Package 'qpNCA'

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Type Package

Title Noncompartmental Pharmacokinetic Analysis by qPharmetra

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Description Computes noncompartmental pharmacokinetic parameters
for drug concentration profiles. For each profile, data
imputations and adjustments are made as necessary and
basic parameters are estimated. Supports single dose, multi-dose,
and multi-subject data. Supports steady-state calculations
and various routes of drug administration. See ?qpNCA and vignettes.
Methodology follows Rowland and Tozer (2011, ISBN:978-0-683-07404-8),
Gabrielsson and Weiner (1997, ISBN:978-91-9765-100-4), and
Gibaldi and Perrier (1982, ISBN:978-0824710422).

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Encoding UTF-8

Suggests rmarkdown, markdown, covr, testthat (>= 2.1.0)

Depends R (>= 3.3.0)

Imports dplyr(>= 0.7.0), tidyr (>= 0.8.2), magrittr, ggplot2, knitr

RoxygenNote 7.1.1

VignetteBuilder knitr

NeedsCompilation no

Repository CRAN

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R topics documented:

`calc.ctmax` *Calculate Cmax and Tmax*

Description

Calculates Cmax and Tmax from raw data for each PK curve defined using `by`.

Usage

```
calc.ctmax(x, by = character(0), timevar = "time", depvar = "dv")
```

Arguments

`x`	data.frame
`by`	column names in x indicating grouping variables
`timevar`	variable name containing the actual sampling time after dose
`depvar`	variable name containing the dependent variable (e.g., concentration)

Details

Input dataset can contain all uncorrected data, including LOQ; estimate first occurence of maximum concentration for each PK curve; if all concentrations are NA, sets Cmax and Tmax also to NA.

Value

A dataset with estimates for the Cmax (maximum concentration) and Tmax (time of first occurence of cmax) parameters: one observation per subject

Examples

```
example(est.thalf)
ctmax <- x %>% calc.ctmax(by = 'subject')
ctmax %>% head
```

`calc.par` *Calculate NCA Parameters*

Description

Calculates PK parameters for which half-life is not needed in the calculation for each PK curve defined using by.

Usage

```
calc.par(
  x,
  by = character(0),
  tau = NA,
  tstart = NA,
  tend = NA,
  teval = NA,
  route = "EV",
  method = 1
)
```

Arguments

`x`	contains all data after time/concentration deviation corrections obtained from `correct.time` and `correct.conc`
`by`	column names in x indicating grouping variables
`tau`	dosing interval (for multiple dosing); NA (default) for if single dose; x$tau overrides
`tstart`	start time of partial AUC (start>0); NA (default) if not requested; x$tstart overrides
`tend`	end time of partial AUC; NA (default) if not requested; x$tend overrides
`teval`	user selected AUC interval; NA (default) if not requested; x$teval overrides
`route`	route of drug administration ("EV","IVB","IVI"); x$route overrides
`method`	method for trapezoidal rule • 1: linear up - linear down • 2: linear up - logarithmic down • 3: linear before first Tmax, logarithmic after first Tmax

Value

A dataset with estimates for the following parameters, one observation per subject:

Parameter	Description
t0.ok	flags if t=0 concentration could be corrected/imputes. If not, no AUCs starting at t=0 are calculated
tlast.ok	flags if there is at least one measurable concentration. If not, no AUClast can be calculated
tlast	time of last sample with measurable concentration
clast.obs	observed concentration at tlast
aucall	auc calculated over all observations, including values below LOQ (which are set to 0)
auclast	auc calculated using all observations up to and including the last measurable concentration (clast.obs at tlast)
aumcall	aumc calculated over all observations, including values below LOQ (which are set to 0)
aumclast	aumc calculated using all observations up to and including the last measurable concentration (clast.obs at tlas
tau	the dosing interval (if specified)
calc.tau	flags if AUCtau could be calculated
auctau	auc calculated over the dosing interval, only calculated if tau is specified
aumctau	aumc calculated over the dosing interval, only calculated if tau is specified
teval	user selected AUC interval starting at t=0 (if specified)
calc.teval	flags if AUCteval could be calculated
aucxx	auc calculated from t=0 up to/including teval, only calculated if teval is specified (xx is substituted by teval)
calc.part	flags if AUCpart could be calculated
tstart	start time of partial AUC (if specified)
tend	end time of partial AUC (if specified)
aucx_y	partial auc from time=x up to/including time=y, where x>0, only calculated if tstart and tend are specified
c0	back-extrapolated concentration at t=0 for IV bolus administration
area.back.extr	area back-extrapolated to 0

Examples

```
example(correct.conc)
par <- x %>% calc.par(by = 'subject')
par %>% head
```

`calc.par.th` *Calculate Lambda_z Parameters*

Description

Calculates PK parameters that need lambda_z.

