Package 'ncappc'

August 29, 2016

Title NCA Calculation and Population PK Model Diagnosis

Version 0.2.1.1

Description A flexible tool is presented here that can perform
(i) traditional non-compartmental analysis (NCA) and
(ii) simulation-based posterior predictive checks for a population
pharmacokinetic (PK) model using NCA metrics.

Depends R (>= 2.15.3), ggplot2, grid, gridExtra

Imports scales, gtable, knitr, xtable, reshape2, testthat, dplyr,
readr (>= 0.2.2), lazyeval

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LazyData true

VignetteBuilder knitr

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R topics documented:

`calc.stat` *Calculates a set of statistics for a given array of numbers.*

Description

calc.stat calculates a set of statistics for a given array of numbers.

Usage

```
calc.stat(x)
```

Arguments

x	a numeric array

Details

calc.stat calculates a set of statistics for a given array of numbers. The calculated statistics are

- Ntot = length of the array
- Nunique = Number of unique elements
- Min = Minimum value of the array
- Max = Maximum value of the array
- Mean = Mean value of the array
- Median = Median value of the array
- SD = Standard deviation value of the array
- SE = Standard error value of the array
- CVp = Percent coefficient of variation of the array
- CI95u = Upper limit of the 95% confidence interval of the array
- cI95l = Lower limit of the 95% confidence interval of the array
- gMean = Geometric mean value of the array
- gCVp = Geometric percent coefficient of variation of the array

Value

An array of calculated statistics of a given set of numbers

dv.plot — *Plots drug plasma concentration vs time data*

Description

dv.plot plots DV vs Time data.

Usage

```
dv.plot(pdata, cunit = "[M].[L]^-3", tunit = "[T]")
```

Arguments

pdata	A data frame with three mandatory columns and one optional column: 1. Time: Time column (mandatory) 2. Conc: DV column (mandatory) 3. ID: Individual ID (mandatory) 4. FCT: Dose identifier and/or population stratifier (optional)
cunit	Unit for concentration (**"[M].[L]^-3"**)
tunit	Unit for time (**"[T]"**)

Details

dv.plot plots DV vs Time data

Value

returns a graphical object created by arrangeGrob function

est.nca — *Estimates individual NCA metrics from concentration vs time data. data.*

Description

est.nca estimates a comprehensive set of NCA metrics for a given individual using concentration vs time profile.

Usage

```
est.nca(time, conc, backExtrp = FALSE, negConcExcl = FALSE,
  doseType = "ns", adminType = "extravascular", doseAmt = NULL,
  method = "linear-log", AUCTimeRange = NULL, LambdaTimeRange = NULL,
  LambdaExclude = NULL, doseTime = doseTime, Tau = NULL, TI = NULL,
  simFile = NULL, dset = "obs")
```

Arguments

time	Numeric array for time
conc	Numeric array for concentration
backExtrp	If back-extrapolation is needed for AUC (TRUE or FALSE) (**FALSE**)
negConcExcl	Exclude -ve conc (**FALSE**)
doseType	Steady-state (ss) or nonsteady-state (ns) dose (**"ns"**)
adminType	Route of administration (iv-bolus,iv-infusion,extravascular) (**"extravascular"**)
doseAmt	Dose amounts (**"NULL"**)
method	linear, log or linear-log (**"linear-log"**)
AUCTimeRange	User-defined window of time used to estimate AUC (**"NULL"**)
LambdaTimeRange	User-defined window of time to estimate elimination rate-constant (**"NULL"**)
LambdaExclude	User-defined excluded observation time points for estimation of elimination rate-constant (**"NULL"**)
doseTime	Dose time prior to the first observation for steady-state data (NULL)
Tau	Dosing interval for steady-state data (**"NULL"**)
TI	Infusion duration (**"NULL"**)
simFile	Name of the simulated concentration-time data if present (**"NULL"**)
dset	Type, i.e., observed or simulated concentration-time data set ("obs" or "sim") (**"obs"**)

Details

est.nca estimates a comprehensive set of NCA metrics using the concentration-time profile of an individual. NCA metrics are eatimated according to traditional PK calculations. The names of the various NCA metrics estimated in this package are assigned mainly following the names used in WinNonlin. This package accepts any of the three different types of drug administration, (i) iv-bolus, (ii) iv-infusion and (iii) extravascular; **ncappc** also can accept both non-steady state and steady-state data. The NCA metrics that are estimated and reported by **ncappc** are listed below.

