Package ‘Rsmlx’

April 30, 2019

Type Package
Title R Speaks 'Monolix'
Version 2.0.2
Description Provides methods for model building and model evaluation of mixed effects models using 'Monolix' <http://monolix.lixoft.com>. 'Monolix' is a software tool for nonlinear mixed effects modeling that must have been installed in order to use 'Rsmlx'. Among other tasks, 'Rsmlx' provides a powerful tool for automatic PK model building, performs statistical tests for model assessment, bootstrap simulation and likelihood profiling for computing confidence intervals. 'Rsmlx' also proposes several automatic covariate search methods for mixed effects models.

URL http://rsmlx.webpopix.org
SystemRequirements 'Monolix' (<http://monolix.lixoft.com>)
Depends R (>= 3.0.0)
Imports tools, methods, graphics, grDevices, utils, stats, tcltk, MASS, ggplot2, gridExtra
Suggests mlxR,
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Copyright Inria
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Repository CRAN

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**bootmlx**

*Bootstrapping - case resampling*

**Description**

Generate replicates of the original data using random sampling with replacement. Population parameters are then estimated from each replicate.

**Usage**

```r
bootmlx(project, nboot = 100, dataFolder = NULL, parametric = FALSE,
         tasks = c(populationParameterEstimation = TRUE), settings = NULL)
```
Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>project</td>
<td>Monolix project</td>
</tr>
<tr>
<td>nboot</td>
<td>[optional] number of bootstrap replicates (default=100)</td>
</tr>
<tr>
<td>dataFolder</td>
<td>[optional] folder where already generated datasets are stored, e.g dataFolder=&quot;./dummy_project/boot/&quot; (default: data set are generated by bootmlx)</td>
</tr>
<tr>
<td>parametric</td>
<td>[optional] boolean to define if parametric bootstrap is performed (new data is drawn from the model), (default: false)</td>
</tr>
<tr>
<td>tasks</td>
<td>[optional] vector of booleans defining the list of tasks to perform (default: estimation of the population parameters)</td>
</tr>
<tr>
<td>settings</td>
<td>[optional] a list of settings for the resampling and the results:</td>
</tr>
<tr>
<td></td>
<td>• N the number of individuals in each bootstrap data set (default value is the number of individuals in the original data set).</td>
</tr>
<tr>
<td></td>
<td>• newResampling boolean to generate the data sets again if they already exist (default=FALSE).</td>
</tr>
<tr>
<td></td>
<td>• covStrat a categorical covariate of the project. The original distribution of this covariate is maintained in each resampled data set if covStrat is defined (default=NULL). Notice that if the categorical covariate is varying within the subject (in case of IOV), it will not be taken into account.</td>
</tr>
<tr>
<td></td>
<td>• plot boolean to choose if the distribution of the bootstrapped estimates is displayed (default = FALSE)</td>
</tr>
<tr>
<td></td>
<td>• level level of the bootstrap confidence intervals of the population parameters (default = 0.90)</td>
</tr>
<tr>
<td></td>
<td>• seed seed for the generation of the data sets (default = NA)</td>
</tr>
</tbody>
</table>

Value

a data frame with the bootstrap estimates

Examples

```r
# RsmlxDemo1.mlxtran is a Monolix project for modelling the PK of warfarin using a PK model with parameters ka, V, Cl.

# In this example, bootmlx will generate 100 random replicates of the original data and will use Monolix to estimate the population parameters from each of these 100 replicates:
r1 <- bootmlx(project="RsmlxDemo1.mlxtran")

# 5 replicates will now be generated, with 50 individuals in each replicate:
r2 <- bootmlx(project="RsmlxDemo1.mlxtran", nboot = 5, settings = list(N = 50))

# Proportions of males and females in the original dataset will be preserved in each replicate:
r3 <- bootmlx(project="RsmlxDemo1.mlxtran", settings = list(covStrat = "sex"))

# See http://rsmlx.webpopix.org/userguide/bootmlx/ for detailed examples of use of bootmlx
# Download the demo examples here: http://rsmlx.webpopix.org/installation
```
**buildmlx**

**Automatic model building**

**Description**

buildmlx uses SAMBA (Stochastic Approximation for Model Building Algorithm), an iterative procedure to accelerate and optimize the process of model building by identifying at each step how best to improve some of the model components. This method allows to find the optimal statistical model which minimizes some information criterion in very few steps.

