Package ‘RsSimulx’

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Type Package

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Description Provide useful tools which supplement the use of Simulx software and R connectors (Monolix Suite). ‘Simulx’ is an easy, efficient and flexible application for clinical trial simulations. You need ‘Simulx’ software to be installed in order to use ‘RsSimulx’ package. Among others tasks, ‘RsSimulx’ provides the same functions as package ‘mlxR’ does with a compatibility with ‘Simulx’ software.

SystemRequirements ‘Simulx’ (<http://simulx.lixoft.com/>)

Depends R (>= 3.0.0), ggplot2

Imports gridExtra, utils, stats, grDevices

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LazyData true

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catplotmlx  
Plot Categorical Longitudinal Data

Description

Plot the empirical distribution of categorical longitudinal data.

Usage

catplotmlx(  
  r,  
  col = NULL,  
  breaks = NULL,  
  plot = TRUE,  
  color = "#194280",  
  group = NULL,  
  facet = TRUE,  
  labels = NULL  
)

Arguments

r .................. a data frame with a column ‘id’, a column ‘time’, a column with values and possibly Hkja column ‘group’.

col .................. a vector of 3 column numbers: (‘id’, ‘time/x’, ‘y’. Default = c(1, 2,3).

breaks .................. one of:
• a vector giving the breakpoints,
• a single number giving the number of segments.

plot
if TRUE the empirical distribution is displayed, if FALSE the values are returned

color
a color to be used for the plots (default="#194280")

group
variable to be used for defining groups (by default, ‘group’ is used when it exists)

facet
makes subplots for different groups if TRUE

labels
vector of strings

Details
See http://simulx.webpopix.org/mlxr/catplotmlx/ for more details.

Value
a ggplot object if plot=TRUE ; otherwise, a list with fields:
• color a vector of colors used for the plot
• y a data frame with the values of the empirical distribution computed at each time point

Examples
## Not run:
catModel <- inlineModel("[LONGITUDINAL]
input = {a,b}
EQUATION:
lp1=a-b*t
lp2=a-b*t/2
DEFINITION:
y = {type=categorical, categories={1,2,3},
logit(P(y<=1))=lp1, logit(P(y<=2))=lp2}
")
y.out <- list(name="y", time=seq(0, 100, by=4))

Ng <- 1000
g1 <- list(size=Ng, parameter=c(a=6,b=0.2))
res <- simulx(model=catModel, output=y.out, group=g1)
catplotmlx(res$y)
catplotmlx(res$y, breaks=seq(-2,102,by=8), color="purple")
catplotmlx(res$y, breaks=5, color="#490917")

g2 <- list(size=Ng, parameter=c(a=10,b=0.2))
res <- simulx(model=catModel, output=y.out, group=list(g1,g2))
catplotmlx(res$y)
catplotmlx(res$y, group="none")

g3 <- list(size=Ng, parameter=c(a=6,b=0.4))
g4 <- list(size=Ng, parameter=c(a=10,b=0.4))
exposure <- simulx(model=catModel, output=y.out, group=list(g1,g2,g3,g4))
catplotmlx(res$y)

res <- simulx(model=catModel, output=y.out, group=list(g1,g2,g3,g4))
catplotmlx(res$y)

## End(Not run)

treatment <- data.frame(id=levels(res$y$id), a=rep(c(6,10,6,10),each=Ng),
b=rep(c(0.2,0.2,0.4,0.4),each=Ng))
catplotmlx(res$y, group=treatment)

exposure

Computation of AUC, Cmax and Cmin

Description

Compute the area under the curve, the maximum and minimum values of a function of time over a given interval or at steady state

Usage

exposure(
  model = NULL,
  output = NULL,
  group = NULL,
  treatment = NULL,
  parameter = NULL,
  data = NULL,
  project = NULL,
  settings = NULL,
  regressor = NULL,
  varlevel = NULL
)

Arguments

model a Mlxtran model used for the simulation
output a list with fields:
  • name: a vector of output names
  • time: = 'steady.state'
  • ntp: number of time points used for computing the exposure (default=100)
  • tol: tolerance number, between 0 and 1, for approximating steaty-state (default=0.01)
  • ngc: number of doses used for estimating the convergence rate to steaty-state (default=5)

group a list, or a list of lists, with fields:
  • size : size of the group (default=1),
  • level : level(s) of randomization,
• parameter: if different parameters per group are defined,
• output: if different outputs per group are defined,
• treatment: if different treatments per group are defined,
• regressor: if different regression variables per group are defined.

