# Package 'PFIM'

June 26, 2025

```
Type Package
Title Population Fisher Information Matrix
Version 7.0
Date 2025
NeedsCompilation no
Description Evaluate or optimize designs for nonlinear mixed effects models using the Fisher Infor-
      mation matrix. Methods used in the package refer to
     Mentré F, Mallet A, Baccar D (1997) < doi:10.1093/biomet/84.2.429 >,
     Retout S, Comets E, Samson A, Mentré F (2007) <doi:10.1002/sim.2910>,
      Bazzoli C, Retout S, Mentré F (2009) <doi:10.1002/sim.3573>,
     Le Nagard H, Chao L, Tenaillon O (2011) <doi:10.1186/1471-2148-11-326>,
     Combes FP, Retout S, Frey N, Mentré F (2013) <doi:10.1007/s11095-013-1079-3> and
     Seurat J, Tang Y, Mentré F, Nguyen TT (2021) <doi:10.1016/j.cmpb.2021.106126>.
URL http://www.pfim.biostat.fr/, https://github.com/packagePFIM
BugReports https://github.com/packagePFIM/Issues
Materials NEWS.md
Depends R (>= 4.0.0)
License GPL (>=3)
Encoding UTF-8
LazyData true
Imports utils,
     Deriv,
     methods,
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     deSolve,
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     S7,
     Matrix,
     ggplot2,
     Rcpp,
     RcppArmadillo,
     pracma,
     kableExtra,
     tibble,
      scales,
     knitr
```

```
Roxygen list(markdown = TRUE, roclets = c(``rd", ``namespace"))
RoxygenNote 7.3.2
VignetteBuilder knitr
Collate 'Administration.R'
      'AdministrationConstraints.R'
      'Model.R'
      'Fim.R'
      'PFIMProject.R'
      'Optimization.R'
      'PGBOAlgorithm.R'
      'PSOAlgorithm.R'
      'SimplexAlgorithm.R'
      'FedorovWynnAlgorithm.R'
      'MultiplicativeAlgorithm.R'
      'Arm.R'
      'BayesianFim.R'
      'ModelError.R'
      'Combined.R'
      'Combined1.R'
      'Constant.R'
      'Design.R'
      'Distribution.R'
      'Evaluation.R'
      'IndividualFim.R'
      'LibraryOfModels.R'
      'LibraryOfPDModels.R'
      'LibraryOfPKModels.R'
      'LogNormal.R'
      'ModelODE.R'
      'ModelAnalytic.R'
      'ModelInfusion.R'
      'ModelAnalyticInfusion.R'
      'ModelAnalyticInfusionSteadyState.R'
      'ModelAnalyticSteadyState.R'
      'ModelODEBolus.R'
      'ModelODEDoseInEquations.R'
      'ModelODEDoseNotInEquations.R'
      'ModelODEInfusion.R'
      'ModelODEInfusionDoseInEquation.R'
      'ModelParameter.R'
      'Normal.R'
      'PFIM-package.R'
      'PopulationFim.R'
      'Proportional.R'
      'SamplingTimeConstraints.R'
      'SamplingTimes.R'
      'zzz.R'
Suggests rmarkdown,
      testthat (>= 3.0.0)
```

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### **Description**

Evaluate or optimize designs for nonlinear mixed effects models using the Fisher Information matrix. Methods used in the package refer to Mentré F, Mallet A, Baccar D (1997) doi:10.1093/biomet/84.2.429, Retout S, Comets E, Samson A, Mentré F (2007) doi:10.1002/sim.2910, Bazzoli C, Retout S, Mentré F (2009) doi:10.1002/sim.3573, Le Nagard H, Chao L, Tenaillon O (2011) doi:10.1186/1471214811326, Combes FP, Retout S, Frey N, Mentré F (2013) doi:10.1007/s11095-01310793 and Seurat J, Tang Y, Mentré F, Nguyen TT (2021) doi:10.1016/j.cmpb.2021.106126.

# Description

Nonlinear mixed effects models (NLMEM) are widely used in model-based drug development and use to analyze longitudinal data. The use of the "population" Fisher Information Matrix (FIM) is a good alternative to clinical trial simulation to optimize the design of these studies. The present version, **PFIM 7.0**, is an R package that uses the S4 object system for evaluating and/or optimizing population designs based on FIM in NLMEMs.

6 PFIM-package

This version of **PFIM** now includes a library of models implemented also using the object oriented system S4 of R. This library contains two libraries of pharmacokinetic (PK) and/or pharmacodynamic (PD) models. The PK library includes model with different administration routes (bolus, infusion, first-order absorption), different number of compartments (from 1 to 3), and different types of eliminations (linear or Michaelis-Menten). The PD model library, contains direct immediate models (e.g. Emax and Imax) with various baseline models, and turnover response models. The PK/PD models are obtained with combination of the models from the PK and PD model libraries. **PFIM** handles both analytical and ODE models and offers the possibility to the user to define his/her own model(s). In **PFIM 7.0**, the FIM is evaluated by first order linearization of the model assuming a block diagonal FIM as in Mentré et al. (1997). The Bayesian FIM is also available to give shrinkage predictions (Combes et al., 2013). **PFIM 7.0** includes several algorithms to conduct design optimization based on the D-criterion, given design constraints: the simplex algorithm (Nelder-Mead) (Nelder & Mead, 1965), the multiplicative algorithm (Seurat et al., 2021), the Fedorov-Wynn algorithm (Fedorov, 1972), PSO (*Particle Swarm Optimization*) and PGBO (*Population Genetics Based Optimizer*) (Le Nagard et al., 2011).

#### **Documentation**

Documentation and user guide are available at http://www.pfim.biostat.fr/

#### Validation

**PFIM 7.0** also provides quality control with tests and validation using the evaluated FIM to assess the validity of the new version and its new features. Finally, **PFIM 7.0** displays all the results with both clear graphical form and a data summary, while ensuring their easy manipulation in R. The standard data visualization package ggplot2 for R is used to display all the results with clear graphical form (Wickham, 2016). A quality control using the D-criterion is also provided.

### Organization of the source files in the /R folder

**PFIM 7.0** contains a hierarchy of S4 classes with corresponding methods and functions serving as constructors. All of the source code related to the specification of a certain class is contained in a file named [Name\_of\_the\_class]-Class.R. These classes include:

- 1. all roxygen @include to insure the correctly generated collate for the DESCRIPTION file,
- 2. \setClass preceded by a roxygen documentation that describes the purpose and slots of the class,
- 3. specification of an initialize method,
- 4. all getter and setter, respectively returning attributes of the object and associated objects.

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#### References

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Eberhart RC, Kennedy J. A new optimizer using particle swarm theory. Proc. of the Sixth International Symposium on Micro Machine and Human Science, Nagoya, 4-6 October 1995, 39-43.

Le Nagard H, Chao L, Tenaillon O. The emergence of complexity and restricted pleiotropy in adapting networks. BMC Evol Biol. 2011;11:326.

Wickham H. ggplot2: Elegant Graphics for Data Analysis, Springer-Verlag New York, 2016.

#### See Also

Useful links:

- http://www.pfim.biostat.fr/
- https://github.com/packagePFIM
- Report bugs at https://github.com/packagePFIM/Issues

adjustGradient

adjustGradient: adjust the gradient for the log normal distribution.

### **Description**

adjustGradient: adjust the gradient for the log normal distribution.

# Arguments

distribution An object Distribution giving the distribution.

gradient The gradient of the model responses.

# Value

The adjusted gradient of the model responses.

8 AdministrationConstraints

Administration Administration

### **Description**

The class Administration represents the administration and stores information concerning the administration for the dosage regimen.

#### Usage

```
Administration(
  outcome = character(0),
  timeDose = numeric(0),
  dose = numeric(0),
  Tinf = numeric(0),
  tau = 0
)
```

### **Arguments**

outcome A string giving the outcome for the administration.

timeDose A vector of double giving the time doses.

dose A vector of double giving the doses.

Tinf A vector of double giving the time for infusion Tinf.

tau An integer giving the tau value for repeated dose or steady state.

#### **Details**

Class Administration

AdministrationConstraints

Administration Constraints

# Description

The class AdministrationConstraints represents the constraint of an input to the system. The class stores information concerning the constraints for the dosage regimen.

# Usage

```
Administration Constraints (outcome = character(0), doses = list()) \\
```

### **Arguments**

outcome A string giving the outcome for the administration.

doses A vector of double giving the doses.

#### **Details**

Class AdministrationConstraints

Arm 9

Arm Arm

### **Description**

The class Arm represents an arm and stores information concerning an arm.

#### Usage

```
Arm(
  name = character(0),
  size = numeric(0),
  administrations = list(),
  initialConditions = list(),
  samplingTimes = list(),
  administrationsConstraints = list(),
  samplingTimesConstraints = list(),
  evaluationModel = list(),
  evaluationGradients = list(),
  evaluationVariance = list(),
  evaluationFim = Fim()
)
```

### **Arguments**

name A string giving the name of the arm.

size A integer giving the size of the arm.

administrations

A list giving the objects of class Administration that define the administrations of the arm.

initialConditions

A list giving the initial conditions for the ode model where the names are string that define the variable and their value are giving by double.

samplingTimes

A list giving the objects of class SamplingTime that define the sampling time of the arm.

administrationsConstraints

A list giving the objects of class AdministrationsConstraints that define the administration constraints of the arm.

samplingTimesConstraints

A list giving the objects of class SamplingTimeConstraints that define the sampling time constraints of the arm.

evaluationModel

A list giving the evaluation of the responses of the arm.

evaluationGradients

A list giving the evaluation of the responses gradient of the arm.

evaluationVariance

A list giving the evaluation of the variance.

evaluationFim A object of class Fim giving the Fisher Information Matrix.

10 BayesianFim

#### **Details**

Class Arm

armAdministration

getArmAdministration: get the administration parameters of an arm.

#### **Description**

getArmAdministration: get the administration parameters of an arm.

### **Arguments**

arm

A object of class Arm giving the arm.

#### Value

A list giving the administration parameters of an arm.

BayesianFim

**BayesianFim** 

### **Description**

The class BayesianFim represents and stores information for the Bayesian Fim.

# Usage

```
BayesianFim(
  fisherMatrix = numeric(0),
  fixedEffects = numeric(0),
  varianceEffects = numeric(0),
  SEAndRSE = list(),
  condNumberFixedEffects = numeric(0),
  condNumberVarianceEffects = numeric(0),
  shrinkage = numeric(0)
)
```

# Arguments

fisherMatrix A matrix giving the numerical values of the Fim.

fixedEffects A matrix giving the numerical values of the fixedEffects of the Fim.

varianceEffects

A matrix giving the numerical values of varianceEffects of the Fim.

SEANDRSE A data frame giving the value of the SE and RSE.

 ${\tt condNumberFixedEffects}$ 

The conditional number of the fixedEffects of the Fim.

condNumberVarianceEffects

The conditional number of the varianceEffects of the Fim.

shrinkage A vector giving the shrinkage values.

#### **Details**

BayesianFim

 $check Sampling Time Constraints For Metaheuristic \\ check Sampling Time Constraints For Metaheuristic$ 

# Description

check Sampling Time Constraints For Metaheuristic

# Arguments

samplingTimesConstraints

 $An\ object\ {\tt SamplingTimeConstraints}.$ 

arm An object Arm.

newSamplings A vector of numeric for the new samplings.

outcome A string giving the outcome.

#### Value

A boolean TRUE/FALSE, with a message error if FALSE.

checkValiditySamplingConstraint

checkValiditySamplingConstraint: check if the constraints used for the design optimization are valid.

# Description

checkValiditySamplingConstraint: check if the constraints used for the design optimization are valid.

# **Arguments**

design An object Design giving the design.

### Value

A boolean TRUE / FALSE, if FALSE it also gives an error message.

12 Combined1

Combined1

Combined1

### **Description**

The class Combined1 represents and stores information for the error model Combined1. The class Combined1 represents and stores information for the error model Combined1.

