Thema08-week1-mRNA

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1 Introduction

Introduction of the research and introduction research questions

1.1 Goal

- Describe Goal (not the educational goal but the research goal)
- Describe how you reach the goal (e.g. make model and figures, use different setting)
- formulate hypothesis

1.2 Theory

- Describe biological model
- Picture of the biological model

Give an explanation of the model with citations of source [1] (replace this with actual source) and formula explanation

$$\frac{\delta R}{\delta t} = -r * R + m$$

Describe each element and the transformations

2 Methods

Over het algemeen biedt de mediaan een beter idee van de data verdeling, bij steekproefproefgemiddelden mits zij een normaal verdeling volgen. Aangezien de mediaan robuuster is dan een gemiddelde (mean), want het is minder afhankelijk van uitbijters/uitschieters, omdat het het middelste punt is van een gesorteerde reeks cijfers/getallen/gegevens en de scores niet worden gedeeld door het aantal n. Een goede illustratie zegt meer dan duizend woorden, om die reden is het beter om een grafiek van de mediaan erbij te plotten.

2.1 The software model

- Describe the software tools used, as well as the libraries
- Describe the software implementation (note: code below is an example)

```
library(deSolve)
# code
```

2.2 Model configuration

Explain chosen initial state, parameter values and time sequence. Use tables with values as for example below

Table 1: Parameter Values

Parameter	Value	Unit
a	0.08	$hour^{-1}$
b	0.06	$hour^{-1}$
c	0.06	$hour^{-1}$

3 Results

De vragen die opkomen tijdens het onderzoeken van een biologisch systeem zal je kunnen beantwoorden aan de hand van een gecreerd model. Hieronder is de code te zien dat zo'n soort model kan produceren:

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

```
##    dose time MPL_conc  mRNA Free_receptor
## 1   0.0    0     0.00 3.459         259.6
## 2   0.0    0     0.00 5.560         256.7
## 3   0.0    0     0.00 4.372         500.9
## 4   0.0    0     0.00 1.971         241.7
## 5   0.0    0     0.00 1.351         388.7
## 6   0.0    0     0.00    NA         287.9
## 7   0.0    0     0.00 3.790         457.1
## 8   0.0    0     0.00 2.907         467.9
## 9   0.0    0     0.00 6.063         298.0
## 10  0.0    0     0.00 1.633         233.9
## 11  0.0    0     0.00 4.307         343.3
## 12  0.0    0     0.00 4.752         230.1
## 13  0.1    6     3.96 1.811         136.5
## 14  0.1    6    13.55 1.594         112.9
## 15  0.1    6     8.81 2.534         179.5
## 16  0.1    6    18.23 1.535          29.8
## 17  0.1   10    10.68 1.777         186.9
## 18  0.1   10    10.78 1.836         128.7
## 19  0.1   10    13.89 1.726         190.8
## 20  0.1   10    18.37 0.895          14.2
## 21  0.1   13     5.36 1.350         183.2
## 22  0.1   13     8.46 2.059         121.8
## 23  0.1   13    19.42 2.502         242.9
## 24  0.1   13    15.43 1.223          51.9
## 25  0.1   18    28.26 3.849         141.7
## 26  0.1   18    82.20 2.976         119.3
## 27  0.1   18    30.28 2.278          75.8
## 28  0.1   18    20.08 1.729          33.2
## 29  0.1   24     6.99 0.654         115.3
## 30  0.1   24    12.31 1.394          88.6
## 31  0.1   24    18.48 1.142          59.9
## 32  0.1   24    13.85 1.269          16.8
## 33  0.1   36       NA 2.014          76.3
## 34  0.1   36    12.75 1.084         119.7
## 35  0.1   36    28.02 0.566          44.5
## 36  0.1   36    15.42 1.265            NA
## 37  0.1   48     8.80 1.093          77.4
## 38  0.1   48     6.78 1.175         162.8
```

```
## 39  0.1   48    18.53 1.210         158.2
## 40  0.1   48    15.94 2.248            NA
## 41  0.1   72   128.35 2.871          61.4
## 42  0.1   72    75.54    NA         125.9
## 43  0.1   72    16.98 3.525         102.1
## 44  0.1   72    10.11 1.164            NA
## 45  0.1   96    29.75 0.689         164.4
## 46  0.1   96    13.68 0.673          99.0
## 47  0.1   96       NA 4.613          74.5
## 48  0.1   96    10.25 0.213          32.5
## 49  0.1  168     4.55    NA          98.1
## 50  0.1  168    19.38    NA           0.0
## 51  0.1  168     8.82 2.380          57.1
## 52  0.1  168    15.29    NA          91.9
## 53  0.1  168       NA 4.912          45.1
## 54  0.3    6    28.44 1.001          66.9
## 55  0.3    6    43.81 1.840         180.5
## 56  0.3    6    34.15 1.858         128.9
## 57  0.3    6    23.83 1.619          20.5
## 58  0.3   10    38.91 1.727          70.7
## 59  0.3   10    40.69 1.616          68.4
## 60  0.3   10    23.64 0.926          34.4
## 61  0.3   10    35.01 1.212         109.0
## 62  0.3   13    38.14 1.760         153.9
## 63  0.3   13    21.19 1.803          25.8
## 64  0.3   13    93.57 1.068          42.8
## 65  0.3   13    25.80 1.621          13.6
## 66  0.3   18    55.96 2.630           7.2
## 67  0.3   18   112.88 2.355           7.6
## 68  0.3   18    19.18 1.538            NA
## 69  0.3   18    36.64 1.182          44.9
## 70  0.3   18       NA 1.438          73.6
## 71  0.3   24    16.81 0.512         212.5
## 72  0.3   24   215.90 1.273          22.3
## 73  0.3   24    64.67 1.022          41.4
## 74  0.3   24    39.28 0.844           5.8
## 75  0.3   36    30.89 3.378          20.5
## 76  0.3   36    60.77 2.547           0.0
## 77  0.3   36    66.85 1.886          27.8
## 78  0.3   36    39.63 2.537          32.6
## 79  0.3   48    25.08 3.404         183.3
## 80  0.3   48    50.13 0.930          80.2
## 81  0.3   48    77.82 0.559          17.8
## 82  0.3   48    50.11 1.812          74.9
## 83  0.3   72    53.22 0.744         115.1
## 84  0.3   72   150.34 1.921          29.0
## 85  0.3   72    46.59 2.087          38.2
## 86  0.3   72    40.22 1.769           0.0
## 87  0.3   96    35.39 5.614           0.0
## 88  0.3   96    36.76 0.313          81.9
## 89  0.3   96    93.43 0.366           0.0
## 90  0.3   96    61.71 1.976          48.9
## 91  0.3  168    17.38    NA           0.0
## 92  0.3  168    38.28 7.387           0.0
```

```
## 93  0.3  168    46.45 1.251          52.1
## 94  0.3  168    52.51 3.285           0.0
```

```
median_MPL_01 <- median(data$MPL_conc[data$dose==0.1], na.rm=T)
head(median_MPL_01)
```

