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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rPBK-package

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Description

A DESCRIPTION OF THE PACKAGE

References

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

Usage

```r
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, 
k_u_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**

*Description*

Compute quantiles 95 credible intervals

*Usage*

\[ df\_quant95\_ (x, \ldots) \]

*Arguments*

- **x**: An object of class `fitPBK`
- **\ldots**: 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*

\[ export\_interpolate(x, xpt, ypt, chain = 1, iter = 1, \ldots) \]

*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
- **\ldots**: Arguments passed to `rstan::sampling`

*Value*

A sample of a stanfit object returning a linear interpolation
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_acccumulation = 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**

\[
\text{ppc}(x, \ldots)
\]

```r
## S3 method for class 'fitPBK'
ppc(x, \ldots)
```

**Arguments**

- **x**: an object used to select a method `ppc`
- `\ldots`: Further arguments to be passed to generic methods

**Value**

a plot of class `ggplot`

**Examples**

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