

2025 National Taiwan University - Population Pharmacokinetics workshop: TEST

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1. Install the C Compiler

Ensure that a C compiler is installed on your system. For installation instructions, refer to `ReadMe.txt`.

2. Restore the R environment

Run the following code chunk to install and restore the required packages. When prompted in the console, type Y at `install.packages()`, select **2** when prompted by `renv::restore()`, and type Y again to proceed.

```
install.packages("renv")
install.packages("pkgbuild")
library(renv)
renv::restore()
has_rtools <- pkgbuild::has_build_tools(debug = TRUE)
```

3. **Run Script** To knit the `.Rmd` document, press `Ctrl + Shift + K` (Windows) or `Cmd + Shift + K` (Mac) in RStudio. This will generate the output document based on the settings defined in the YAML header.

4. **Validate the Run** `test.html` is an outcome after successful run from `test.Rmd` script. Compare with `test_run_complete.pdf` if anything is missing. Compare this file with `test_run_complete.pdf` to ensure that no content is missing. If any issues are encountered, please contact the author for troubleshooting.

Load Packages

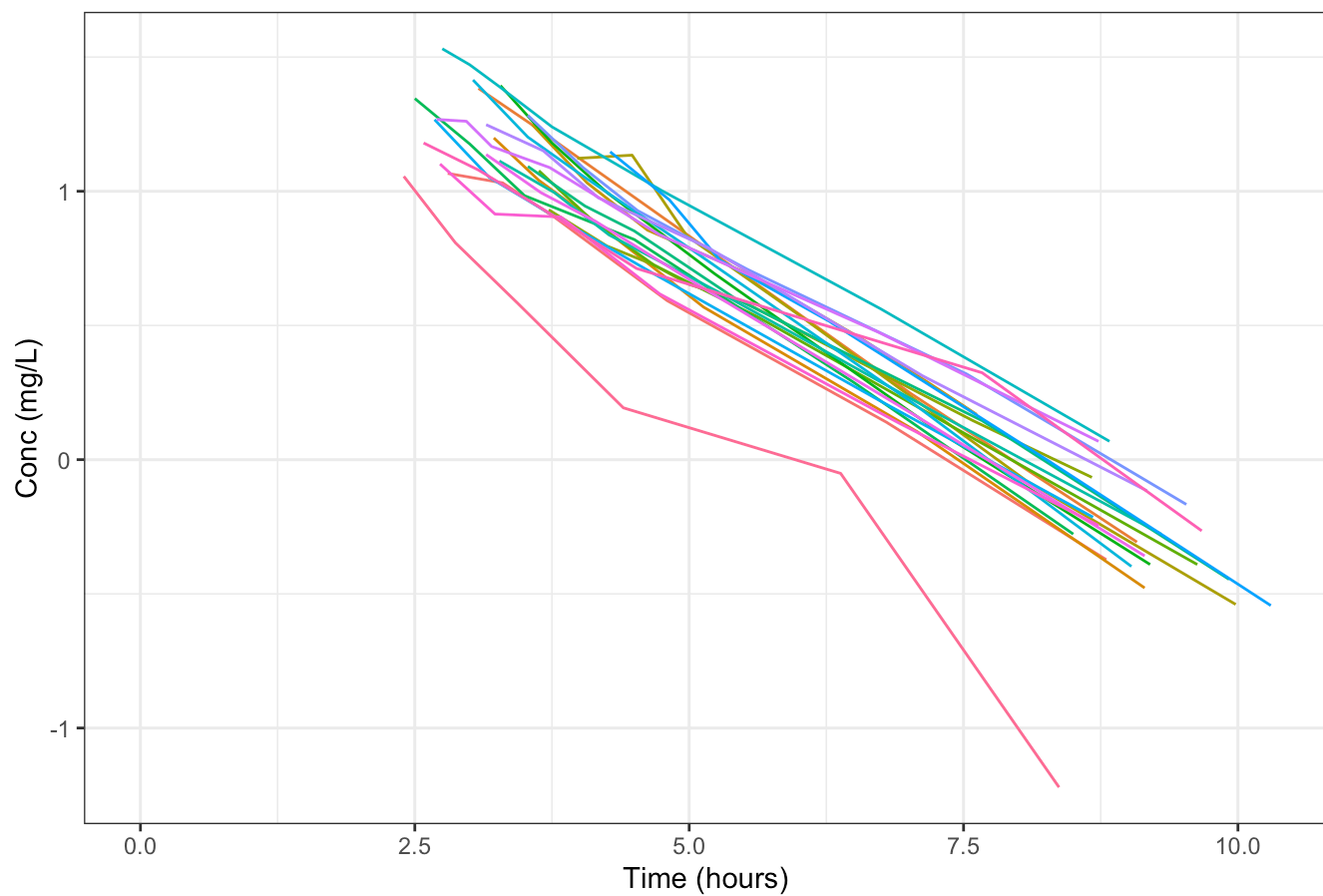
```
rm(list=ls())
library(tidyverse)
library(ggplot2)
library(nlmixr2)
library(xpose4)
library(xpose.nlmixr2)
library(rxode2)
library(gridExtra)
library(ggPMX)
library(ggpubr)
library(mrgsolve)
```

