# Virus Dynamics in R

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# Preface

This represents an attempt to write reproduce the code from "Virus Dynamics: Mathematical Principles of Immunology and Virology" by Nowak and May.

No guarantees that anything in this is correct, but just an attempt to reproduce what is in the book.

This book is written in Rmarkdown and rendered using the phenomenal Quarto engine.

To learn more about Quarto books visit https://quarto.org/docs/books.

# 1 Introduction

This is a book created from markdown and executable code.

# 2 The Basic Model of Virus Dynamics

```
library(deSolve)
library(tidyverse)
```

Set Up the ODE

```
base_ode <- function(time, state, parameters){
    with(as.list(c(state, parameters)),{

        dx <- lambda - d*x - beta * x * v
        dy <- beta * x * v - a * y
        dv <- k * y - u * v

        return(list(c(dx,dy,dv)))
    })

}

t <- seq(0,30,.1)

params <- c(
    lambda =1e5,# Uninfected cell production rate
    d = .1, # Cell Death Rate
    a = .5, # Infected Cell Death Rate
    beta = 2e-7, # "Rate Constant"
    k = 100, # Virus productin from Infected cell
    u = 5 # Free Virus lifestapn
)
```

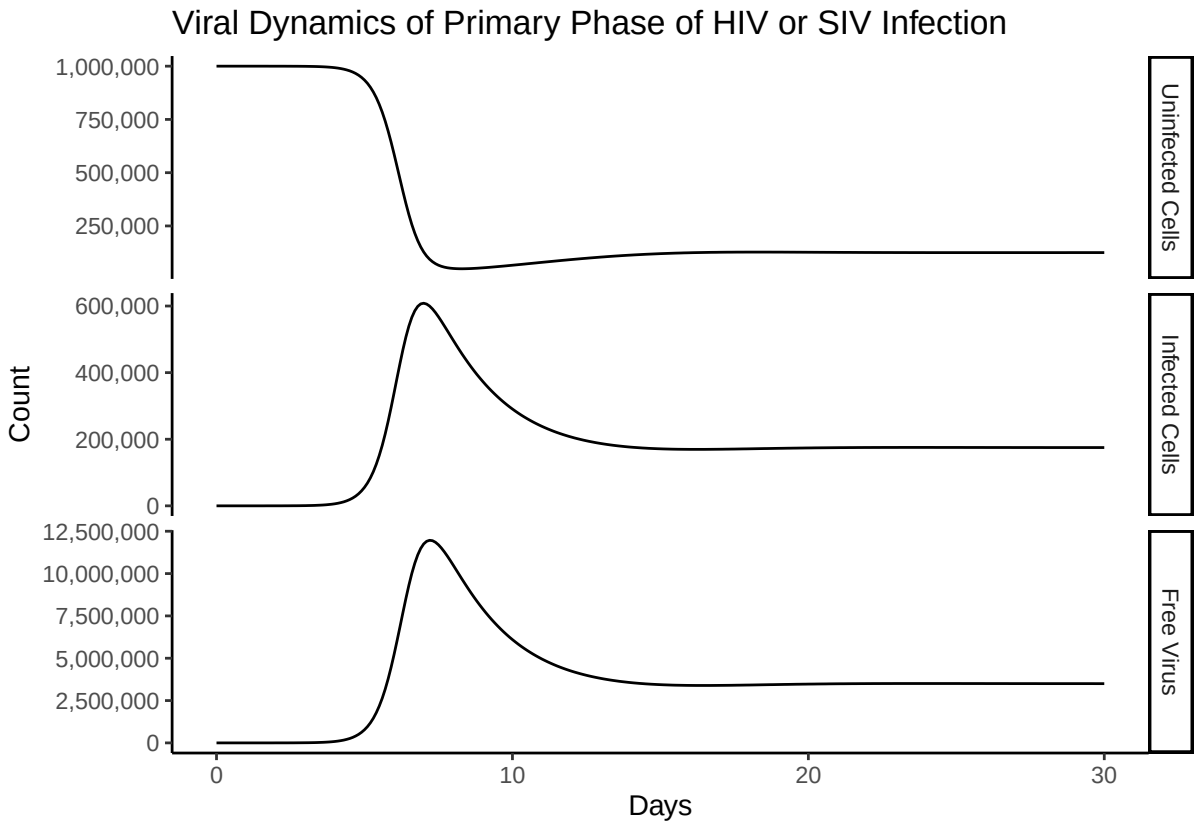
Guessing Initial values from a graph

```
x0 <- params["lambda"][1]/params["d"][1]
init <- c(x = unname(x0),
                    y = 1, v = 1)
```

```
out <- ode(init, t, base_ode, params)

out_df <- as_tibble(as.data.frame(out))
```

