Package 'PKNCA'

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Type Package

Title Perform Pharmacokinetic Non-Compartmental Analysis

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Imports dplyr (>= 0.5.0), digest, nlme, parallel, rlang, stats, tidyr, utils

Suggests cowplot, ggplot2, knitr, rmarkdown, testthat

Description Compute standard Non-Compartmental Analysis (NCA) parameters and summarize them. In addition to this core work, it also provides standardized plotting routines, basic assessments for biocomparison or drug interaction, and model-based estimation routines for calculating doses to reach specific values of AUC or Cmax.

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URL `https://github.com/billdenney/pknca`

BugReports `https://github.com/billdenney/pknca/issues`

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R topics documented:

`add.interval.col` *Add columns for calculations within PKNCA intervals*

Description

Add columns for calculations within PKNCA intervals

Usage

```
add.interval.col(name, FUN, values = c(FALSE, TRUE), depends = c(),
  desc = "", formalsmap = list(), datatype = c("interval",
  "individual", "population"))
```

Arguments

`name`	The column name as a character string
`FUN`	The function to run (as a character string) or `NA` if the parameter is automatically calculated when calculating another parameter.
`values`	Valid values for the column
`depends`	Character vector of columns that must be run before this column.
`desc`	A human-readable description of the parameter (<=40 characters to comply with SDTM)
`formalsmap`	A named list mapping parameter names in the function call to NCA parameter names. See the details for information on use of `formalsmap`.
`datatype`	The type of data used for the calculation

Details

The `formalsmap` argument enables mapping some alternate formal argument names to parameters. It is used to generalize functions that may use multiple similar arguments (such as the variants of mean residence time). The names of the list should correspond to function formal parameter names and the values should be one of the following:

- For the current interval:

  character strings of NCA parameter name The value of the parameter calculated for the current interval.

  "conc" Concentration measurements for the current interval.

  "time" Times associated with concentration measurements for the current interval (values start at 0 at the beginning of the current interval).

"volume" Volume associated with concentration measurements for the current interval (typically applies for excretion parameters like urine).

"duration.conc" Durations assocuated with concentration measurements for the current interval.

"dose" Dose amounts assocuated with the current interval.

"time.dose" Time of dose start associated with the current interval (values start at 0 at the beginning of the current interval).

"duration.dose" Duration of dose (typically infusion duration) for doses in the current interval.

"route" Route of dosing for the current interval.

"start" Time of interval start.

"end" Time of interval end.

"options" PKNCA.options governing calculations.

- For the current group:

"conc.group" Concentration measurements for the current group.

"time.group" Times associated with concentration measurements for the current group (values start at 0 at the beginning of the current interval).

"volume.group" Volume associated with concentration measurements for the current interval (typically applies for excretion parameters like urine).

"duration.conc.group" Durations assocuated with concentration measurements for the current group.

"dose.group" Dose amounts assocuated with the current group.

"time.dose.group" Time of dose start associated with the current group (values start at 0 at the beginning of the current interval).

"duration.dose.group" Duration of dose (typically infusion duration) for doses in the current group.

"route.group" Route of dosing for the current group.

Value

NULL (Calling this function has a side effect of changing the available intervals for calculations)

See Also

Other Interval specifications: `check.interval.deps`, `check.interval.specification`, `choose.auc.intervals`, `get.interval.cols`, `get.parameter.deps`

Examples

```
## Not run:
add.interval.col("cmax",
                 FUN="pk.calc.cmax",
                 values=c(FALSE, TRUE),
                 desc="Maximum observed concentration",
                 depends=c())
add.interval.col("cmax.dn",
                 FUN="pk.calc.dn",
```

```
                    values=c(FALSE, TRUE),
                    desc="Maximum observed concentration, dose normalized",
                    formalsmap=list(parameter="cmax"),
                    depends=c("cmax"))

## End(Not run)
```

`addProvenance` *Add a hash and associated information to enable checking object provenance.*

Description

Add a hash and associated information to enable checking object provenance.

Usage

```
addProvenance(object, replace = FALSE)
```

Arguments

`object`	The object to add provenance
`replace`	Replace provenance if the object already has a provenance attribute. (If the object already has provenance and `replace` is `FALSE`, then an error will be raised.)

Value

The object with provenance as an added item

See Also

`checkProvenance`

`adj.r.squared` *Calculate the adjusted r-squared value*

Description

Calculate the adjusted r-squared value

Usage

```
adj.r.squared(r.sq, n)
```

Arguments

r.sq	The r-squared value
n	The number of points

Value

The numeric adjusted r-squared value

AIC.list *Assess the AIC for all models in a list of models*

Description

Assess the AIC for all models in a list of models

Usage

```
## S3 method for class 'list'
AIC(object, ..., assess.best = TRUE)
```

Arguments

object	the list of models
...	parameters passed to the underlying AIC function (typically the parameter k)
assess.best	determine which model is the best (by lowest AIC)

Value

a data frame with row names matching the names of the list x and columns for degrees of freedom (df) and AIC. If assess.best is true, then there will be another column isBest.

See Also

get.best.model

as.data.frame.PKNCAresults

Extract the parameter results from a PKNCAresults and return them as a data frame.

Description

Extract the parameter results from a PKNCAresults and return them as a data frame.

Usage

```
## S3 method for class 'PKNCAresults'
as.data.frame(x, ..., out.format = c("long",
  "wide"))
```

Arguments

x	The object to extract results from
...	Ignored (for compatibility with generic as.data.frame)
out.format	Should the output be 'long' (default) or 'wide'?

Value

A data frame of results

business.mean

Generate functions to do the named function (e.g. mean) applying the business rules.

Description

Generate functions to do the named function (e.g. mean) applying the business rules.

Usage

```
business.mean(x, ...)

business.sd(x, ...)

business.cv(x, ...)

business.geomean(x, ...)

business.geocv(x, ...)
```

```
business.min(x, ...)

business.max(x, ...)

business.median(x, ...)

business.range(x, ...)
```

Arguments

x	vector to be passed to the various functions
...	Additional arguments to be passed to the underlying function.

Value

The value of the various functions or NA if too many values are missing

Functions

- business.sd: Compute the standard deviation with business rules.
- business.cv: Compute the coefficient of variation with business rules.
- business.geomean: Compute the geometric mean with business rules.
- business.geocv: Compute the geometric coefficient of variation with business rules.
- business.min: Compute the minimum with business rules.
- business.max: Compute the maximum with business rules.
- business.median: Compute the median with business rules.
- business.range: Compute the range with business rules.

See Also

pk.business

---

check.conc.time *Verify that the concentration and time are valid*

Description

If the concentrations or times are invalid, will provide an error. Reasons for being invalid are

- time is not a number
- conc is not a number
- Any time value is NA
- time is not monotonically increasing
- conc and time are not the same length

Usage

```
check.conc.time(conc, time, monotonic.time = TRUE)
```

Arguments

conc	Measured concentrations
time	Time of the measurement of the concentrations
monotonic.time	Must the time be unique and monotonically increasing?

Details

Some cases may generate warnings but allow the data to proceed.

- A negative concentration is often but not always an error; it will generate a warning.

Value

None

---

check.conversion *Check that the conversion to a data type does not change the number of NA values*

Description

Check that the conversion to a data type does not change the number of NA values

Usage

```
check.conversion(x, FUN, ...)
```

Arguments

x	the value to convert
FUN	the function to use for conversion
...	arguments passed to FUN

Value

FUN(x,...) or an error if the set of NAs change.

check.interval.deps

Take in a single row of an interval specification and return that row updated with any additional calculations that must be done to fulfill all dependencies.

Description

Take in a single row of an interval specification and return that row updated with any additional calculations that must be done to fulfill all dependencies.

Usage

```
check.interval.deps(x)
```

Arguments

x	A data frame with one or morw rows of the PKNCA interval

Value

The interval specification with additional calculations added where requested outputs require them.

See Also

Other Interval specifications: `add.interval.col`, `check.interval.specification`, `choose.auc.intervals`, `get.interval.cols`, `get.parameter.deps`

check.interval.specification

Check the formatting of a calculation interval specification data frame.

Description

Calculation interval specifications are data frames defining what calculations will be required and summarized from all time intervals. Note: parameters which are not requested may be calculated if it is required for (or computed at the same time as) a requested parameter.

Usage

```
check.interval.specification(x)
```

Arguments

x	The data frame specifying what to calculate during each time interval

Details

`start` and `end` time must always be given as columns, and the `start` must be before the `end`. Other columns define the parameters to be calculated and the groupings to apply the intervals to.

Value

x The potentially updated data frame with the interval calculation specification.

See Also

The vignette "Selection of Calculation Intervals"

Other Interval specifications: `add.interval.col`, `check.interval.deps`, `choose.auc.intervals`, `get.interval.cols`, `get.parameter.deps`

---

checkProvenance *Check the hash of an object to confirm its provenance.*

Description

Check the hash of an object to confirm its provenance.

Usage

```
checkProvenance(object)
```

Arguments

`object`	The object to check provenance for

Value

`TRUE` if the provenance is confirmed to be consistent, `FALSE` if the provenance is not consistent, or `NA` if provenance is not present.

See Also

`addProvenance`

`choose.auc.intervals` *Choose intervals to compute AUCs from time and dosing information*

Description

Intervals for AUC are selected by the following metrics:

1. If only one dose is administered, use the `PKNCA.options("single.dose.auc")`
2. If more than one dose is administered, estimate the AUC between any two doses that have PK taken at both of the dosing times and at least one time between the doses.
3. For the final dose of multiple doses, try to determine the dosing interval (τ) and estimate the AUC in that interval if multiple samples are taken in the interval.
4. If there are samples $> \tau$ after the last dose, calculate the half life after the last dose.

Usage

```
choose.auc.intervals(time.conc, time.dosing, options = list(),
  single.dose.aucs = NULL)
```

Arguments

`time.conc`	Time of concentration measurement
`time.dosing`	Time of dosing
`options`	List of changes to the default `PKNCA.options` for calculations.
`single.dose.aucs`	The AUC specification for single dosing.

Value

A data frame with columns for `start`, `end`, `auc.type`, and `half.life`. See `check.interval.specification` for column definitions. The data frame may have zero rows if no intervals could be found.

See Also

`pk.calc.auc`, `pk.calc.aumc`, `pk.calc.half.life`, `PKNCA.options`

Other Interval specifications: `add.interval.col`, `check.interval.deps`, `check.interval.specificatio` `get.interval.cols`, `get.parameter.deps`

Other Interval determination: `find.tau`

`clean.conc.blq` *Handle BLQ values in the concentration measurements as requested by the user.*

Description

Handle BLQ values in the concentration measurements as requested by the user.

Usage

```
clean.conc.blq(conc, time, ..., options = list(), conc.blq = NULL,
  conc.na = NULL, check = TRUE)
```

Arguments

`conc`	Measured concentrations
`time`	Time of the concentration measurement
`...`	Additional arguments passed to clean.conc.na
`options`	List of changes to the default `PKNCA.options` for calculations.
`conc.blq`	How to handle a BLQ value that is between above LOQ values? See details for description.
`conc.na`	How to handle NA concentrations. (See `clean.conc.na`)
`check`	Run `check.conc.time`?

Details

NA concentrations (and their associated times) will be handled as described in `clean.conc.na` before working with the BLQ values. The method for handling NA concentrations can affect the output of which points are considered BLQ and which are considered "middle". Values are considered BLQ if they are 0.

