Detailed Analysis

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```
packages <- c("deSolve", "ggplot2", "formatR", "scales")
invisible(lapply(packages, library, character.only = T))
```

```
MPL_data <- read.csv("MPL.csv", na.strings = "NA")

median_MPL_01 <- median(MPL_data$MPL_conc[MPL_data$dose==0.1], na.rm=T)
median_MPL_03 <- median(MPL_data$MPL_conc[MPL_data$dose==0.3], na.rm=T)

cat("Median of dose 0.1: ", median_MPL_01)
```

```
## Median of dose 0.1:  14.59
```

```
cat("Median of dose 0.3: ", median_MPL_03)
```

```
## Median of dose 0.3:  39.925
```

```
medians <- aggregate(MPL_data[,c("MPL_conc","mRNA","Free_receptor")],
                     list(MPL_data$dose, MPL_data$time), median, na.rm=T)
names(medians)[1:2] <- c("dose","time")

median_01 <- subset(medians, medians$dose == 0 | medians$dose == 0.1)
median_03 <- subset(medians, medians$dose == 0 | medians$dose == 0.3)

head(medians)
```

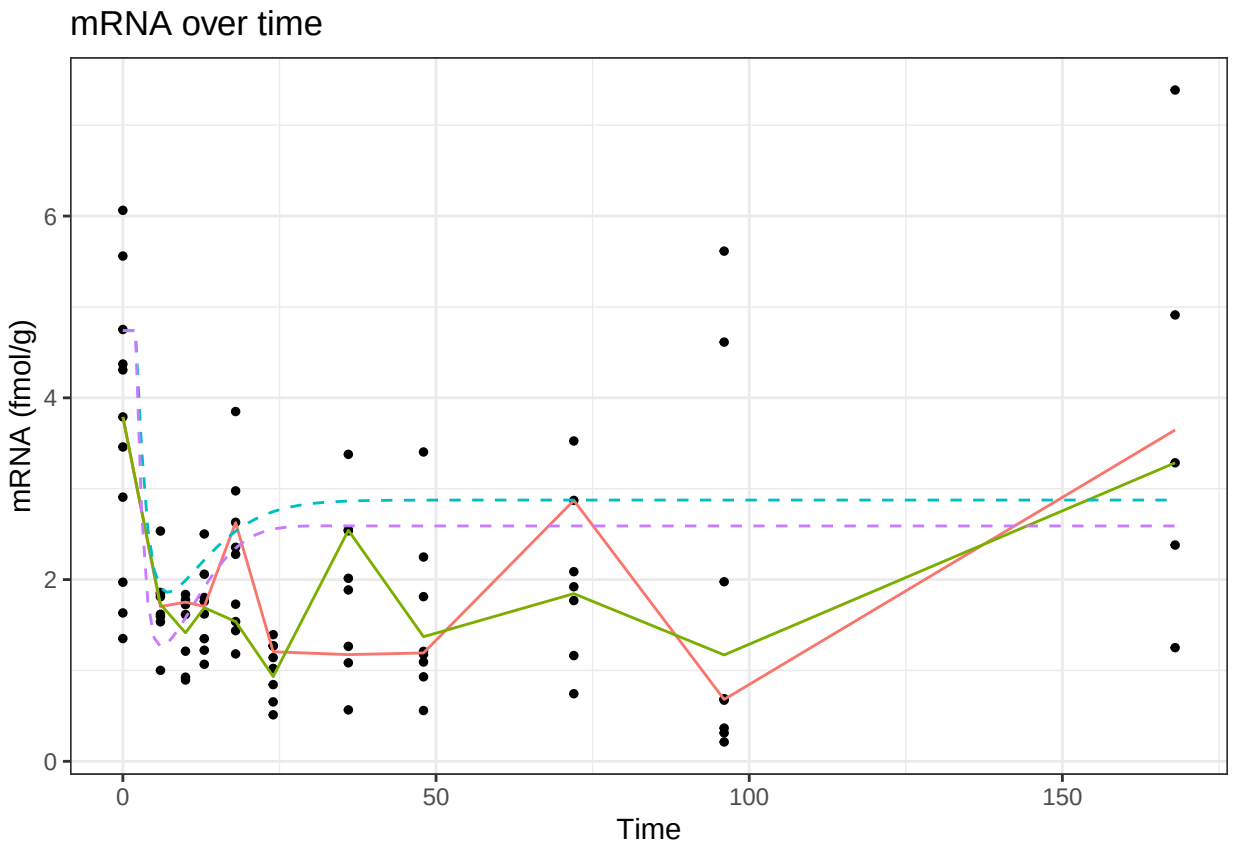
```
##   dose time MPL_conc   mRNA Free_receptor
## 1  0.0    0    0.000 3.7900        292.95
## 2  0.1    6   11.180 1.7025        124.70
## 3  0.3    6   31.295 1.7295         97.90
## 4  0.1   10   12.335 1.7515        157.80
## 5  0.3   10   36.960 1.4140         69.55
## 6  0.1   13   11.945 1.7045        152.50
```

