

Dept. of Clinical Pharmacology and Therapeutics

**Manual for Clinical Trial**

**Noncompartmental Analysis**

**Implemented in NonCompart R package**

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## [1] Preparation

This is just for the preparation of data for the subsequent R scripts.

```
Adm = c("BOLUS", "INFUSION", "EXTRAVASCULAR")[3] # Drug Administration Method
Dose = 320 # mg
x = x0 = Theoph[Theoph$Subject==1, "Time"] # h
y = y0 = Theoph[Theoph$Subject==1, "conc"] # ug/L

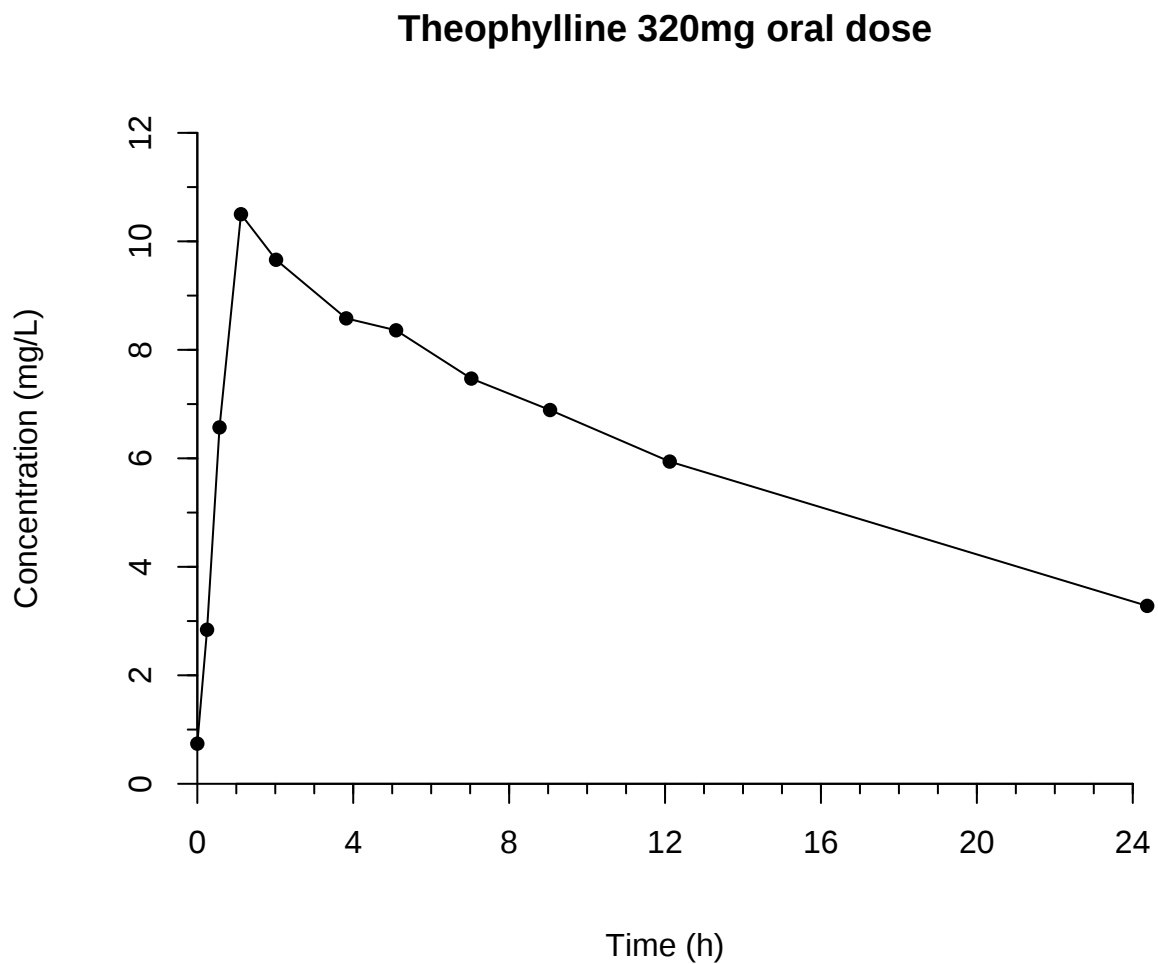
# For the calculation of AUClast
iLastNonZero = max(which(y > 0)) # index of last non-zero concentration
x1 = x0[1:iLastNonZero]
y1 = y0[1:iLastNonZero]

# For the log-concentration vs. time regression
x2 = x0[y0 > 0]
y2 = y0[y0 > 0]

# Print data
cbind(Time=x0, Conc=y0)
#      Time Conc
# [1,] 0.00 0.74
# [2,] 0.25 2.84
# [3,] 0.57 6.57
# [4,] 1.12 10.50
# [5,] 2.02 9.66
# [6,] 3.82 8.58
# [7,] 5.10 8.36
# [8,] 7.03 7.47
```

```
# [9,] 9.05 6.89
# [10,] 12.12 5.94
# [11,] 24.37 3.28
```