`conc.blq` can be set either a scalar indicating what should be done for all BLQ values or a list with elements named "first", "middle", and "last" each set to a scalar.

The meaning of each of the list elements is:

first Values up to the first non-BLQ value. Note that if all values are BLQ, this includes all values.

middle Values that are BLQ between the first and last non-BLQ values.

last Values that are BLQ after the last non-BLQ value

The valid settings for each are:

"drop" Drop the BLQ values

"keep" Keep the BLQ values

a number Set the BLQ values to that number

Value

The concentration and time measurements (data frame) filtered and cleaned as requested relative to BLQ in the middle.

See Also

Other Data cleaners: `clean.conc.na`

`clean.conc.na` *Handle NA values in the concentration measurements as requested by the user.*

Description

NA concentrations (and their associated times) will be removed then the BLQ values in the middle

Usage

```
clean.conc.na(conc, time, ..., options = list(), conc.na = NULL,
  check = TRUE)
```

Arguments

`conc`	Measured concentrations
`time`	Time of the concentration measurement
`...`	Additional items to add to the data frame
`options`	List of changes to the default `PKNCA.options` for calculations.
`conc.na`	How to handle NA concentrations? Either 'drop' or a number to impute.
`check`	Run `check.conc.time`?

Value

The concentration and time measurements (data frame) filtered and cleaned as requested relative to NA in the concentration.

See Also

Other Data cleaners: `clean.conc.blq`

exclude *Exclude data points or results from calculations or summarization.*

Description

Exclude data points or results from calculations or summarization.

Usage

```
exclude(object, reason, mask, FUN)

## Default S3 method:
exclude(object, reason, mask, FUN)
```

Arguments

object	The object to exclude data from.
reason	The reason to add as a reason for exclusion.
mask	A logical vector or numeric index of values to exclude (see details).
FUN	A function to operate on the data (one group at a time) to select reasons for exclusions (see details).

Details

Only one of mask or FUN may be given. If FUN is given, it will be called with two arguments: a data.frame (or similar object) that consists of a single group of the data and the full object (e.g. the PKNCAconc object), FUN(current_group,object), and it must return a logical vector equivalent to mask or a character vector with the reason text given when data should be excluded or NA_character_ when the data shoudl be included (for the current exclusion test).

Value

The object with updated information in the exclude column. The exclude column will contain the reason if mask or FUN indicate. If a previous reason for exclusion was given, then subsequent reasons for exclusion will be added to the first with a semicolon space ("; ") separator.

Methods (by class)

- default: The general case for data exclusion

See Also

Other Result exclusions: exclude_nca

Examples

```
myconc <- PKNCAconc(data.frame(subject=1,
                               time=0:6,
                               conc=c(1, 2, 3, 2, 1, 0.5, 0.25)),
                    conc~time|subject)
exclude(myconc,
        reason="Carryover",
        mask=c(TRUE, rep(FALSE, 6)))
```

---

exclude_nca *Exclude NCA parameters based on examining the parameter set.*

Description

Exclude NCA parameters based on examining the parameter set.

Usage

```
exclude_nca_span.ratio(min.span.ratio)

exclude_nca_max.aucinf.pext(max.aucinf.pext)

exclude_nca_min.hl.r.squared(min.hl.r.squared)
```

Arguments

`min.span.ratio`
: The minimum acceptable span ratio (uses `PKNCA.options("min.span.ratio")` if not provided).

`max.aucinf.pext`
: The maximum acceptable percent AUC extrapolation (uses `PKNCA.options("max.aucinf.pext"` if not provided).

`min.hl.r.squared`
: The minimum acceptable r-squared value for half-life (uses `PKNCA.options("min.hl.r.squared` if not provided).

Functions

- `exclude_nca_span.ratio`: Exclude based on span.ratio
- `exclude_nca_max.aucinf.pext`: Exclude based on AUC percent extrapolated (both observed and predicted)
- `exclude_nca_min.hl.r.squared`: Exclude based on half-life r-squared

See Also

Other Result exclusions: `exclude`

Examples

```
my_conc <- PKNCAconc(data.frame(conc=1.1^(3:0),
                                time=0:3,
                                subject=1),
                     conc~time|subject)
my_data <- PKNCAdata(my_conc,
                     intervals=data.frame(start=0, end=Inf,
                                          aucinf.obs=TRUE,
                                          aucpext.obs=TRUE))
my_result <- pk.nca(my_data)
my_result_excluded <- exclude(my_result,
                              FUN=exclude_nca_max.aucinf.pext())
as.data.frame(my_result_excluded)
```

---

find.tau *Find the repeating interval within a vector of doses*

Description

This is intended to find the interval over which x repeats by the rule unique(mod(x, interval)) is minimized.

Usage

```
find.tau(x, na.action = na.omit, options = list(),
  tau.choices = NULL)
```

Arguments

x	the vector to find the interval within
na.action	What to do with NAs in x
options	List of changes to the default PKNCA.options for calculations.
tau.choices	the intervals to look for if the doses are not all equally spaced.

Value

A scalar indicating the repeating interval with the most repetition.

1. If all values are NA then NA is returned.
2. If all values are the same, then 0 is returned.
3. If all values are equally spaced, then that spacing is returned.
4. If one of the choices can minimize the number of unique values, then that is returned.
5. If none of the choices can minimize the number of unique values, then -1 is returned.

See Also

Other Interval determination: choose.auc.intervals

`findOperator` *Find the first occurrence of an operator in a formula and return the left, right, or both sides of the operator.*

Description

Find the first occurrence of an operator in a formula and return the left, right, or both sides of the operator.

Usage

```
findOperator(x, op, side)
```

Arguments

`x`	The formula to parse
`op`	The operator to search for (e.g. +, −, ⋆, /, ...)
`side`	Which side of the operator would you like to see: 'left', 'right', or 'both'.

Value

The side of the operator requested, NA if requesting the left side of a unary operator, and NULL if the operator is not found.

See Also

Other Formula parsing: `formula.parseFormula`, `parseFormula`

`fit_half_life` *Perform the half-life fit given the data. The function simply fits the data without any validation. No selection of points or any other components are done.*

Description

Perform the half-life fit given the data. The function simply fits the data without any validation. No selection of points or any other components are done.

Usage

```
fit_half_life(data, tlast)
```

Arguments

`data`	The data to fit. Must have two columns named "log_conc" and "time"
`tlast`	The time of last observed concentration above the limit of quantification.

Value

A data.frame with one row and columns named "r.squared", "adj.r.squared", "PROB", "lambda.z", "clast.pred", "lambda.z.n.points", "half.life", "span.ratio"

See Also

`pk.calc.half.life`

`formula.parseFormula` *Convert the parsed formula back into the original*

Description

Convert the parsed formula back into the original

Usage

```
## S3 method for class 'parseFormula'
formula(x, drop.groups = FALSE,
  drop.lhs = FALSE, ...)
```

Arguments

`x`	The parsed formula object to revert to the original
`drop.groups`	logical. Should the returned formula drop the groups?
`drop.lhs`	logical. Should the returned formula be one-sided dropping the left hand side?
`...`	Unused.

Value

A formula (optionally with portions removed)

See Also

Other Formula parsing: `findOperator`, `parseFormula`

formula.PKNCAconc *Extract the formula from a PKNCAconc object.*

Description

Extract the formula from a PKNCAconc object.

Usage

```
## S3 method for class 'PKNCAconc'
formula(x, ...)

## S3 method for class 'PKNCAdose'
formula(x, ...)
```

Arguments

x	The object to extract the formula from.
...	Unused

Value

A formula object

geomean *Compute the geometric mean, sd, and CV*

Description

Compute the geometric mean, sd, and CV

Usage

```
geomean(x, na.rm = FALSE)

geosd(x, na.rm = FALSE)

geocv(x, na.rm = FALSE)
```

Arguments

x	A vector to compute the geometric mean of
na.rm	Should missing values be removed?

Value

The scalar value of the geometric mean, geometric standard deviation, or geometric coefficient of variation.

Functions

- `geosd`: Compute the geometric standard deviation, `exp(sd(log(x)))`.
- `geocv`: Compute the geometric coefficient of variation, `sqrt(exp(sd(log(x))^2)-1)*100`.

References

Kirkwood T. B.L. Geometric means and measures of dispersion. Biometrics 1979; 35: 908-909

`get.best.model` *Extract the best model from a list of models using AIC.list.*

Description

Extract the best model from a list of models using AIC.list.

Usage

```
get.best.model(object, ...)
```

Arguments

`object`	the list of models
`...`	Parameters passed to AIC.list

Value

The model which is assessed as best. If more than one are equal, the first is chosen.

See Also

`AIC.list`

get.first.model *Get the first model from a list of models*

Description

Get the first model from a list of models

Usage

```
get.first.model(object)
```

Arguments

object	the list of (lists of, ...) models

Value

The first item in the object that is not a list or NA. If NA is passed in or the list (of lists) is all NA, then NA is returned.

get.interval.cols *Get the columns that can be used in an interval specification*

Description

Get the columns that can be used in an interval specification

Usage

```
get.interval.cols()
```

Value

A list with named elements for each parameter. Each list element contains the parameter definition.

See Also

check.interval.specification and the vignette "Selection of Calculation Intervals"

Other Interval specifications: add.interval.col, check.interval.deps, check.interval.specificatio
choose.auc.intervals, get.parameter.deps

Examples

```
get.interval.cols()
```

get.parameter.deps *Get all columns that depend on a parameter*

Description

Get all columns that depend on a parameter

Usage

```
get.parameter.deps(x)
```

Arguments

x	The parameter name (as a character string)

Value

A character vector of parameter names that depend on the parameter x. If none depend on x, then the result will be an empty vector.

See Also

Other Interval specifications: add.interval.col, check.interval.deps, check.interval.specificatio
choose.auc.intervals, get.interval.cols

getAttributeColumn *Retrieve the value of an attribute column.*

Description

Retrieve the value of an attribute column.

Usage

```
getAttributeColumn(object, attr_name, warn_missing = c("attr", "column"))
```

Arguments

object	The object to extract the attribute value from.
attr_name	The name of the attribute to extract
warn_missing	Give a warning if the "attr"ibute or "column" is missing. Character vector with zero, one, or both of "attr" and "column".

Value

The value of the attribute (or NULL if the attribute is not set or the column does not exist)

`getColumnValueOrNot` *Get the value from a column in a data frame if the value is a column there, otherwise, the value should be a scalar or the length of the data.*

Description

Get the value from a column in a data frame if the value is a column there, otherwise, the value should be a scalar or the length of the data.

Usage

```
getColumnValueOrNot(data, value, prefix = "X")
```

Arguments

`data`	A data.frame or similar object
`value`	A character string giving the name of a column in the `data`, a scalar, or a vector the same length as the `data`
`prefix`	The prefix to use if a column must be added (it will be used as the full column name if it is not already in the dataset or it will be prepended to the maximum column name if not.)

Value

A list with elements named "data", "name" giving the `data` with a column named "name" with the value in that column.

`getData.PKNCAconc` *Extract all the original data from a PKNCAconc or PKNCAdose object*

Description

Extract all the original data from a PKNCAconc or PKNCAdose object

Usage

```
## S3 method for class 'PKNCAconc'
getData(object)

## S3 method for class 'PKNCAdose'
getData(object)
```

Arguments

`object`	R object to extract the data from.

`getData.PKNCAdata` *Extract all the original data from a PKNCAconc or PKNCAdose object*

Description

Extract all the original data from a PKNCAconc or PKNCAdose object

Usage

```
## S3 method for class 'PKNCAdata'
getData(object)
```

Arguments

`object`	R object to extract the data from.

