Package ‘rPBK’

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Title  Inference and Prediction of Generic Physiologically-Based Kinetic Models

Version 0.2.4

BugReports https://gitlab.in2p3.fr/mosaic-software/rPBK/-/issues

URL https://gitlab.in2p3.fr/mosaic-software/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>.

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Encoding UTF-8

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Biarch true

Depends R (>= 3.4.0)

Imports ggplot2, methods, Rcpp (>= 0.12.0), rstan (>= 2.26.0), rstantools

LinkingTo BH (>= 1.66.0), Rcpp (>= 0.12.0), RcppEigen (>= 0.3.3.3.0), RcppParallel (>= 5.0.1), rstan (>= 2.26.0), StanHeaders (>= 2.26.0)

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dataCompartment4

LazyData true
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R topics documented:

  dataCompartment4 ............................................. 2
  dataMaleGammarusSingle ..................................... 3
  dataPBK ....................................................... 3
  df_quant95_ .................................................. 5
  export_interpolate ........................................... 6
  fitPBK ......................................................... 6
  fitPBK_C4 ..................................................... 7
  plot.fitPBK ................................................... 8
  ppc ............................................................. 8

Index 10

 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'
dataMaleGammarusSingle

caecum compartment 'caecum'
cephalon compartment 'cephalon'
reste compartment 'reste' #'

---

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 #'

---

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, 
)
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

```r
# (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**

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

**Arguments**

- `x`: An object returned by `fitPBK`
- `...`: Additional arguments

**Value**

A plot of class `ggplot`

**Examples**

```r
# (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**

```r
ppc(x, ...)
```

**Examples**

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

* datasets
  dataCompartment4, 2
  dataMaleGammarusSingle, 3
  fitPBK_C4, 7
  dataCompartment4, 2
  dataMaleGammarusSingle, 3
  dataPBK, 3
  df_quant95_, 5
  export_interpolate, 6
  fitPBK, 6
  fitPBK_C4, 7
  nested_model (dataPBK), 3
  plot.fitPBK, 8
  ppc, 8