Usage

```
calc.par.th(
  x,
  by = character(0),
```

```
  th = th,
  covariates = NA,
  dose = "dose",
  factor = 1,
  reg = "SD",
  ss = "N",
  route = "EV"
)
```

Arguments

x	result parameter dataset from calc.par
by	column names in x indicating grouping variables
th	result dataset from est.thalf
covariates	covariates dataset (containing at least dose for CL calculation); defaults to unique combinations of by and dose evaluated on x; can be character name of csv file or local object
dose	variable containing the dose amount; default 'dose' set to 1 if not in names(x)
factor	conversion factor for CL and V calculation (e.g. dose in mg, conc in ng/mL, factor=1000); x$factor overrides
reg	regimen, "sd" or "md"; x$reg overrides
ss	is steady state reached (y/n); x$ss overrides
route	of drug administration ("EV","IVB","IVI"); x$route overrides

Value

A dataset containing all parameters calculated in est.thalf and calc.par
with estimates for the following parameters added, one observation per subject:

Parameter	Description
clast.pred	predicted concentration at tlast
aucinf.obs	aucinf based on observed concentration at tlast
aucinf.pred	aucinf based on predicted concentration at tlast
aumcinf.obs	area under the first moment curve extrapolated to infinity, based on observed concentration at tlast
aumcinf.pred	area under the first moment curve extrapolated to infinity, based on predicted concentration at tlast
cl.obs, cl.f.obs	clearance based on aucinf.obs, at steady state based on auctau
cl.pred, cl.f.pred	clearance based on aucinf.pred
cl.ss, cl.f.ss	clearance at steady state, based on auctau
mrt.obs	mean residence time based on aumcinf.obs and aucinf.obs
mrt.pred	mean residence time based on aumcinf.pred and aucinf.pred
vz.obs, vz.f.obs	distribution volume based on cl.f.obs, at steady state based on auctau
vz.pred, vz.f.pred	distribution based on cl.pred/cl.f.pred
vss.obs	steady-state volume based on cl.obs and mrt.obs
vss.pred	steady-state volume based on cl.pred and mrt.pred
pctextr.pred	percentage of AUC extrapolated to infinity, based on aucinf.pred
pctextr.obs	percentage of AUC extrapolated to infinity, based on aucinf.obs
pctback.pred	percentage of AUC extrapolated back to 0, based on aucinf.pred

pctback.obs percentage of AUC extrapolated back to 0, based on aucinf.obs

Note: ctmax must be merged separately as those were calculated from uncorrected data.

Examples

```
example(calc.par) # creates par
# notice x includes (optional) loqrule, includeCmax, reg, method, route, ss
covs <- Theoph %>%
  select(subject = Subject, Wt, dose = Dose) %>%
  unique %>%
  mutate(dose = dose * Wt, subject=as.numeric(as.character(subject))) # see ?Theoph
y <- x %>% select(subject, reg, ss, loqrule) %>% unique
y %<>% mutate(factor = 1)
par %<>% left_join(y, by = 'subject')
par %<>% calc.par.th(by = 'subject', th = th, covariates = covs)
par %<>% left_join(ctmax, ., by = 'subject')
par %>% head
par %>% data.frame %>% head(2)
```

---

check.input *Check qpNCA function arguments for validity*

Description

Checks whether all function arguments are valid and entered column names are present in input data
See qpNCA for description of the arguments

Usage

```
check.input(
  x,
  by = NA,
  nomtimevar = NA,
  timevar = NA,
  depvar = NA,
  bloqvar = NA,
  loqvar = NA,
  loqrule = NA,
  includeCmax = NA,
  exclvar = NA,
  plotdir = NA,
  timelab = NA,
  deplab = NA,
```

```
  tau = NA,
  tstart = NA,
  tend = NA,
  teval = NA,
  covariates = NA,
  dose = NA,
  factor = NA,
  reg = NA,
  ss = NA,
  route = NA,
  method = NA
)
```