`getData.PKNCAresults` *Extract all the original data from a PKNCAconc or PKNCAdose object*

Description

Extract all the original data from a PKNCAconc or PKNCAdose object

Usage

```
## S3 method for class 'PKNCAresults'
getData(object)
```

Arguments

`object`	R object to extract the data from.

`getDataName.PKNCAconc` *Get the name of the element containing the data for the current object.*

Description

Get the name of the element containing the data for the current object.

Usage

```
## S3 method for class 'PKNCAconc'
getDataName(object)

## S3 method for class 'PKNCAdata'
getDataName(object)

## S3 method for class 'PKNCAdose'
getDataName(object)

## S3 method for class 'PKNCAresults'
getDataName(object)

getDataName(object)

## Default S3 method:
getDataName(object)
```

Arguments

`object`	The object to get the data name from.

Value

A character scalar with the name of the data object (or NULL if the method does not apply).

Methods (by class)

- `default`: If no data name exists, returns NULL.

See Also

Other PKNCA object extractors: `getDepVar`, `getIndepVar`

`getDepVar` *Get the dependent variable (left hand side of the formula) from a PKNCA object.*

Description

Get the dependent variable (left hand side of the formula) from a PKNCA object.

Usage

```
getDepVar(x, ...)
```

Arguments

`x`	The object to extract the formula from
`...`	Unused

Value

The vector of the dependent variable from the object.

See Also

Other PKNCA object extractors: `getDataName.PKNCAconc`, `getIndepVar`

`getGroups.PKNCAconc` *Get the groups (right hand side after the | from a PKNCA object).*

Description

Get the groups (right hand side after the | from a PKNCA object).

Usage

```
## S3 method for class 'PKNCAconc'
getGroups(object, form = formula(object), level,
  data = getData(object), sep)

## S3 method for class 'PKNCAdose'
getGroups(...)

## S3 method for class 'PKNCAresults'
getGroups(object,
  form = formula(object$data$conc), level, data = object$result, sep)
```

Arguments

object	The object to extract the data from
form	The formula to extract the data from (defaults to the formula from object)
level	optional. If included, this specifies the level(s) of the groups to include. If a numeric scalar, include the first level number of groups. If a numeric vector, include each of the groups specified by the number. If a character vector, include the named group levels.
data	The data to extract the groups from (defaults to the data from object)
sep	Unused (kept for compatibility with the nlme package)
...	Arguments passed to other getGroups functions

Value

A data frame with the (selected) group columns.

---

getIndepVar *Get the independent variable (right hand side of the formula) from a PKNCA object.*

Description

Get the independent variable (right hand side of the formula) from a PKNCA object.

Usage

```
getIndepVar(x, ...)
```

Arguments

x	The object to extract the formula from
...	Unused

Value

The vector of the independent variable from the object.

See Also

Other PKNCA object extractors: getDataName.PKNCAconc, getDepVar

`interp.extrap.conc` *Interpolate concentrations between measurements or extrapolate concentrations after the last measurement.*

Description

`interpolate.conc` and `extrapolate.conc` returns an interpolated (or extrapolated) concentration. `interp.extrap.conc` will choose whether interpolation or extrapolation is required and will also operate on many concentrations. These will typically be used to estimate the concentration between two measured concentrations or after the last measured concentration. Of note, these functions will not extrapolate prior to the first point.

Usage

```
interp.extrap.conc(conc, time, time.out, lambda.z = NA,
  clast = pk.calc.clast.obs(conc, time), options = list(),
  interp.method = NULL, extrap.method = "AUCinf", ...,
  conc.blq = NULL, conc.na = NULL, check = TRUE)

interpolate.conc(conc, time, time.out, options = list(),
  interp.method = NULL, conc.blq = NULL, conc.na = NULL,
  conc.origin = 0, ..., check = TRUE)

extrapolate.conc(conc, time, time.out, lambda.z = NA,
  clast = pk.calc.clast.obs(conc, time), extrap.method = "AUCinf",
  options = list(), conc.na = NULL, conc.blq = NULL, ...,
  check = TRUE)

interp.extrap.conc.dose(conc, time, time.dose,
  route.dose = "extravascular", duration.dose = NA, time.out,
  out.after = FALSE, options = list(), conc.blq = NULL,
  conc.na = NULL, ..., check = TRUE)
```

Arguments

`conc`	Measured concentrations
`time`	Time of the concentration measurement
`time.out`	Time when interpolation is requested (vector for `interp.extrap.conc`, scalar otherwise)
`lambda.z`	The elimination rate constant. `NA` will prevent extrapolation.
`clast`	The last observed concentration above the limit of quantification. If not given, `clast` is calculated from `pk.calc.clast.obs`
`options`	List of changes to the default `PKNCA.options` for calculations.
`interp.method`	The method for interpolation (either 'lin up/log down' or 'linear')

`extrap.method`
: The method for extrapolation: "AUCinf", "AUClast", or "AUCall". See details for usage.

`...`
: Additional arguments passed to `interpolate.conc` or `extrapolate.conc`.

`conc.blq`
: How to handle BLQ values. (See `clean.conc.blq` for usage instructions.)

`conc.na`
: How to handle NA concentrations. (See `clean.conc.na`)

`check`
: Run `check.conc.time`, `clean.conc.blq`, and `clean.conc.na`?

`conc.origin`
: The concentration before the first measurement. `conc.origin` is typically used to set predose values to zero (default), set a predose concentration for endogenous compounds, or set predose concentrations to `NA` if otherwise unknown.

`time.dose`
: Time of the dose

`route.dose`
: What is the route of administration ("intravascular" or "extravascular"). See the details below for how this parameter is used.

`duration.dose`
: What is the duration of administration? See the details below for how this parameter is used.

`out.after`
: Should interpolation occur from the data before (`FALSE`) or after (`TRUE`) the interpolated point? See the details below for how this parameter is used. It only has a meaningful effect at the instant of an IV bolus dose.

Details

extrap.method 'AUCinf' Use lambda.z to extrapolate beyond the last point with the half-life.

'AUCall' If the last point is above the limit of quantification or missing, this is identical to 'AUCinf'. If the last point is below the limit of quantification, then linear interpolation between the Clast and the next BLQ is used for that interval and all additional points are extrapolated as 0.

'AUClast' Extrapolates all points after the last above the limit of quantification as 0.

`duration.dose` and `direction.out` are ignored if `route.dose == "extravascular"`. `direction.out` is ignored if `duration.dose > 0`.

`route.dose` and `duration.dose` affect how interpolation/extrapolation of the concentration occurs at the time of dosing. If `route.dose == "intravascular"` and `duration.dose == 0` then extrapolation occurs for an IV bolus using `pk.calc.c0` with the data after dosing. Otherwise (either `route.dose == "extravascular"` or `duration.dose > 0`), extrapolation occurs using the concentrations before dosing and estimating the half-life (or more precisely, estimating `lambda.z`). Finally, `direction.out` can change the direction of interpolation in cases with `route.dose == "intravascular"` and `duration.dose == 0`. When `direction.out == "before"` interpolation occurs only with data before the dose (as is the case for `route.dose == "extravascular"`), but if `direction.out == "after"` interpolation occurs from the data after dosing.

Value

The interpolated or extrapolated concentration value as a scalar float.

Functions

- `interpolate.conc`: Interpolate concentrations through Tlast (inclusive)
- `extrapolate.conc`: Extrapolate concentrations after Tlast
- `interp.extrap.conc.dose`: Interpolate and extrapolate concentrations without interpolating or extrapolating beyond doses.

See Also

`pk.calc.clast.obs`, `pk.calc.half.life`, `pk.calc.c0`

`merge.splitlist` *Merge two or more lists with a data.frame 'groupid' attribute defining the matching.*

Description

Merge two or more lists with a data.frame 'groupid' attribute defining the matching.

Usage

```
## S3 method for class 'splitlist'
merge(...)
```

Arguments

`...`	lists with 'groupid' attributes

Details

The merge is equivalent to a `full_join` where items missing from one or the other item will be missing, but the element(s) will exist.

Value

A list of lists with elements for the matching items between the 'groupid's of each of the input lists. The output list will have a new 'groupid' attribute added with additional columns to indicate the of each input to its output location. If the inputs are named, then each list item will be named the same as the input name.

model.frame.PKNCAconc *Extract the columns used in the formula (in order) from a PKNCAconc or PKNCAdose object.*

Description

Extract the columns used in the formula (in order) from a PKNCAconc or PKNCAdose object.

Usage

```
## S3 method for class 'PKNCAconc'
model.frame(formula, ...)

## S3 method for class 'PKNCAdose'
model.frame(formula, ...)
```

Arguments

formula	The object to use (parameter name is formula to use the generic function)
...	Unused

Value

A data frame with the columns from the object in formula order.

normalize_exclude *Normalize the exclude column by setting blanks to NA*

Description

Normalize the exclude column by setting blanks to NA

Usage

```
normalize_exclude(object)
```

Arguments

object	The object to extract the exclude column from

Value

The exclude vector where NA indicates not to exclude and anything else indicates to exclude.

`parseFormula` *Parse a formula into its component parts.*

Description

This function supports parsing

Usage

```
parseFormula(form, require.groups = FALSE, require.two.sided = FALSE)
```

Arguments

`form`	the formula to extract into its parts
`require.groups`	is it an error not to have groups?
`require.two.sided`	is it an error to have a one-sided formula?

Details

This function extracts the left hand side (`lhs`), right hand side (`rhs`), groups (`groups` and as a formula, `grpFormula`), the environment (`env`, and the original left/right hand side of the model (`model`).

This function borrows heavily from the `parseGroupFormula` function in the doBy package.

Value

A parseFormula class list with elements of

model The left~right side of the model (excluding groups)

lhs The call for the left hand side

rhs The call for the right hand side (excluding groups)

groups The call for the groups

groupFormula A formula form of the groups

env The original formula's environment

See Also

Other Formula parsing: `findOperator`, `formula.parseFormula`

Examples

```
parseFormula("a~b", require.groups=FALSE)
## parseFormula("a~b", require.groups=TRUE) # This is an error
parseFormula("a~b|c")
parseFormula("a~b|c")$groups
```

pk.business — *Run any function with a maximum missing fraction of X and 0s possibly counting as missing. The maximum fraction missing comes from* `PKNCA.options("max.missing")`.

Description

Note that all missing values are removed prior to calling the function. The function is called with the

Usage

```
pk.business(FUN, zero.missing = FALSE, max.missing)
```

Arguments

`FUN`	function to run. The function is called as FUN(x, ...) with missing values removed.
`zero.missing`	Are zeros counted as missing? If `TRUE` then include them in the missing count.
`max.missing`	The maximum fraction of the data allowed to be missing (a number between 0 and 1, inclusive).

Value

A version of FUN that can be called with parameters that are checked for missingness (and zeros) with missing (and zeros) removed before the call. If `max.missing` is exceeded, then NA is returned.

pk.calc.ae — *Calculate amount excreted (typically in urine or feces)*

Description

Calculate amount excreted (typically in urine or feces)

Usage

```
pk.calc.ae(conc, volume, check = TRUE)
```

Arguments

`conc`	The concentration in the sample
`volume`	The volume (or mass) of the sample
`check`	Should the concentration and volume data be checked?

Details

ae is `sum(conc*volume)`.

