

Package ‘NonCompart’

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Title Noncompartmental Analysis for Pharmacokinetic Data

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) Use of 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)

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NonCompart-package	<i>Noncompartmental Analysis for Pharmacokinetic Data</i>
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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

tblNCA to perform NCA for many subjects.

sNCA to perform NCA for one subject.

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.

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.

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

BestSlope	<i>Choose the best-fit slope for the log(y) and x regression by the criteria of adjusted R-square.</i>
-----------	--

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 picks 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 Phoenix 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. Phoenix 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

Author(s)

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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	<i>Determine slope for the log(y) and x regression manually</i>
----------	---

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

Author(s)

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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)

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](#), [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 $\log(y) \sim x$
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)

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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	<i>Area Under the Curve(AUC) and Area Under the first Moment Curve(AUMC) by linear trapezoidal method</i>
--------	---

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)

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
```

LogAUC	<i>Area Under the Curve(AUC) and Area Under the first Moment Curve(AUMC) by linear-up log-down method</i>
--------	---

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

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

[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 $\log(y) \sim x$ **Description**

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

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

Author(s)

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See Also

[BestSlope](#)

Examples

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

sNCA	<i>Simplest NCA</i>
------	---------------------

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

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}
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
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
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, 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	<i>Table output NCA</i>
--------	-------------------------

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

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

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")
```

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 multiplication 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")
```

UnitUrine	<i>Returns a conversion factor for the amount calculation from urine concentration and volume</i>
-----------	---

Description

You can get a conversion factor for the multiplication: $\text{conc} * \text{vol} * \text{factor} = \text{amount}$ 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
--------	--

Author(s)

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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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