Package 'pkr'

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Title Pharmacokinetics in R

Description Conduct a noncompartmental analysis as closely as possible to the most widely used commercial software.
The core noncompartmental computations are delegated to the 'NonCompart' package so that the two share a single, maintained engine.
Some features are
1) CDISC SDTM terms
2) Automatic slope selection with the same criterion of WinNonlin(R), restricted by default to samples after the end of an infusion
3) Supporting both 'linear-up linear-down' and 'linear-up log-down' method
4) Interval(partial) AUCs with 'linear' or 'log' interpolation method
5) Steady-state analysis over the dosing interval (AUCTAU, CAVG, CL and Vz from AUCTAU)
* Reference: Gabrielsson J, Weiner D. Pharmacokinetic and Pharmacodynamic Data Analysis - Concepts and Applications. 5th ed. 2016. (ISBN:9198299107).

Depends R (>= 3.6.0)

Imports NonCompart (>= 0.8.5), foreign, grDevices, graphics, grid, stats, utils

Suggests binr, forestplot, rtf

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NeedsCompilation no

URL https://cran.r-project.org/package=pkr

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`pkr-package` *Pharmacokinetics in R*

Description

It conducts a noncompartmental analysis(NCA) as closely as possible to the most widely used commercial pharmacokinetic analysis software.

Details

The main functions are

```
NCA      to perform NCA for many subjects.

IndiNCA  to perform NCA for one subject.
```

Author(s)

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References

1. Gabrielsson J, Weiner D. Pharmacokinetic and Pharmacodynamic Data Analysis - Concepts and Applications. 5th ed. 2016.
2. Shargel L, Yu A. Applied Biopharmaceutics and Pharmacokinetics. 7th ed. 2015.
3. Rowland M, Tozer TN. Clinical Pharmacokinetics and Pharmacodynamics - Concepts and Applications. 4th ed. 2011.
4. Gibaldi M, Perrier D. Pharmacokinetics. 2nd ed. revised and expanded. 1982.

Examples

```
# Theoph and Indometh data: dose in mg, conc in mg/L, time in h
NCA(Theoph, "Subject", "Time", "conc", dose=320, uConc="mg/L")
NCA(Indometh, "Subject", "time", "conc", dose=25, adm="Bolus", uConc="mg/L")

iAUC = data.frame(Name=c("AUC[0-12h]","AUC[0-24h]"), Start=c(0,0), End=c(12,24)) ; iAUC
NCA(Theoph, "Subject", "Time", "conc", dose=320, iAUC=iAUC, uConc="mg/L")
NCA(Indometh, "Subject", "time", "conc", dose=25, adm="Bolus", iAUC=iAUC, uConc="mg/L")

# writeLines(NCA(Theoph, "Subject", "Time", "conc", dose=320, report="Text", uConc="mg/L"),
#            "Theoph_Linear_CoreOutput.txt")
# writeLines(NCA(Theoph, "Subject", "Time", "conc", dose=320, fit="Log", report="Text",
#            uConc="mg/L"), "Theoph_Log_CoreOutput.txt")
# writeLines(NCA(Indometh, "Subject", "time", "conc", dose=25, adm="Bolus", report="Text",
#            uConc="mg/L"), "Indometh_Bolus_Linear_CoreOutput.txt")
# writeLines(NCA(Indometh, "Subject", "time", "conc", dose=25, adm="Bolus", fit="Log",
#            report="Text", uConc="mg/L"), "Indometh_Bolus_Log_CoreOutput.txt")
# writeLines(NCA(Indometh, "Subject", "time", "conc", dose=25, adm="Infusion", dur=0.25,
#            report="Text", uConc="mg/L"), "Indometh_Infusion_Linear_CoreOutput.txt")
# writeLines(NCA(Indometh, "Subject", "time", "conc", dose=25, adm="Infusion", dur=0.25,
#        fit="Log", report="Text", uConc="mg/L"), "Indometh_Infusion_Log_CoreOutput.txt")

sNCA(Theoph[Theoph$Subject==1,"Time"], Theoph[Theoph$Subject==1, "conc"], dose=320, concUnit="mg/L")
sNCA(Indometh[Indometh$Subject==1,"time"], Indometh[Indometh$Subject==1, "conc"], dose=25,
        adm="Bolus", concUnit="mg/L")
sNCA(Indometh[Indometh$Subject==1,"time"], Indometh[Indometh$Subject==1, "conc"], dose=25,
        adm="Infusion", dur=0.25, concUnit="mg/L")

iAUC = data.frame(Name=c("AUC[0-12h]","AUC[0-24h]"), Start=c(0,0), End=c(12,24)) ; iAUC
sNCA(Theoph[Theoph$Subject==1,"Time"], Theoph[Theoph$Subject==1, "conc"], dose=320,
        iAUC=iAUC, concUnit="mg/L")
sNCA(Indometh[Indometh$Subject==1,"time"], Indometh[Indometh$Subject==1, "conc"], dose=25,
        adm="Bolus", iAUC=iAUC, concUnit="mg/L")
sNCA(Indometh[Indometh$Subject==1,"time"], Indometh[Indometh$Subject==1, "conc"], dose=25,
        adm="Infusion", dur=0.25, iAUC=iAUC, concUnit="mg/L")
```

AUC *Calculate Area Under the Curve (AUC) and Area Under the first Moment Curve (AUMC) in a table format*

Description

Calculate Area Under the Curve(AUC) and the first Moment Curve(AUMC) in two ways; 'linear trapezoidal method' or 'linear-up and log-down' method. Return a table of cumulative values.

Usage

```
AUC(x, y, down = "Linear")
```

Arguments

x	vector values of independent variable, usually time
y	vector values of dependent variable, usually concentration
down	either of "Linear" or "Log" to indicate the way to calculate AUC and AUMC

Details

down="Linear" means linear trapezoidal rule with linear interpolation. down="Log" means linear-up and log-down method.

Value

Table with two columns, AUC and AUMC; the first column values are cumulative AUCs and the second column values cumulative AUMCs.

Author(s)

Kyun-Seop Bae <k@acr.kr>

References

Rowland M, Tozer TN. Clinical Pharmacokinetics and Pharmacodynamics - Concepts and Applications. 4th ed. pp687-689. 2011.

See Also

LinAUC, LogAUC

Examples

```
AUC(Theoph[Theoph$Subject==1, "Time"], Theoph[Theoph$Subject==1, "conc"])
AUC(Theoph[Theoph$Subject==1, "Time"], Theoph[Theoph$Subject==1, "conc"], down="Log")
```

BestSlope *Choose best fit slope for the log(y) and x regression by the criteria of adjusted R-square*

Description

It sequentially fits (log(y) ~ x) from the last point of x to the previous points with at least 3 points. It chooses a slope the highest adjusted R-square. If the difference is less then 1e-4, it chooses longer slope.

Usage

```
BestSlope(x, y, adm = "Extravascular", TOL=1e-4)
```

Arguments

x	vector values of x-axis, usually time
y	vector values of y-axis, usually concentration
adm	one of "Bolus" or "Infusion" or "Extravascular" to indicate drug administration mode
TOL	tolerance. Adjusted R-squared values that differ by less than this are considered equal, and the fit with more points is then chosen.

Details

Choosing the best terminal slope (y in log scale) in pharmacokinetic analysis is somewhat challenging, and it could vary by analysis performer. The slope with the highest adjusted R-squared is chosen, and among those the longest one. Difference of adjusted R-Squared less than TOL considered to be 0. This function uses ordinary least square method (OLS).

Value

R2	R-squared
R2ADJ	adjusted R-squared
LAMZNPT	number of points used for slope
LAMZ	negative of slope, lambda_z
b0	intercept of regression line
CORRXY	correlation of log(y) and x
LAMZLL	earliest x for lambda_z
LAMZUL	last x for lambda_z
CLSTP	predicted y value at last point, predicted concentration for the last time point

Author(s)

Kyun-Seop Bae <k@acr.kr>

See Also

Slope

Examples

```
BestSlope(Theoph[Theoph$Subject==1, "Time"], Theoph[Theoph$Subject==1, "conc"])
BestSlope(Indometh[Indometh$Subject==1, "time"], Indometh[Indometh$Subject==1, "conc"],
          adm="Bolus")
```

---

combXPT *Combine XPT files*

Description

This function combines specified CDISC domain XPT files across the folders.

Usage

```
combXPT(folders, domain)
```

Arguments

folders	where to find specified CDISC domain XPT files
domain	domain XPT files to be comined across the folders

Details

You need to designate only one CDISC domain name. You may specify one or more folders to find the domain XPT files.