The units for the concentration and volume should match such that `sum(conc*volume)` has units of mass or moles.

Value

The amount excreted during the interval

See Also

`pk.calc.clr`, `pk.calc.fe`

`pk.calc.aucint` *Calculate the AUC over an interval with interpolation and/or extrapolation of concentrations for the beginning and end of the interval.*

Description

Calculate the AUC over an interval with interpolation and/or extrapolation of concentrations for the beginning and end of the interval.

Usage

```
pk.calc.aucint(conc, time, interval = NULL, start = NULL, end = NULL,
  clast = pk.calc.clast.obs(conc, time), lambda.z = NA,
  time.dose = NULL, route = "extravascular", duration.dose = 0,
  method = NULL, auc.type = "AUClast", conc.blq = NULL,
  conc.na = NULL, check = TRUE, ..., options = list())

pk.calc.aucint.last(conc, time, start = NULL, end = NULL, time.dose,
  ..., options = list())

pk.calc.aucint.all(conc, time, start = NULL, end = NULL, time.dose,
  ..., options = list())

pk.calc.aucint.inf.obs(conc, time, start = NULL, end = NULL, time.dose,
  lambda.z, clast.obs, ..., options = list())

pk.calc.aucint.inf.pred(conc, time, start = NULL, end = NULL,
  time.dose, lambda.z, clast.pred, ..., options = list())
```

Arguments

conc	Concentration measured
time	Time of concentration measurement (must be monotonically increasing and the same length as the concentration data)
interval	Numeric vector of two numbers for the start and end time of integration
start, end	The start and end of the interval (cannot be given if interval is given)
clast, clast.obs, clast.pred	The last concentration above the limit of quantification; this is used for AUCinf calculations. If provided as clast.obs (observed clast value, default), AUCinf is AUCinf,obs. If provided as clast.pred, AUCinf is AUCinf,pred.
lambda.z	The elimination rate (in units of inverse time) for extrapolation
time.dose, route, duration.dose	The time of doses, route of administration, and duration of dose used with interpolation and extrapolation of concentration data (see interp.extrap.conc.dose). If NULL, interp.extrap.conc will be used instead (assuming that no doses affecting concentrations are in the interval).
method	The method for integration (either 'lin up/log down' or 'linear')
auc.type	The type of AUC to compute. Choices are 'AUCinf', 'AUClast', and 'AUCall'.
conc.blq	How to handle BLQ values in between the first and last above LOQ concentrations. (See clean.conc.blq for usage instructions.)
conc.na	How to handle missing concentration values. (See clean.conc.na for usage instructions.)
check	Run check.conc.time, clean.conc.blq, and clean.conc.na?
...	Additional arguments passed to pk.calc.auxc and interp.extrap.conc
options	List of changes to the default PKNCA.options for calculations.

Functions

- pk.calc.aucint.last: Interpolate or extrapolate concentrations for AUClast
- pk.calc.aucint.all: Interpolate or extrapolate concentrations for AUCall
- pk.calc.aucint.inf.obs: Interpolate or extrapolate concentrations for AUCinf.obs
- pk.calc.aucint.inf.pred: Interpolate or extrapolate concentrations for AUCinf.pred

See Also

PKNCA.options, interp.extrap.conc.dose

Other AUC calculations: pk.calc.auxc

pk.calc.aucpext *Calculate the AUC percent extrapolated*

Description

Calculate the AUC percent extrapolated

Usage

```
pk.calc.aucpext(auclast, aucinf)
```

Arguments

auclast	the area under the curve from time 0 to the last measurement above the limit of quantification
aucinf	the area under the curve from time 0 to infinity

Details

aucpext is `100*(1-auclast/aucinf)`.

Value

The numeric value of the AUC percent extrapolated or `NA_real_` if andy of the following are true `is.na(aucinf)`, `is.na(auclast)`, `aucinf <= 0`, or `auclast <= 0`.

pk.calc.auxc *A compute the Area Under the (Moment) Curve*

Description

Compute the area under the curve (AUC) and the area under the moment curve (AUMC) for pharmacokinetic (PK) data. AUC and AUMC are used for many purposes when analyzing PK in drug development.

Usage

```
pk.calc.auxc(conc, time, interval = c(0, Inf),
  clast = pk.calc.clast.obs(conc, time, check = FALSE), lambda.z = NA,
  auc.type = "AUClast", options = list(), method = NULL,
  conc.blq = NULL, conc.na = NULL, check = TRUE, fun.linear, fun.log,
  fun.inf)

pk.calc.auc(conc, time, ..., options = list())
```

```
pk.calc.auc.last(conc, time, ..., options = list())

pk.calc.auc.inf(conc, time, ..., options = list(), lambda.z)

pk.calc.auc.inf.obs(conc, time, clast.obs, ..., options = list(),
  lambda.z)

pk.calc.auc.inf.pred(conc, time, clast.pred, ..., options = list(),
  lambda.z)

pk.calc.auc.all(conc, time, ..., options = list())

pk.calc.aumc(conc, time, ..., options = list())

pk.calc.aumc.last(conc, time, ..., options = list())

pk.calc.aumc.inf(conc, time, ..., options = list(), lambda.z)

pk.calc.aumc.inf.obs(conc, time, clast.obs, ..., options = list(),
  lambda.z)

pk.calc.aumc.inf.pred(conc, time, clast.pred, ..., options = list(),
  lambda.z)

pk.calc.aumc.all(conc, time, ..., options = list())
```

Arguments

conc	Concentration measured
time	Time of concentration measurement (must be monotonically increasing and the same length as the concentration data)
interval	Numeric vector of two numbers for the start and end time of integration
clast, clast.obs, clast.pred	The last concentration above the limit of quantification; this is used for AUCinf calculations. If provided as clast.obs (observed clast value, default), AUCinf is AUCinf,obs. If provided as clast.pred, AUCinf is AUCinf,pred.
lambda.z	The elimination rate (in units of inverse time) for extrapolation
auc.type	The type of AUC to compute. Choices are 'AUCinf', 'AUClast', and 'AUCall'.
options	List of changes to the default PKNCA.options for calculations.
method	The method for integration (either 'lin up/log down' or 'linear')
conc.blq	How to handle BLQ values in between the first and last above LOQ concentrations. (See clean.conc.blq for usage instructions.)
conc.na	How to handle missing concentration values. (See clean.conc.na for usage instructions.)
check	Run check.conc.time, clean.conc.blq, and clean.conc.na?

fun.linear	The function to use for integration of the linear part of the curve (not required for AUC or AUMC functions)
fun.log	The function to use for integration of the logarithmic part of the curve (if log integration is used; not required for AUC or AUMC functions)
fun.inf	The function to use for extrapolation from the final measurement to infinite time (not required for AUC or AUMC functions.
...	For functions other than pk.calc.auxc, these values are passed to pk.calc.auxc

Details

pk.calc.auc.last is simply a shortcut setting the interval parameter to c(0,"last").

Extrapolation beyond Clast occurs using the half-life and Clast,obs; Clast,pred is not yet supported.

Value

A numeric value for the AU(M)C

Functions

- pk.calc.auc: Compute the area under the curve
- pk.calc.auc.last: Compute the AUClast.
- pk.calc.auc.inf: Compute the AUCinf
- pk.calc.auc.inf.obs: Compute the AUCinf with the observed Clast.
- pk.calc.auc.inf.pred: Compute the AUCinf with the predicted Clast.
- pk.calc.auc.all: Compute the AUCall.
- pk.calc.aumc: Compute the area under the moment curve
- pk.calc.aumc.last: Compute the AUMClast.
- pk.calc.aumc.inf: Compute the AUMCinf
- pk.calc.aumc.inf.obs: Compute the AUMCinf with the observed Clast.
- pk.calc.aumc.inf.pred: Compute the AUMCinf with the predicted Clast.
- pk.calc.aumc.all: Compute the AUMCall.

References

Gabrielsson J, Weiner D. "Section 2.8.1 Computation methods - Linear trapezoidal rule." Pharmacokinetic & Pharmacodynamic Data Analysis: Concepts and Applications, 4th Edition. Stockholm, Sweden: Swedish Pharmaceutical Press, 2000. 162-4.

Gabrielsson J, Weiner D. "Section 2.8.3 Computation methods - Log-linear trapezoidal rule." Pharmacokinetic & Pharmacodynamic Data Analysis: Concepts and Applications, 4th Edition. Stockholm, Sweden: Swedish Pharmaceutical Press, 2000. 164-7.

See Also

clean.conc.blq

Other AUC calculations: pk.calc.aucint

Examples

```
myconc <- c(0, 1, 2, 1, 0.5, 0.25, 0)
mytime <- c(0, 1, 2, 3, 4,   5,    6)
pk.calc.auc(myconc, mytime, interval=c(0, 6))
pk.calc.auc(myconc, mytime, interval=c(0, Inf))
```

---

pk.calc.c0 *Estimate the concentration at dosing time for an IV bolus dose.*

Description

Estimate the concentration at dosing time for an IV bolus dose.

Usage

```
pk.calc.c0(conc, time, time.dose = 0, method = c("c0", "logslope",
  "c1", "cmin", "set0"), check = TRUE)

pk.calc.c0.method.logslope(conc, time, time.dose = 0, check = TRUE)

pk.calc.c0.method.c0(conc, time, time.dose = 0, check = TRUE)

pk.calc.c0.method.c1(conc, time, time.dose = 0, check = TRUE)

pk.calc.c0.method.set0(conc, time, time.dose = 0, check = TRUE)

pk.calc.c0.method.cmin(conc, time, time.dose = 0, check = TRUE)
```

Arguments

`conc`	The observed concentrations
`time`	The observed times
`time.dose`	The time when dosing occurred
`method`	The order of methods to test (see details)
`check`	Check the `conc` and `time` inputs

Details

Methods available for interpolation are below, and each has its own specific function.

`c0` If the observed `conc` at `time.dose` is nonzero, return that. This method should usually be used first for single-dose IV bolus data in case nominal time zero is measured.

`logslope` Compute the semilog line between the first two measured times, and use that line to extrapolate backward to `time.dose`

`c1` Use the first point after `time.dose`

`cmin` Set c0 to cmin during the interval. This method should usually be used for multiple-dose oral data and IV infusion data.

`set0` Set c0 to zero (regardless of any other data). This method should usually be used first for single-dose oral data.

Value

The estimated concentration at time 0.

Functions

- `pk.calc.c0.method.logslope`: Semilog regress the first and second points after time.dose. This method will return `NA` if the second `conc` after `time.dose` is 0 or greater than the first.
- `pk.calc.c0.method.c0`: Use `C0` = `conc[time time.dose]` if it is nonzero.
- `pk.calc.c0.method.c1`: Use `C0` = `C1`.
- `pk.calc.c0.method.set0`: Use `C0` = 0 (typically used for single dose oral and IV infusion)
- `pk.calc.c0.method.cmin`: Use `C0` = Cmin (typically used for multiple dose oral and IV infusion but not IV bolus)

`pk.calc.cav` *Calculate the average concentration during an interval.*

Description

Calculate the average concentration during an interval.

Usage

```
pk.calc.cav(auclast, start, end)
```

Arguments

`auclast`	The area under the curve during the interval
`start`	The starting time of the interval
`end`	The ending time of the interval

Details

cav is `auclast/(end-start)`.

