PIPET
Pharmacometrics Institute for Practical Education and Training

제약사 연구원을 위한 약동학 코스

Excel, R을 사용한 비구획분석 (NCA) Hands-on

가톨릭대학교 약리학교실
한성필

다운로드: bit.ly/pharma-pk-course

앱: asan.shinyapps.io/pkrshiny

목적

- Excel을 사용한 수작업 비구획분석을 수행하고 이론을 이해합니다.
- R을 사용하여 (= 코딩하여) 비구획분석을 수행할 수 있도록 안내할 것입니다.

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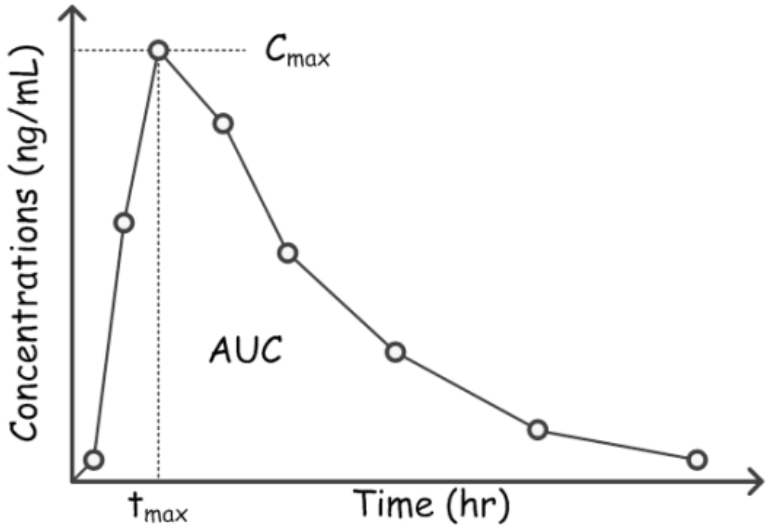
Excel을 사용한 비구획분석 (NCA) Hands-on

비구획 분석이란

- 시간, 농도가 표현되어 있는 곡선에서 아무런 가정을 하지 않고 분석
- 최대농도 (C_{max}) 및 최대농도에 도달하는 시간 (T_{max}), 전체 시간-농도 곡선의 면적 (Area under the time-concentration curve, AUC)



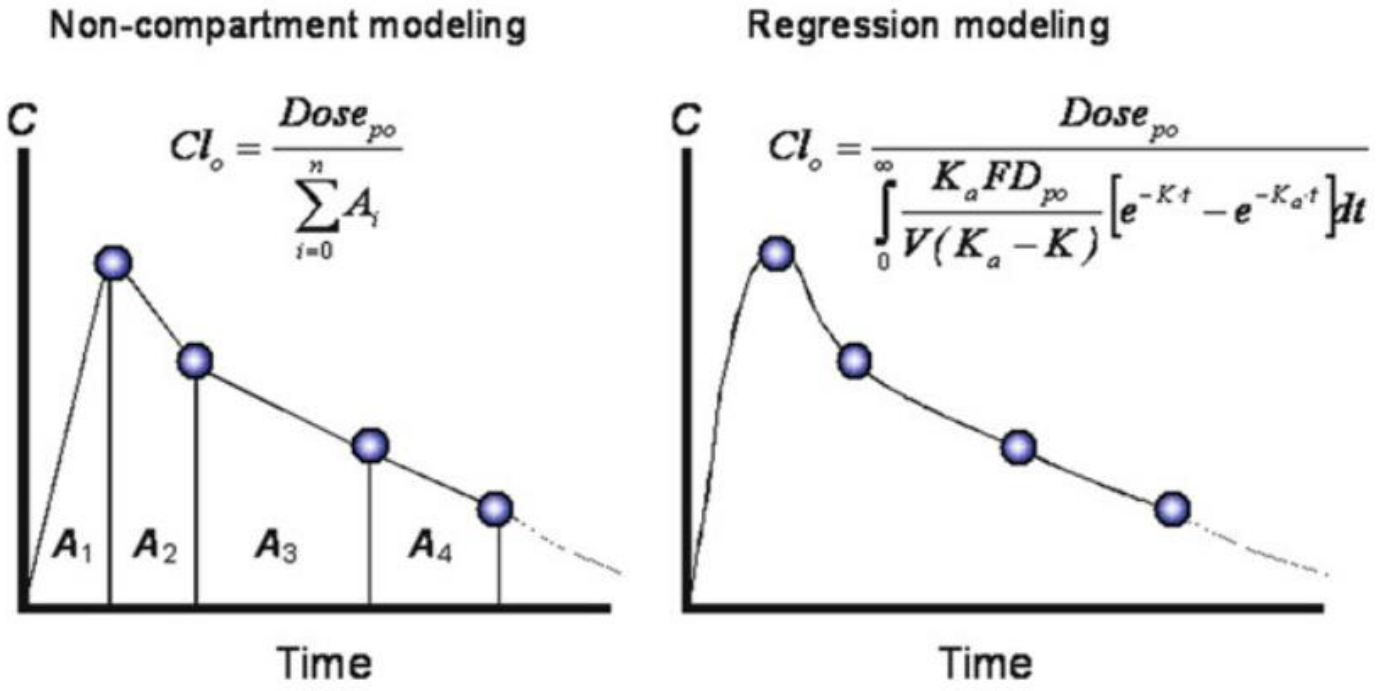


Fig. 1. Comparison of NCA (*left*) and nonlinear regression modeling (*right*). K_a, K, and V in the *right-hand panel* indicate the model parameters to be estimated by regressing the model to data.

$$\mu_m \text{ or } m\text{th moment} = \int_0^\infty t^m f(t)\, dt$$ Eq.1

where $f(t)$ is the probability density function, t is time, and m is the mth moment.

For example, when $m = 0$, substituting for $m = 0$ yields Equation 2 called the *zero moment*, μ_0:

$$\mu_0 = \int_0^\infty f(t)\, dt \quad [\text{AUC}]_0^\infty = \int C\, dt$$

If the distribution is a true probability function, the area under the zero moment curve is 1.

Substituting into Equation 1 with $m = 1$, Equation 3 gives the first moment μ_1

$$\mu_1 = \int_0^\infty t^1 f(t)\, dt \quad [\text{AUMC}]_0^\infty = \int t \times C\, dt$$

The area under the curve $f(t)$ times t is called the AUMC, or the *area under the first moment curve*. The *first moment*, μ_1, defines the *mean* of the distribution.

I.V. bolus injection – Calculation of AUC and AUMC

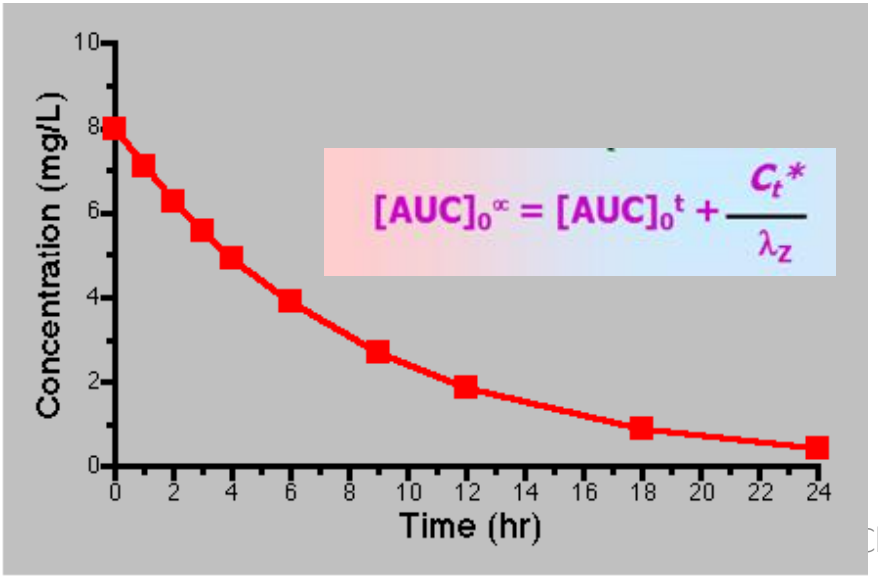
Time (hr)	Cp (mg/L)	Cp•t (mg.hr/L)	AUC (mg.hr/L)	AUMC (mg.hr^2/L)
0	0	0	0	0
1	7.09	7.09	7.54	3.54
2	6.29	12.6	14.2	13.4
3	5.58	16.7	20.2	28.1
4	4.95	19.8	25.4	46.3
6	3.89	23.4	34.3	89.5
9	2.71	24.5	44.2	161.2
12	1.89	22.7	51.1	232
18	0.92	16.6	59.6	350
24	0.44	10.8	63.7	432
∞			67.4	553

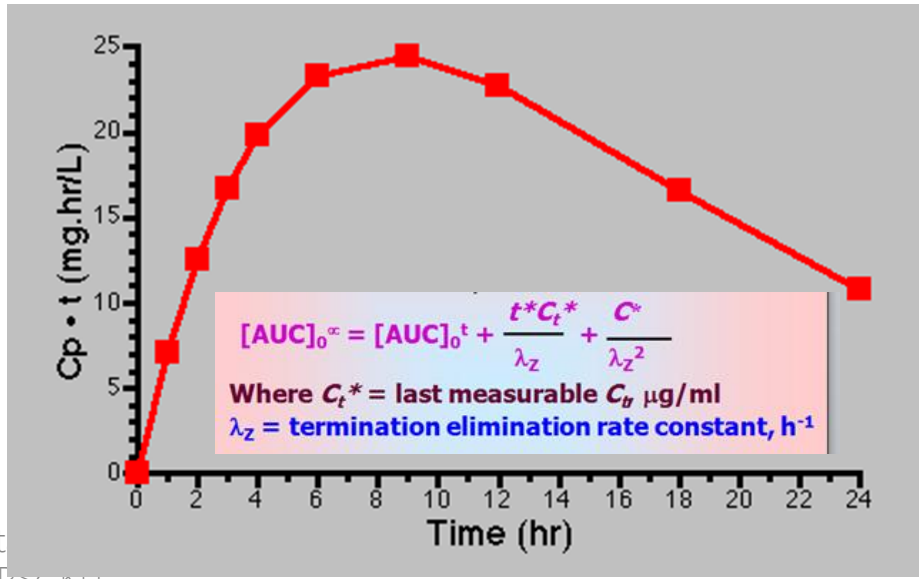
$$AUC_0^{t_{last}} = \sum_{i=1}^{n} \frac{C_i + C_{i+1}}{2} \cdot \Delta t,$$

$$AUC_{t_{last}}^{\infty} = \int_{t_{last}}^{\infty} C_{last} \cdot e^{-\lambda_z (t - t_{last})} dt = C_{last} \left[\frac{e^{-\lambda_z (t - t_{last})}}{-\lambda_z} \right]_{t_{last}}^{\infty}$$
$$= C_{last} \left[0 - \frac{1}{-\lambda_z} \right] = \frac{C_{last}}{\lambda_z},$$

$$AUMC_0^{t_{last}} = \sum_{i=1}^{n} \frac{t_i \cdot C_i + t_{i+1} \cdot C_{i+1}}{2} \cdot \Delta t.$$

$$AUMC_{t_{last}}^{\infty} = \int_{t_{last}}^{\infty} t \cdot C dt = \int_{t_{last}}^{\infty} t \cdot C_{last} e^{-\lambda_z (t - t_{last})} dt$$
$$= C_{last} \cdot e^{\lambda_z t_{last}} \left[\frac{t \cdot e^{-\lambda_z t_{last}}}{-\lambda_z} + \frac{e^{-\lambda_z t_{last}}}{-\lambda_z^2} \right]_{t_{last}}^{\infty}$$
$$= \frac{C_{last} \cdot t_{last}}{\lambda_z} + \frac{C_{last}}{\lambda_z^2}.$$





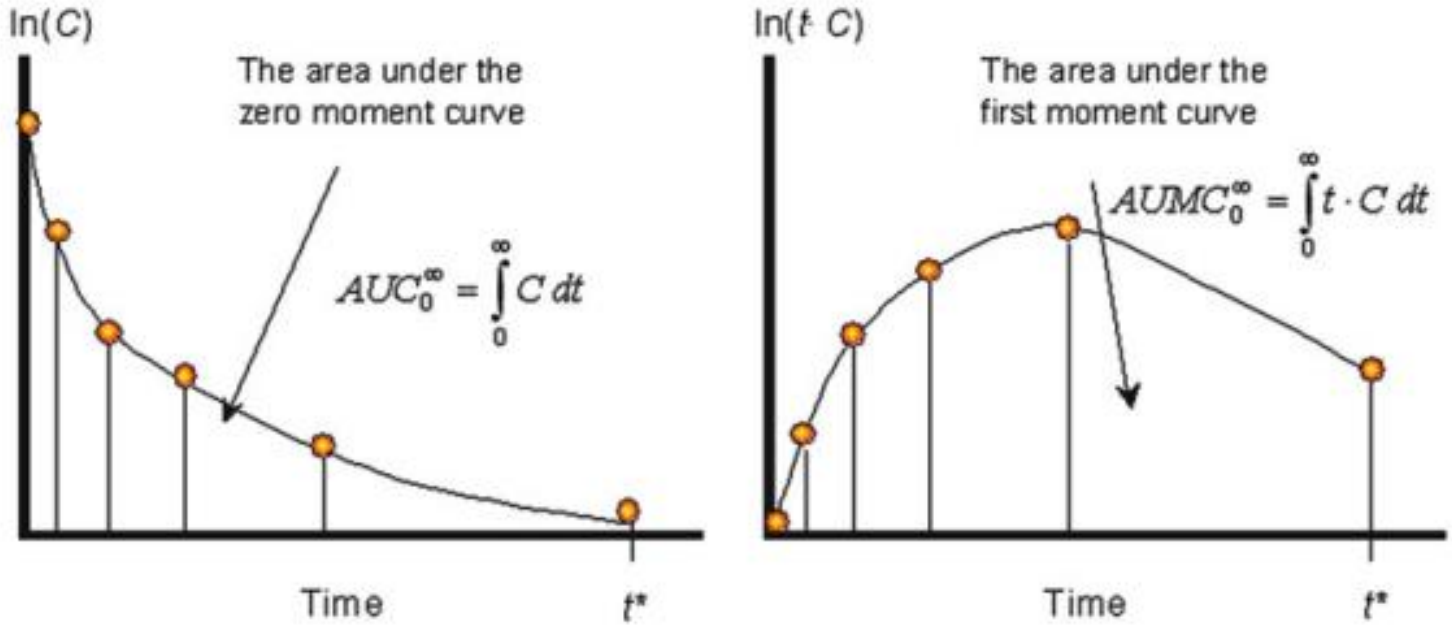


Fig. 9. Comparison of shape of area under the zero moment curve AUC and area under the first moment ($t \cdot C$) curve AUMC. The latter area contains usually an extensive extrapolated area as compared to AUC.