Value

XPT	combined table

Author(s)

Kyun-Seop Bae <k@acr.kr>

See Also

help, readEX, readPC

---

foreNCA *Forest plot to compare NCA results*

Description

This function compares NCA results usually from rNCA function

Usage

```
foreNCA(NCAres = "", PPTESTCD = "", PCTESTCD = "", title = "", ...)
```

Arguments

NCAres	NCA results from rNCA function
PPTESTCD	CDISC SDTM PP domain Test Code to coompare
PCTESTCD	Molecular species to compare specified in PCTESTCD of CDISC SDTM PC domain
title	Title of the plot
...	further aguments to pass to the forestplot function

Details

This functio calls forestplot in forest package.

Value

Currently, this just plots.

Author(s)

Kyun-Seop Bae <k@acr.kr>

See Also

help, rNCA

IndiNCA *Noncompartmental Analysis for an Individual*

Description

It performs a noncompartmental analysis with one subject data. This will be deprecated. Use `sNCA()` instead.

Usage

```
IndiNCA(x, y, dose = 0, fit = "Linear", adm = "Extravascular", dur = 0,
            report = "Table", iAUC = "", uTime = "h", uConc = "ug/L", uDose = "mg")
```

Arguments

`x`	vector values of independent variable, usually time
`y`	vector values of dependent variable, usually concentration
`dose`	administered dose for the subject
`fit`	either of `"Linear"` or `"Log"` to indicate the way to calculate AUC and AUMC
`adm`	one of `"Bolus"` or `"Infusion"` or `"Extravascular"` to indicate drug administration mode
`dur`	infusion duration for constant infusion, otherwise 0
`report`	either of `"Table"` or `"Text"` to specify the type of return value
`iAUC`	data.frame with three columns, "Name", "Start", "End" to specify the invervals for partial (interval) AUC
`uTime`	unit of time
`uConc`	unit of concentration
`uDose`	unit of dose

Details

This performs a noncompartmental analysis for a subject. It returns practically the same result with the most popular commercial software.

Value

`CMAX`	maximum concentration, Cmax
`CMAXD`	dose normalized Cmax, CMAX / Dose, Cmax / Dose
`TMAX`	time of maximum concentration, Tmax
`TLAG`	time to observe the first non-zero concentration, for extravascular administration only
`CLST`	last positive concentration observed, Clast
`CLSTP`	last positive concentration predicted, Clast_pred
`TLST`	time of last positive concentration, Tlast
`LAMZHL`	half-life by lambda z, ln(2)/LAMZ
`LAMZ`	lambda_z negative of best fit terminal slope

LAMZLL	earliest time for LAMZ
LAMZUL	last time for LAMZ
LAMZNPT	number of points for LAMZ
CORRXY	correlation of log(concentration) and time
R2	R-squared
R2ADJ	R-squared adjusted
C0	back extrapolated concentration at time 0, for bolus intravascular administration only
AUCLST	AUC from 0 to TLST
AUCALL	AUC using all the given points, including trailing zero concentrations
AUCIFO	AUC infinity observed
AUCIFOD	AUCIFO / Dose
AUCIFP	AUC infinity predicted using CLSTP instead of CLST
AUCIFPD	AUCIFP / Dose
AUCPEO	AUC % extrapolation observed
AUCPEP	AUC % extrapolated for AUCIFP
AUCPBEO	AUC % back extrapolation observed, for bolus IV administration only
AUCPBEP	AUC % back extrapolation predicted with AUCIFP, for bolus IV administration only
AUMCLST	AUMC to the TLST
AUMCIFO	AUMC infinity observed using CLST
AUMCIFP	AUMC infinity determined by CLSTP
AUMCPEO	AUMC % extrapolated observed
AUMCPEP	AUMC % extrapolated predicted
MRTIVLST	mean residence time (MRT) to TLST, for intravascular administration
MRTIVIFO	mean residence time (MRT) infinity using CLST, for intravascular administration
MRTIVIFP	mean residence time (MRT) infinity using CLSTP, for intravascular administration
MRTEVLST	mean residence time (MRT) to TLST, for extravascular administration
MRTEVIFO	mean residence time (MRT) infinity using CLST, for extravascular administration
MRTEVIFP	mean residence time (MRT) infinity using CLSTP, for extravascular administration
VZO	volume of distribution determined by LAMZ and AUCIFO, for intravascular administration
VZP	volume of distribution determined by LAMZ and AUCIFP, for intravascular administration
VZFO	VZO for extravascular administration, VZO/F, F is bioavailability
VZFP	VZP for extravascular administration, VZP/F, F is bioavailability
CLO	clearance using AUCIFO, for intravascular administration
CLP	clearance using AUCIFP, for intravascular administration

CLFO	CLO for extravascular administration, CLO/F, F is bioavailability
CLFP	CLP for extravascular administration, CLP/F, F is bioavailability
VSSO	volume of distribution at steady state using CLST, for intravascular administration only
VSSP	volume of distribution at stead state using CLSTP, for intravascular administration only

Author(s)

Kyun-Seop Bae <k@acr.kr>

References

1. Gabrielsson J, Weiner D. Pharmacokinetic and Pharmacodynamic Data Analysis - Concepts and Applications. 5th ed. 2016.
2. Shargel L, Yu A. Applied Biopharmaceutics and Pharmacokinetics. 7th ed. 2015.
3. Rowland M, Tozer TN. Clinical Pharmacokinetics and Pharmacodynamics - Concepts and Applications. 4th ed. 2011.
4. Gibaldi M, Perrier D. Pharmacokinetics. 2nd ed. revised and expanded. 1982.

See Also

AUC, BestSlope

Examples

```
IndiNCA(Theoph[Theoph$Subject==1,"Time"], Theoph[Theoph$Subject==1, "conc"], dose=320, uConc="mg/L")
IndiNCA(Indometh[Indometh$Subject==1,"time"], Indometh[Indometh$Subject==1, "conc"], dose=25,
        adm="Bolus", uConc="mg/L")
IndiNCA(Indometh[Indometh$Subject==1,"time"], Indometh[Indometh$Subject==1, "conc"], dose=25,
        adm="Infusion", dur=0.25, uConc="mg/L")

IndiNCA(Theoph[Theoph$Subject==1,"Time"], Theoph[Theoph$Subject==1, "conc"], dose=320,
        report="Text", uConc="mg/L")
IndiNCA(Indometh[Indometh$Subject==1,"time"], Indometh[Indometh$Subject==1, "conc"], dose=25,
        adm="Bolus", report="Text", uConc="mg/L")
IndiNCA(Indometh[Indometh$Subject==1,"time"], Indometh[Indometh$Subject==1, "conc"], dose=25,
        adm="Infusion", dur=0.25, report="Text", uConc="mg/L")

iAUC = data.frame(Name=c("AUC[0-12h]","AUC[0-24h]"), Start=c(0,0), End=c(12,24)) ; iAUC
IndiNCA(Theoph[Theoph$Subject==1,"Time"], Theoph[Theoph$Subject==1, "conc"], dose=320,
        iAUC=iAUC, uConc="mg/L")
IndiNCA(Indometh[Indometh$Subject==1,"time"], Indometh[Indometh$Subject==1, "conc"], dose=25,
        adm="Bolus", iAUC=iAUC, uConc="mg/L")
IndiNCA(Indometh[Indometh$Subject==1,"time"], Indometh[Indometh$Subject==1, "conc"], dose=25,
        adm="Infusion", dur=0.25, iAUC=iAUC, uConc="mg/L")
```

IntAUC *Calculate interval AUC*

Description

It calculates interval AUC

Usage

```
IntAUC(x, y, t1, t2, Res, down = "Linear")
```

Arguments

x	vector values of independent variable, usually time
y	vector values of dependent variable, usually concentration
t1	start time for AUC
t2	end time for AUC
Res	result from IndiNCA function
down	either of "Linear" or "Log" to indicate the way to calculate AUC

Details

This calculates an interval (partial) AUC (from t1 to t2) with the given series of x and y. If t1 and/or t2 cannot be found within x vector, it interpolates according to the down option.

Value

return interval AUC value (scalar)

Author(s)

Kyun-Seop Bae <k@acr.kr>

References

1. Gabrielsson J, Weiner D. Pharmacokinetic and Pharmacodynamic Data Analysis - Concepts and Applications. 5th ed. 2016.
2. Shargel L, Yu A. Applied Biopharmaceutics and Pharmacokinetics. 7th ed. 2015.
3. Rowland M, Tozer TN. Clinical Pharmacokinetics and Pharmacodynamics - Concepts and Applications. 4th ed. 2011.
4. Gibaldi M, Perrier D. Pharmacokinetics. 2nd ed. revised and expanded. 1982.