Data Import

```
# Import busulfan two compartment dataset
busulfan_dataset <- read.csv("dataset/busulfan_First_Dose.csv", na.strings = ".")

# Plasma drug concentration decline in two phases shown in semi-log plot
ggplot(busulfan_dataset, aes(TIME/60, log(DV), group = ID, color = as.factor(ID))) +
  geom_line() +
  theme_bw() +
  labs(title = "Busulfan semi-log plot", x = "Time (hours)", y = "Conc (mg/L)") +
  theme(legend.position = "blank")
```

Busulfan semi-log plot



Fit

```

# One compartment model structure
busulfan_1cmt_base_model <- function() {
  ini({
    # Typical value (THETAs)
    tvcl <- log(5)
    tvv1 <- log(50)

    # Interindividual variability (OMEGAs)
    eta_cl ~ 0.0322
    eta_v1 ~ 0.0222

    # Residual variability
    add.error <- 0.0955
  })

  model({
    # Individual value
    cl <- exp(tvcl + eta_cl)
    v1 <- exp(tvv1 + eta_v1)

    # Conversion
    k10 <- cl / v1

    # ODEs
    d / dt(central) = -k10 * central

    # Concentration
    cp = central / v1

    # Error model
    IPRED = cp
    IPRED ~ add(add.error)
  })
}

# 1 compartment model fitting
one_cmt_pk_fit <- nlmixr2(
  busulfan_1cmt_base_model,
  busulfan_dataset,
  "focei",
  table = list(cwres = TRUE)
)

```

```
## i parameter labels from comments are typically ignored in non-interactive mode
```

```
## i Need to run with the source intact to parse comments
```

```
## → loading into symengine environment...
```

→ pruning branches (`if`/`else`) of full model...

✓ done

→ calculate jacobian

→ calculate sensitivities

→ calculate $\partial(f)/\partial(\eta)$

→ calculate $\partial(R^2)/\partial(\eta)$

→ finding duplicate expressions in inner model...

→ optimizing duplicate expressions in inner model...

→ finding duplicate expressions in EBE model...

→ optimizing duplicate expressions in EBE model...

→ compiling inner model...

using C compiler: 'Apple clang version 16.0.0 (clang-1600.0.26.6)'
using SDK: 'MacOSX15.2.sdk'

✓ done

→ finding duplicate expressions in FD model...

→ optimizing duplicate expressions in FD model...

→ compiling EBE model...

using C compiler: 'Apple clang version 16.0.0 (clang-1600.0.26.6)'
using SDK: 'MacOSX15.2.sdk'

✓ done

→ compiling events FD model...

```
## using C compiler: 'Apple clang version 16.0.0 (clang-1600.0.26.6)'  
## using SDK: 'MacOSX15.2.sdk'
```

```
## ✓ done
```

```
## → Calculating residuals/tables
```

```
## ✓ done
```

```
## → compress origData in nlmixr2 object, save 9504
```

```
## → compress parHistData in nlmixr2 object, save 3768
```