Arguments

x	data.frame
by	column names in x indicating grouping variables
nomtimevar	variable name containing the nominal sampling time after dose
timevar	variable name containing the actual sampling time after dose
depvar	variable name containing the dependent variable (e.g., concentration)
bloqvar	variable name containing the BLOQ flag (0: no, 1: yes)
loqvar	variable name containing the LOQ value
loqrule	rule number to be applied to the LOQ values in the curve; x$loqrule overrides if provided
includeCmax	include Cmax in half-life estimation? (y/n); x$includeCmax overrides if provided
exclvar	variable name indicating points to be excluded in half-life estimation (these should have exclvar = 1)
plotdir	directory where regression plots (.PNG) will be saved; NA gives default location, NULL skips regression plots
timelab	label for time axis in regression plots
deplab	label for dependent variable axis in regression plots
tau	dosing interval (for multiple dosing); NA (default) if single dose; x$tau overrides
tstart	start time of partial AUC (start>0); NA (default) if not requested; x$tstart overrides
tend	end time of partial AUC; NA (default) if not requested; x$tend overrides
teval	user selected AUC interval (starting at t=0); NA (default) if not requested; x$teval overrides
covariates	covariates dataset; Must contain the dose variable
dose	variable containing the dose amount
factor	conversion factor for CL and V calculation (e.g. dose in mg, conc in ng/mL, factor=1000); x$factor overrides if provided

reg	regimen, "SD" or "MD"; x$reg overrides if provided
ss	is steady state reached (y/n); x$ss overrides if provided
route	route of drug administration ("EV","IVB", "IVI"); x$route overrides if provided
method	method for trapezoidal rule; x$method overrides if provided

Value

Check results

`correct.conc` *Correct Missing Concentration*

Description

Corrects missing concentration at critical time points (e.g, predose, TAU, start and end of user selected AUC interval).

Usage

```
correct.conc(
  x,
  by = character(0),
  nomtimevar = "ntad",
  tau = NA,
  tstart = NA,
  tend = NA,
  teval = NA,
  th = NA,
  reg = "SD",
  ss = "N",
  route = "EV",
  method = 1
)
```

Arguments

x	input dataset name (after Time Deviation Correction Rules have been applied by `correct.time`)
by	column names in x indicating grouping variables
nomtimevar	variable name containing the nominal sampling time after dose
tau	dosing interval (for multiple dosing); NA (default) for if single dose; x$tau overrides
tstart	start time of partial AUC (start>0); NA (default) if not requested; x$tstart overrides
tend	end time of partial AUC; NA (default) if not requested; x$tend overrides

`teval`	user selected AUC interval; NA (default) if not requested; x$teval overrides
`th`	lamdba_z information for each curve; like output of `est.thalf`
`reg`	regimen, "sd" or "md"; x$reg overrides
`ss`	is steady state reached (y/n); x$ss overrides
`route`	route of drug administration ("EV","IVB","IVI"); x$route overrides
`method`	method for trapezoidal rule; x$method overrides • 1: linear up - linear down • 2: linear up - logarithmic down • 3: linear before first Tmax, logarithmic after first Tmax

Details

- Use interpolation if there is a measurable concentration BEFORE and AFTER the missing concentration
- Use extrapolation if there is NO measurable concentration AFTER the missing concentration
- Set missing concentration at predose to 0 (SD, non-endogenous) or value at t=TAU (steady state only)
- Set missing concentration at t=TAU to value at t=0 (steady state only)

The following Concentration Deviation Correction Rules will be applied to critical time points (t=0, tau, tstart, tend, teval), if needed:

Rule	Regimen	Description
SDC-1	sd	Set concentration to 0 (only non-endogenous compounds)
SDC-2	sd	impute missing concentration by interpolation
SDC-3	sd	impute missing concentration by extrapolation
SDC-4	sd (IVB)	impute missing concentration by back-extrapolation
MDC-1	md	impute missing concentration by existing conc at t=0 or t=tau (only if steady state has been reached)
MDC-2	md	impute missing concentration by interpolation
MDC-3	md	impute missing concentration by extrapolation
MDC-4	md (IVB)	impute missing concentration by back-extrapolation

Value

a dataset with missing concentrations imputed. The following variables are added:

Variable	Description
crule.nr	correction rule number
crule.txt	text explaining what was altered
applies.to.conc	lists all critical time points to which the concentration correction rule applies

Examples

```
example(correct.time)
```

```
x %<>% mutate(ss = 'N', route = 'EV')
# route redefined for completeness
x %<>% correct.conc(by = 'subject') # ignoring th
x %>% head
```

`correct.loq` *Impute Concentrations Below the Limit of Quantitation*

Description

Imputes LOQ values according to the chosen LOQ substitution rule.

