



## Fc-OPG / uNTx PKPD model vignette.

<https://www.github.com/metrumresearchgroup>

<https://www.github.com/mrgsolve/examples>

[https://mrgsolve.github.io/user\\_guide](https://mrgsolve.github.io/user_guide)

```
library(mrgsolve)
library(ggplot2)
library(dplyr)
library(knitr)
library(parallel)
opts_chunk$set(comment='.', message=FALSE)
```

Compile and load the OPG/NTX model

```
mod <- mread("opg", end=528,delta=6)
```

A dosing event object for a single 3 mg/kg dose (assuming 70 kg individual)

```
e <- ev(amt=70*3,cmt=1)
```

Execute the simulation

```
sim <-
  mod %>% Req(PKDV,NTX) %>% zero_re(sigma) %>%
  mrgsim(events=e,nid=50,atol=1E-30,obsonly=TRUE,add=0.01) %>%
  filter(time > 0)
```

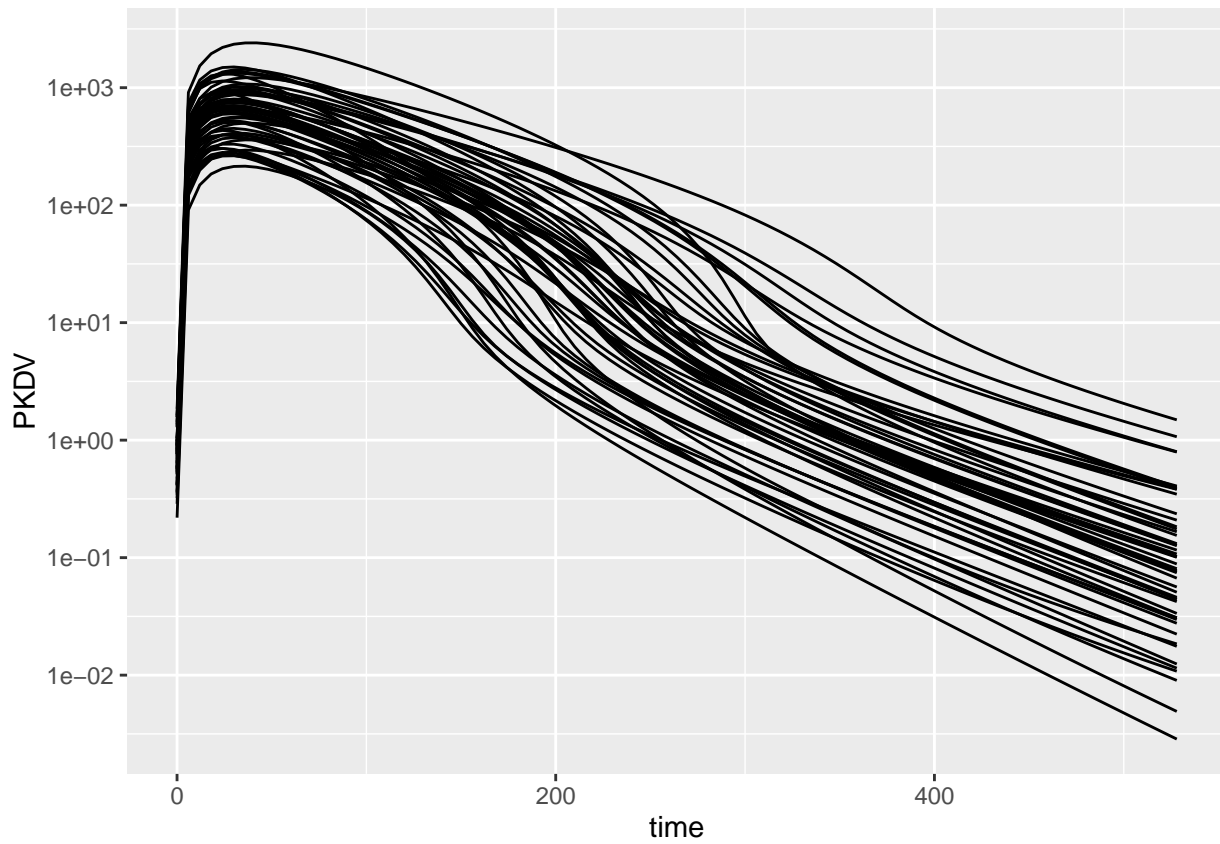
```
sim
```

```
. # A tibble: 4,450 × 4
.   ID time    NTX    PKDV
.   <dbl> <dbl>   <dbl>   <dbl>
. 1     1  0.01 84.05850  0.5672433
. 2     1  6.00 72.95543 253.0925321
. 3     1 12.00 62.50845 406.3002681
. 4     1 18.00 53.51580 494.1143938
```

```
. 5      1 24.00 45.82219 538.5557163  
. 6      1 30.00 39.25534 554.3529342  
. 7      1 36.00 33.65814 551.4017298  
. 8      1 42.00 28.89288 536.3707827  
. 9      1 48.00 24.84054 513.7650683  
. 10     1 54.00 21.39888 486.6331152  
. # ... with 4,440 more rows
```