### Usage

```
Combined1(
  output = "output",
  equation = expression(sigmaInter + sigmaSlope * output),
  derivatives = list(),
  sigmaInter = NULL,
  sigmaSlope = NULL,
  sigmaInterFixed = FALSE,
  sigmaSlopeFixed = FALSE,
  cError = NULL
)
Combined1(
  output = "output",
  equation = expression(sigmaInter + sigmaSlope * output),
  derivatives = list(),
  sigmaInter = NULL,
  sigmaSlope = NULL,
  sigmaInterFixed = FALSE,
  sigmaSlopeFixed = FALSE,
  cError = NULL
)
```

# Arguments

output A string giving the model error output. A expression giving the model error equation. equation derivatives A list giving the derivatives of the model error equation. sigmaInter A double giving the sigma inter. sigmaSlope A double giving the sigma slope sigmaInterFixed A boolean giving if the sigma inter is fixed or not. - not in the v7.0 sigmaSlopeFixed A boolean giving if the sigma slope is fixed or not. - not in the v7.0 A integer giving the power parameter. cError

# **Details**

Combined1

Combined1

computeVMat 13

computeVMat	computeVMat
-------------	-------------

# Description

computeVMat

### Usage

```
computeVMat(varParam1, varParam2, invCholV)
```

#### **Arguments**

```
varParam1 varParam1
varParam2 varParam2
invCholV invCholV
```

#### Value

VMat

Constant Constant

# **Description**

The class Constant represents and stores information for the error model Constant.

### Usage

```
Constant(
  output = "output",
  equation = expression(sigmaInter),
  derivatives = list(),
  sigmaInter = NULL,
  sigmaSlope = NULL,
  sigmaInterFixed = FALSE,
  sigmaSlopeFixed = FALSE,
  cError = NULL
)
```

# Arguments

output A string giving the model error output.

equation A expression giving the model error equation.

derivatives A list giving the derivatives of the model error equation.

sigmaInter A double giving the sigma inter.
sigmaSlope A double giving the sigma slope

sigmaInterFixed

A boolean giving if the sigma inter is fixed or not.

sigmaSlopeFixed

A boolean giving if the sigma slope is fixed or not.

cError

A integer giving the power parameter.

#### **Details**

Constant

constraintsTableForReport

constraintsTableForReport: table of the PGBOAlgorithm constraints for the report.

# Description

constraintsTableForReport: table of the PGBOAlgorithm constraints for the report.

constraintsTableForReport: table of the PSOAlgorithm constraints for the report.

constraintsTableForReport: table of the SimplexAlgorithm constraints for the report.

constraints Table For Report

constraintsTableForReport: table of the MultiplicativeAlgorithm constraints for the report.

### Arguments

 $optimization {\tt Algorithm}$ 

 $A\ object\ {\tt Multiplicative Algorithm}.$ 

arms

List of the arms.

### Value

The table for the constraints in the arms.

The table for the constraints in the arms.

The table for the constraints in the arms.

arms Constraints Table

The table for the constraints in the arms.

convertPKModelAnalyticToPKModelODE

convertPKModelAnalyticToPKModelODE: conversion from analytic to ode

# **Description**

convertPKModelAnalyticToPKModelODE: conversion from analytic to ode convertPKModelAnalyticToPKModelODE: conversion from analytic to ode convertPKModelAnalyticToPKModelODE: conversion from analytic infusion to ode

### **Arguments**

pkModel An object of class ModelAnalyticInfusion that defines the model.

Dcriterion Dcriterion: get the D-criterion of the Fim.

# **Description**

Dcriterion: get the D-criterion of the Fim.

# **Arguments**

Fim A object Fim giving the Fim.

# Value

A double giving the D-criterion of the Fim.

defineFim define the type of Fisher information matrix: population, individual or Bayesian

# Description

define the type of Fisher information matrix: population, individual or Bayesian

# **Arguments**

pfimproject An object PFIMProject.

# Value

An object Fim.

defineModelAdministration

defineModelAdministration: define the administration

### **Description**

defineModelAdministration: define the administration defineModelAdministration: define the administration

### **Arguments**

model An object of class ModelODEInfusionDoseInEquation that defines the model.

arm An object of class Arm that defines the arm.

#### Value

The model with samplings, solverInputs

The model with samplings, solverInputs

The model with samplings, solverInputs

The model with updated slots.

The model with samplings, solverInputs

The model with samplings, solverInputs

The model with updated slots.

 $define {\tt Model Equations From Library Of Model}$ 

defineModelEquationsFromLibraryOfModel: define the model equations giving the models in the library of models.

# Description

defineModelEquationsFromLibraryOfModel: define the model equations giving the models in the library of models.

# **Arguments**

pfimproject An object PFIMProject giving the evaluation to be run.

### Value

A list giving the model equations.

defineModelType 17

defineModelType	defineModelType: define the class of the model to be evaluated.

#### **Description**

defineModelType: define the class of the model to be evaluated.

#### **Arguments**

pfimproject An object PFIMProject giving the evaluation to be run.

#### Value

An object Model giving the model to be evaluated with its modelParameters, odeSolverParameters, modelError, modelEquations.

 ${\tt define Model Wrapper: define \ the \ model \ wrapper \ for \ the \ ode \ solver}$ 

# **Description**

defineModelWrapper: define the model wrapper for the ode solver defineModelWrapper: define the model wrapper for the ode solver defineModelWrapper: define the model wrapper for the ode solver defineModelWrapper: define the model wrapper for the ode solver defineModelWrapper: define the model wrapper for the ode solver defineModelWrapper: define the model wrapper for the ode solver defineModelWrapper: define the model wrapper for the ode solver defineModelWrapper: define the model wrapper for the ode solver defineModelWrapper: define the model wrapper for the ode solver

#### **Arguments**

model An object of class ModelODEInfusionDoseInEquation that defines the model.

evaluation An object of class Evaluation that defines the evaluation

#### Value

 $The \ model \ with \ wrapper Model Analytic, function Arguments Model Analytic, function Arguments Symbol Model Analytic, output Names, outcomes With Administration$ 

The model with wrapperModelAnalyticInfusion, functionArgumentsModelAnalyticInfusion, functionArgumentsSymbolModelAnalyticInfusion, outputNames, outcomesWithAdministration

The model with wrapperModelAnalyticInfusion, functionArgumentsModelAnalyticInfusion, functionArgumentsSymbolModelAnalyticInfusion, outputNames, outcomesWithAdministration

 $The \ model \ with \ wrapper Model Analytic, function Arguments Model Analytic, function Arguments Symbol Model Analytic, output Names, outcomes With Administration$ 

The model with updated slots.

18 definePKModel

The model with the updated slots.

The model with the updated slots.

The model with updated slots.

 ${\tt defineOptimizationAlgorithm}$ 

Define optimization algorithm

### **Description**

Define optimization algorithm

# **Arguments**

optimization An Optimization object.

#### Value

An optimization algorithm.

definePKModel

definePKModel: define a PK model from library of model

### **Description**

definePKModel: define a PK model from library of model

 $define PKModel\ Model Analytic Infusion$ 

definePKModel definePKModel

definePKModel: define PK model ode bolus

definePKModel: define a PK model from library of model definePKModel: define a PK model from library of model

definePKModel: define PK model ode bolus

# Arguments

 $\label{lem:pkModel} An object of class \verb|ModelODEInfusionDoseInEquation| that defines the PK model.$ 

pfimproject An object of class PFIMProject that defines the pfimproject.

definePKPDModel 19

definePKPDModel

definePKPDModel: define a PKPD model from library of model

# Description

definePKPDModel: define a PKPD model from library of model definePKPDModel: define a PKPD model from library of model definePKPDModel ModelAnalyticInfusion, ModelAnalytic definePKPDModel ModelAnalyticInfusion, ModelODE definePKPDModel definePKPDModel definePKPDModel definePKPDModel definePKPDModel

#### Arguments

pkModel An object of class ModelODE that defines the PD model.

pfimproject An object of class PFIMProject that defines the pfimproject.

Design

Design

# Description

The class Design represents and stores information for the Design.

# Usage

```
Design(
  name = character(0),
  size = numeric(0),
  arms = list(),
  evaluationArms = list(),
  numberOfArms = numeric(0),
  fim = Fim()
)
```

### **Arguments**

name A string giving the name of the design.
size A integer gving the size of the design.
arms A list giving the arms of the design.

evaluationArms A list giving the valuation of the arms of the design.

numberOfArms A integer giving the number of arms.

fim A object Fim giving the Fim of the design.

20 evaluateArm

#### **Details**

Design

Distribution

Distribution

# Description

The class Distribution represents and stores information for the parameter distribution.

# Usage

```
Distribution(name = character(0), mu = numeric(0), omega = numeric(0))
```

### **Arguments**

name A string giving the name of the distribution.

mu A double giving the mean mu.

omega A double giving omega.

#### **Details**

Distribution

evaluateArm

evaluateArm: evaluation of the model with the arm parameters.

# Description

evaluateArm: evaluation of the model with the arm parameters.

# Arguments

arm A object of class Arm giving the arm.

Model A object of class Model giving the model.

fim A object of class Fim giving the fim.

### Value

The object arm with the slots evaluationModel, evaluationGradients, evaluationVariance and evaluationFim.

evaluateDesign 21

# Description

evaluateDesign: evaluation of a design.

# Arguments

design An object Design giving the design.

model An object Model giving the model.

fim An object Fim giving the Fim.

### Value

The object Design with its evaluation results.

evaluateErrorModelDerivatives

evaluateErrorModelDerivatives; evaluate the derivatives of the model error.

# Description

evaluateErrorModelDerivatives; evaluate the derivatives of the model error.

# Arguments

modelError An object ModelError that defines the model error.

 ${\it evaluation} {\it Model}$ 

A dataframe giving the outputs for the model evaluation.

#### Value

The matrices sigmaDerivatives and errorVariance.

22 evaluateInitialConditions

evaluateFim: evaluation of the Fim

### **Description**

evaluateFim: evaluation of the Fim evaluateFim: evaluation of the Fim evaluateFim: evaluation of the Fim

#### **Arguments**

fim An object PopulationFim giving the Fim.

model An object Model giving the model.

arm An object Arm giving the arm.

### Value

The object Fim with the fisherMatrix and the shrinkage.

The object IndividualFim with the fisherMatrix and the shrinkage.

The object IndividualFim with the fisherMatrix and the shrinkage.

evaluateInitialConditions

evaluateInitialConditions: evaluate the initial conditions.

# Description

evaluateInitialConditions: evaluate the initial conditions. evaluateInitialConditions: evaluate the initial conditions. evaluateInitialConditions: evaluate the initial conditions.

# **Arguments**

arm A object of class Arm giving the arm.

model A object of class ModelODEInfusion giving the model.

doseEvent A data frame giving the dose event for the ode solver.

#### Value

A list giving the evaluated initial conditions.

evaluateModel 23

evaluateModel

evaluateModel: evaluate the model

### **Description**

evaluateModel: evaluate the model

evaluateModel: evaluate the ModelAnalyticInfusion evaluateModel: evaluate the ModelAnalyticInfusion evaluateModel: evaluate the ModelAnalyticInfusion

evaluateModel evaluateModel

evaluateModel: evaluate the model evaluateModel: evaluate the model

evaluateModel

#### **Arguments**

arm A object of class Arm giving the arm.

model A object of class ModelODEInfusionDoseInEquation giving the model.

#### Value

A list of dataframes that contains the results for the evaluation of the model.

A list of dataframes that contains the results for the evaluation of the model.

A list of dataframes that contains the results for the evaluation of the model.

A list of dataframes that contains the results for the evaluation of the model.

A list of dataframes that contains the evaluation of the model.

A data frame giving the output of the model evaluation.

A list of dataframes that contains the results for the evaluation of the model.

A list of dataframes that contains the results for the evaluation of the model.