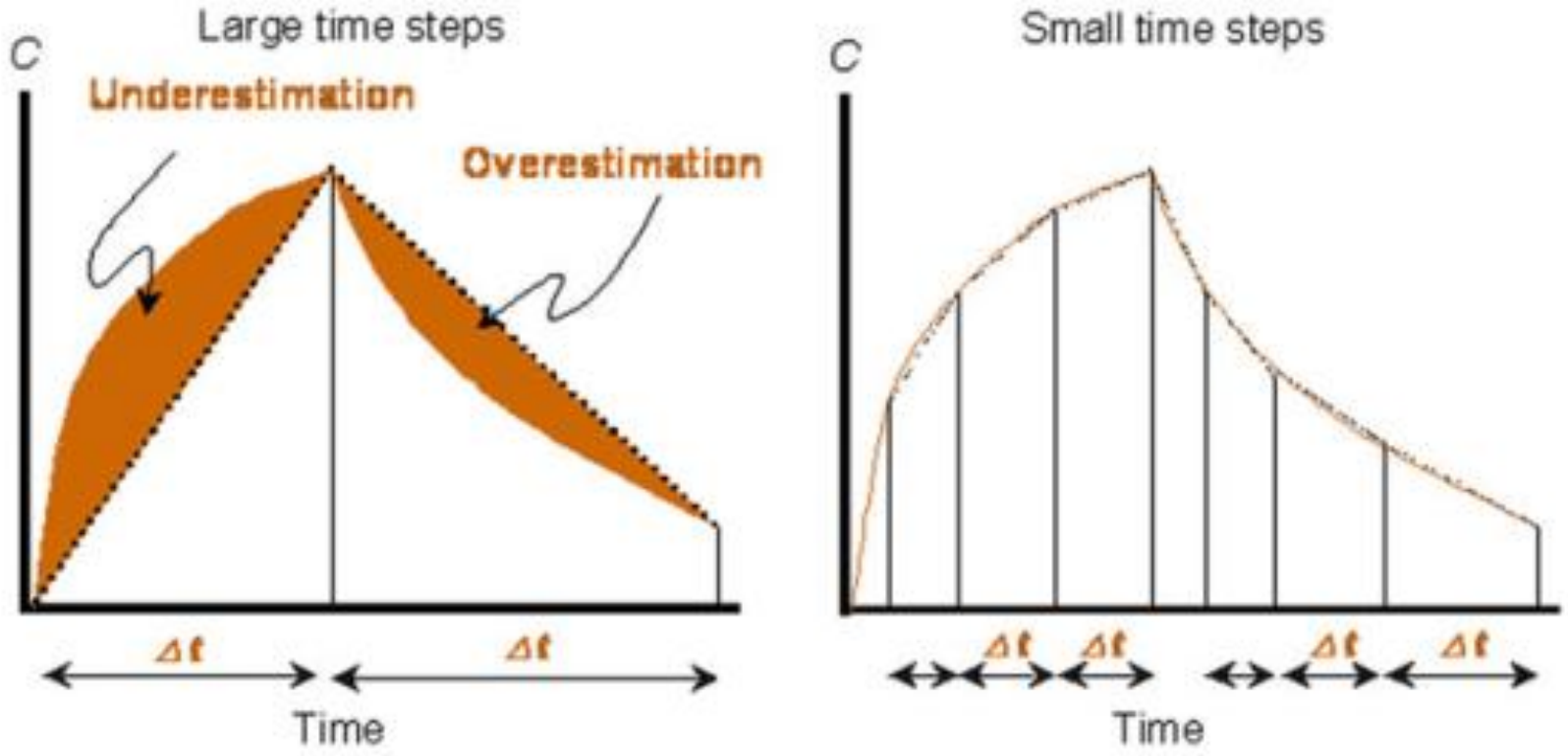


Fig. 3. Concentration versus time during and after a constant rate infusion. The *shaded area* represents underestimation of the area during ascending concentrations and overestimation of the area during descending concentrations. By decreasing the time step (Δt) between observations, this under- or overestimation of the area is minimized.

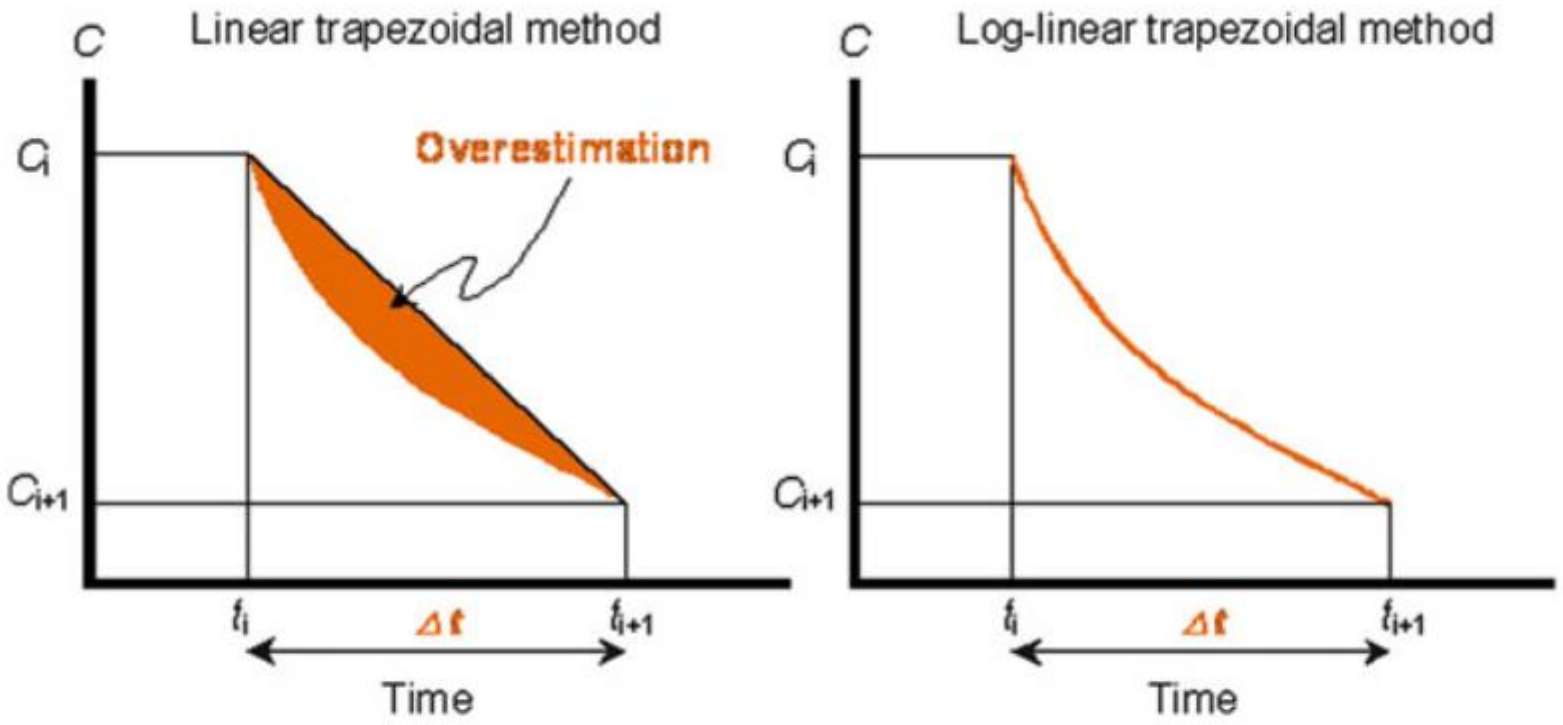


Fig. 5. The principal difference between the linear (*left*) and the log-linear (*right*) trapezoidal methods. The *shaded region* represents the over-predicted area with the linear trapezoidal rule. Note that the log-linear approximation is only true if the decay is truly mono-exponential between t_i and t_{i+1}.

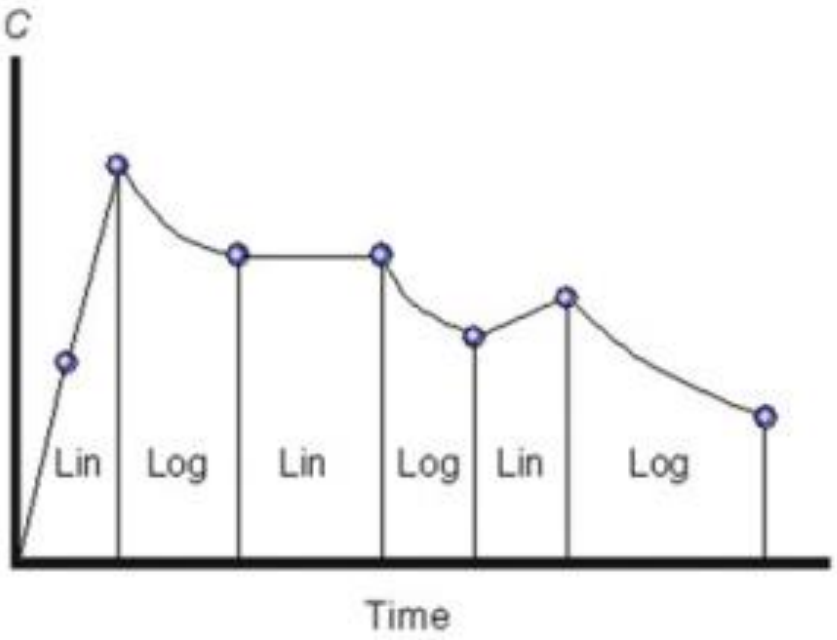


Fig. 6. NCA using a combination of the linear and log-linear trapezoidal methods. The linear method is used for consecutively increasing or consecutively equal concentrations. The log-linear method is used for decreasing concentrations.

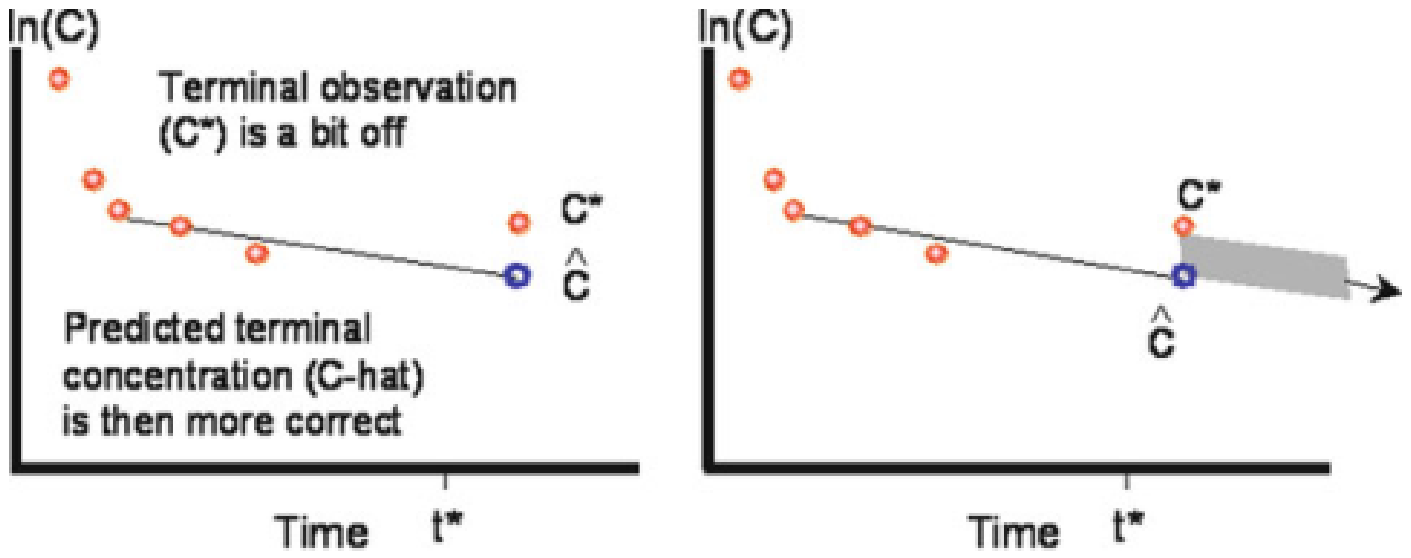


Fig. 8. Impact on the extrapolated area of using observed terminal concentration versus predicted concentration. The *shaded area* from t_{last} to infinity symbolizes the overestimation that would result. Note that if the observed terminal concentration lies below the predicted terminal concentration, then the extrapolated area would be underestimated. The *open circle* is the predicted concentration at t_{last}. The last observation is not included in the regression.

Hands-on exercise 1: IV infusion

- Hands-on-NCA-using-Excel-blank.xlsx 을 열고,

1. Indomethacin IV infusion (25mg) data를 탐색합니다.
2. 빈칸을 채웁니다.
    1. Log(농도)를 계산 Hint) =log
    2. Time interval 계산 Hint) =B1-B2
    3. Segmental, cumulative AUC와 AUMC를 구합니다.
    4. Terminal slope를 마지막 세 Log(농도)를 이용하여 구합니다.
    5. Cmax, Tmax, AUC, AUMC, MRT, Clearance 등을 계산합니다.
3. Hands-on-NCA-using-Excel.xlsx의 정답과 비교합니다.

Hands-on exercise 2: oral dosing - Drug-drug interaction study

- Hands-on-NCA-using-Excel-blank.xlsx 을 열고,

1. 약물 120mg 경구 투여 후 혈장농도 자료를 탐색합니다.
   - Fluconazole이 투여되었을때와 아닐때의 비교.
2. 빈칸을 채웁니다.
   - Log(농도)를 계산 Hint) =log
   - Time interval 계산 Hint) =B1-B2
   - Segmental, cumulative AUC와 AUMC를 구합니다.
   - Terminal slope를 마지막 세 Log(농도)를 이용하여 구합니다.
   - Cmax, Tmax, AUC, AUMC, MRT, Clearance 등을 계산합니다.
3. Control과 Test의 AUC, Cl/F, Cmax 등을 비교합니다.
4. Hands-on-NCA-using-Excel.xlsx의 정답과 비교합니다.