See Also

AUC, Interpol

Examples

```
Res = sNCA(Theoph[Theoph$Subject==1,"Time"], Theoph[Theoph$Subject==1, "conc"],
           dose=320, concUnit="mg/L")
IntAUC(Theoph[Theoph$Subject==1, "Time"], Theoph[Theoph$Subject==1, "conc"], t1=0.5, t2=11, Res)
```

`Interpol` *Interpolate y value*

Description

It interpolates y value when a corresponding x value (xnew) does not exist within x vector

Usage

```
Interpol(x, y, xnew, Slope, b0, down = "Linear")
```

Arguments

`x`	vector values of x-axis, usually time
`y`	vector values of y-axis, usually concentration
`xnew`	new x point to be interpolated, usually new time point
`Slope`	slope of regression log(y) ~ x
`b0`	y value of just left point of xnew
`down`	either of `"Linear"` or `"Log"` to indicate the way to interpolate

Details

This function interpolate y value, if xnew is not in x vector. If xnew is in x vector, it just returns the given x and y vector. This function usually is called by `IntAUC` function Returned vector is sorted in the order of increasing x values.

Value

new x and y vector containing xnew and ynew point

Author(s)

Kyun-Seop Bae <k@acr.kr>

See Also

`IntAUC`

Examples

```
x = 10:1 + 0.1
y = -2*x + 40.2
Interpol(x, y, 1.5)
Interpol(x, y, 1.5, down="Log")
```

LinAUC *Area Under the Curve(AUC) and Area Under the first Moment Curve(AUMC) by linear trapezoidal method*

Description

It calculates AUC and AUMC using linear trapezoidal method

Usage

```
LinAUC(x, y)
```

Arguments

x	vector values of independent variable, usually time
y	vector values of dependent variable, usually concentration

Details

This function returns AUC and AUMC by linear trapezoidal method.

Value

AUC	area under the curve
AUMC	area under the first moment curve

Author(s)

Kyun-Seop Bae <k@acr.kr>

References

1. Gabrielsson J, Weiner D. Pharmacokinetic and Pharmacodynamic Data Analysis - Concepts and Applications. 5th ed. 2016.
2. Shargel L, Yu A. Applied Biopharmaceutics and Pharmacokinetics. 7th ed. 2015.
3. Rowland M, Tozer TN. Clinical Pharmacokinetics and Pharmacodynamics - Concepts and Applications. 4th ed. 2011.
4. Gibaldi M, Perrier D. Pharmacokinetics. 2nd ed. revised and expanded. 1982.

See Also

LogAUC, AUC

Examples

```
LinAUC(Theoph[Theoph$Subject==1, "Time"], Theoph[Theoph$Subject==1, "conc"])
AUC(Theoph[Theoph$Subject==1, "Time"], Theoph[Theoph$Subject==1, "conc"]) # compare the last line
```

loadEXPC *Load EX and PC domain files in folders*

Description

This loads and returns EX and PC domain files in the specified folders

Usage

```
loadEXPC(folders)
```

Arguments

folders	folders where to find EX and PC domain files

Details

This reads EX and PC domain files in the specified folder. This calls readEX and readPC functions.

Value

EX	combined EX domain data
PC	combined PC doamin data

Author(s)

Kyun-Seop Bae <k@acr.kr>

See Also

help, readEX, readPC

LogAUC *Area Under the Curve(AUC) and Area Under the first Moment Curve(AUMC) by linear-up log-down method*

Description

It calculates AUC and AUMC using linear-up log-down method

Usage

```
LogAUC(x, y)
```

Arguments

x	vector values of independent variable, usually time
y	vector values of dependent variable, usually concentration

Details

This function returns AUC and AUMC by linear-up log-down method.

Value

AUC	area under the curve
AUMC	area under the first moment curve

Author(s)

Kyun-Seop Bae <k@acr.kr>

References

1. Gabrielsson J, Weiner D. Pharmacokinetic and Pharmacodynamic Data Analysis - Concepts and Applications. 5th ed. 2016.
2. Shargel L, Yu A. Applied Biopharmaceutics and Pharmacokinetics. 7th ed. 2015.
3. Rowland M, Tozer TN. Clinical Pharmacokinetics and Pharmacodynamics - Concepts and Applications. 4th ed. 2011.
4. Gibaldi M, Perrier D. Pharmacokinetics. 2nd ed. revised and expanded. 1982.

See Also

LinAUC,AUC

Examples

```
LogAUC(Theoph[Theoph$Subject==1, "Time"], Theoph[Theoph$Subject==1, "conc"])
# Compare the last line with the above
AUC(Theoph[Theoph$Subject==1, "Time"], Theoph[Theoph$Subject==1, "conc"], down="Log")
```

NCA *Noncompartmental analysis for a dataset with multiple subjects*

Description

conduct noncompartmental analysis for many subjects in a data table

Usage

```
NCA(concData, id, Time, conc, trt="", fit = "Linear", dose = 0,
           adm = "Extravascular", dur = 0, report = "Table", iAUC = "",
           uTime = "h", uConc = "ug/L", uDose = "mg")
```

Arguments

concData	name of data table containing time-concentration data of multiple subjects
id	column name for subject ID
Time	column name for the time
conc	column name for the concentration
trt	column name for the treatment code. This is useful for crossover study like bioequivalence trial.
fit	one of "Linear" or "Log" to indicate the way to calculate AUC
dose	administered dose. One should be careful for the unit. This can be a vector containing dose for each subject in order.
adm	one of "Bolus" or "Infusion" or "Extravascular" to indicate drug administration mode
dur	infusion duration for constant infusion, otherwise 0. This can be a vector containing values for each subject in order.
report	either of "Table" or "Text" to specify the type of return value
iAUC	data.frame with three columns, "Name", "Start", "End" to specify partial interval AUC
uTime	unit of time
uConc	unit of concentration
uDose	unit of dose

Details

This function calls sNCA repeatedly to do NCA for each subject. If you specify report="Text", this function returns in free text format to be used in a report file.

Value

CMAX	maximum concentration, Cmax
CMAXD	dose normalized Cmax, CMAX / Dose, Cmax / Dose
TMAX	time of maximum concentration, Tmax
TLAG	time to observe the first non-zero concentration, for extravascular administration only
CLST	last positive concentration observed, Clast
CLSTP	last positive concentration predicted, Clast_pred
TLST	time of last positive concentration, Tlast
LAMZHL	half-life by lambda z, ln(2)/LAMZ
LAMZ	lambda_z negative of best fit terminal slope
LAMZLL	earliest time for LAMZ
LAMZUL	last time for LAMZ
LAMZNPT	number of points for LAMZ
CORRXY	correlation of log(concentration) and time
R2	R-squared
R2ADJ	R-squared adjusted

C0	back extrapolated concentration at time 0, for bolus intravascular administration only
AUCLST	AUC from 0 to TLST
AUCALL	AUC using all the given points, including trailing zero concentrations
AUCIFO	AUC infinity observed
AUCIFOD	AUCIFO / Dose
AUCIFP	AUC infinity predicted using CLSTP instead of CLST
AUCIFPD	AUCIFP / Dose
AUCPEO	AUC % extrapolation observed
AUCPEP	AUC % extrapolated for AUCIFP
AUCPBEO	AUC % back extrapolation observed, for bolus IV administration only
AUCPBEP	AUC % back extrapolation predicted with AUCIFP, for bolus IV administration only
AUMCLST	AUMC to the TLST
AUMCIFO	AUMC infinity observed using CLST
AUMCIFP	AUMC infinity determined by CLSTP
AUMCPEO	AUMC % extrapolated observed
AUMCPEP	AUMC % extrapolated predicted
MRTIVLST	mean residence time (MRT) to TLST, for intravascular administration
MRTIVIFO	mean residence time (MRT) infinity using CLST, for intravascular administration
MRTIVIFP	mean residence time (MRT) infinity using CLSTP, for intravascular administration
MRTEVLST	mean residence time (MRT) to TLST, for extravascular administration
MRTEVIFO	mean residence time (MRT) infinity using CLST, for extravascular administration
MRTEVIFP	mean residence time (MRT) infinity using CLSTP, for extravascular administration
VZO	volume of distribution determined by LAMZ and AUCIFO, for intravascular administration
VZP	volume of distribution determined by LAMZ and AUCIFP, for intravascular administration
VZFO	VZO for extravascular administration, VZO/F, F is bioavailability
VZFP	VZP for extravascular administration, VZP/F, F is bioavailability
CLO	clearance using AUCIFO, for intravascular administration
CLP	clearance using AUCIFP, for intravascular administration
CLFO	CLO for extravascular administration, CLO/F, F is bioavailability
CLFP	CLP for extravascular administration, CLP/F, F is bioavailability
VSSO	volume of distribution at steady state using CLST, for intravascular administration only
VSSP	volume of distribution at stead state using CLSTP, for intravascular administration only

Author(s)

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References

1. Gabrielsson J, Weiner D. Pharmacokinetic and Pharmacodynamic Data Analysis - Concepts and Applications. 5th ed. 2016.
2. Shargel L, Yu A. Applied Biopharmaceutics and Pharmacokinetics. 7th ed. 2015.
3. Rowland M, Tozer TN. Clinical Pharmacokinetics and Pharmacodynamics - Concepts and Applications. 4th ed. 2011.
4. Gibaldi M, Perrier D. Pharmacokinetics. 2nd ed. revised and expanded. 1982.