A data frame giving the output of the model evaluation.

evaluateModelGradient evaluateModelGradient: evaluate the gradient of the model

### **Description**

evaluateModelGradient: evaluate the gradient of the model

# **Arguments**

model An object Model that defines the model.

arm A object Arm giving the arm

#### Value

A data frame that contains the gradient of the model.

24 evaluate Variance FIM

evaluateModelVariance evaluateModelVariance: evaluate the variance of the model

# Description

evaluateModelVariance: evaluate the variance of the model

# Arguments

model A object Model giving the model.

arm A object Arm giving the arm

#### Value

A list giving errorVariance and sigmaDerivatives.

evaluateVarianceFIM evaluateVarianceFIM: evaluate the variance

# **Description**

evaluate Variance FIM: evaluate the variance evaluate Variance FIM: evaluate the variance evaluate Variance FIM: evaluate the variance

# **Arguments**

arm A object of class Arm giving the arm.

model A object of class Model giving the model.

fim A object of class PopulationFim giving the Fim.

# Value

The matrices MFbeta and V.

The matrices MFbeta and V.

The matrices MFVar and V.

Evaluation 25

Evaluation

Evaluation

### **Description**

The class Evaluation represents and stores information for the evaluation of a design

#### Usage

```
Evaluation(
  name = character(0),
  modelEquations = list(),
  modelFromLibrary = list(),
  modelParameters = list(),
  modelError = list(),
  optimizer = character(0),
  optimizerParameters = list(),
  outputs = list(),
  designs = list(),
  fimType = character(0),
  fim = Fim(),
  odeSolverParameters = list(),
  evaluationDesign = list()
)
```

# **Arguments**

name A string giving the name of the design evaluation. modelEquations A list giving the model equations.

modelFromLibrary

A list giving the model equations from the library of model.

modelParameters

A list giving the model parameters.

modelError A list giving the model error.

 $\begin{tabular}{ll} \textbf{optimizer} & A string giving the name of the optimization algorithm being used.} \\ \textbf{optimizerParameters} & \end{tabular}$ 

A list giving the parameters of the optimization algorithm.

outputs A list giving the model outputs.

designs A list giving the designs to be evaluated.

fimType A string giving the type of Fim being evaluated.

fim A object Fim giving the Fim.

odeSolverParameters

A list giving the atol and rtol parameters for the ode solver.

evaluationDesign

A list giving the evaluation of the design.

# **Details**

Evaluation

FedorovWynnAlgorithm FedorovWynnAlgorithm

#### **Description**

The class FedorovWynnAlgorithm implements the FedorovWynn algorithm.

# Usage

```
FedorovWynnAlgorithm(
  name = character(0),
  modelEquations = list(),
  modelFromLibrary = list(),
  modelParameters = list(),
  modelError = list(),
  optimizer = character(0),
  optimizerParameters = list(),
  outputs = list(),
  designs = list(),
  fimType = character(0),
  fim = Fim(),
  odeSolverParameters = list(),
  optimisationDesign = list(),
  optimisationAlgorithmOutputs = list(),
  elementaryProtocols = list(),
  numberOfSubjects = logical(0),
  proportionsOfSubjects = logical(0),
  showProcess = logical(0),
  FedorovWynnAlgorithmOutputs = list()
)
```

#### **Arguments**

```
name
                  A string giving the name.
model Equations A list giving the model equations.
modelFromLibrary
                   A list giving the model equations from the library of model.
modelParameters
                   A list giving the model parameters.
modelError
                   A list giving the model error.
optimizer
                  A string giving the name of the optimization algorithm being used.
optimizerParameters
                  A list giving the parameters of the optimization algorithm.
outputs
                  A list giving the model outputs.
designs
                  A list giving the designs to be evaluated.
                  A string giving the type of Fim being evaluated.
fimType
fim
                  A object Fim giving the Fim.
```

```
{\tt odeSolverParameters}
                  A list giving the atol and rtol parameters for the ode solver.
optimisationDesign
                  A list giving the evaluation of initial and optimal design.
optimisationAlgorithmOutputs
                  A list giving the outputs of the optimization process.
elementaryProtocols
                  A lit giving the elementaryProtocols.
numberOfSubjects
                  A numeric giving the numberOfSubjects.
proportionsOfSubjects
                  A numeric giving the proportionsOfSubjects.
showProcess
                  A boolean giving showProcess.
FedorovWynnAlgorithmOutputs
                  A list giving the output of the optimization algorithm.
```

### **Details**

Class "FedorovWynnAlgorithm"

```
FedorovWynnAlgorithm_Rcpp
```

Fedorov-Wynn algorithm in Rcpp.

### **Description**

Run the FedorovWynnAlgorithm in Rcpp

#### Usage

```
FedorovWynnAlgorithm_Rcpp(
   protocols_input,
   ndimen_input,
   nbprot_input,
   numprot_input,
   freq_input,
   nbdata_input,
   vectps_input,
   fisher_input,
   nok_input,
   protdep_input,
   freqdep_input
)
```

### **Arguments**

28 Fim

```
nbprot_input
                 parameter nbprot_input
numprot_input
                 parameter numprot_input
                 parameter freq_input
freq_input
nbdata_input
                 parameter nbdata_input
vectps_input
                 parameter vectps_input
fisher_input
                 parameter fisher_input
                 parameter nok_input
nok_input
protdep_input
                 parameter protdep_input
freqdep_input
                 parameter freqdep_input
```

#### Value

A list giving the results of the outputs of the FedorovWynn algorithm.

Fim Fim

# Description

The class Fim represents and stores information for the Fim.

# Usage

```
Fim(
   fisherMatrix = numeric(0),
   fixedEffects = numeric(0),
   varianceEffects = numeric(0),
   SEAndRSE = list(),
   condNumberFixedEffects = numeric(0),
   condNumberVarianceEffects = numeric(0),
   shrinkage = numeric(0)
)
```

### **Arguments**

 $\label{eq:fisherMatrix} \textbf{A matrix giving the numerical values of the Fim.}$ 

 ${\tt fixedEffects} \qquad A \ matrix \ giving \ the \ numerical \ values \ of \ the \ fixedEffects \ of \ the \ Fim.$ 

varianceEffects

A matrix giving the numerical values of varianceEffects of the Fim.

SEAndRSE A data frame giving the value of the SE and RSE.

 ${\tt condNumberFixedEffects}$ 

The conditional number of the fixedEffects of the Fim.

condNumberVarianceEffects

The conditional number of the varianceEffects of the Fim.

shrinkage A vector giving the shrinkage values.

### **Details**

Fim

finiteDifferenceHessian 29

finiteDifferenceHessian

finiteDifferenceHessian: compute the Hessian

# Description

finiteDifferenceHessian: compute the Hessian

### **Arguments**

model

A object Model giving the model.

#### Value

The model with the slots parametersForComputingGradient with XcolsInv, shifted, frac.

fisherSimplex

Compute the fisher.simplex

### **Description**

Compute the fisher.simplex

# Arguments

simplex A list giving the parameters of the simplex.

optimizationObject

An object Optimization.

outcomes A vector giving the outcomes of the arms.

# Value

A list giving the results of the optimization.

fun.amoeba

Compute the fun.amoeba

# Description

Compute the fun.amoeba

# Usage

```
fun.amoeba(p, y, ftol, itmax, funk, outcomes, data, showProcess)
```

### **Arguments**

p parameter p
y parameter y
ftol parameter ftol
itmax parameter itmax
funk parameter funk

outcomes The model outcomes.

data parameter data

showProcess Boolean.

#### Value

fun.amoeba

generateDosesCombination

generateDosesCombination: generate the combination for the doses.

# Description

generateDosesCombination: generate the combination for the doses.

# Arguments

design

An object Design giving the design.

# Value

dosesForFIMs, numberOfDoses used in the design optimization.

generateFimsFromConstraints

Generate FIMs from constraints

### **Description**

Generate FIMs from constraints

### **Arguments**

optimization An Optim

 $An \ {\tt Optimization} \ object.$ 

# Value

A list containing FIMs from constraints.

generateReportEvaluation

generateReportEvaluation: generate the report for the model evaluation.

#### **Description**

generateReportEvaluation: generate the report for the model evaluation. generateReportEvaluation: generate the report for the model evaluation. generateReportEvaluation: generate the report for the model evaluation.

# Arguments

fim An object PopulationFim giving the Fim.
tablesForReport
The output list giving by the method tablesForReport.

#### Value

The html report for the design evaluation.

The html report for the model evaluation.

The html report for the model evaluation.

generateReportOptimization

generateReportOptimization: generate the report for the design optimization.

# Description

generateReportOptimization: generate the report for the design optimization. generateReportOptimization: generate the report for the design optimization.

### **Arguments**

```
\begin{tabular}{ll} fim & An object PopulationFim giving the Fim. \\ optimizationAlgorithm \\ & An object PGBOAlgorithm giving the PGBOAlgorithm \\ tablesForReport \\ & The output list giving by the method tablesForReport. \\ \end{tabular}
```

#### Value

The html report for the design optimization.

The html report for the design optimization.

The html report.

 $generate Sampling Sampling Constraints \\ generate Sampling From Sampling Constraints$ 

# Description

generate Samplings From Sampling Constraints

# **Arguments**

```
{\bf Sampling Time Constraints} \\ {\bf An \ object \ Sampling Time Constraints}
```

# Value

A list intervalsConstraints.

generateSamplingTimesCombination

generateSamplingTimesCombination: generate the combination for the samplings.

#### **Description**

generateSamplingTimesCombination: generate the combination for the samplings.

### **Arguments**

design

An object Design giving the design.

#### Value

samplingTimesCombinations used in the design optimization.

getArmConstraints

getArmConstraints: get the administration and sampling time constraints for the MultiplicativeAlgorithm.

### **Description**

getArmConstraints: get the administration and sampling time constraints for the MultiplicativeAlgorithm.

getArmConstraints: get the administration and sampling time constraints for the FedorovWynnAlgorithm.

getArmConstraints: get the administration and sampling time constraints for the SimplexAlgorithm. getArmConstraints: get the administration and sampling time constraints for the PSOAlgorithm.

getArmConstraints: get the administration and sampling time constraints for the PGBOAlgorithm.

# **Arguments**

 $\begin{array}{ll} \text{arm} & \text{A object of class Arm giving the arm.} \\ \text{optimizationAlgorithm} \end{array}$ 

A object of class Optimization giving the optimization algorithm.

#### Value

A list giving the administration and sampling time constraints for the MultiplicativeAlgorithm.

A list giving the administration and sampling time constraints for the FedorovWynnAlgorithm.

A list giving the administration and sampling time constraints for the SimplexAlgorithm.

A list giving the administration and sampling time constraints for the PSOAlgorithm.

A list giving the administration and sampling time constraints for the PGBOAlgorithm.

34 getDcriterion

getArmData

getArmData: extract arm data for The Report

# Description

getArmData: extract arm data for The Report

# **Arguments**

arm

A object of class Arm giving the arm.

#### Value

A list giving the name, Number of subjects, Outcome, Dose and Sampling times of the arm.

getCorrelationMatrix getCorrelationMatrix : get the correlation matrix

# Description

getCorrelationMatrix : get the correlation matrix getCorrelationMatrix : get the correlation matrix

# Arguments

pfimproject

A object PFIMProject giving the Evaluation.

### Value

The correlation matrix

The Dcriterion

getDcriterion

getDcriterion : get the Dcriterion

### **Description**

getDcriterion : get the Dcriterion getDcriterion : get the Dcriterion

### **Arguments**

pfimproject A object PFIMProject giving the Evaluation.

# Value

The Dcriterion of the FIM.

The Dcriterion

getDeterminant 35

getDeterminant

getDeterminant: get the determinant

# Description

getDeterminant: get the determinant getDeterminant: get the determinant

#### **Arguments**

pfimproject A object PFIMProject giving the Evaluation.

# Value

The determinant of the FIM.

The determinant

getFim

getFim: get the Fisher matrix.

# **Description**

getFim: get the Fisher matrix.

# **Arguments**

evaluation

An object Evaluation giving the evaluation to be run.

### Value

The matrices fisherMatrix, fixedEffects, varianceEffects.