- **C0** is the initial concentration at the dosing time. It is the observed concentration at the dosing time, if available. Otherwise it is approximated using the following rules.
- **Cmax, Tmax and Cmax_D** are the value and the time of maximum observed concentration, respectively. If the maximum concentration is not unique, the first maximum is used. For steady state data, The maximum value between the dosing intervals is considered. Cmax_D is the dose normalized maximum observed concentration.
- **Clast and Tlast** are the last measurable positive comcentration and the corresponding time, respectively.
- **AUClast** is the area under the concentration vs. time curve from the first observed to last measurable concentration.
- **AUMClast** is the first moment of the concentration vs. time curve from the first observed to last measurable concentration.

- **MRTlast** is the mean residence time from the first observed to last measurable concentration.
- **No_points_Lambda_z** is the number of observed data points used to determine the best fitting regression line in the elimination phase.
- **AUC_pBack_Ext_obs** is the percentage of AUCINF_obs that is contributed by the back extrapolation to estimate C0.
- **AUC_pBack_Ext_pred** is the percentage of AUCINF_pred that is contributed by the back extrapolation to estimate C0.
- **AUClower_upper** is the AUC under the concentration-time profile within the user-specified window of time privided as the "AUCTimeRange" argument. In case of empty "AUCTimeRange" argument, AUClower_upper is equal to the AUClast.
- **Rsq, Rsq_adjusted and Corr_XY** are regression coefficient of the regression line used to estimate the elimination rate constant, the adjusted value of Rsq and the square root of Rsq, respectively.
- **Lambda_z** is the elimination rate constant estimated from the regression line representing the terminal phase of the concentration-time prifile.
- **Lambda_lower and Lambda_upper** are the lower and upper limit of the time values from the concentration-time profile used to estimate Lambda_z, respectively, in case the "LambdaTimeRange" is used to specify the time range.
- **HL_Lambda_z** is terminal half-life of the drug.
- **AUCINF_obs and AUCINF_obs_D** are AUC estimated from the first sampled data extrapolated to infinity and its dose normalized version, respectively. The extrapolation in the terminal phase is based on the last observed concentration Clast_obs.
- **AUC_pExtrap_obs** is the percentage of the AUCINF_obs that is contributed by the extrapolation from the last sampling time to infinity.
- **AUMCINF_obs** is AUMC estimated from the first sampled data extrapolated to infinity. The extrapolation in the terminal phase is based on the last observed concentration.
- **AUMC_pExtrap_obs** is the percentage of the AUMCINF_obs that is contributed by the extrapolation from the last sampling time to infinity.
- **Vz_obs** is the volume of distribution estimated based on total AUC
- **Cl_obs** is total body clearance.
- **AUCINF_pred and AUCINF_pred_D** are AUC from the first sampled data extrapolated to infinity and its dose normalized version, respectively. The extrapolation in the terminal phase is based on the last predicted concentration obtained from the regression line used to estimate Lambda_z (Clast_pred).
- **AUC_pExtrap_pred** is the percentage of the AUCINF_pred that is contributed by the extrapolation from the last sampling time to infinity.
- **AUMCINF_pred** is AUMC estimated from the first sampled data extrapolated to infinity. The extrapolation in the terminal phase is based on the last predicted concentration obtained from the regression line used to estimate Lambda_z (Clast_pred).
- **AUMC_pExtrap_pred** is the percentage of the AUMCINF_pred that is contributed by the extrapolation from the last sampling time to infinity.
- **Vz_pred** is the volume of distribution estimated based on AUCINF_pred.

