

Package ‘mapbayr’

July 27, 2021

Title MAP-Bayesian Estimation of PK Parameters

Version 0.5.0

Description Performs maximum a posteriori Bayesian estimation of individual pharmacokinetic parameters from a model defined in `mrgsolve`, typically for model-based therapeutic drug monitoring. Internally computes an objective function value from model and data, performs optimization and returns predictions in a convenient format.

License GPL-3

Encoding UTF-8

RoxygenNote 7.1.1

Imports dplyr, ggplot2, magrittr, mrgsolve (>= 0.10.9), optimx, purrr, rlang, stats, stringr, tibble, tidyr

URL <https://github.com/FelicienLL/mapbayr>

BugReports <https://github.com/FelicienLL/mapbayr/issues>

Suggests knitr

NeedsCompilation no

Author Felicien Le Louedec [aut, cre]
(<https://orcid.org/0000-0003-3699-2729>)

Maintainer Felicien Le Louedec <louedec.felicien@iuct-oncopole.fr>

Repository CRAN

Date/Publication 2021-07-27 11:40:02 UTC

R topics documented:

add_covariates.mrgmod	2
adm_0_cmt	3
adm_cmt	3
adm_lines.mrgmod	4
as.data.frame.mapbayests	4
augment	5
augment.mapbayests	5

check_mapbayr_model	6
compute_ofv	6
data_helpers	7
derivatives	8
get_data.mapbayests	9
get_data.mrgmod	9
get_eta.mapbayests	10
get_param.mapbayests	10
get_x	11
hist.mapbayests	11
mapbayest	12
mbrlib	13
obs_cmt	13
obs_lines.mrgmod	14
plot.mapbayests	14
postprocess	15
preprocess.ofv	16
preprocess.optim	16
print.mapbayests	17
use_posterior	17

Index **19**

add_covariates.mrgmod *Add covariates columns to data*

Description

Add covariates columns to data

Usage

```
## S3 method for class 'mrgmod'
add_covariates(x, covariates = list(), ...)
```

Arguments

x	model object
covariates	a list of named covariates, with a single value or exact number of lines than data
...	not used

Value

model object with dataset

`adm_0_cmt`*Get zero-order infusion compartment from mrgsolve model*

Description

Get zero-order infusion compartment from mrgsolve model

Usage

```
adm_0_cmt(x)
```

Arguments

x model object

Value

vector of integer

Examples

```
model <- mrgsolve::mread("ex_mbr1", mbrlib())
adm_0_cmt(model)
```

`adm_cmt`*Get administration compartment numbers from mrgsolve model*

Description

Get administration compartment numbers from mrgsolve model

Usage

```
adm_cmt(x)
```

Arguments

x model object

Value

vector of integer

Examples

```
model <- mrgsolve::mread("ex_mbr1", mbrlib())
adm_cmt(model)
```

adm_lines.mrgmod	<i>Add administrations lines to data</i>
------------------	--

Description

Add administrations lines to data

Usage

```
## S3 method for class 'mrgmod'
adm_lines(x, ...)
```

Arguments

x	model object
...	passed to mrgsolve::ev

Value

model object with dataset

as.data.frame.mapbayests	<i>Return the mapbay_tab as a data.frame</i>
--------------------------	--

Description

Return the mapbay_tab as a data.frame

Usage

```
## S3 method for class 'mapbayests'
as.data.frame(x, row.names = NULL, optional = FALSE, ...)
```

Arguments

x	A mapbayests object.
row.names, optional, ...	passed to as.data.frame

Value

a data.frame (the mapbay_tab from estimation)

augment	<i>Compute full PK profile prediction from mapbayr estimates.</i>
---------	---

Description

Compute full PK profile prediction from mapbayr estimates.

Usage

```
augment(x, ...)
```

Arguments

x	object to augment
...	additional arguments

Value

an augmented object (depending on the object passed)

augment.mapbayests	<i>Compute full PK profile prediction from mapbayr estimates.</i>
--------------------	---

Description

Compute full PK profile prediction from mapbayr estimates.