treatment
a list with fields
• tfd: time of first dose (default=0),
• ii: inter dose interval (mandatory),
• amount: the amount for each dose,
• rate: the infusion rate (default=Inf),
• tinf: the time of infusion (default=0),
• type: the type of input (default=1),
• target: the target compartment (default=NULL).

parameter
a vector of parameters with their names and values

data
a list

project
the name of a Monolix project

settings
a list of optional settings
• result.file: name of the datafile where the simulated data is written (string),
• seed: initialization of the random number generator (integer),
• load.design: TRUE/FALSE (if load.design is not defined, a test is automatically performed to check if a new design has been defined),
• data.in: TRUE/FALSE (default=FALSE)
• id.out: add columns id (when N=1) and group (when #group=1), TRUE/FALSE (default=FALSE)
• Nmax: maximum group size used in a single call of mlxCompute (default=100)

regressor
a list, or a list of lists, with fields
• name: a vector of regressor names,
• time: a vector of times,
• value: a vector of values.

varlevel
a list, or a list of lists, with fields
• name: a vector of names of variability levels,
• time: a vector of times that define the occasions.

Details

Input arguments are the input arguments of Simulx (http://simulx.webpopix.org)
Specific input arguments can be also used for computing the exposure at steady state, i.e. after the administration of an "infinite" number of doses. See http://simulx.webpopix.org/exposure/ for more details.
Value
A list of data frames. One data frame per output is created with columns id (if number of subject >1), group (if number of groups >1), t1 (beginning of time interval), t2 (end of time interval), step (time step), auc (area under the curve), tmax (time of maximum value), cmax (maximum value), tmin (time of minimum value), cmin (minimum value).

---

ggplotmlx  wrapper for ggplot

Description
wrapper around ggplot with a custom theme

Usage
ggplotmlx(...)

Arguments

...  parameters passed to ggplot

Value
see ggplot

---

initRsSimulx  Initialize RsSimulx library

Description
Initialize RsSimulx library

Usage
initRsSimulx(path = NULL, ...)

Arguments

path  (character) (optional) Path to installation directory of the Lixoft suite. If RsSimulx library is not already loaded and no path is given, the directory written in the lixoft.ini file is used for initialization.

...  (optional) Extra arguments passed to lixoftConnectors package when RsSimulx is used with a version of Lixoft/@) software suite.

  • force (bool) (optional) Should RsSimulx initialization overpass lixoftConnectors software switch security or not. Equals FALSE by default.
Value

A list:

- software: the software that is used (should be monolix with Rsmlx)
- path: the path to MonolixSuite
- version: the version of MonolixSuite that is used
- status: boolean equaling TRUE if the initialization has been successful.

Examples

```r
## Not run:
initRsSimulx(path = "/path/to/lixoftRuntime/")
## End(Not run)
```

**inlineDataFrame**

**Inline dataframe**

Description

Convert a string in dataframe and save it in a temporary file

Usage

```r
inlineDataFrame(str)
```

Arguments

- `str` *(string)* Dataframe in string format

Value

dataframe object

Examples

```r
## Not run:
occ <- inlineDataFrame("id time occ
1 0 1
1 12 2
1 24 3
2 0 1
2 24 2
3 0 1
")
## End(Not run)
```
inlineModel 

Inline model

Description

Save a string in a temporary file to be used as a model file

Usage

inlineModel(srtIn, filename = NULL)

Arguments

srtIn 
(string) Model in string format,

filename 
(string) name of the model file (by default the model is saved in a temporary file)

Value

Name of the model file

Examples

## Not run:
myModel <- inlineModel("[
[LONGITUDINAL]
input = {A, k, c, a}
EQUATION:
t0 = 0
f_0 = A
ddt_f = -k*f/(c+f)
DEFINITION:
y = {distribution=normal, prediction=f, sd=a}
[INDIVIDUAL]
input = {k_pop, omega}
DEFINITION:
k = {distribution=lognormal, prediction=k_pop, sd=omega}
")

## End(Not run)
kmplotmlx

Kaplan Meier plot

Description
Plot empirical survival functions using the Kaplan Meier estimate.