See Also

sNCA

Examples

```
# Theoph and Indometh data: dose in mg, conc in mg/L, time in h
NCA(Theoph, "Subject", "Time", "conc", dose=320, uConc="mg/L")
NCA(Indometh, "Subject", "time", "conc", dose=25, adm="Bolus", uConc="mg/L")

iAUC = data.frame(Name=c("AUC[0-12h]","AUC[0-24h]"), Start=c(0,0), End=c(12,24)) ; iAUC
NCA(Theoph, "Subject", "Time", "conc", dose=320, iAUC=iAUC, uConc="mg/L")
NCA(Indometh, "Subject", "time", "conc", dose=25, adm="Bolus", iAUC=iAUC, uConc="mg/L")

# writeLines(NCA(Theoph, "Subject", "Time", "conc", dose=320, report="Text", uConc="mg/L"),
#            "Theoph_Linear_CoreOutput.txt")
# writeLines(NCA(Theoph, "Subject", "Time", "conc", dose=320, fit="Log", report="Text",
#            uConc="mg/L"), "Theoph_Log_CoreOutput.txt")
# writeLines(NCA(Indometh, "Subject", "time", "conc", dose=25, adm="Bolus", report="Text",
#            uConc="mg/L"), "Indometh_Bolus_Linear_CoreOutput.txt")
# writeLines(NCA(Indometh, "Subject", "time", "conc", dose=25, adm="Bolus", fit="Log",
#            report="Text", uConc="mg/L"), "Indometh_Bolus_Log_CoreOutput.txt")
# writeLines(NCA(Indometh, "Subject", "time", "conc", dose=25, adm="Infusion", dur=0.25,
#            report="Text", uConc="mg/L"), "Indometh_Infusion_Linear_CoreOutput.txt")
# writeLines(NCA(Indometh, "Subject", "time", "conc", dose=25, adm="Infusion", dur=0.25,
#        fit="Log", report="Text", uConc="mg/L"), "Indometh_Infusion_Log_CoreOutput.txt")
```

NCA0 *NCA of SDTM data for single subject*

Description

This performs Noncompartmental Analysis(NCA) for one dosing record from the CDISC EX and PC domain.

Usage

```
NCA0(EX0, PC0, fit="Linear", excludeInfusion=TRUE, label="")
```

Arguments

EX0	One EX record: a named character vector, a one-row data.frame or a one-row matrix. It needs the names EXDOSE, EXDOSU, EXROUTE, EXSTDTC and EXENDTC.
PC0	The concentration records of that dosing interval, with the columns PCDTC, PCSTRESN and PCSTRESU
fit	either of "Linear" or "Log" to indicate the way to calculate AUC and AUMC
excludeInfusion	when the administration is an infusion, estimate the terminal slope from post-infusion samples only; TRUE by default. See rNCA for what this changes.
label	identifier used only in warning messages

Details

The administration method is taken from EXROUTE first: an EXROUTE of "INTRAVENOUS" gives "Infusion" when EXENDTC is later than EXSTDTC and "Bolus" otherwise, and any other route gives "Extravascular". Time after dose is computed from EXSTDTC and negative values are set to zero, so a pre-dose sample is placed at time zero.

This calls sNCA. This is called by rNCA function.

Value

This returns a named character vector: AdmMethod, Dose, UnitDose, Dur, UnitTime, UnitConc, followed by the NCA parameters. Which parameters are present depends on the administration method.

Author(s)

Kyun-Seop Bae <k@acr.kr>

See Also

help, rNCA, sNCA

---

pdfNCA *NCA output to pdf file*

Description

This output NCA result in a pdf file.

Usage

```
pdfNCA(fileName = "Temp-NCA.pdf", concData, colSubj = "Subject", colTime = "Time",
      colConc = "conc", dose = 0, adm = "Extravascular", dur = 0, doseUnit = "mg",
       timeUnit = "h", concUnit = "ug/L", down="Linear", MW = 0,
       SS = FALSE, tau = NA, unitTau = "h")
```

Arguments

fileName	file name to save
concData	concentration data table
colSubj	column name for subject ID
colTime	column name for time
colConc	column name for concentration
dose	administered dose
adm	one of "Bolus" or "Infusion" or "Extravascular" to indicate drug administration mode
dur	duration of infusion
doseUnit	unit of dose
timeUnit	unit of time
concUnit	unit of concentration
down	either of "Linear" or "Log" to indicate the way to calculate AUC and AUMC
MW	molecular weight of drug
SS	if steady-state, this should be TRUE and tau must be given. AUCTAU (AUC over one dosing interval, 0 to tau) is then used instead of AUCIFO for the calculation of Vz (VZFO, VZO) and CL (CLFO, CLO), CMAX and TMAX are taken from the samples within the dosing interval, the MRT to infinity is (AUMC from 0 to tau + tau * (AUCinf - AUCTAU)) / AUCTAU, Vdss (VSSO, VSSP) is that MRT times CLO, and AUCTAU and CAVG are reported.
tau	dosing interval, a positive scalar in the unit of unitTau, applied to every subject. Required when SS = TRUE.
unitTau	unit of tau: "h" (default), "min", "s", "d", "wk" or their common spellings. tau is converted into timeUnit before use.

Value

CMAX	maximum concentration, Cmax
CMAXD	dose normalized Cmax, CMAX / Dose, Cmax / Dose
TMAX	time of maximum concentration, Tmax
TLAG	time to observe the first non-zero concentration, for extravascular administration only
CLST	last positive concentration observed, Clast
CLSTP	last positive concentration predicted, Clast_pred
TLST	time of last positive concentration, Tlast
LAMZHL	half-life by lambda z, ln(2)/LAMZ
LAMZ	lambda_z negative of best fit terminal slope
LAMZLL	earliest time for LAMZ
LAMZUL	last time for LAMZ
LAMZNPT	number of points for LAMZ
CORRXY	correlation of log(concentration) and time
R2	R-squared

R2ADJ	R-squared adjusted
C0	back extrapolated concentration at time 0, for bolus intravascular administration only
AUCLST	AUC from 0 to TLST
AUCALL	AUC using all the given points, including trailing zero concentrations
AUCIFO	AUC infinity observed
AUCIFOD	AUCIFO / Dose
AUCIFP	AUC infinity predicted using CLSTP instead of CLST
AUCIFPD	AUCIFP / Dose
AUCPEO	AUC % extrapolation observed
AUCPEP	AUC % extrapolated for AUCIFP
AUCPBEO	AUC % back extrapolation observed, for bolus IV administration only
AUCPBEP	AUC % back extrapolation predicted with AUCIFP, for bolus IV administration only
AUMCLST	AUMC to the TLST
AUMCIFO	AUMC infinity observed using CLST
AUMCIFP	AUMC infinity determined by CLSTP
AUMCPEO	AUMC % extrapolated observed
AUMCPEP	AUMC % extrapolated predicted
MRTIVLST	mean residence time (MRT) to TLST, for intravascular administration
MRTIVIFO	mean residence time (MRT) infinity using CLST, for intravascular administration
MRTIVIFP	mean residence time (MRT) infinity using CLSTP, for intravascular administration
MRTEVLST	mean residence time (MRT) to TLST, for extravascular administration
MRTEVIFO	mean residence time (MRT) infinity using CLST, for extravascular administration
MRTEVIFP	mean residence time (MRT) infinity using CLSTP, for extravascular administration
VZO	volume of distribution determined by LAMZ and AUCIFO, for intravascular administration
VZP	volume of distribution determined by LAMZ and AUCIFP, for intravascular administration
VZFO	VZO for extravascular administration, VZO/F, F is bioavailability
VZFP	VZP for extravascular administration, VZP/F, F is bioavailability
CLO	clearance using AUCIFO, for intravascular administration
CLP	clearance using AUCIFP, for intravascular administration
CLFO	CLO for extravascular administration, CLO/F, F is bioavailability
CLFP	CLP for extravascular administration, CLP/F, F is bioavailability
VSSO	volume of distribution at steady state using CLST, for intravascular administration only
VSSP	volume of distribution at steady state using CLSTP, for intravascular administration only
AUCTAU	AUC over one dosing interval, from 0 to tau; with SS = TRUE only
CAVG	average concentration over the dosing interval at steady state, AUCTAU / tau; with SS = TRUE only

Author(s)

Kyun-Seop Bae <k@acr.kr>

See Also

help, txtNCA, rtfNCA

Examples

```
#pdfNCA(fileName="NCA-Theoph.pdf", Theoph, colSubj="Subject", colTime="Time",
#       colConc="conc", dose=320, doseUnit="mg", timeUnit="h", concUnit="mg/L")
#pdfNCA(fileName="NCA-Indometh.pdf", Indometh, colSubj="Subject", colTime="time",
#       colConc="conc", adm="Infusion", dur=0.5, dose=25, doseUnit="mg",
#       timeUnit="h", concUnit="mg/L")
```

---

plotFit *Plot best fit slope*

Description

Automatically select best fit slope for the given x(usually time) and log(y)(usually concentration) values.