Usage

```
## S3 method for class 'mapbayests'  
augment(x, data = NULL, end = NULL, ...)
```

Arguments

x	A mapbayests object.
data	dataset to pass to mrgsolve for simulation (default is dataset used for estimation)
end	end of infusion time (passed to mrgsim)
...	additional argument to pass to mrgsim

Value

a mapbayests object, augmented of an aug_tab

check_mapbayr_model *Check if model is valid for mapbayr*

Description

Check if model is valid for mapbayr

Usage

```
check_mapbayr_model(x)
```

Arguments

x model file

Value

TRUE value if check is passed, a vector of character with errors otherwise.

Examples

```
library(mapbayr)
library(mrgsolve)
check_mapbayr_model(house())
```

compute_ofv *Compute the objective function value*

Description

Compute the objective function value

Usage

```
compute_ofv(
  eta,
  mrgsolve_model,
  data,
  sigma,
  log_transformation,
  DVobs,
  omega.inv,
  obs_cmt
)
```

Arguments

eta	a named vector of numeric (ETA1, ETA2...)
mrgsolve_model	model object (updated for purpose)
data	NMTRAN-like data (of one individual)
sigma	matrix
log_transformation	logical. If TRUE, prediction will be log-transformed to compute ofv (useful for log-additive model)
DVobs	vector of observation to fit
omega.inv	inverse of omega matrix
obs_cmt	vector of compartments with observations to fit

Details

This function is called iteratively by the optimization function. Arguments should not be passed directly, but generated by the pre-processing functions (see [preprocess.ofv](#))

Value

a single numeric value (the objective function value)

data_helpers

Data helpers

Description

Helpful functions to pass information about administrations (`adm_lines()`), observations (`obs_lines()`) and covariates (`add_covariates()`). These functions are passed to a `mrgmod` object (`mrgsolve` model), and return a `mrgmod` object with a dataset inside, so that `mrgsolve` or `mapbayr` functions can be passed along within a pipe-friendly workflow.

Usage

```
adm_lines(x, ...)
```

```
obs_lines(x, time, DV, mdv = 0, cmt = NULL, DVmet = NULL, ...)
```

```
add_covariates(x, covariates, ...)
```

```
see_data(x, ...)
```

Arguments

x model object
... passed to `mrgsolve::ev()` in `adm_lines()`
time, DV, mdv, cmt, DVmet
 passed to `obs_lines()`
covariates a list of named covariates, with a single value or same number of lines than data

Value

a `mrgmod` object, with a dataset in the `@args$data` slot.

derivatives	<i>Compute the derivatives</i>
-------------	--------------------------------

Description

Compute the derivatives

Usage

```
derivatives(v_DV, v_cmt, cmts)
```

Arguments

v_DV vector of concentrations to derive (typically `output$DV`)
v_cmt vector of compartment associated to the concentrations (typically `output$cmt`)
cmts numbers of compartment compartment associated with an observations, to derive concentration (typically `obs_cmt`)

Value

a matrix

Examples

```

derivatives(
  v_DV = c(400, 40, 200, 20),
  v_cmt = c(2, 3, 2, 3),
  cmts = c(2,3)
)

```

get_data.mapbayests *Return data from a mapbayests*

Description

Return data from a mapbayests

Usage

```
## S3 method for class 'mapbayests'  
get_data(x, ...)
```

Arguments

x	mapbayests object
...	not used

Value

a tibble

get_data.mrgmod *Return data from a mrgmod*

Description

Return data from a mrgmod

Usage

```
## S3 method for class 'mrgmod'  
get_data(x, ...)
```

Arguments

x	model object
...	not used

Value

a tibble

get_eta.mapbayests *Return eta from a mapbayests*

Description

Return eta from a mapbayests

Usage

```
## S3 method for class 'mapbayests'
get_eta(x, ..., output = NULL)
```

Arguments

x	mapbayests object
...	not used
output	either a list ("list"), a data.frame ("df") or a vector of numeric ("num"). Default to "num" if only one ID.

Value

a tibble

get_param.mapbayests *Return a posteriori param from a mapbayests*

Description

Return a posteriori param from a mapbayests

Usage

```
## S3 method for class 'mapbayests'
get_param(x, ..., output = NULL, keep_ID = NULL, keep_names = NULL)
```

Arguments

x	mapbayests object
...	passed along
output	either a data.frame ("df") or a vector of numeric ("num"). Default to "num" if only one ID
keep_ID	a logical. By default, the ID variable is dropped if one ID in data.
keep_names	a logical. By default, names are dropped if one parameter is requested, and output is not a data frame.

