

Assignment week 2  
Glucocorticoid receptor dynamica



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# 1 Introduction

## 1.1 About corticosteroids

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## 1.2 How they work and when they are used

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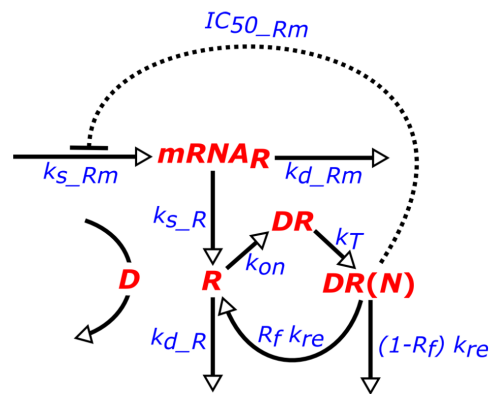


Figure 1: flowdiagram glucocorticoide receptor dynamica

## 1.3 Effect of medicine on receptor production

text

## 2 Model for Glucocorticoids Receptor Dynamics

### 2.1 Differential equations

$$\begin{aligned}\frac{\Delta mRNA_R}{\Delta t} &= k_{s\_Rm} * (1 - \frac{DR(N)}{IC_{50\_Rm} + DR(N)}) - k_{d\_Rm} * mRNA_R \\ \frac{\Delta R}{\Delta t} &= k_{s\_R} * mRNA_R + R_f * K_{re} * DR(N) - K_{on} * D * R - k_{d\_R} * R \\ \frac{\Delta DR}{\Delta t} &= k_{on} * D * R - k_T * DR \\ \frac{\Delta DR(N)}{\Delta t} &= k_T * DR - k_{re} * DR(N)\end{aligned}$$

### 2.2 Creating an R function of the GRD model

```
# Create function of GRD model
model <- function(time, cur.state, parameters) {
  # Unpack the current state and the parameters for instant access
  with(as.list(c(cur.state, parameters)), {
    # Calculate delta for each equation
    delta.mRNA.R <- k.s_Rm * ( 1 - DR_N / ( IC.50_Rm + DR_N )) - k.d_Rm * mRNA.R
    delta.R <- k.s_R * mRNA.R + R.f * k.re * DR_N - k.on * D * R - k.d_R * R
    delta.DR <- k.on * D * R - k.T * DR
    delta.DR_N <- k.T * DR - k.re * DR_N
    # Return delta's in a list for `ode` function to use
    return(list(c(delta.mRNA.R, delta.R, delta.DR, delta.DR_N)))
  })
}
```

### 2.3 Simulating the model for MPL using given values

For this assignment the corticosteroid that is used is methylprednisolon (MPL). Parameters for MPL to use in the model are already given, they were previously determined by performing experiments on rats.

```
# Initial values and time frame
initial.values <- c(mRNA.R = 4.74, R = 267, DR = 0, DR_N = 0)
times <- seq(0, 48, by = 1)

## Convert concentration of MPL from ng/mL to nmol/L
D <- 20 * 1000 * ( 1 / 374.471)
# Define parameters determined for methylprednisolon (MPL)
parameters <- c(k.s_Rm = 2.9, IC.50_Rm = 26.2, k.on = 0.00329, k.T = 0.63, k.re = 0.57,
  R.f = 0.49, k.d_R = 0.0572, k.d_Rm = 0.612, k.s_R = 3.22, D = D)

# Perform ODE function using the model with the given values for MPL
out <- ode(times = times, y = initial.values, parms = parameters,
  func = model, method = "euler")
plot(out)
```

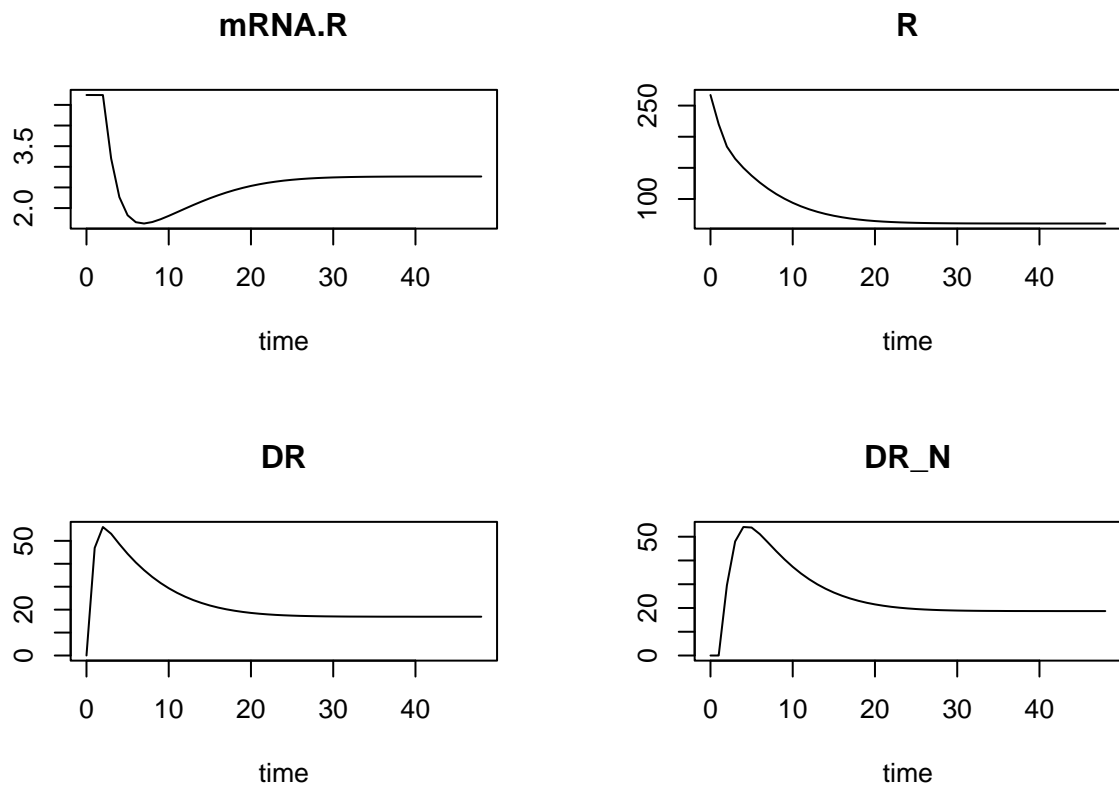


Figure 2: plot of glucocorticoids receptor dynamics simulation with given determined parameter values

## 3 Results

### 3.1 Concentration changes

- Concentration of receptor mRNA ( $\Delta mRNA_R$ )
- Concentration of free receptor ( $R$ )
- Concentration of MPL-receptor complex in cytosol ( $DR$ )
- Concentration of activated MPL-receptor complex ( $DR(N)$ )
- Total receptor concentration

## 4 Discussion and Conclusion

Changes over time explained by interactions between variables.

## References

- [1] Barnes, P.J. (2011), *Glucocorticosteroids: current and future directions*, British Journal of Pharmacology, 163: 29-43, <https://doi.org/10.1111/j.1476-5381.2010.01199.x> (accessed May 11, 2022).