Package 'rPBK'

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Title Inference and Prediction of Generic Physiologically-Based Kinetic Models

Version 0.2.0

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>.

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Encoding UTF-8

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Biarch true

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R topics documented:

`rPBK-package` *The 'rPBK' package.*

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 compartiment 'intestin'

caecum compartiment 'caecum'

cephalon compartiment 'cephalon'

reste compartiment '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 iterpolation 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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