## [2] Plot of raw data



## [3] Cmax (CMAX)

Maximum concentration.

```
CMAX = NA
CMAX = max(y, na.rm=TRUE) ; CMAX
# [1] 10.5
```

#### [4] Cmax\_D (CMAXD)

Dose normalized Cmax.

```
CMAXD = NA  
CMAXD = CMAX/Dose ; CMAXD  
# [1] 0.0328125
```

#### [5] Tmax (TMAX)

Time of maximum concentration.

```
TMAX = NA  
if (CMAX > 0) TMAX = x[which.max(y)]  
TMAX  
# [1] 1.12
```

#### [6] Tlag (TLAG)

Time until first non-zero concentration.

```
TLAG = NA  
if (CMAX > 0) TLAG = x[max(1, min(which(y > 0)) - 1)]  
TLAG  
# [1] 0
```

#### [7] Clast (CLST)

Last non-zero concentration.

```
CLST = y[iLastNonZero] ; CLST  
# [1] 3.28
```

## [8] Tlast (TLST)

Time of last non-zero concentration.

```
TLST = x[iLastNonZero] ; TLST  
# [1] 24.37
```

## [9] Rsq (R2)

R-squared value from the log concentration and time regression.

## [10] Rsq\_adjusted (R2ADJ)

Adjusted R-squared value.

