Package ‘rbioacc’

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Title  Inference and Prediction of ToxicoKinetic (TK) Models

Version  1.1-0

Description  The MOSAICbioacc application is a turnkey package providing bioaccumulation factors (BCF/BMF/BSAF) from a toxicokinetic (TK) model fitted to accumulation-depuration data. It is designed to fulfil the requirements of regulators when examining applications for market authorization of active substances. See Ratier et al. (2021) <doi:10.1101/2021.09.08.459421>.

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BugReports  https://github.com/aursiber/rbioacc/issues

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Biarch  true

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SystemRequirements  GNU make

Config/testthat/edition  3

Suggests  knitr, rmarkdown, testthat

VignetteBuilder  knitr

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Author  Virgile Baudrot [aut], Sandrine Charles [aut], Ophélie Gestin [ctb], Mélina Kaag [aut], Christelle Lopes [ctb], Gauthier Multari [ctb],
R topics documented:

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The 'rbioacc' package.

Description
A DESCRIPTION OF THE PACKAGE

References

.fonte
A simple implementation of to pivot_longer of tidyr

Description
A simple implementation of to pivot_longer of tidyr

Usage
.fonte(df, names_to, values_to)

Arguments
df A data frame to pivot.
names_to A string specifying the name of the column to create from the data stored in the column names of df.
values_to A string specifying the name of the column to create from the data stored in cell values.

Value
The data frame with a "lengthens" shape: more rows, less columns
.index_col_exposure

Return column matching "expw", "exps", "expf", "exppw" of a data.frame

Description

Return column matching "expw", "exps", "expf", "exppw" of a data.frame

Usage

.index_col_exposure(data_frame)

Arguments

data_frame a dataframe

Value

A vector of numeric

.index_col_metabolite

Return column matching "concX" of a data.frame where X is metabolite

Description

Return column matching "concX" of a data.frame where X is metabolite

Usage

.index_col_metabolite(data_frame)

Arguments

data_frame a dataframe

Value

A vector of numeric
.is_equal_rmInf

---

Check if two vectors `x` and `y` are equal after remove Inf

**Description**

Check if two vectors `x` and `y` are equal after remove Inf

**Usage**

`.is_equal_rmInf(x, y)`

**Arguments**

- `x`: A vector
- `y`: A vector

**Value**

A logical value

---

bioacc_metric

---

Biaccumulation metrics

**Description**

Biaccumulation metrics

**Usage**

`bioacc_metric(fit, ...)`

```r
## S3 method for class 'fitTK'
bioacc_metric(fit, type = "k", route = "all", ...)
```

**Arguments**

- `fit`: An `stanFit` object
- `...`: Further arguments to be passed to generic methods
- `type`: A string with the type of metric: `k` for the kinetics BioConcentration Factor, `ss` for the steady state BioConcentration Factor.
- `route`: Provide exposure route: `all`

**Value**

A data frame
Chironomus_benzoapyrene

Data on Chironomus exposed to benzoapyrene

Description

Data on Chironomus exposed to benzoapyrene

Usage

data(Chironomus_benzoapyrene)

Chiro_Creuzot

Data on Chironomus with several exposure routes.

Description

Data on Chironomus with several exposure routes.

Usage

data(Chiro_Creuzot)

Format

A dataframe with 24 observations on the following four variables:

- **time**: A vector of class numeric with the time points in days.
- **expw**: A vector of class numeric with the exposure in water.
- **expw**: A vector of class numeric with the exposure in pore water.
- **replicate**: A vector of class integer for replicate identification.
- **conc**: A vector of class numeric with concentration in organism.
- **concm1**: A vector of class numeric with metabolite concentration in organism.
- **concm2**: A vector of class numeric with metabolite concentration in organism.
corrMatrix

Correlations between parameters: colored matrix

Description
Correlations between parameters: colored matrix

Usage
corrMatrix(fit)

Arguments
fit
An object of class fitTK

Value
A heatmap of class ggplot.

corrPlot
Correlations between parameters: pairs plot

Description
Correlations between parameters: pairs plot

Usage
corrPlot(fit, plots = c("all", "deterministic", "stochastic"))

Arguments
fit
An object of class fitTK
plots
A string selecting the parameters. Defaults is "all" and select all parameters. Deterministic parameters can be selected by setting "deterministic" and stochastic parameter with "stochastic"

Value
A pairsplot of class ggmatrix containing planes of parameter pairs (lower triangle), marginal posterior distribution of each parameter (diagonal) and Pearson correlation coefficients (upper triangle)
df_ppc

### Description

This is the generic ppc S3 method for plots of the predicted values along with 95\% versus the observed values for fitTK objects.