Value

The Cav (average concentration during the interval)

pk.calc.ceoi *Determine the concentration at the end of infusion*

Description

Determine the concentration at the end of infusion

Usage

```
pk.calc.ceoi(conc, time, duration.dose = NA, check = TRUE)
```

Arguments

conc	Concentration measured
time	Time of concentration measurement
duration.dose	The duration for the dosing administration (typically from IV infusion)
check	Run check.conc.time?

Value

The concentration at the end of the infusion, NA if duration.dose is NA, or NA if all time != duration.dose

pk.calc.cl *Calculate the (observed oral) clearance*

Description

Calculate the (observed oral) clearance

Usage

```
pk.calc.cl(dose, auc)
```

Arguments

dose	the dose administered
auc	The area under the concentration-time curve.

Details

cl is dose/auc.

If dose is the same length as the other inputs, then the output will be the same length as all of the inputs; the function assumes that you are calculating for multiple intervals simultaneously. If the inputs other than dose are scalars and dose is a vector, then the function assumes multiple doses were given in a single interval, and the sum of the doses will be used for the calculation.

Value

the numeric value of the total (CL) or observed oral clearance (CL/F)

References

Gabrielsson J, Weiner D. "Section 2.5.1 Derivation of clearance." Pharmacokinetic & Pharmacodynamic Data Analysis: Concepts and Applications, 4th Edition. Stockholm, Sweden: Swedish Pharmaceutical Press, 2000. 86-7.

`pk.calc.clast.obs` *Determine the last observed concentration above the limit of quantification (LOQ).*

Description

If Tlast is NA (due to no non-missing above LOQ measurements), this will return NA.

Usage

```
pk.calc.clast.obs(conc, time, check = TRUE)
```

Arguments

`conc`	Concentration measured
`time`	Time of concentration measurement
`check`	Run `check.conc.time`?

Value

The last observed concentration above the LOQ

`pk.calc.clr` *Calculate renal clearance*

Description

Calculate renal clearance

Usage

```
pk.calc.clr(ae, auc)
```

Arguments

`ae`	The amount excreted in urine (as a numeric scalar or vector)
`auc`	The area under the curve (as a numeric scalar or vector)

Details

clr is `sum(ae)/auc`.

The units for the `ae` and `auc` should match such that `ae/auc` has units of volume/time.

Value

The renal clearance as a number

See Also

`pk.calc.ae`, `pk.calc.fe`

`pk.calc.cmax` *Determine maximum observed PK concentration*

Description

Determine maximum observed PK concentration

Usage

```
pk.calc.cmax(conc, check = TRUE)

pk.calc.cmin(conc, check = TRUE)
```

Arguments

`conc`	Concentration measured
`check`	Run `check.conc.time`?

Value

a number for the maximum concentration or NA if all concentrations are missing

Functions

- `pk.calc.cmin`: Determine the minimum observed PK concentration

pk.calc.ctrough *Determine the trough (predose) concentration*

Description

Determine the trough (predose) concentration

Usage

```
pk.calc.ctrough(conc, time, end)
```

Arguments

conc	Observed concentrations during the interval
time	Times of conc observations
end	End time of the interval

Value

The concentration when time == end. If none match, then NA

pk.calc.deg.fluc *Determine the degree of fluctuation*

Description

Determine the degree of fluctuation

Usage

```
pk.calc.deg.fluc(cmax, cmin, cav)
```

Arguments

cmax	The maximum observed concentration
cmin	The minimum observed concentration
cav	The average concentration in the interval

Details

deg.fluc is 100*(cmax-cmin)/cav.

Value

The degree of fluctuation around the average concentration.

pk.calc.dn *Determine dose normalized NCA parameter*

Description

Determine dose normalized NCA parameter

Usage

```
pk.calc.dn(parameter, dose)
```

Arguments

parameter	Parameter to dose normalize
dose	Dose in units compatible with the area under the curve

Value

a number for dose normalized AUC

Examples

```
pk.calc.dn(90, 10)
```

pk.calc.f *Calculate the absolute (or relative) bioavailability*

Description

Calculate the absolute (or relative) bioavailability

Usage

```
pk.calc.f(dose1, auc1, dose2, auc2)
```

Arguments

dose1	The dose administered in route or method 1
auc1	The AUC from 0 to infinity or 0 to tau administered in route or method 1
dose2	The dose administered in route or method 2
auc2	The AUC from 0 to infinity or 0 to tau administered in route or method 2

Details

f is `(auc2/dose2)/(auc1/dose1)`.

pk.calc.fe *Calculate fraction excreted (typically in urine or feces)*

Description

Calculate fraction excreted (typically in urine or feces)

Usage

```
pk.calc.fe(ae, dose)
```

Arguments

ae	The amount excreted (as a numeric scalar or vector)
dose	The dose (as a numeric scalar or vector)

Details

fe is `sum(ae)/dose`

The units for `ae` and `dose` should be the same so that `ae/dose` is a unitless fraction.

Value

The fraction of dose excreted.

See Also

`pk.calc.ae`, `pk.calc.clr`

pk.calc.half.life *Compute the half-life and associated parameters*

Description

The terminal elimination half-life is estimated from the final points in the concentration-time curve using semi-log regression (`log(conc)~time`) with automated selection of the points for calculation (unless `manually.selected.points` is `TRUE`).

Usage

```
pk.calc.half.life(conc, time, tmax, tlast,
  manually.selected.points = FALSE, options = list(),
  min.hl.points = NULL, adj.r.squared.factor = NULL, conc.blq = NULL,
  conc.na = NULL, first.tmax = NULL, allow.tmax.in.half.life = NULL,
  check = TRUE)
```

Arguments

conc	Concentration measured
time	Time of concentration measurement
tmax	Time of maximum concentration (will be calculated and included in the return data frame if not given)
tlast	Time of last concentration above the limit of quantification (will be calculated and included in the return data frame if not given)
manually.selected.points	Have the points being input been manually selected? The impact of setting this to TRUE is that no selection for the best points will be done. When TRUE, this option causes the options of adj.r.squared.factor, min.hl.points, and allow.tmax.in.half.life to be ignored.
options	List of changes to the default PKNCA.options for calculations.
min.hl.points	The minimum number of points that must be included to calculate the half-life
adj.r.squared.factor	The allowance in adjusted r-squared for adding another point.
conc.blq	See clean.conc.blq
conc.na	See clean.conc.na
first.tmax	See pk.calc.tmax.
allow.tmax.in.half.life	Allow the concentration point for tmax to be included in the half-life slope calculation.
check	Run check.conc.time, clean.conc.blq, and clean.conc.na?

Details

If manually.selected.points is FALSE (default), the half-life is calculated by computing the best fit line for all points at or after tmax (based on the value of allow.tmax.in.half.life. The best half-life is chosen by the following rules in order:

- At least min.hl.points points included
- A lambda.z > 0
- The best adjusted r-squared (within adj.r.squared.factor)
- The one with the most points included

If manually.selected.points is TRUE, the conc and time data are used as-is without any form of selection for the best-fit half-life.

Value

A data frame with one row and columns for

tmax Time of maximum observed concentration (only included if not given as an input)

tlast Time of last observed concentration above the LOQ (only included if not given as an input)

r.squared coefficient of determination

adj.r.squared adjusted coefficient of determination

lambda.z elimination rate

lambda.z.time.first first time for half-life calculation

lambda.z.n.points number of points in half-life calculation

clast.pred Concentration at tlast as predicted by the half-life line

half.life half-life

span.ratio span ratio [ratio of half-life to time used for half-life calculation

References

Gabrielsson J, Weiner D. "Section 2.8.4 Strategies for estimation of lambda-z." Pharmacokinetic & Pharmacodynamic Data Analysis: Concepts and Applications, 4th Edition. Stockholm, Sweden: Swedish Pharmaceutical Press, 2000. 167-9.

`pk.calc.kel` *Calculate the elimination rate (Kel)*

Description

Calculate the elimination rate (Kel)

Usage

```
pk.calc.kel(mrt)
```

Arguments

`mrt`	the mean residence time
`kel`	is `1/mrt`, not to be confused with lambda.z.

Value

the numeric value of the elimination rate

`pk.calc.mrt` *Calculate the mean residence time (MRT) for single-dose data or linear multiple-dose data.*

Description

Calculate the mean residence time (MRT) for single-dose data or linear multiple-dose data.

Usage

```
pk.calc.mrt(auc, aumc)

pk.calc.mrt.iv(auc, aumc, duration.dose)
```

Arguments

`auc`	the AUC from 0 to infinity or 0 to tau
`aumc`	the AUMC from 0 to infinity or 0 to tau
`duration.dose`	The duration of the dose (usually an infusion duration for an IV infusion)

Details

mrt is `aumc/auc -duration.dose/2` where `duration.dose = 0` for oral administration.

Value

the numeric value of the mean residence time

Functions

- `pk.calc.mrt.iv`: MRT for an IV infusion

See Also

`pk.calc.mrt.md`

pk.calc.mrt.md *Calculate the mean residence time (MRT) for multiple-dose data with nonlinear kinetics.*

Description

Calculate the mean residence time (MRT) for multiple-dose data with nonlinear kinetics.

Usage

```
pk.calc.mrt.md(auctau, aumctau, aucinf, tau)
```

Arguments

auctau	the AUC from time 0 to the end of the dosing interval (tau).
aumctau	the AUMC from time 0 to the end of the dosing interval (tau).
aucinf	the AUC from time 0 to infinity (typically using single-dose data)
tau	the dosing interval

Details

mrt.md is `aumctau/auctau + tau*(aucinf-auctau)/auctau` and should only be used for multiple dosing with equal intervals between doses.

Note that if `aucinf == auctau` (as would be the assumption with linear kinetics), the equation becomes the same as the single-dose MRT.

See Also

`pk.calc.mrt`

pk.calc.ptr *Determine the peak-to-trough ratio*

Description

Determine the peak-to-trough ratio

Usage

```
pk.calc.ptr(cmax, ctrough)
```

Arguments

cmax	The maximum observed concentration
ctrough	The last concentration in an interval

Details

ptr is `cmax/ctrough`.

Value

The ratio of cmax to ctrough (if ctrough == 0, NA)

`pk.calc.swing` *Determine the PK swing*

Description

Determine the PK swing

Usage

```
pk.calc.swing(cmax, cmin)
```

Arguments

`cmax`	The maximum observed concentration
`cmin`	The minimum observed concentration

Details

swing is `100*(cmax -cmin)/cmin`.

Value

The swing above the minimum concentration. If `cmin` is zero, then the result is infinity.

`pk.calc.thalf.eff` *Calculate the effective half-life*

Description

Calculate the effective half-life

Usage

```
pk.calc.thalf.eff(mrt)
```

Arguments

`mrt`	the mean residence time to infinity

Details

thalf.eff is `log(2)*mrt`.

Value

the numeric value of the effective half-life

`pk.calc.tlag` *Determine the observed lag time (time before the first concentration above the limit of quantification or above the first concentration in the interval)*

Description

Determine the observed lag time (time before the first concentration above the limit of quantification or above the first concentration in the interval)

Usage

```
pk.calc.tlag(conc, time)
```

Arguments

`conc`	The observed concentrations
`time`	The observed times

Value

The time associated with the first increasing concentration

`pk.calc.tlast` *Determine time of last observed concentration above the limit of quantification.*

Description

`NA` will be returned if all `conc` are `NA` or 0.

Usage

```
pk.calc.tlast(conc, time, check = TRUE)

pk.calc.tfirst(conc, time, check = TRUE)
```

Arguments

conc	Concentration measured
time	Time of concentration measurement
check	Run check.conc.time?