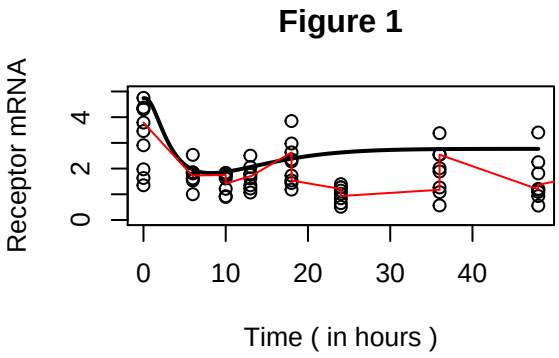
```
## [1] 14.59
```

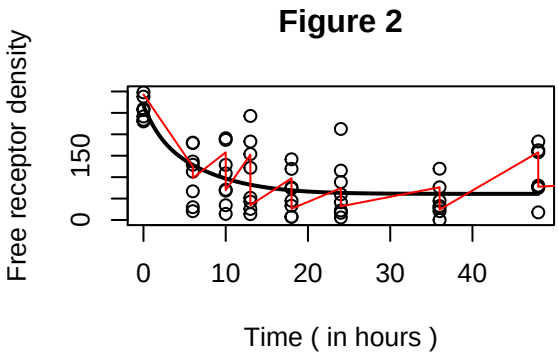
```
medians <- aggregate(data[,c("MPL_conc","mRNA","Free_receptor")],list(data$dose,data$time), median, na.
names(medians)[1:2] <- c("dose","time")
medians <- as.data.frame(medians)
head(medians)
```