Value

a tibble

get_x	<i>Get content from object</i>
-------	--------------------------------

Description

Helpful functions to get content from a mrgmod object (i.e. data) or from a mapbayests object (data, eta, param).

Usage

```
get_data(x, ...)
```

```
get_eta(x, ...)
```

```
get_param(x, ...)
```

Arguments

x	object to get content from
...	passed along

Value

the class of the object returned depends on the function, and on their arguments. Typically, a data.frame or a vector if the output can be reduced to one line.

hist.mapbayests	<i>Plot posterior distribution of bayesian estimates</i>
-----------------	--

Description

Plot posterior distribution of bayesian estimates

Usage

```
## S3 method for class 'mapbayests'
hist(x, ...)
```

Arguments

x	A mapbayests object.
...	additional arguments (not used)

Value

a ggplot object, representing prior parameter density distribution, and a histogram of patients estimates.

 mapbayest

Estimate parameters (maximum a posteriori)

Description

The main function of the mapbayr package. Performs a *maximum a posteriori* Bayesian estimation of parameters, from a mrgsolve model object and a dataset containing information about administrations and observed concentrations.

Usage

```
mapbayest(
  x,
  data = NULL,
  method = "L-BFGS-B",
  force_initial_eta = NULL,
  quantile_bound = 0.001,
  control = list(),
  check = TRUE,
  verbose = TRUE,
  reset = TRUE,
  output = NULL
)

mbrest(...)
```

Arguments

x	the model object
data	NMTRAN-like data set
method	optimization method; possible values are L-BFGS-B (the default) and newuoa
force_initial_eta	a vector of numeric values to start the estimation from (default to 0 for "L-BFGS-B")
quantile_bound	a numeric value representing the quantile of the normal distribution admitted to define the bounds for L-BFGS-B (default is 0.001, i.e. 0.1%)
control	a list passed to the optimizer (see optimx documentation)
check	check model code for mapbayr specification (a logical, default is TRUE)
verbose	print the steps of the estimations to the console (a logical, default is TRUE)
reset	reset optimizer with new initial eta values if numerical difficulties, or with new bounds (L-BFGS-B) if estimate equal to a bound. (a logical, default is TRUE)

output	if NULL (the default) a mapbayests object is returned; if df a <i>mapbay_tab</i> dataframe is returned
...	passed to mapbayest

Value

a mapbayests model object

mbrlib	<i>Internal "mapbayr" model examples</i>
--------	--

Description

Internal "mapbayr" model examples

Usage

```
mbrlib()
```

Value

a character string, the location of the example models.

obs_cmt	<i>Get observation compartment numbers from mrgsolve model</i>
---------	--

Description

Get observation compartment numbers from mrgsolve model

Usage

```
obs_cmt(x)
```

Arguments

x	model object
---	--------------

Value

vector of integer

Examples

```
model <- mrgsolve::mread("ex_mbr1", mbrlib())
obs_cmt(model)
```

obs_lines.mrgmod *Add observations lines to data*

Description

Add observations lines to data

Usage

```
## S3 method for class 'mrgmod'  
obs_lines(x, time, DV, mdv = 0, cmt = NULL, DVmet = NULL, ...)
```

Arguments

x	model object
time	vector of time
DV	vector of values to fit
mdv	optional should the DV be ignored (1) or not (0)
cmt	an integer. Optional, cmt where observation is measured
DVmet	optional : metabolite data to fit
...	not used

Value

model object with dataset

plot.mapbayests *Plot predictions from mapbayests object*

Description

Plot predictions from mapbayests object

Usage

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

Arguments

x	A mapbayests object.
...	additional arguments (not used)

Value

a ggplot object. Observed and predicted concentration vs time profile for every patients.

postprocess	<i>Postprocess mapbayr</i>
-------------	----------------------------

Description

Functions to generate postprocess after optimization.