**Usage**

```r
buildmlx(project, final.project = NULL, model = "all",
paramToUse = "all", covToTest = "all", covToTransform = "none",
criterion = "BICc", direction = NULL, max.iter = 20,
print = TRUE, nb.model = 1, linearization = FALSE, seqcc = FALSE,
p.max = 1, steps = 1000, exp.iter = 2)
```

**Arguments**

- `project`: a string: the initial Monolix project
- `final.project`: a string: the final Monolix project (default adds ".built" to the original project)
- `model`: components of the model to optimize c("residualError", "covariate", "correlation"), (default="all")
- `paramToUse`: list of parameters possibly function of covariates (default="all")
- `covToTest`: components of the covariate model that can be modified (default="all")
- `covToTransform`: list of (continuous) covariates to be log-transformed (default="none")
- `criterion`: penalization criterion to optimize c("AIC", "BIC", "BICc", gamma)
- `direction`: method for covariate search c("full", "both", "backward", "forward"), (default="full" or "both")
- `max.iter`: maximum number of iterations (default=20)
- `print`: TRUE/FALSE display the results (default=TRUE)
- `nb.model`: number of models to display at each iteration (default=1)
- `linearization`: TRUE/FALSE whether the computation of the likelihood is based on a linearization of the model (default=FALSE)
- `seqcc`: TRUE/FALSE whether the covariate model is built before the correlation model (default=FALSE)
- `p.max`: maximum p-value (for the correlation test) for keeping a covariate in a model (default=1)
- `steps`: maximum number of iteration for stepAIC (default=1000)
- `exp.iter`: number of iterations during the exploratory phase (default=1)
Details

Penalization criterion can be either a custom penalization of the form $\gamma \cdot \text{(number of parameters)}$, AIC ($\gamma = 2$) or BIC ($\gamma = \log(N)$).

Several strategies can be used for building the covariate model at each iteration of the algorithm: direction = "full" means that all the possible models are compared (default when the number of covariates is less than 10). Otherwise, direction is the mode of stepwise search of stepAIC (MASS), can be one of "both", "backward", or "forward", with a default of "both" when there are at least 10 covariates.

See http://rsmlx.webpopix.org for more details.

Value

a new Monolix project with a new statistical model.

Examples

# RsmlxDemo1.mlxtran is a Monolix project for modelling the pharmacokinetics (PK) of warfarin
# using a PK model with parameters $ka$, $V$, $Cl$.

# By default, buildmlx will compute the best statistical model in term of BIC, i.e.,
# the best covariate model, the best correlation model for the three random effects and the best
# residual error model in terms of BIC.
# In this example, three covariates (wt, age, sex) are available with the data and will be used
# for building the covariate model for the three PK parameters:
# r1 <- buildmlx(project="RsmlxDemo1.mlxtran")

# Here, the covariate model will be built for $V$ and $Cl$ only and log-transformation of all
# continuous covariates will also be considered:
# r2 <- buildmlx(project="RsmlxDemo1.mlxtran", paramToUse=c("V", "Cl"), covToTransform="all")

# Only the covariate model will be built, using AIC instead of BIC:
# r3 <- buildmlx(project="RsmlxDemo1.mlxtran", model="covariate", criterion="AIC")

# See http://rsmlx.webpopix.org/userguide/buildmlx/ for detailed examples of use of buildmlx
# Download the demo examples here: http://rsmlx.webpopix.org/installation

confintmlx

Confidence intervals for population parameters

Description

Compute confidence intervals for the population parameters estimated by Monolix.