Usage
```r
descript mlx(  
r,  
index = 1,  
level = NULL,  
time = NULL,  
cens = TRUE,  
plot = TRUE,  
color = "#e05969",  
group = NULL,  
facet = TRUE,  
labels = NULL  
)
```

Arguments
- `r`: a data frame with a column ‘id’, a column ‘time’, a column with values and possibly a column ‘group’.
- `index`: an integer: index=k means that the survival function for the k-th event is displayed. Default is index=1.
- `level`: a number between 0 and 1: confidence interval level.
- `time`: a vector of time points where the survival function is evaluated.
- `cens`: if TRUE right censoring times are displayed.
- `plot`: if TRUE the estimated survival function is displayed, if FALSE the values are returned.
- `color`: color to be used for the plots (default=”#e05969”)
- `group`: variable to be used for defining groups (by default, ‘group’ is used when it exists)
- `facet`: makes subplots for different groups if TRUE
- `labels`: vector of strings

Details
See http://simulx.webpopix.org/mlxr/kmplotmlx/ for more details.
Value

a ggplot object if plot=TRUE; otherwise, a list with fields:

- surv a data frame with columns T (time), S (survival), possibly (S1, S2) (confidence interval) and possibly group
- cens a data frame with columns T0 (time), S0 (survival) and possibly group

Examples

```r
## Not run:
tteModel1 <- inlineModel(
  [LONGITUDINAL]
  input = (beta,lambda)
  EQUATION:
  h=(beta/lambda)*(t/lambda)^{(beta-1)}
  DEFINITION:
  e = {type=event, maxEventNumber=1, rightCensoringTime=70, hazard=h}
)

p1 <- c(beta=2.5,lambda=50)
e <- list(name='e', time=0)
res1 <- simulx(model=tteModel1, parameter=p1, output=e, group=list(size=100))
pl1 <- kmplotmlx(res1$e,level=0.95)
print(pl1)

p2 <- c(beta=2,lambda=45)
g1 <- list(size=50, parameter=p1)
g2 <- list(size=100, parameter=p2)
res2 <- simulx(model=tteModel1, output=e, group=list(g1,g2))
pl2 <- kmplotmlx(res2$e)
print(pl2)

## End(Not run)
```

lixoft.read.table Read Lixoft@ files

Description

Utility function to read Lixoft@ formatted input/output files

Usage

```r
lixoft.read.table(file, sep = "", ...) 
```

Arguments

```r
file file path of the file to read
sep separator
... see read.table
```
Value

a dataframe object

prctilemlx Percentiles of the empirical distribution of longitudinal data

Description

Compute and display percentiles of the empirical distribution of longitudinal data.

Usage

prctilemlx(
  r = NULL,
  col = NULL,
  project = NULL,
  outputVariableName = NULL,
  number = 8,
  level = 80,
  plot = TRUE,
  color = NULL,
  group = NULL,
  facet = TRUE,
  labels = NULL,
  band = NULL
)

Arguments

r a data frame with a column ‘id’, a column ‘time’ and a column with values. The times should be the same for each individual.
col a vector with the three column indexes for ‘id’, ‘time’ and ‘y’. Default = c(1, 2,3).
project simulx project filename (with extension ".smlx")
outputVariableName name of the output to consider. By default the first output will be consider. You must define either a 'r' dataframe and the associated 'col' argument or a simulx project and the name of the output 'outputVariableName'
number the number of intervals (i.e. the number of percentiles minus 1).
level the largest interval (i.e. the difference between the lowest and the highest percentile).
plot if TRUE the empirical distribution is displayed, if FALSE the values are returned
color colors to be used for the plots In case of one group or facet = TRUE, only the first color will be used
group variable to be used for defining groups (by default, ‘group’ is used when it exists)
facet makes subplots for different groups if TRUE
labels vector of strings
band is deprecated (use number and level instead); a list with two fields
  • number the number of intervals (i.e. the number of percentiles minus 1).
  • level the largest interval (i.e. the difference between the lowest and the highest percentile).

Details
See http://simulx.webpopix.org/mlxr/prctilemlx/ for more details.