$$R_{\text{adj}}^2 = 1 - (1 - R^2) \frac{n - 1}{n - 2}$$

## [11] Corr\_XY (CORRXY)

Correlation value of the regression

## [12] b0

Intercept of the simple linear regression of log(y) vs x

## [13] Lambda\_z (LAMZ)

Terminal slope as a positive value

## [14] No\_points\_Lambda\_z (LAMZNPT)

Number of points used for the regression

## [15] Lambda\_z\_lower (LAMZLL)

First time point used for the regression

## [16] Lambda\_z\_upper (LAMZUL)

Last time point used for the regression

## [17] R2, R2ADJ, CORRXY, b0, LAMZ, LAMZNPT, LAMZLL, LAMZUL

Only positive concentrations are used. In case of oral administration, the first possible point is next to Tmax point. In case of intravascular administration, the first point can be Tmax point. If the difference of R2ADJ (R2-squared adjusted) is less than 1e-4, the longer slope is chosen. Regression points should be at least 3.

```
x = x2 ; y = y2

if (toupper(Adm) == "EXTRAVASCULAR") {
  iFirst = which.max(y) + 1 # for oral administration
} else {
  iFirst = which.max(y)      # for intravenous administration
}
iLast = iLastNonZero

ColNames = c("R2", "R2ADJ", "CORRXY", "b0", "LAMZ", "LAMZNPT", "LAMZLL", "LAMZUL")
mRes = matrix(nrow = iLast - iFirst + 1 - 2, ncol=length(ColNames))
colnames(mRes) = ColNames
for (i in iFirst:(iLast - 2)) {
  Res = lm(log(y[i:iLast]) ~ x[i:iLast])
  mRes[i - iFirst + 1, "R2"]      = summary(Res)$r.squared
  mRes[i - iFirst + 1, "R2ADJ"]  = summary(Res)$adj.r.squared
  mRes[i - iFirst + 1, "CORRXY"] = cor(log(y[i:iLast]), x[i:iLast])
  mRes[i - iFirst + 1, "b0"]     = Res$coefficients[1]
  mRes[i - iFirst + 1, "LAMZ"]   = -Res$coefficients[2]
  mRes[i - iFirst + 1, "LAMZNPT"] = iLast - i + 1
  mRes[i - iFirst + 1, "LAMZLL"] = x[i]
  mRes[i - iFirst + 1, "LAMZUL"] = x[iLast]
} ; mRes
```

```
#           R2      R2ADJ      CORRXY      b0      LAMZ LAMZNPT LAMZLL LAMZUL
# [1,] 0.9988013 0.9985615 -0.9994005 2.355187 0.04778625      7  2.02  24.37
# [2,] 0.9987305 0.9984131 -0.9993650 2.350845 0.04751440      6  3.82  24.37
# [3,] 0.9995671 0.9994229 -0.9997836 2.362429 0.04817356      5  5.10  24.37
# [4,] 0.9996109 0.9994164 -0.9998054 2.356834 0.04787556      4  7.03  24.37
# [5,] 0.9999997 0.9999995 -0.9999999 2.368785 0.04845700      3  9.05  24.37

OKs = abs(max(mRes[, "R2ADJ"]) - mRes[, "R2ADJ"]) < 1e-4
resNCA = as.data.frame(mRes[which(OKs)[1],,drop=FALSE]) ; resNCA
#           R2      R2ADJ      CORRXY      b0      LAMZ LAMZNPT LAMZLL LAMZUL
# 1 0.9999997 0.9999995 -0.9999999 2.368785 0.048457      3  9.05  24.37
attach(resNCA, warn.conflicts=FALSE)
```

If you want to manually omit some points, use an R package for convenience.

## [18] HL\_Lambda\_z (LAMZHL)

Terminal half-life calculated by  $\ln(2)/\lambda_Z$

```
LAMZHL = NA
if (LAMZ > 0) LAMZHL = log(2)/LAMZ
LAMZHL
# [1] 14.30438
```

## [19] Clast\_pred (CLSTP)

Predicted Clast, predicted concentration at Tlast.

$$C_{\text{last,pred}} = \exp(\beta_0 - \lambda \cdot T_{\text{last}})$$

```
CLSTP = NA
if (LAMZ > 0) CLSTP = exp(b0 - LAMZ*x[iLast])
CLSTP
# [1] 3.280146
```

## [20] C0 (C0)

Concentration at time 0, initial concentration. This is calculated only for BOLUS administration.

$$C_0 = \exp \left( \log(C_1) - t_1 \frac{\log(C_2) - \log(C_1)}{t_2 - t_1} \right)$$

```
x = x0 ; y = y0
if (toupper(Adm) == "BOLUS") {
  if (y[1] > y[2] & y[2] > 0) {
    C0 = exp(log(y[1]) - x[1]*(log(y[2]) - log(y[1]))/(x[2] - x[1]))
  } else {
    C0 = y[x==min(x[y > 0])]
  }
} else {
  C0 = NA
}
```

## [21] AUClast (AUCLAST)

Area under the time-concentration curve from dosing to the last positive concentration.

For linear trapezoidal method,

$$AUC_{\text{last}} = \sum_{i=2} \frac{(t_i - t_{i-1}) \times (C_i + C_{i-1})}{2}$$

```
n = length(x1)
AUCLAST = sum((y1[-1] + y1[-n]) * (x1[-1] - x1[-n]))/2 ; AUCLAST
# [1] 148.923
```

For 'linear-up log-down' method,

```
AUCLAST = 0
for (i in 2:n) {
  if (y1[i] < y1[i-1] & y1[i] > 0) {
    k = (log(y1[i - 1]) - log(y1[i]))/(x1[i] - x1[i - 1]) # slope in log
    AUCLAST = AUCLAST + (y1[i - 1] - y1[i])/k
  } else {
    AUCLAST = AUCLAST + (x1[i] - x1[i - 1])*(y1[i] + y1[i - 1])/2
  }
} ; AUCLAST
```

## [22] AUCall (AUCALL)

AUC values including all zero concentrations.