Usage

confintmlx(project, parameters = "all", method = "fim", level = 0.9,
linearization = TRUE, nboot = 100, settings = NULL)
Arguments

- **project**: a Monolix project
- **parameters**: list of parameters for which confidence intervals are computed (default="all")
- **method**: method c("fim", "proflike", "bootstrap")
- **level**: confidence level, a real number between 0 and 1 (default=0.90)
- **linearization**: TRUE/FALSE whether the calculation of the standard errors or the profile likelihood is based on a linearization of the model (default=TRUE)
- **nboot**: number of bootstrap replicates (default=100, used when method="bootstrap")
- **settings**: a list of settings for the profile likelihood method:
  - **max.iter**: maximum number of iterations to find the solution (default=10)
  - **tol.LL**: absolute tolerance for -2LL (default=0.001)
  - **tol.param**: relative tolerance for the parameter (default=0.01)
  - **print**: TRUE/FALSE display the results (default=TRUE)

Details

The method used for computing the confidence intervals can be either based on the standard errors derived from an estimation of the Fisher Information Matrix ("fim"), on the profile likelihood ("proflike") or on nonparametric bootstrap estimate ("bootstrap"). method=",fim" is used by default.

When method="fim", the FIM can be either estimated using a linearization of the model or a stochastic approximation. When method="proflike", the observed likelihood can be either estimated using a linearization of the model or an importance sampling Monte Carlo procedure. When method="bootstrap", the bootstrap estimates are obtained using the bootmlx function.

Value

a list with the computed confidence intervals, the method used and the level.

Examples

```r
# Rsm1xDemo2 mlxtran is a Monolix project for modelling the PK of warfarin using a PK model
# with parameters ka, V, Cl.

# confintmlx will compute a 90% confidence interval for all the population parameters
# using the population estimates obtained by Monolix and the Fisher Information Matrix
# estimated by linearization
r1 <- confintmlx(project="Rsm1xDemo2 mlxtran")

# 95% confidence intervals are now computed, using the FIM estimated by Monolix using a
# stochastic approximation algorithm:
r2 <- confintmlx(project="Rsm1xDemo2 mlxtran", linearization=FALSE, level=0.95)

# Confidence intervals are computed for ka_pop and omega_ka only,
# using the profile likelihood method:
r <- confintmlx(project = "Rsm1xDemo2 mlxtran",
               method = "proflike",
               parameters = c("ka_pop", "omega_ka"))
```
# Covariate Search

Confidence intervals are computed using 200 bootstrap samples:
```
r3 <- confintmlx(project="Rsm1xDemo2.mlxtran", method="bootstrap", nboot=200)
```

See [http://rsm1x.webpopix.org/userguide/confintmlx/](http://rsm1x.webpopix.org/userguide/confintmlx/) for detailed examples of use of confintmlx.
Download the demo examples here: [http://rsm1x.webpopix.org/installation](http://rsm1x.webpopix.org/installation)

---

**Description**

Automatic search of the best covariate model. Two methods for covariate model building are proposed:

- **SCM**: stepwise covariate modeling method. In the forward selection, at each step, each of the remaining (i.e., not yet included) parameter-covariate relationships are added to the model in an univariate model (one model per relationship), and run. Among all models, the model that improves some criteria (LRT, BIC or AIC) most is selected and taken forward to the next step. During backward elimination, parameter-covariate relationships are removed in an univariate manner.

- **COSSAC**: COnditional Sampling for Stepwise Approach based on Correlation tests method. COSSAC makes use of the information contained in the base model run to choose which covariate to try first (instead of trying all covariates "blindly" as in SCM). Indeed, the correlation between the individual parameters (or random effects) and the covariates hints at possibly relevant parameter-covariate relationships. If the EBEs (empirical Bayes estimates) are used, shrinkage may bias the result. COSSAC instead uses samples from the a posteriori conditional distribution (available as "conditional distribution" task in MonolixSuite2018) to calculate the correlation between the random effects and covariates. A p-value can be derived using the Pearson’s correlation test for continuous covariate and ANOVA for categorical covariate. The p-values are used to sort all the random effect-covariate relationships. Relationships with the lowest p-value are added first, run and confirmed using a likelihood ratio test, AIC or BIC criteria.