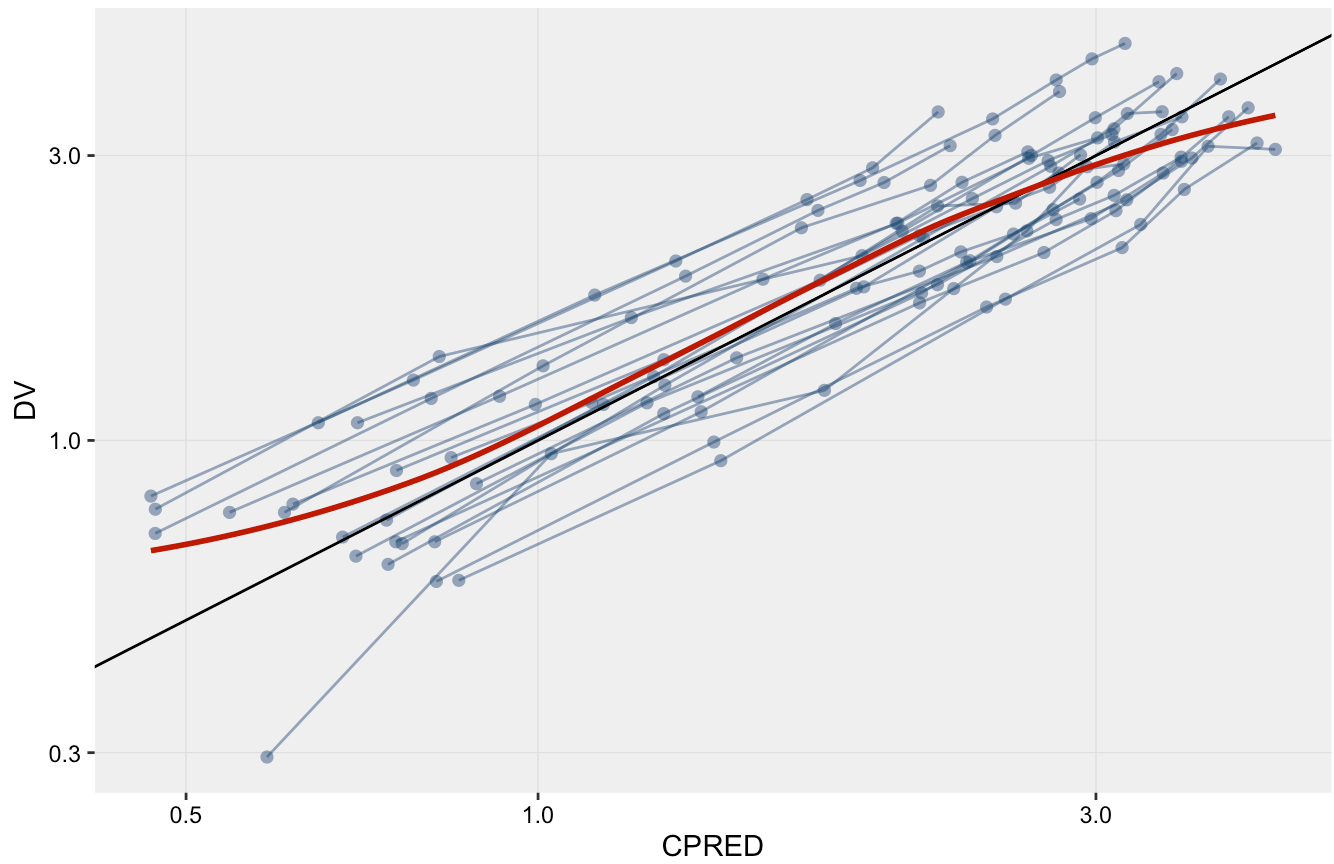
Plot

```
# Convert to XPOSE for goodness of fit  
one_cmt_xpdb_pk <- xpose_data_nlmixr2(one_cmt_pk_fit,  
                                     xp_theme = theme_xp_nlmixr2()  
                                     )
```

```
# observation vs population prediction plot  
dv_vs_pred(one_cmt_xpdb_pk,  
            type="pls",  
            title = "One Compartment",  
            log = 'xy',  
            subtitle = NULL,  
            guide = TRUE)
```

```
## `geom_smooth()` using formula = 'y ~ x'  
## `geom_smooth()` using formula = 'y ~ x'
```

One Compartment



n/Library/CloudStorage/OneDrive-TheOhioStateUniversity/Desktop/PMx_workspace/taiwan_workshop/2025_NTUSP_Workshop