of replicates to simulate |
| scenarios | total number of scenarios to simulate |
| iterations | total number of iterations to simulate |
| slices | total number of slices to simulate |
| replicate | current replicate number being simulated |
| scenario | current scenario number being simulated |
| iteration | current iteration number being simulated |
| slice | current slice number being simulated |
| progressor | progressor progressor |
| hardware | hardware settings |

simulation_settings-class
Simulation settings class.

Description

Simulation settings class.

Slots

| | |
|----------|----------------------------------|
| hardware | hardware settings object |
| solver | solver settings object |
| nocb | NOCB settings object |
| declare | declare settings (mrgsolve only) |
| internal | internal settings |

Solver *Create solver settings.*

Description

Create solver settings.

Usage

```
Solver(
  atol = 1e-08,
  rtol = 1e-08,
  hmax = NA,
  maxsteps = 70000L,
  method = "liblsoda"
)
```

Arguments

| | |
|----------|---|
| atol | absolute solver tolerance, default is 1e-08 |
| rtol | relative solver tolerance, default is 1e-08 |
| hmax | limit how big a solver step can be, default is NA |
| maxsteps | max steps between 2 integration times (e.g. when observations records are far apart), default is 70000 |
| method | solver method, for RxODE/rxode2 only: 'liblsoda' (default), 'lsoda', 'dop853', 'indLin'. Mrgsolve's method is always 'lsoda'. |

Value

solver settings

solver_settings-class *Solver settings class. See ?mrgsolve::update. See ?rxode2::rxSolve.*

Description

Solver settings class. See ?mrgsolve::update. See ?rxode2::rxSolve.

Slots

`atol` absolute solver tolerance, default is 1e-08
`rtol` relative solver tolerance, default is 1e-08
`hmax` limit how big a solver step can be, default is NA
`maxsteps` max steps between 2 integration times (e.g. when observations records are far apart), default is 70000
`method` solver method, for R_xODE/rxode2 only: 'liblsoda' (default), 'lsoda', 'dop853', 'indLin'. Mrgsolve's method is always 'lsoda'.

| | |
|---------------|------------------------|
| spaghettiPlot | <i>Spaghetti plot.</i> |
|---------------|------------------------|

Description

Spaghetti plot.

Usage

```
spaghettiPlot(x, output, scenarios = NULL)
```

Arguments

| | |
|------------------------|------------------|
| <code>x</code> | data frame |
| <code>output</code> | variable to show |
| <code>scenarios</code> | scenarios |

Value

plot

| | |
|----------------------|--|
| TimeVaryingCovariate | <i>Create a time-varying covariate. This covariate will be implemented using EVID=2 rows in the exported dataset and will not use interruption events.</i> |
|----------------------|--|

Description

Create a time-varying covariate. This covariate will be implemented using EVID=2 rows in the exported dataset and will not use interruption events.

Usage

```
TimeVaryingCovariate(name, table)
```

Arguments

| | |
|-------|---|
| name | covariate name, character |
| table | data.frame, must contain the mandatory columns 'TIME' and 'VALUE'. An 'ID' column may also be specified. In that case, ID's between 1 and the max number of subjects in the dataset/arm can be used. All ID's must have a VALUE defined for TIME 0. |

Value

a time-varying covariate

time_varying_covariate-class
Time-varying covariate class.

Description

Time-varying covariate class.

treatment-class *Treatment class.*

Description

Treatment class.

treatment_iov-class *Treatment IOV class.*

Description

Treatment IOV class.

Slots

colname name of the column that will be output in dataset
distribution distribution
dose_numbers associated dose numbers, integer vector, same length as values

treatment_iovs-class *Treatment IOV's class.*

Description

Treatment IOV's class.

undefined_distribution-class

Undefined distribution class. This type of object is automatically created in method toExplicitDistribution() when the user does not provide a concrete distribution. This is because S4 objects do not accept NULL values.

Description

Undefined distribution class. This type of object is automatically created in method toExplicitDistribution() when the user does not provide a concrete distribution. This is because S4 objects do not accept NULL values.

UniformDistribution *Create an uniform distribution.*

Description

Create an uniform distribution.

Usage

UniformDistribution(min, max)

Arguments

| | |
|-----|-----------|
| min | min value |
| max | max value |

Value

an uniform distribution

| | |
|-----|--|
| VPC | <i>Compute the VPC summary. Input data frame must contain the following columns: - replicate: replicate number - low: low percentile value in replicate (and in scenario if present) - med: median value in replicate (and in scenario if present) - up: up percentile value in replicate (and in scenario if present) - any scenario column</i> |
|-----|--|

Description

Compute the VPC summary. Input data frame must contain the following columns: - replicate: replicate number - low: low percentile value in replicate (and in scenario if present) - med: median value in replicate (and in scenario if present) - up: up percentile value in replicate (and in scenario if present) - any scenario column

Usage

```
VPC(x, scenarios = NULL, level = 0.9)
```

Arguments

| | |
|-----------|--|
| x | data frame |
| scenarios | scenarios, character vector, NULL is default |
| level | PI level, default is 0.9 (90% PI) |

Value

VPC summary with columns TIME, <scenarios> and all combinations of low, med, up (i.e. low_low, low_med, low_up, etc.)

| | |
|---------|------------------|
| vpcPlot | <i>VPC plot.</i> |
|---------|------------------|

Description

VPC plot.

Usage

```
vpcPlot(x, scenarios = NULL, level = 0.9, alpha = 0.15)
```

Arguments

| | |
|-----------|---|
| x | data frame, output of CAMPSIS with replicates |
| scenarios | scenarios, character vector, NULL is default |
| level | PI level, default is 0.9 (90% PI) |
| alpha | alpha parameter (transparency) given to geom_ribbon |

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Value

a ggplot object

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