**Usage**

```r
covariateSearch(project, final.project = NULL, method = NULL, 
                 covToTest = NULL, covToTransform = NULL, paramToUse = NULL, 
                 testRelations = NULL, settings = NULL)
```

**Arguments**

- `project` a Monolix project
- `final.project` [optional] string corresponding to the final Monolix project (default: 'runFinal.mlxtran' in covariate search output folder)
method [optional] string correspondig to the method. It can be 'COSSAC' or 'SCM'. By default, COSSAC’ is used.

covToTest [optional] vector of covariates to test. Cannot be used if testRelations is defined. By default, all covariates are tested.

covToTransform [optional] vector of covariates to transform. The transformation consists in a log transform of the covariate with centering by the mean value (ex: WT is transformed into log(WT/mean) with mean the mean WT value over the individuals of the data set). Both the transformed and untransformed covariate are tested by the algorithm. By default, no covariate is transformed. Note: adding a non-transformed covariate on a lognormally distributed parameter results in an exponential relationship: $\log(V) = \log(V_{pop}) + \beta*WT + \eta \implies V = V_{pop} * \exp(\beta*WT) * \exp(\eta)$ adding a log-transformed covariate on a lognormally distributed parameter results in a power law relationship: $\log(V) = \log(V_{pop}) + \beta*\log(WT/70) + \eta \implies V = V_{pop} * (WT/70)^{\beta} * \exp(\eta)$

paramToUse [optional] vector of parameters which may be function of covariates. Cannot be used if testRelations is defined. By default, all parameters are tested.

testRelations [optional] list of parameter-covariate relationships to test, ex: list(V=c("WT","SEX"),Cl=c("CRCL")) Cannot be used if covToTest or paramToUse is defined. By default, all parameter-covariate relationships are tested.

settings [optional] list of settings for the covariate search:

- pInclusion [positive double] threshold on the LRT p-value to accept the model with the added parameter-covariate relationship during forward selection (default = .1). Only used if criteria="LRT".
- pElimination [positive double] threshold on the LRT p-value to accept the model without the removed parameter-covariate relationship during the backward elimination (default = .05). Only used if criteria="LRT".
- criteriaThreshold [positive double] the threshold on the AIC or BIC difference to accept the model with added/removed parameter-covariate relationship (default = 0). Only used if criteria="BIC" or "AIC.
- linearization [boolean] whether the computation of the likelihood is based on a linearization of the model (default = FALSE).
- criteria [string] criteria to optimize. It can be the "BIC", "AIC", or "LRT" (default="LRT")
- direction [string] method for covariate search. It can be "backward", "forward", or "both" (default = "both")
- updateInit [boolean] whether to update or not the initial parameters using the estimates of the parent model (default = FALSE)
- saveRun [boolean] whether to save or not each run (default = TRUE)

Examples

# RsmlxDemo1.mlxtran is a Monolix project for modelling the pharmacokinetics (PK) of warfarin
# using a PK model with parameters ka, V, Cl.

# In this example, three covariates (wt, age, sex) are available with the data
# covariatesearch will compute the best covariate model, in term of BIC,
getEstimatedCovarianceMatrix

Get estimated covariance and correlation matrices

Description

Get estimated covariance and correlation matrices

Usage

getEstimatedCovarianceMatrix()

Value

a list of two matrices.

Examples

## Not run:
# Assume that the Monolix project "warfarinPKPD.mltran" has been loaded
r = getEstimatedCovarianceMatrix() # r is a list with elements "cor.matrix" and "cov.matrix"

# See http://rsmlx.webpopix.org/userguide/newconnectors/ for more detailed examples
# Download the demo examples here: http://rsmlx.webpopix.org/installation

## End(Not run)
getEstimatedIndividualParameters2

Get estimated individual and population parameters

Description

Get the individual parameters, the population parameters with the population covariates and the population parameters with the individual covariates.

Usage

getEstimatedIndividualParameters2()

Value

a list of data frames.