```
params <- c(
        k.s_Rm = 2.90, # fmol/g liver/h, Oe k voor GR mRNA synthese
        IC.50_Rm = 26.2, # fmol/mg protein, concentratie DR(N) wat mRNAR inhibeert
        k.on = 0.00329, # L/nmol/h, 2e orde k voor vorming MPL-receptor complex
        k.T = 0.63, # 1/h, 1e orde k voor translocatie MPL-receptor complex naar nucleus
        k.re = 0.57, # 1/h, 1e orde k voor 'recovery' receptor (celkern -> cytosol)
        R.f = 0.49, # fractie vrije receptor die gerecycled wordt
        k.d_R = 0.0572, # 1/h, 1e orde k voor afbraak van de receptor
        k.d_Rm = 0.612, # 1e orde k voor GR mRNA afbraak
        k.s_R = 3.22, # 1e orde k voor aanmaak receptor
        D = (0 * 1000)/374.471 # nmol/L, als molgewicht[MPL] = 374.471 g/mol
)
```

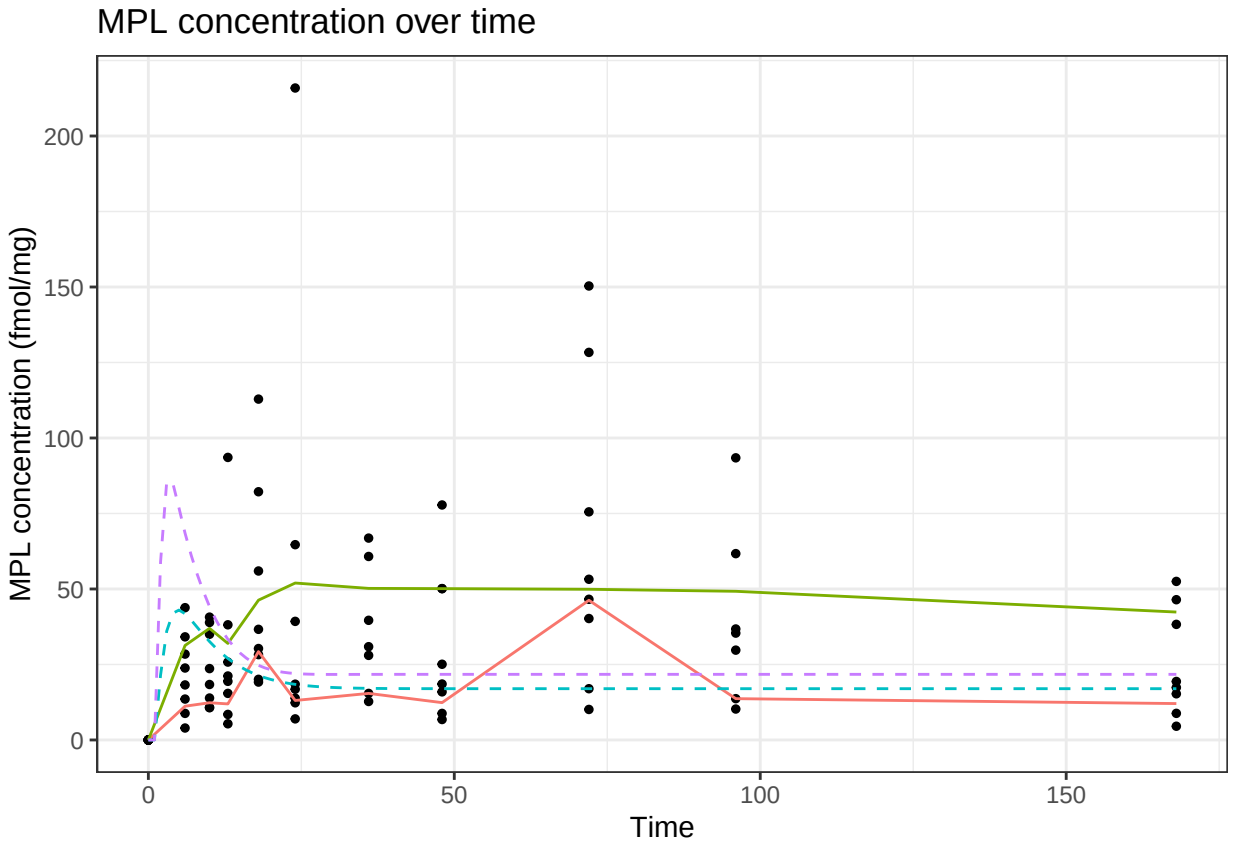
```
state <- c(
        mRNA = 4.74, # fmol / g liver, basisniveau concentratie receptor mRNA
        Free_receptor = 267, # fmol/mg protein, basisniveau concentratie vrije receptor
        DR = 0, # fmol/mg protein, dichtheid MPL
        MPL_conc = 0 # fmol/mg protein, hoeveelheid MPL
)