 ${\tt getFisherMatrix}$ 

getFisherMatrix: display the Fisher matrix components

# Description

getFisherMatrix: display the Fisher matrix components getFisherMatrix: display the Fisher matrix components

# Arguments

evaluation

An object Evaluation giving the evaluation to be run.

### Value

The matrices fisherMatrix, fixedEffects, varianceEffects.

The matrices fisherMatrix, fixedEffects, varianceEffects.

getListLastName: routine to get the names of last element of a nested list.

### **Description**

getListLastName: routine to get the names of last element of a nested list.

# Usage

getListLastName(list)

### **Arguments**

list

The list to be used.

#### Value

The names of last element.

getModelErrorData

getModelErrorData: get the parameters sigma slope and sigma inter (used for the report).

#### **Description**

getModelErrorData: get the parameters sigma slope and sigma inter (used for the report).

# **Arguments**

modelError

An object ModelError that defines the model error.

#### Value

A list of dataframe with outcome, type of model error and sigma slope and inter.

getModelParametersData

getModelParametersData: get model parameters data for report.

# Description

getModelParametersData: get model parameters data for report.

### **Arguments**

modelParameter An object if class Model giving the model.

#### Value

A data frame with the data of all the parameters.

getRSE 37

getRSE

getRSE: get the RSE

## **Description**

getRSE: get the RSE getRSE: get the RSE

### **Arguments**

pfimproject

A object PFIMProject giving the Evaluation.

#### Value

The RSE of the parameters.

The RSE

getSamplingData

getSamplingData: extract sampling times and max sampling time used for plot.

### **Description**

getSamplingData: extract sampling times and max sampling time used for plot.

## **Arguments**

arm

A object of class Arm giving the arm.

#### Value

A list giving the samplingTimes object, the vector samplings and the double samplingMax.

getSE

getSE: get the SE

## Description

getSE: get the SE getSE: get the SE

## **Arguments**

pfimproject

A object PFIMProject giving the Evaluation.

#### Value

The SE of the parameters.

The SE.

38 IndividualFim

getShrinkage

getShrinkage: get the shrinkage

### **Description**

```
getShrinkage: get the shrinkage
getShrinkage: get the shrinkage
```

### **Arguments**

pfimproject A object PFIMProject giving the Evaluation.

#### Value

The shrinkage of the FIM.

The shrinkage

IndividualFim

IndividualFim

### Description

The class IndividualFim represents and stores information for the IndividualFim.

### Usage

```
IndividualFim(
  fisherMatrix = numeric(0),
  fixedEffects = numeric(0),
  varianceEffects = numeric(0),
  SEAndRSE = list(),
  condNumberFixedEffects = numeric(0),
  condNumberVarianceEffects = numeric(0),
  shrinkage = numeric(0)
)
```

### **Arguments**

fisherMatrix A matrix giving the numerical values of the Fim.

 $\label{thm:continuous} \mbox{fixedEffects} \qquad \mbox{A matrix giving the numerical values of the fixedEffects of the Fim.}$ 

varianceEffects

A matrix giving the numerical values of varianceEffects of the Fim.

SEAndRSE A data frame giving the value of the SE and RSE.

 ${\tt condNumberFixedEffects}$ 

The conditional number of the fixedEffects of the Fim.

condNumberVarianceEffects

The conditional number of the varianceEffects of the Fim.

shrinkage A vector giving the shrinkage values.

LibraryOfModels 39

### **Details**

IndividualFim

LibraryOfModels

**LibraryOfModels** 

## Description

 $The \ class \ Library Of Models \ represents \ and \ stores \ information \ for \ the \ Library Of Models.$ 

## Usage

```
LibraryOfModels(models = list())
```

## **Arguments**

models

A list giving all the PK and PD models.

### **Details**

LibraryOfModels

LibraryOfPDModels

LibraryOfPDModels

# Description

The class LibraryOfPDModels represents and stores information for the LibraryOfPDModels.

## Usage

LibraryOfPDModels

# **Format**

An object of class PFIM: LibraryOfPDModels (inherits from PFIM: LibraryOfModels,  $S7\_object$ ) of length 1.

## **Details**

LibraryOfPDModels

LibraryOfPKModels

 ${\it Library Of PKModels}$ 

### **Description**

The class LibraryOfPKModels represents and stores information for the LibraryOfPKModels.

## Usage

LibraryOfPKModels

#### **Format**

An object of class PFIM: :LibraryOfPKModels (inherits from PFIM: :LibraryOfModels, S7\_object) of length 1.

#### **Details**

LibraryOfPKModels

Linear2BolusSingleDose\_ClQV1V2

Model Linear2BolusSingleDose\_ClQV1V2

## Description

 $Model\ Linear 2 Bolus Single Dose\_ClQV1V2$ 

# Usage

Linear2BolusSingleDose\_ClQV1V2()

Linear2BolusSingleDose\_kk12k21V

Model Linear2BolusSingleDose\_kk12k21V

## Description

 $Model\ Linear 2 Bolus Single Dose\_kk 12k 21V$ 

# Usage

Linear2BolusSingleDose\_kk12k21V()

 $Linear 2 Bolus Steady State\_ClQV1V2 tau \\ {\it Model Linear 2 Bolus Steady State\_ClQV1V2} tau$ 

### **Description**

Model Linear2BolusSteadyState\_ClQV1V2tau

#### Usage

 $Linear 2 Bolus Steady State\_ClQV1V2 tau()$ 

Linear2BolusSteadyState\_kk12k21Vtau

Model Linear2BolusSteadyState\_kk12k21Vtau

## Description

 $Model\ Linear 2 Bolus Steady State\_kk 12k 21V tau$ 

#### Usage

Linear2BolusSteadyState\_kk12k21Vtau()

 $Linear 2 First Order Single Dose\_ka ClQV1V2 \\ Model\ Linear 2 First Order Single Dose\_ka ClQV1V2$ 

### **Description**

 $Model\ Linear 2 First Order Single Dose\_ka ClQV 1V 2$ 

## Usage

Linear2FirstOrderSingleDose\_kaClQV1V2()

 $Linear 2 First Order Single Dose\_kakk 12k 21V \\ Model\ Linear 2 First Order Single Dose\_kakk 12k 21V$ 

# Description

Model Linear2FirstOrderSingleDose\_kakk12k21V

### Usage

Linear2FirstOrderSingleDose\_kakk12k21V()

 $Linear 2 First Order Steady State\_ka ClQV1V2 tau \\ Model\ Linear 2 First Order Steady State\_ka ClQV1V2 tau$ 

### **Description**

 $Model\ Linear 2 First Order Steady State\_ka ClQV 1 V 2 tau$ 

#### Usage

Linear2FirstOrderSteadyState\_kaClQV1V2tau()

 $Linear 2 First Order Steady State\_kakk 12k 21V tau \\ \textit{Model Linear 2 First Order Steady State\_kakk 12k 21V tau}$ 

### **Description**

Model Linear2FirstOrderSteadyState\_kakk12k21Vtau

### Usage

Linear2FirstOrderSteadyState\_kakk12k21Vtau()

 $Linear 2 Infusion Single Dose\_C1QV1V2 \\ Model\ Linear 2 Infusion Single Dose\_ClQV1V2$ 

## **Description**

 $Model\ Linear 2 Infusion Single Dose\_ClQV1V2$ 

## Usage

Linear2InfusionSingleDose\_ClQV1V2()

 $Linear 2 Infusion Single Dose\_kk 12k 21V \\ Model\ Linear 2 Infusion Single Dose\_kk 12k 21V$ 

# Description

Model Linear2InfusionSingleDose\_kk12k21V

### Usage

Linear2InfusionSingleDose\_kk12k21V()

Linear2InfusionSteadyState\_ClQV1V2tau

Model Linear2InfusionSteadyState\_ClQV1V2tau

## Description

Model Linear2InfusionSteadyState\_ClQV1V2tau

## Usage

Linear2InfusionSteadyState\_ClQV1V2tau()

Linear2InfusionSteadyState\_kk12k21Vtau

Model Linear2InfusionSteadyState\_kk12k21Vtau

### **Description**

Model Linear2InfusionSteadyState\_kk12k21Vtau

## Usage

Linear2InfusionSteadyState\_kk12k21Vtau()

LogNormal

LogNormal

### **Description**

The class LogNormal represents and stores information for the LogNormal distribution.

## Usage

```
LogNormal(name = character(\emptyset), mu = numeric(\emptyset), omega = numeric(\emptyset))
```

# Arguments

name A string giving the name of the distribution.

mu A double giving the mean mu.

omega A double giving omega.

### **Details**

LogNormal

44 Model

Model Model

#### **Description**

The class Model represents and stores information for a model.

#### Usage

```
Model(
  name = character(0),
  modelParameters = list(),
  samplings = numeric(0),
  modelEquations = list(),
  wrapper = function() NULL,
  outputFormula = list(),
  outputNames = character(0),
  variableNames = character(0),
  outcomesWithAdministration = character(0),
  outcomesWithNoAdministration = character(0),
  modelError = list(),
  odeSolverParameters = list(),
  parametersForComputingGradient = list(),
  initialConditions = numeric(0),
  functionArguments = character(0),
  functionArgumentsSymbol = list()
)
```

### **Arguments**

name A string giving the name of the model.

modelParameters

A list giving the model parameters.

samplings A vector of double giving the samplings of the model.

modelEquations A list giving the model equations.

wrapper The method wrapper used to get the ode solver format.

outputFormula A list giving the formula of the evaluation outputs.

outputNames A string giving the names of the model outputs.

variableNames A string giving the names of the model variables.

outcomesWithAdministration

A vector giving the outcomes with administration.

outcomesWithNoAdministration

A vector giving the outcomes with no administration.

modelError A list of the models error.

odeSolverParameters

A list of the parameters for the ode solver.

parametersForComputingGradient

A list for the parameters used in the computation of the Hessian.

ModelAnalytic 45

```
initialConditions
```

A list giving the initial conditions of the model.

functionArguments

A list giving the functionArguments of the wrapper.

functionArgumentsSymbol

A list giving the functionArgumentsSymbol of the wrapper.

#### **Details**

Model

ModelAnalytic

ModelAnalytic

## **Description**

The class ModelAnalytic is used to defined an analytic model.

## Usage

```
ModelAnalytic(
  name = character(0),
  modelParameters = list(),
  samplings = numeric(0),
  modelEquations = list(),
  wrapper = function() NULL,
  outputFormula = list(),
  outputNames = character(0),
  variableNames = character(0),
  outcomesWithAdministration = character(0),
  outcomesWithNoAdministration = character(0),
  modelError = list(),
  odeSolverParameters = list(),
  parametersForComputingGradient = list(),
  initialConditions = numeric(0),
  functionArguments = character(0),
  functionArgumentsSymbol = list(),
  modelAnalytic = function() NULL,
  wrapperModelAnalytic = list(),
  functionArgumentsModelAnalytic = list(),
  functionArgumentsSymbolModelAnalytic = list(),
  solverInputs = list()
)
```

#### **Arguments**

name A string giving the name of the model.

modelParameters

A list giving the model parameters.

samplings A vector of double giving the samplings of the model.

model Equations A list giving the model equations.

wrapper The method wrapper used to get the ode solver format.

 $\hbox{outputFormula} \quad A \ list \ giving \ the \ formula \ of \ the \ evaluation \ outputs.$ 

 $\hbox{outputNames} \qquad \hbox{A string giving the names of the model outputs}.$ 

variableNames A string giving the names of the model variables.

outcomesWithAdministration

A vector giving the outcomes with administration.

outcomes With No Administration

A vector giving the outcomes with no administration.

modelError A list of the models error.

odeSolverParameters

A list of the parameters for the ode solver.

parameters For Computing Gradient

A list for the parameters used in the computation of the Hessian.

initialConditions

A list giving the initial conditions of the model.

functionArguments

A list giving the functionArguments of the wrapper.

functionArgumentsSymbol

A list giving the functionArgumentsSymbol of the wrapper.

modelAnalytic An object ModelAnalytic

wrapperModelAnalytic

Wrapper for the ode solver.

function Arguments Model Analytic

A list giving the functionArguments of the wrapper for the analytic model.

functionArgumentsSymbolModelAnalytic

A list giving the functionArgumentsSymbol of the wrapper for the analytic

model.

solverInputs A list giving the solver inputs.

