Computer Lab Exercise

Finding parameters for an HIV infection

Handout for the *Immunobiology* lecture, at Utrecht University.

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Objectives of this exercise:

1. Learn to think in a quantitative manner about the immune system
2. Learn to parametrize simple mathematical models using quantitative information about steady states
3. Learn to fit mathematical models to experimental data to obtain quantitative parameter estimates.
4. Identify the mechanisms underlying the immunodominance ranking of primary immune reactions.

Background

Models are typicall defined as ordinary differential equations (ODEs) that give the rate of change of the variables defining the system. The ODEs that we need today are solved numerically on a computer, and we will use the R environment for that. This exercise introduces you to modeling, and teaches you to estimate parameter values from our knowledge on the steady states of the system. This is partly a paper and pencil exercise!

Exercise 1 Finding parameter values

A simple model for a viral infection is

$$\frac{\mathrm{d}T}{\mathrm{d}t} = \sigma - dT - \beta TI\,, \quad \frac{\mathrm{d}I}{\mathrm{d}t} = \beta TI - \delta I\,, \tag{1}$$

where T are target cells, and I the infected cells. This looks like a simple host-parasite model. To simulate a model like this on a computer you will have to give numerical values to the parameters. Let us try to estimate them from some basic knowledge on HIV-1 infection, because the parameters of this infection has been studied extensively by interdisciplinary teams of virologists, immunologists and mathematical modelers. For HIV-1 infection we know from the classical Ho *et al.* (1995) paper that $\delta \simeq 1$ d^{-1}. Since HIV-1 uses memory CD4$^+$ T cells as its major target cell, and we know from labeling studies that human CD4$^+$ memory T cells have an average life span of about 150 days (Vrisekoop *et al.*, 2008; Westera *et al.*, 2013) (see later in the course), we estimate that $1/d = 150$ days, or $d = 0.0067$ per day. In healthy uninfected individuals there are about $T = 500$ memory CD4$^+$ T cells in one μl of blood.

a. What would you estimate for the daily production, σ cells per day, of memory CD4$^+$ T cells per μl of blood? Hint: compute the steady state of Eq. (1) in the absence of infection.

b. Consider a HIV$^+$ patient approaching a set-point viral load with a CD4 T cell count in which the number of memory CD4$^+$ T cells has decreased 5-fold. What would you estimate for his infection rate β? Hint: compute the steady state of Eq. (1) in the presence of infection.

c. Play with this model in R. The required code is available as hiv.R and is listed below.

d. Try to add an immune response. An example code is available as ctl.R.

hiv.R

```
library(deSolve)

model <- function(t, state, parms){
  with(as.list(c(state,parms)),{
```

```
    dS <- s - dT*S - beta*S*I
    dI <- beta*S*I - delta*I

    return(list(c(dS, dI)))

  }) # end of 'with'
}

run <- function(finish=200,step=1,state=s,parms=p) {       # run and make a table
  as.data.frame(ode(times=seq(0,finish,by=step),
    func=model,y=state,parms=parms,rtol=1e-12))
}

timeplt <- function(finish=200,step=1,state=s,parms=p) {   # run and make a time plot
  data <- run(finish,step,state,parms)
  plot(range(0:finish),range(-6:3),type='n',xlab="Time in days",ylab="Log10 population
      size")
  attach(data)
  lines(time,log10(S),col="blue",lwd=2)
  if (I[1] > 0) lines(time,log10(I),col="red",lwd=2)
  legend("topright",legend=c("T","I"), col=c("blue", "red"), lty=1, lwd=2)
  detach(data)
}

# Here the session starts:

p <- c(dT=1/150, delta=1, s=500/150, beta=0.01)
s <- c(S=500, I=0)

run()
timeplt()
s["I"] <- 1
timeplt()
```

References

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