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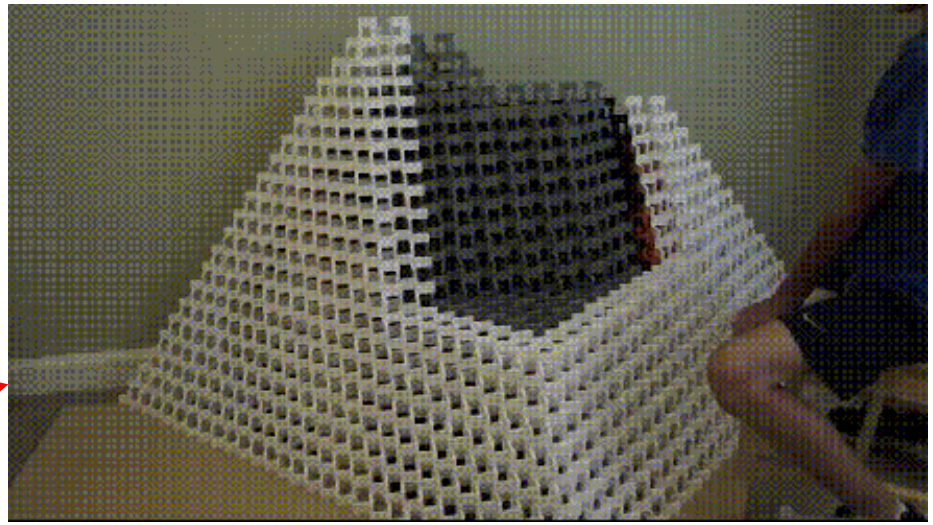
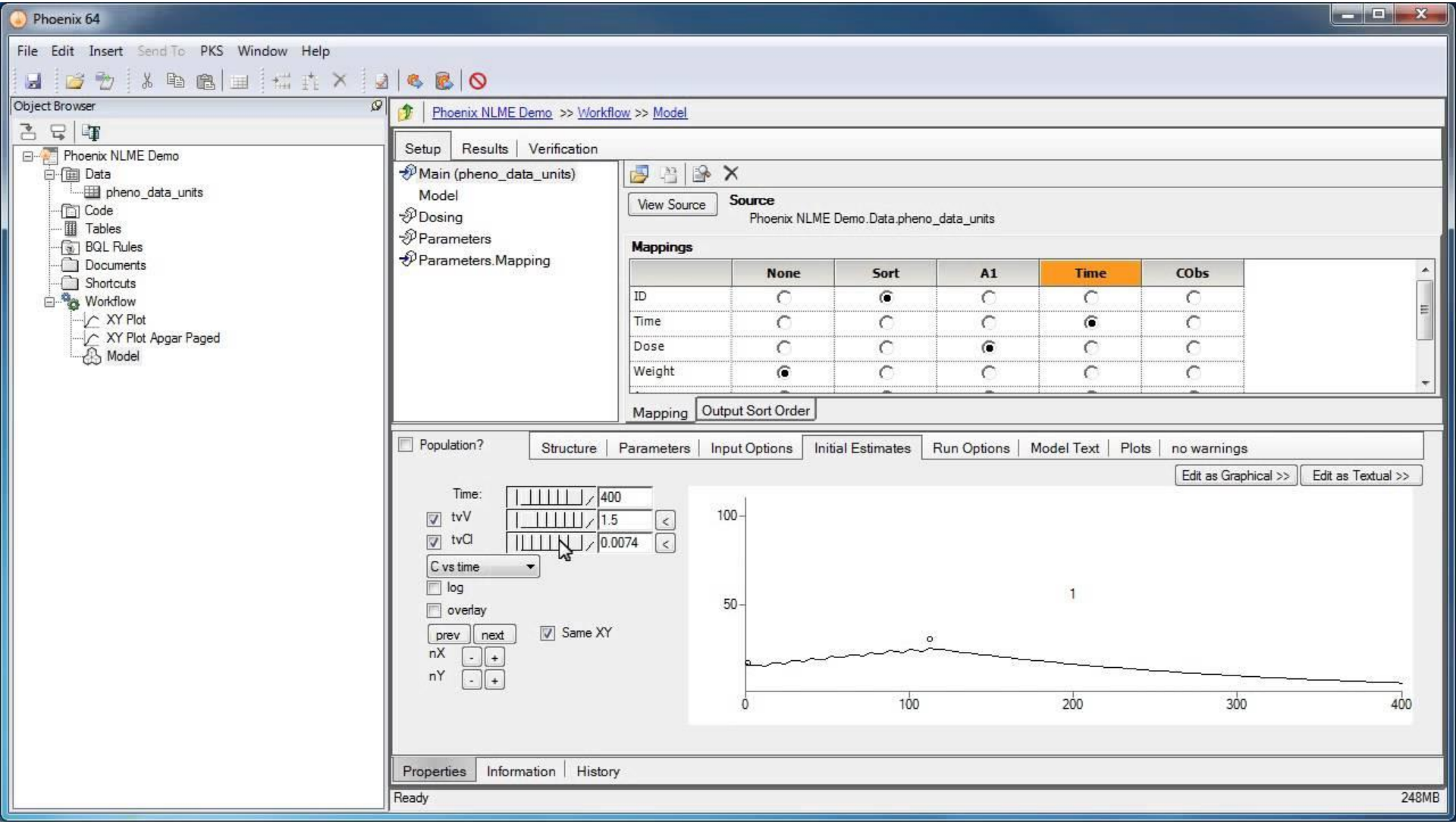
R을 사용한 비구획분석 (NCA) Hands-on

비구획 분석 작업 흐름

- WNL
  - 임상시험 자료
  - R에서 자료 변형
  - 파일 생성 (WNL용)
  - WNL에서 비구획분석
  - 파일 생성 (통계 용)
  - 통계분석 (R or SAS)
  - 보고서 작성
- R
  - 임상시험 자료
  - R에서 자료 변형 / 비구획분석 / 통계 분석/ 보고서 작성

임상시험 자료의 오류발견!

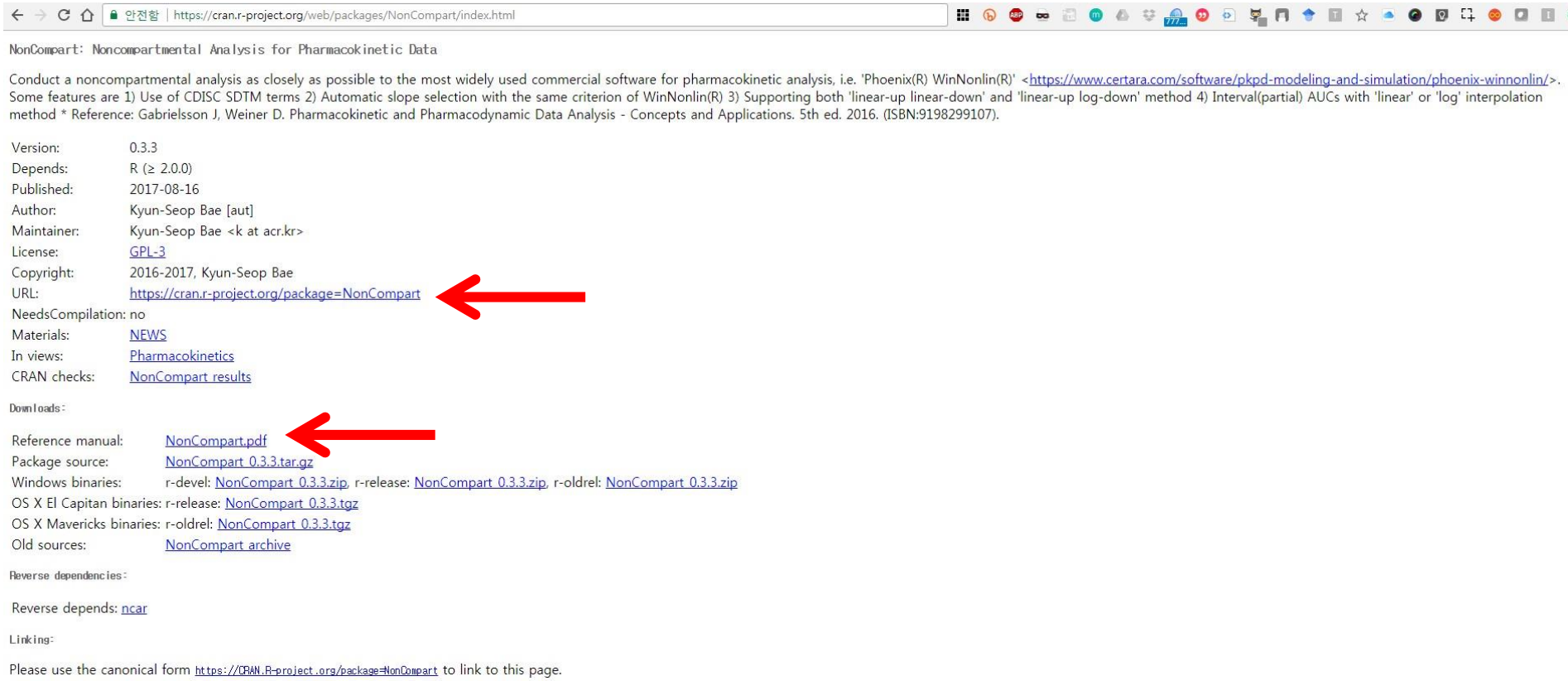



Phoenix 64
File Edit Insert Send To PKS Window Help
Object Browser
Phoenix NLME Demo
Data
pheno_data_units
Code
Tables
BQL Rules
Documents
Shortcuts
Workflow
XY Plot
XY Plot Apgar Paged
Model
Phoenix NLME Demo >> Workflow >> Model
Setup Results Verification
Main (pheno_data_units)
Model
Dosing
Parameters
Parameters.Mapping
View Source
Source
Phoenix NLME Demo.Data.pheno_data_units
Mappings
None Sort A1 Time CObs
ID
Time
Dose
Weight
Mapping Output Sort Order
Population?
Structure Parameters Input Options Initial Estimates Run Options Model Text Plots no warnings
Edit as Graphical >> Edit as Textual >>
Time: 400
tvV 1.5
tvCl 0.0074
C vs time
log
overlay
prev next
Same XY
nX
nY
100
50
1
0
100
200
300
400
Properties Information History
Ready
248MB

NonCompart, ncar, pkr

- 비구획 약동학 분석을 쉽게 해 주는 프로그램
- 장점
  - **비용:** WinNonLin (~$5k/yr) 와 동일한 결과를 얻을 수 있음을 반복적으로 확인
  - **시각화:** 숫자 계산 뿐만 아니라 시각화 가능
    - 농도-시간 곡선, 용량군 별 파라메터의 forest plot 등의 유용한 그림도 쉽게 그릴 수 있습니다.-
  - **표준:** CDISC SDTM 표준을 따르는 용어를 사용
  - **속도:** R을 통한 빠른 계산
  - **연속성:** 재현가능한 연구

CRAN



안전함 | https://cran.r-project.org/web/packages/NonCompart/index.html

NonCompart: Noncompartmental Analysis for Pharmacokinetic Data

Conduct a noncompartmental analysis as closely as possible to the most widely used commercial software for pharmacokinetic analysis, i.e. 'Phoenix(R) WinNonlin(R)' <https://www.certara.com/software/pkpd-modeling-and-simulation/phoenix-winnonlin/>. Some features are 1) Use of CDISC SDTM terms 2) Automatic slope selection with the same criterion of WinNonlin(R) 3) Supporting both 'linear-up linear-down' and 'linear-up log-down' method 4) Interval(partial) AUCs with 'linear' or 'log' interpolation method * Reference: Gabrielsson J, Weiner D. Pharmacokinetic and Pharmacodynamic Data Analysis - Concepts and Applications. 5th ed. 2016. (ISBN:9198299107).

Version:	0.3.3
Depends:	R (≥ 2.0.0)
Published:	2017-08-16
Author:	Kyun-Seop Bae [aut]
Maintainer:	Kyun-Seop Bae <k at acr.kr>
License:	GPL-3
Copyright:	2016-2017, Kyun-Seop Bae
URL:	https://cran.r-project.org/package=NonCompart
NeedsCompilation:	no
Materials:	NEWS
In views:	Pharmacokinetics
CRAN checks:	NonCompart results

Downloads:

Reference manual:	NonCompart.pdf
Package source:	NonCompart_0.3.3.tar.gz
Windows binaries:	r-devel: NonCompart_0.3.3.zip, r-release: NonCompart_0.3.3.zip, r-oldrel: NonCompart_0.3.3.zip
OS X El Capitan binaries:	r-release: NonCompart_0.3.3.tgz
OS X Mavericks binaries:	r-oldrel: NonCompart_0.3.3.tgz
Old sources:	NonCompart archive

Reverse dependencies:

Reverse depends: ncar

Linking:

Please use the canonical form https://CRAN.R-project.org/package=NonCompart to link to this page.

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

예시 자료

- R에는 theophylline과 Indomethacin의 약동학 데이터가 내장되어 있습니다.
- Theoph:
  - theophylline의 약동학 데이터,
  - 12명,
  - 320mg PO 단회투여,
  - 0~24시간 채혈,
  - NONMEM 의 run 폴더의 THEOPP 데이터와 동일
- Indometh:
  - Indomethacin의 약동학 데이터,
  - 6명,
  - 25mg IV bolus 단회투여,
  - 0~8시간 채혈(0, 0.25, 0.5, 0.75, 1, 1.25, 2, 3, 4, 5, 6, 8 h)

기초 작업

- 설치하기 & 불러오기

```{r eval = FALSE}
install.packages('NonCompart')
install.packages('ncar')
install.packages('pkr')
```

-

```{r}
library(NonCompart)
library(ncar)
library(pkr)
```

```{r}
?NonCompart
?tblNCA
```

tblNCA {NonCompart} R Documentation

Table output NCA

Description

Do multiple NCA and returns a result table.

Usage

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

Arguments

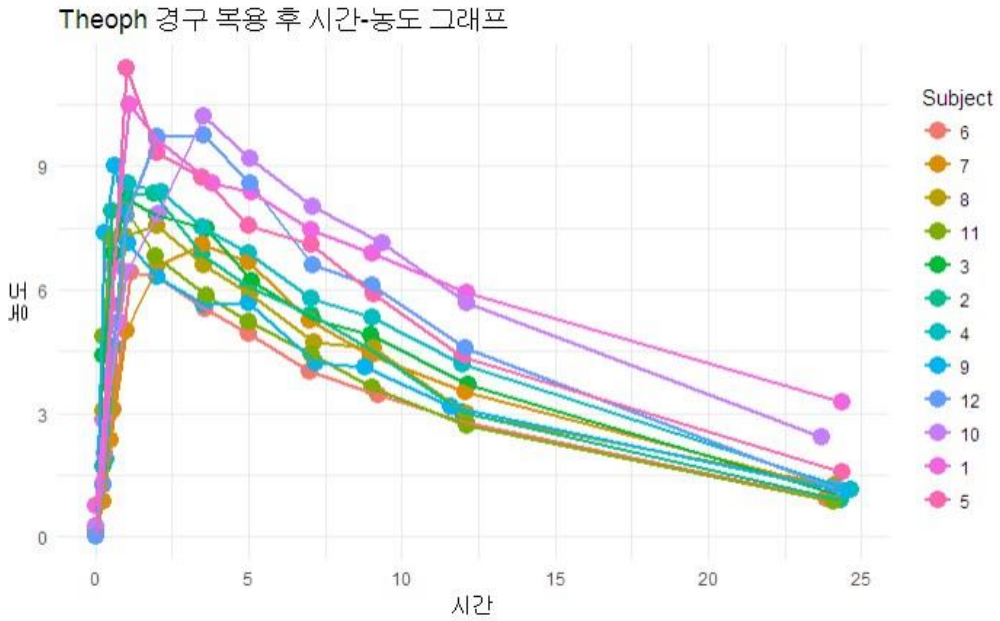
concData	concentration data table
key	column names of concData to be shown at the output table
colTime	column name for time
colConc	column name for concentration
dose	administered dose
adm	one of "Bolus" or "Infusion" or "Extravascular" to indicate drug administration mode
dur	duration of infusion
doseUnit	unit of dose
timeUnit	unit of time
concUnit	unit of concentration
down	method to calculate AUC, "Linear" or "Log"
MW	molecular weight of drug