### Usage

```r
df_ppc(fit, ...)
```

```r
## S3 method for class 'fitTK'
df_ppc(fit, ...)
```

```r
ppc(fit, ...)
```

```r
## S3 method for class 'fitTK'
ppc(fit, ...)
```

### Arguments

- **fit**: An object returned by fitTK
- **...**: Additional arguments

### Details

The black points show the observed number of survivors (pooled replicates, on \(X\)-axis) against the corresponding predicted number (\(Y\)-axis). Predictions come along with 95\% intervals, which are depicted in green when they contain the observed value and in red otherwise. Samples with equal observed value are shifted on the \(X\)-axis. For that reason, the bisecting line (\(y = x\)), is represented by steps when observed values are low. That way we ensure green intervals do intersect the bisecting line.

### Value

A data frame with median and 95\% a plot of class ggplot
**df_PriorPost**

*Data frame of Posterior over Prior*

### Description
Data frame of Posterior over Prior

### Usage

```r
df_PriorPost(fit, ...)  
```

### Arguments

- `fit` An object of class `fitTK` returned by the function `fitTK()`.
- `select` A string selecting the parameters. Defaults is "all" and select all parameters. Deterministic parameters can be selected by setting "deterministic" and stochastic parameter with "stochastic".

### Value
An object of class `data.frame`

---

**equations**

*Equations of the mathematical model used for the fit*

### Description
Equations of the mathematical model used for the fit

### Usage

```r
equations(fit, object)
```

### Arguments

- `fit` An object of class `fitTK`.
- `object` The `data.frame` used as the base as the fit object.

### Value
A vector of strings each containing an equation
### exposure_names

Retrieves exposure routes names from object

**Description**

Retrieve exposure routes names from object

**Usage**

```r
exposure_names(object)
```

**Arguments**

- `object`: a data frame.

**Value**

A vector of strings

### Exposure_Sialis_lutaria

Data on Sialis lutaria exposure time series

**Description**

Data on Sialis lutaria exposure time series

**Usage**

```r
data(Exposure_Sialis_lutaria)
```

### fitTK

Posterior predictive check

**Description**

Posterior predictive check

- Bayesian inference of TK model with Stan
- Bayesian inference of TK model with variable exposure profile (BETA version)
Gammarus_azoxistrobine_1d_Rosch2017

Usage

fitTK(stanTKdata, ...)

## S3 method for class 'stanTKdataCST'
fitTK(stanTKdata, ...)

## S3 method for class 'stanTKdataVAR'
fitTK(stanTKdata, ...)

Arguments

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

Value

An object of class fitTK containing two object: stanTKdata the data set used for inference and stanfit returned by rstan::sampling

Gammarus_azoxistrobine_1d_Rosch2017

Data on Gammarus exposed to azoxistrobine

Description

Data on Gammarus exposed to azoxistrobine

Usage

data(Gammarus_azoxistrobine_1d_Rosch2017)

Internal_Sialis_lutaria

Data on Sialis lutaria internal time series

Description

Data on Sialis lutaria internal time series

Usage

data(Internal_Sialis_lutaria)
Male Gammarus fossarum exposed to Hg spiked water. Three exposure concentrations were tested in triplicates. The duration of the accumulation phase is 4 days for 0.0000708021 and 0.000283208 µg.mL$^{-1}$ exposure concentrations, and 7 days for 0.000141604 µg.mL$^{-1}$ exposure concentration.

**Description**

Male Gammarus fossarum exposed to Hg spiked water. Three exposure concentrations were tested in triplicates. The duration of the accumulation phase is 4 days for 0.0000708021 and 0.000283208 µg.mL$^{-1}$ exposure concentrations, and 7 days for 0.000141604 µg.mL$^{-1}$ exposure concentration.

**Usage**

data(Male_Gammarus_Merged)

**Format**

A dataframe with 72 observations on the following four variables:

time A vector of class numeric with the time points in days.
extpw A vector of class numeric with Hg exposure in water in µg.mL$^{-1}$.
replicate A vector of class integer for replicate identification.
conc A vector of class numeric with Hg concentration in organism in µg.mL$^{-1}$.

**References**


Male Gammarus pulex exposed to seanine spiked water. A single exposure concentration was tested. The duration of the accumulation phase is 1.417 days. Three metabolites were quantified. The growth of organism was included.