Value

The time of the last observed concentration measurement

Functions

- pk.calc.tfirst: Determine the first concentration above the limit of quantification.

---

pk.calc.tmax *Determine time of maximum observed PK concentration*

Description

Input restrictions are:

1. the conc and time must be the same length,
2. the time may have no NAs,

NA will be returned if:

1. the length of conc and time is 0
2. all conc is 0 or NA

Usage

```
pk.calc.tmax(conc, time, options = list(), first.tmax = NULL,
  check = TRUE)
```

Arguments

conc	Concentration measured
time	Time of concentration measurement
options	List of changes to the default PKNCA.options for calculations.
first.tmax	If there is more than time that matches the maximum concentration, should the first be considered as Tmax? If not, then the last is considered Tmax.
check	Run check.conc.time?

Value

the time of the maximum concentration

pk.calc.vd — *Calculate the volume of distribution (Vd) or observed volume of distribution (Vd/F)*

Description

Calculate the volume of distribution (Vd) or observed volume of distribution (Vd/F)

Usage

```
pk.calc.vd(dose, aucinf, lambda.z)
```

Arguments

dose	One or more doses given during an interval
aucinf	Area under the curve to infinity (either predicted or observed).
lambda.z	Elimination rate constant

Details

vd is `dose/(aucinf * lambda.z)`.

If `dose` is the same length as the other inputs, then the output will be the same length as all of the inputs; the function assumes that you are calculating for multiple intervals simultaneously. If the inputs other than `dose` are scalars and `dose` is a vector, then the function assumes multiple doses were given in a single interval, and the sum of the `dose`s will be used for the calculation.

Value

The observed volume of distribution

pk.calc.vss — *Calculate the steady-state volume of distribution (Vss)*

Description

Calculate the steady-state volume of distribution (Vss)

Usage

```
pk.calc.vss(cl, mrt)
```

Arguments

cl	the clearance
mrt	the mean residence time

Details

vss is `cl*mrt`.

Value

the volume of distribution at steady-state

---

pk.calc.vz *Calculate the terminal volume of distribution (Vz)*

Description

Calculate the terminal volume of distribution (Vz)

Usage

```
pk.calc.vz(cl, lambda.z)
```

Arguments

`cl`	the clearance (or apparent observed clearance)
`lambda.z`	the elimination rate

Details

vz is `cl/lambda.z`.

---

pk.nca *Compute NCA parameters for each interval for each subject.*

Description

The `pk.nca` function computes the NCA parameters from a `PKNCAdata` onject. All options for the calculation and input data are set in prior functions (`PKNCAconc`, `PKNCAdose`, and `PKNCAdata`). Options for calculations are set either in `PKNCAdata` or with the current default options in `PKNCA.options`.

Usage

```
pk.nca(data)
```

Arguments

`data`	A PKNCAdata object

Details

When performing calculations, all time results are relative to the start of the interval. For example, if an interval starts at 168 hours, ends at 192 hours, and and the maximum concentration is at 169 hours, `tmax=169-168=1`.

Value

A `PKNCAresults` object.

See Also

`PKNCAdata`, `PKNCA.options`, `summary.PKNCAresults`, `as.data.frame.PKNCAresults`, `exclude`

`pk.nca.interval` *Compute all PK parameters for a single concentration-time data set*

Description

For one subject/time range, compute all available PK parameters. All the internal options should be set by `PKNCA.options` prior to running. The only part that changes with a call to this function is the `conc`entration and `time`.

Usage

```
pk.nca.interval(conc, time, volume, duration.conc, dose, time.dose,
  duration.dose, route, conc.group = NULL, time.group = NULL,
  volume.group = NULL, duration.conc.group = NULL, dose.group = NULL,
  time.dose.group = NULL, duration.dose.group = NULL,
  route.group = NULL, include_half.life = NULL,
  exclude_half.life = NULL, interval, options = list())
```

Arguments

`conc`, `conc.group`
: Concentration measured for the current interval or all data for the group

`time`, `time.group`
: Time of concentration measurement for the current interval or all data for the group

`volume`, `volume.group`
: The volume (or mass) of the concentration measurement for the current interval or all data for the group (typically for urine and fecal measurements)

`duration.conc`, `duration.conc.group`
: The duration of the concentration measurement for the current interval or all data for the group (typically for urine and fecal measurements)

dose, dose.group
: Dose amount (may be a scalar or vector) for the current interval or all data for the group

time.dose, time.dose.group
: Time of the dose for the current interval or all data for the group (must be the same length as dose or dose.group)

duration.dose, duration.dose.group
: The duration of the dose administration for the current interval or all data for the group (typically zero for extravascular and intravascular bolus and nonzero for intravascular infusion)

route, route.group
: The route of dosing for the current interval or all data for the group

include_half.life
: An optional boolean vector of the concentration measurements to include in the half-life calculation. If given, no half-life point selection will occur.

exclude_half.life
: An optional boolean vector of the concentration measurements to exclude from the half-life calculation.

interval
: One row of an interval definition (see check.interval.specification for how to define the interval.

options
: List of changes to the default PKNCA.options for calculations.

Value

A data frame with the start and end time along with all PK parameters for the interval

See Also

check.interval.specification

---

pk.tss *Compute the time to steady-state (tss)*

Description

Compute the time to steady-state (tss)

Usage

```
pk.tss(..., type = c("monoexponential", "stepwise.linear"),
  check = TRUE)
```

Arguments

...
: Passed to pk.tss.monoexponential or pk.tss.stepwise.linear.

type
: The type of Tss to calculate, either stepwise.linear or monoexponential

check
: See pk.tss.data.prep

Value

A data frame with columns as defined from `pk.tss.monoexponential` and/or `pk.tss.stepwise.linear`.

See Also

Other Time to steady-state calculations: `pk.tss.monoexponential`, `pk.tss.stepwise.linear`

`pk.tss.data.prep` *Clean up the time to steady-state parameters and return a data frame for use by the tss calculators.*

Description

Clean up the time to steady-state parameters and return a data frame for use by the tss calculators.

Usage

```
pk.tss.data.prep(conc, time, subject, treatment, subject.dosing,
  time.dosing, options = list(), conc.blq = NULL, conc.na = NULL,
  check = TRUE, ...)
```

Arguments

`conc`	Concentration measured
`time`	Time of concentration measurement
`subject`	Subject identifiers (used as a random effect in the model)
`treatment`	Treatment description (if missing, all subjects are assumed to be on the same treatment)
`subject.dosing`	Subject number for dosing
`time.dosing`	Time of dosing
`options`	List of changes to the default `PKNCA.options` for calculations.
`conc.blq`	See `clean.conc.blq`
`conc.na`	See `clean.conc.na`
`check`	Run `check.conc.time`?
`...`	Discarded inputs to allow generic calls between tss methods.

Value

a data frame with columns for `conc`entration, `time`, `subject`, and `treatment`.

`pk.tss.monoexponential` *Compute the time to steady state using nonlinear, mixed-effects modeling of trough concentrations.*

Description

Trough concentrations are selected as concentrations at the time of dosing. An exponential curve is then fit through the data with a different magnitude by treatment (as a factor) and a random steady-state concentration and time to stead-state by subject (see `random.effects` argument).

Usage

```
pk.tss.monoexponential(..., tss.fraction = 0.9,
  output = c("population", "popind", "individual", "single"),
  check = TRUE, verbose = FALSE)
```

Arguments

`...`	See `pk.tss.data.prep`
`tss.fraction`	The fraction of steady-state required for calling steady-state
`output`	Which types of outputs should be produced? `population` is the population estimate for time to steady-state (from an nlme model), `popind` is the individual estimate (from an nlme model), `individual` fits each individual separately with a gnls model (requires more than one individual; use `single` for one individual), and `single` fits all the data to a single gnls model.
`check`	See `pk.tss.data.prep`.
`verbose`	Describe models as they are run, show convergence of the model (passed to the nlme function), and additional details while running.

Value

A scalar float for the first time when steady-state is achieved or `NA` if it is not observed.

References

Maganti L, Panebianco DL, Maes AL. Evaluation of Methods for Estimating Time to Steady State with Examples from Phase 1 Studies. AAPS Journal 10(1):141-7. doi:10.1208/s12248-008-9014-y

See Also

Other Time to steady-state calculations: `pk.tss.stepwise.linear`, `pk.tss`

pk.tss.monoexponential.individual

A helper function to estimate individual and single outputs for mono-exponential time to steady-state.

Description

This function is not intended to be called directly. Please use `pk.tss.monoexponential`.

Usage

```
pk.tss.monoexponential.individual(data, output = c("individual",
  "single"), verbose = FALSE)
```

Arguments

`data`	a data frame as prepared by `pk.tss.data.prep`. It must contain at least columns for `subject`, `time`, `conc`, and `tss.constant`.
`output`	a character vector requesting the output types.
`verbose`	Show verbose output.

Details

If no model converges, then the `tss.monoexponential.single` and/or `tss.monoexponential.individual` column will be set to NA.

Value

A data frame with either one row (if `population` output is provided) or one row per subject (if `popind` is provided). The columns will be named `tss.monoexponential.population` and/or `tss.monoexponential.popind`.

pk.tss.monoexponential.population

A helper function to estimate population and popind outputs for mo-noexponential time to steady-state.

Description

This function is not intended to be called directly. Please use `pk.tss.monoexponential`.

Usage

```
pk.tss.monoexponential.population(data, output = c("population",
  "popind"), verbose = FALSE)
```

Arguments

data	a data frame as prepared by pk.tss.data.prep. It must contain at least columns for subject, time, conc, and tss.constant.
output	a character vector requesting the output types.
verbose	Show verbose output.

Details

If no model converges, then the tss.monoexponential.population column will be set to NA. If the best model does not include a random effect for subject on Tss then the tss.monoexponential.popind column of the output will be set to NA.

Value

A data frame with either one row (if population output is provided) or one row per subject (if popind is provided). The columns will be named tss.monoexponential.population and/or tss.monoexponential.popind.

---

pk.tss.stepwise.linear

Compute the time to steady state using stepwise test of linear trend

---

Description

A linear slope is fit through the data to find when it becomes non-significant. Note that this is less preferrred than the pk.tss.monoexponential due to the fact that with more time or more subjects the performance of the test changes (see reference).

Usage

```
pk.tss.stepwise.linear(..., min.points = 3, level = 0.95,
  verbose = FALSE, check = TRUE)
```

Arguments

...	See pk.tss.data.prep
min.points	The minimum number of points required for the fit
level	The confidence level required for assessment of steady-state
verbose	Describe models as they are run, show convergence of the model (passed to the nlme function), and additional details while running.
check	See pk.tss.data.prep

Details

The model is fit with a different magnitude by treatment (as a factor, if given) and a random slope by subject (if given). A minimum of min.points is required to fit the model.

Value

A scalar float for the first time when steady-state is achieved or NA if it is not observed.

References

Maganti L, Panebianco DL, Maes AL. Evaluation of Methods for Estimating Time to Steady State with Examples from Phase 1 Studies. AAPS Journal 10(1):141-7. doi:10.1208/s12248-008-9014-y

See Also

Other Time to steady-state calculations: pk.tss.monoexponential, pk.tss

---

PKNCA *Compute noncompartmental pharmacokinetics*

Description

Compute pharmacokinetic (PK) noncompartmental analysis (NCA) parameters.