기본 자료

```{r}
head(Theoph, n=20)
```

```
Grouped Data: conc ~ Time | Subject
   Subject   Wt Dose  Time  conc
1        1 79.6 4.02  0.00  0.74
2        1 79.6 4.02  0.25  2.84
3        1 79.6 4.02  0.57  6.57
4        1 79.6 4.02  1.12 10.50
5        1 79.6 4.02  2.02  9.66
6        1 79.6 4.02  3.82  8.58
7        1 79.6 4.02  5.10  8.36
8        1 79.6 4.02  7.03  7.47
9        1 79.6 4.02  9.05  6.89
10       1 79.6 4.02 12.12  5.94
11       1 79.6 4.02 24.37  3.28
12       2 72.4 4.40  0.00  0.00
13       2 72.4 4.40  0.27  1.72
14       2 72.4 4.40  0.52  7.91
15       2 72.4 4.40  1.00  8.31
16       2 72.4 4.40  1.92  8.33
17       2 72.4 4.40  3.50  6.85
18       2 72.4 4.40  5.02  6.08
19       2 72.4 4.40  7.03  5.40
20       2 72.4 4.40  9.00  4.55
```

```{r}
ggplot(Theoph, aes(Time, conc, group = Subject, color = Subject)) +
  geom_point(size = 4) + geom_line(size = 1) +
  theme_minimal() +
  labs(title = 'Theoph 경구 복용 후 시간-농도 그래프',
       x = '시간', y = '농도')
```



NonCompart

비구획 분석의 계산

tblNCA(): 전체 대상자 비구획분석

```
tblNCA(Theoph, key="Subject", dose=320, concUnit="mg/L")
```

```
tblNCA(Theoph, key="Subject", dose=320, concUnit="mg/L")
```

```
   Subject b0                CMAX    CMAXD       TMAX   TLAG CLST   CLSTP                TLST    LAMZHL               LAMZ                 LAMZLL LAMZUL  LAMZNPT CORRXY               R2
 [1,] "1"     "2.36878509420585" "10.5"  "0.0328125" "1.12" "0" "3.28" "3.28014647414312" "24.37" "14.304377571097" "0.0484569969657749" "9.05" "24.37" "3"     "-0.99999986483748"  "0.999999729674979"
 [2,] "2"     "2.41123733696293" "8.33"  "0.02603125" "1.92" "0" "0.9"  "0.888639849106919" "24.3"  "6.65934156262252"  "0.104086443688432"  "7.03" "24.3"  "4"     "-0.998596709529913" "0.99719538828397"
 [3,] "3"     "2.52971150145858" "8.2"   "0.025625"  "1.02" "0" "1.05" "1.05509670837553" "24.17" "6.76608737718236"  "0.102444314109434"  "9"    "24.17" "3"     "-0.999662423945811" "0.999324961849213"
 [4,] "4"     "2.59275546723663" "8.6"   "0.026875"  "1.07" "0" "1.15" "1.15642160174997" "24.65" "6.98124666099893"  "0.0992870205306231" "9.02" "24.65" "3"     "-0.999461923749821" "0.998924137025692"
 [5,] "5"     "2.55109229061238" "11.4"  "0.035625"  "1"    "0" "1.57" "1.55569511595616" "24.35" "8.0022640410078"   "0.0866188839818201" "7.02" "24.35" "4"     "-0.999323363372814" "0.998647184582752"
 [6,] "6"     "2.0334043955261"  "6.44"  "0.020125"  "1.15" "0" "0.92" "0.941271173708175" "23.85" "7.89499786796582"  "0.0877957400561702" "2.03" "23.85" "7"     "-0.999120281624298" "0.998241337153017"
 [7,] "7"     "2.28854976005424" "7.09"  "0.02215625" "3.48" "0" "1.15" "1.16071921229933" "24.22" "7.84666826130148"  "0.0883364961379133" "6.98" "24.22" "4"     "-0.999334862622512" "0.998670167652754"
 [8,] "8"     "2.17040271754659" "7.56"  "0.023625"  "2.02" "0" "1.25" "1.22852675835656" "24.12" "8.51003788342506"  "0.0814505399453019" "3.53" "24.12" "6"     "-0.995496052943785" "0.991012391426654"
 [9,] "9"     "2.12464810390587" "9.03"  "0.02821875" "0.63" "0" "1.12" "1.11648311706515" "24.43" "8.40599880716182"  "0.0824586341803179" "8.8"  "24.43" "3"     "-0.99972179371205"  "0.999443664822839"
[10,] "10"    "2.65770546248091" "10.21" "0.03190625" "3.55" "0" "2.42" "2.41369227401111" "23.7"  "9.24691582297898"  "0.0749598237757766" "9.38" "23.7"  "3"     "-0.999754311749369" "0.999508683861454"
[11,] "11"    "2.1475943307927"  "8"     "0.025"     "0.98" "0" "0.86" "0.859806606884089" "24.08" "7.26123651504339"  "0.0954585598642772" "9.03" "24.08" "3"     "-0.999999127979356" "0.999998255959473"
[12,] "12"    "2.82449347826545" "9.75"  "0.03046875" "3.52" "0" "1.17" "1.17553904959565" "24.15" "6.28650816367189"  "0.110259489451627"  "9.03" "24.15" "3"     "-0.999698355328196" "0.9993968016459"
      R2ADJ                AUCLST             AUCALL             AUCIFO             AUCIFOD                AUCIFP             AUCIFPD                AUCPEO             AUCPEP             AUMCLST            AUMCIFO
 [1,] "0.999999459349959" "148.92305" "148.92305" "216.611933038226" "0.676912290744456" "216.614955803818" "0.67692173688693"  "31.2489169404534" "31.2498763313113" "1459.0711035" "4505.53481941065"
 [2,] "0.995793082425955" "91.5268"   "91.5268"   "100.173459143183" "0.313042059822447" "100.064317640308" "0.312700992625963" "8.63168669340252" "8.53203003991598" "706.586566"   "999.772287999786"
 [3,] "0.998649923698427" "99.2865"   "99.2865"   "109.535970740547" "0.342299908564208" "109.585721753278" "0.342455380478994" "9.3571734209797"  "9.39832451573008" "803.18587"    "1150.96476871455"
 [4,] "0.997848274051385" "106.7963"  "106.7963"  "118.378881427603" "0.369934004461258" "118.44355857992"  "0.370136120562249" "9.7843308603032"  "9.83359392402986" "901.0842105"  "1303.25240140958"
 [5,] "0.997970776874129" "121.2944"  "121.2944"  "139.419777837118" "0.435686805740995" "139.254630430615" "0.435170720095671" "13.0005786254328" "12.8974026752838" "1017.1143165" "1667.72161189007"
 [6,] "0.99788960458362"  "73.77555"  "73.77555"  "84.2544183301878" "0.263295057281837" "84.4966985785753" "0.264052183058048" "12.4371736674055" "12.688245527848"  "609.1523875"  "978.428485741731"
 [7,] "0.998005251479131" "90.7534"   "90.7534"   "103.771801796293" "0.324286880613414" "103.893147024686" "0.324666084452144" "12.5452209279821" "12.6473664538854" "782.41986"    "1245.09840831465"
 [8,] "0.988765489283318" "88.55995"  "88.55995"  "103.906686815243" "0.324708396297635" "103.643051464786" "0.323884535827455" "14.7697297311878" "14.5529307094073" "739.534598"   "1298.11575468474"
 [9,] "0.998887329645677" "86.32615"  "86.32615"  "99.9087179279482" "0.312214743524838" "99.8660676588793" "0.312081461433998" "13.5949777052926" "13.5580763078894" "705.2296255"  "1201.77153812025"
[10,] "0.999017367722909" "138.3681"  "138.3681"  "170.652060635217" "0.533287689485054" "170.567912545332" "0.533024726704162" "18.9180022292417" "18.8780011813617" "1278.180042"  "2473.99342735889"
[11,] "0.999996511918946" "80.0936"   "80.0936"   "89.1027449234385" "0.278446077885745" "89.1007189855217" "0.278439746829755" "10.1109622730249" "10.1089184106194" "617.2422125"  "928.559971386069"
[12,] "0.998793603291801" "119.9775"  "119.9775"  "130.588831558118" "0.408090098619118" "130.639068046815" "0.408247087646298" "8.12575733430562" "8.16108703637935" "977.8807235"  "1330.38400236898"
      AUMCIFP            AUMCPEO            AUMCPEP            VZFO               VZFP               CLFO               CLFP               MRTEVLST           MRTEVIFO           MRTEVIFP
 [1,] "4505.67086458209" "67.6160286851172" "67.6170064935417" "30.4867482345887" "30.4863228055447" "1.47729626669981" "1.47727565168591" "9.79748335465867" "20.8000305256292" "20.8003683211179"
 [2,] "996.071583509104" "29.3252499112927" "29.0626720309864" "30.6904415765423" "30.7239160557228" "3.19445891892989" "3.19794315842211" "7.71999639449866" "9.98041094468705" "9.95431345556755"
 [3,] "1152.65289026304" "30.2162940315685" "30.318495985664"  "28.5170999496524" "28.5041534217657" "2.92141474473231" "2.92008844656286" "8.08957783787323" "10.5076420187191" "10.5182762117325"
 [4,] "1305.4981091996"  "30.8588106551423" "30.9777467963968" "27.2259641330176" "27.2110971545992" "2.70318485984093" "2.70170876184947" "8.43741038313125" "11.0091630001303" "11.0221115006327"
 [5,] "1661.79367436228" "39.0117445712149" "38.7941877387202" "26.4979946505636" "26.5294196385914" "2.29522672438806" "2.29794872178016" "8.38550103302378" "11.9618725389051" "11.9334895308224"
 [6,] "986.966459689532" "37.7417566662308" "38.280335514986"  "43.2597344953234" "43.13569439204l"  "3.79802040465035" "3.78713021198604" "8.25683288704727" "11.612785479182"  "11.6805328053348"
 [7,] "1249.41106012833" "37.1599983764277" "37.376906210544"  "34.9084408430805" "34.8676684452056" "3.08368934971535" "3.08008765894795" "8.62138344128154" "11.9984271908357" "12.0259237101698"
 [8,] "1288.52011616077" "43.0301500208197" "42.605894256157"  "37.8105081118408" "37.9066861615621" "3.07968630131565" "3.08752005539633" "8.3506663903943"  "12.4930915850769" "12.4322865638375"
 [9,] "1200.2123597462"  "41.3174964516894" "41.2412628670872" "38.8427934436931" "38.8593822173436" "3.20292369511514" "3.20429158273309" "8.1693626496722"  "12.0286954236259" "12.0182198807093"
[10,] "2470.87654175199" "48.3353501320931" "48.2701777931124" "25.0155401378403" "25.0278813214113" "1.87516048038837" "1.87608557333405" "9.23753409926132" "14.4972959491374" "14.4861744795951"
[11,] "928.489963582081" "33.5269415524517" "33.5219295081337" "37.6221852019531" "37.6230406407462" "3.59135961832556" "3.59144127728081" "7.70651103833515" "10.4212274513421" "10.4206786898426"
[12,] "1332.05283411623" "26.4963558071417" "26.5884431567018" "22.2242935639128" "22.2157473419508" "2.45043926178l"  "2.44949695970983" "8.15053425433936" "10.1875787270284" "10.1964355229393"
attr(,"units")
 [1] ""          ""          "mg/L"      "mg/L/mg"   "h"         "h"         "mg/L"      "mg/L"      "h"         "h"         "/h"        "h"         "h"         ""          ""          ""
[17] ""          "h*mg/L"    "h*mg/L"    "h*mg/L"    "h*mg/L/mg" "h*mg/L"    "h*mg/L/mg" "%"         "%"         "h2*mg/L"   "h2*mg/L"   "h2*mg/L"   "%"         "%"         "L"         "L"
[33] "L/h"       "L/h"       "h"         "h"         "h"
```

sNCA(): 한명만 비구획분석

```r
head(Theoph, n=20)
```

```
Grouped Data: conc ~ Time | Subject
   Subject   Wt Dose  Time   conc
1        1 79.6 4.02  0.00  0.74
2        1 79.6 4.02  0.25  2.84
3        1 79.6 4.02  0.57  6.57
4        1 79.6 4.02  1.12 10.50
5        1 79.6 4.02  2.02  9.66
6        1 79.6 4.02  3.82  8.58
7        1 79.6 4.02  5.10  8.36
8        1 79.6 4.02  7.03  7.47
9        1 79.6 4.02  9.05  6.89
10       1 79.6 4.02 12.12  5.94
11       1 79.6 4.02 24.37  3.28
12       2 72.4 4.40  0.00  0.00
13       2 72.4 4.40  0.27  1.72
14       2 72.4 4.40  0.52  7.91
15       2 72.4 4.40  1.00  8.31
16       2 72.4 4.40  1.92  8.33
17       2 72.4 4.40  3.50  6.85
18       2 72.4 4.40  5.02  6.08
19       2 72.4 4.40  7.03  5.40
20       2 72.4 4.40  9.00  4.55
```

```r
# For one subject
x = Theoph[Theoph$Subject=="1","Time"]
y = Theoph[Theoph$Subject=="1","conc"]

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

```
        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     CORRXY         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"
```

```r
ggplot(Theoph %>% filter(Subject == 1), aes(Time, conc, group = Subject, color = Subject)) +
  geom_point(size = 4) + geom_line(size = 1) +
  theme_minimal() +
  labs(title = 'Theoph 경구 복용 후 시간-농도 그래프 (Subject 1)',
       x = '시간', y = '농도')
```

각 파라메터의 의미를 알고싶으면?

```
?ncar::txtNCA()
```

Value

CMAX	maximum concentration, Cmax
CMAXD	dose normalized Cmax, CMAX / Dose, Cmax / Dose
TMAX	time of maximum concentration, Tmax
TLAG	time to observe the first non-zero concentration, for extravascular administration only
CLST	last positive concentration observed, Clast
CLSTP	last positive concentration predicted, Clast_pred
TLST	time of last positive concentration, Tlast
LAMZHL	half-life by lambda z, ln(2)/LAMZ
LAMZ	lambda_z negative of best fit terminal slope
LAMZLL	earliest time for LAMZ
LAMZUL	last time for LAMZ
LAMZNPT	number of points for LAMZ
CORRXY	correlation of log(concentration) and time
R2	R-squared
R2ADJ	R-squared adjusted

...