For linear trapezoidal method,

```
AUCALL = sum((y0[-1] + y0[-n]) * (x0[-1] - x0[-n]))/2 ; AUCALL
# [1] 148.923
```

For 'linear-up log-down' method,

```
AUCALL = 0
for (i in 2:n) {
  if (y0[i] < y0[i-1] & y0[i] > 0) {
    k = (log(y0[i - 1]) - log(y0[i]))/(x0[i] - x0[i - 1]) # slope in log
    AUCALL = AUCALL + (y0[i - 1] - y0[i])/k
  } else {
    AUCALL = AUCALL + (x0[i] - x0[i - 1])*(y0[i] + y0[i - 1])/2
  }
} ; AUCALL
```

Zero concentrations to be log-transformed need not be removed, because R can handle infinity value.

## [23] AUCtau (AUCTAU)

Area under the curve over one dosing interval, from dosing (time 0) to  $\tau$ , the dosing interval. This is calculated only at steady state (SS=TRUE), when tau is required; its unit unitTau defaults to "h" and is converted into the unit of time. Available since NonCompart 0.8.4.

$$\text{AUC}_{\text{tau}} = \int_0^{\tau} C(t) dt$$

The same trapezoidal rules as for AUClast (linear, or linear-up log-down) are applied over  $0 \leq t \leq \tau$ . When  $\tau$  is not a sampling time, the concentration at  $\tau$  is interpolated between the two neighboring samples (linearly, or log-linearly for a descending segment under the log-down method). When  $\tau$  is later than  $T_{\text{last}}$ , the concentration at  $\tau$  is predicted from the terminal regression,  $\exp(\beta_0 - \lambda_z \tau)$ ,

and the segment after  $T_{\text{last}}$  is integrated by the log-down rule; without a terminal slope AUCTAU is NA. This is the interval AUC that iAUC with Start=0 and End=tau gives.

For a steady-state profile sampled over one 12 h dosing interval (pre-dose trough 2 mg/L, then 6, 10, 8, 4 and 2 mg/L at 1, 2, 4, 8 and 12 h), the linear trapezoidal method gives

```
tau = 12
xs = c(0, 1, 2, 4, 8, 12)
ys = c(2, 6, 10, 8, 4, 2)
ns = length(xs)
AUCTAU = sum((ys[-1] + ys[-ns]) * (xs[-1] - xs[-ns]))/2 ; AUCTAU
# [1] 66
```

## [24] Cavg (CAVG)

Average concentration over the dosing interval at steady state. This is calculated only at steady state (SS=TRUE).

$$C_{\text{avg}} = \frac{\text{AUC}_{\text{tau}}}{\tau}$$

```
CAVG = AUCTAU/tau ; CAVG
# [1] 5.5
```

## [25] AUCinf\_obs (AUCIFO)

AUCinf observed.

$$\text{AUC}_{\text{inf,obs}} = \text{AUC}_{\text{last}} + \frac{C_{\text{last}}}{\lambda_z}$$

## [26] AUC\_%Extrap\_obs (AUCPEO)

AUC percent extrapolated observed.

$$\text{AUC}_{\% \text{Extrap,obs}} = \left( 1 - \frac{\text{AUC}_{\text{last}}}{\text{AUC}_{\text{inf,obs}}} \right) \times 100$$

### [27] AUCinf\_D\_obs (AUCIFOD)

Dose normalized AUCinf observed.

$$AUC_{\text{dose,inf,obs}} = \frac{AUC_{\text{inf,obs}}}{\text{Dose}}$$

### [28] AUCinf\_pred (AUCIFP)

AUCinf predicted.

$$AUC_{\text{inf,pred}} = AUC_{\text{last}} + \frac{C_{\text{last,pred}}}{\lambda_z}$$

### [29] AUC\_%Extrap\_pred (AUCPEP)

AUC percent extrapolated predicted.

$$AUC_{\% \text{Extrap,pred}} = \left( 1 - \frac{AUC_{\text{last}}}{AUC_{\text{inf,pred}}} \right) \times 100$$

### [30] AUCinf\_D\_pred (AUCIFPD)

Dose normalized AUCinf predicted.

$$AUC_{\text{dose,inf,pred}} = \frac{AUC_{\text{inf,pred}}}{\text{Dose}}$$

### [31] AUMClast (AUMCLST)

$$AUMC_{\text{last}} = \int_0^{t_{\text{last}}} t C(t) dt$$

For linear trapezoidal method;

$$AUMC_{\text{last}} \approx \sum_{i=2} \frac{(t_i - t_{i-1}) \times (t_i C_i + t_{i-1} C_{i-1})}{2}$$

```
AUMCLST = sum((x1[-1] - x1[-n])*(x1[-1]*y1[-1] + x1[-n]*y1[-n]))/2
```