Examples

```r
## Not run:
# Assume that the Monolix project "warfarinPKPD.mlxtran" has been loaded
r = getEstimatedIndividualParameters2()

# r is a list with elements "saem", "conditionalMean", "conditionalSD", "conditionalMode",
# "popPopCov" and "popIndCov"

# See http://rsmlx.webpopix.org/userguide/newconnectors/ for more detailed examples
# Download the demo examples here: http://rsmlx.webpopix.org/installation

## End(Not run)
```

getEstimatedPredictions

Get estimated predictions

Description

Get the individual predictions obtained with the estimated individual parameters:

Usage

getEstimatedPredictions()

Value

a list of data frames (one data frame per output).
getEstimatedResiduals  

Examples

```r
## Not run:
# Assume that the Monolix project "warfarinPKPD.mlxtran" has been loaded
r = getEstimatedPredictions()  # r is a list with elements "y1" and "y2"

# See http://rsmlx.webpopix.org/userguide/newconnectors/ for more detailed examples
# Download the demo examples here: http://rsmlx.webpopix.org/installation

## End(Not run)
```

getEstimatedResiduals  Get estimated residuals

Description

Get the residuals computed from the individual predictions obtained with the estimated individual parameters:

Usage

```r
getEstimatedResiduals()
```

Value

A list of data frames (one data frame per output).

Examples

```r
## Not run:
# Assume that the Monolix project "warfarinPKPD.mlxtran" has been loaded
r = getEstimatedResiduals()  # r is a list with elements "y1" and "y2"

# See http://rsmlx.webpopix.org/userguide/newconnectors/ for more detailed examples
# Download the demo examples here: http://rsmlx.webpopix.org/installation

## End(Not run)
```

getSimulatedPredictions  Get simulated predictions

Description

Get the individual predictions obtained with the simulated individual parameters:

```r
## Not run:
# Assume that the Monolix project "warfarinPKPD.mlxtran" has been loaded
r = getSimulatedPredictions()  # r is a list with elements "y1" and "y2"

# See http://rsmlx.webpopix.org/userguide/newconnectors/ for more detailed examples
# Download the demo examples here: http://rsmlx.webpopix.org/installation

## End(Not run)
```
**getSimulatedResiduals**

**Usage**

```r
getsimulatedpredictions()
```

**Value**

a list of data frames (one data frame per output).

**Examples**

```r
## Not run:
# Assume that the Monolix project "warfarinPKPD.mlxtan" has been loaded
r = getsimulatedPredictions()  # r is a list with elements "Cc" and "E"

# See http://rsmlx.webpopix.org/userguide/newconnectors/ for more detailed examples
# Download the demo examples here: http://rsmlx.webpopix.org/installation

## End(Not run)
```

---

**getSimulatedResiduals**  *Get simulated residuals*

**Description**

Get the residuals computed from the individual predictions obtained with the simulated individual parameters:

**Usage**

```r
getSimulatedResiduals()
```

**Value**

a list of data frames (one data frame per output).

**Examples**

```r
## Not run:
# Assume that the Monolix project "warfarinPKPD.mlxtan" has been loaded
r = getSimulatedResiduals()  # r is a list with elements "y1" and "y2"

# See http://rsmlx.webpopix.org/userguide/newconnectors/ for more detailed examples
# Download the demo examples here: http://rsmlx.webpopix.org/installation

## End(Not run)
```
initRsmlx  

*Initialize Rsmlx library*

**Description**

Initialize Rsmlx library

**Usage**

initRsmlx()

**Value**

A boolean equaling TRUE if the initialization has been successful and FALSE if not.

**Examples**

```r
# Not run:
initRsmlx()

# End(Not run)
```

pkbuild  

*Automatic PK model building*

**Description**

Fit several structural PK models and select the best one based on a Bayesian Information Criterion. Models to compare can be defined by rate constants and/or clearances and can include or not nonlinear elimination models. See [http://rsmlx.webpopix.org/pkbuild/](http://rsmlx.webpopix.org/pkbuild/) for more details.