Value
a ggplot object if plot=TRUE; otherwise, a list with fields:
  • proba a vector of probabilities of length band$number+1
  • color a vector of colors used for the plot of length band$number
  • y a data frame with the values of the empirical percentiles computed at each time point

Examples
```r
## Not run:
myModel <- inlineModel("[LONGITUDINAL]
input = {ka, V, Cl}
EQUATION:
C = pkmodel(ka,V,Cl)

[INDIVIDUAL]
input = {ka_pop, V_pop, Cl_pop, omega_ka, omega_V, omega_Cl}
DEFINITION:
ka = (distribution=lognormal, reference=ka_pop, sd=omega_ka)
V = (distribution=lognormal, reference=V_pop, sd=omega_V)
Cl = (distribution=lognormal, reference=Cl_pop, sd=omega_Cl)
")

N=2000

pop.param <- c(
  ka_pop = 1, omega_ka = 0.5,
  V_pop = 10, omega_V = 0.4,
  Cl_pop = 1, omega_Cl = 0.3)

res <- simulx(model = myModel,
  parameter = pop.param,
  treatment = list(time=0, amount=100),
  group = list(size=N, level='individual'),
  output = list(name='C', time=seq(0,24,by=0.1)))
```
# res$C is a data.frame with 2000x241=482000 rows and 3 columns
head(res$C)
# we can display the empirical percentiles of C using the default
# settings (i.e. percentiles of order 10%, 20%, ... 90%)
prctilemlx(res$C)
# The 3 quartiles (i.e. percentiles of order 25%, 50% and 75%) are displayed by
# selecting a 50% interval splitted into 2 subintervals
prctilemlx(res$C, number=2, level=50)
# A one 90% interval can be displayed using only one interval
prctilemlx(res$C, number=1, level=90)
# or 75 subintervals in order to better represent the continuous distribution
# of the data within this interval
prctilemlx(res$C, number=75, level=90)
# prctilemlx produces a ggplot object that can be modified
pl <- prctilemlx(res$C, number=4, level=80)
pl + ylab("concentration") + ggtitle("predictive distribution")
# The percentiles are not plotted by setting plot=FALSE
pr.out <- prctilemlx(res$C, number=4, level=80, plot=FALSE)
print(pr.out$proba)
print(pr.out$color)
print(pr.out$y[1:5,])

## End(Not run)

---

**read.vector**

*Reads a table into a vector*

**Description**

Reads a table into a vector

**Usage**

```r
read.vector(f, header = FALSE, sep = "", quote = "\"")
```

**Arguments**

- `f` : path to table file
- `header` : bool, use the header or not
- `sep` : the separator
- `quote` : the quote character

**Value**

the vector
**Description**

Model definition corresponding to rssimulxDemo.smlx project

**Usage**

rssimulxDemo.model

**Format**

A vector of string

**Source**

Simulx model

---

**Description**

rssimulxDemo.smlx is a Simulx project. In this demo three groups with different dose levels are simulated: low, medium and high. Groups have the same number of individuals, population parameters, distribution of covariates and outputs.

**Usage**

rssimulxDemo.project

**Format**

A vector of string

**Source**

Simulx project
**Description**

Creates a Shiny application for longitudinal data model

**Usage**

```r
shinymlx(
  model,
  parameter = NULL,
  output = NULL,
  treatment = NULL,
  regressor = NULL,
  group = NULL,
  data = NULL,
  appname = "shinymlxApp",
  style = "basic",
  settings = NULL,
  title = ""
)
```

**Arguments**

- **model** a Mlxtran model used for the simulation
- **parameter** a vector, or a list of shiny widgets
- **output** a list - or a list of lists - with fields:
  - name: a vector of output names
  - time: a vector of times, or a vector (min, max, step)
- **treatment** a list with fields
  - tfd: first time of dose,
  - amount: amount,
  - nd: number of doses,
  - ii: interdose interval,
  - type: the type of input,
  Input argument of Simulx can also be used, i.e. a list with fields time, amount, rate, tinf, type, target.
- **regressor** a list, or a list of lists, with fields
  - name: a vector of regressor names
  - time: a vector of times,
  - value: a vector of values.
- **group** a list, or a list of lists, with fields:
• size: size of the group (default=1),
• level: level(s) of randomization,
• parameter: if different parameters per group are defined,
• output: if different outputs per group are defined,
• treatment: if different treatments per group are defined,
• regressor: if different regression variables per group are defined.

