Package 'campsis'

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Type Package

Title Generic PK/PD Simulation Platform CAMPSIS

Version 1.5.4

Description A generic, easy-to-use and intuitive pharmacokinetic/pharmacodynamic (PK/PD) simulation platform based on R packages 'rxode2' 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' 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 (>= 1.1.0), R (>= 4.0.0)

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

Suggests bookdown, devtools, gridExtra, knitr, mrgsolve, pkgdown, rmarkdown, roxygen2, rxode2, stringr, testthat, tictoc, vdiffr

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LazyData true

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Collate 'global.R' 'utilities.R' 'time_utilities.R' 'check.R' 'generic.R' 'data.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' 'outfun.R'
'hardware_settings.R' 'simulation_progress.R'
'solver_settings.R' 'nocb_settings.R' 'declare_settings.R'
'progress_settings.R' 'internal_settings.R'
'simulation_settings.R' 'plan_setup.R' 'simulate_preprocess.R'
'simulate.R' 'results_processing.R' 'default_plot.R'

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Contents

`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` *Create a treatment arm.*

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 trough 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 *Arm class.*

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.

BinomialDistribution *Binomial distribution.*

Description

Binomial distribution.

Usage

```
BinomialDistribution(trials, prob)
```

Arguments

`trials`	number of Bernoulli trials per observation (=subject), integer
`prob`	probability of success for each trial

Value

a binomial distribution

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 *Bolus class.*

Description

Bolus class.

Bootstrap *Create a bootstrap object.*

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 *Bootstrap class.*

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

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

`convertTime` *Convert numeric time vector based on the provided units.*

Description

Convert numeric time vector based on the provided units.

Usage

```
convertTime(x, from, to)
```

Arguments

`x`	numeric time vector
`from`	unit of x, single character value
`to`	destination unit, single character value

Value

numeric vector with the converted times

`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 *Covariates class.*

Description

Covariates class.

Dataset *Create a dataset.*

Description

Create a dataset.

Usage

```
Dataset(subjects = NULL, label = as.character(NA))
```

Arguments

`subjects`	number of subjects in the default arm
`label`	label of the default arm, NA by default

Value

a dataset

`dataset-class` *Dataset class.*

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

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,
  timeUnitDataset = "hour",
  timeUnitExport = "hour"
)
```

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
`timeUnitDataset`	unit of time in dataset, character ('hour' by default)
`timeUnitExport`	unit of time in export, character ('hour' by default)

Value

a dataset configuration

dataset_config-class *Dataset configuration class.*

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

`time_unit_dataset` unit of time in dataset, character ('hour' by default)

`time_unit_export` unit of time in export, character ('hour' by default)

days *Convert days to hours.*

Description

Convert days to hours.

Usage

```
days(x)
```

Arguments

x	numeric vector in days

Value

numeric vector in hours

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

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` *Create an interruption event.*

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 *Event class.*

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

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 *Create a list of interruption events.*

Description

Create a list of interruption events.

Usage

```
Events()
```

Value

a events object

events-class *Events class.*

Description

Events class.

event_covariate-class *Event covariate class.*

Description

Event covariate class.

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

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 *Generate IIV matrix for the given Campsis model.*

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_ *Generate IIV matrix for the given OMEGA matrix.*

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

getAvailableTimeUnits *Return the list of available time units.*

Description

Return the list of available time units.

Usage

```
getAvailableTimeUnits()
```

Value

character vector

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

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 *Get all event-related covariates.*

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` *Get all IOV objects.*

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 *Get all occasions.*

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 *Get all distinct times for the specified object.*

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 *Get all time-varying covariates.*

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

hours *Convert hours to hours (do nothing).*

Description

Convert hours to hours (do nothing).

Usage

```
hours(x)
```

Arguments

x	numeric vector in hours

Value

numeric vector in hours

`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` *Infusion class.*

Description

Infusion class.

Slots

`duration` infusion duration, distribution

`rate` infusion rate, distribution

`internal_settings-class` *Internal settings class (transient object from the simulation settings).*

Description

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

Slots

`dataset_summary` dataset summary

`progress` simulation progress

`iterations` list of event iterations

`IOV` *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.*

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

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

Value

an IOV object

---

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

Description

Return the number of subjects contained in this arm.

Usage

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

Arguments

x	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

---

minutes *Convert minutes to hours.*

Description

Convert minutes to hours.

Usage

```
minutes(x)
```

Arguments

x	numeric vector in minutes

Value

numeric vector in hours

months *Convert pharma months (1 month = 4 weeks) to hours.*

Description

Convert pharma months (1 month = 4 weeks) to hours.

Usage

```
months(x)
```

Arguments

x	numeric vector in months

Value

numeric vector in hours

mrgsolve_engine-class *mrgsolve engine class.*

Description

mrgsolve engine class.

nhanes *NHANES database (demographics and body measure data combined, from 2017-2018).*

Description

NHANES database (demographics and body measure data combined, from 2017-2018).

Usage

