

Package ‘pkr’

July 10, 2017

Version 0.1.1

Date 2017-07-10

Title Pharmacokinetics in R

Description Conduct a noncompartmental analysis as closely as possible to the most widely used commercial software for pharmacokinetic analysis, i.e. 'Phoenix(R) WinNonlin(R)' <<https://www.certara.com/software/pkpd-modeling-and-simulation/phoenix-winnonlin/>>. Some features are

- 1) CDISC SDTM terms
- 2) Automatic slope selection with the same criterion of WinNonlin(R)
- 3) Supporting both 'linear-up linear-down' and 'linear-up log-down' method
- 4) Interval(partial) AUCs with 'linear' or 'log' interpolation method

* Reference: Gabrielsson J, Weiner D. Pharmacokinetic and Pharmacodynamic Data Analysis - Concepts and Applications. 5th ed. 2016. (ISBN:9198299107).

Depends R (>= 2.0.0), foreign, binr, forestplot

Author Kyun-Seop Bae [aut], Jee Eun Lee [aut]

Maintainer Kyun-Seop Bae <k@acr.kr>

Copyright 2017, Kyun-Seop Bae, Jee Eun Lee

License GPL-3

NeedsCompilation no

Repository CRAN

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

Date/Publication 2017-07-10 05:02:21 UTC

R topics documented:

pkr-package	2
AUC	3
BestSlope	4
combXPT	6
foreNCA	6
IndiNCA	7

IntAUC	10
Interpol	11
LinAUC	12
loadEXPC	13
LogAUC	14
NCA	15
NCA0	18
plotFit	19
plotPK	20
readEX	22
readPC	22
rNCA	23
Round	24
RptCfg	25
Slope	26
unit	27
Index	28

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)

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

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")

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")

```

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, fit = "Linear")
```

Arguments

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

Details

fit="Linear" means linear trapezoidal rule with linear interpolation. fit="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"]) # Default is "Linear"
AUC(Theoph[Theoph$Subject==1, "Time"],Theoph[Theoph$Subject==1, "conc"], fit="Log")
```

BestSlope

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

Description

It sequentially fits ($\log(y) \sim x$) 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 than $1e-4$, it chooses longer slope.

Usage