#### **Details**

ModelAnalytic

 ${\tt Model Analytic Infusion} \ \ \textit{Model Analytic Infusion}$ 

## **Description**

The class ModelAnalyticInfusion is used to defined an analytic model in infusion.

#### Usage

```
ModelAnalyticInfusion(
  name = character(0),
 modelParameters = list(),
  samplings = numeric(0),
 modelEquations = list(),
 wrapper = function() NULL,
 outputFormula = list(),
 outputNames = character(0),
  variableNames = character(0),
  outcomesWithAdministration = character(0),
 outcomesWithNoAdministration = character(0),
 modelError = list(),
  odeSolverParameters = list(),
  parametersForComputingGradient = list(),
  initialConditions = numeric(0),
  functionArguments = character(0),
  functionArgumentsSymbol = list(),
 wrapperModelAnalyticInfusion = list(),
  functionArgumentsModelAnalyticInfusion = list(),
  functionArgumentsSymbolModelAnalyticInfusion = list(),
  solverInputs = list()
```

#### **Arguments**

name A string giving the name of the model.

modelParameters

A list giving the model parameters.

samplings A vector of double giving the samplings of the model.

model Equations A list giving the model equations.

wrapper The method wrapper used to get the ode solver format.

outputFormula A list giving the formula of the evaluation outputs.

outputNames A string giving the names of the model outputs.

variableNames A string giving the names of the model variables.

outcomesWithAdministration

A vector giving the outcomes with administration.

outcomesWithNoAdministration

A vector giving the outcomes with no administration.

modelError A list of the models error.

odeSolverParameters

A list of the parameters for the ode solver.

parametersForComputingGradient

A list for the parameters used in the computation of the Hessian.

initialConditions

A list giving the initial conditions of the model.

functionArguments

A list giving the functionArguments of the wrapper.

 ${\tt function Arguments Symbol}$ 

A list giving the functionArgumentsSymbol of the wrapper.

wrapperModelAnalyticInfusion

Wrapper for the ode solver.

function Arguments Model Analytic Infusion

A list giving the functionArguments of the wrapper for the analytic model in infusion.

function Arguments Symbol Model Analytic Infusion

A list giving the functionArgumentsSymbol of the wrapper for the analytic model in infusion.

solverInputs A list giving the solver inputs.

#### **Details**

ModelAnalyticInfusion

ModelAnalyticInfusionSteadyState

Model Analytic Infusion Steady State

#### **Description**

The class ModelAnalyticInfusionSteadyState is used to defined an analytic model in infusion steady state.

```
ModelAnalyticInfusionSteadyState(
  name = character(0),
  modelParameters = list(),
  samplings = numeric(0),
  modelEquations = list(),
  wrapper = function() NULL,
  outputFormula = list(),
  outputNames = character(0),
  variableNames = character(0),
  outcomesWithAdministration = character(0),
  outcomesWithNoAdministration = character(0),
  modelError = list(),
  odeSolverParameters = list(),
  parametersForComputingGradient = list(),
  initialConditions = numeric(0),
  functionArguments = character(0),
  functionArgumentsSymbol = list(),
  wrapperModelAnalyticInfusion = list(),
  functionArgumentsModelAnalyticInfusion = list(),
  functionArgumentsSymbolModelAnalyticInfusion = list(),
  solverInputs = list()
)
```

#### **Arguments**

name A string giving the name of the model.

modelParameters

A list giving the model parameters.

samplings A vector of double giving the samplings of the model.

model Equations A list giving the model equations.

wrapper The method wrapper used to get the ode solver format.

outputFormula A list giving the formula of the evaluation outputs.

outputNames A string giving the names of the model outputs.

variableNames A string giving the names of the model variables.

outcomesWithAdministration

A vector giving the outcomes with administration.

outcomesWithNoAdministration

A vector giving the outcomes with no administration.

modelError A list of the models error.

odeSolverParameters

A list of the parameters for the ode solver.

parameters For Computing Gradient

A list for the parameters used in the computation of the Hessian.

initial Conditions

A list giving the initial conditions of the model.

functionArguments

A list giving the functionArguments of the wrapper.

 ${\tt functionArgumentsSymbol}$ 

A list giving the functionArgumentsSymbol of the wrapper.

 $wrapper {\tt Model Analytic Infusion}$ 

Wrapper for the ode solver.

function Arguments Model Analytic Infusion

A list giving the functionArguments of the wrapper for the analytic model in infusion.

function Arguments Symbol Model Analytic Infusion

A list giving the functionArgumentsSymbol of the wrapper for the analytic

model in infusion.

solverInputs A list giving the solver inputs.

### **Details**

Model Analytic Infusion Steady State

ModelAnalyticSteadyState

Model Analytic Steady State

### **Description**

The class ModelAnalyticSteadyState is used to defined an analytic model in steady state.

### Usage

```
ModelAnalyticSteadyState(
  name = character(0),
  modelParameters = list(),
  samplings = numeric(0),
  modelEquations = list(),
  wrapper = function() NULL,
  outputFormula = list(),
  outputNames = character(0),
  variableNames = character(0),
  outcomesWithAdministration = character(0),
  outcomesWithNoAdministration = character(0),
  modelError = list(),
  odeSolverParameters = list(),
  parametersForComputingGradient = list(),
  initialConditions = numeric(0),
  functionArguments = character(0),
  functionArgumentsSymbol = list(),
  modelAnalytic = function() NULL,
  wrapperModelAnalytic = list(),
  functionArgumentsModelAnalytic = list(),
  functionArgumentsSymbolModelAnalytic = list(),
  solverInputs = list()
)
```

#### **Arguments**

name A string giving the name of the model.

modelParameters

A list giving the model parameters.

samplings A vector of double giving the samplings of the model.

modelEquations A list giving the model equations.

wrapper The method wrapper used to get the ode solver format.

outputFormula A list giving the formula of the evaluation outputs.

outputNames A string giving the names of the model outputs.

variableNames A string giving the names of the model variables.

outcomesWithAdministration

A vector giving the outcomes with administration.

outcomesWithNoAdministration

A vector giving the outcomes with no administration.

ModelError 51

modelError A list of the models error.

odeSolverParameters

A list of the parameters for the ode solver.

parametersForComputingGradient

A list for the parameters used in the computation of the Hessian.

initialConditions

A list giving the initial conditions of the model.

functionArguments

A list giving the functionArguments of the wrapper.

 ${\tt function Arguments Symbol}$ 

A list giving the functionArgumentsSymbol of the wrapper.

modelAnalytic A object ModelAnalytic giving the analytic model.

wrapperModelAnalytic

Wrapper for the ode solver.

function Arguments Model Analytic

A list giving the functionArguments of the wrapper for the analytic model in steady state.

functionArgumentsSymbolModelAnalytic

A list giving the functionArgumentsSymbol of the wrapper for the analytic model in steady state.

solverInputs A list giving the solver inputs.

#### **Details**

ModelAnalyticSteadyState

ModelError

ModelError

#### **Description**

The class ModelError is used to defined a model error.

```
ModelError(
  output = character(0),
  equation = expression(),
  derivatives = list(),
  sigmaInter = numeric(0),
  sigmaSlope = numeric(0),
  sigmaInterFixed = logical(0),
  sigmaSlopeFixed = logical(0),
  cError = numeric(0)
)
```

52 ModelInfusion

## **Arguments**

 $\label{eq:Astring} \text{output} \qquad \quad A \text{ string giving the model error output.}$ 

equation A expression giving the model error equation.

derivatives A list giving the derivatives of the model error equation.

sigmaInter A double giving the sigma inter.
sigmaSlope A double giving the sigma slope

sigmaInterFixed

A boolean giving if the sigma inter is fixed or not. - not in the v7.0

sigmaSlopeFixed

A boolean giving if the sigma slope is fixed or not. - not in the v7.0

cError A integer giving the power parameter.

#### **Details**

ModelError

ModelInfusion

ModelInfusion

### **Description**

The class ModelInfusion is used to defined a model in infusion.

```
ModelInfusion(
  name = character(0),
  modelParameters = list(),
  samplings = numeric(0),
  modelEquations = list(),
  wrapper = function() NULL,
  outputFormula = list(),
  outputNames = character(0),
  variableNames = character(0),
  outcomesWithAdministration = character(0),
  outcomesWithNoAdministration = character(0),
  modelError = list(),
  odeSolverParameters = list(),
  parametersForComputingGradient = list(),
  initialConditions = numeric(0),
  functionArguments = character(0),
  functionArgumentsSymbol = list()
)
```

ModelODE 53

## Arguments

name A string giving the name of the model.

modelParameters

A list giving the model parameters.

samplings A vector of double giving the samplings of the model.

model Equations A list giving the model equations.

wrapper The method wrapper used to get the ode solver format.

outputFormula A list giving the formula of the evaluation outputs.

outputNames A string giving the names of the model outputs.

variableNames A string giving the names of the model variables.

outcomesWithAdministration

A vector giving the outcomes with administration.

 $\verb"outcomesWithNoAdministration"$ 

A vector giving the outcomes with no administration.

modelError A list of the models error.

odeSolverParameters

A list of the parameters for the ode solver.

parametersForComputingGradient

A list for the parameters used in the computation of the Hessian.

initialConditions

A list giving the initial conditions of the model.

functionArguments

A list giving the functionArguments of the wrapper.

 ${\tt function Arguments Symbol}$ 

A list giving the functionArgumentsSymbol of the wrapper.

#### **Details**

ModelInfusion

ModelODE ModelODE

### **Description**

The class ModelODE is used to defined a ode model.

```
ModelODE(
  name = character(0),
  modelParameters = list(),
  samplings = numeric(0),
  modelEquations = list(),
  wrapper = function() NULL,
  outputFormula = list(),
  outputNames = character(0),
```

54 ModelODE

```
variableNames = character(0),
outcomesWithAdministration = character(0),
outcomesWithNoAdministration = character(0),
modelError = list(),
odeSolverParameters = list(),
parametersForComputingGradient = list(),
initialConditions = numeric(0),
functionArguments = character(0),
functionArgumentsSymbol = list()
)
```

#### **Arguments**

name A string giving the name of the model.

modelParameters

A list giving the model parameters.

samplings A vector of double giving the samplings of the model.

model Equations A list giving the model equations.

wrapper The method wrapper used to get the ode solver format.

outputFormula A list giving the formula of the evaluation outputs.

outputNames A string giving the names of the model outputs.

variableNames A string giving the names of the model variables.

 $\verb"outcomesWithAdministration"$ 

A vector giving the outcomes with administration.

 $\verb"outcomesWithNoAdministration"$ 

A vector giving the outcomes with no administration.

modelError A list of the models error.

odeSolverParameters

A list of the parameters for the ode solver.

parameters For Computing Gradient

A list for the parameters used in the computation of the Hessian.

initialConditions

A list giving the initial conditions of the model.

 $function {\tt Arguments}$ 

A list giving the functionArguments of the wrapper.

 ${\tt function Arguments Symbol}$ 

A list giving the functionArgumentsSymbol of the wrapper.

#### **Details**

ModelODE

ModelODEBolus 55

ModelODEBolus ModelODEBolus

### **Description**

The class ModelODEBolus is used to defined a model ode admin bolus.