- **Cl_pred** is the total body clearance estimated based on AUCINF_pred.
- **MRTINF_obs** is the mean residence time from the first sampled time extrapolated to infinity based on the last observed concentration (Clast_obs).
- **MRTINF_pred** is the mean residence time from the first sampled time extrapolated to infinity based on the last predicted concentration obtained from the regression line used to estimate Lambda_z (Clast_pred).
- **Tau** is the dosing interval for steady-state data. This value is assumed equarion over multiple doses.
- **Cmin and Tmin** are the minimum concentration between 0 and Tau and the corresponding time, respectively.
- **Cavg** is the average concentration between 0 and Tau for steady-state data.
- **AUCtau and AUMCtau** are AUC and AUMC between 0 and Tau for steady-state data.
- **Clss** is an estimate of the total body clearance for steady-state data.
- **Vss_obs and Vss_pred** are estimated volume of distribution at steady-state based on Clast_obs and Clast_pred, respectively.
- **p_Fluctuation** is the percentage of the fluctuation of the concentration between 0 and Tau for steady-state data.
- **Accumulation_Index** is $1/(1 - e^(- \lambda_z * \tau))$

Value

An array of estimated NCA metrics

`histobs.plot` *Plots histogram of selected set of NCA metrics.*

Description

histobs.plot plots histogram of selected set of NCA metrics (e.g. AUClast, AUCINF_obs, Cmax and Tmax).

Usage

```
histobs.plot(plotData, figlbl = NULL, param = c("AUClast", "AUCINF_obs",
  "Cmax", "Tmax"), cunit = "[M].[L]^-3", tunit = "[T]", spread = "npi")
```

Arguments

`plotData`	A data frame with the estimated NCA metrics
`figlbl`	Figure label based on dose identifier and/or population stratifier (**NULL**)
`param`	A character array of the NCA metrics. The allowed NCA metrics for this histograms are "AUClast", "AUClower_upper", "AUCINF_obs", "AUCINF_pred", "AUMClast", "Cmax", "Tmax" and "HL_Lambda_z". (**c("AUClast", "AUCINF_obs", "Cmax", "Tmax")**)

cunit	Unit for concentration (**"[M].[L]^-3"**)
tunit	Unit for time (**"[T]"**)
spread	Measure of the spread of simulated data (ppi (95% parametric prediction interval) or npi (95% nonparametric prediction interval)) (**"npi"**)

Details

histobs.plot plots histogram of selected set of NCA metrics. The allowed NCA metrics for this histograms are "AUClast", "AUClower_upper", "AUCINF_obs", "AUCINF_pred", "AUMClast", "Cmax", "Tmax" and "HL_Lambda_z". By default, this function produces histogram of AUClast, AUCINF_obs, Cmax and Tmax.

Value

returns a graphical object created by arrangeGrob function

---

histpop.plot *Plots population histogram of the NCA metrics selected for model diagnosis.*

Description

histpop.plot plots population histogram of the NCA metrics selected for model diagnosis (e.g. AUClast, AUCINF_obs, Cmax and Tmax).

Usage

```
histpop.plot(obsdata = outData, simdata = smeanData, figlbl = NULL,
  param = c("AUClast", "Cmax"), cunit = "[M].[L]^-3", tunit = "[T]",
  spread = "npi")
```

Arguments

obsdata	Data frame with the values of the NCA metrics estimated from the observed data
simdata	Data frame with the values of the NCA metrics estimated from the simulated data
figlbl	Figure label based on dose identifier and/or population stratifier (**NULL**)
param	A character array of the NCA metrics. The allowed NCA metrics for this histograms are "AUClast", "AUClower_upper", "AUCINF_obs", "AUCINF_pred", "AUMClast", "Cmax", "Tmax" and "HL_Lambda_z". (**c("AUClast", "Cmax")**)
cunit	Unit for concentration (**"[M].[L]^-3"**)
tunit	Unit for time (**"[T]"**)
spread	Measure of the spread of simulated data (ppi (95% parametric prediction interval) or npi (95% nonparametric prediction interval)) (**"npi"**)

Details

histpop.plot plots histogram of the NCA metrics selected for the model diagnosis and compares with the corresponding metrics estimated from the observed data. The allowed NCA metrics for this histograms are "AUClast", "AUClower_upper", "AUCINF_obs", "AUCINF_pred", "AUMClast", "Cmax", "Tmax" and "HL_Lambda_z". By default, this function produces histogram of AUClast and Cmax.

Value

returns a graphical object created by arrangeGrob function

`nca.deviation.plot` *Plot individual deviation of NCA metrics estimated from observed and simulated data*

Description

nca.deviation.plot plots individual deviation of selected NCA metrics estimated from observed and simulated data.