Usage

```
postprocess.optim(x, data, opt.value)
```

```
postprocess.output(
  x,
  arg.optim,
  arg.ofv.fix,
  arg.ofv.id,
  opt.value,
  post,
  output,
  times
)
```

Arguments

x	the model object
data	NMTRAN-like data set
opt.value	value returned by optimizer
arg.optim, arg.ofv.fix, arg.ofv.id	argument passed to optimizer
post, times	output of the post.process function
output	if NULL (the default) a mapbayests object is returned; if df a <i>mapbay_tab</i> dataframe is returned

Value

postprocess.optim() returns a list with final parameters and mapbay_tab. postprocess.output() returns a mapbayests class object.

```
preprocess.ofv
```

Preprocess model and data for ofv computation

Description

Functions to generate arguments passed to `compute_ofv`. Arguments that are fixed between individuals are created once (`preprocess.ofv.fix`), while other are specific of each individual (`preprocess.ofv.id`).

Usage

```
preprocess.ofv.fix(x, data)
```

```
preprocess.ofv.id(x, iddata)
```

Arguments

<code>x</code>	the model object
<code>data, iddata</code>	NMTRAN-like data set. <code>iddata</code> is likely a dataset of one individual

Value

a list of arguments use to `compute_ofv()`.

```
preprocess.optim
```

Pre-process: arguments for optimization function

Description

Pre-process: arguments for optimization function

Usage

```
preprocess.optim(x, method, control, force_initial_eta, quantile_bound)
```

Arguments

<code>x</code>	the model object
<code>method</code>	optimization method; possible values are L-BFGS-B (the default) and newuoa
<code>control</code>	a list passed to the optimizer (see optimx documentation)
<code>force_initial_eta</code>	a vector of numeric values to start the estimation from (default to 0 for "L-BFGS-B")
<code>quantile_bound</code>	a numeric value representing the quantile of the normal distribution admitted to define the bounds for L-BFGS-B (default is 0.001, i.e. 0.1%)

Value

a list of named arguments passed to optimizer (i.e. arg.optim)

print.mapbayests	<i>Print a mapbayests object</i>
------------------	----------------------------------

Description

Print a mapbayests object

Usage

```
## S3 method for class 'mapbayests'
print(x, ...)
```

Arguments

x	A mapbayests object.
...	additional arguments

Value

print the results of the estimation to the console, and returns it invisibly.

use_posterior	<i>Use posterior param and covariates</i>
---------------	---

Description

Use posterior param and covariates

Usage

```
use_posterior(x, .zero_re = c("both", "omega", "sigma"))
```

Arguments

x	A mapbayests object.
.zero_re	Default is "both", meaning all matrices are zeroed. Pass "omega" to zero between-subject variability, and keep simulating residual error.

Details

Updates the param values of the model object with the estimated etas, and the covariates of the individual. Returns an updated mrgmod, so that the user can derive simulations from it. Works only with one individual. Does not handle time-varying covariates.

Value

a mrgmod

Index

`add_covariates (data_helpers)`, 7
`add_covariates.mrgmod`, 2
`adm_0_cmt`, 3
`adm_cmt`, 3
`adm_lines (data_helpers)`, 7
`adm_lines.mrgmod`, 4
`as.data.frame.mapbayests`, 4
`augment`, 5
`augment.mapbayests`, 5

`check_mapbayr_model`, 6
`compute_ofv`, 6, 16

`data_helpers`, 7
`derivatives`, 8

`get_data (get_x)`, 11
`get_data.mapbayests`, 9
`get_data.mrgmod`, 9
`get_eta (get_x)`, 11
`get_eta.mapbayests`, 10
`get_param (get_x)`, 11
`get_param.mapbayests`, 10
`get_x`, 11

`hist.mapbayests`, 11

`mapbayest`, 12
`mbrest (mapbayest)`, 12
`mbrlib`, 13

`obs_cmt`, 13
`obs_lines (data_helpers)`, 7
`obs_lines.mrgmod`, 14
`optimx`, 12, 16

`plot.mapbayests`, 14
`postprocess`, 15
`preprocess.ofv`, 7, 16
`preprocess.optim`, 16
`print.mapbayests`, 17

`see_data (data_helpers)`, 7
`use_posterior`, 17