data a data file to display with the plot
appname the name of the application (and possibly its path)
style the style of the Shiny app
  • "basic": basic Shiny app with a single side bar (default)
  • "navbar1": navigation bar and tabPanels (including outputs)
  • "navbar2": navigation bar and tabPanels (outputs separated)
  • "dashboard1": Shiny dashboard,
settings a list of settings
  • "tabstyle": look of the tabs c("tabs","pills"),
  • "select.x": display the list of variables available for the x-axis c(TRUE,FALSE),
  • "select.y": display the list of variables available for the y-axis c(TRUE,FALSE),
  • "select.log": log scale option c(TRUE,FALSE),
  • "select.ref": reference curves option c(TRUE,FALSE)
title the title of the application

Details

shinynmlx automatically generates files ui.R and server.R required for a Shiny application.

Elements of parameters and treatment can be either scalars or lists. A scalar automatically
generates a slider with default minimum and maximum values and default step. A list may contain
the type of widget ("slider", "select", "numeric") and the settings defining the widget: (value, min,
max, step) for slider, (selected, choices) for select and value for numeric.

See http://simulx.webpopix.org/mlxr/shinynmlx/ for more details.

Value

A Shiny app with files ui.R, server.R and model.txt

Examples

```r
## Not run:
PKPDmodel <- inlineModel("[LONGITUDINAL]
input={ka,V,Cl,Imax,IC50,S0,kout}
EQUATION:
C    = pkmodel(ka, V, Cl)
E_0   = S0
ddt_E = kout*(((1-Imax*C/(C+IC50))*S0- E)
")
```

p1 <- c(ka=0.5, V=10, Cl=1)
p2 <- c(Imax=0.5, IC50=0.03, S0=100, kout=0.1)
adm <- list(tfd=5, nd=15, ii=12, amount=1)
f1 <- list(name = 'C', time = seq(0, 250, by=1))
f2 <- list(name = 'E', time = seq(0, 250, by=1))
f <- list(f1, f2)

shinymlx(model=PKPDmodel, treatment=adm, parameter=list(p1,p2), output=f, style="dashboard1")

#----------------------------------------------------------
p1 <- list(ka = list(widget="slider", value=0.5, min=0.1, max=2, step=0.1), V = list(widget="slider", value=10, min=2, max=20, step=2), Cl = list(widget="slider", value=1, min=0.1, max=2, step=0.1))
adm <- list(tfd = list(widget="slider", value=5, min=0, max=100, step=5), nd = list(widget="numeric", value=15), ii = list(widget="select", selected=12, choices=c(3,6,12,18,24), amount = list(widget="slider", value=40, min=0, max=50, step=5))
)s <- list(select.x=FALSE, select.y=FALSE)
shinymlx(model=PKPDmodel, treatment=adm, parameter=list(p1,p2), output=f, style="navbar1", settings=s)

## End(Not run)

---

**simpopmlx**  
*Population parameters simulation*

---

**Description**

Draw population parameters using the covariance matrix of the estimates

**Usage**

```r
simpopmlx(
  n = 1,
  project = NULL,
  fim = NULL,
  parameter = NULL,
  corr = NULL,
  kw.max = 100,
  outputFilename = NULL,
  sep = ",",
  seed = NULL
)
```
Arguments

n (integer) the number of vectors of population parameters (default = 1).

project (string) a Monolix project, assuming that the Fisher information Matrix was estimated by Monolix.

fim the (string) Fisher Information Matrix estimated by Monolix. fim="sa", "lin" (default="sa")

parameter (data.frame) a data frame with the following columns

- pop.param (no default) population parameters
- sd (no default) standard deviation of the distribution
- trans (default ='N') distribution (N: normal, L: logNormal, G: logitnormal, P: probitnormal, R)
- lim.a: lower bound of logit distribution (if trans != G set lim.a to NA)
- lim.b: upper bound of logit distribution (if trans != G set lim.b to NA)

Only when project is not used.

corr (matrix) correlation matrix of the population parameters (default = identity). Only when project is not used.

kw.max (integer) maximum number of trials for generating a positive definite covariance matrix (default = 100)

outputFilename (string) when defined, path where the population parameters dataframe will be saved. It must be a file with a csv or txt extension. If no extension is specified, file will be saved by default in csv format

sep (string) file separator when outputFilename is defined (default = ",")

seed (integer) initialization of the random number generator (integer) (by default a random seed will be generated)

Details

See http://simulx.webpopix.org/mlxr/simpopmlx/ for more details.

