Pulsed Vaccination[*]

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1 Introduction

In the lecture, we saw that analytical treatment of the SIR model under pulsed vaccination is possible (though too advanced for us) and leads to the following condition for eradication:

$$\frac{(\mu T_v - p_v)(e^{\mu T_v} - 1) + \mu p_v T_v}{\mu T_v (p_v - 1 + e^{\mu T_v})} < \frac{1}{R_0}$$

Recall that μ is the per capita birth rate, T is the time between pulses, and pV is the fraction of susceptibles vaccinated per pulse. In this lab, we will implement this model numerically to explore some ideas. Using techniques developed in our earlier study of open deterministic compartmental models, we numerically integrate the SIR equations.

$$\begin{aligned}\frac{dS}{dt} &= b - \lambda(I,t)\,S - \mu\,S\\ \frac{dI}{dt} &= \lambda(I,t)\,S - \gamma\,I - \mu\,I\\ \frac{dR}{dt} &= \gamma\,I - \mu\,R\end{aligned}$$

where S, I, and R are the number of susceptible, infected, and recovered individuals, $\lambda(I,t) = \beta SI$ is the *force of infection*, $b = \mu(S + I + R)$ is the birth rate, and γ is the recovery rate.

2 Solving differential equations revisited

To solve this model, we first define a function that specifies the set of differential equations describing our system.

```
> require(deSolve)                          #deSolve library needed for this computing session
> sir.model.open <- function (t, x, params) {    #here we begin a function with three arguments
+   S <- x[1]                               #create local variable S, the first element of x
+   I <- x[2]                               #create local variable I
+   R <- x[3]                               #create local variable R
+   with(                                   #we can simplify code using "with"
+        as.list(params),                   #this argument to "with" lets us use the variable names
```

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```
+        {                                  #the system of rate equations
+          dS <- mu*(S+I+R) - beta*S*I - mu*S
+          dI <- beta*S*I - gamma*I - mu*I
+          dR <- gamma*I - mu*R
+          dx <- c(dS,dI,dR)                #combine results into a single vector dx
+          list(dx)                         #return result as a list
+        }
+        )
+ }
```

Now, we specify some parameters,

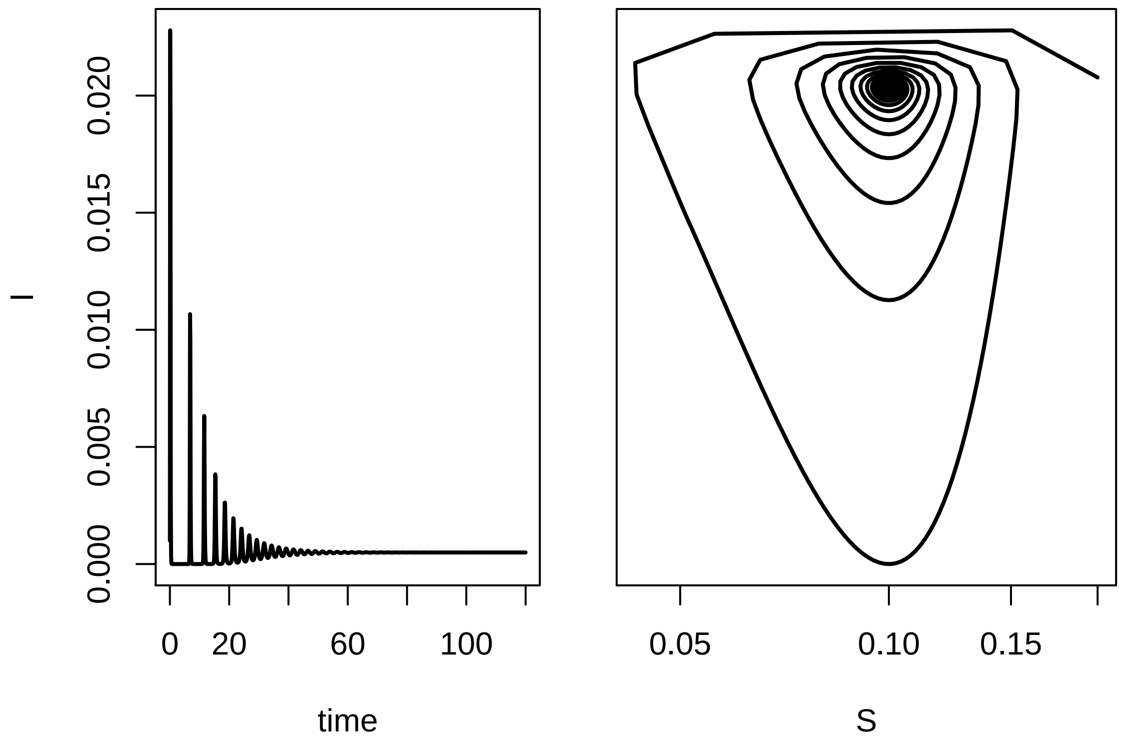
```
> R0 <- 10
> N <-  1                                                                #population size
> mu <- 0.02                          #per capita birth/death rate
> gamma <- 365/10                                         #recovery rate (in years)
> beta <- R0*(gamma+mu)/N                   #transmission rate
> xstart <- c(S=0.2, I=0.001, R=1-0.2-0.001)        #initial conditions, must sum to one
> Tmax <- 120                         #integrate for 200 years after transients
> params <- c(beta=beta, gamma=gamma, mu=mu)          #parameter vector
> tau <- 0.1                          #size of time step
> times <- seq(0, Tmax, by=tau)       #function seq returns a sequence
```

and solve. (Note that under these initial conditions the system may get very close to the boundary at $I = 0$. Therefore, we will specify that higher order solver should be used `ode45` and under more stringent constraints, specifically relative error tolerance of no more than 1×10^{-7}.)