For ‘linear-up log-down’ method;

```
AUMCLST = 0
for (i in 2:n) {
  if (y1[i] < y1[i-1] & y1[i] > 0) {
    k = (log(y1[i-1]) - log(y1[i]))/(x1[i] - x1[i-1]) # slope in log
    AUMCLST = AUMCLST + (x1[i-1]*y1[i-1] - x1[i]*y1[i])/k + (y1[i-1] - y1[i])/k/k
  } else {
    AUMCLST = AUMCLST + (x1[i] - x1[i-1])*(x1[i]*y1[i] + x1[i-1]*y1[i-1])/2
  }
}
```

### [32] AUMC<sub>inf\_obs</sub> (AUMCIFO)

AUMC infinity observed.

$$\text{AUMC}_{\text{inf,obs}} = \text{AUMC}_{\text{last}} + \frac{C_{\text{last}} T_{\text{last}}}{\lambda_z} + \frac{C_{\text{last}}}{\lambda_z^2}$$

### [33] AUMC\_%Extrap\_obs (AUMCPEO)

AUMC percent extrapolated observed.

$$\text{AUMC}_{\%Extrap,obs} = \left(1 - \frac{\text{AUMC}_{\text{last}}}{\text{AUMC}_{\text{inf,obs}}}\right) \times 100$$

### [34] AUMC<sub>inf\_pred</sub> (AUMCIFP)

AUMC infinity predicted.

$$\text{AUMC}_{\text{inf,pred}} = \text{AUMC}_{\text{last}} + \frac{C_{\text{last,pred}} T_{\text{last}}}{\lambda_z} + \frac{C_{\text{last,pred}}}{\lambda_z^2}$$

### [35] AUMC\_%Extrap\_pred (AUMCPEP)

AUMC percent extrapolated predicted.

$$\text{AUMC}_{\% \text{Extrap, pred}} = \left( 1 - \frac{\text{AUMC}_{\text{last}}}{\text{AUMC}_{\text{inf, pred}}} \right) \times 100$$

### [36] AUC\_Back\_Ext\_obs (AUCBEO)

AUC back extrapolated observed. This is only for BOLUS administration.

For trapezoidal method;

$$\text{AUC}_{\text{backextrap}} = \frac{t_1 \times (C_0 + C_1)}{2}$$

For log-down method;

$$\text{AUC}_{\text{backextrap}} = \frac{t_1 \times (C_0 - C_1)}{\log(C_0) - \log(C_1)}$$

### [37] AUC\_%Back\_Ext\_obs (AUCPBEO)

AUC percent back extrapolated observed. This is only for BOLUS administration.

$$\text{AUC}_{\% \text{backextrap, obs}} = \frac{\text{AUC}_{\text{backextrap}}}{\text{AUC}_{\text{inf, obs}}} \times 100$$

### [38] AUC\_%Back\_Ext\_pred (AUCPBEP)

AUC percent back extrapolated predicted. This is only for BOLUS administration.

$$\text{AUC}_{\% \text{backextrap, pred}} = \frac{\text{AUC}_{\text{backextrap}}}{\text{AUC}_{\text{inf, pred}}} \times 100$$

### [39] MRTlast (MRTEVLST, MRTIVLST)

Mean Residence Time (MRT) from 0 to Tlast.

$$\text{MRT}_{\text{EV,last}} = \frac{\text{AUMC}_{\text{last}}}{\text{AUC}_{\text{last}}}$$

$$\text{MRT}_{\text{IV,last}} = \frac{\text{AUMC}_{\text{last}}}{\text{AUC}_{\text{last}}} - \frac{\text{Dur}}{2}$$

EV: extravascular

IV: intravascular

Dur: duration of infusion

### [40] MRTinf\_obs (MRTEVIFO, MRTIVIFO)

MRT infinity observed. Not calculated (NA) at steady state (SS=TRUE).

$$\text{MRT}_{\text{EV,inf,obs}} = \frac{\text{AUMC}_{\text{inf,obs}}}{\text{AUC}_{\text{inf,obs}}}$$

$$\text{MRT}_{\text{IV,inf,obs}} = \frac{\text{AUMC}_{\text{inf,obs}}}{\text{AUC}_{\text{inf,obs}}} - \frac{\text{Dur}}{2}$$