```
ncar::RptCfg
```

PPTESTCD <chr>	SYNONYM <chr>	NCI <chr>
b0	Intercept	Intercept of regression
TLAG	Time Until First Nonzero Conc	Time until First Nonzero Concentration
MRTEVLST	MRT Extravasc to Last Nonzero Conc	Mean Residence Time to Last Nonzero Concentration by Extravascular
MRTEVIFO	MRT Extravasc Infinity Obs	Mean Residence Time Infinity Observed by Extravascular Dose
MRTEVIFP	MRT Extravasc Infinity Pred	Mean Residence Time Infinity Predicted by Extravascular Dose
VZFO	Vz Obs by F	Observed Volume of Distribution of Absorbed Fraction
VZFP	Vz Pred by F	Predicted Volume of Distribution of Absorbed Fraction
CLFO	Total CL Obs by F	Observed Total Body Clearance by Fraction of Dose Absorbed

...

ncar

비구획 분석 보고서 작성

ncar 소개

- 보고서를 통해 다른 사람/기관과 정보 공유
- pdf, rtf, text 형식 지원

txtNCA()

```
txtNCA(Theoph[Theoph$Subject=="1","Time"], Theoph[Theoph$Subject=="1","conc"],
       dose=320, doseUnit="mg", concUnit="mg/L", timeUnit="h")
```

```
                    NONCOMPARTMENTAL ANALYSIS REPORT
                    Package version 0.3.7 (2017-08-16 KST)
                      R version 3.4.2 (2017-09-28)

Date and Time: 2017-11-01 18:00:30 Asia/Seoul

Calculation Setting
-------------------
Drug Administration: Extravascular
Observation count excluding trailing zero: 11
Dose at time 0: 320 mg
AUC Calculation Method: Linear-up Linear-down
Weighting for lambda z: Uniform (Ordinary Least Square, OLS)
Lambda z selection criterion: Heighest adjusted R-squared value with precision=1e-


Fitting, AUC, AUMC Result
-------------------------
      Time         Conc.      Pred.    Residual       AUC       AUMC
------------------------------------------------------------------------
     0.0000       0.7400                           0.0000     0.0000
     0.2500       2.8400                           0.4475     0.0888
     0.5700       6.5700                           1.9531     0.8015
     1.1200      10.5000                           6.6474     5.0654
     2.0200       9.6600                          15.7194    19.1383
     3.8200       8.5800                          32.1354    66.1982
     5.1000       8.3600                          42.9769   114.4617
     7.0300       7.4700                          58.2529   206.2815
     9.0500 *     6.8900     6.8912 -1.228e-03    72.7565   322.2988
    12.1200 *     5.9400     5.9387 +1.324e-03    92.4505   528.5219
    24.3700 *     3.2800     3.2801 -1.465e-04   148.9231  1459.0711

*: Used for the calculation of Lambda z.
```

```
Calculated Values
-----------------
CMAX       Max Conc                                10.5000 mg/L
CMAXD      Max Conc Norm by Dose                    0.0328 mg/L/mg
TMAX       Time of CMAX                             1.1200 h
TLAG       Time Until First Nonzero Conc            0.0000 h
CLST       Last Nonzero Conc                        3.2800 mg/L
CLSTP      Last Nonzero Conc Pred                   3.2801 mg/L
TLST       Time of Last Nonzero Conc               24.3700 h
LAMZHL     Half-Life Lambda z                      14.3044 h
LAMZ       Lambda z                                 0.0485 /h
LAMZLL     Lambda z Lower Limit                     9.0500 h
LAMZUL     Lambda z Upper Limit                    24.3700 h
LAMZNPT    Number of Points for Lambda z            3
CORRXY     Correlation Between TimeX and Log ConcY -1.0000
R2         R Squared                                1.0000
R2ADJ      R Squared Adjusted                       1.0000
AUCLST     AUC to Last Nonzero Conc               148.9231 h*mg/L
AUCALL     AUC All                                148.9231 h*mg/L
AUCIFO     AUC Infinity Obs                       216.6119 h*mg/L
AUCIFOD    AUC Infinity Obs Norm by Dose            0.6769 h*mg/L/mg
AUCIFP     AUC Infinity Pred                      216.6150 h*mg/L
AUCIFPD    AUC Infinity Pred Norm by Dose           0.6769 h*mg/L/mg
AUCPEO     AUC %Extrapolation Obs                  31.2489 %
AUCPEP     AUC %Extrapolation Pred                 31.2499 %
AUMCLST    AUMC to Last Nonzero Conc             1459.0711 h2*mg/L
AUMCIFO    AUMC Infinity Obs                     4505.5348 h2*mg/L
AUMCIFP    AUMC Infinity Pred                    4505.6709 h2*mg/L
AUMCPEO    AUMC %Extrapolation Obs                 67.6160 %
AUMCPEP    AUMC % Extrapolation Pred               67.6170 %
VZFO       Vz Obs by F                             30.4867 L
VZFP       Vz Pred by F                            30.4863 L
CLFO       Total CL Obs by F                        1.4773 L/h
CLFP       Total CL Pred by F                       1.4773 L/h
MRTEVLST   MRT Extravasc to Last Nonzero Conc       9.7975 h
MRTEVIFO   MRT Extravasc Infinity Obs              20.8000 h
MRTEVIFP   MRT Extravasc Infinity Pred             20.8004 h
```

pdfNCA()

