

Package ‘rPBK’

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Title Inference and Prediction of Generic Physiologically-Based Kinetic Models

Version 0.2.1

BugReports <https://gitlab.com/qonfluens/model/rPBK>

Description Fit and simulate any kind of physiologically-based kinetic ('PBK') models whatever the number of compartments. Moreover, it allows to account for any link between pairs of compartments, as well as any link of each of the compartments with the external medium. Such generic PBK models have today applications in pharmacology (PBPK models) to describe drug effects, in toxicology and ecotoxicology (PBTk models) to describe chemical substance effects. In case of exposure to a parent compound (drug or chemical) the 'rPBK' package allows to consider metabolites, whatever their number and their phase (I, II, ...). Last but not least, package 'rPBK' can also be used for dynamic flux balance analysis (dFBA) to deal with metabolic networks. See also Charles et al. (2022) <[doi:10.1101/2022.04.29.490045](https://doi.org/10.1101/2022.04.29.490045)>.

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Biarch true

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rPBK-package	<i>The 'rPBK' package.</i>
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Description

A DESCRIPTION OF THE PACKAGE

References

Stan Development Team (2022). RStan: the R interface to Stan. R package version 2.21.5.
<https://mc-stan.org>

dataCompartment4 *An example data set with 4 compartment*

Description

A dataset containing an example with 4 compartments.

Usage

```
data(dataCompartment4)
```

Format

A data frame with 21 rows and 7 variables:

temps vector of time

condition exposure concentration

replicat replicate of experiment

intestin compartment 'intestin'

caecum compartment 'caecum'

cephalon compartment 'cephalon'

reste compartment 'reste'##'

dataMaleGammarusSingle

An example data set with 1 compartment

Description

A dataset containing an example with a single compartment.

Usage

```
data(dataMaleGammarusSingle)
```

Format

A data frame with 22 rows and 4 variables:

time vector of time

expw exposure concentration

replicate replicat of experiment

conc internal measured concentration##'

 dataPBK

Create a list giving data and parameters to use in the model inference.

Description

Create a list giving data and parameters to use in the model inference.

Usage

```
dataPBK(object, ...)

## S3 method for class 'data.frame'
dataPBK(
  object,
  col_time = NA,
  col_replicate = NA,
  col_exposure = NA,
  col_compartment = NA,
  time_accumulation = NA,
  ku_nest = NA,
  ke_nest = NA,
  k_nest = NA,
  ...
)

nested_model(object)

## S3 method for class 'stanPBKdata'
nested_model(object)
```

Arguments

object	An object of class stanPBKdata (from dataPBK() function).
...	Further arguments to be passed to generic methods
col_time	Column name of the time column
col_replicate	Column name of the replicate column
col_exposure	Column name of the exposure column.
col_compartment	Column names of the compartment column. If several columns, give a vector with the column names.
time_accumulation	A scalar giving accumulation time.
ku_nest	Vector of binary (0 or 1) to select the uptake route. Use the nested_model() on the stanPBKdata object to check it.

ke_nest	Vector of binary (0 or 1) to select the excretion route. Use the nested_model() on the stanPBKdata object to check it.
k_nest	Matrix of binary (0 or 1) to select interaction routes. Use the nested_model() on the stanPBKdata object to check it.

Value

A list with data and parameters require for model inference.

Examples

```
# (1) load data file
data("dataCompartment4")
# (2) prepare data set
dataPBK_C4 <- dataPBK(
  object = dataCompartment4,
  col_time = "temps",
  col_replicate = "replicat",
  col_exposure = "condition",
  col_compartment = c("intestin", "reste", "caecum", "cephalon"),
  time_accumulation = 7)

# (1) load data file
data("dataCompartment4")
# (2) prepare data set
dataPBK_C4 <- dataPBK(
  object = dataCompartment4,
  col_time = "temps",
  col_replicate = "replicat",
  col_exposure = "condition",
  col_compartment = c("intestin", "reste", "caecum", "cephalon"),
  time_accumulation = 7)
# (3) check nesting
nested_model(dataPBK_C4)
# (2bis)
dataPBK_C42 <- dataPBK(
  object = dataCompartment4,
  col_time = "temps",
  col_replicate = "replicat",
  col_exposure = "condition",
  col_compartment = c("intestin", "reste", "caecum", "cephalon"),
  time_accumulation = 7,
  ku_nest = c(1,1,1,1), # No Change here
  ke_nest = c(1,1,1,1), # No Change here
  k_nest = matrix(c(
    c(0,1,1,1),
    c(0,0,1,1),
    c(0,0,0,0),
    c(0,0,0,0)),
    ncol=4,nrow=4,byrow=TRUE) # Remove
)
# (3bis) re-checking nesting
```

```
nested_model(dataPBK_C42)
```