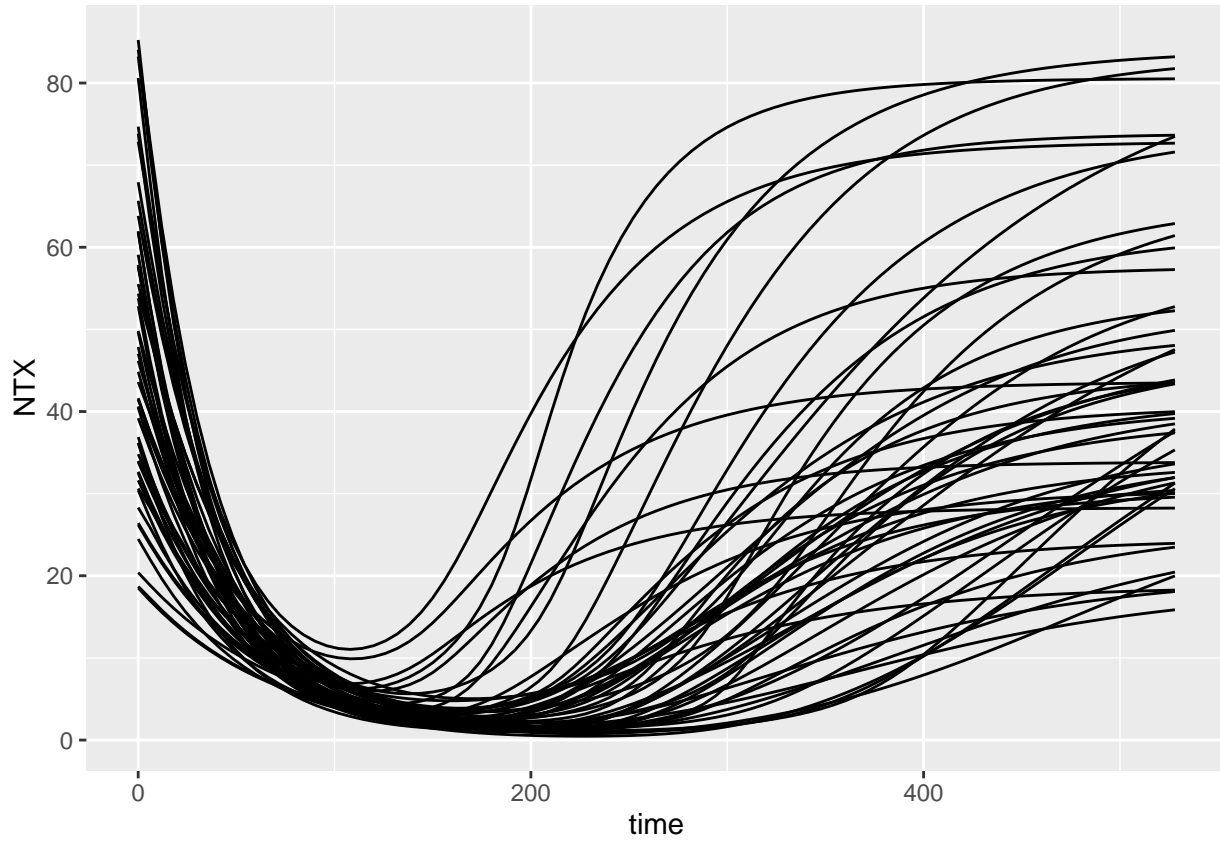
**Fc-OPG versus time**

```
ggplot(sim, aes(time,PKDV,group=ID)) + geom_line() +  
  scale_y_continuous(trans='log',breaks=10^seq(-4,4))
```