```
pdfNCA(fileName="NCA-Theoph.pdf", Theoph, colSubj="Subject", colTime="Time",
       colConc="conc", dose=320, doseUnit="mg", timeUnit="h", concUnit="mg/L")
```

Subject ID = 1

NONCOMPARTMENTAL ANALYSIS REPORT
Package version 0.3.7 (2017-08-16 KST)
R version 3.4.2 (2017-09-28)

Date and Time: 2017-11-01 18:04:59 Asia/Seoul

Calculation Setting

Drug Administration: Extravascular
Observation count excluding trailing zero: 11
Dose at time 0: 320 mg
AUC Calculation Method: Linear-up Linear-down
Weighting for lambda z: Uniform (Ordinary Least Square, OLS)
Lambda z selection criterion: Heighest adjusted R-squared value with precision=1e-4

Fitting, AUC, AUMC Result

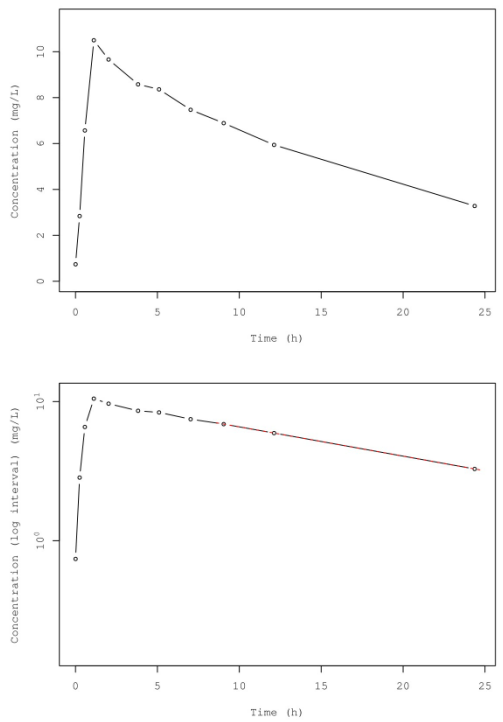
	Time	Conc.	Pred.	Residual	AUC	AUMC
	0.0000	0.7400			0.0000	0.0000
	0.2500	2.8400			0.4475	0.0888
	0.5700	6.5700			1.9531	0.8015
	1.1200	10.5000			6.6474	5.0654
	2.0200	9.6600			15.7194	19.1383
	3.8200	8.5800			32.1354	66.1982
	5.1000	8.3600			42.9769	114.4617
	7.0300	7.4700			58.2529	206.2815
	9.0500	* 6.8900	6.8912	-1.228e-03	72.7565	322.2988
	12.1200	* 5.9400	5.9387	+1.324e-03	92.4505	528.5219
	24.3700	* 3.2800	3.2801	-1.465e-04	148.9231	1459.0711

*: Used for the calculation of Lambda z.

Calculated Values

CMAX	Max Conc	10.5000 mg/L
CMAXD	Max Conc Norm by Dose	0.0328 mg/L/mg
TMAX	Time of CMAX	1.1200 h
TLAG	Time Until First Nonzero Conc	0.0000 h
CLST	Last Nonzero Conc	3.2800 mg/L
CLSTP	Last Nonzero Conc Pred	3.2801 mg/L
TLST	Time of Last Nonzero Conc	24.3700 h
LAMZHL	Half-Life Lambda z	14.3044 h
LAMZ	Lambda z	0.0485 /h
LAMZLL	Lambda z Lower Limit	9.0500 h
LAMZUL	Lambda z Upper Limit	24.3700 h
LAMZNPT	Number of Points for Lambda z	3
CORRXY	Correlation Between TimeX and Log ConcY	-1.0000
R2	R Squared	1.0000
R2ADJ	R Squared Adjusted	1.0000
AUCLST	AUC to Last Nonzero Conc	148.9231 h*mg/L
AUCALL	AUC All	148.9231 h*mg/L

Subject ID = 1

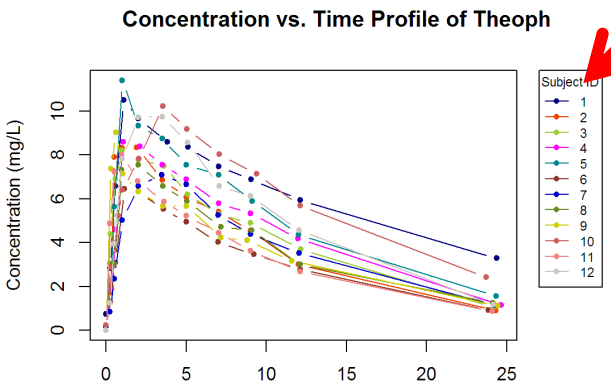


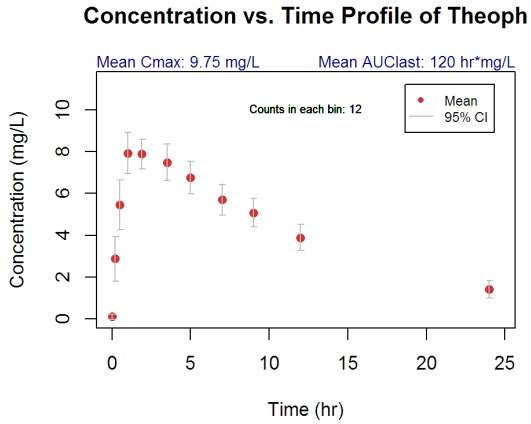
pkr

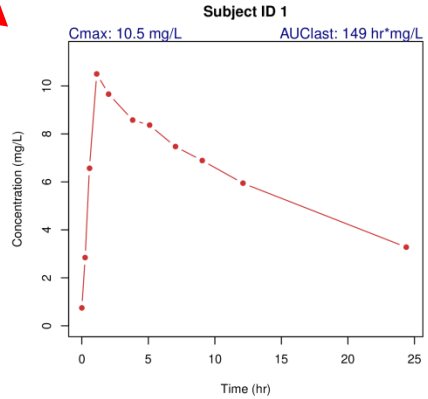
비구획 분석 시각화 & SDTM

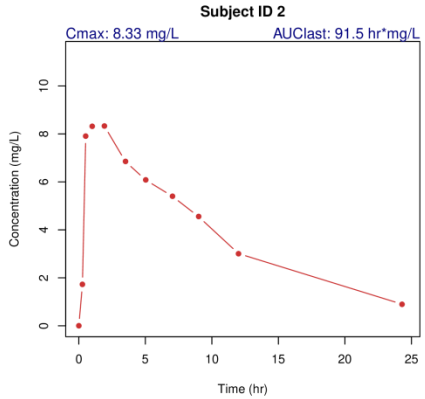
plotPK()

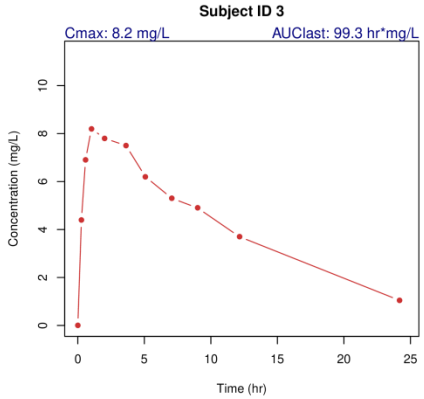
```
plotPK(Theoph, "Subject", "Time", "conc", unitTime="hr", unitConc="mg/L", dose=320)
```

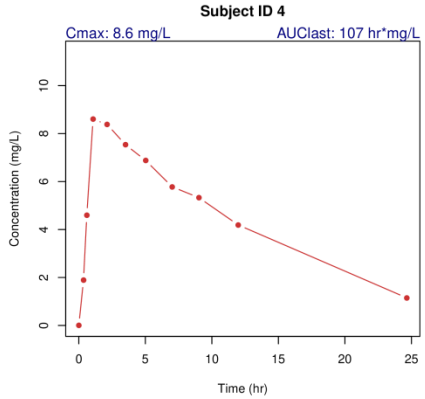






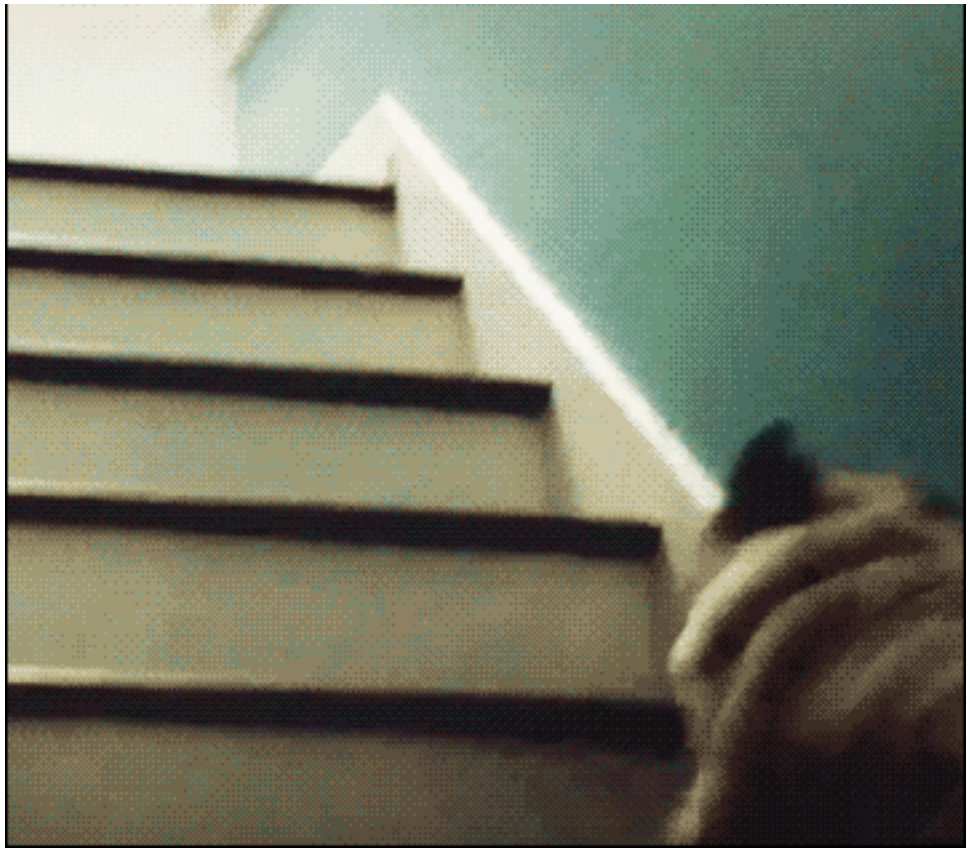






인터넷 웹브라우져를 통한 비구획분석

https://asan.shinyapps.io/pkrshiny

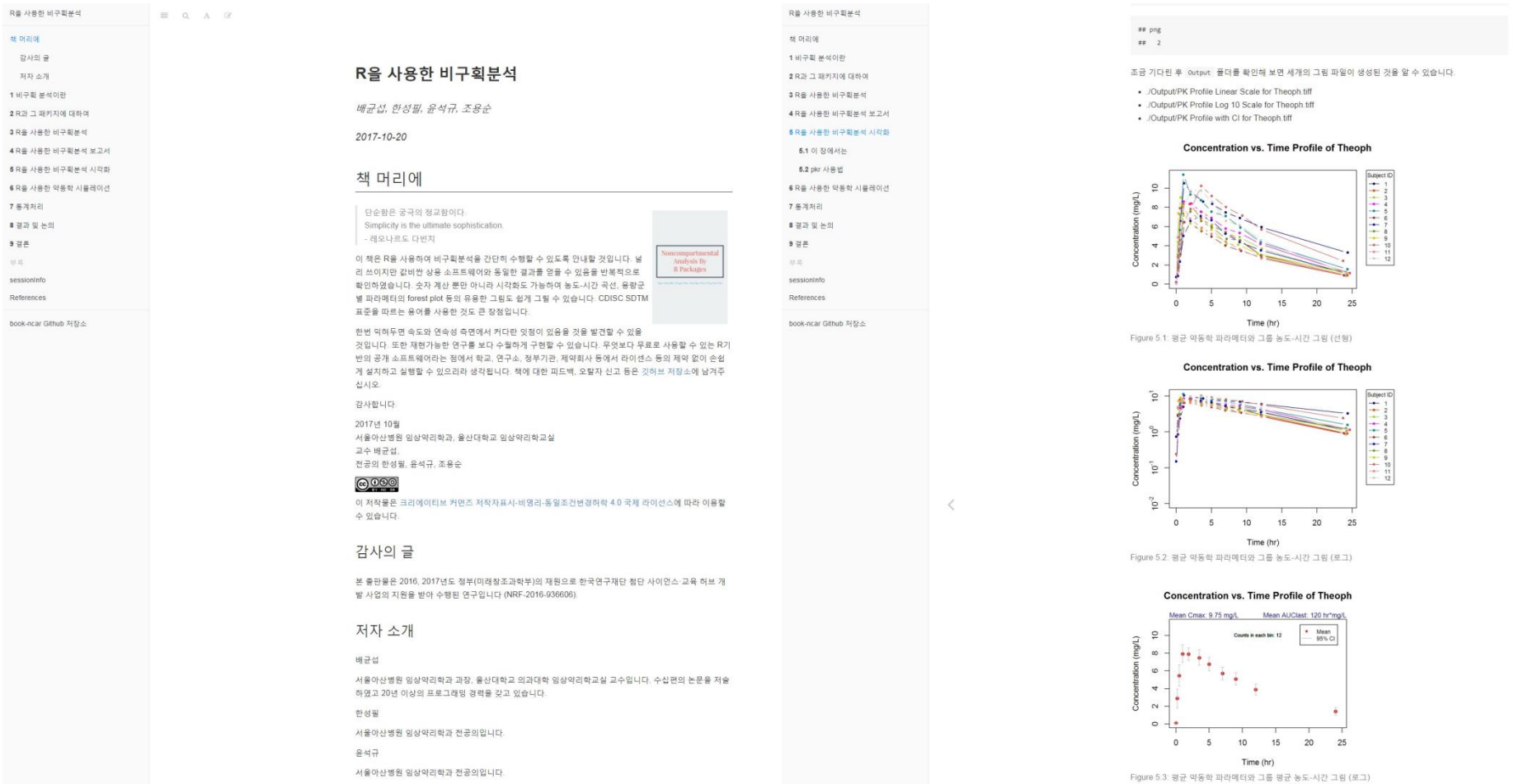


결론

- 무료 소프트웨어인 R과 그 패키지를 통해서 상용 소프트웨어와 동일한 결과를 얻을 수 있음. ($0)
- R을 사용하여 이후 여러 통계 분석을 연속적으로 행할 수 있음. (Bioequivalence, ANOVA, linear regression, glm, nlme 등)
- 자료의 오류가 있을 때 재분석을 쉽게 할 수 있고 보고서와 그림의 수정도 한번에 행할 수 있음 → Continuous Integration & Reproducible Research

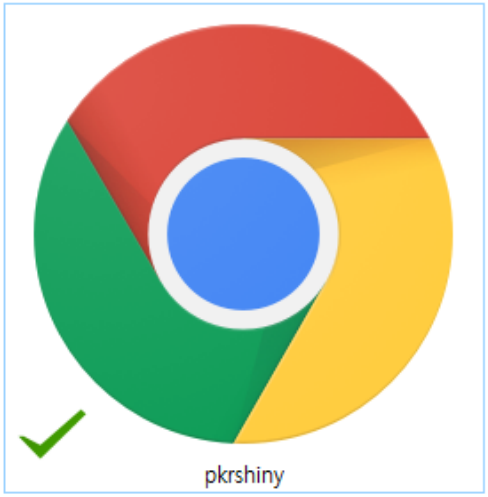
매뉴얼 책

- Gitbook: https://asancpt.github.io/book-ncar/



Hands-on Exercise 1

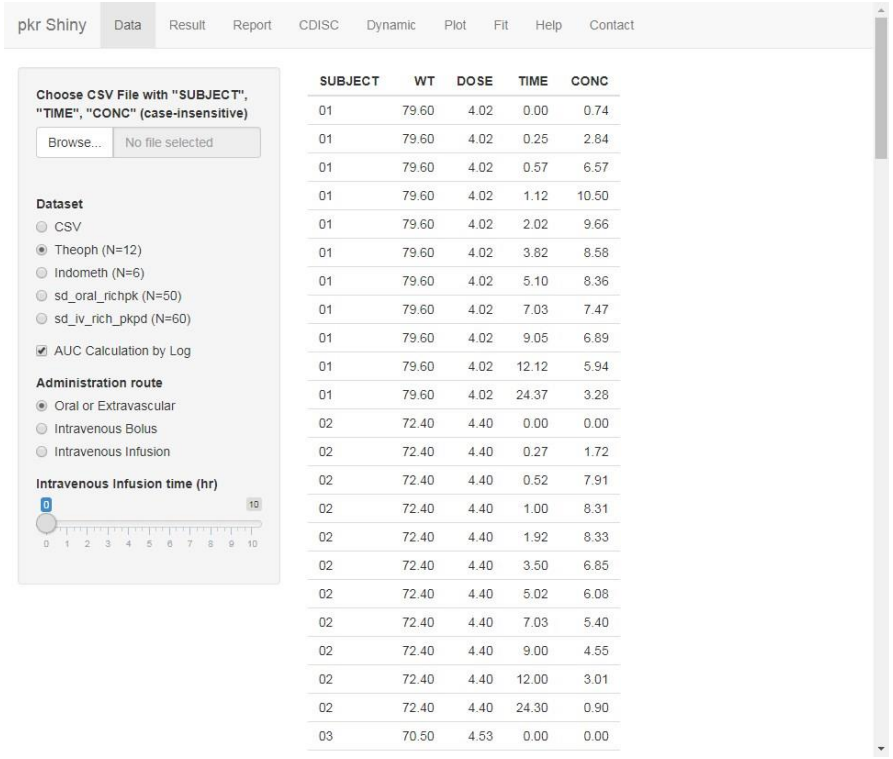
- 웹브라우저로 접속
- CSV 파일 업로드
- 이것 저것 눌러서 기능 확인해보기.



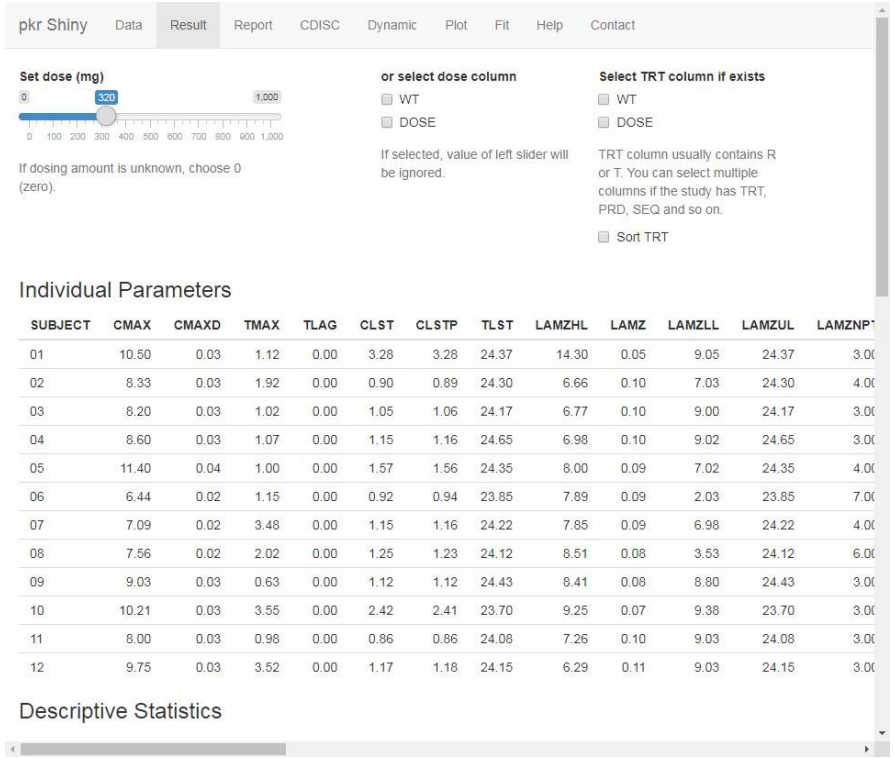
pkrshiny

- Shiny를 이용한 간편한 비구획분석
  - Csv 업로드 하여 NonCompart, ncar, pkr의 핵심 기능을 클릭하여 수행.
  - R이 설치되어 있지 않은 PC, Mac, Linux, 혹은 휴대폰으로도 접속 가능
- http://asan.shinyapps.io/pkrshiny

예시



SUBJECT	WT	DOSE	TIME	CONC
01	79.60	4.02	0.00	0.74
01	79.60	4.02	0.25	2.84
01	79.60	4.02	0.57	6.57
01	79.60	4.02	1.12	10.50
01	79.60	4.02	2.02	9.66
01	79.60	4.02	3.82	8.58
01	79.60	4.02	5.10	8.36
01	79.60	4.02	7.03	7.47
01	79.60	4.02	9.05	6.89
01	79.60	4.02	12.12	5.94
01	79.60	4.02	24.37	3.28
02	72.40	4.40	0.00	0.00
02	72.40	4.40	0.27	1.72
02	72.40	4.40	0.52	7.91
02	72.40	4.40	1.00	8.31
02	72.40	4.40	1.92	8.33
02	72.40	4.40	3.50	6.85
02	72.40	4.40	5.02	6.08
02	72.40	4.40	7.03	5.40
02	72.40	4.40	9.00	4.55
02	72.40	4.40	12.00	3.01
02	72.40	4.40	24.30	0.90
03	70.50	4.53	0.00	0.00



SUBJECT	CMAX	CMAXD	TMAX	TLAG	CLST	CLSTP	TLST	LAMZHL	LAMZ	LAMZLL	LAMZUL	LAMZNP
01	10.50	0.03	1.12	0.00	3.28	3.28	24.37	14.30	0.05	9.05	24.37	3.0
02	8.33	0.03	1.92	0.00	0.90	0.89	24.30	6.66	0.10	7.03	24.30	4.0
03	8.20	0.03	1.02	0.00	1.05	1.06	24.17	6.77	0.10	9.00	24.17	3.0
04	8.60	0.03	1.07	0.00	1.15	1.16	24.65	6.98	0.10	9.02	24.65	3.0