### Usage

```
ModelODEBolus(
  name = character(0),
  modelParameters = list(),
  samplings = numeric(0),
  modelEquations = list(),
  wrapper = function() NULL,
  outputFormula = list(),
  outputNames = character(0),
  variableNames = character(0),
  outcomesWithAdministration = character(0),
  outcomesWithNoAdministration = character(0),
  modelError = list(),
  odeSolverParameters = list(),
  parametersForComputingGradient = list(),
  initialConditions = numeric(0),
  functionArguments = character(0),
  functionArgumentsSymbol = list(),
  modelODE = function() NULL,
  doseEvent = list(),
  solverInputs = list()
)
```

# Arguments

name A string giving the name of the model.

modelParameters

A list giving the model parameters.

samplings A vector of double giving the samplings of the model.

model Equations A list giving the model equations.

wrapper The method wrapper used to get the ode solver format.

outputFormula A list giving the formula of the evaluation outputs.

outputNames A string giving the names of the model outputs.

variableNames A string giving the names of the model variables.

outcomesWithAdministration

A vector giving the outcomes with administration.

outcomes With No Administration

A vector giving the outcomes with no administration.

modelError A list of the models error. odeSolverParameters

A list of the parameters for the ode solver.

#### **Details**

ModelODEBolus

 ${\tt ModelODEDoseInEquations}$ 

Model ODE Dose Not In Equations

## Description

The class ModelODEDoseNotInEquations is used to defined a ModelODEDoseNotInEquations

```
ModelODEDoseInEquations(
  name = character(0),
  modelParameters = list(),
  samplings = numeric(0),
  modelEquations = list(),
  wrapper = function() NULL,
  outputFormula = list(),
  outputNames = character(0),
  variableNames = character(0),
  outcomesWithAdministration = character(0),
  outcomesWithNoAdministration = character(0),
  modelError = list(),
  odeSolverParameters = list(),
  parametersForComputingGradient = list(),
  initialConditions = numeric(0),
  functionArguments = character(0),
  functionArgumentsSymbol = list(),
  modelODEDoseInEquations = function() NULL,
  solverInputs = list()
)
```

#### **Arguments**

name A string giving the name of the model.

modelParameters

variableNames

A list giving the model parameters.

samplings A vector of double giving the samplings of the model.

modelEquations A list giving the model equations.

wrapper The method wrapper used to get the ode solver format.

outputFormula A list giving the formula of the evaluation outputs.

OutputNames A string giving the names of the model outputs.

outcomesWithAdministration

A vector giving the outcomes with administration.

A string giving the names of the model variables.

 $\verb"outcomesWithNoAdministration"$ 

A vector giving the outcomes with no administration.

modelError A list of the models error.

odeSolverParameters

A list of the parameters for the ode solver.

parameters For Computing Gradient

A list for the parameters used in the computation of the Hessian.

initialConditions

A list giving the initial conditions of the model.

functionArguments

A list giving the functionArguments of the wrapper.

functionArgumentsSymbol

A list giving the functionArgumentsSymbol of the wrapper.

 ${\tt modelODEDoseInEquations}$ 

An object modelODEDoseInEquations.

solverInputs A list giving the solver inputs.

#### **Details**

ModelODEDoseNotInEquations

 ${\tt ModelODEDoseNotInE} quations$ 

Model ODE Dose Not In Equations

## **Description**

The class ModelODEDoseNotInEquations is used to defined a ModelODEDoseNotInEquations

#### **Usage**

```
ModelODEDoseNotInEquations(
  name = character(0),
  modelParameters = list(),
  samplings = numeric(0),
  modelEquations = list(),
  wrapper = function() NULL,
  outputFormula = list(),
  outputNames = character(0),
  variableNames = character(0),
  outcomesWithAdministration = character(0),
  outcomesWithNoAdministration = character(0),
  modelError = list(),
  odeSolverParameters = list(),
  parametersForComputingGradient = list(),
  initialConditions = numeric(0),
  functionArguments = character(0),
  functionArgumentsSymbol = list(),
  modelODE = function() NULL,
  doseEvent = list(),
  solverInputs = list()
)
```

#### **Arguments**

name A string giving the name of the model.

modelParameters

A list giving the model parameters.

samplings A vector of double giving the samplings of the model.

modelEquations A list giving the model equations.

wrapper The method wrapper used to get the ode solver format.

 $\label{eq:continuity} \mbox{outputFormula} \quad \mbox{$A$ list giving the formula of the evaluation outputs.}$ 

outputNames A string giving the names of the model outputs.

variableNames A string giving the names of the model variables.

outcomesWithAdministration

A vector giving the outcomes with administration.

 $\verb"outcomesWithNoAdministration"$ 

A vector giving the outcomes with no administration.

modelError A list of the models error.

odeSolverParameters

A list of the parameters for the ode solver.

parameters For Computing Gradient

A list for the parameters used in the computation of the Hessian.

initialConditions

A list giving the initial conditions of the model.

functionArguments

A list giving the functionArguments of the wrapper.

functionArgumentsSymbol

A list giving the functionArgumentsSymbol of the wrapper.

ModelODEInfusion 59

modelODE An object modelODE.

doseEvent A dataframge given the doseEvent for the ode solver.

solverInputs A list giving the solver inputs.

#### Details

Model ODE Dose Not In Equations

ModelODEInfusion ModelODEInfusion

### **Description**

The class ModelODEInfusion is used to defined a model ModelODEInfusion.

### Usage

```
ModelODEInfusion(
  name = character(0),
  modelParameters = list(),
  samplings = numeric(0),
  modelEquations = list(),
  wrapper = function() NULL,
  outputFormula = list(),
  outputNames = character(0),
  variableNames = character(0),
  outcomesWithAdministration = character(0),
  outcomesWithNoAdministration = character(0),
  modelError = list(),
  odeSolverParameters = list(),
  parametersForComputingGradient = list(),
  initialConditions = numeric(0),
  functionArguments = character(0),
  functionArgumentsSymbol = list()
)
```

### **Arguments**

name A string giving the name of the model.

modelParameters

A list giving the model parameters.

samplings A vector of double giving the samplings of the model.

model Equations A list giving the model equations.

wrapper The method wrapper used to get the ode solver format.

outputFormula A list giving the formula of the evaluation outputs.

outputNames A string giving the names of the model outputs.

variableNames A string giving the names of the model variables.

outcomesWithAdministration

A vector giving the outcomes with administration.

```
outcomesWithNoAdministration
```

A vector giving the outcomes with no administration.

modelError A list of the models error.

odeSolverParameters

A list of the parameters for the ode solver.

parametersForComputingGradient

A list for the parameters used in the computation of the Hessian.

initialConditions

A list giving the initial conditions of the model.

functionArguments

A list giving the functionArguments of the wrapper.

 ${\tt functionArgumentsSymbol}$ 

A list giving the functionArgumentsSymbol of the wrapper.

#### **Details**

ModelODEInfusion

ModelODEInfusionDoseInEquation

Model ODE Infusion Dose In Equation

### **Description**

 $The \ class \ Model ODE Infusion Dose In Equation \ is \ used \ to \ defined \ a \ Model ODE Infusion Dose In Equation$ 

```
ModelODEInfusionDoseInEquation(
  name = character(0),
  modelParameters = list(),
  samplings = numeric(0),
  modelEquations = list(),
  wrapper = function() NULL,
  outputFormula = list(),
  outputNames = character(0),
  variableNames = character(0),
  outcomesWithAdministration = character(0),
  outcomesWithNoAdministration = character(0),
  modelError = list(),
  odeSolverParameters = list(),
  parametersForComputingGradient = list(),
  initialConditions = numeric(0),
  functionArguments = character(0),
  functionArgumentsSymbol = list(),
  modelODE = function() NULL,
  wrapperModelInfusion = list(),
  solverInputs = list()
```

ModelParameter 61

#### **Arguments**

name A string giving the name of the model.

modelParameters

A list giving the model parameters.

samplings A vector of double giving the samplings of the model.

modelEquations A list giving the model equations.

wrapper Wrapper for solver.

outputFormula A list giving the formula of the evaluation outputs.

outputNames A string giving the names of the model outputs.

variableNames A string giving the names of the model variables.

outcomesWithAdministration

A vector giving the outcomes with administration.

 $\verb"outcomesWithNoAdministration"$ 

A vector giving the outcomes with no administration.

modelError A list of the models error.

odeSolverParameters

A list of the parameters for the ode solver.

parameters For Computing Gradient

A list for the parameters used in the computation of the Hessian.

initialConditions

A list giving the initial conditions of the model.

functionArguments

A list giving the functionArguments of the wrapper.

functionArgumentsSymbol

A list giving the functionArgumentsSymbol of the wrapper..

modelODE An object modelODE.

wrapperModelInfusion

Wrapper for solver.

solverInputs A list giving the solver inputs.

# **Details**

Model ODE Infusion Dose In Equation

ModelParameter

ModelParameter

#### **Description**

The class ModelParameter is used to defined the model parameters.

```
ModelParameter(
  name = character(0),
  distribution = Distribution(),
  fixedMu = FALSE,
  fixedOmega = FALSE
)
```

#### **Arguments**

name A string giving the name of the parameter.

distribution A string giving the distribution of the parameter.

fixedMu A boolean setting TRUE/FALSE if the mu is estimated or not.

fixedOmega A boolean setting TRUE/FALSE if the omega is estimated or not.

#### **Details**

ModelParameter

MultiplicativeAlgorithm

MultiplicativeAlgorithm

## Description

The class MultiplicativeAlgorithm implements the multiplicative algorithm.

# Usage

```
MultiplicativeAlgorithm(
  name = character(0),
  modelEquations = list(),
  modelFromLibrary = list(),
  modelParameters = list(),
  modelError = list(),
  optimizer = character(0),
  optimizerParameters = list(),
  outputs = list(),
  designs = list(),
  fimType = character(0),
  fim = Fim(),
  odeSolverParameters = list(),
  optimisationDesign = list(),
  optimisationAlgorithmOutputs = list(),
  lambda = integer(0),
  delta = integer(0),
  numberOfIterations = integer(0),
  weightThreshold = integer(0),
  showProcess = logical(0),
  multiplicativeAlgorithmOutputs = list()
)
```

#### **Arguments**

```
name A string giving the name of the optimization process.

modelEquations A list giving the model equations.

modelFromLibrary
```

A list giving the name of the model for the mode equations.

```
modelParameters
```

A list giving the model parameters.

modelError A list giving the model error.

optimizer A string giving the name of the optimization algorithm.

optimizerParameters

A list giving the parameters of the optimization algorithm.

outputs A list giving the ouput of the model.

designs A list giving the designs.

fimType A string giving the type of the Fim.

fim A object Fim giving the Fim.

odeSolverParameters

A list giving the ode parameters for solver.

optimisationDesign

A list giving the evaluation of initial and optimal design.

optimisation Algorithm Outputs

A list giving the outputs of the optimization process.

lambda A numeric giving the parameter lambda. delta A numeric giving the parameter delta

numberOfIterations

A numeric giving the number of iterations.

weightThreshold

A numeric giving the weight threshold.

showProcess A boolean for displaying the process or not.

 $\verb|multiplicativeAlgorithmOutputs|\\$ 

A list giving the output of the optimization algorithm.

#### **Details**

Class "MultiplicativeAlgorithm"

MultiplicativeAlgorithm\_Rcpp

Function MultiplicativeAlgorithm\_Rcpp

## **Description**

Run the MultiplicativeAlgorithm\_Rcpp in Rcpp.

```
MultiplicativeAlgorithm_Rcpp(
   fisherMatrices_input,
   numberOfFisherMatrices_input,
   weights_input,
   numberOfParameters_input,
   dim_input,
   lambda_input,
   delta_input,
   iterationInit_input
)
```

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## **Arguments**

fisherMatrices\_input

The parameter fotfisherMatrices\_input.

numberOfFisherMatrices\_input

The parameter numberOfFisherMatrices\_input.

weights\_input The parameter weights\_input.

numberOfParameters\_input

The parameter numberOfParameters\_input.

dim\_input The parameter dim\_input.

lambda\_input The parameter lambda\_input.

delta\_input The parameter delta\_input.

iterationInit\_input

The parameter iterationInit\_input.

## Value

The list output with the outputs of the MultiplicativeAlgorithm\_Rcpp.

Normal Normal

### Description

The class Normal implements the Normal distribution.