Usage

```
correct.loq(
  x,
  by = character(0),
  nomtimevar = "ntad",
  timevar = "time",
  depvar = "dv",
  bloqvar = "bloq",
  loqvar = "loq",
  loqrule = 1
)
```

Arguments

`x`	input dataset name contains all uncorrected data, including LOQ
`by`	column names in x indicating grouping variables
`nomtimevar`	variable name containing the nominal sampling time after dose
`timevar`	variable name containing the actual sampling time after dose
`depvar`	variable name containing the dependent variable (e.g., concentration)
`bloqvar`	variable name containing the BLOQ flag (0: no, 1: yes)
`loqvar`	variable name containing the LOQ value
`loqrule`	rule number to be applied to the LOQ values in the curve. x$loqrule overrides if provided • 1: 0 before first measurable concentration (FMC); NA after FMC • 2: 0 before FMC; 0 after FMC • 3: 0 before FMC; 0.5xLOQ for first consecutive LOQ after FMC, NA for other LOQ • 4: 0 before FMC; 0.5xLOQ for first consecutive LOQ after FMC, 0 for other LOQ

Details

Imputations will be applied to the original depvar (no new concentration variable will be created).

Value

A dataset with imputed BLOQ concentrations using the chosen imputation rule

Examples

```
library(magrittr)
library(dplyr)
library(qpNCA)
x <- Theoph
ntad <- c(0,0.25,0.5,1,2,4,5,7,9,12,24)
for(i in 1:nrow(x)){
  time  <- x$Time[[i]]
  delta <- abs(ntad - time)
  best  <- min(delta)
  index <- match(best, delta)
  nom   <- ntad[[index]]
  x$ntad[[i]] <- nom
}
rm(list = c('time','delta','best','index','nom', 'i','ntad'))
x %<>% rename(time = Time, dv = conc)
x %<>% mutate(bloq = ifelse(dv==0,1,0), loq = 0.01, tad = time, loqrule = 1,
              subject=as.numeric(Subject), ntad=as.numeric(ntad))
x %>% head
x %<>% correct.loq('subject')
x %>%  head
```

`correct.time` *Correct Concentrations for Time Deviations*

Description

Corrects concentrations at critical, but deviating time points (e.g, predose, TAU, start and end of user selected AUC interval), and adds missing records at these critical time points.

Usage

```
correct.time(
  x,
  by = character(0),
  nomtimevar = "ntad",
  timevar = "time",
  depvar = "dv",
  tau = NA,
```

```
  tstart = NA,
  tend = NA,
  teval = NA,
  th = NA,
  reg = "SD",
  method = 1
)
```

Arguments

x	input dataset name (after LOQ values have been imputed by correct.loq)
by	column names in x indicating grouping variables
nomtimevar	variable name containing the nominal sampling time after dose
timevar	variable name containing the actual sampling time after dose
depvar	variable name containing the dependent variable (e.g., concentration)
tau	dosing interval (for multiple dosing); NA (default) if single dose; x$tau overrides
tstart	start time of partial AUC (start>0); NA (default) if not requested; x$tstart overrides
tend	end time of partial AUC; NA (default) if not requested; x$tend overrides
teval	user selected AUC interval, starting at t=0; NA (default) if not requested; x$teval overrides
th	lamdba_z information for each curve; like output of est.thalf
reg	regimen, "sd" or "md"; x$reg overrides
method	method for trapezoidal rule; x$method overrides if provided • 1: linear up - linear down • 2: linear up - logarithmic down • 3: linear before first Tmax, logarithmic after first Tmax

Details

- Records with missing NOMINAL time will be removed and this must be corrected before the function is called
- If a record at the critical time point is missing, add it and set time to nominal time and set dv conc to NA
- Use interpolation if there is a measurable concentration AFTER the nominal time point (i.e. sample is taken too late)
- Use extrapolation if there is NO measurable concentration AFTER the nominal time point (i.e. sample is taken too early)
- Set deviating time at predose after single dose to 0
- Original time and conc will be kept in original variables.