### [41] MRTinf\_pred (MRTEVIFP, MRTIVIFP)

MRT infinity predicted. Not calculated (NA) at steady state (SS=TRUE).

$$\text{MRT}_{\text{EV,inf,pred}} = \frac{\text{AUMC}_{\text{inf,pred}}}{\text{AUC}_{\text{inf,pred}}}$$

$$\text{MRT}_{\text{IV,inf,pred}} = \frac{\text{AUMC}_{\text{inf,pred}}}{\text{AUC}_{\text{inf,pred}}} - \frac{\text{Dur}}{2}$$

#### [42] Vz\_obs (VZO) or Vz\_F\_obs (VZFO)

Volume of distribution by AUCIFO. VZO is for intravascular administration and VZFO for extravascular administration.

$$V_{z,obs} = \frac{\text{Dose}}{\text{AUC}_{inf,obs} \times \lambda_z}$$

At steady state (SS=TRUE) the area over one dosing interval takes the place of  $\text{AUC}_{inf,obs}$ :

$$V_{z,obs} = \frac{\text{Dose}}{\text{AUC}_{\tau} \times \lambda_z}$$

Up to NonCompart 0.8.3,  $\text{AUC}_{last}$  was used here at steady state; it equals  $\text{AUC}_{\tau}$  only when the last sample falls exactly at  $\tau$ .

#### [43] Vz\_pred (VZP) or Vz\_F\_pred (VZFP)

Volume of distribution by AUCIFP. VZP is for intravascular administration and VZFP for extravascular administration. Not calculated (NA) at steady state.

$$V_{z,pred} = \frac{\text{Dose}}{\text{AUC}_{inf,pred} \times \lambda_z}$$

#### [44] CL\_obs (CLO) or CL\_F\_obs (CLFO)

Clearance observed. CLO is for intravascular administration and CLFO for extravascular administration.

$$\text{CL}_{obs} = \frac{\text{Dose}}{\text{AUC}_{inf,obs}}$$

At steady state (SS=TRUE) the dose given in one dosing interval is cleared over that interval, so

$$\text{CL}_{obs} = \frac{\text{Dose}}{\text{AUC}_{\tau}}$$

Up to NonCompart 0.8.3,  $\text{AUC}_{last}$  was used here at steady state; it equals  $\text{AUC}_{\tau}$  only when the last sample falls exactly at  $\tau$ .

#### [45] CL\_pred (CLP) or CL\_F\_pred (CLFP)

Clearance predicted. CLP is for intravascular administration and CLFP for extravascular administration. Not calculated (NA) at steady state.

$$CL_{pred} = \frac{Dose}{AUC_{inf,pred}}$$

#### [46] Vss\_obs (VSSO)

Volume of distribution at steady state, observed. This is for intravascular administration only.

$$V_{ss,obs} = MRT_{IV,inf,obs} \times CL_{obs}$$

With SS=TRUE, where  $MRT_{IV,inf,obs}$  is not calculated,  $MRT_{IV,last}$  is used with  $CL_{obs} = Dose/AUC_{tau}$ :

$$V_{ss,obs} = MRT_{IV,last} \times CL_{obs}$$

#### [47] Vss\_pred (VSSP)

Volume of distribution at steady state, predicted. This is for intravascular administration only. Not calculated (NA) at steady state (SS=TRUE).

$$V_{ss,pred} = MRT_{IV,inf,pred} \times CL_{pred}$$

#### [48] AmtRecLast (RCAMLST)

Amount recovered in urine.

$$Ae_{last} = \sum_{i=1} Vol_i Conc_i$$

#### [49] CL<sub>renal</sub> (RENALCL)

Renal clearance.

$$CL_R = \frac{Ae_{last}}{AUC_{last}}$$

#### [50] fe (FE)

Fraction excreted unchanged.

$$fe = \frac{CL_R}{CL_{obs}} = \frac{Ae_{last}/AUC_{last}}{Dose/AUC_{inf,obs}} = \frac{Ae_{last}}{Dose} \times \frac{AUC_{inf,obs}}{AUC_{last}}$$