Usage

```
plotFit(concData, id, Time, conc, mol = "", adm = "Extravascular", ID = "", Mol = "")
```

Arguments

concData	name of data table containing time-concentration data of multiple subjects
id	column name for subject ID
Time	column name for the time
conc	column name for the concentration
mol	column name for molecular species
adm	one of "Bolus" or "Infusion" or "Extravascular" to indicate drug administration mode
ID	Subject ID for this plot
Mol	the name of molecular species to see

Details

Find the best fit slope then plot it. Currently this function uses ordinary least square method(OLS) only. This function calles BestSlope function.

Value

R2	R-squared
R2ADJ	adjusted R-squared
LAMZNPT	number of points used for slope
LAMZ	negative of slope, lambda_z
b0	intercept of regression line
CORRXY	correlation of log(y) and x
LAMZLL	earliest x for lambda_z
LAMZUL	last x for lambda_z
CLSTP	predicted y value at last point, predicted concentration for the last time point

Author(s)

Jee Eun Lee <JeeEun.Lee@fda.hhs.gov>

See Also

BestSlope

Examples

```
plotFit(Theoph, "Subject", "Time", "conc", ID="1")
plotFit(Indometh, "Subject", "time", "conc", adm="Bolus", ID="1")
```

---

plotPK *Plot concentration vs. time curve for individuals and collectively.*

Description

Generates individual and superposed concentration vs. time curves and saves them in pdf and tiff files.

Usage

```
plotPK(concData, id, Time, conc, unitTime = "hr", unitConc = "ng/mL", trt = "",
      fit = "Linear", dose = 0, adm = "Extravascular", dur = 0, outdir = "Output",
       name = "")
```

Arguments

concData	name of data table containing time-concentration data of multiple subjects
id	column name for subject ID
Time	column name for the time
conc	column name for the concentration
unitTime	unit for the time
unitConc	unit for the concentration

trt	column name for the treatment code. This is useful for crossover study like bioequivalence trial.
fit	one of "Linear" or "Log" to indicate the way to calculate AUC
dose	administered dose. One should be careful for the unit. This can be a vector containing dose for each subject and treatment in order.
adm	one of "Bolus" or "Infusion" or "Extravascular" to indicate drug administration mode
dur	infusion duration for constant infusion, otherwise 0. This can be a vector containing values for each subject and treatment in order.
outdir	name of the folder to be used for the output files. "" means the current working directory.
name	stem used in the output file names. "" means the deparsed concData argument, sanitized so that it is a valid file name.

Details

This function generates five figures: individual linear and semi-logarithmic profiles (one pdf each, several panels per page) and pooled linear, semi-logarithmic and mean with 95% confidence interval profiles (one tiff each, or png where the R build has no tiff device).

Each subject gets its own colour and plotting symbol whatever the number of subjects, and the subject legend is drawn in a panel of its own so that it cannot overlap the curves. When there are more subjects than can be labelled legibly, the count is shown instead of an unreadable legend. Treatment panels are laid out in a grid of at most four columns, so a study with many treatments neither exhausts the figure margins nor produces an enormous raster.

Non-finite times and concentrations are dropped from the axis ranges, and the semi-logarithmic figures use only positive concentrations. The semi-logarithmic axis is aligned to whole decades enclosing the data, so a labelled tick is always visible.

This function calls NCA().

Value

Invisibly, a character vector of the paths written. The files are saved in the outdir folder.

Author(s)

Jee Eun Lee <JeeEun.Lee@fda.hhs.gov>, Kyun-Seop Bae <k@acr.kr>

See Also

NCA

Examples

```
# plotPK(Theoph, "Subject", "Time", "conc", unitTime="hr", unitConc="mg/L", dose=320)
# plotPK(Indometh, "Subject", "time", "conc", unitTime="hr", unitConc="mg/L", adm="Bolus", dose=25)
```

readEX *Read EX domain files*

Description

This reads EX domain files from the specified folders.

Usage

```
readEX(folders)
```

Arguments

folders	folders where to find EX doamin files

Details

This calls combXPT function. This is called by loadEXPC function.

Value

This returns combined table of EX doamin.

Author(s)

Kyun-Seop Bae <k@acr.kr>

See Also

help, combXPT, loadEXPC

readPC *Read PC domain files*

Description

This reads PC domain files from the specified folders.

Usage

```
readPC(folders)
```

Arguments

folders	folders where to find PC doamin files

Details

This calls combXPT function. This is called by loadEXPC function.

Value

This returns combined table of PC doamin.

Author(s)

Kyun-Seop Bae <k@acr.kr>

See Also

help, combXPT, loadEXPC

---

rNCA *Do NCA for review*

Description

This performs NCA from the CDISC EX and PC datasets.

Usage

```
rNCA(ex, pc, study = "", trt = "", id = "", analyte = "",
     codeBQL = c("< 0", "<0", "NQ", "BLQ", "BQL", "BQoL", "<LOQ"),
     fit="Linear", MinPoints = 5, excludeInfusion = TRUE)
```

Arguments

ex	EX domain data, usually from the loadEXPC
pc	PC domain data, usually form the loadEXPC
study	vector of study names in EX and PC domain to do NCA. "" means all.
trt	vector of treatment names in EXTRT to do NCA. "" means all. Placebo is always excluded, since a dose of zero has no pharmacokinetics to characterize.
id	vector of subject IDs in USUBJID to do NCA. "" means all.
analyte	vector of molecular species in PCTESTCD to do NCA. "" means all. Matching is case-insensitive.
codeBQL	symbols of below the quantitation limit
fit	either of "Linear" or "Log" to indicate the way to calculate AUC and AUMC
MinPoints	an analysis is done only when the number of quantifiable (greater than zero) concentrations in the dosing interval is strictly greater than this value. Note that this counts quantifiable concentrations, not sampling points: BQL and zero records do not count.
excludeInfusion	estimate the terminal slope of an infusion from post-infusion samples only; TRUE by default. Set FALSE for the unrestricted automatic search. See Details. No effect on a bolus or an extravascular dose.

Details

One row of result is produced for each subject, dosing interval and analyte. A dosing interval starts at its own EXSTDTC and ends at the subject's next real dose of any treatment in the same study, so that in a crossover trial the first period is not extended into the second; a placebo or zero dose delivers no drug and does not end an interval. The final interval is open-ended, so terminal and follow-up samples still contribute to the elimination phase.

The last concentration in the 24 hours before the dose is carried into the interval as the pre-dose sample, and placed at time zero. The lookback is bounded because an unbounded one would report a sample from an earlier period as this dose's initial concentration. In an interval that is followed by another dose the trailing trough is dropped when its nominal time (PCTPTNUM) equals the pre-dose one, so that it is not counted twice.

EX and PC records are sorted by date and time before use, so the result does not depend on the row order of the input. Records whose date and time cannot be read as a full `YYYY-MM-DDTHH:MM:SS` value are dropped with a warning naming the subjects affected.

The automatic terminal-slope search restricts itself to samples after the maximum concentration. That is the right rule for an extravascular dose but says nothing about an infusion, so a sample drawn while drug is still being infused can win on adjusted R-squared and be reported as terminal elimination. Because a terminal phase does not exist while drug is still going in, `excludeInfusion` defaults to `TRUE`: the search is given only the samples after the end of infusion, and the same maximum-adjusted-R-squared criterion then selects the window among them; within that window it still starts after the largest of those samples. Set `excludeInfusion=FALSE` for the unrestricted search over all samples.