Value

dataframe object with generated population parameters

Examples

```r
## Not run:
param <- data.frame(pop.param=c(1.5, 0.5, 0.02, 0.4, 0.15, 0.2, 0.7),
                     sd=c(0.2, 0.05, 0.004, 0.05, 0.02, 0.02, 0.05),
                     trans=c("N","N","N","L","L","L","N"))
pop <- simpopmlx(n=3, parameter=param)
## End(Not run)
```
Simulation of mixed effects models and longitudinal data

Description

Compute predictions and sample data from \texttt{Mlxtran} and \texttt{R} models

Usage

\begin{verbatim}
simulx(
  model = NULL,
  parameter = NULL,
  covariate = NULL,
  output = NULL,
  treatment = NULL,
  regressor = NULL,
  occasion = NULL,
  varlevel = NULL,
  group = NULL,
  project = NULL,
  nrep = 1,
  npop = NULL,
  fim = NULL,
  saveSmlxProject = NULL,
  result.file = NULL,
  addlines = NULL,
  settings = NULL
)
\end{verbatim}

Arguments

- **model** a \texttt{Mlxtran} model used for the simulation. It can be a text file or an output of the \texttt{inLine} function.
- **parameter** One of
  - a vector of parameters with their names and values,
  - a dataframe with parameters defined for each id or each pop
  - a string, path to a data frame (csv or txt file)
  - a string corresponding to the parameter elements automatically generated by monolix (only when simulation is based on a Monolix project). One of the following \texttt{mlx} parameter elements: "mlx_Pop", "mlx_PopUncertainSA", "mlx_PopUncertainLin", "mlx_PopIndiv", "mlx_PopIndivCov", "mlx_CondMean", "mlx_EBEs", "mlx_CondDistSample"
- **covariate** One of
  - a vector of covariates with their names and values.
  - a dataframe with covariates defined for each id
• a string, path to a data frame (csv or txt file)
• a string corresponding to the covariate elements automatically generated by monolix (only when simulation is based on a Monolix project). One of the following mlx covariate elements: "mlx_Cov" and "mlx_CovDist"

output
output or list of outputs. An output can be defined by
• a string corresponding to the output elements automatically generated by monolix (only when simulation is based on a Monolix project) - the format is mlx_nameofoutput.
• a list with fields
  – name: a vector of output names
  – time:
    * a vector of times
    * a dataframe with columns id, time (columns lloq, uloq, limit are optional)
    * a string, path to a data frame (csv or txt file)
  – lloq: lower limit of quantification (when time is a vector of times)
  – uloq: upper limit of quantification (when time is a vector of times)
  – limit: lower bound of the censoring interval (when time is a vector of times)

• treatment
treatment or list of treatments. A treatment can be defined by
• A list with fields
  – time: a vector of input times,
  – amount: a scalar or a vector of amounts,
  – rate: a scalar or a vector of infusion rates (default=Inf),
  – tinf: a scalar or a vector of infusion times (default=0),
  – washout: a scalar or a vector of boolean (default=F),
  – adm: (or type) the administration type (default=1),
  – repeats: the treatment cycle (optional), a vector with fields
    * cycleDuration: the duration of a cycle,
    * NumberOfRepetitions: the number of cycle repetition
  – probaMissDose: the probability to miss each dose (optional).
• a dataframe with treatments defined for each id
• a string, path to a data frame (csv or txt file)
• a string corresponding to the treatment elements automatically generated by monolix (only when simulation is based on a Monolix project) - for example mlx_Adm1.

regressor
treatment or list of treatments. A treatment can be defined by
• A list with fields
  – name: a vector of regressor names,
  – time: a vector of times,
  – value: a vector of values.
• A dataframe with columns id, time, and regressor values
occasion

An occasion can be defined by
- A list with fields
  - name: name of the variable which defines the occasions,
  - time: a vector of times (beginnings of occasions)
- A dataframe with columns id, time, occasion
- a string, path to a data frame (csv or txt file)
- "none", to delete an occasion structure

varlevel

deprecated, use occasion instead.

group

a list, or a list of lists, with fields:
- size: size of the group (default=1),
- parameter: if different parameters per group are defined,
- covariate: if different covariates per group are defined,
- output: if different outputs per group are defined,
- treatment: if different treatments per group are defined,
- regressor: if different regression variables per group are defined.

