Package 'NonCompart'

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Title Noncompartmental Analysis for Pharmacokinetic Data

Description Conduct a noncompartmental analysis with industrial strength.
Some features are
1) Use of CDISC SDTM terms
2) Automatic or manual slope selection
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).

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LazyLoad yes

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

R topics documented:

NonCompart-package *Noncompartmental Analysis for Pharmacokinetic Data*

Description

It conducts a noncompartmental analysis(NCA) with industrial strength.

Details

The main functions are

`tblNCA` to perform NCA for many subjects.

`sNCA` 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
tblNCA(Theoph, key="Subject", colTime="Time", colConc="conc", dose=320,
       adm="Extravascular", doseUnit="mg", concUnit="mg/L")

tblNCA(Indometh, key="Subject", colTime="time", colConc="conc", dose=25,
       adm="Infusion", dur=0.5, doseUnit="mg", concUnit="mg/L", R2ADJ=0.9)

# For individual NCA
iAUC = data.frame(Name=c("AUC[0-12h]","AUC[0-24h]"), Start=c(0,0), End=c(12,24)) ; iAUC

x = Theoph[Theoph$Subject=="1","Time"]
y = Theoph[Theoph$Subject=="1","conc"]

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

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.

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

`BestSlope` *Choose the 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 pickes 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. See Phoneix WinNonlin 6.4 User's Guide p33 for the detail.

Details

Choosing the best terminal slope (y in log scale) in pharmacokinetic analysis is somewhat challenging, and it could vary by analysis performer. Pheonix WinNonlin chooses a slope with highest adjusted R-squared and the longest one. The 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 the slope, lambda_z
`b0`	intercept of the 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 the last point, predicted concentration for the last time point

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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")
```

DetSlope *Determine slope for the log(y) and x regression manually*

Description

You choose a slope for terminal half-life.

Usage

```
DetSlope(x, y, sel.1=0, sel.2=0)
```

Arguments

x	vector values of x-axis, usually time
y	vector values of y-axis, usually concentration
sel.1	default index of the first element to use
sel.2	default index of the last element to use

Details

Sometimes BestSlope cannot find terminal slope satisfactorily. Then you can use this function to choose manually. It returns the same format result with BestSlope with an attribute indicating used points.

Value

R2	R-squared
R2ADJ	adjusted R-squared
LAMZNPT	number of points used for the slope
LAMZ	negative of the slope, lambda_z
b0	intercept of the 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 the last point, predicted concentration for the last time point

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See Also

Slope

Examples

```
DetSlope(Theoph[Theoph$Subject==1, "Time"], Theoph[Theoph$Subject==1, "conc"])
DetSlope(Indometh[Indometh$Subject==2, "time"], Indometh[Indometh$Subject==2, "conc"])
```

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)

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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, 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

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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 the linear trapezoidal method

Usage

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

Arguments

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

Details

This function returns AUC and AUMC by the linear trapezoidal method.

Value

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

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

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
```

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 the linear-up log-down method

Usage

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

Arguments

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

Details

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

Value

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

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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

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")
```

`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 the independent variable, usually time
`y`	vector values of the 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 the slope, lambda_z
`b0`	intercept of the 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 the last point, predicted concentration for the last time point

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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", R2ADJ = 0.9, MW = 0, returnNA = FALSE)
```

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
R2ADJ	Minimum adjusted R-square value to determine terminal slope automatically
MW	molecular weight of the drug
returnNA	deprecated, just for backward compatibility

Details

This will replace IndiNCA.

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 the 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 intravascular bolus 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

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")

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

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. See sNCA for more detail i.e. iAUC

Usage

```
tblNCA(concData, key = "Subject", colTime = "Time", colConc = "conc", dose = 0,
       adm = "Extravascular", dur = 0, doseUnit = "mg", timeUnit = "h",
       concUnit = "ug/L", down = "Linear", R2ADJ = 0.9, MW = 0, iAUC="")
```

Arguments

concData	concentration data table
key	column names of concData to be shown in 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"
R2ADJ	Lowest threshold of adjusted R-square value to do manual slope determination
MW	molecular weight of drug
iAUC	data.frame for interval AUC

Value

Basically same with sNCA

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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")
```

`Unit` *Display 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 mulitplication factor

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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")
```

UnitUrine	*Retuns a conversion factor for the amount calculation from urine concentration and volume*

Description

You can get a conversion factor for the multiplication: conc * vol * factor = amount in the given unit.

Usage

```
UnitUrine(conU = "ng/mL", volU = "mL", amtU = "mg", MW = 0)
```

Arguments

conU	concentration unit
volU	volume unit
amtU	amount unit
MW	molecular weight

Value

Factor	conversion factor for multiplication with the unit in name

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Examples

```
UnitUrine()
UnitUrine("ng/mL", "mL", "mg")
UnitUrine("ug/L", "mL", "mg")
UnitUrine("ug/L", "L", "mg")

UnitUrine("ng/mL", "mL", "g")

UnitUrine("ng/mL", "mL", "mol", MW=500)
UnitUrine("ng/mL", "mL", "mmol", MW=500)
UnitUrine("ng/mL", "mL", "umol", MW=500)
```

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