df_quant95_ *Compute 95 credible intervals*

Description

Compute quantiles 95 credible intervals

Usage

```
df_quant95_(x, ...)
```

Arguments

x An object of class fitPBK
 ... Additional arguments

Value

An object of class data.frame returning median and 95 credible interval

export_interpolate *Interpolate function implemented in Stan only export for checking*

Description

This function export the linear interpolation implemented in Stan. It can be use to re-sample the exposure profiles.

Usage

```
export_interpolate(x, xpt, ypt, chain = 1, iter = 1, ...)
```

Arguments

x interpolation point x
 xpt a vector of x axis (has to be same size as ypt vector)
 ypt a vector of y axis (has to be same size as ypt vector)
 chain number of chain
 iter number of iteration
 ... Arguments passed to rstan::sampling

Value

A sample of a stanfit object returning a linear interpolation

`fitPBK`*Bayesian inference of TK model with Stan*

Description

Bayesian inference of TK model with Stan

Usage

```
fitPBK(stanPBKdata, ...)  
  
## S3 method for class 'stanPBKdata'  
fitPBK(stanPBKdata, ...)
```

Arguments

```
stanPBKdata    List of Data require for computing  
...           Arguments passed to rstan::sampling (e.g. iter, chains).
```

Value

An object of class `fitPBK` containing two object: `stanPBKdata` the data set used for inference and `stanfit` returned by `rstan::sampling`

Examples

```
# (1) load data file  
data("dataCompartment4")  
# (2) prepare data set  
dataPBK_C4 <- dataPBK(  
  object = dataCompartment4,  
  col_time = "temps",  
  col_replicate = "replicat",  
  col_exposure = "condition",  
  col_compartment = c("intestin", "reste", "caecum", "cephalon"),  
  time_accumulation = 7)  
# (3) run Bayesian fitting: <5 sec to be executed  
# 1 chain and 10 iterations is fast to run but provide  
# bad goodness-of-fit  
fitPBK_C4_FASTbadGOF <- fitPBK(dataPBK_C4, chains = 1, iter = 10)  
  
# (3) run Bayesian fitting: > 5 sec to be executed  
# 4 chains and 2000 iterations provides better estimates  
fitPBK_C4 <- fitPBK(dataPBK_C4, chains = 4, iter = 2000)
```

fitPBK_C4

An example of fitPBK object

Description

A fitPBK object containing Bayesian inference of the dataCompartment4 data set.

Usage

```
data(fitPBK_C4)
```

Format

A fitPBK object with:

stanPBKdata original data frame wrap in a formatted list for inference

stanfit a stanfit object resulting from inference with stan

plot.fitPBK

Plotting method for fitPBK objects

Description

This is the generic plot S3 method for the fitTK. It plots the fit obtained for each variable in the original dataset.

Usage

```
## S3 method for class 'fitPBK'  
plot(x, ...)
```

Arguments

x And object returned by fitPBK
... Additional arguments

Value

a plot of class ggplot

Examples

```
# (1) load a fitPBK object  
data("fitPBK_C4")  
# (2) plot result of bayesian fitting  
plot(fitPBK_C4)
```

ppc *Posterior predictive check plot*

Description

Plots posterior predictive check for fitPBK

Usage

```
ppc(x, ...)  
  
## S3 method for class 'fitPBK'  
ppc(x, ...)
```

Arguments

x an object used to select a method ppc
... Further arguments to be passed to generic methods

Value

a plot of class ggplot

Examples

```
# (1) load a fitPBK object  
data("fitPBK_C4")  
# (2) plot ppc of bayesian fitting  
ppc(fitPBK_C4)
```

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