"level" field is not supported anymore in RsSimulx.

project

the name of a Monolix project

nrep

Samples with or without uncertainty depending which element is given as "parameter".

npop

deprecated, Set parameter = "mlx_popUncertainSA" or "mlx_popUncertainLin" instead.

fim

deprecated, Set parameter = "mlx_popUncertainSA" or "mlx_popUncertainLin" instead.

saveSmlxProject

If specified, smlx project will be save in th path location (by default smlx project is not saved)

result.file

deprecated

addlines

a list with fields:
- formula: string, or vector of strings, to be inserted.

"section", "block" field are not supported anymore in RsSimulx. You only need to specify a formula. The additional lines will be added in a new section EQUATION.

settings

a list of optional settings
- seed: initialization of the random number generator (integer) (by default a random seed will be generated)
- id.out: add (TRUE) / remove (FALSE) columns id and group when only one element (N = 1 or group = 1) (default=FALSE)
- kw.max: deprecated.
- replacement: deprecated, use samplingMethod instead
- samplingMethod: str, Sampling method used for the simulation. One of "keepOrder", "withReplacement", "withoutReplacement" (default "keepOrder")
• `out.trt`: TRUE/FALSE (default = TRUE) output of simulx includes treatment
• `sharedIds`: Vector of Elements that share ids. Available types are "covariate", "output", "treatment", "regressor", "population", "individual" (default c())
• `sameIndividualsAmongGroups`: boolean, if True same individuals will be simulated among all groups (default False)
• `exportData`: boolean, if True and if a path to save the smlx project (saveSmLxProject) is specified, export the simulated dataset (smlx project directory/Simulation/simulatedData.txt) (default False)

Details

simulx takes advantage of the modularity of hierarchical models for simulating different components of a model: models for population parameters, individual covariates, individual parameters and longitudinal data.

Furthermore, simulx allows to draw different types of longitudinal data, including continuous, count, categorical, and time-to-event data.

The models are encoded using either the model coding language `Mlxtran`. `Mlxtran` models are automatically converted into C++ codes, compiled on the fly and linked to R using the `RJSONIO` package. That allows one to implement very easily complex models and to take advantage of the numerical solvers used by the C++ `mlxLibrary`.

See http://simulx.lixoft.com for more details.

Value

A list of data frames. Each data frame is an output of simulx

Examples

```r
## Not run:
myModel <- inlineModel("  [LONGITUDINAL]
  input = {A, k, c, a}
  EQUATION:
  t0 = 0
  f_0 = A
  ddt_f = -k*f/(c+f)
  DEFINITION:
  y = {distribution=normal, prediction=f, sd=a}
  [INDIVIDUAL]
  input = {k_pop, omega}
  DEFINITION:
  k = {distribution=lognormal, prediction=k_pop, sd=omega}
")

f <- list(name="f", time=seq(0, 30, by=0.1))
y <- list(name="y", time=seq(0, 30, by=2))
parameter <- c(A=100, k_pop=6, omega=0.3, c=10, a=2)
```

```r
res <- simulx(model = myModel,
              parameter = parameter,
              occasion = data.frame(time=c(0, 0), occ=c(1, 2)),
              output = list(f,y),
              group = list(size=4),
              saveSmlxProject = "/project.smlx")

res <- simulx(model = myModel,
              parameter = parameter,
              occasion = data.frame(time = c(0, 0, 0, 0),
                                     occ1 = c(1, 1, 2, 2),
                                     occ2 = c(1, 2, 3, 4)),
              output = list(f,y),
              group = list(size=4))

res <- simulx(model = myModel,
              parameter = parameter,
              output = list(f,y),
              group = list(size=4))

plot(ggplotmlx() + geom_line(data=res$f, aes(x=time, y=f, colour=id)) +
     geom_point(data=res$y, aes(x=time, y=y, colour=id)))

print(res$parameter)

## End(Not run)
```

---

### statmlx

#### Summary of data

**Description**

Compute statistical summaries (mean, quantile, variance, survival rate,...)