Usage

```
nca.deviation.plot(plotdata, xvar = NULL, devcol = NULL, figlbl = NULL,
  spread = "npi", cunit = "[M].[L]^-3", tunit = "[T]")
```

Arguments

`plotdata`	A data frame containing the scaled deviation values of the NCA metrics
`xvar`	x-variable against which the deviation data will be plotted (**NULL**)
`devcol`	column names/numbers of the data frame containing deviation data (**NULL**)
`figlbl`	Figure label based on dose identifier and/or population stratifier (**NULL**)
`spread`	Measure of the spread of simulated data (ppi (95% parametric prediction interval) or npi (95% nonparametric prediction interval)) (**"npi"**)
`cunit`	Unit for concentration (**"[M].[L]^-3"**)
`tunit`	Unit for time (**"[T]"**)

Details

nca.deviation.plot plots individual deviation of selected NCA metrics estimated from observed and simulated data. This function requires three mandatory arguments, (i) deviation data, (ii) independent variable and (iii) dependent variables. The deviation of the NCA metrics values estimated from the observed and simulated data are scaled by the "spread" of the simulated metrics values. The "spead" of the simulated data is measured either by the standard deviation or the 95

Value

returns the data frame with the NPDE values based on the input data.

`nca.npde` *Calculates individual normalized prediction distribution errors (NPDE) from PDE data.*

Description

nca.npde calculates individual normalized prediction distribution errors (NPDE) of selected NCA metrics from the PDE data.

Usage

```
nca.npde(pdedata, pdecol)
```

Arguments

`pdedata`	A data frame containing the prediction distribution errors (PDE) of NCA metrics
`pdecol`	The range of column numbers in the data frame containing the PDE values, which will be used to calculate the corresponding NPDE

Details

nca.npde calculates individual normalized prediction distribution errors (NPDE) of selected NCA metrics from PDE data. The The deviation of each estimated NCA metrics is scaled by the "spread" of the simulated values. By default, this function calculates the NPDE values of all columns of the input data frame.

Value

returns the data frame with the NPDE values based on the input data.

`nca.npde.plot` *Plots population histogram of the NCA metrics selected for model diagnosis.*

Description

nca.npde.plot plots individual NPDE values and histogram of the NPDE values within a population group

Usage

```
nca.npde.plot(plotdata, xvar = NULL, npdecol = NULL, figlbl = NULL,
  cunit = "[M].[L]^-3", tunit = "[T]")
```

Arguments

plotdata	Data frame with the values of the NPDE values of each individual for the NCA metrics
xvar	Name of the independent variable column against which NPDE values will be plotted
npdecol	Column names or column numbers of containing the NPDE values
figlbl	Figure label based on dose identifier and/or population stratifier (**NULL**)
cunit	Unit for concentration (**"M.L^-3"**)
tunit	Unit for time (**"T"**)

Details

nca.npde.plot individual NPDE values and histogram of the NPDE values of NCA metrics within a population group.

Value

returns a data frame with the mean and SD of population NPDE values of each NCA metric and two graphical objects created by arrangeGrob function for the individual and population histogram of the NPDE values

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nca.pde.deviation.outlier

Calculates individual prediction distribution errors (PDE) and scaled deviation of NCA metrics estimated from observed and simulated data. Identifies outlier to population PK model.

Description

nca.pde.deviation.outlier calculates individual prediction distribution errors (PDE) and scaled deviation of NCA metrics estimated from observed and simulated data. Identifies outlier to population PK model.

Usage

```
nca.pde.deviation.outlier(obsdata, simdata, idNm = "ID", id = NULL,
  spread = "npi", figlbl = NULL, calcparam = c("AUClast", "Cmax"),
  diagparam = c("AUClast", "Cmax"), cunit = "[M].[L]^-3", tunit = "[T]",
  noPlot = FALSE)
```