**uNTX versus time**

```
ggplot(sim, aes(time,NTX,group=ID)) + geom_line()
```



## Simulation to evaluate 3 mg/kg dose

- Simulate the median percent change from baseline at 2 weeks after single 3 mg/kg dose

```
mod <- mread("opg")
mod %<>% mrgsolve::collapse_omega() %>% mrgsolve::collapse_sigma()
```

### Read in our simulated posterior

```
set.seed(770090)
post <- readRDS("opgpost.RDS") %>% sample_n(500)
omegas <- as_bmat(post, "OMEGA")
sigmas <- as_bmat(post, "SIGMA")
```

### 3 mg/kg SC dose in N=200 70 kg patient

```
sc3 <- expand.ev(amt=210, ID=1:200, IV=0)
```

```
sim <- function(i, data, des) {
  mod %>%
    Req(PKDV, PDDV) %>%
    param(slice(post, i)) %>%
    omat(omegas[[i]]) %>% smat(sigmas[[i]]) %>%
    carry_out(dose, IV) %>%
    mrgsim(data=data, tgrid=des, obsonly=TRUE) %>%
    mutate(irep=i)
}
```

### Simulate

- If we're on a unix-like system, parallelize
- If windows, just use regular lapply

```
if(.Platform$OS.type=="windows") mclapply <- lapply
```

```
mcRNG()
set.seed(2331991)
out <- mclapply(1:300, sim, data=sc3,
               des=tgrid(end=-1, add=c(0, 336))) %>% bind_rows
```

### Summarise the simulations:

- Group by ID and irep
- Get the baseline uNTX observation
- Calculate percent change from baseline

- Filter down to the week 2 observation
- Summarize (median)

```
sum <-  
  out %>%  
  group_by(ID, irep) %>%  
  mutate(BASE = dplyr::first(PDDV), dDV = 100*(PDDV-BASE)/BASE) %>%  
  ungroup %>%  
  filter(time==336) %>%  
  group_by(irep) %>%  
  summarise(med = median(dDV))
```

### The bottom line

- The summarise the distribution of median percent change from baseline at week 2

```
quantile(sum$med, c(0.025, 0.5, 0.975))
```

```
.      2.5%      50%      97.5%  
. -58.67022 -43.97501 -33.27235
```

`sessionInfo()`

```
. R version 3.3.0 (2016-05-03)
. Platform: x86_64-apple-darwin13.4.0 (64-bit)
. Running under: OS X 10.9.5 (Mavericks)
.
. locale:
. [1] en_US.UTF-8/en_US.UTF-8/en_US.UTF-8/C/en_US.UTF-8/en_US.UTF-8
.
. attached base packages:
. [1] parallel stats grDevices utils datasets graphics methods
. [8] base
.
. other attached packages:
. [1] knitr_1.14 dplyr_0.5.0 ggplot2_2.1.0
. [4] mrgsolve_0.7.6.9028
.
. loaded via a namespace (and not attached):
. [1] Rcpp_0.12.7 magrittr_1.5
. [3] munsell_0.4.3 colorspace_1.2-6
. [5] R6_2.2.0 RcppArmadillo_0.7.400.2.0
. [7] stringr_1.1.0 plyr_1.8.4
. [9] tools_3.3.0 grid_3.3.0
. [11] gtable_0.2.0 DBI_0.5-1
. [13] htmltools_0.3.5 yaml_2.1.13
. [15] lazyeval_0.2.0 assertthat_0.1.0.99
. [17] digest_0.6.10 tibble_1.2
. [19] formatR_1.4 evaluate_0.9
. [21] rmarkdown_1.0 labeling_0.3
. [23] stringi_1.1.1 scales_0.4.0
```