The following Time Deviation Correction Rules will be applied to critical time points (t = 0, tau, tstart, tend, teval), if needed:

Rule	Regimen	Description	Applied to
SDT-1	sd	Set actual time to 0	t = 0
SDT-2	sd	Correct concentration at deviating time by interpolation	t = tau,tstart,tend,teval
SDT-3	sd	Correct concentration at deviating time by extrapolation	t = tau,tend,teval
MDT-1	md	If predose sample taken after dosing, set actual time to 0 and conc to NA	t = 0
MDT-2	md	Correct concentration at deviating time by interpolation (too late)	t = tau,tstart,tend,teval
MDT-3	md	Correct concentration at deviating time by extrapolation (too early)	t = 0,tau,tend,teval
MDT-3a	md	Set actual time to zero if concentration is BLOQ (too early)	t = 0

Value

a dataset with time deviation corrections applied (timevar and depvar adapted). The following variables are added:

Variable	Description
create.nr	is a missing record created?
create.txt	explanation of what is created
trule.nr	correction rule number
trule.txt	text explaining what was altered
applies.to.time	lists all critical time points to which the time deviation rule applies
time.tau, conc.tau	time and conc, corrected for AUCtau calculation
time.teval, conc.teval	time and conc, corrected for AUCteval calculation (AUC0-teval)
time.part, conc.part	time and conc, corrected for partial AUC calculation (AUCstart-end, start>0)
time.lastall, conc.lastall	time and conc, corrected for AUClast and AUCall calculation
t0.flag, tau.flag, tstart.flag, tend.flag, teval.flag	flags for what timepoint the correction was needed

The following are preserved if present in x: tau, tstart, tend, teval, reg, ss, route, method.

Examples

```
example(calc.ctmax)
x %<>% mutate(reg = 'SD', method = 1, route = 'EV')
# route not used yet, but still preserved
x %<>% correct.time(by = 'subject', th = th)
x %>% head
```

`est.thalf` *Calculate Lambda_z and Elimination Half-life*

Description

Calculates lambda_z and thalf for each PK curve identified using `by`.

Usage

```
est.thalf(
  x,
  by = character(0),
  timevar = "time",
  depvar = "dv",
  includeCmax = "Y",
  exclvar = NA
)
```

Arguments

x	a dataset
by	column names in x indicating grouping variables
timevar	variable name containing the actual sampling time after dose
depvar	variable name containing the dependent variable (e.g., concentration)
includeCmax	include results of regression including Cmax in selection? (y/n); x$includeCmax overrides if provided
exclvar	a variable name containing information about points to be excluded (these should have exclvar = 1)

Details

The function starts with the last three sample points and performs log-linear regression on it. It then adds one sampling point at a time (including and ending at tmax) and performs the regression again. The results of the regression with the highest adjusted R-squared are returned.

Visual outliers can be excluded from the regression analysis.

Value

a dataset with estimates for each regression analysis in one observation. The following parameters are available.

- **no.points** number of data points used in the regression analysis
- **intercept** estimated intercept
- **lambda_z** -1*estimated slope
- **r.squared** square of the correlation coefficient
- **adj.r.squared** adjusted square of the correlation coefficient
- **thalf** elimination half-life
- **start_th** time of first sample included in the thalf estimation
- **end_th time** of last sample included in the thalf estimation
- **includeCmax** include results of regression including Cmax in selection? (y/n)
- **points_excluded** are time points excluded from the half-life estimation? (y/n)

Examples

```
example(correct.loq)
x %<>% mutate(includeCmax = 'Y')
th <- x %>% est.thalf(by='subject',exclvar=)
th %>%  head
```

`filenamefun` *Create File Name for Regression Plots*

Description

Creates file name for regression plots (*.png) from by-variables in plot_reg function

Usage

```
filenamefun(x, by)
```

Arguments

x	data.frame
by	column names in x indicating grouping variables

Value

character

`interpol` *Interpolate Concentrations*

Description

Interpolates concentrations. Used by correct.xx functions to interpolate concentrations. Uses linear interpolation unless method is 2 (log down), c1 > c2, and both concentrations are non-zero.

Usage

```
interpol(c1 = NA, c2 = NA, t1 = NA, t2 = NA, t3 = NA, method = 1)
```

Arguments

c1	concentration 1 lagconc
c2	concentration 2 leadconc
t1	time 1 tiem where conc should be calculated
t2	time 2 lagtime
t3	time 3 leadtime
method	calculation method (1, 2, or 3)

---

lag_lead *Estimate Lagging and Leading Times and Concentrations*

Description

Estimates lagging and leading times and concentrations. Used by correct.xx functions to estimate lagging and leading timepoints and concentrations for each timepoint.