Details

A common workflow would load data from a file or database into a data.frame then run the following

Examples

```
## Not run:
# Load concentration-time data into a data.frame called d.conc
# with columns named "conc", "time", and "subject".
my.conc <- PKNCAconc(d.conc, conc~time|subject)
# Load dose-time data into a data.frame called d.dose
# with columns named "dose", "time", and "subject".
my.dose <- PKNCAdose(d.dose, dose~time|subject)
# Combine the concentration-time and dose-time data into an object
# ready for calculations.
my.data <- PKNCAdata(my.conc, my.dose)
# Perform the calculations
my.results <- pk.nca(my.data)
# Look at summary results
summary(my.results)
# Look at a listing of results
as.data.frame(my.results)

## End(Not run)
```

PKNCA.choose.option *Choose either the value from an option list or the current set value for an option.*

Description

Choose either the value from an option list or the current set value for an option.

Usage

```
PKNCA.choose.option(name, value = NULL, options = list())
```

Arguments

name	The option name requested.
value	A value to check for the option (NULL to choose not to check the value).
options	The non-default options to choose from.

Value

The value of the option first from the options list and if it is not there then from the current settings.

See Also

Other PKNCA calculation and summary settings: PKNCA.options, PKNCA.set.summary

PKNCA.options *Set default options for PKNCA functions*

Description

This function will set the default PKNCA options. If given no inputs, it will provide the current option set. If given name/value pairs, it will set the option (as in the options function). If given a name, it will return the value for the parameter. If given the default option as true, it will provide the default options.

Usage

```
PKNCA.options(..., default = FALSE, check = FALSE, name, value)
```

Arguments

`...`	options to set or get the value for
`default`	(re)sets all default options
`check`	check a single option given, but do not set it (for validation of the values when used in another function)
`name`	An option name to use with the `value`.
`value`	An option value (paired with the `name`) to set or check (if `NULL`,).

Details

Options are either for calculation or summary functions. Calculation options are required for a calculation function to report a result (otherwise the reported value will be `NA`). Summary options are used during summarization and are used for assessing what values are included in the summary.

See the vignette 'Options for Controlling PKNCA' for a current list of options.

Value

If...

no arguments are given returns the current options.

a value is set (including the defaults) returns `NULL`

a single value is requested the current value of that option is returned as a scalar

multiple values are requested the current values of those options are returned as a list

See Also

Other PKNCA calculation and summary settings: `PKNCA.choose.option`, `PKNCA.set.summary`

Examples

```
PKNCA.options()
PKNCA.options(default=TRUE)
PKNCA.options("auc.method")
PKNCA.options(name="auc.method")
PKNCA.options(auc.method="lin up/log down", min.hl.points=3)
```

PKNCA.options.describe *Describe a PKNCA.options option by name.*

Description

Describe a PKNCA.options option by name.

Usage

```
PKNCA.options.describe(name)
```

Arguments

name	The option name requested.

Value

A character string of the description.

See Also

PKNCA.options

PKNCA.set.summary *Define how NCA parameters are summarized.*

Description

Define how NCA parameters are summarized.

Usage

```
PKNCA.set.summary(name, description, point, spread,
  rounding = list(signif = 3), reset = FALSE)
```

Arguments

name	The parameter name or a vector of parameter names. It must have already been defined (see add.interval.col).
description	A single-line description of the summary
point	The function to calculate the point estimate for the summary. The function will be called as point(x) and must return a scalar value (typically a number, NA, or a string).

spread	Optional. The function to calculate the spread (or variability). The function will be called as `spread(x)` and must return a scalar or two-long vector (typically a number, NA, or a string).
rounding	Instructions for how to round the value of point and spread. It may either be a list or a function. If it is a list, then it must have a single entry with a name of either "signif" or "round" and a value of the digits to round. If a function, it is expected to return a scalar number or character string with the correct results for an input of either a scalar or a two-long vector.
reset	Reset all the summary instructions

Value

All current summary settings (invisibly)

See Also

`summary.PKNCAresults`

Other PKNCA calculation and summary settings: `PKNCA.choose.option`, `PKNCA.options`

Examples

```
## Not run:
PKNCA.set.summary(
  name="half.life",
  description="arithmetic mean and standard deviation",
  point=business.mean,
  spread=business.sd,
  rounding=list(signif=3)
)

## End(Not run)
```

PKNCAconc *Create a PKNCAconc object*

Description

Create a PKNCAconc object

Usage

```
PKNCAconc(data, ...)

## Default S3 method:
PKNCAconc(data, ...)

## S3 method for class 'tbl_df'
```

```
PKNCAconc(data, ...)

## S3 method for class 'data.frame'
PKNCAconc(data, formula, subject, time.nominal,
  exclude, duration, volume, exclude_half.life, include_half.life, ...)
```

Arguments

data	A data frame with concentration (or amount for urine/feces), time, and the groups defined in formula.
...	Ignored.
formula	The formula defining the concentration~time|groups or amount~time|groups for urine/feces (In the remainder of the documentation, "concentration" will be used to describe concentration or amount.) One special aspect of the groups part of the formula is that the last group is typically assumed to be the subject; see the documentation for the subject argument for exceptions to this assumption.
subject	The column indicating the subject number (used for plotting). If not provided, this defaults to the beginning of the inner groups: For example with concentration~time|Study+S the inner groups start with the first grouping variable before a /, Subject. If there is only one grouping variable, it is assumed to be the subject (e.g. concentration~time|Subject), and if there are multiple grouping variables without a /, subject is assumed to be the last one. For single-subject data, it is assigned as NULL.
time.nominal	(optional) The name of the nominal time column (if the main time variable is actual time. The time.nominal is not used during calculations; it is available to assist with data summary and checking.
exclude	(optional) The name of a column with concentrations to exclude from calculations and summarization. If given, the column should have values of NA or "" for concentrations to include and non-empty text for concentrations to exclude.
duration	(optional) The duration of collection as is typically used for concentration measurements in urine or feces.
volume	(optional) The volume (or mass) of collection as is typically used for urine or feces measurements.
exclude_half.life, include_half.life	Points to exclude from the half-life calculation (still using normal selection rules for the other points) or to include for the half-life (using specifically those points and bypassing automatic point selection).

Value

A PKNCAconc object that can be used for automated NCA.

See Also

Other PKNCA objects: PKNCAdata, PKNCAdose, PKNCAresults

PKNCAdata *Create a PKNCAdata object.*

Description

PKNCAdata combines PKNCAconc and PKNCAdose and adds in the intervals for PK calculations.

Usage

```
PKNCAdata(data.conc, data.dose, ...)

## S3 method for class 'PKNCAconc'
PKNCAdata(data.conc, data.dose, ...)

## S3 method for class 'PKNCAdose'
PKNCAdata(data.conc, data.dose, ...)

## Default S3 method:
PKNCAdata(data.conc, data.dose, ..., formula.conc,
  formula.dose, intervals, options = list())
```

Arguments

data.conc	Concentration data as a PKNCAconc object or a data frame
data.dose	Dosing data as a PKNCAdose object (see details)
...	arguments passed to PKNCAdata.default
formula.conc	Formula for making a PKNCAconc object with data.conc. This must be given if data.conc is a data.frame, and it must not be given if data.conc is a PKNCAconc object.
formula.dose	Formula for making a PKNCAdose object with data.dose. This must be given if data.dose is a data.frame, and it must not be given if data.dose is a PKNCAdose object.
intervals	A data frame with the AUC interval specifications as defined in check.interval.specification. If missing, this will be automatically chosen by choose.auc.intervals. (see details)
options	List of changes to the default PKNCA.options for calculations.

Details

If data.dose is not given or is NA, then the intervals must be given. At least one of data.dose and intervals must be given.

Value

A PKNCAdata object with concentration, dose, interval, and calculation options stored (note that PKNCAdata objects can also have results after a NCA calculations are done to the data).

See Also

choose.auc.intervals, pk.nca

Other PKNCA objects: PKNCAconc, PKNCAdose, PKNCAresults

PKNCAdose *Create a PKNCAdose object*

Description

Create a PKNCAdose object

Usage

```
PKNCAdose(data, ...)

## Default S3 method:
PKNCAdose(data, ...)

## S3 method for class 'tbl_df'
PKNCAdose(data, ...)

## S3 method for class 'data.frame'
PKNCAdose(data, formula, route, rate, duration,
  time.nominal, exclude, ...)
```

Arguments

data	A data frame with time and the groups defined in formula.
...	Ignored.
formula	The formula defining the dose.amount~time|groups where time is the time of the dosing and dose.amount is the amount administered at that time (see Details).
route	Define the route of administration. The value may be either a column name from the data (checked first) or a character string of either "extravascular" or "intravascular" (checked second). If given as a column name, then every value of the column must be either "extravascular" or "intravascular".
rate, duration	(optional) for "intravascular" dosing, the rate or duration of dosing. If given as a character string, it is the name of a column from the data, and if given as a number, it is the value for all doses. Only one may be given, and if neither is given, then the dose is assumed to be a bolus (duration=0). If rate is given, then the dose amount must be given (the left hand side of the formula).
time.nominal	(optional) The name of the nominal time column (if the main time variable is actual time. The time.nominal is not used during calculations; it is available to assist with data summary and checking.

exclude (optional) The name of a column with concentrations to exclude from calculations and summarization. If given, the column should have values of NA or "" for concentrations to include and non-empty text for concentrations to exclude.

Details

The formula for a PKNCAdose object can be given three ways: one-sided (missing left side), one-sided (missing right side), or two-sided. Each of the three ways can be given with or without groups. When given one-sided missing the left side, the left side can either be omitted or can be given as a period (.): ~time|treatment+subject and .~time|treatment+subject are identical, and dose-related NCA parameters will all be reported as not calculable (for example, clearance). When given one-sided missing the right side, the right side must be specified as a period (.): dose~.|treatment+subject, and only a single row may be given per group. When the right side is missing, PKNCA assumes that the same dose is given in every interval. When given as a two-sided formula

Value

A PKNCAconc object that can be used for automated NCA.

See Also

Other PKNCA objects: PKNCAconc, PKNCAdata, PKNCAresults

PKNCAresults *Generate a PKNCAresults object*

Description

This function should not be run directly. The object is created for summarization and plotting.

Usage

```
PKNCAresults(result, data, exclude)
```

Arguments

result	a data frame with NCA calculation results and groups. Each row is one interval and each column is a group name or the name of an NCA parameter.
data	The PKNCAdata used to generate the result
exclude	(optional) The name of a column with concentrations to exclude from calculations and summarization. If given, the column should have values of NA or "" for concentrations to include and non-empty text for concentrations to exclude.

Value

A PKNCAresults object with each of the above within.

See Also

Other PKNCA objects: `PKNCAconc`, `PKNCAdata`, `PKNCAdose`

`print.PKNCAconc` *Print and/or summarize a PKNCAconc or PKNCAdose object.*

Description

Print and/or summarize a PKNCAconc or PKNCAdose object.