Only lambda z and the parameters derived from it (half-life, AUCIFO, AUCPEO, Vz) are affected - Cmax, AUClast and the other observed parameters cannot change. When there are too few post-infusion samples to fit a slope, a warning names the profile and the unrestricted selection is used, so no profile is lost silently.

The restriction applies to this function and to `NCA0`, which know the dosing record and so the end of infusion. `sNCA` and `tblNCA` take times and concentrations without a dosing record and remain faithful wrappers around **NonCompart**; give `sNCA` an explicit `UsePoints` to fix the window there.

This calls NCA0. Results of this can be further processed by foreNCA to plot and compare between studies and dose groups.

Value

This returns a table of NCA results, or invisibly `NULL` with a warning when no subject meets the `MinPoints` criterion.

Author(s)

Kyun-Seop Bae <k@acr.kr>

See Also

`help`, `NCA0`, `loadEXPC`, `foreNCA`

Round *Round Half Away from Zero*

Description

This is an ordinary rounding function, so called round half away from zero

Usage

```
Round(x, n = 0)
```

Arguments

x	numeric to be rounded
n	indicating decimal digits

Details

The function round in R base rounds to the even number, i.e. `round(0.5)` is 0 not 1. If you want rounding 0.5 be 1, you can use this Round function. This function is for the consistency with other software like MS-Excel, SAS.

Value

ordinarily rounded value

Author(s)

Kyun-Seop Bae <k@acr.kr>

References

See wikipedia subject "Rounding"

Examples

```
(x = 1:10 - 0.5)
Round(x)
round(x) # compare with the above
```

RptCfg *NCA Report Configuation Table*

Description

Contains the names and order of colum of return table/text by IndiNCA and NCA functions

Usage

```
RptCfg
```

Format

A data frame with 50 observations on the following 10 variables.

PPTESTCD a character vector of CDISC SDTM PPTESTCD

SYNONYM a character vector of CDISC SDTM PPTESTCD Synonym

NCI a character vector of NCI peferred terms

WNL a character vector of WinNonlin(R) software variables

ExtravascularDefault a numeric vector of ordering in report for extravascular administration, Zero means exclusion in the report.

ExtravascularWNL a numeric vector of ordering in report in the style of the WNL variables for extravascular administration, Zero means exclusion in the report.

BolusDefault a numeric vector of ordering in report for extravascular administration, Zero means exclusion in the report.

BolusWNL a numeric vector of ordering in report in the style of the WNL variables for extravascular administration, Zero means exclusion in the report.

InfusionDefault a numeric vector of ordering in report for extravascular administration, Zero means exclusion in the report.

InfusionWNL a numeric vector of ordering in report in the style of the WNL variables for extravascular administration, Zero means exclusion in the report.

Details

This table should exist in pkr package. User can edit this table for shaping the report in one's own style.

rtfNCA *NCA output to rtf file*

Description

This output NCA result in a rtf file.

Usage

```
rtfNCA(fileName = "Temp-NCA.rtf", concData, colSubj = "Subject", colTime = "Time",
      colConc = "conc", dose = 0, adm = "Extravascular", dur = 0, doseUnit = "mg",
       timeUnit = "h", concUnit = "ug/L", down="Linear", MW = 0,
       SS = FALSE, tau = NA, unitTau = "h")
```

Arguments

fileName	file name to save
concData	concentration data table
colSubj	column name for subject ID
colTime	column name for time
colConc	column name for concentration
dose	administered dose
adm	one of "Bolus" or "Infusion" or "Extravascular" to indicate drug administration mode
dur	duration of infusion
doseUnit	unit of dose
timeUnit	unit of time
concUnit	unit of concentration
down	either of "Linear" or "Log" to indicate the way to calculate AUC and AUMC
MW	molecular weight of drug
SS	if steady-state, this should be TRUE and tau must be given. AUCTAU (AUC over one dosing interval, 0 to tau) is then used instead of AUCIFO for the calculation of Vz (VZFO, VZO) and CL (CLFO, CLO), CMAX and TMAX are taken from the samples within the dosing interval, the MRT to infinity is (AUMC from 0 to tau + tau * (AUCinf - AUCTAU)) / AUCTAU, Vdss (VSSO, VSSP) is that MRT times CLO, and AUCTAU and CAVG are reported.
tau	dosing interval, a positive scalar in the unit of unitTau, applied to every subject. Required when SS = TRUE.
unitTau	unit of tau: "h" (default), "min", "s", "d", "wk" or their common spellings. tau is converted into timeUnit before use.

Value

CMAX	maximum concentration, Cmax
CMAXD	dose normalized Cmax, CMAX / Dose, Cmax / Dose
TMAX	time of maximum concentration, Tmax
TLAG	time to observe the first non-zero concentration, for extravascular administration only
CLST	last positive concentration observed, Clast
CLSTP	last positive concentration predicted, Clast_pred
TLST	time of last positive concentration, Tlast
LAMZHL	half-life by lambda z, ln(2)/LAMZ
LAMZ	lambda_z negative of best fit terminal slope
LAMZLL	earliest time for LAMZ
LAMZUL	last time for LAMZ
LAMZNPT	number of points for LAMZ
CORRXY	correlation of log(concentration) and time
R2	R-squared
R2ADJ	R-squared adjusted
C0	back extrapolated concentration at time 0, for bolus intravascular administration only
AUCLST	AUC from 0 to TLST
AUCALL	AUC using all the given points, including trailing zero concentrations
AUCIFO	AUC infinity observed
AUCIFOD	AUCIFO / Dose
AUCIFP	AUC infinity predicted using CLSTP instead of CLST
AUCIFPD	AUCIFP / Dose
AUCPEO	AUC % extrapolation observed
AUCPEP	AUC % extrapolated for AUCIFP
AUCPBEO	AUC % back extrapolation observed, for bolus IV administration only
AUCPBEP	AUC % back extrapolation predicted with AUCIFP, for bolus IV administration only
AUMCLST	AUMC to the TLST
AUMCIFO	AUMC infinity observed using CLST
AUMCIFP	AUMC infinity determined by CLSTP
AUMCPEO	AUMC % extrapolated observed
AUMCPEP	AUMC % extrapolated predicted
MRTIVLST	mean residence time (MRT) to TLST, for intravascular administration
MRTIVIFO	mean residence time (MRT) infinity using CLST, for intravascular administration
MRTIVIFP	mean residence time (MRT) infinity using CLSTP, for intravascular administration
MRTEVLST	mean residence time (MRT) to TLST, for extravascular administration

MRTEVIFO	mean residence time (MRT) infinity using CLST, for extravascular administration
MRTEVIFP	mean residence time (MRT) infinity using CLSTP, for extravascular administration
VZO	volume of distribution determined by LAMZ and AUCIFO, for intravascular administration
VZP	volume of distribution determined by LAMZ and AUCIFP, for intravascular administration
VZFO	VZO for extravascular administration, VZO/F, F is bioavailability
VZFP	VZP for extravascular administration, VZP/F, F is bioavailability
CLO	clearance using AUCIFO, for intravascular administration
CLP	clearance using AUCIFP, for intravascular administration
CLFO	CLO for extravascular administration, CLO/F, F is bioavailability
CLFP	CLP for extravascular administration, CLP/F, F is bioavailability
VSSO	volume of distribution at steady state using CLST, for intravascular administration only
VSSP	volume of distribution at steady state using CLSTP, for intravascular administration only
AUCTAU	AUC over one dosing interval, from 0 to tau; with SS = TRUE only
CAVG	average concentration over the dosing interval at steady state, AUCTAU / tau; with SS = TRUE only

Author(s)

Kyun-Seop Bae <k@acr.kr>

See Also

help, txtNCA, pdfNCA

Examples

```
#rtfNCA(fileName="NCA-Theoph.rtf", Theoph, colSubj="Subject", colTime="Time",
#       colConc="conc", dose=320, doseUnit="mg", timeUnit="h", concUnit="mg/L")
#rtfNCA(fileName="NCA-Indometh.rtf", Indometh, colSubj="Subject", colTime="time",
#       colConc="conc", adm="Infusion", dur=0.5, dose=25, doseUnit="mg",
#       timeUnit="h", concUnit="mg/L")
```

Slope *Get the Slope of regression log(y) ~ x*

Description

It calculates the slope with linear regression of log(y) ~ x

Usage

```
Slope(x, y)
```

Arguments

x	vector values of independent variable, usually time
y	vector values of dependent variable, usually concentration

Details

With time-concentration curve, you frequently need to estimate slope in log(concentration) ~ time. This function is usually called by `BestSlope` function and you seldom need to call this function directly.

