# Package 'pkr'

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**Version** 0.1.0

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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

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

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

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**NeedsCompilation** no

**Repository** CRAN

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

## R topics documented:

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`pkr-package` *Pharmacokinetics in R*

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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

```
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) ~ 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)

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) ~ 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)
```

### Arguments

| | |
|---|---|
| EX0 | Data of one subject from EX domain |
| PC0 | Data of one subject from PC domain |

### 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"), 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 |
| 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")
```

# Index