05	11.40	0.04	1.00	0.00	1.57	1.56	24.35	8.00	0.09	7.02	24.35	4.0
06	6.44	0.02	1.15	0.00	0.92	0.94	23.85	7.89	0.09	2.03	23.85	7.0
07	7.09	0.02	3.48	0.00	1.15	1.16	24.22	7.85	0.09	6.98	24.22	4.0
08	7.56	0.02	2.02	0.00	1.25	1.23	24.12	8.51	0.08	3.53	24.12	6.0
09	9.03	0.03	0.63	0.00	1.12	1.12	24.43	8.41	0.08	8.80	24.43	3.0
10	10.21	0.03	3.55	0.00	2.42	2.41	23.70	9.25	0.07	9.38	23.70	3.0
11	8.00	0.03	0.98	0.00	0.86	0.86	24.08	7.26	0.10	9.03	24.08	3.0
12	9.75	0.03	3.52	0.00	1.17	1.18	24.15	6.29	0.11	9.03	24.15	3.0

pkr Shiny | Data | Result | Report | CDISC | Dynamic | Plot | Fit | Help | Contact

Study ID

Drug

PP

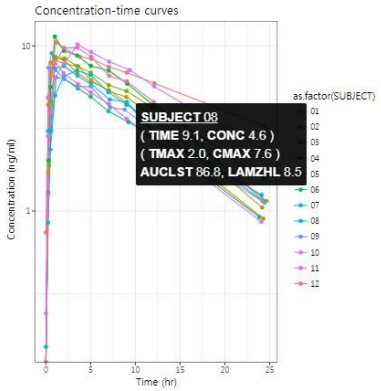
STUDYID	DOMAIN	USUBJID	PPSEQ	PPGRPID	PPTESTCD	PPTEST	PPSCAT	PPORRES
	PP	01	1		CMAX	Max Conc	NON-COMPARTMENTAL	10.50
	PP	01	2		CMAXD	Max Conc Norm by Dose	NON-COMPARTMENTAL	0.03
	PP	01	3		TMAX	Time of CMAX	NON-COMPARTMENTAL	1.12
	PP	01	4		TLAG	Time Until First Nonzero Conc	NON-COMPARTMENTAL	0.00
	PP	01	5		CLST	Last Nonzero Conc	NON-COMPARTMENTAL	3.28
	PP	01	6		CLSTP	Last Nonzero Conc Pred	NON-COMPARTMENTAL	3.28
	PP	01	7		TLST	Time of Last Nonzero Conc	NON-COMPARTMENTAL	24.37
	PP	01	8		LAMZHL	Half-Life Lambda z	NON-COMPARTMENTAL	14.30
	PP	01	9		LAMZ	Lambda z	NON-COMPARTMENTAL	0.05
	PP	01	10		LAMZLL	Lambda z Lower Limit	NON-COMPARTMENTAL	9.05
	PP	01	11		LAMZUL	Lambda z Upper Limit	NON-	24.37

pkr Shiny | Data | Result | Report | CDISC | Dynamic | Plot | Fit | Help | Contact

Hovering a cursor over a plot shows dynamic results.

Y axis

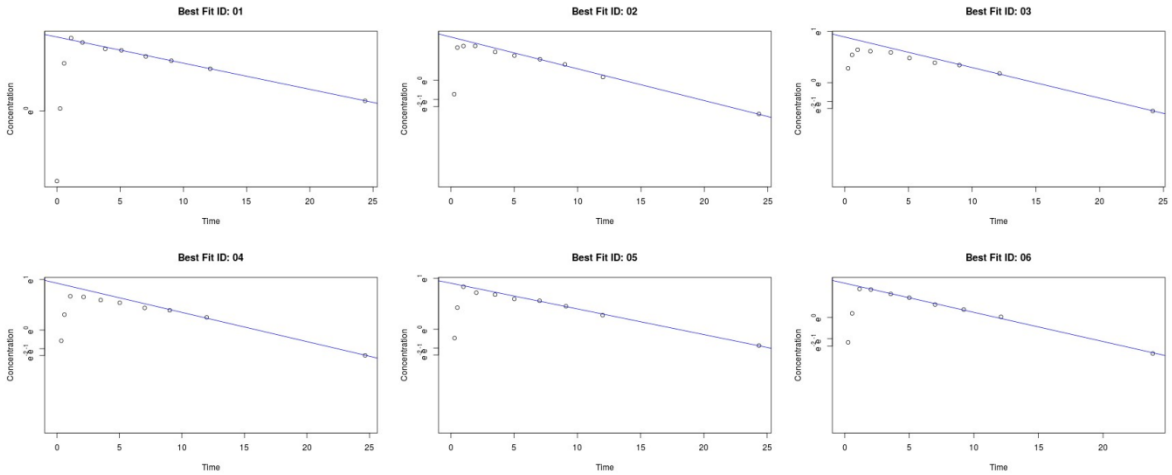
- (•) Log
- ( ) Linear



pkr Shiny | Data | Result | Report | CDISC | Dynamic | Plot | Fit | Help | Contact

Generating plots takes a while. Please wait.

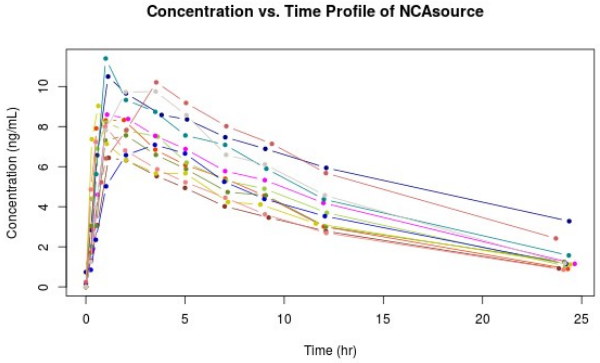
Individual Plots

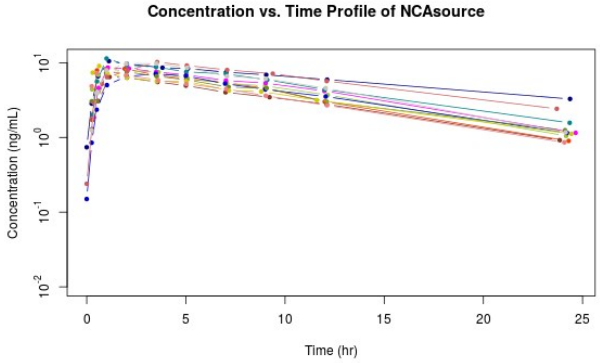


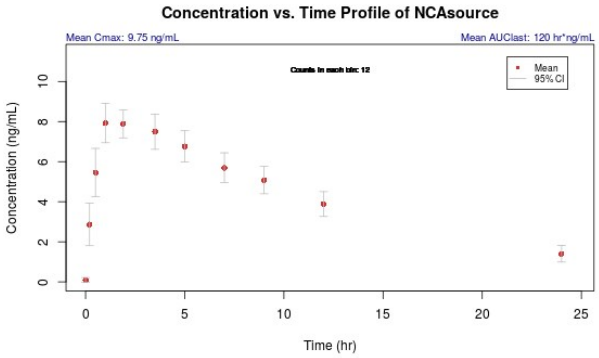
Generating plots takes a while. Please wait.

Concentration-time curve

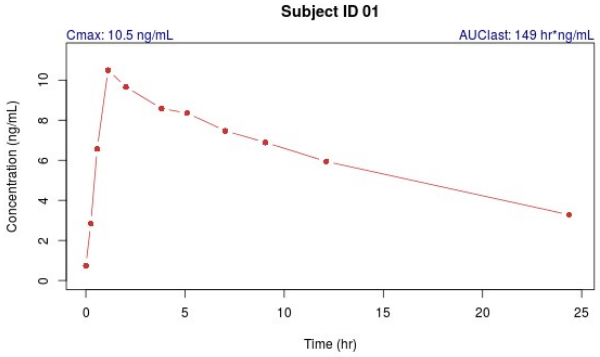
Group

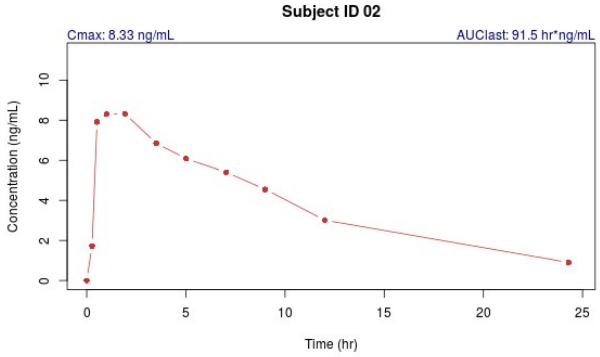


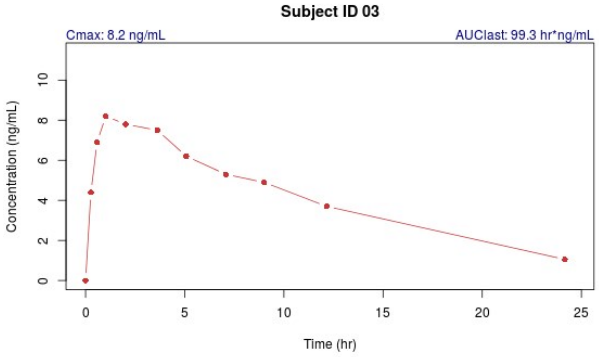


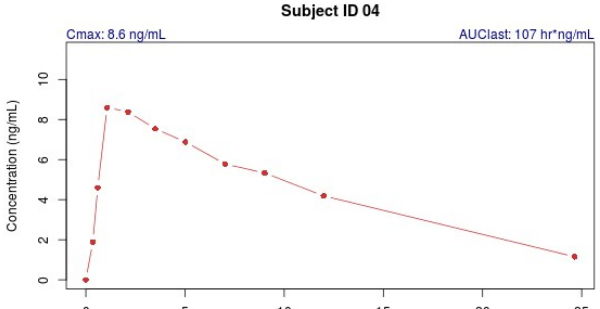


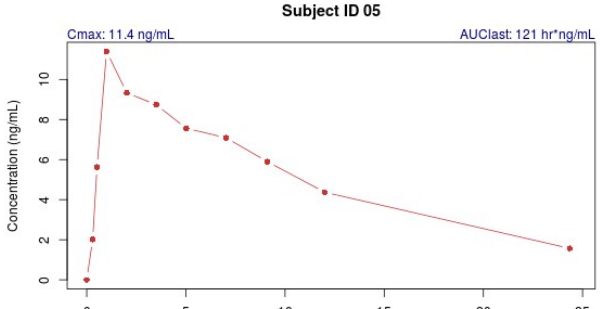
Individual

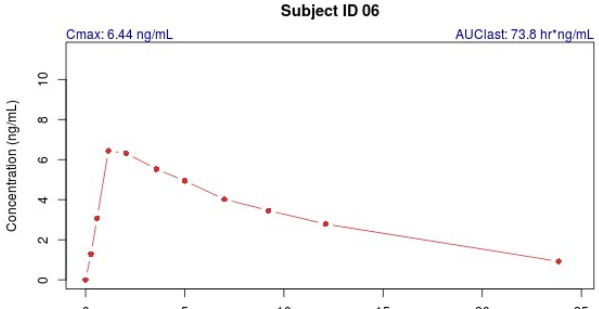






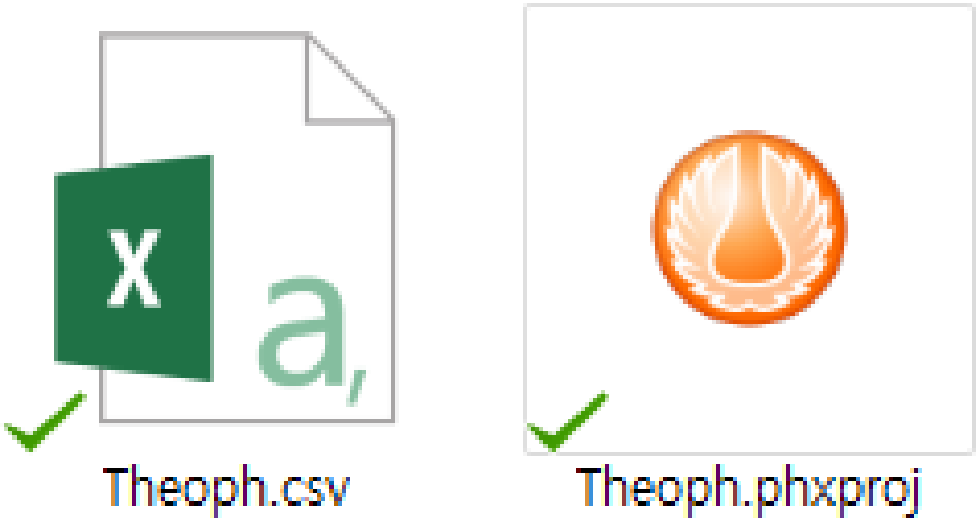




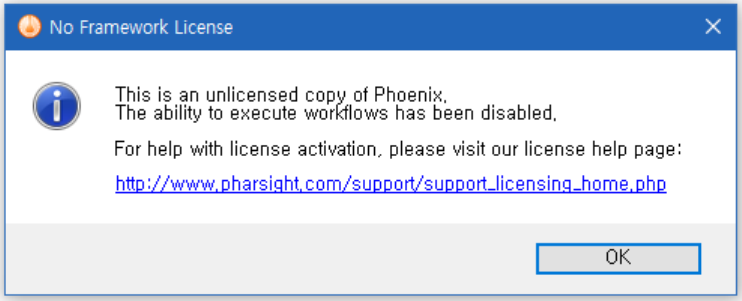


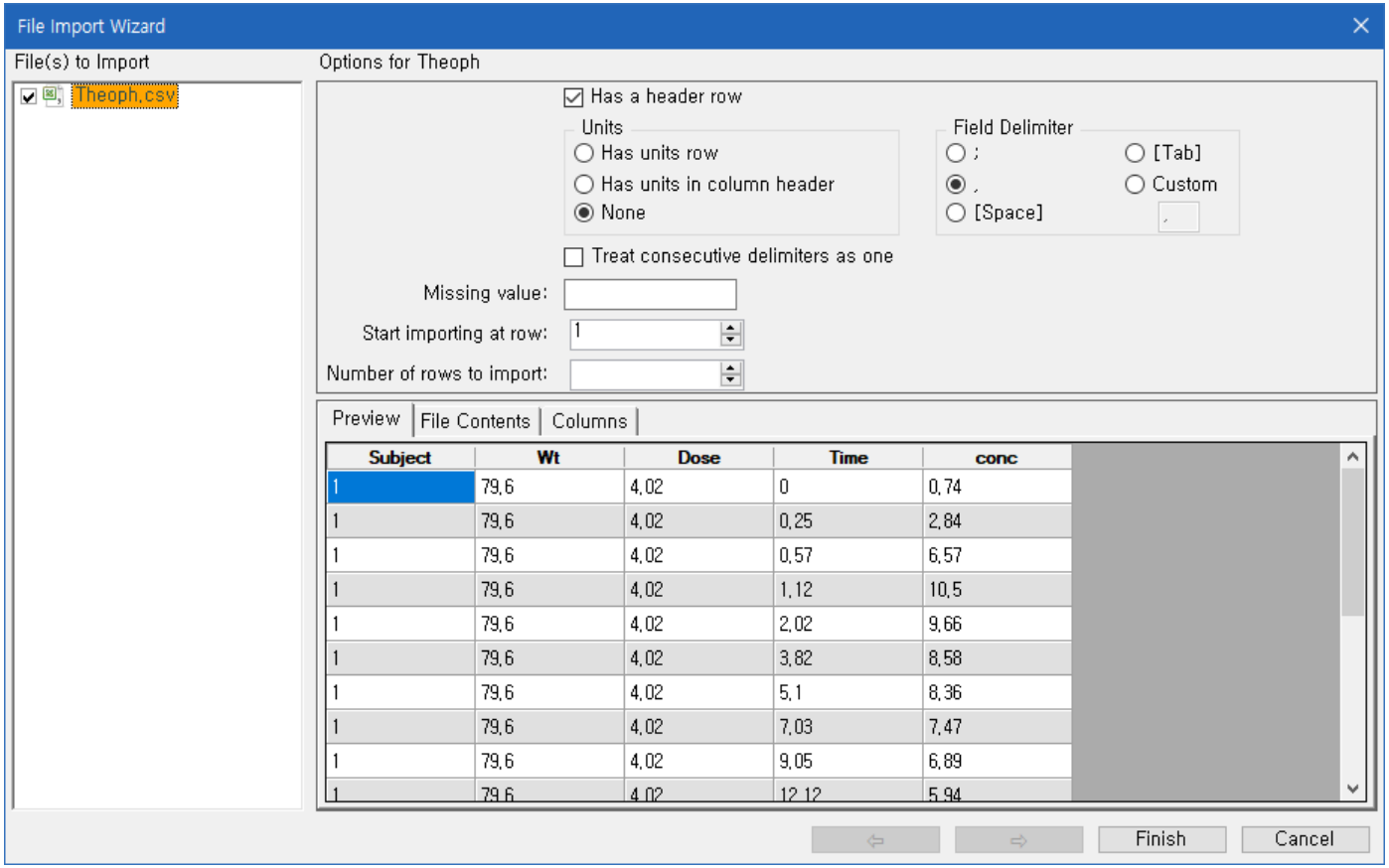
Hands-on Exercise 2

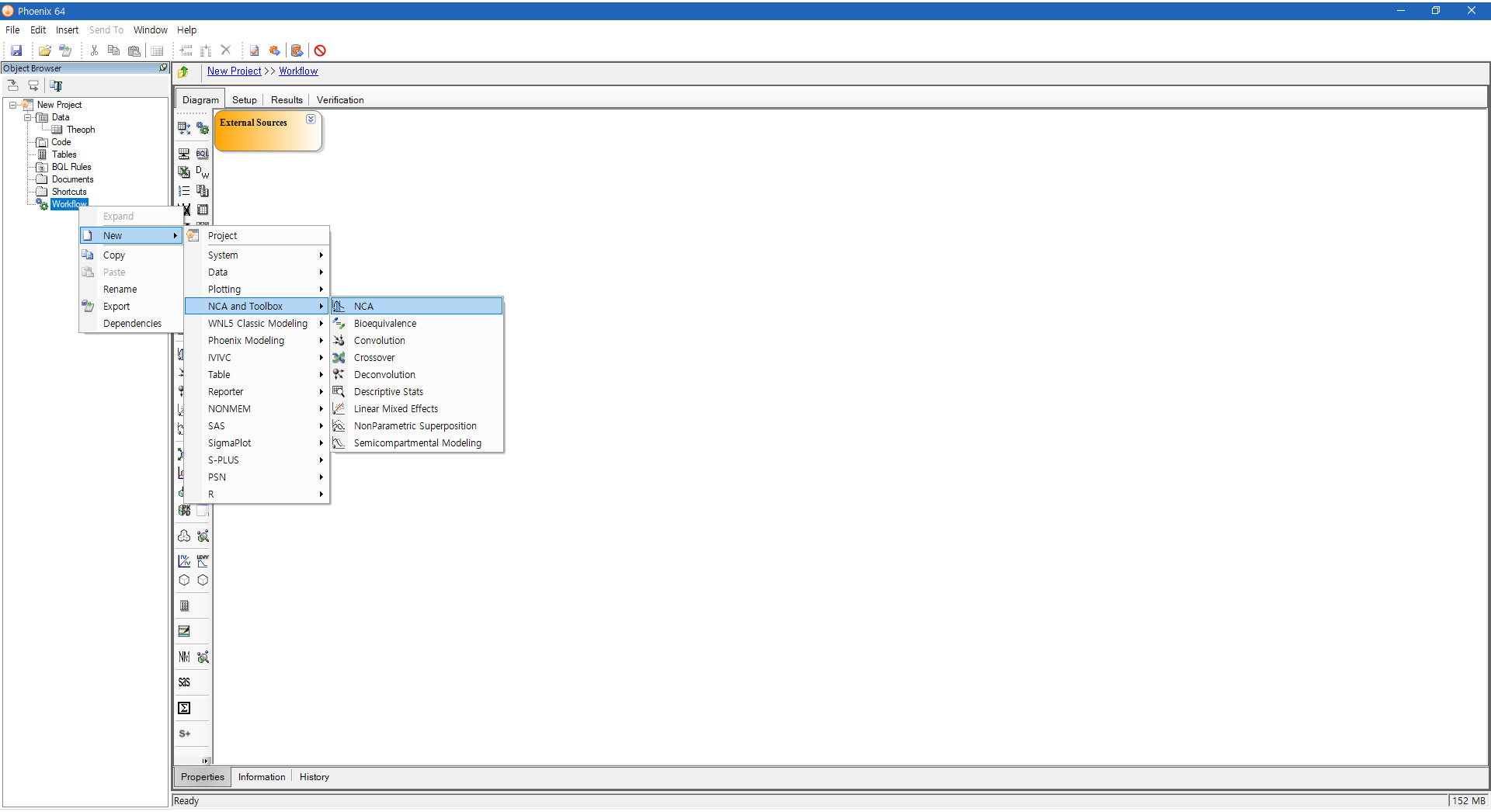
- Phoenix Winnonlin



유료 사용?


No Framework License
This is an unlicensed copy of Phoenix.
The ability to execute workflows has been disabled.
For help with license activation, please visit our license help page:
http://www.pharsight.com/support/support_licensing_home.php
OK


File Import Wizard
File(s) to Import
Theoph.csv
Options for Theoph
Has a header row
Units
Has units row
Has units in column header
None
Field Delimiter
;
,
[Space]
[Tab]
Custom
Treat consecutive delimiters as one
Missing value:
Start importing at row:
1
Number of rows to import:
Preview
File Contents
Columns
Subject Wt Dose Time conc
1 79,6 4,02 0 0,74
1 79,6 4,02 0,25 2,84
1 79,6 4,02 0,57 6,57
1 79,6 4,02 1,12 10,5
1 79,6 4,02 2,02 9,66
1 79,6 4,02 3,82 8,58
1 79,6 4,02 5,1 8,36
1 79,6 4,02 7,03 7,47
1 79,6 4,02 9,05 6,89
1 79,6 4,02 12,12 5,94
Finish
Cancel


Phoenix 64
File
Edit
Insert
Send To
Window
Help
Object Browser
New Project
Data
Theoph
Code
Tables
BQL Rules
Documents
Shortcuts
Workflow
Expand
New
Copy
Paste
Rename
Export
Dependencies
Project
System
Data
Plotting
NCA and Toolbox
WNL5 Classic Modeling
Phoenix Modeling
IVIVC
Table
Reporter
NONMEM
SAS
SigmaPlot
S-PLUS
PSN
R
NCA
Bioequivalence
Convolution
Crossover
Deconvolution
Descriptive Stats
Linear Mixed Effects
NonParametric Superposition
Semicompartmental Modeling
New Project >> Workflow
Diagram
Setup
Results
Verification
External Sources
Properties
Information
History
Ready
152 MB

Setup | Results | Verification

4.53

	Subject	Rsq	Rsq_adjusted	Corr_XY	No_points_lambda_z	Lambda_z (1/hr)	Lambda_z_lower (hr)	Lambda_z_upper (hr)	HL_Lambda_z (hr)	Tlag (hr)	Tmax (hr)	Cmax (ug/mL	Cmax_D (ug/mL/m	Tlast (hr)	Clast (ug/m	AUClast (hr*ug/m	AUCall (hr*ug/m	AUCINF_obs (hr*ug/mL)	AUCINF_D_obs (hr*ug/mL/mg)	AUC_%Extrap_obs ({%})	Vz_F_obs (mL)	Cl_F_o (mL/h