Funny side note is that the differences in the scales are almost immediately reproduced as in the book.

```
compartment_names <- c("Uninfected Cells",
"Infected Cells",
"Free Virus")

p <- out_df %>%
    setNames(c("time", compartment_names)) %>%
    gather(compartment, value, -time) %>%
    mutate(compartment = factor(compartment, compartment_names)) %>%
    ggplot(aes(time, y = value))+
    geom_line()+
    facet_grid(rows = vars(compartment),scales = "free_y")+
    theme_classic()+
    labs(
        title = "Viral Dynamics of Primary Phase of HIV or SIV Infection",
        x = "Days",
        y = "Count"
    )+
    scale_y_continuous(labels = scales::comma_format(accuracy = 1000))

p
```


Viral Dynamics of Primary Phase of HIV or SIV Infection
Count
1,000,000
750,000
500,000
250,000
600,000
400,000
200,000
0
12,500,000
10,000,000
7,500,000
5,000,000
2,500,000
0
0
10
20
30
Days
Uninfected Cells
Infected Cells
Free Virus

# 3 Anti-viral Drug Therapy

From pages 35-37.

```
library(deSolve)
library(tidyverse)
```

## 3.1 Set Up the ODE

Represents infected cells becoming:

- Latently infected: do not produce new virions, but contain replication competent virus that can be re-activated to become virus producing
- long-lived chronic producers: produce small amounts of virus over long periods
- cells which harbor defective provirus

These dynamics can be represented by the below equations:

$$\frac{dx}{dt} = \lambda - dx - \beta xv$$
$$\frac{dy_1}{dt} = q_1\beta xv - a_1 y_1 + \alpha y_2$$
$$\frac{dy_2}{dt} = q_2\beta xv - a_2 y_2 - \alpha y_2$$
$$\frac{dy_3}{dt} = q_3\beta xv - a_3 y_3$$
$$\frac{dv}{dt} = k y_1 - uv$$

These equations can then be coded as follows:

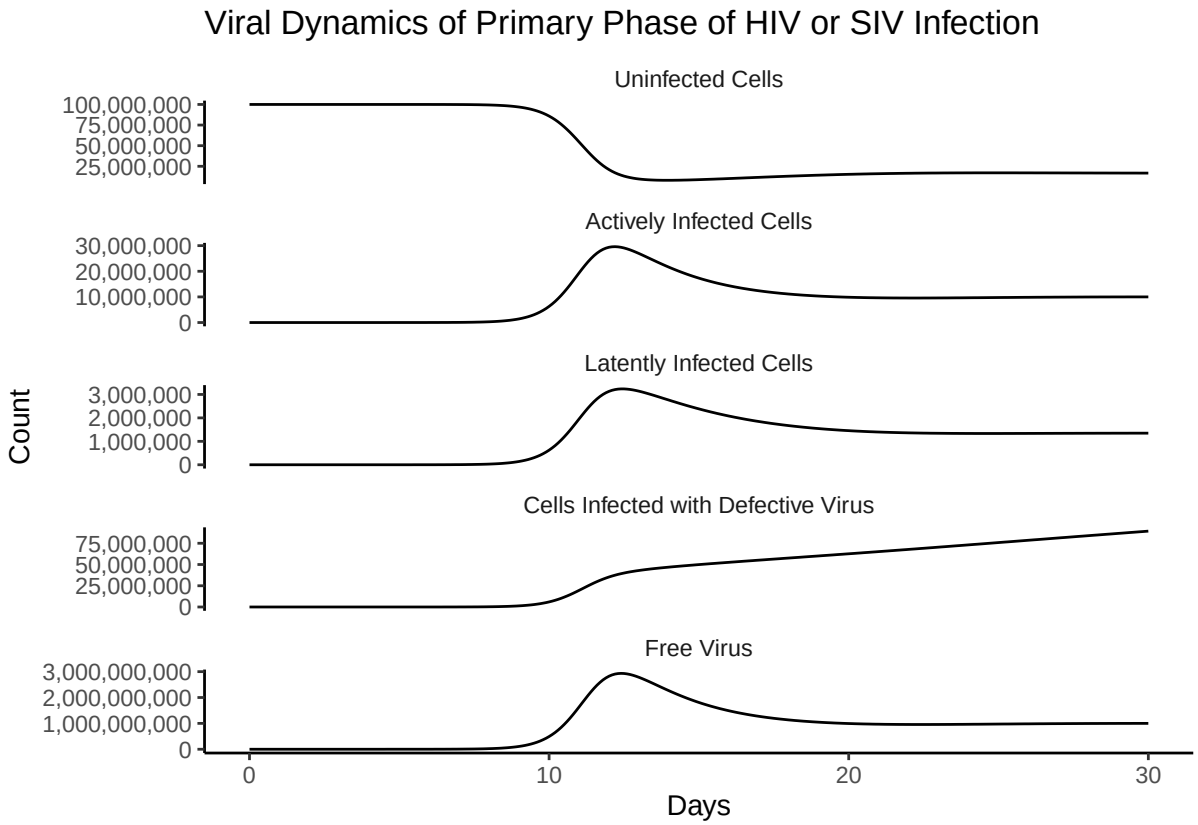
```
base_ode <- function(time, state, parameters){
  with(as.list(c(state, parameters)),{

    dx <- lambda - d*x - beta * x * v
    dy1 <- q1*beta * x * v - a1 * y1 + alpha * y2
    dy2 <- q2*beta * x * v - a2 * y2 - alpha * y2
    dy3 <- q3*beta * x * v - a3 * y3
    dv <- k * y1 - u * v

    return(list(c(dx, dy1, dy2, dy3, dv)))
  })

}
```