**Description**

Male Gammarus pulex exposed to seanine spiked water. A single exposure concentration was tested. The duration of the accumulation phase is 1.417 days. Three metabolites were quantified. The growth of organism was included.
Usage

data(Male_Gammarus_seanine_growth)

Format

A dataframe with 22 observations on the following four variables:

- `time` A vector of class numeric with the time points in days.
- `expw` A vector of class numeric with seanine exposure in water in $\mu g.mL^{-1}$.
- `replicate` A vector of class integer for replicate identification.
- `conc` A vector of class numeric with concentration in organism.
- `concm1` A vector of class numeric with metabolite concentration in organism.
- `concm2` A vector of class numeric with metabolite concentration in organism.
- `concm3` A vector of class numeric with metabolite concentration in organism.
- `growth` A vector of class numeric with growth of the organism.

References


---

Male_Gammarus_Single Bio-accumulation data set for Gammarus fossarum exposed to Hg spiked water.

Description

Male *Gammarus fossarum* exposed to Hg spiked water. A single exposure concentration was tested. The duration of the accumulation phase is 4 days.

Usage

data(Male_Gammarus_Single)

Format

A dataframe with 23 observations on the following four variables:

- `time` A vector of class numeric with the time points in days.
- `expw` A vector of class numeric with Hg exposure in water in $\mu g.mL^{-1}$.
- `replicate` A vector of class integer for replicate identification.
- `conc` A vector of class numeric with Hg concentration in organism in $\mu g.mL^{-1}$.

References

**mcmcTraces**

*Traces of MCMC iterations*

**Description**

Traces of MCMC iterations

**Usage**

```r
mcmcTraces(fit, plots = "all")
```

**Arguments**

- `fit`: An object of class `fitTK`
- `plots`: A string selecting the parameters. Defaults is "all" and select all parameters. Deterministic parameters can be selected by setting "deterministic" and stochastic parameter with "stochastic"

**Value**

A traceplot of class `ggplot`.

---

**modelData**

*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**

```r
modelData(object, ...)
```

```r
## S3 method for class 'data.frame'
modelData(object, time_accumulation, elimination_rate = NA, ...)
```

**Arguments**

- `object`: An object of class `data.frame`
- `...`: Further arguments to be passed to generic methods
- `time_accumulation`: A scalar giving accumulation time
- `elimination_rate`: A scalar for the elimination rate. Default is `NA`. To remove elimination rate, set `elimination_rate = 0`. 
**modelData_ode**

**Value**

A list with data and parameters required for model inference.

---

**modelData_ode**

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**

```r
modelData_ode(
  df_exposure,
  df_internal,
  y0 = 1,
  t0 = -0.001,
  unifMax = 10,
  time_accumulation = NULL,
  minK = -5,
  maxK = 5,
  ...
)
```

```r
modelData_ode(
  df_exposure,
  df_internal,
  y0 = 1,
  t0 = -0.001,
  unifMax = 10,
  time_accumulation = NULL,
  minK = -5,
  maxK = 5,
  ...
)
```

**Arguments**

- `df_exposure` Dataframe of exposure with 2 column (time and value)
- `df_internal` Dataframe of internal concentration with 2 column (time and value)
- `y0` Initial concentration
- `t0` initial time point
- `unifMax` Hyperparameter value
- `time_accumulation` Time of accumulation
plot.bioaccMetric

---

**minK**  Hyperparameter value

**maxK**  Hyperparameter value

...  Additional arguments

**Value**

A list with data and parameters require for model inference.

---

### Oncorhynchus_two  Data on Oncorhynchus exposition

---

**Description**

Data on Oncorhynchus exposition

**Usage**

```r
data(Oncorhynchus_two)
```

---

### plot.bioaccMetric  Plot function for object of class bioaccMetric

---

**Description**

Plot function for object of class bioaccMetric

**Usage**

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

**Arguments**

- **x**  a data frame
- ...  Additional arguments

**Value**

A plot of class ggplot
plot.fitTK

---

**plot.fitTK**

*Plotting method for fitTK 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 'fitTK'
plot(x, time_interp = NULL, ...)
```

**Arguments**

- `x`: An object returned by fitTK
- `time_interp`: A vector with additional time point to interpolate. Time point of the original data set are conserved.
- `...`: Additional arguments

**Value**

A plot of class ggplot

---

plot.predictTK

---

**plot.predictTK**

*Plotting method for predictTK objects*

---

**Description**

This is the generic plot S3 method for the predictTK.

**Usage**

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