Arguments

obsdata	A data frame containing the NCA metrics values estimated from the observed data
simdata	A data frame containing the NCA metrics values estimated from the simulated data
idNm	Column name for ID (**"ID"**)
id	ID of the individual whose data is being evaluated
spread	Measure of the spread of simulated data (ppi (95% parametric prediction interval) or npi (95% nonparametric prediction interval)) (**"npi"**)
figlbl	Figure label based on dose identifier and/or population stratifier, in addition to ID (**NULL**)
calcparam	A character array of the NCA metrics used for calculations of PDE and deviation. The allowed NCA metrics for this histograms are "AUClast", "AUClower_upper", "AUCINF_obs", "AUCINF_pred", "AUMClast", "Cmax", "Tmax" and "HL_Lambda_z". (**c("AUClast", "Cmax")**)
diagparam	A character array of the NCA metrics used for diagnostic test. The allowed NCA metrics for this histograms are "AUClast", "AUClower_upper", "AUCINF_obs", "AUCINF_pred", "AUMClast", "Cmax", "Tmax" and "HL_Lambda_z". (**c("AUClast", "Cmax")**)
cunit	Unit for concentration (**"[M].[L]^-3"**)
tunit	Unit for time (**"[T]"**)
noPlot	Perform only NCA calculations without any plot generation (TRUE, FALSE) (**FALSE**)

Details

nca.pde.deviation.outlier calculates individual prediction distribution errors (PDE) and scaled deviation of NCA metrics estimated from observed and simulated data. The deviation of each estimated NCA metrics is scaled by the "spread" of the simulated values. The "spread" is measured either by the 95% parametric prediction interval or 95% non-parametric prediction interval. Any individual yielding an absolute value of the scaled deviation for any of the selected NCA metrics greater than 1, is assigned as an outlier to the corresponding population PK model. The allowed NCA metrics for this diagnostic tests are "AUClast", "AUClower_upper", "AUCINF_obs", "AUCINF_pred", "AUMClast", "Cmax", "Tmax" and "HL_Lambda_z". By default, this function uses AUClast and Cmax metrics for the comparison.

Value

returns the observed data frame with added distance and simulation mean of the nCA metrics, and a data frame with the PDE values of the NCA metrics. If the individual is identified as an outlier for the PK model, histograms of the diagnostic NCA metrics are produced and a graphical object created by arrangeGrob function is returned.

ncappc *Performs NCA calculations and population PK model diagnosis.*

Description

ncappc is a flexible tool, to

1. perform a traditional NCA
2. perform simulation-based posterior predictive checks for a population PK model using NCA metrics.

Usage

```
ncappc(obsFile = "nca_original.npctab.dta",
  simFile = "nca_simulation.1.npctab.dta", str1Nm = NULL, str1 = NULL,
  str2Nm = NULL, str2 = NULL, str3Nm = NULL, str3 = NULL,
  concUnit = NULL, timeUnit = NULL, doseUnit = NULL,
  doseNormUnit = NULL, obsLog = FALSE, simLog = FALSE, psnOut = TRUE,
  idNmObs = "ID", timeNmObs = "TIME", concNmObs = "DV", idNmSim = "ID",
  timeNmSim = "TIME", concNmSim = "DV", AUCTimeRange = NULL,
  backExtrp = FALSE, LambdaTimeRange = NULL, LambdaExclude = NULL,
  doseAmtNm = NULL, adminType = "extravascular", doseType = "ns",
  doseTime = NULL, Tau = NULL, TI = NULL, method = "linear-log",
  blqNm = NULL, blqExcl = 1, evid = TRUE, evidIncl = 0, mdv = FALSE,
  filterNm = NULL, filterExcl = NULL, negConcExcl = FALSE,
  param = c("AUClast", "Cmax"), timeFormat = "number", dateColNm = NULL,
  dateFormat = NULL, spread = "npi", tabCol = c("AUClast", "Cmax", "Tmax",
  "AUCINF_obs", "Vz_obs", "Cl_obs", "HL_Lambda_z"), figFormat = "tiff",
  noPlot = FALSE, printOut = TRUE, studyName = NULL,
  new_data_method = TRUE, overwrite_SIMDATA = NULL, outFileNm = NULL)
```