volume <- function(t, y, parms){
  with(as.list(c(parms, y)),{
    delta.mRNA_R <- k.s_Rm * (1 - ( MPL_conc / (IC.50_Rm + MPL_conc) ) ) - k.d_Rm * mRNA
    delta.R <- k.s_R * mRNA + R.f * k.re * MPL_conc -
            k.on * D * Free_receptor - k.d_R * Free_receptor
    delta.DR <- k.on * D * Free_receptor - k.T * DR
    delta.MPL_conc <- k.T * DR - k.re * MPL_conc
    return( list( c(delta.mRNA_R, delta.R, delta.DR, delta.MPL_conc ) ) )
  })
}

times <- seq(0, 168, by = 1)

# model_00 <- ode(times = times, y = state,
#                 parms = params, func = volume, method = "euler")
# model_00 <- as.data.frame(model_00)

params$D <- (median_MPL_01 * 1000)/374.471
model_01 <- ode(times = times, y = state,
                parms = params, func = volume, method = "euler")
model_01 <- as.data.frame(model_01)

params$D <- (median_MPL_03 * 1000)/374.471
model_03 <- ode(times = times, y = state,
                parms = params, func = volume, method = "euler")
model_03 <- as.data.frame(model_03)
```

Assignment 1

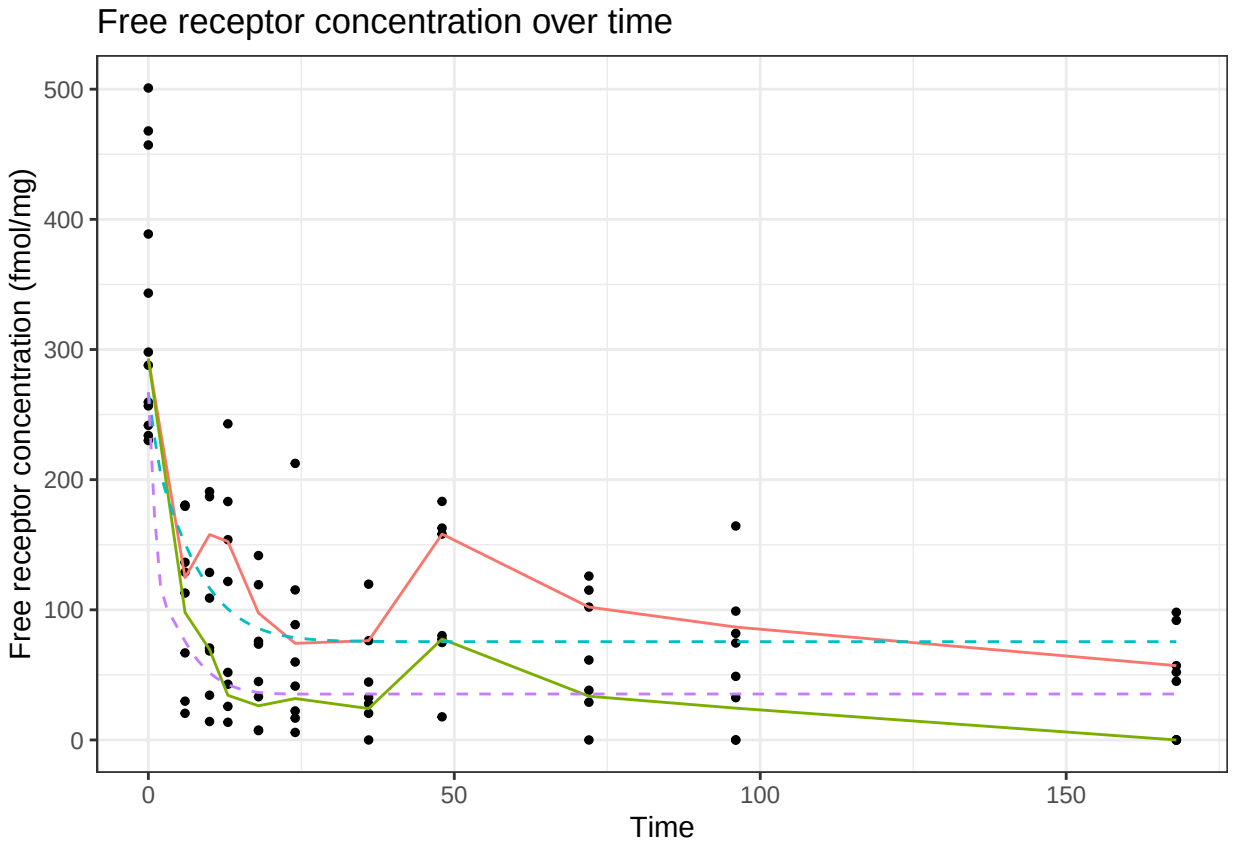
```
group.cols <- hue_pal()(4)
colours <- c("Median 0.1" = group.cols[1], "Median 0.3" = group.cols[2],
             "Model 0.1" = group.cols[3], "Model 0.3" = group.cols[4])
ggplot(data = MPL_data, mapping = aes(x = time, y = mRNA)) +
        geom_point(size = 1) +
        geom_line(data = median_01, color = colours["Median 0.1"]) +
        geom_line(data = median_03, color = colours["Median 0.3"]) +
        geom_line(data = model_01, linetype = "dashed", color = colours["Model 0.1"]) +
        geom_line(data = model_03, linetype = "dashed", color = colours["Model 0.3"]) +