Value

R2	R-squared
R2ADJ	adjusted R-squared
LAMZNPT	number of points used for slope
LAMZ	negative of slope, lambda_z
b0	intercept of regression line
CORRXY	correlation of log(y) and x
LAMZLL	earliest x for lambda_z
LAMZUL	last x for lambda_z
CLSTP	predicted y value at last point, predicted concentration for the last time point

Author(s)

Kyun-Seop Bae <k@acr.kr>

See Also

`BestSlope`

Examples

```
Slope(Indometh[Indometh$Subject==1, "time"], Indometh[Indometh$Subject==1, "conc"])
```

---

sNCA *Simplest NCA*

Description

This is the work-horse function for NCA.

Usage

```
sNCA(x, y, dose = 0, adm = "Extravascular", dur = 0, doseUnit = "mg", timeUnit = "h",
     concUnit = "ug/L", iAUC = "", down = "Linear", MW = 0, returnNA = TRUE,
     UsePoints = NULL, SS = FALSE, tau = NA, unitTau = "h")
```

Arguments

x	usually time
y	usually concentration
dose	given amount
adm	one of "Bolus" or "Infusion" or "Extravascular" to indicate drug administration mode
dur	duration of infusion
doseUnit	unit of dose
timeUnit	unit of time
concUnit	unit of concentration
iAUC	interval AUCs to calculate
down	either of "Linear" or "Log" to indicate the way to calculate AUC and AUMC
MW	molecular weight of the drug
returnNA	if returnNA is TRUE, it returns NA values also.
UsePoints	indices into x and y, counted after non-finite points are dropped, to be used for the terminal slope in place of the automatic search. NULL leaves the automatic selection in place. y at those indices must be positive.
SS	if steady-state, this should be TRUE and tau must be given. AUCTAU (AUC over one dosing interval, 0 to tau) is then used instead of AUCIFO for the calculation of Vz (VZFO, VZO) and CL (CLFO, CLO), CMAX and TMAX are taken from the samples within the dosing interval, the MRT to infinity is (AUMC from 0 to tau + tau * (AUCinf - AUCTAU)) / AUCTAU, Vdss (VSSO, VSSP) is that MRT times CLO, and AUCTAU and CAVG are returned. The Pred-based twins of Vz and CL (VZFP, CLFP, VZP, CLP) are NA at steady state. Passed through to sNCA.
tau	dosing interval, a positive scalar in the unit of unitTau. Required when SS = TRUE; ignored, with a warning, otherwise.
unitTau	unit of tau: "h" (default), "min", "s", "d", "wk" or their common spellings. tau is converted into timeUnit before use.

Details

This will replace IndiNCA. With returnNA = TRUE the result is the fixed 50-parameter vector; AUCTAU and CAVG occupy the last two positions, so the first 48 positions are those of earlier versions.

Value

CMAX	maximum concentration, Cmax
CMAXD	dose normalized Cmax, CMAX / Dose, Cmax / Dose
TMAX	time of maximum concentration, Tmax
TLAG	time to observe the first non-zero concentration, for extravascular administration only
CLST	last positive concentration observed, Clast
CLSTP	last positive concentration predicted, Clast_pred
TLST	time of last positive concentration, Tlast

LAMZHL	half-life by lambda z, ln(2)/LAMZ
LAMZ	lambda_z negative of best fit terminal slope
LAMZLL	earliest time for LAMZ
LAMZUL	last time for LAMZ
LAMZNPT	number of points for LAMZ
CORRXY	correlation of log(concentration) and time
R2	R-squared
R2ADJ	R-squared adjusted
C0	back extrapolated concentration at time 0, for bolus intravascular administration only
AUCLST	AUC from 0 to TLST
AUCALL	AUC using all the given points, including trailing zero concentrations
AUCIFO	AUC infinity observed
AUCIFOD	AUCIFO / Dose
AUCIFP	AUC infinity predicted using CLSTP instead of CLST
AUCIFPD	AUCIFP / Dose
AUCPEO	AUC % extrapolation observed
AUCPEP	AUC % extrapolated for AUCIFP
AUCPBEO	AUC % back extrapolation observed, for bolus IV administration only
AUCPBEP	AUC % back extrapolation predicted with AUCIFP, for bolus IV administration only
AUMCLST	AUMC to the TLST
AUMCIFO	AUMC infinity observed using CLST
AUMCIFP	AUMC infinity determined by CLSTP
AUMCPEO	AUMC % extrapolated observed
AUMCPEP	AUMC % extrapolated predicted
MRTIVLST	mean residence time (MRT) to TLST, for intravascular administration
MRTIVIFO	mean residence time (MRT) infinity using CLST, for intravascular administration
MRTIVIFP	mean residence time (MRT) infinity using CLSTP, for intravascular administration
MRTEVLST	mean residence time (MRT) to TLST, for extravascular administration
MRTEVIFO	mean residence time (MRT) infinity using CLST, for extravascular administration
MRTEVIFP	mean residence time (MRT) infinity using CLSTP, for extravascular administration
VZO	volume of distribution determined by LAMZ and AUCIFO, for intravascular administration
VZP	volume of distribution determined by LAMZ and AUCIFP, for intravascular administration
VZFO	VZO for extravascular administration, VZO/F, F is bioavailability
VZFP	VZP for extravascular administration, VZP/F, F is bioavailability

CLO	clearance using AUCIFO, for intravascular administration
CLP	clearance using AUCIFP, for intravascular administration
CLFO	CLO for extravascular administration, CLO/F, F is bioavailability
CLFP	CLP for extravascular administration, CLP/F, F is bioavailability
VSSO	volume of distribution at steady state using CLST, for intravascular administration only
VSSP	volume of distribution at steady state using CLSTP, for intravascular administration only
AUCTAU	AUC over one dosing interval, from 0 to tau; with SS = TRUE only
CAVG	average concentration over the dosing interval at steady state, AUCTAU / tau; with SS = TRUE only

Author(s)

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References

Gabrielsson J, Weiner D. Pharmacokinetic and Pharmacodynamic Data Analysis - Concepts and Applications. 5th ed. 2016.

See Also

help, tblNCA

Examples

```
# For one subject
x = Theoph[Theoph$Subject=="1","Time"]
y = Theoph[Theoph$Subject=="1","conc"]

sNCA(x, y, dose=320, doseUnit="mg", concUnit="mg/L", timeUnit="h")
sNCA(x, y, dose=320, concUnit="mg/L", returnNA=FALSE)

iAUC = data.frame(Name=c("AUC[0-12h]","AUC[0-24h]"), Start=c(0,0), End=c(12,24))
sNCA(x, y, dose=320, doseUnit="mg", concUnit="mg/L", timeUnit="h", iAUC=iAUC)

MW = 180.164 # Molecular weight of theophylline

sNCA(x, y/MW, dose=320, doseUnit="mg", concUnit="mmol/L", timeUnit="h")
sNCA(x, y/MW, dose=320, doseUnit="mg", concUnit="mmol/L", timeUnit="h", MW=MW)
sNCA(x, y, dose=320/MW, doseUnit="mmol", concUnit="mg/L", timeUnit="h", MW=MW)
sNCA(x, y/MW, dose=320/MW, doseUnit="mmol", concUnit="mmol/L", timeUnit="h", MW=MW)

sNCA(x, y/MW, dose=320/MW, doseUnit="mmol", concUnit="mmol/L", timeUnit="h", MW=MW,
     returnNA=FALSE)
sNCA(x, y/MW, doseUnit="mmol", concUnit="mmol/L", timeUnit="h", MW=MW, returnNA=FALSE)
sNCA(x, y/MW, dose=as.numeric(NA), doseUnit="mmol", concUnit="mmol/L", timeUnit="h",
     MW=MW, returnNA=FALSE)

sNCA(x, y, dose=320, concUnit="mg/L", timeUnit="hr")
sNCA(x*60, y, dose=320, concUnit="mg/L", timeUnit="min")
```

tblNCA *Table output NCA*

Description

do multiple NCA and returns a result table.