**Usage**

pkbuild(data = NULL, project = NULL, stat = FALSE, 
param = "clearance", new.dir = ".", MM = FALSE, level = NULL, 
settings.stat = NULL)

**Arguments**

- `data` a list with fields
  - `dataFile`: path of a formatted data file
  - `headerTypes`: a vector of strings
  - `administration`: route of administration ("iv", "bolus", "infusion", "oral", "ev")

- `project` a Monolix project
pkpopini

Compute initial population PK parameters

Description

Use the pooled PK data to derive population PK parameters for a "standard" PK model (i.e. a model of the Monolix PK library). The structural model is automatically defined using the names of the PK parameters. Allowed names are: 'Tlag', 'Mt', 'Kr', 'ka', 'Tk0', 'V', 'V1', 'V2', 'V3', 'Q', 'Q2', 'Q3', 'Cl', 'k', 'k12', 'k21', 'k13', 'k31', 'Vm', 'Km'.

Usage

pkpopini(data = NULL, project = NULL, parameter = NULL, new.project = NULL, new.dir = NULL, par.ini = NULL)
Arguments

data a list with fields
  • datafile: path to a formatted data file
  • headertypes: a vector of strings

project a Monolix project

parameter a vector of strings (names of the PK parameters)

new.project name of the new Monolix project (a default name is created if not provided)

new.dir name of the directory where the created files are stored (default is the current working directory)

par.ini a vector of PK parameter values

Details

A Monolix project is then automatically created using these values as initial population parameters.

See http://rsmlx.webpopix.org/pkpopini/ for more details.

Value

A list of results

Examples

## Not run:
# Create in the working directory a Monolix project for a 1 cpt model with
# lag time, 0 order absorption and linear elimination
warf.ini1 <- pkpopini(data=warfarin, param=c("Tlag", "Tk0", "V", "Cl"))

# Create in directory 'warfarin' a Monolix project called 'warfPK2 mlxtran'
# for a 2 cpt model with 1st order absorption and nonlinear elimination
warf.ini3 <- pkpopini(data=warfarin, param=c("ka", "V", "k12", "k21", "Vm", "Km"),
                      new.dir="warfarin", new.project="warfPK2 mlxtran")

## End(Not run)

resMonolix Monolix results

Description

Monolix results used by the Rsmlx examples

Usage

resMonolix
**RsmlxDemo1.project**

**Format**
A R list

**Source**
Monolix demos

**References**
Rsmlx website: http://rsmlx.webpopix.org

---

**RsmlxDemo1.project**  
*Monolix project for warfarin PK - 1*

**Description**
RsmlxDemo2.mlxtran is a Monolix project for modelling the pharmacokinetics (PK) of warfarin using a PK model with parameters ka, V, Cl. There is no covariate in the model.

**Usage**
RsmlxDemo1.project

**Format**
A text file

**Source**
Monolix project

**References**
Rsmlx documentation
Description

RsmlxDemo2.mlxtan is a Monolix project for modelling the pharmacokinetics (PK) of warfarin using a PK model with parameters $ka$, $V$, $Cl$. Here, $V$ and $Cl$ are function of weight.

Usage

RsmlxDemo2.project

Format

A text file

Source

Monolix project

References

Rsmlx documentation

setSettings  

Easy tuning of the settings of a Monolix project

Description

Use a single accuracy level, between 1 and 9, to automatically tune all the settings of a Monolix project. When the accuracy level is equal to 1, the algorithms are very fast but the results may be not precise. When the accuracy level is equal to 9, the algorithms are slow but the results are accurate. Default Monolix settings are obtained with level=5.