1	1	0.99999973	0.99999946	-0.99999986	3	0.048456997	9.05	24.37	14.304378	0	1.12	10.5	0.0328125	24.37	3.28	148.92305	148.92305	216.61193	0.67691229	31.248917	30486.748	1477.
2	2	0.99719539	0.99579308	-0.99859671	4	0.10408644	7.03	24.3	6.6593416	0	1.92	8.33	0.02603125	24.3	0.9	91.5268	91.5268	100.17346	0.31304206	8.6316867	30690.442	3194.
3	3	0.99932496	0.99864992	-0.99966242	3	0.10244431	9	24.17	6.7660874	0	1.02	8.2	0.025625	24.17	1.05	99.2865	99.2865	109.53597	0.34229991	9.3571734	28517.1	2921.
4	4	0.99892414	0.99784827	-0.99946192	3	0.099287021	9.02	24.65	6.9812467	0	1.07	8.6	0.026875	24.65	1.15	106.7963	106.7963	118.37888	0.369934	9.7843309	27225.964	2703.
5	5	0.99864718	0.99797078	-0.99932336	4	0.086618884	7.02	24.35	8.002264	0	1	11.4	0.035625	24.35	1.57	121.2944	121.2944	139.41978	0.43568681	13.000579	26497.995	2295.
6	6	0.99824134	0.9978896	-0.99912028	7	0.08779574	2.03	23.85	7.8949979	0	1.15	6.44	0.020125	23.85	0.92	73.77555	73.77555	84.254418	0.26329506	12.437174	43259.734	3798.
7	7	0.99867017	0.99800525	-0.99933486	4	0.088336496	6.98	24.22	7.8466683	0	3.48	7.09	0.02215625	24.22	1.15	90.7534	90.7534	103.7718	0.32428688	12.545221	34908.441	3083.
8	8	0.99101239	0.98876549	-0.99549605	6	0.08145054	3.53	24.12	8.5100379	0	2.02	7.56	0.023625	24.12	1.25	88.55995	88.55995	103.90669	0.3247084	14.76973	37810.508	3079.
9	9	0.99944366	0.99888733	-0.99972179	3	0.082458634	8.8	24.43	8.4059988	0	0.63	9.03	0.02821875	24.43	1.12	86.32615	86.32615	99.908718	0.31221474	13.594978	38842.793	3202.
10	10	0.99950868	0.99901737	-0.99975431	3	0.074959824	9.38	23.7	9.2469158	0	3.55	10.21	0.03190625	23.7	2.42	138.3681	138.3681	170.65206	0.53328769	18.918002	25015.54	1875.
11	11	0.99999826	0.99999651	-0.99999913	3	0.09545856	9.03	24.08	7.2612365	0	0.98	8	0.025	24.08	0.86	80.0936	80.0936	89.102745	0.27844608	10.110962	37622.185	3591.
12	12	0.9993968	0.9987936	-0.99969836	3	0.11025949	9.03	24.15	6.2865082	0	3.52	9.75	0.03046875	24.15	1.17	119.9775	119.9775	130.58883	0.4080901	8.1257573	22224.294	2450.

Filter:

- Output Data
  - Dosing Used
  - Exclusions
  - Final Parameters
  - Final Parameters Pivo
  - Partial Areas
  - Plot Titles
  - Slopes Settings
  - Summary Table
- Plots
  - Observed Y and Predi
- Text Output
  - Core output
  - Settings

Options | Plots

Model Type: Plasma (200 - 202)

Sparse | Weighting: Uniform | 0

Titles (up to 5 lines)

Calculation Method: Linear Trapezoidal Linear Interpolation

Model Settings
- Page Breaks
- Intermediate Output
- Exclude Profiles with Insufficient data
- Disable Curve Stripping

Dose Options
Type: Extravascular | Preview
Unit: mg | Normalization: None

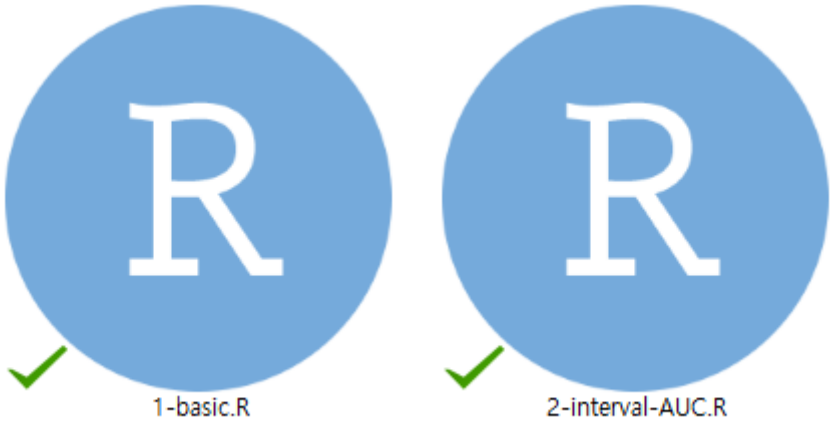
Fit Slopes
Clear: Selections, Exclusions | Fit
Max # of Profiles for User Range Selections: 100

력하십시오.

오전 11:37

Hands-on Exercise 3

- Basic NCA,
- Find Interval AUC

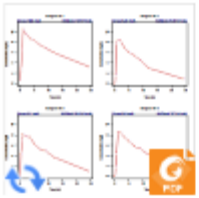


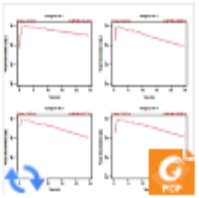
Hands-on Exercise 4

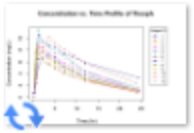
- Report Generation

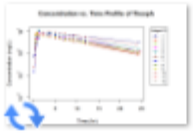
Hands-on Exercise 5

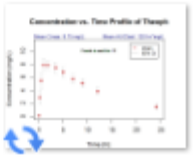
- plotPK


Individual PK Linear Scale for Theoph.pdf


Individual PK Log 10 Scale for Theoph.pdf

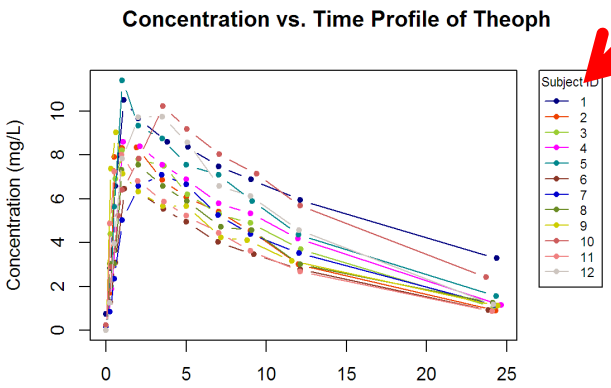

PK Profile Linear Scale for Theoph.tiff

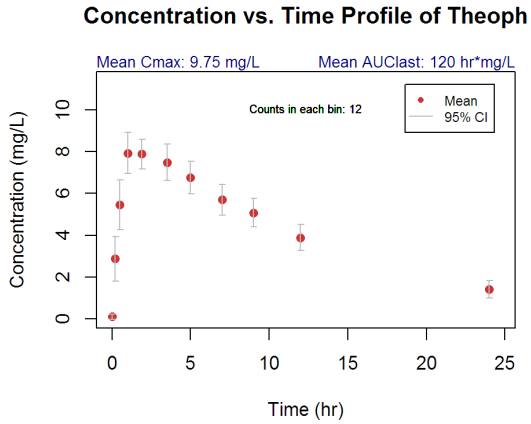

PK Profile Log 10 Scale for Theoph.tiff

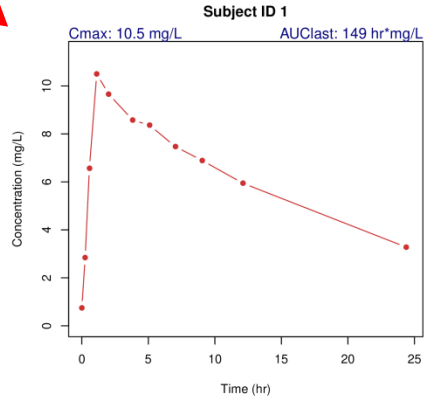

PK Profile with CI for Theoph.tiff

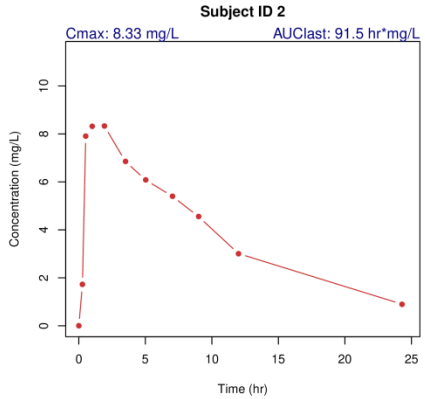
plotPK()

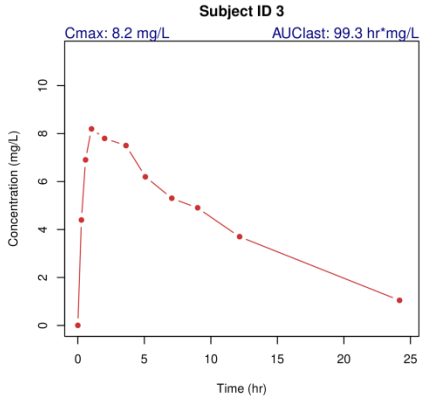
```
plotPK(Theoph, "Subject", "Time", "conc", unitTime="hr", unitConc="mg/L", dose=320)
```

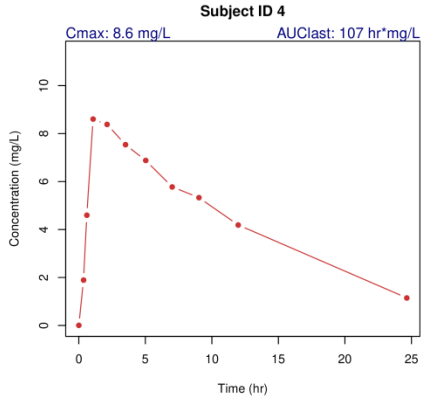






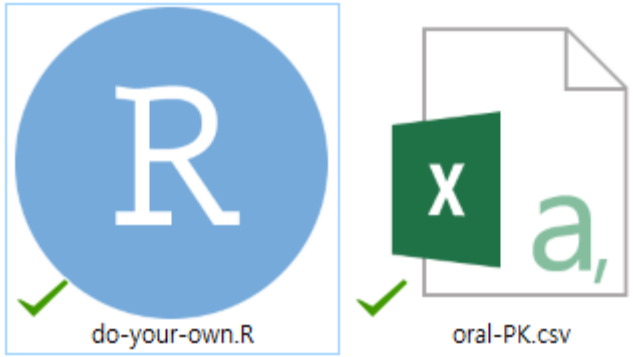






Hands-on Exercise 6

- 50세 이하 흑인 여자의 AUC_{last}를 50세 이하 흑인 남자의 비교해 보세요.



감사합니다.

사용후 궁금한 점이 있다면 shan@catholic.ac.kr 로 알려주세요.

Reference

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