#### [51] AI (ARCMAX, ARAUC, ARCMIN)

Accumulation index, accumulation ratio.

$$R_{ac} = \frac{C_{max,ss}}{C_{max,1}} = \frac{AUC_{tau,ss}}{AUC_{tau,1}} = \frac{AUC_{inf,ss}}{AUC_{inf,1}} = \frac{C_{min,ss}}{C_{min,1}}$$

## Example using NonCompart::sNCA

```
require(NonCompart)
# Loading required package: NonCompart
x = Theoph[Theoph$Subject==1, "Time"]
y = Theoph[Theoph$Subject==1, "conc"]
r1 = sNCA(x, y, dose=320, concUnit="mg/L") ; r1
#           b0           CMAX           CMAXD           TMAX           TLAG           CLST
# 2.3687851 10.5000000 0.0328125 1.1200000 0.0000000 3.2800000
#           CLSTP           TLST           LAMZHL           LAMZ           LAMZLL           LAMZUL
# 3.2801465 24.3700000 14.3043776 0.0484570 9.0500000 24.3700000
#           LAMZNPT           CORRX           R2           R2ADJ           AUCLST           AUCALL
# 3.0000000 -0.9999999 0.9999997 0.9999995 148.9230500 148.9230500
#           AUCIFO           AUCIFOD           AUCIFP           AUCIFPD           AUCPEO           AUCPEP
# 216.6119330 0.6769123 216.6149558 0.6769217 31.2489169 31.2498763
#           AUMCLST           AUMCIFO           AUMCIFP           AUMCPEO           AUMCPEP           VZFO
# 1459.0711035 4505.5348194 4505.6708646 67.6160287 67.6170065 30.4867482
#           VZFP           CLFO           CLFP           MRTEVLST           MRTEVIFO           MRTEVIFP
# 30.4863228 1.4772963 1.4772757 9.7974834 20.8000305 20.8003683
# attr(,"units")
# [1] "" "mg/L" "mg/L/mg" "h" "h" "mg/L" "mg/L"
# [8] "h" "h" "/h" "h" "h" "" ""
# [15] "" "" "h*mg/L" "h*mg/L" "h*mg/L" "h*mg/L/mg" "h*mg/L"
# [22] "h*mg/L/mg" "%" "%" "h2*mg/L" "h2*mg/L" "h2*mg/L" "%"
# [29] "%" "L" "L" "L/h" "L/h" "h" "h"
# [36] "h"
# attr(,"UsedPoints")
# [1] 9 10 11
```

```
r2 = data.frame(VALUE=r1, UNIT=attr(r1, "units")) ; r2
```

| #          | VALUE        | UNIT      |
|------------|--------------|-----------|
| # b0       | 2.3687851    |           |
| # CMAX     | 10.5000000   | mg/L      |
| # CMAXD    | 0.0328125    | mg/L/mg   |
| # TMAX     | 1.1200000    | h         |
| # TLAG     | 0.0000000    | h         |
| # CLST     | 3.2800000    | mg/L      |
| # CLSTP    | 3.2801465    | mg/L      |
| # TLST     | 24.3700000   | h         |
| # LAMZHL   | 14.3043776   | h         |
| # LAMZ     | 0.0484570    | /h        |
| # LAMZLL   | 9.0500000    | h         |
| # LAMZUL   | 24.3700000   | h         |
| # LAMZNPT  | 3.0000000    |           |
| # CORRX    | -0.9999999   |           |
| # R2       | 0.9999997    |           |
| # R2ADJ    | 0.9999995    |           |
| # AUCLST   | 148.9230500  | h*mg/L    |
| # AUCALL   | 148.9230500  | h*mg/L    |
| # AUCIFO   | 216.6119330  | h*mg/L    |
| # AUCIFOD  | 0.6769123    | h*mg/L/mg |
| # AUCIFP   | 216.6149558  | h*mg/L    |
| # AUCIFPD  | 0.6769217    | h*mg/L/mg |
| # AUCPEO   | 31.2489169   | %         |
| # AUCPEP   | 31.2498763   | %         |
| # AUMCLST  | 1459.0711035 | h2*mg/L   |
| # AUMCIFO  | 4505.5348194 | h2*mg/L   |
| # AUMCIFP  | 4505.6708646 | h2*mg/L   |
| # AUMCPEO  | 67.6160287   | %         |
| # AUMCPEP  | 67.6170065   | %         |
| # VZFO     | 30.4867482   | L         |
| # VZFP     | 30.4863228   | L         |
| # CLFO     | 1.4772963    | L/h       |
| # CLFP     | 1.4772757    | L/h       |
| # MRTEVLST | 9.7974834    | h         |
| # MRTEVIFO | 20.8000305   | h         |
| # MRTEVIFP | 20.8003683   | h         |