**Usage**

```r
statmlx(r, FUN = "mean", probs = c(0.05, 0.5, 0.95), surv.time = NULL)
```

**Arguments**

- `r` a data frame
- `FUN` a string, or a vector of strings, with the name of the functions to apply to the result of the simulation
- `probs` a vector of quantiles between 0 and 1. Only used when "quantile" has been defined in `FUN`
- `surv.time` a scalar or a vector of times. Only used when "event" has been defined in type
Details

See [http://simulx.webpopix.org/stamlx](http://simulx.webpopix.org/stamlx) for more details.

Value

A data frame.

Examples

```r
## Not run:
modelPK <- inlineModel("[LONGITUDINAL]
input={V,Cl,alpha, beta,b}
EQUATION:
C = pkmodel(V, Cl)
h = alpha*exp(beta*C)
g = b*C
DEFINITION:
y = {distribution=normal, prediction=C, sd=g}
e = {type=event, maxEventNumber=1, rightCensoringTime=30, hazard=h}

[INDIVIDUAL]
input={V_pop,Cl_pop,omega_V,omega_Cl}
DEFINITION:
V = {distribution=lognormal, prediction=V_pop, sd=omega_V}
Cl = {distribution=lognormal, prediction=Cl_pop, sd=omega_Cl}
")

adm <- list(amount=100, time=0)
p <- c(V_pop=10, Cl_pop=1, omega_V=0.2, omega_Cl=0.2, alpha=0.02, beta=0.1, b=0.1)
out.y <- list(name=c("Var"y"), time=seq(0, to=25, by=5))
out.e <- list(name=c("Var"e"), time=0)
out <- list(out.y, out.e)
g <- list(size=100)
res1 <- simulx(model=modelPK, treatment=adm, parameter=p, output=out, group=g)

statmlx(res1$parameter, FUN = "mean", probs = c(0.05, 0.5, 0.95))
statmlx(res1$parameter, FUN = "quantile", probs = c(0.05, 0.5, 0.95))
statmlx(res1$parameter, FUN = c("sd", "quantile"), probs = c(0.05, 0.95))
statmlx(res1$y, FUN = c("mean", "sd", "quantile"), probs = c(0.05, 0.95))
statmlx(res1$e, surv.time=c(10,20))

res2 <- simulx(model=modelPK, treatment=adm, parameter=p, output=out, group=g, nrep=3)

statmlx(res2$parameter, FUN = c("sd", "quantile"), probs = c(0.05, 0.95))
statmlx(res2$y, FUN = c("mean", "sd", "quantile"), probs = c(0.05, 0.95))
statmlx(res2$e, surv.time=c(10,20,30))

## End(Not run)
```
writeData

Write Simulx Dataset

Description

Format outputs of simulx simulations and write datasets in monolix and pkanalix project format.

Usage

writeData(
  project = NULL,
  filename = "simulated_dataset.csv",
  sep = ",",
  ext = "csv",
  nbdigits = 5
)

Arguments

project (string) a simulx project. If no project specified, the function will run on the project that is already loaded.

filename (string) (optional) file path to dataset. (default "simulated_dataset.csv") In case of multiple replicates, the function creates one dataset per replicate with name $filename_repi If filename contains an extension, it must be "csv" or "txt". If it does not, extension is defined by ext argument.

sep (string) (optional) Separator used to write dataset file. (default ",") It must be one of "\t", " " , "", "".

ext (bool) (optional) Extension used to write dataset file. (default "csv") It must be one of "csv", "txt". To defined only if filename with no extension.

nbdigits (integer) (optional) number of decimal digits in output file. (default = 5)

Details

WARNING: writeData function is not implemented for simulx project with regressors in MonolixSuite version 2020R1

Value

a dataframe if one single simulation, a list of dataframe if multiple replicates.

Examples

## Not run:
# rssimulxDemo.smlx is a Simulx project. This demo simulates three groups
# with different dose levels: low, medium and high.
# Groups have the same number of individuals, population parameters,
# distribution of covariates and outputs.
# In this example we write data in the home directory with the name demo_simulx
# and a txt extension
writeData("rssimulxDemo.smlx", filename = "demo_simulx", ext = "txt")

## End(Not run)
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