Usage

```
lag_lead(
  x,
  nomtimevar1 = NA,
  depvar1 = NA,
  timevar1 = NA,
  lagc = NA,
  lagt = NA,
  leadc = NA,
  leadt = NA,
  ...
)
```

Arguments

x	data.frame
nomtimevar1	column name in x indicating nominal time after dose
depvar1	column name in x indicating concentration
timevar1	column name in x indicating actual time after dose
lagc	concentration at previous sampling time
lagt	previous sampling time
leadc	concentration at next sampling time
leadt	next sampling time
...	ignored

Value

data.frame

plot_reg *Plot Regression Curves*

Description

Plots regression curves for each set of records defined using by. A log-linear plot will be made for each curve.

Usage

```
plot_reg(
  x,
  by = character(0),
  th = NA,
  bloqvar = "bloq",
  timevar = "tad",
  depvar = "dv",
  timelab = "timevar",
  deplab = "depvar",
  exclvar = NA,
  plotdir = NA,
  ...
)
```

Arguments

x	input dataset name
by	column names in x indicating grouping variables
th	file name of file with half-life estimation information for each curve
bloqvar	variable name containing the BLOQ flag (0: no, 1: yes)
timevar	variable name containing the actual sampling time after dose
depvar	variable name containing the dependent variable (e.g., concentration)
timelab	X-axis label (default: "timevar")
deplab	Y-axis label (default: "depvar")
exclvar	variable name containing information about points to be excluded (these should have exclvar = 1)
plotdir	directory where individual plot files will be saved
...	ignored

Details

If elimination half-life was estimated for that curve, the following will be indicated in the plot:

- Cmax (Yellow, even if no half-life was estimated)

- points used in regression and resulting regression line (green)
- points excluded from regression (red crossed)
- estimate of elimination half-life and adjusted R-squared

Input dataset:

- uncorrected dataset, used for half-life estimation
- dataset containing results of the half-life estimation

Value

(invisible) plotdir. If the attribute 'plotdir' is empty, plots will be generated in standard output, otherwise plots will be saved as PNG file in the designated directory.

Examples

```
example(est.thalf)
x %>% filter(dv > 0) %>% plot_reg(by = 'subject', th = th)
```

---

qpNCA *Perform Non-compartmental Analysis*

Description

Consecutively executes the following NCA steps:

- correct.loq impute LOQ values
- est.thalf calculate lambda_z and half-life
- plot_reg plot each regression curve
- calc.ctmax calculate Cmax and Tmax
- correct.time correct time deviations at critical time points
- correct.conc impute missing concentrations at critical time points
- tab.corr tabulate data alterations
- calc.par calculates parameters not dependent on lambda_z
- calc.par.th calculates parameters dependent on lambda_z

Usage

```
qpNCA(
  x,
  by = character(0),
  nomtimevar = "ntad",
  timevar = "time",
  depvar = "dv",
  bloqvar = "bloq",
  loqvar = "loq",
  loqrule = 1,
  includeCmax = "Y",
  exclvar = NA,
  plotdir = NA,
  timelab = "timevar",
  deplab = "depvar",
  tau = NA,
  tstart = NA,
  tend = NA,
  teval = NA,
  covariates = NA,
  dose = "dose",
  factor = 1,
  reg = "SD",
  ss = "N",
  route = "EV",
  method = 1
)
```

Arguments

x	input dataset name
by	column names in x indicating grouping variables
nomtimevar	variable name containing the nominal sampling time after dose
timevar	variable name containing the actual sampling time after dose
depvar	variable name containing the dependent variable (e.g., concentration)
bloqvar	variable name containing the BLOQ flag (0: no, 1: yes)
loqvar	variable name containing the LOQ value
loqrule	rule number to be applied to the LOQ values in the curve; x$loqrule overrides if provided
includeCmax	include Cmax in half-life estimation? (y/n); x$includeCmax overrides if provided
exclvar	variable name indicating points to be excluded in half-life estimation (these should have exclvar = 1)
plotdir	directory where regression plots (.PNG) will be saved; NA gives default location, NULL skips regression plots