Usage

setSettings(project = NULL, new.project = NULL, level = 5)

Arguments

<table>
<thead>
<tr>
<th>argument</th>
<th>description</th>
</tr>
</thead>
<tbody>
<tr>
<td>project</td>
<td>a string: a Monolix project (the loaded project if NULL)</td>
</tr>
<tr>
<td>new.project</td>
<td>a string: the new created Monolix project (default is the original project)</td>
</tr>
<tr>
<td>level</td>
<td>an integer between 1 and 9 (default=5)</td>
</tr>
</tbody>
</table>
Examples

## Not run:

# RsmlxDemo1 mlxtran is a Monolix project for modelling the PK of warfarin.
# All settings of the project are set so that algorithms used by Monolix converge as
# quickly as possible possible:
setSettings(project="RsmlxDemo1 mlxtran", level=1)

# A new project will be created with settings set in order to obtain the most
# precise results possible:
new.project= file.path(tempdir(,"RsmlxDemoNew mlxtran")
setSettings(project="RsmlxDemo1 mlxtran", new.project=new.project, level=9)

# See http:OOrsmlx NwebpopixNorgOuserguideOsetsettingsO for detailed examples of use of setSettings
# Download the demo examples here: http:OOrsmlx NwebpopixNorgOinstallation

## End(Not run)

testmlx

### Statistical tests for model assessment

#### Description

Perform several statistical tests using the results of a Monolix run to assess the statistical components of the model in use.

#### Usage

```r
testmlx(project, tests = c("covariate", "randomEffect", "correlation", "residual"), plot = FALSE, adjust = "edf", n.sample = NULL)
```

#### Arguments

- **project**: a Monolix project
- **tests**: a vector of strings: the list of tests to perform among c("covariate", "randomEffect", "correlation", "residual")
- **plot**: FALSE/TRUE display some diagnostic plots associated to the tests (default=FALSE)
- **adjust**: method to take into account the dependency of MCMC sample c("edf", "BH")
- **n.sample**: number of samples from the conditional distribution to be used (default = number of available samples in the project)

#### Details

The tests used are: 1) F-tests (or, equivalently, correlation tests) to evaluate the effect of each covariate on each parameter ("covariate"), 2) correlation tests to assess the correlation structure of the random effects ("correlation"), 3) Shapiro-Wilk and Miao-Gel-Gastwirth tests to assess, respectively the normality and the symmetry of the distribution of the random effects ("randomEffect"), 4) Shapiro-Wilk and Miao-Gel-Gastwirth tests to assess, respectively the normality and the symmetry of the distribution of residual errors ("residual").
By default, the four tests are performed. When several samples of the conditional
distributions are used, two methods are proposed in order
to take into the dependance of the samples for the Shapiro-Wilk and Miao-Gel-Gastwirth tests:
"edf" computes an effective degrees of freedom, "BH" performs one test per replicates and adjust
the smallest p-value using the Benjamini-Hochberg correction.

Value

a list of data frames and ggplot objects if plot=TRUE

Examples

# RsmlxDemo2.mltran is a Monolix project for modelling the PK of warfarin using a PK model
# with parameters ka, V, Cl.

testmlx will perform statistical tests for the different component of the statistical model:
r1 <- testmlx(project="RsmlxDemo2.mltran")

testmlx will perform statistical tests for the covariate model and the correlation model only.
r2 <- testmlx(project="RsmlxDemo2.mltran", tests=c("covariate","correlation"))

# See http://rsmlx.webpopix.org/userguide/testmlx/ for detailed examples of use of testmlx
# Download the demo examples here: http://rsmlx.webpopix.org/installation

---

warfarin.data warfarin PKPD data

Description

The warfarin PK and PD data for 32 patients

Usage

warfarin.data

Format

A csv file

Source

Monolix demos

References

O’Reilly (1968). Studies on coumarin anticoagulant drugs. Initiation of warfarin therapy without a
whichPKmodel

Find a Monolix PK model

Description

Return the path of the Monolix PK model defined by a list of parameter names. See http://rsmlx.webpopix.org/whichPKmodel/ for more details.

Usage

whichPKmodel(parameter, mlxPath = NULL, pkPath = NULL)

Arguments

- parameter: a vector of PK parameter names
- mlxPath: path to Monolix install
- pkPath: path to the Monolix PK library

Examples

```r
## Not run:
whichPKmodel(parameter = c("Tlag", "Tk0", "V", "Cl"))

## End(Not run)
```
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