        labs(x = "Time", y = "mRNA (fmol/g)", title = "mRNA over time") +
        theme_bw()
```




```
ggplot(data = MPL_data, mapping = aes(x = time, y = MPL_conc)) +
        geom_point(size = 1) +
        geom_line(data = median_01, color = colours["Median 0.1"]) +
        geom_line(data = median_03, color = colours["Median 0.3"]) +
        geom_line(data = model_01, linetype = "dashed", color = colours["Model 0.1"]) +
        geom_line(data = model_03, linetype = "dashed", color = colours["Model 0.3"]) +
        labs(x = "Time", y = "MPL concentration (fmol/mg)",
             title = "MPL concentration over time") +
        theme_bw()
```




```
ggplot(data = MPL_data, mapping = aes(x = time, y = Free_receptor)) +
        geom_point(size = 1) +
        geom_line(data = median_01, color = colours["Median 0.1"]) +
        geom_line(data = median_03, color = colours["Median 0.3"]) +
        geom_line(data = model_01, linetype = "dashed", color = colours["Model 0.1"]) +
        geom_line(data = model_03, linetype = "dashed", color = colours["Model 0.3"]) +
        labs(x = "Time", y = "Free receptor concentration (fmol/mg)",
             title = "Free receptor concentration over time") +
        theme_bw()
```



- [1] Why is it best practice to plot the median for the experimental data? >The median does not change with huge outliers, so the data is more reliable. If there is a significant difference, it will show.
- [2] How do the results of the simulations depend on the dose and concentration of the drug? >
- [3] Are the results of the model in line with experimental data?