## Usage

```
Normal(name = character(\theta), mu = numeric(\theta), omega = numeric(\theta))
```

### **Arguments**

name A string giving the name of the distribution.

mu A double giving the mean mu.

omega A double giving omega.

## Details

Normal

Optimization 65

Optimization Optimization

### **Description**

The class Optimization implements the Optimization.

#### Usage

```
Optimization(
  name = character(0),
  modelEquations = list(),
  modelFromLibrary = list(),
  modelParameters = list(),
  modelError = list(),
  optimizer = character(0),
  optimizerParameters = list(),
  outputs = list(),
  designs = list(),
  fimType = character(0),
  fim = Fim(),
  odeSolverParameters = list(),
  optimisationDesign = list(),
  optimisationAlgorithmOutputs = list()
)
```

#### **Arguments**

name A string giving the name of the design evaluation.

modelEquations A list giving the model equations.

 ${\tt modelFromLibrary}$ 

A list giving the model equations from the library of model.

modelParameters

A list giving the model parameters.

modelError A list giving the model error.

 $\label{eq:continuous} \text{Optimizer} \qquad \text{A string giving the name of the optimization algorithm being used.}$ 

optimizerParameters

A list giving the parameters of the optimization algorithm.

outputs A list giving the model outputs.

designs A list giving the designs to be evaluated.

fimType A string giving the type of Fim being evaluated.

fim A object Fim giving the Fim.

odeSolverParameters

A list giving the atol and rtol parameters for the ode solver.

optimisationDesign

A list giving the evaluation of initial and optimal design.

optimis at ion Algorithm Outputs

A list giving the outputs of the optimization process.

PFIMProject

### **Details**

Optimization

```
optimize Design: optimization of a design. 
 Optimization \ PGBOAlgorithm
```

## **Description**

Optimization PGBOAlgorithm

Optimization PSOAlgorithm

Optimization SimplexAlgorithm

Optimization FedorovWynnAlgorithm

Optimization MultiplicativeAlgorithm

#### **Arguments**

 $\label{eq:continuous} Optimization Object \\ A object Optimization.$ 

 ${\tt optimizationAlgorithm}$ 

 $A\ object\ {\tt MultiplicativeAlgorithm}.$ 

## Value

The object optimizationObject with the slots updated.

The object optimizationObject with the slots updated.

The object optimization Object with the slots updated.

The object optimizationObject with the slots updated.

The object optimizationObject with the slots updated.

PFIMProject

PFIMProject

## Description

The class PFIMProject implements the PFIM project.

PGBOAlgorithm 67

#### Usage

```
PFIMProject(
  name = character(0),
  modelEquations = list(),
  modelFromLibrary = list(),
  modelParameters = list(),
  modelError = list(),
  optimizer = character(0),
  optimizerParameters = list(),
  outputs = list(),
  designs = list(),
  fimType = character(0),
  fim = Fim(),
  odeSolverParameters = list()
)
```

#### **Arguments**

name A string giving the name of the design evaluation.

modelEquations A list giving the model equations.

modelFromLibrary

A list giving the model equations from the library of model.

modelParameters

A list giving the model parameters.

modelError A list giving the model error.

optimizer A string giving the name of the optimization algorithm being used.

 ${\tt optimizerParameters}$ 

A list giving the parameters of the optimization algorithm.

outputs A list giving the model outputs.

designs A list giving the designs to be evaluated.

fimType A string giving the type of Fim being evaluated.

fim A object Fim giving the Fim.

odeSolverParameters

A list giving the atol and rtol parameters for the ode solver.

#### **Details**

PFIMProject

PGBOAlgorithm PGBOAlgorithm

## Description

The class PGBOAlgorithm implements the PGBO algorithm.

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#### **Usage**

muteEffect

```
PGBOAlgorithm(
      name = character(0),
      modelEquations = list(),
      modelFromLibrary = list(),
      modelParameters = list(),
      modelError = list(),
      optimizer = character(0),
      optimizerParameters = list(),
      outputs = list(),
      designs = list(),
      fimType = character(0),
      fim = Fim(),
      odeSolverParameters = list(),
      optimisationDesign = list(),
      optimisationAlgorithmOutputs = list(),
      N = integer(0),
      muteEffect = integer(0),
      maxIteration = integer(0),
      purgeIteration = integer(0),
      seed = integer(0),
      showProcess = logical(0)
Arguments
    name
                     A string giving the name.
   model Equations A list giving the model equations.
   modelFromLibrary
                     A list giving the model equations from the library of model.
   modelParameters
                     A list giving the model parameters.
   modelError
                     A list giving the model error.
                     A string giving the name of the optimization algorithm being used.
    optimizer
    optimizerParameters
                     A list giving the parameters of the optimization algorithm.
   outputs
                     A list giving the model outputs.
   designs
                     A list giving the designs to be evaluated.
    fimType
                     A string giving the type of Fim being evaluated.
    fim
                     A object Fim giving the Fim.
    odeSolverParameters
                     A list giving the atol and rtol parameters for the ode solver.
   optimisationDesign
                     A list giving the evaluation of initial and optimal design.
   optimis at ion Algorithm Outputs\\
                     A list giving the outputs of the optimization process.
                     A numeric giving the parameter N.
```

A numeric giving the parameter muteEffect.

plotEvaluation 69

maxIteration A numeric giving the parameter maxIteration.

purgeIteration A numeric giving the parameter purgeIteration.

seed A numeric giving the parameter seed.

showProcess A boolean giving showProcess.

#### **Details**

Class "PGBOAlgorithm"

plotEvaluation plotEvaluation: plots for the evaluation of the model responses.

## Description

plotEvaluation: plots for the evaluation of the model responses.

#### **Arguments**

#### Value

All the plots for the evaluation of the model responses.

 $plot \verb|Evaluation| Results| \textit{plotEvaluationResults}| \textit{process for the evaluation of the responses}|.$ 

### **Description**

plotEvaluationResults: process for the evaluation of the responses.

# **Arguments**

arm A object of class Arm giving the arm.

 $\hbox{\it evaluation} \hbox{\it Model}$ 

A list giving the evaluation of the model.

outputNames A list of string giving the output of the evaluation of the model.

samplingData A list giving the sampling data from the method getSamplingData.

unitYAxis A list giving the unit of the x-axis.
unitYAxis A list giving the unit of the y-axis.
designName A string giving the design name.

#### Value

A list giving the plot of the evaluation of the model responses.

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plotEvaluationSI	plotEvaluationSI: process for the evaluation of the gradient of the responses.
------------------	--

## Description

plotEvaluationSI: process for the evaluation of the gradient of the responses.

### **Arguments**

arm A object of class Arm giving the arm.

 $evaluation {\tt ModelGradient}$ 

A list giving the evaluation of the gradient of the model responses.

parametersNames

A vector of string giving the parameter names?

outputNames A list of string giving the name of the outputs.

samplingData A list giving the sampling data from the method getSamplingData.

unitXAxis A list giving the unit of the x-axis.
unitYAxis A list giving the unit of the y-axis.
designName A string giving the design name.

## Value

A list giving the plot of the evaluation of gradient of the model responses.

plotFrequencies	Plot frequencies for the FedorovWynn algorithm

# Description

Plot frequencies for the FedorovWynn algorithm

# Arguments

optimization An Optimization object.

### Value

Graph of the optimal frequencies.

 $plot Frequencies Fedorov Wynn Algorithm \\ plot Frequencies Fedorov Wynn Algorithm$ 

## **Description**

plotFrequenciesFedorov Wynn Algorithm

## **Arguments**

```
\begin{array}{ll} \text{optimization} & \text{optimization} \\ \\ \text{optimizationAlgorithm} \\ \\ \text{optimizationAlgorithm} \end{array}
```

### Value

plotFrequenciesFedorovWynnAlgorithm

plotRSE

Plot relative standard errors

## Description

Plot relative standard errors

plotRSE: bar plot of the RSE.

## Arguments

optimization An Optimization object.

pfimproject A object PFIMProject giving the Evaluation.

#### Value

Graph of relative standard errors

The bar plot of the RSE.

72 plotSE

plotRSEFIM

plotRSEFIM: barplot for the RSE

## Description

plotRSEFIM: barplot for the RSE plotRSEFIM: barplot for the RSE plotRSEFIM: barplot for the RSE

## **Arguments**

fim An object PopulationFim giving the Fim.

evaluation An object Evaluation giving the evaluation of the model.

### Value

The bar plot of the RSE.

The bar plot of the RSE.

The bar plot of the RSE.

plotSE

Plot standard errors

## Description

Plot standard errors

plotSE: bar plot of the SE.

## **Arguments**

optimization An Optimization object.

pfimproject A object PFIMProject giving the Evaluation.

## Value

Graph of standard errors

The bar plot of the SE.

plotSEFIM 73

plotSEFIM: barplot for the SE

# Description

plotSEFIM: barplot for the SE plotSEFIM: barplot for the SE plotSEFIM: barplot for the SE

## **Arguments**

fim An object PopulationFim giving the Fim.

evaluation An object Evaluation giving the evaluation of the model.

## Value

The bar plot of the SE.

The bar plot of the SE.

The bar plot of the SE.

 ${\tt plotSensitivityIndices}$ 

Plot sensitivity indices.

# Description

Plot sensitivity indices.

 $plotSensitivity Indices:\ plots\ for\ the\ evaluation\ of\ the\ gradient\ of\ the\ model\ responses.$ 

## **Arguments**

optimization An Optimization object.

pfimproject A object PFIMProject giving the Evaluation.

plotOptions A list giving the plot options.

## Value

Graph of sensitivity indices.

All the plots for the evaluation of the gradient of the model responses.

plotShrinkage

plotShrinkage: plot the shrinkage values.

# **Description**

plotShrinkage: plot the shrinkage values.

## **Arguments**

fim An object BayesianFim giving the Fim.

evaluation An object Evaluation giving the evaluation of the model.

#### Value

The bar plot of the shrinkage.

plotWeights

Plot weights for the multiplicative algorithm

# Description

Plot weights for the multiplicative algorithm

## **Arguments**

optimization An Optimization object.

## Value

Plot of weights

plotWeightsMultiplicativeAlgorithm

 $plot Weights Multiplicative Algorithm:\ plot\ the\ optimal\ weight.$ 

# Description

plotWeightsMultiplicativeAlgorithm: plot the optimal weight.

# Arguments

optimization A object Optimization.
optimizationAlgorithm

A object MultiplicativeAlgorithm.

# Value

The graph plotWeight.

PopulationFim 75

PopulationFim

**PopulationFim** 

## **Description**

 $The \ class \ Population Fim \ implements \ the \ Population Fim.$ 

# Usage

```
PopulationFim(
  fisherMatrix = numeric(0),
  fixedEffects = numeric(0),
  varianceEffects = numeric(0),
  SEAndRSE = list(),
  condNumberFixedEffects = numeric(0),
  condNumberVarianceEffects = numeric(0),
  shrinkage = numeric(0)
)
```

## **Arguments**

fisherMatrix A matrix of numeric giving the fisherMatrix.

fixedEffects A matrix of numeric giving the fixedEffects.

varianceEffects

A matrix of numeric giving the varianceEffects.

SEAndRSE A data frame giving the SEAndRSE.

 ${\tt condNumberFixedEffects}$ 

A numeric giving the condNumberFixedEffects.

 $cond {\tt Number Variance Effects}$ 

A numeric giving the condNumberVarianceEffects.

shrinkage A vector of numeric giving the shrinkage.

## **Details**

PopulationFim

processArmEvaluationResults

processArmEvaluationResults: process for the evaluation of an arm.

# **Description**

processArmEvaluationResults: process for the evaluation of an arm.

#### **Arguments**

arm A object of class Arm giving the arm.

Model A object of class Model giving the model.

A object of class Fim giving the fim.

A string giving the name of the design.

PlotOptions A list giving the plot options.

#### Value

A list of ggplot object giving the plot of the responses ans the gradient responses of the the model.

```
processArmEvaluationSI
```

processArmEvaluationSI: process for the evaluation of the gradient of the responses.