Now we can set up the initial conditions and constants to simulate the outputs from this system of equations.

```
t <- seq(0,30,.1)

params <- c(
  lambda =1e7,# Uninfected cell production rate
  d = .1, # Cell Death Rate
  a1 = .5, # Infected Cell Death Rate
  a2 = .01, # Infected Cell Death Rate
  a3 = .008, # Infected Cell Death Rate
  beta = 5e-10, # "Rate Constant"
  alpha = .3, # Virus Production rate of reactivated latent
  k = 500, # Virus productin from Infected cell
  u = 5, # Free Virus lifestapn
  q1 = .55, # P(Infected State | Infected)
  q2 = .05, # P(Latent State | Infected)
  q3 = .4 # P(Defective Provirus | Infected)
)

#' Guessing Initial values from a graph
x0 <- params["lambda"][1]/params["d"][1]
init <- c(x = unname(x0),
          y1 = 1,y2=0,y3=0, v = 1)

out <- ode(init, t, base_ode, params)

out_df <- as_tibble(as.data.frame(out))
```

Funny side note is that the differences in the scales are almost immediately reproduced as in the book.

```
compartment_names <- c("Uninfected Cells",
"Actively Infected Cells",
"Latently Infected Cells",
"Cells Infected with Defective Virus",
"Free Virus")

p <- out_df %>%
  setNames(c("time", compartment_names)) %>%
  gather(compartment, value, -time) %>%
  mutate(compartment = factor(compartment,
                              compartment_names)) %>%
  ggplot(aes(time, y = value))+
  geom_line()+
  facet_wrap(~compartment, ncol = 1,scales = "free_y")+
  theme_classic()+
  labs(
    title = "Viral Dynamics of Primary Phase of HIV or SIV Infection",
    x = "Days",
    y = "Count"
  )+
  scale_y_continuous(labels = scales::comma_format(accuracy = 1000))+
  theme(strip.background = element_blank())

p
```




### 3.1.1 Equilibrium Conditions

$$\hat{x} = \frac{x_0}{R_0}$$

$$\hat{y_1} = (R_0 - 1)\frac{du}{\beta k} = \hat{v}\frac{u}{k}$$

$$\hat{y_2} = \frac{\hat{y_1}\frac{a_1}{q_1}}{\frac{\alpha+a_2}{q_2} + \frac{\alpha}{q_1}}$$

$$\hat{y_3} = \hat{y_2}\frac{\frac{\alpha+a_2}{q_2}}{\frac{a_3}{q_3}}$$

$$\hat{v} = (R_0 - 1)\frac{d}{\beta}$$

With $R_0$ given by:

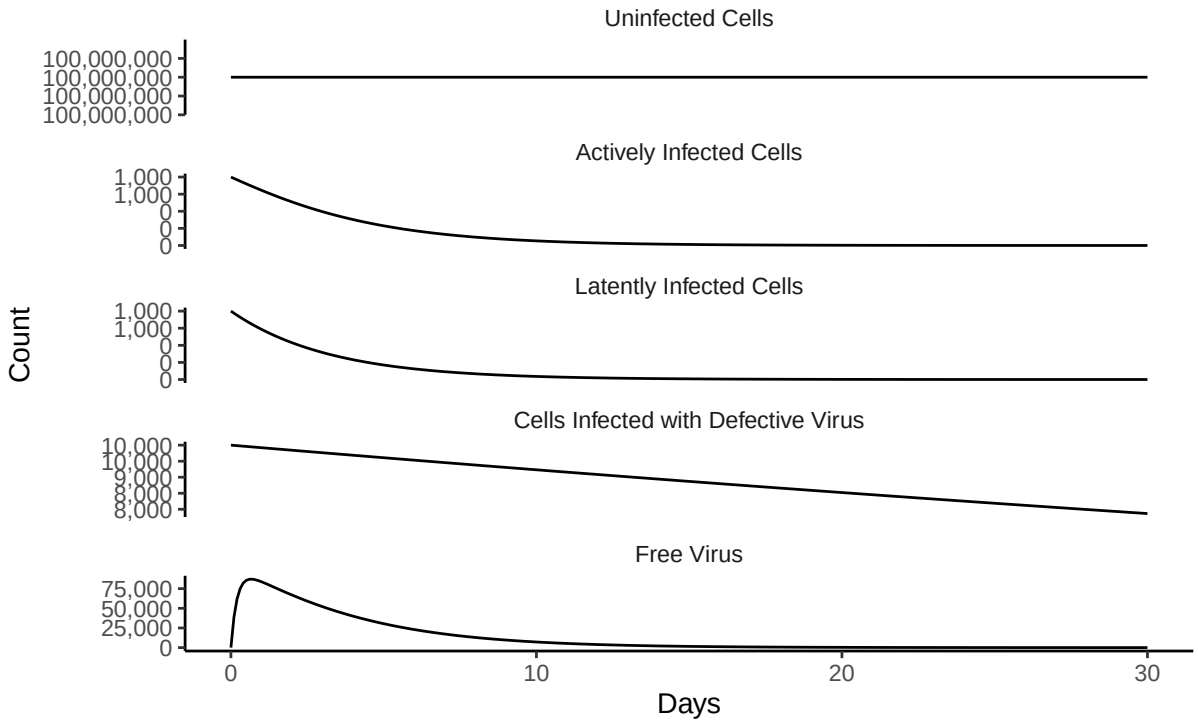
$$R_0 = \frac{\beta\lambda\ k}{a_1 du}(q_1 + q_2\frac{\alpha}{\alpha + a_2})$$

## 3.2 Effect of Anti-Virals

The big take-away from these equations is that introduction of an anti-viral should reduce the contact rate, $\beta$, to zero (or some much lower value).

```
params["beta"] <- 0

init <- c(x = unname(x0),
          y1 = 1000,y2=1000,y3=10000, v = 50)

out_antiviral <- ode(init, t, base_ode, params)

out_df_av <- as_tibble(as.data.frame(out_antiviral))
```

```
p <- out_df_av %>%
  setNames(c("time", compartment_names)) %>%
  gather(compartment, value, -time) %>%
  mutate(compartment = factor(compartment,
                              compartment_names)) %>%
  ggplot(aes(time, y = value))+
  geom_line()+
  facet_wrap(~compartment, ncol = 1,scales = "free_y")+
  theme_classic()+
  labs(
    title = "Viral Dynamics of Primary Phase of HIV or SIV Infection",
    subtitle = "With Anti-viral therapy",
    x = "Days",
    y = "Count"
  )+
  scale_y_continuous(labels = scales::comma_format(accuracy = 1000))+
  theme(strip.background = element_blank())

p
```


Viral Dynamics of Primary Phase of HIV or SIV Infection
With Anti−viral therapy
Uninfected Cells
100,000,000
100,000,000
100,000,000
100,000,000
Actively Infected Cells
1,000
1,000
0
0
0
Latently Infected Cells
1,000
1,000
0
0
0
Count
Cells Infected with Defective Virus
10,000
10,000
9,000
8,000
8,000
Free Virus
75,000
50,000
25,000
0
0
10
20
30
Days

# 4 Dynamics of Hepatitis B Virus

More to come.

# 5 Dynamics of Immune Response

May and Nowak argue that:

(1) virus load in an important determinant of disease
(2) immune responses limit virus load
(3) individual variation in immune responsiveness accounts for much of the observed variation in the outcome of a disease

## 5.1 Predatory Prey Dynamics of the Immune System

$$\frac{dx}{dt} = \lambda - dx - \beta xv$$
$$\frac{dy}{dt} = \beta xv - ay - pyz$$
$$\frac{dv}{dt} = ky - uv$$
$$\frac{dz}{dt} = c - bz$$

With the basic reproduction number defined for this system as

$$R_0 = \frac{\beta \lambda k}{adu}$$

And the basic reproduction number in the presence of an immune response (CTL)

$$R_1 = \frac{\beta \lambda k}{(a + a')du}$$

Where:

$$a' = \frac{cp}{b}$$

representing the rate at which infected cells are eliminated by the CTL response at equilibrium.

If R1 <1 then the infection will clear. The virus may spread initially, but once the immune response is activated, each infected cell will on average give rise to less than one newly infected cell and thus the infection will die out.

# 6 Summary

In summary, there will be more to come.

# References