Arguments

obsFile	Observed concentration-time data from an internal data frame or an external table with comma, tab or space as separator (**"nca_original.npctab.dta"**)
simFile	NONMEM simulation output with the simulated concentration-time data from an internal data frame or an external table (**"nca_simulation.1.npctab.dta"**). NULL produces just the traditional NCA output, a filename or data frame prduces the NCA output as well as the PopPK diagnosis. If new_data_method=TRUE then this can be a compressed file as well.
str1Nm	Column name for 1st level population stratifier (NULL)
str1	Stratification ID of the members within 1st level stratification (e.g c(1,2)) (NULL)
str2Nm	Column name for 2nd level population stratifier (NULL)
str2	Stratification ID of the members within 2nd level stratification (e.g c(1,2)) (NULL)
str3Nm	Column name for 3rd level population stratifier (NULL)

str3	Stratification ID of the members within 3rd level stratification (e.g c(1,2)) (NULL)
concUnit	Unit of concentration (e.g. "ng/mL") (**"M.L^-3"**)
timeUnit	Unit of time (e.g. "h") (**"T"**)
doseUnit	Unit of dose amount (e.g. "ng") (**"M"**)
doseNormUnit	Normalization factor of dose amount if used (e.g. "kg") (NULL)
obsLog	Concentration in observed data in logarithmic form (TRUE, FALSE) (FALSE)
simLog	Concentration in simulated data in logarithmic form (TRUE, FALSE) (FALSE)
psnOut	observed data is an output from PsN or in NONMEM output format (TRUE, FALSE) (TRUE)
idNmObs	Column name for ID in observed data (**"ID"**)
timeNmObs	Column name for time in observed data (**"TIME"**)
concNmObs	Column name for concentration in observed data (**"DV"**)
idNmSim	Column name for ID in simulated data (**"ID"**)
timeNmSim	Column name for time in simulated data (**"TIME"**)
concNmSim	Column name for concentration in simulated data (**"DV"**)
AUCTimeRange	User-defined window of time used to estimate AUC (NULL)
backExtrp	If back-extrapolation is needed for AUC (TRUE or FALSE) (FALSE)
LambdaTimeRange	User-defined window of time to estimate elimination rate-constant. This argument lets the user to choose a specific window of time to be used to estimate the elimination rate constant (Lambda) in the elimination phase. The accepted format for the input to this argument is a numeric array of two elements; c(14,24) will estimate the Lambda using the data within the time units 14 to 24. If NULL then all times are considered.
LambdaExclude	User-defined excluded observation time points for estimation of elimination rate-constant (NULL)
doseAmtNm	Column name to specify dose amount (NULL)
adminType	Route of administration (iv-bolus,iv-infusion,extravascular) (**"extravascular"**)
doseType	Steady-state (ss) or nonsteady-state (ns) dose (**"ns"**)
doseTime	Dose time prior to the first observation for steady-state data (NULL)
Tau	Dosing interval for steady-state data (NULL)
TI	Infusion duration (NULL)
method	linear, log or linear-log (**"linear-log"**)
blqNm	Name of BLQ column if used (NULL)
blqExcl	Excluded BLQ value or logical condition (e.g. 1 or ">=1" or c(1,">3")) (**"1"**)
evid	Use EVID (TRUE, FALSE) (TRUE)
evidIncl	Included EVID (**"0"**)
mdv	Use MDV (TRUE(includes data for MDV==0), FALSE) (FALSE)
filterNm	Column name for filter (NULL)

filterExcl	Filter identifier or logical condition used for row exclusion (e.g. c(1, 2, "<20", ">=100", "!=100")) (NULL)
negConcExcl	Exclude -ve conc (FALSE)
param	NCA parameters (AUClast, AUClower_upper, AUCINF_obs, AUCINF_pred, AUMClast, Cmax, Tmax, HL_Lambda_z) (c(**"AUClast", "Cmax"**))
timeFormat	time format (number, H:M, H:M:S) (**"number"**)
dateColNm	colunm name for date if used (Date, DATE) (NULL)
dateFormat	date format (D-M-Y, D/M/Y or any other combination of D,M,Y) (NULL)
spread	Measure of the spread of simulated data ("ppi" (95% parametric prediction interval) or "npi" (95% nonparametric prediction interval))
tabCol	Output columns to be printed in the report in addition to ID, dose and population strata information (list of NCA metrics in a string array) (**c("AUClast", "Cmax", "Tmax", "AUCINF_obs", "Vz_obs", "Cl_obs", "HL_Lambda_z"**))
figFormat	format of the produced figures (bmp, jpeg, tiff, png) (**"tiff"**)
noPlot	Perform only NCA calculations without any plot generation (TRUE or FALSE)
printOut	Write/print output on the disk. No plot will be saved if noPlot is set to TRUE (TRUE, FALSE) (TRUE)
studyName	Name of the study to be added as a description in the report (NULL)
new_data_method	TRUE or FALSE. For testing a faster method of reading data. (TRUE)
overwrite_SIMDATA	Can be TRUE, to create new information in the SIMDATA directory, FALSE, to use the information in the SIMDATA directory or NULL to have a dialog come up to ask the user what to do. (NULL)
outFileNm	Additional tag to the name of the output html and pdf output file hyphenated to the standard ncappc report file name standard ncappc report file name (**Name of the observed data file**)