```
BestSlope(x, y, adm = "Extravascular")
```

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

Details

Choosing the best terminal slope (y in log scale) in pharmacokinetic analysis is somewhat challenging, and it could vary by analysis performer. Currently this function uses ordinary least square method(OLS) only.

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

<code>folders</code>	where to find specified CDISC domain XPT files
<code>domain</code>	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 compare
PCTestCD	Molecular species to compare specified in PCTestCD of CDISC SDTM PC domain
title	Title of the plot
...	further arguments to pass to the forestplot function

Details

This function 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

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 intervals 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

C _{MAX}	maximum concentration, C _{max}
C _{MAXD}	dose normalized C _{max} , C _{MAX} / Dose, C _{max} / Dose
T _{MAX}	time of maximum concentration, T _{max}
T _{LAG}	time to observe the first non-zero concentration, for extravascular administration only
CL _{ST}	last positive concentration observed, C _{last}
CL _{STP}	last positive concentration predicted, C _{last_pred}
T _{LST}	time of last positive concentration, T _{last}
L _{AMZHL}	half-life by lambda z, ln(2)/L _{AMZ}
L _{AMZ}	lambda_z negative of best fit terminal slope
L _{AMZLL}	earliest time for L _{AMZ}
L _{AMZUL}	last time for L _{AMZ}
L _{AMZNPT}	number of points for L _{AMZ}
C _{ORRXY}	correlation of log(concentration) and time
R ²	R-squared
R ² _{ADJ}	R-squared adjusted
C ₀	back extrapolated concentration at time 0, for bolus intravascular administration only
AUC _{LST}	AUC from 0 to T _{LST}
AUC _{ALL}	AUC using all the given points, including trailing zero concentrations
AUC _{IFO}	AUC infinity observed
AUC _{IFO} _D	AUC _{IFO} / Dose
AUC _{IFP}	AUC infinity predicted using CL _{STP} instead of CL _{ST}
AUC _{IFP} _D	AUC _{IFP} / Dose
AUC _{PEO}	AUC % extrapolation observed
AUC _{PEP}	AUC % extrapolated for AUC _{IFP}

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

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, fit = "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
fit	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 Method.

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 = IndiNCA(Theoph[Theoph$Subject==1,"Time"], Theoph[Theoph$Subject==1, "conc"], dose=320)
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, fit = "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 $\log(y) \sim x$
b0	y value of just left point of xnew
fit	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, fit="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 domain 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"], fit="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 IndiNCA 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

C _{MAX}	maximum concentration, C _{max}
C _{MAXD}	dose normalized C _{max} , C _{MAX} / Dose, C _{max} / Dose
T _{MAX}	time of maximum concentration, T _{max}
T _{LAG}	time to observe the first non-zero concentration, for extravascular administration only
C _{LST}	last positive concentration observed, C _{last}
C _{LSTP}	last positive concentration predicted, C _{last_pred}
T _{LST}	time of last positive concentration, T _{last}
L _{AMZHL}	half-life by lambda z, ln(2)/L _{AMZ}
L _{AMZ}	lambda_z negative of best fit terminal slope
L _{AMZLL}	earliest time for L _{AMZ}
L _{AMZUL}	last time for L _{AMZ}
L _{AMZNPT}	number of points for L _{AMZ}
C _{ORRXY}	correlation of log(concentration) and time
R ₂	R-squared
R _{2ADJ}	R-squared adjusted
C ₀	back extrapolated concentration at time 0, for bolus intravascular administration only
A _{UCLST}	AUC from 0 to T _{LST}
A _{UCALL}	AUC using all the given points, including trailing zero concentrations
A _{UCIFO}	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
AUCPBE0	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
VSS0	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

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

[IndiNCA](#)

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 only one subject from the CDISC EX and PC domain.

Usage

```
NCA0(EX0, PC0, fit="Linear")
```

Arguments

EX0	Data of one subject from EX domain
PC0	Data of one subject from PC domain
fit	either of "Linear" or "Log" to indicate the way to calculate AUC and AUMC

Details

This calls IndiNCA function. This is called by rNCA function.

Value

This returns NCA results vector.

Author(s)

Kyun-Seop Bae <k@acr.kr>

See Also

[help](#), [rNCA](#), [IndiNCA](#)

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 calls 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 curve and save it in pdf files.

Usage

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

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 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.
outdir	name of the folder to be used for the output files

Details

This function generates plots for individual and summary concentration vs. time curve. This function calls `NCA()`.

Value

This function saves pdf files and tiff files in the `outdir` folder.

Author(s)

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

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	<i>Read EX domain files</i>
--------	-----------------------------

Description

This reads EX domain files from the specified folders.

Usage

```
readEX(folders)
```

Arguments

folders folders where to find EX domain files

Details

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

Value

This returns combined table of EX domain.

Author(s)

Kyun-Seop Bae <k@acr.kr>

See Also

[help](#), [combXPT](#), [loadEXPC](#)

readPC	<i>Read PC domain files</i>
--------	-----------------------------

Description

This reads PC domain files from the specified folders.

Usage

```
readPC(folders)
```

Arguments

folders folders where to find PC domain files

Details

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

Value

This returns combined table of PC domain.

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", "NQ", "BQL", "BQoL", "<LOQ"), fit="Linear", MinPoints = 5)
```

Arguments

ex	EX domain data, usually from the loadEXPC
pc	PC domain data, usually from the loadEXPC
study	vector of study names in EX and PC domain to do NCA
trt	vector of treatment names in EXTRT to do NCA
id	vector of subject IDs in USUBJID to do NCA
analyte	vector of molecular species in PCTESTCD to do NCA
codeBQL	symbols of below the quantitation limit
fit	either of "Linear" or "Log" to indicate the way to calculate AUC and AUMC
MinPoints	minimum number of sampling points for NCA

Details

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

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 Configuration Table*

Description

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

Usage

RptCfg

Format

A data frame with 48 observations on the following 10 variables.