```
nhanes
```

Format

data frame

BS_ID Original identifier

SEX Sex: 1 for males, 2 for females

AGE Age in years

BW Body weight in kg

BMI Body mass index

HT Height in cm

Source

https://wwwn.cdc.gov/Nchs/Nhanes/2017-2018/DEMO_J.XPT

https://wwwn.cdc.gov/Nchs/Nhanes/2017-2018/BMX_J.XPT

`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` *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.*

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 *Occasion class.*

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 *Occasions class.*

Description

Occasions class.

Outfun *Create a new output function*

Description

Create a new output function

Usage

```
Outfun(
  fun = function(x, ...) {
     x
 },
  args = list(),
  packages = NULL,
  level = "scenario"
)
```

Arguments

`fun`	function or purrr-style lambda formula, first argument 'x' must be the results
`args`	extra arguments, named list
`packages`	packages that must be loaded to execute the given function, character vector
`level`	either 'scenario' or 'replicate'. Default is 'scenario'.

Value

an output function

`output_function-class` *Output function class.*

Description

Output function class.

Slots

`fun` function or purrr-style lambda formula, first argument 'x' must be the results

`args` extra arguments, named list

`packages` packages that must be loaded to execute the given function, character vector

`level` either 'scenario' or 'replicate'. Default is 'scenario'.

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

Description

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

Usage

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

Arguments

`model`	model
`theta`	corresponding THETA name, character
`omega`	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

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

Value

a summary table

Progress *Create progress settings.*

Description

Create progress settings.

Usage

```
Progress(tick_slice = TRUE)
```

Arguments

tick_slice	tick() is called after each simulated slice, default is TRUE. In some cases, when the number of subjects per slice is low, it may be useful disable this flag, to improve performance issues.

Value

progress settings

progress_settings-class *Progress settings class.*

Description

Progress settings class.

Slots

`tick_slice` tick() is called after each simulated slice, default is TRUE. In some cases, when the number of subjects per slice is low, it may be useful disable this flag, to improve performance issues.

protocol-class *Protocol class.*

Description

Protocol class.

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

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 *RxODE/rxode2 engine class.*

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` *Scatter plot (or X vs Y plot).*

Description

Scatter plot (or X vs Y plot).

Usage

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

Arguments

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

Value

a ggplot object

Scenario *Create an scenario.*

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 *Scenario class.*

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 — *Create a list of scenarios.*

Description

Create a list of scenarios.

Usage

```
Scenarios()
```

Value

a scenarios object

scenarios-class — *Scenarios class.*

Description

Scenarios class.

seconds — *Convert seconds to hours.*

Description

Convert seconds to hours.

Usage

```
seconds(x)
```

Arguments

x	numeric vector in seconds

Value

numeric vector in hours

setLabel *Set the label.*

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 *Set the number of subjects.*

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, ?Declare or ?Progress settings

Value

advanced simulation settings

`setupPlanDefault` *Setup default plan for the given simulation or hardware settings. This plan will prioritise the distribution 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 distribution 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,
  colour = NULL,
  strat_extra = NULL,
  level = 0.9,
  alpha = 0.25
)
```

Arguments

x	data frame
output	variable to show
colour	variable(s) to colour
strat_extra	variable(s) to stratify, but not to colour (useful for use with facet_wrap)
level	PI level, default is 0.9 (90% PI)
alpha	alpha parameter (transparency) given to geom_ribbon

Value

a ggplot object

simulate *Simulate function.*

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,
##   output_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,
##   output_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,
##   output_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,
##   output_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,
##   output_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	an output function to apply on the simulation results. Type ?Outfun for more info.
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	progressr 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	progressr 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)

progress progress settings

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 RxODE/rxode2 only: 'liblsoda' (default), 'lsoda', 'dop853', 'indLin'. Mrgsolve's method is always 'lsoda'.

---

spaghettiPlot *Spaghetti plot.*

Description

Spaghetti plot.

Usage

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

Arguments

`x`	data frame
`output`	variable to show
`colour`	variable(s) to colour

Value

plot

---

standardiseTime *Standardise time to hours.*

Description

Standardise time to hours.

Usage

```
standardiseTime(x, unit)
```

Arguments

`x`	numeric time vector
`unit`	unit of x, single character value

Value

numeric vector with the times converted to hours

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

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` *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*

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 *VPC plot.*

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

Value

a ggplot object

---

weeks *Convert weeks to hours.*

Description

Convert weeks to hours.

Usage

```
weeks(x)
```

Arguments

x	numeric vector in weeks

Value

numeric vector in hours

`years` *Convert pharma years (1 year = 12*4 weeks) to hours.*

Description

Convert pharma years (1 year = 12*4 weeks) to hours.

Usage

```
years(x)
```

Arguments

`x`	numeric vector in years

Value

numeric vector in hours

Index