Details

Non-compartmental analysis (NCA) calculates pharmacokinetic (PK) metrics related to the systemic exposure to a drug following administration, e.g. area under the concentration-time curve and peak concentration. **ncappc** performs a traditional NCA using the observed plasma concentration-time data. In the presence of simulated plasma concentration-time data, **ncappc** also performs simulation-based posterior predictive checks (ppc) using NCA metrics for the corresponding population PK (PopPK) model used to generate the simulated data. The diagnostic analysis is performed at the population as well as the individual level. The distribution of the simulated population means of each NCA metric is compared with the corresponding observed population mean. The individual level comparison is performed based on the deviation of the mean of any NCA metric based on simulations for an individual from the corresponding NCA metric obtained from the observed data. Additionaly, **ncappc** reports the normalized prediction distribution error (NPDE) of the simulated NCA metrics for each individual and their distribution within a population. **ncappc** produces two default outputs depending on the type of analysis performed, i.e., traditional NCA and PopPK diagnosis. The PopPK diagnosis feature of **ncappc** produces 7 sets of graphical outputs to assess the ability of a population model to simulate the concentration-time profile of a drug and thereby

identify model misspecification. In addition, tabular outputs are generated showing the values of the NCA metrics estimated from the observed and the simulated data, along with the deviation, NPDE, regression parameters used to estimate the elimination rate constant and the related population statistics. The default values of the arguments used in **ncappc** are shown in the **Useage** section of this document and/or in **bold** in the **Arguments** section.

Value

NCA results and diagnostic test results

Examples

```
ncappc(obsFile=system.file("extdata","pkdata.csv",package="ncappc"),
psnOut=FALSE,noPlot=TRUE,printOut=FALSE)
```

`read_nm_table` *Read nonmem table files produced.*

Description

The function reads in nonmem table files. The files can be created from the `$EST` line or from the `$SIM` line in a NONMEM model file.

Usage

```
read_nm_table(nm_table, only_obs = FALSE, method = "default",
  quiet = TRUE, sim_num = FALSE, sim_name = "NSIM")
```

Arguments

`nm_table`	The NONMEM table file to read. A text string. If `dplyr` and `readr` are available and `method="default"` or `method="readr_*"` then `nm_table` can either a path to a file, a connection, or literal data (either a single string or a raw vector). Files ending in .gz, .bz2, .xz, or .zip will be automatically uncompressed. Files starting with http://, https://, ftp://, or ftps:// will be automatically downloaded. Remote gz files can also be automatically downloaded & decompressed.
`only_obs`	Should the non-observation lines in the data set be removed? Currently filtered uisng the expected `MDV` column. `TRUE` or `FALSE`.
`method`	Can be one of `default`, `readr_1`, `readr_2`, `readr_3`, `slow`. `readr_1` should be fastest. All but `slow` require `dplyr` and `readr` (version >= 0.2.2).
`quiet`	Should there be verbose messages about what the function is doing?
`sim_num`	Should the function add a column to the returned data frame that identifies the simulation number (if present)?
`sim_name`	The name of the resulting column in the returned data frame if `sim_num` is true.

Details

Currently the function searches the `$TABLE` for multiple header lines, and uses that to identify multiple simulations. The function expects at least one header line (`NOHEADER` option is not allowed in NONMEM table files).

Value

Returns a data frame of the simulated table with an added column for the simulation number. The data frame is given class `c("tbl_df", "tbl", "data.frame")` for easy use with dplyr.

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