## [1] Steady state

One dosing interval of a q12h regimen at steady state, sampled from the pre-dose trough to the next dose. tau is the dosing interval; AUCTAU, CAVG, CLF0 and VZF0 are derived over it, and the Pred twins and the MRT to infinity are NA.

```
xs = c(0, 1, 2, 4, 8, 12)
ys = c(2, 6, 10, 8, 4, 2)
r3 = snca(xs, ys, dose=100, concUnit="mg/L", SS=TRUE, tau=12)
data.frame(VALUE=r3, UNIT=attr(r3, "units"))
```

| #         | VALUE       | UNIT      |
|-----------|-------------|-----------|
| # b0      | 2.7725887   |           |
| # CMAX    | 10.0000000  | mg/L      |
| # CMAXD   | 0.1000000   | mg/L/mg   |
| # TMAX    | 2.0000000   | h         |
| # TLAG    | 0.0000000   | h         |
| # CLST    | 2.0000000   | mg/L      |
| # CLSTP   | 2.0000000   | mg/L      |
| # TLST    | 12.0000000  | h         |
| # LAMZHL  | 4.0000000   | h         |
| # LAMZ    | 0.1732868   | /h        |
| # LAMZLL  | 4.0000000   | h         |
| # LAMZUL  | 12.0000000  | h         |
| # LAMZNPT | 3.0000000   |           |
| # CORRX   | -1.0000000  |           |
| # R2      | 1.0000000   |           |
| # R2ADJ   | 1.0000000   |           |
| # AUCLST  | 66.0000000  | h*mg/L    |
| # AUCALL  | 66.0000000  | h*mg/L    |
| # AUCIF0  | 77.5415603  | h*mg/L    |
| # AUCIF0D | 0.7754156   | h*mg/L/mg |
| # AUCIFP  | 77.5415603  | h*mg/L    |
| # AUCIFPD | 0.7754156   | h*mg/L/mg |
| # AUCPE0  | 14.8843540  | %         |
| # AUCPEP  | 14.8843540  | %         |
| # AUMCLST | 308.0000000 | h2*mg/L   |
| # AUMCIF0 | 513.1025313 | h2*mg/L   |
| # AUMCIFP | 513.1025313 | h2*mg/L   |
| # AUMCPE0 | 39.9730110  | %         |
| # AUMCPEP | 39.9730110  | %         |
| # AUCTAU  | 66.0000000  | h*mg/L    |
| # CAVG    | 5.5000000   | mg/L      |

|            |           |     |
|------------|-----------|-----|
| # VZF0     | 8.7436063 | L   |
| # VZFP     | NA        | L   |
| # CLF0     | 1.5151515 | L/h |
| # CLFP     | NA        | L/h |
| # MRTEVLST | 4.6666667 | h   |
| # MRTEVIF0 | NA        | h   |
| # MRTEVIFP | NA        | h   |

## Session Information

### Compile Time

```
# [1] "2026-09-11 09:35:14 KST"
```

### Session Information

```
# R version 4.6.1 (2026-06-24 ucrt)
# Platform: x86_64-w64-mingw32/x64
# Running under: Windows 11 x64 (build 26100)
#
# Matrix products: default
# LAPACK version 3.12.1
#
# locale:
# [1] LC_COLLATE=Korean_Korea.utf8 LC_CTYPE=Korean_Korea.utf8
# [3] LC_MONETARY=Korean_Korea.utf8 LC_NUMERIC=C
# [5] LC_TIME=Korean_Korea.utf8
#
# time zone: Asia/Seoul
# tzcode source: internal
#
# attached base packages:
# [1] stats      graphics  grDevices  utils      datasets  methods   base
#
# other attached packages:
# [1] NonCompart_0.8.4 knitr_1.51
```