Usage

```
## S3 method for class 'PKNCAconc'
print(x, n = 6, summarize = FALSE, ...)

## S3 method for class 'PKNCAconc'
summary(object, n = 0, summarize = TRUE, ...)

## S3 method for class 'PKNCAdose'
print(x, n = 6, summarize = FALSE, ...)

## S3 method for class 'PKNCAdose'
summary(object, n = 0, summarize = TRUE, ...)
```

Arguments

`x`	The object to print
`n`	The number of rows of data to show (see `head`)
`summarize`	Summarize the nested number of groups
`...`	Arguments passed to `print.formula` and `print.data.frame`
`object`	The object to summarize

`print.PKNCAdata` *Print a PKNCAdata object*

Description

Print a PKNCAdata object

Usage

```
## S3 method for class 'PKNCAdata'
print(x, ...)
```

Arguments

x	The object to print
...	Arguments passed on to print.PKNCAconc and print.PKNCAdose

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print.provenance *Print the summary of a provenance object*

Description

Print the summary of a provenance object

Usage

```
## S3 method for class 'provenance'
print(x, ...)
```

Arguments

x	The object to be printed
...	Ignored

Value

invisible text of the printed information

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print.summary_PKNCAresults *Print the results summary*

Description

Print the results summary

Usage

```
## S3 method for class 'summary_PKNCAresults'
print(x, ...)
```

Arguments

x	A summary_PKNCAresults object
...	passed to print.data.frame (row.names is always set to FALSE)

Value

x invisibly

See Also

summary.PKNCAresults

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roundingSummarize *During the summarization of PKNCAresults, do the rounding of values based on the instructions given.*

Description

During the summarization of PKNCAresults, do the rounding of values based on the instructions given.

Usage

```
roundingSummarize(x, name)
```

Arguments

x	The values to summarize
name	The NCA parameter name (matching a parameter name in PKNCA.set.summary)

Value

A string of the rounded value

---

roundString *Round a value to a defined number of digits printing out trailing zeros, if applicable.*

Description

Round a value to a defined number of digits printing out trailing zeros, if applicable.

Usage

```
roundString(x, digits = 0, sci_range = Inf, sci_sep = "e", si_range)
```

Arguments

x	The number to round
digits	integer indicating the number of decimal places
sci_range	See help for signifString (and you likely want to round with signifString if you want to use this argument)
sci_sep	The separator to use for scientific notation strings (typically this will be either "e" or "x10^" for computer- or human-readable output).
si_range	Deprecated, please use sci_range

Details

Values that are not standard numbers like Inf, NA, and NaN are returned as "Inf", "NA", and NaN.

Value

A string with the value

See Also

round, signifString

---

setAttributeColumn *Add an attribute to an object where the attribute is added as a name to the names of the object.*

Description

Add an attribute to an object where the attribute is added as a name to the names of the object.

Usage

```
setAttributeColumn(object, attr_name, col_or_value, col_name,
  default_value, stop_if_default, warn_if_default, message_if_default)
```

Arguments

object	The object to set the attribute column on.
attr_name	The attribute name to set
col_or_value	If this exists as a column in the data, it is used as the col_name. If not, this becomes the default_value.
col_name	The name of the column within the dataset to use (if missing, uses attr_name)
default_value	The value to fill in the column if the column does not exist (the column is filled with NA if it does not exist and no value is provided).

`stop_if_default, warn_if_default, message_if_default`
: A character string to provide as an error, a warning, or a messagemessage to the user if the `default_value` is used. They are tested in order (if stop, the code stops; if warning, the message is ignored; and message last).

Value

The object with the attribute column added to the data.

See Also

`getAttributeColumn`

`setDuration` *Set the duration of dosing or measurement*

Description

Set the duration of dosing or measurement

Usage

```
setDuration(object, ...)

## S3 method for class 'PKNCAdose'
setDuration(object, duration, rate, dose, ...)
```

Arguments

`object`	An object to set a duration on
`...`	Arguments passed to another setDuration function
`duration`	The value to set for the duration or the name of the column in the data to use for the duration.
`rate`	(for PKNCAdose objects only) The rate of infusion
`dose`	(for PKNCAdose objects only) The dose amount

Value

The object with duration set

setExcludeColumn *Set the exclude parameter on an object*

Description

This function adds the exclude column to an object. To change the exclude value, use the `exclude` function.

Usage

```
setExcludeColumn(object, exclude, dataname = "data")
```

Arguments

`object`	The object to set the exclude column on.
`exclude`	The column name to set as the exclude value.
`dataname`	The name of the data.frame within the object to add the exclude column to.

Value

The object with an exclude column and attribute

setRoute *Set the dosing route*

Description

Set the dosing route

Usage

```
setRoute(object, ...)

## S3 method for class 'PKNCAdose'
setRoute(object, route, ...)
```

Arguments

`object`	A PKNCAdose object
`...`	Arguments passed to another setRoute function
`route`	A character string indicating one of the following: the column from the data which indicates the route of administration, a scalar indicating the route of administration for all subjects, or a vector indicating the route of administration for each dose in the dataset.

Value

The object with an updated route

`signifString` *Round a value to a defined number of significant digits printing out trailing zeros, if applicable.*

Description

Round a value to a defined number of significant digits printing out trailing zeros, if applicable.

Usage

```
signifString(x, ...)

## S3 method for class 'data.frame'
signifString(x, ...)

## Default S3 method:
signifString(x, digits = 6, sci_range = 6,
  sci_sep = "e", si_range, ...)
```

Arguments

`x`	The number to round
`...`	Arguments passed to methods.
`digits`	integer indicating the number of significant digits
`sci_range`	integer (or `Inf`) indicating when to switch to scientific notation instead of floating point. Zero indicates always use scientific; `Inf` indicates to never use scientific notation; otherwise, scientific notation is used when `abs(log10(x)) > si_range`.
`sci_sep`	The separator to use for scientific notation strings (typically this will be either "e" or "x10^" for computer- or human-readable output).
`si_range`	Deprecated, please use `sci_range`

Details

Values that are not standard numbers like `Inf`, `NA`, and `NaN` are returned as `"Inf"`, `"NA"`, and `NaN`.

Value

A string with the value

See Also

`signif`, `roundString`

sort.interval.cols *Sort the interval columns by dependencies.*

Description

Columns are always to the right of columns that they depend on.

Usage

```
## S3 method for class 'interval.cols'
sort()
```

split.PKNCAconc *Divide into groups*

Description

`split.PKNCAconc` divides data into individual groups defined by `getGroups.PKNCAconc`.

Usage

```
## S3 method for class 'PKNCAconc'
split(x, f = getGroups(x), drop = TRUE, ...)

## S3 method for class 'PKNCAdata'
split(x, ...)

## S3 method for class 'PKNCAdose'
split(x, f = getGroups(x), drop = TRUE, ...)
```

Arguments

`x`	the object to split
`f`	the groups to use for splitting the object
`drop`	logical indicating if levels that do not occur should be dropped.
`...`	Ignored.

Details

If `x` is `NA` then a list with NA as the only element and a "groupid" attribute of an empty data.frame is returned.

Value

A list of objects with an attribute of groupid consisting of a data.frame with columns for each group.

summary.PKNCAdata *Summarize a PKNCAdata object showing important details about the concentration, dosing, and interval information.*

Description

Summarize a PKNCAdata object showing important details about the concentration, dosing, and interval information.

Usage

```
## S3 method for class 'PKNCAdata'
summary(object, ...)
```

Arguments

object	The PKNCAdata object to summarize.
...	arguments passed on to print.PKNCAdata

summary.PKNCAresults *Summarize PKNCA results*

Description

Summarize PKNCA results

Usage

```
## S3 method for class 'PKNCAresults'
summary(object, ...,
  drop.group = object$data$conc$subject, summarize.n.per.group = TRUE,
  not.requested.string = ".", not.calculated.string = "NC")
```

Arguments

object	The results to summarize
...	Ignored.
drop.group	Which group(s) should be dropped from the formula?
summarize.n.per.group	Should a column for N be added (TRUE or FALSE)? Note that N is maximum number of parameter results for any parameter; if no parameters are requested for a group, then N will be NA.

not.requested.string
: A character string to use when a parameter summary was not requested for a parameter within an interval.

not.calculated.string
: A character string to use when a parameter summary was requested, but the point estimate AND spread calculations (if applicable) returned NA.

Details

Excluded results will not be included in the summary.

Value

A data frame of NCA parameter results summarized according to the summarization settings.

See Also

PKNCA.set.summary, print.summary_PKNCAresults

Examples

```
conc_obj <- PKNCAconc(as.data.frame(datasets::Theoph), conc~Time|Subject)
d_dose <- unique(datasets::Theoph[datasets::Theoph$Time == 0,
                                  c("Dose", "Time", "Subject")])
dose_obj <- PKNCAdose(d_dose, Dose~Time|Subject)
data_obj_automatic <- PKNCAdata(conc_obj, dose_obj)
results_obj_automatic <- pk.nca(data_obj_automatic)
# To get standard results run summary
summary(results_obj_automatic)
# To enable numeric conversion and extraction, do not give a spread function
# and subsequently run as.numeric on the result columns.
PKNCA.set.summary(
  name=c("auclast", "cmax", "half.life", "aucinf.obs"),
  point=business.geomean,
  description="geometric mean"
)
PKNCA.set.summary(
  name=c("tmax"),
  point=business.median,
  description="median"
)
summary(results_obj_automatic, not.requested.string="NA")
```

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superposition *Compute noncompartmental superposition for repeated dosing*

Description

Compute noncompartmental superposition for repeated dosing

Usage

```
superposition(conc, ...)

## S3 method for class 'PKNCAconc'
superposition(conc, ...)

## S3 method for class 'numeric'
superposition(conc, time, dose.input, tau,
  dose.times = 0, dose.amount, n.tau = Inf, options = list(),
  lambda.z, clast.pred = FALSE, tlast, additional.times = c(),
  check.blq = TRUE, interp.method = NULL, extrap.method = "AUCinf",
  steady.state.tol = 0.001, ...)
```

Arguments

conc	Concentration measured
...	Additional arguments passed to the half.life function if required to compute lambda.z.
time	Time of concentration measurement
dose.input	The dose given to generate the conc and time inputs. If missing, output doses will be assumed to be equal to the input dose.
tau	The dosing interval
dose.times	The time of dosing within the dosing interval. The min(dose.times) must be >= 0, and the max(dose.times) must be < tau. There may be more than one dose times given as a vector.
dose.amount	The doses given for the output. Linear proportionality will be used from the input to output if they are not equal. The length of dose.amount must be either 1 or matching the length of dose.times.
n.tau	The number of tau dosing intervals to simulate or Inf for steady-state.
options	The PKNCA.options to use for the calculation (passed on to subsequent functions like pk.calc.half.life).
lambda.z	The elimination rate (from the half life calculation, used to extrapolate beyond the maximum time observed).
clast.pred	To use predicted as opposed to observed Clast, either give the value for clast.pred here or set it to true (for automatic calculation from the half-life).
tlast	The time of last observed concentration above the limit of quantificaiton. This is calculated if not provided.
additional.times	Times to include in the final outputs in addition to the standard times (see details). All min(additional.times) must be >= 0, and the max(additional.times) must be <= tau.
check.blq	Must the first concentration measurement be below the limit of quantification?
interp.method	See interp.extrap.conc

`extrap.method`
: See `interp.extrap.conc`

`steady.state.tol`
: The tolerance for assessing if steady-state has been achieved (between 0 and 1, exclusive).

Details

The returned superposition times will include all of the following times: 0 (zero), `dose.times`, `time` `modulo` `tau` (shifting `time` for each dose time as well), `additional.times`, and `tau`.

Value

A data frame with columns named "conc" and "time".

See Also

`interp.extrap.conc`

`tss.monoexponential.generate.formula` *A helper function to generate the formula and starting values for the parameters in monoexponential models.*

Description

A helper function to generate the formula and starting values for the parameters in monoexponential models.

Usage

```
tss.monoexponential.generate.formula(data)
```

Arguments

`data`	The data used for the model

Value

a list with elements for each of the variables