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 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

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NeedsCompilation no

Repository CRAN

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

R topics documented:

`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")

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)

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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) ~ 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")
```

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

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

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)

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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

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) ~ 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 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"], 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

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

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

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
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 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 48 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 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) ~ 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"])
```

---

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")
```

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