## **Description**

processArmEvaluationSI: process for the evaluation of the gradient of the responses.

## **Arguments**

arm A object of class Arm giving the arm.

model A object of class Model giving the model.

fim A object of class Fim giving the fim.

designName A string giving the name of the design.

## Value

A list giving the ggplot object of the plots of the gradient.

Proportional Proportional

## **Description**

The class Proportional is used to defined a model error.

## Usage

```
Proportional(
  output = "output",
  equation = expression(sigmaSlope),
  derivatives = list(),
  sigmaInter = NULL,
  sigmaSlope = NULL,
  sigmaInterFixed = FALSE,
  sigmaSlopeFixed = FALSE,
  cError = NULL
)
```

**PSOAlgorithm** 77

#### **Arguments**

A string giving the model error output. output equation A expression giving the model error equation. derivatives A list giving the derivatives of the model error equation. A double giving the sigma inter. sigmaInter sigmaSlope A double giving the sigma slope sigmaInterFixed A boolean giving if the sigma inter is fixed or not. - not in the v7.0

sigmaSlopeFixed

A boolean giving if the sigma slope is fixed or not. - not in the v7.0

A integer giving the power parameter. cError

#### **Details**

Proportional

**PSOAlgorithm PSOAlgorithm** 

## **Description**

The class PSOAlgorithm implements the PSO algorithm.

## Usage

```
PSOAlgorithm(
  name = character(0),
  modelEquations = list(),
  modelFromLibrary = list(),
  modelParameters = list(),
  modelError = list(),
  optimizer = character(0),
  optimizerParameters = list(),
  outputs = list(),
  designs = list(),
  fimType = character(0),
  fim = Fim(),
  odeSolverParameters = list(),
  optimisationDesign = list(),
  optimisationAlgorithmOutputs = list(),
  maxIteration = integer(0),
  populationSize = integer(0),
  seed = integer(0),
  personalLearningCoefficient = integer(0),
  globalLearningCoefficient = integer(0),
  showProcess = logical(0),
  iterationAndCriteria = list()
)
```

#### **Arguments**

name A string giving the name.

model Equations A list giving the model equations.

modelFromLibrary

A list giving the model equations from the library of model.

modelParameters

A list giving the model parameters.

modelError A list giving the model error.

optimizer A string giving the name of the optimization algorithm being used.

optimizerParameters

A list giving the parameters of the optimization algorithm.

outputs A list giving the model outputs.

designs A list giving the designs to be evaluated.

fimType A string giving the type of Fim being evaluated.

fim A object Fim giving the Fim.

odeSolverParameters

A list giving the atol and rtol parameters for the ode solver.

 $optimis at ion {\tt Design}$ 

A list giving the evaluation of initial and optimal design.

optimis at ion Algorithm Outputs

A list giving the outputs of the optimization process.

maxIteration A numeric giving the maxIteration.

 ${\tt populationSize} \ \ A \ numeric \ giving \ the \ populationSize.$ 

seed A numeric giving the seed.

personalLearningCoefficient

A numeric giving the personalLearningCoefficient.

globalLearningCoefficient

A numeric giving the globalLearningCoefficient.

showProcess A boolean giving the showProcess.

iterationAndCriteria

A numeric giving the iterationAndCriteria.

#### **Details**

Class "PSOAlgorithm"

replaceVariablesLibraryOfModels

 $replace \textit{VariablesLibraryOfModels: replace variable in the \textit{LibraryOf-nodels: replace variable in the LibraryOf-nodels: replace variable in the \textit{LibraryOf-nodels: replace variable in the LibraryOf-nodels: replace variable in the \textit{LibraryOf-nodels: replace variable in the LibraryOf-nodels: replace variable in the \textit{LibraryOf-nodels: replace variable in the LibraryOf-nodels: replace variable in the \textit{LibraryOf-nodels: replace variable in the LibraryOf-nodels: replace variable in the \textit{LibraryOf-nodels: replace variable in the LibraryOf-nodels: replace variable in the \textit{LibraryOf-nodels: replace variable in the LibraryOf-nodels: replace variable in the \textit{LibraryOf-nodels: replace variable in the LibraryOf-nodels: replace variable in the \textit{LibraryOf-nodels: replace variable in the libraryOf-nodels: replace variable va$ 

Models

## **Description**

replace Variables Library Of Models: replace variable in the Library Of Models

Report 79

# Usage

replaceVariablesLibraryOfModels(text, old, new)

## **Arguments**

text the text old old string new new string

## Value

text with new string

Report Generate optimization report

## **Description**

Generate optimization report Report: generate the report.

## **Arguments**

optimization An Optimization object.

pfimproject A object PFIMProject giving the Evaluation or Optimization.

outputPath A string giving the path where the output are saved.

outputFile A string giving the name of the output file.

plotOptions A list giving the plot options.

## Value

Generated report.

The html report of the design evaluation or optimization.

run Run optimization

# Description

Run optimization

run: run the evaluation of a design.

## **Arguments**

optimization An Optimization object.

pfimproject A object PFIMProject giving the Evaluation.

#### Value

The optimization design results.

The object Evaluation giving the design evaluation.

SamplingTimeConstraints

Sampling Time Constraints

## **Description**

The class "SamplingTimeConstraints" implements the constraints for the sampling times.

## Usage

```
SamplingTimeConstraints(
  outcome = character(0),
  initialSamplings = logical(0),
  fixedTimes = logical(0),
  numberOfsamplingsOptimisable = integer(0),
  samplingsWindows = list(),
  numberOfTimesByWindows = logical(0),
  minSampling = integer(0)
)
```

## Arguments

outcome A string giving the outcome.

initialSamplings

A vector of numeric giving the initialSamplings.

fixedTimes A vector of numeric giving the fixedTimes.

number Of samplings Optimisable

A vector of numeric giving the numberOfsamplingsOptimisable.

samplingsWindows

A vector of numeric giving the samplingsWindows.

numberOfTimesByWindows

A vector of numeric giving the numberOfTimesByWindows.

minSampling A vector of numeric giving the minSampling.

### **Details**

Class "SamplingTimeConstraints"

Sampling Times 81

## **Description**

The class SamplingTimes is used to defined SamplingTimes.

## Usage

```
SamplingTimes(outcome = character(0), samplings = numeric(0))
```

## **Arguments**

outcome A string giving the outcome.

samplings A vector of numeric giving the samplings.

## **Details**

SamplingTimes

setEvaluationFim setEvaluationFim: set the Fim results.

# Description

setEvaluationFim: set the Fim results. setEvaluationFim: set the Fim results. setEvaluationFim: set the Fim results.

## **Arguments**

fim An object PopulationFim giving the Fim.

evaluation An object Evaluation giving the evaluation of the model.

## Value

The object Fim with its fisherMatrix, fixedEffects, shrinkage, condNumberFixedEffects, SEAndRSE.

The object IndividualFim with its fisherMatrix, fixedEffects, shrinkage, condNumberFixedEffects, SEAndRSE.

The object PopulationFim with its fisherMatrix, fixedEffects, shrinkage, condNumberFixedEffects, SEAndRSE.

setOptimalArms

setOptimalArms: set the optimal arms of an optimization algorithm.

## **Description**

setOptimalArms: set the optimal arms of an optimization algorithm. setOptimalArms: set the optimal arms of an optimization algorithm. setOptimalArms: set the optimal arms of an optimization algorithm. setOptimalArms: set the optimal arms of an optimization algorithm. setOptimalArms: set the optimal arms of an optimization algorithm. setOptimalArms: set the optimal arms of an optimization algorithm.

# **Arguments**

fim An object PopulationFim giving the Fim. optimizationAlgorithm

An object FedorovWynnAlgorithm giving the optimization algorithm.

## Value

The optimal arms.

The optimal arms.

The list optimalArms.

The list optimalArms.

The list optimalArms.

The list optimalArms.

 $\verb|setSamplingConstraintForOptimization| \\$ 

setSamplingConstraintForOptimization: set the sampling time constraints for an arm for the design optimization.

## **Description**

setSamplingConstraintForOptimization: set the sampling time constraints for an arm for the design optimization.

# Arguments

design An object Design giving the design.

## Value

The arm with the sampling time constraint for the design optimization.

show 83

show Show optimization results

# Description

Show optimization results

show: show the evaluation in the R console.

## **Arguments**

optimization An Optimization object.

pfimproject A object PFIMProject giving the Evaluation.

## Value

Prints results to console.

The show of the evaluation of the design.

showFIM

showFIM: show the Fim in the R console.

# Description

showFIM: show the Fim in the R console. showFIM: show the Fim in the R console. showFIM: show the Fim in the R console.

# **Arguments**

fim An object IndividualFim giving the Fim.

# Value

The fisherMatrix, fixedEffects, Determinant, condition numbers and D-criterion, Shrinkage and Parameters estimation

The fisherMatrix, fixedEffects, Determinant, condition numbers and D-criterion, Shrinkage and Parameters estimation

The fisherMatrix, fixedEffects, Determinant, condition numbers and D-criterion, Shrinkage and Parameters estimation

84 SimplexAlgorithm

SimplexAlgorithm

SimplexAlgorithm

## **Description**

The class SimplexAlgorithm implements the Simplex algorithm.

# Usage

```
SimplexAlgorithm(
 name = character(0),
 modelEquations = list(),
 modelFromLibrary = list(),
 modelParameters = list(),
 modelError = list(),
 optimizer = character(0),
 optimizerParameters = list(),
 outputs = list(),
  designs = list(),
  fimType = character(0),
  fim = Fim(),
 odeSolverParameters = list(),
  optimisationDesign = list(),
 optimisationAlgorithmOutputs = list(),
 pctInitialSimplexBuilding = integer(0),
 maxIteration = integer(0),
 tolerance = integer(0),
 seed = integer(0),
  showProcess = logical(0)
)
```

## **Arguments**

```
name
                  A string giving the name.
model Equations A list giving the model equations.
modelFromLibrary
                   A list giving the model equations from the library of model.
modelParameters
                   A list giving the model parameters.
modelError
                   A list giving the model error.
optimizer
                  A string giving the name of the optimization algorithm being used.
optimizerParameters
                  A list giving the parameters of the optimization algorithm.
outputs
                  A list giving the model outputs.
designs
                  A list giving the designs to be evaluated.
                  A string giving the type of Fim being evaluated.
fimType
fim
                  A object Fim giving the Fim.
```

tablesForReport 85

 ${\tt odeSolverParameters}$ 

A list giving the atol and rtol parameters for the ode solver.

optimisationDesign

A list giving the evaluation of initial and optimal design.

optimisationAlgorithmOutputs

A list giving the outputs of the optimization process.

pctInitialSimplexBuilding

A numeric giving the pctInitialSimplexBuilding.

 $\label{eq:maxIteration} \mbox{ A numeric giving the maxIteration.}$ 

tolerance A numeric giving the tolerance.

seed A numeric giving the seed.

showProcess A boolean giving the showProcess.

#### **Details**

Class "SimplexAlgorithm"

tablesForReport

tablesForReport: generate the table for the report.

# Description

tablesForReport: generate the table for the report. tablesForReport: generate the table for the report. tablesForReport: generate the table for the report.

## **Arguments**

fim An object PopulationFim giving the Fim.

evaluation An object Evaluation giving the evaluation of the model.

## Value

fixed Effects Table, FIMC riteria Table, SEAndRSE Table.

fixed Effects Table, FIMC riteria Table, SEAndRSE Table.

fixedEffectsTable, FIMCriteriaTable, SEAndRSETable.

updateSamplingTimes	updateSamplingTimes: plot	update sampling times for plotting used for	r
---------------------	------------------------------	---	---

# Description

updateSamplingTimes: update sampling times for plotting used for plot

# Arguments

arm A object of class Arm giving the arm.

 ${\tt samplingData} \qquad {\tt The\ list\ giving\ as\ output\ in\ the\ method\ getSamplingData}.$ 

# Value

The updated sampling times.

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