PPTTESTCD a character vector of CDISC SDTM PPTTESTCD

SYNONYM a character vector of CDISC SDTM PPTTESTCD Synonym

NCI a character vector of NCI preferred 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 WinNonlin(R) style ordering in report 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 WinNonlin(R) style ordering in report 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 WinNonlin(R) style ordering in report 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.

Slope

Get the Slope of regression $\log(y) \sim x$ **Description**

It calculates the slope with linear regression of $\log(y) \sim x$

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 $\log(\text{concentration}) \sim \text{time}$. 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"])
```

unit	Returns unit of CDISC PP domain Pptestcd
------	--

Description

This function returns the unit for the Pptestcd like CMAX, CMAXD, AUCLST, MRTEVLST.

Usage

```
unit(code, uTime = "h", uConc = "ng/mL", uDose = "mg")
```

Arguments

code	Pptestcd
uTime	unit of time
uConc	unit of concentration
uDose	unit of dose

Details

It is called by IndiNCA.

Value

[1]	unit character
[2]	conversion factor

Author(s)

Kyun-Seop Bae <k@acr.kr>

See Also

[IndiNCA](#)

Examples

```
unit("AUCLST")
unit("CMAXD")
unit(code="MRTEVLST", uTime="h", uConc="ug/L", uDose="mg")
```

Index

- *Topic **AUC**
 - AUC, 3
 - IntAUC, 10
 - LinAUC, 12
 - LogAUC, 14
 - *Topic **AUMC**
 - AUC, 3
 - *Topic **Forest Plot**
 - foreNCA, 6
 - *Topic **NCA**
 - IndiNCA, 7
 - NCA, 15
 - NCA0, 18
 - pkc-package, 2
 - rNCA, 23
 - *Topic **Plot**
 - plotFit, 19
 - plotPK, 20
 - *Topic **Slope**
 - BestSlope, 4
 - *Topic **XPT**
 - combXPT, 6
 - loadEXPC, 13
 - readEX, 22
 - readPC, 22
 - *Topic **best fit slope**
 - BestSlope, 4
 - *Topic **datasets**
 - RptCfg, 25
 - *Topic **interpolation**
 - Interpol, 11
 - *Topic **interval AUC**
 - IntAUC, 10
 - Interpol, 11
 - *Topic **noncompartmental analysis**
 - IndiNCA, 7
 - *Topic **package**
 - pkc-package, 2
 - *Topic **partial AUC**
 - IntAUC, 10
 - Interpol, 11
 - *Topic **rounding**
 - Round, 24
 - *Topic **round**
 - Round, 24
 - *Topic **slope**
 - Slope, 26
 - *Topic **unit**
 - unit, 27
- AUC, 3, 10, 11, 13, 15
- BestSlope, 4, 10, 20, 26
- combXPT, 6, 22, 23
- foreNCA, 6, 24
- help, 6, 7, 14, 19, 22–24
- IndiNCA, 7, 18, 19, 27
- IntAUC, 10, 12
- Interpol, 11, 11
- LinAUC, 4, 12, 15
- loadEXPC, 13, 22–24
- LogAUC, 4, 13, 14
- NCA, 15, 21
- NCA0, 18, 24
- pkc (pkc-package), 2
- pkc-package, 2
- plotFit, 19
- plotPK, 20
- readEX, 6, 14, 22
- readPC, 6, 14, 22
- rNCA, 7, 19, 23
- Round, 24

RptCfg, [25](#)

Slope, [5](#), [26](#)

unit, [27](#)