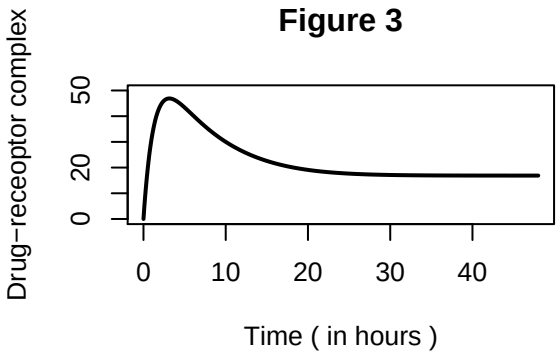
```
##   dose time MPL_conc   mRNA Free_receptor
## 1  0.0    0    0.000 3.7900        292.95
## 2  0.1    6   11.180 1.7025        124.70
## 3  0.3    6   31.295 1.7295         97.90
## 4  0.1   10   12.335 1.7515        157.80
## 5  0.3   10   36.960 1.4140         69.55
## 6  0.1   13   11.945 1.7045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

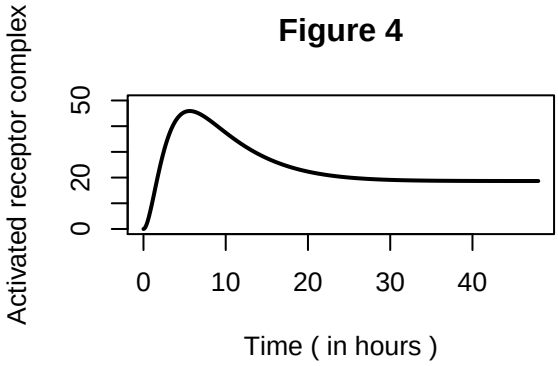
```
# Parameters to be used in the Glucocorticoid function
parameters <- c(ks_Rm = 2.90, IC50_Rm = 26.2, kon = 0.00329,
                kT = 0.63, kre = 0.57, Rf = 0.49, kd_R = 0.0572,
                kd_Rm = 0.612, ks_r = 3.22, D = 53, Rm0 = 4.74,
                DR = 0, DRN = 0)

# this function calculates the derivatives and returns it as a list.
Glucocorticoid_func <- function(t, y, parms) {
    with(as.list(c(y, parms)),{

      # Dit model bevat 4 afgeleide functies:
      # Afgeleide 1:

      dmRNAr_dt <- ks_Rm * ( 1 - (DRN / (IC50_Rm + DRN))) - kd_Rm * mRNAr

      # Afgeleide 2:

      dR_dt <- ks_r * mRNAr + Rf * kre * DRN - kon * D * R - kd_R * R

      # Afgeleide 3:

      dDR_dt <- kon * D * R - kT * DR

      # Afgeleide 4:

      dDRN_dt <- kT * DR - kre * DRN

      return(list(c(dmRNAr_dt, dR_dt, dDR_dt, dDRN_dt)))
       }
       )
}

# Set initial values
state <- c(mRNAr = 4.74, R = 267, DR = 0, DRN = 0)
t <- seq(0, 48, by = 0.1)
```

```r
# Use the ode function from deSolve to create a line using our created function.
# We use the method: "lsode" to get a smooth curve.
out <- deSolve::ode(times = t, y = state, parms = parameters,
                    func = Glucocorticoid_func, method = "lsoda")

# Make a dataframe from the data of 'out'
out <- as.data.frame(out)

# Make a grid so the plotted output looks nice and organised.
par(mfrow = c(2,2) )

# Plot all the functions
plot(out$time, out$mRNAr, xlab = "Time ( in hours )", ylab = "Receptor mRNA",
     type = "l", lwd = 2, ylim = c(0,5), main= "Figure 1")

points(data$time, data$mRNA, xlab = "Time ( in hours )", ylab = "Free receptor density",
     lwd = 1, ylim = c(0,300), main= "Figure 2")

lines(medians$time, medians$mRNA, col = "red")

plot(out$time, out$R, xlab = "Time ( in hours )", ylab = "Free receptor density",
     type = "l", lwd = 2, ylim = c(0,300), main= "Figure 2")

points(data$time, data$Free_receptor, xlab = "Time ( in hours )", ylab = "Free receptor density",
     lwd = 1, ylim = c(0,300), main= "Figure 2")

lines(medians$time, medians$Free_receptor, col = "red")

plot(out$time, out$DR, xlab = "Time ( in hours )", ylab = "Drug-receoptor complex",
     type = "l", lwd = 2, ylim = c(0,50), main= "Figure 3")

plot(out$time, out$DRN, xlab = "Time ( in hours )", ylab = "Activated receptor complex",
     type = "l", lwd = 2, ylim = c(0,50), main= "Figure 4")
```









- Describe what can be seen in such way that it leads to an answer to your research questions
- Give your figures a number and a descriptive title.
- Provide correct axis labels (unit and quantity), legend and caption.
- Always refer to and discuss your figures and tables in the text - they never stand alone.

4 Discussion and Conclusion

4.1 Discussion

- Compare your results with what is expecting from the literature and discuss differences with them.
- Discuss striking and surprising results.
- Discuss weaknesses in your research and how they could be addressed.

4.2 General conclusion and perspective

Discuss what your goal was, what the end result is and how you could continue working from here.

References

[1] Soetaert, K., Petzoldt, T., and Woodrow Setzer, R.: *Solving differential equations in R: package deSolve*, J. Stat. Softw., 33, 1-25, 2010.

Soetaert, K., Petzoldt, T., and Woodrow Setzer, R.: *Solving differential equations in R: package deSolve*, J. Stat. Softw., 33, 1-25, 2010.