Usage

```
tblNCA(concData, key = "Subject", colTime = "Time", colConc = "conc", dose = 0,
       adm = "Extravascular", dur = 0, doseUnit = "mg", timeUnit = "h",
       concUnit = "ug/L", down = "Linear", MW = 0, returnNA = FALSE,
       SS = FALSE, tau = NA, unitTau = "h")
```

Arguments

concData	concentration data table
key	column names of concData to be shown at the output table
colTime	column name for time
colConc	column name for concentration
dose	administered dose
adm	one of "Bolus" or "Infusion" or "Extravascular" to indicate drug administration mode
dur	duration of infusion
doseUnit	unit of dose
timeUnit	unit of time
concUnit	unit of concentration
down	method to calculate AUC, "Linear" or "Log"
MW	molecular weight of drug
returnNA	if returnNA is TRUE, it returns NA values also.
SS	if steady-state, this should be TRUE and tau must be given. AUCTAU (AUC over one dosing interval, 0 to tau) is then used instead of AUCIFO for the calculation of Vz (VZFO, VZO) and CL (CLFO, CLO), CMAX and TMAX are taken from the samples within the dosing interval, the MRT to infinity is (AUMC from 0 to tau + tau * (AUCinf - AUCTAU)) / AUCTAU, Vdss (VSSO, VSSP) is that MRT times CLO, and the columns AUCTAU and CAVG are added. Passed through to tblNCA.
tau	dosing interval in the unit of unitTau, a positive scalar or one value per NCA (subject). Required when SS = TRUE; ignored, with a warning, otherwise.
unitTau	unit of tau: "h" (default), "min", "s", "d", "wk" or their common spellings. tau is converted into timeUnit before use.

Value

Basically same with sNCA

Author(s)

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See Also

help, sNCA

Examples

```
tblNCA(Theoph, key="Subject", dose=320, concUnit="mg/L")
tblNCA(Indometh, key="Subject", colTime="time", colConc="conc", dose=25,
       adm="Infusion", dur=0.5, concUnit="mg/L")
```

---

txtNCA *Text output of NCA for one subject*

Description

This is the text form output.

Usage

```
txtNCA(x, y, dose = 0, adm = "Extravascular", dur = 0, doseUnit = "mg", timeUnit = "h",
       concUnit = "ug/L", iAUC = "", down="Linear", MW = 0, returnNA = FALSE,
       SS = FALSE, tau = NA, unitTau = "h")
```

Arguments

x	usually time
y	usually concentration
dose	given amount
adm	one of "Bolus" or "Infusion" or "Extravascular" to indicate drug administration mode
dur	duration of infusion
doseUnit	unit of dose
timeUnit	unit of time
concUnit	unit of concentration
iAUC	interval AUCs to calculate
down	either of "Linear" or "Log" to indicate the way to calculate AUC and AUMC
MW	molecular weight of the drug
returnNA	if returnNA is TRUE, it returns NA values also.
SS	if steady-state, this should be TRUE and tau must be given. AUCTAU (AUC over one dosing interval, 0 to tau) is then used instead of AUCIFO for the calculation of Vz (VZFO, VZO) and CL (CLFO, CLO), CMAX and TMAX are taken from the samples within the dosing interval, the MRT to infinity is (AUMC from 0 to tau + tau * (AUCinf - AUCTAU)) / AUCTAU, Vdss (VSSO, VSSP) is that MRT times CLO, and AUCTAU and CAVG are reported. The report states the dosing interval it used.

tau	dosing interval, a positive scalar in the unit of unitTau. Required when SS = TRUE; ignored, with a warning, otherwise.
unitTau	unit of tau: "h" (default), "min", "s", "d", "wk" or their common spellings. tau is converted into timeUnit before use.

Value

CMAX	maximum concentration, Cmax
CMAXD	dose normalized Cmax, CMAX / Dose, Cmax / Dose
TMAX	time of maximum concentration, Tmax
TLAG	time to observe the first non-zero concentration, for extravascular administration only
CLST	last positive concentration observed, Clast
CLSTP	last positive concentration predicted, Clast_pred
TLST	time of last positive concentration, Tlast
LAMZHL	half-life by lambda z, ln(2)/LAMZ
LAMZ	lambda_z negative of best fit terminal slope
LAMZLL	earliest time for LAMZ
LAMZUL	last time for LAMZ
LAMZNPT	number of points for LAMZ
CORRXY	correlation of log(concentration) and time
R2	R-squared
R2ADJ	R-squared adjusted
C0	back extrapolated concentration at time 0, for bolus intravascular administration only
AUCLST	AUC from 0 to TLST
AUCALL	AUC using all the given points, including trailing zero concentrations
AUCIFO	AUC infinity observed
AUCIFOD	AUCIFO / Dose
AUCIFP	AUC infinity predicted using CLSTP instead of CLST
AUCIFPD	AUCIFP / Dose
AUCPEO	AUC % extrapolation observed
AUCPEP	AUC % extrapolated for AUCIFP
AUCPBEO	AUC % back extrapolation observed, for bolus IV administration only
AUCPBEP	AUC % back extrapolation predicted with AUCIFP, for bolus IV administration only
AUMCLST	AUMC to the TLST
AUMCIFO	AUMC infinity observed using CLST
AUMCIFP	AUMC infinity determined by CLSTP
AUMCPEO	AUMC % extrapolated observed
AUMCPEP	AUMC % extrapolated predicted
MRTIVLST	mean residence time (MRT) to TLST, for intravascular administration

MRTIVIFO	mean residence time (MRT) infinity using CLST, for intravascular administration
MRTIVIFP	mean residence time (MRT) infinity using CLSTP, for intravascular administration
MRTEVLST	mean residence time (MRT) to TLST, for extravascular administration
MRTEVIFO	mean residence time (MRT) infinity using CLST, for extravascular administration
MRTEVIFP	mean residence time (MRT) infinity using CLSTP, for extravascular administration
VZO	volume of distribution determined by LAMZ and AUCIFO, for intravascular administration
VZP	volume of distribution determined by LAMZ and AUCIFP, for intravascular administration
VZFO	VZO for extravascular administration, VZO/F, F is bioavailability
VZFP	VZP for extravascular administration, VZP/F, F is bioavailability
CLO	clearance using AUCIFO, for intravascular administration
CLP	clearance using AUCIFP, for intravascular administration
CLFO	CLO for extravascular administration, CLO/F, F is bioavailability
CLFP	CLP for extravascular administration, CLP/F, F is bioavailability
VSSO	volume of distribution at steady state using CLST, for intravascular administration only
VSSP	volume of distribution at steady state using CLSTP, for intravascular administration only
AUCTAU	AUC over one dosing interval, from 0 to tau; with SS = TRUE only
CAVG	average concentration over the dosing interval at steady state, AUCTAU / tau; with SS = TRUE only

Author(s)

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See Also

help, pdfNCA, rtfNCA

Examples

```
# For one subject
txtNCA(Theoph[Theoph$Subject=="1","Time"], Theoph[Theoph$Subject=="1","conc"],
       dose=320, doseUnit="mg", concUnit="mg/L", timeUnit="h")

# or equivalently
x = Theoph[Theoph$Subject=="1","Time"]
y = Theoph[Theoph$Subject=="1","conc"]
txtNCA(x, y, dose=320, doseUnit="mg", concUnit="mg/L", timeUnit="h")

# For all subjects
IDs = sort(as.numeric(unique(Theoph[,"Subject"])))
nID = length(IDs)
```

```
Res = vector()
for (i in 1:nID) {
  tRes = txtNCA(Theoph[Theoph[,"Subject"]==IDs[i],"Time"],
                Theoph[Theoph[,"Subject"]==IDs[i],"conc"],
                dose=320, concUnit="mg/L", returnNA=FALSE)
  tRes = c(paste("ID =", IDs[i]), tRes, "")
  Res = c(Res, tRes)
}
Res
```

`Unit` *Disply CDISC standard units and multiplied factor of NCA results*

Description

It displays CDISC PP output units and multiplication factor for them.

Usage

```
Unit(code = "", timeUnit = "h", concUnit = "ng/mL", doseUnit = "mg", MW = 0)
```

Arguments

`code`	vector of PPTESTCD
`timeUnit`	unit of time
`concUnit`	unit of concentration
`doseUnit`	unit of dose
`MW`	molecular weight of drug

Value

`row names`	PPTESTCD
`Unit`	unit
`Factor`	internal mulitpilcation factor

Author(s)

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Examples

```
Unit(concUnit="ug/L", doseUnit="mg")
Unit(concUnit="ng/L", doseUnit="mg")

Unit(concUnit="umol/L", doseUnit="mmol")
Unit(concUnit="nmol/L", doseUnit="mmol")

Unit(concUnit="mmol/L", doseUnit="mg", MW=500)
Unit(concUnit="umol/L", doseUnit="mg", MW=500)
Unit(concUnit="nmol/L", doseUnit="mg", MW=500)
Unit(concUnit="nmol/mL", doseUnit="mg", MW=500)
```

```
Unit(concUnit="ug/L", doseUnit="mmol", MW=500)
Unit(concUnit="ug/L", doseUnit="mol", MW=500)
Unit(concUnit="ng/L", doseUnit="mmol", MW=500)
Unit(concUnit="ng/mL", doseUnit="mmol", MW=500)

Unit(concUnit="nmol/L", doseUnit="mg")
Unit(concUnit="ug/L", doseUnit="mmol")
```

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