timelab	label for time axis in regression plots
deplab	label for dependent variable axis in regression plots
tau	dosing interval (for multiple dosing); NA (default) if single dose; x$tau overrides
tstart	start time of partial AUC (start>0); NA (default) if not requested; x$tstart overrides
tend	end time of partial AUC; NA (default) if not requested; x$tend overrides
teval	user selected AUC interval (starting at t=0); NA (default) if not requested; x$teval overrides
covariates	covariates dataset; Must contain the dose variable
dose	variable containing the dose amount
factor	conversion factor for CL and V calculation (e.g. dose in mg, conc in ng/mL, factor=1000); x$factor overrides if provided
reg	regimen, "SD" or "MD"; x$reg overrides if provided
ss	is steady state reached (y/n); x$ss overrides if provided
route	route of drug administration ("EV","IVB", "IVI"); x$route overrides if provided
method	method for trapezoidal rule; x$method overrides if provided • 1: linear up - linear down • 2: linear up - logarithmic down • 3: linear before first Tmax, logarithmic after first Tmax

Value

(list)

- **covariates** covariates selected with the `covariates` argument
- **half_life** linear regression parameters
- **ct_corr** the time and concentration corrected dataset
- **corrections** descriptions of the corrections applied
- **pkpar** all estimated PK parameters
- **plots** generated plots

Examples

```
library(magrittr)
library(dplyr)
library(qpNCA)
x <- Theoph
ntad <- c(0,0.25,0.5,1,2,4,5,7,9,12,24)
for(i in 1:nrow(x)){
  time  <- x$Time[[i]]
  delta <- abs(ntad - time)
  best  <- min(delta)
```

```
  index <- match(best, delta)
  nom   <- ntad[[index]]
  x$ntad[[i]] <- nom
}
rm(list = c('time','delta','best','index','nom', 'i','ntad'))
x %<>% rename(time = Time, dv = conc, subject = Subject)
x %<>% mutate(bloq = 0, loq = 0.01, tad = time,excl_th=0,
              subject=as.numeric(subject),ntad=as.numeric(ntad))
x %<>% filter(dv > 0)
covs <- x %>%
  select(subject, Wt, dose = Dose) %>%
  distinct(subject,.keep_all=TRUE) %>%
  mutate(dose = dose * Wt) # see ?Theoph
z <- qpNCA(x, by = 'subject', covariates = covs, exclvar='excl_th')
```

---

tab.corr *Tabulate Corrections*

Description

Tabulates what records were added, time deviations and concentration imputations were applied, for each subject.

Usage

```
tab.corr(x, by = character(0), nomtimevar = "time")
```

Arguments

x	concentration dataset created by the correct.time and correct.conc functions, containing time and conc corrected data
by	column names in x indicating grouping variables
nomtimevar	column in x containing the nominal time after dose

Value

dataset with applied corrections (rule number and rule text) listed by by-variable(s) and nominal time

Examples

```
example(correct.conc)
corrtab <- x %>% tab.corr(by = 'subject')
corrtab %>% head
```

titlefun *Create Title for Regression Plots*

Description

Creates title for regression plots in plot_reg() using by-variables.

Usage

```
titlefun(x, by)
```

Arguments

x	dataset containing concentration-time information of the current curve
by	column names in x indicating grouping variables

Value

character

trap *Calculate Area Under the Curve Using Trapezoids*

Description

Calculates AUC using the trapezoidal method. Assumes data represent a single profile. Despite choice of method, only linear interpolation is used for areas of intervals beginning or ending with y: 0.

Usage

```
trap(x = NA, y = NA, method = 1)
```

Arguments

x	x variable, i.e. time
y	y variable, i.e. concentration
method	method: • 1: linear up - linear down • 2: linear up - logarithmic down • 3: linear before Tmax, logarithmic after Tmax

Value

area (length-one numeric)

`trapm` *Calculate Area Under the Moment Curve Using Trapezoids*

Description

Calculates AUMC using the trapezoidal method. Assumes data represent a single profile. Despite choice of method, only linear interpolation is used for areas of intervals beginning or ending with y: 0.

Usage

```
trapm(x = NA, y = NA, method = 1)
```

Arguments

`x`	variable names of x coordinates
`y`	variable names of y coordinates
`method`	method: • 1: linear up - linear down • 2: linear up - logarithmic down • 3: linear before Tmax, logarithmic after Tmax

Value

area (length-one numeric)

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