```r
## S3 method for class 'predictTKstan'
plot(x, add_data = FALSE, ...)
```

**Arguments**

- `x`: An object of class predictTK returned by predict
- `...`: Additional arguments
- `add_data`: logical TRUE or FALSE to add the original data of the fit object x
plot_PriorPost

Value

A plot of class `ggplot`

---

plot_exposure  

Plot exposure profile

Description

Plot exposure profile

Usage

plot_exposure(object)

Arguments

- `object`  
a data frame with exposure column

Value

a plot of class `ggplot`

---

plot_PriorPost  

Plot Posterior over Prior

Description

Plot Posterior over Prior

Usage

plot_PriorPost(x, ...)

## S3 method for class 'fitTK'
plot_PriorPost(x, select = "all", ...)

## S3 method for class 'df_PP'
plot_PriorPost(x, select = "all", ...)

Arguments

- `x`  
A data.frame of class `df_PP` returned by the function `df_PriorPost()`.

- `...`  
addition arguments

- `select`  
A string selecting the parameters. Defaults is "all" and select all parameters. Deterministic parameters can be selected by setting "deterministic" and stochastic parameter with "stochastic".
predict.fitTK

Value

A plot of class `ggplot`.

A plot of class `ggplot`.

predict.fitTK  
Prediction function using fitTK object

Description

Use when parameter are manually given by the user.

Usage

```r
## S3 method for class 'fitTK'
predict(object, data, mcmc_size = NULL, fixed_init = TRUE, ...)
```

```r
predict_stan(
  object,
  data,
  mcmc_size = NULL,
  fixed_init = TRUE,
  time_interp = NULL,
  iter = 1000,
  ...
)
```

```r
predict_manual(
  param,
  data,
  time_accumulation = NULL,
  C0 = 0,
  G0 = NA,
  gmax = NA
)
```

Arguments

- `object`  
  An object of `stanfit`
- `data`  
  A data set with one column `time` and 1 to 4 exposure
- `mcmc_size`  
  Size of mcmc chain if needed to be reduced
- `fixed_init`  
  If `TRUE` fix the initial conditions of internal concentration. columns with name in `expw`, `exp`, `expf` and `exppw`
- `time_interp`  
  A vector with additional time point to interpolate. Time point of the original data set are conserved.
iter       Number of time steps
param      A dataframe with name of parameters kee, keg, ku1, ku2, ..., km1, km2, ... and kem1, kem2, ..., sigmaConc, sigmaCmet (if metabolites) and sigmaGrowth (if growth). The parameter kee is mandatory.
time_accumulation
            the time of accumulation.
C0         Gives the initial conditions of internal concentration.
G0         initial condition of G0 (require if keg is provided)
gmax       gmax (require if keg is provided) columns with name in expw, exps, expf and exppw

Value

An object of class predictTK
An object of class predictTK

psrf

*Potential Scale Reduction Factors (PSRF) of the parameters*

Description

Potential Scale Reduction Factors (PSRF) of the parameters

Usage

psrf(fit)

Arguments

fit       An object of class fitTK

Value

An object of class data.frame with two columns: PSRF and parameter
a data frame with Potential Scale Reduction Factors
**quantile_table**

---

**Quantiles of parameters**

**Description**
Quantiles of parameters

**Usage**

```r
car::quantile_table(fit, probs = c(0.025, 0.5, 0.975))
```

**Arguments**
- `fit`: An object of class `fitTK`
- `probs`: Scalar or Vector of quantiles. Default is 0.025, 0.5 and 0.975 giving median and 95% credible interval

**Value**
A data frame with quantiles

---

**replace_**

---

**Replace element of a vector**

**Description**
Replace element of a vector

**Usage**

```r
replace_(x, from, to)
```

**Arguments**
- `x`: a vector
- `from`: a vector of elements to replace
- `to`: a vector with replacing elements

**Value**
a vector
Examples

```r
replace_(1:10, c(2,4,5,8), c(0,0,0,0))
replace_(c(1,2,2,3,2),c(3,2), c(4,5))
```

**t95**

*Return the time at 95% depuration of the parent component*

Description

Return the time at 95% depuration of the parent component

Usage

```r
t95(fit)
```

Arguments

- `fit` An object of class `fitTK`

Value

A numeric object

**waic**

*Widely Applicable Information Criterion (WAIC)*

Description

Compute WAIC using the `waic()` method of the `loo` package.

Usage

```r
waic(fit)
```

Arguments

- `fit` An object of class `fitTK`

Value

A numeric containing the WAIC
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