```
> out <- ode(xstart,times,sir.model.open,params, method='ode45', rtol=1e-7)
```

We plot the results to inspect the period of transient behavior.

```
> op <- par(fig=c(0,0.5,0,1),mar=c(4,4,1,1))                          #set graphical parameters
> plot(I~time,data=out, type='l', lwd=2)                              #plot the I variable against time
> par(fig=c(0.5,1,0,1),mar=c(4,1,1,1),new=T)                          #re-set graphical parameters
> plot(I~S,data=out,log='xy',yaxt='n',xlab='S', type='l', lwd=2)  #plot phase portrait
> par(op)                                                             #re-set graphical parameters
```



Evidently, the system has settled down to the endemic equilibrium by around $t = 50$. We can use the system state at this time to initilize our study of pulsed vaccination.

```
> xstart <- out[which(out[,1]==50),2:4]
```

3 Adding pulsed vaccination

To study pulsed vaccination we define some additional parameters.

```
> pv <- 0.1                       # fraction of susceptibles vaccomated
> Tv <- 4                         # number of years between pulses
> vacc.events <- floor(Tmax/Tv) # number of pulses in Tmax years
```

We also initialize a data frame at the initial condition to store the result.

```
> data <- data.frame(S=out[which(out[,1]==50),2],
+                    I=out[which(out[,1]==50),3],
+                    R=out[which(out[,1]==50),4])
```

Now, we use the terminal conditions of the transient period as the initial condition, run the model forward T_v units of time, vaccinate (move p_v from the susceptible to infected class), and repeat until time exceeds T_{max}.

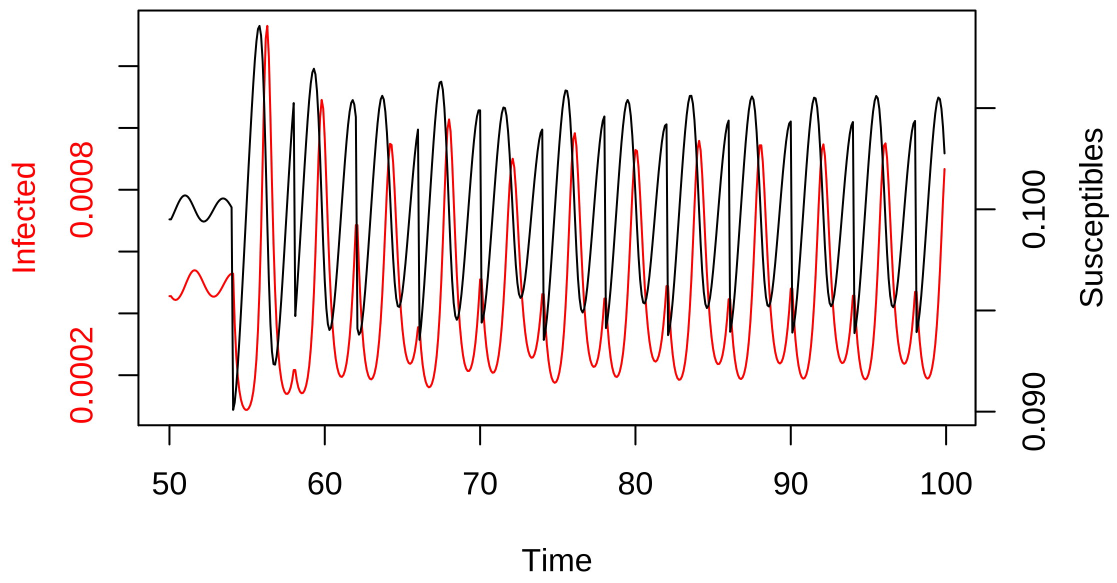
We can execute this algorithm using a `for` loop.

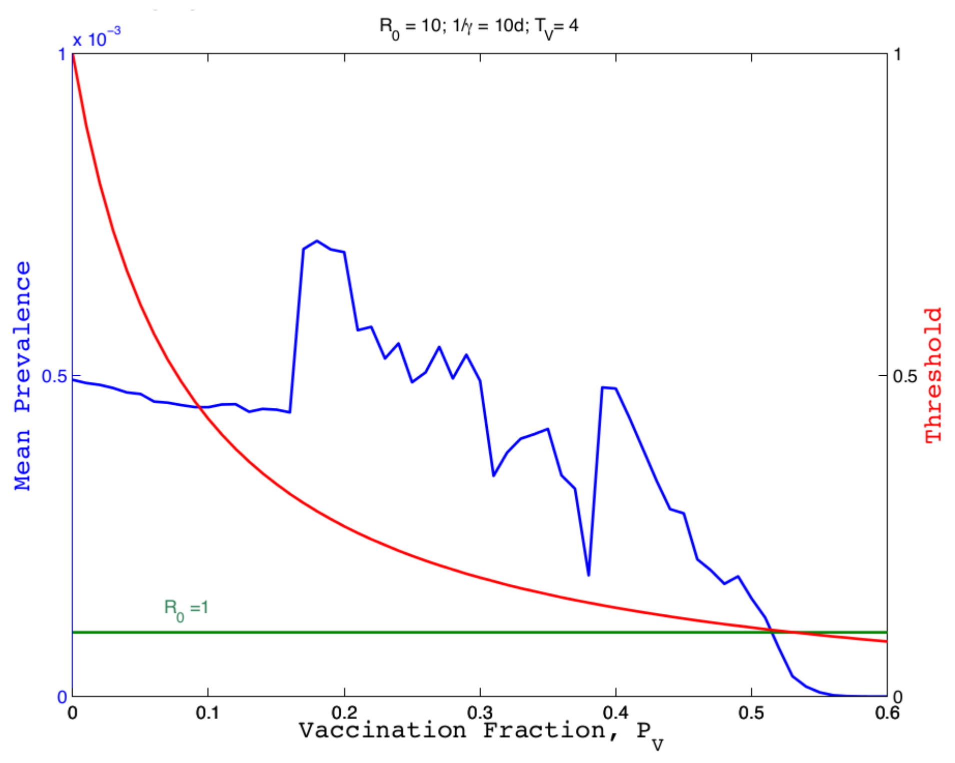
```
> for(i in 1:vacc.events){
+   out <- ode(xstart, seq(tau, Tv, by=tau), sir.model.open, params, method='ode45', rtol=1e-7)
+   xstart <- out[dim(out)[1],2:4]        # reset initial condition
+   xstart[1] <- (1-pv)*(tail(out,1)[2])  # vaccinate susceptibles
+   xstart[3] <- xstart[3]+(pv)*(tail(out,1)[2])  # move to recovered class
+   data <- rbind(data,out[,2:4])         # store result
+ }
```

Notice how this loop simulates pulsed vaccination. Vaccination is represented by modifying the initial conditions of the system, which is then allowed to evolve autonopmously for T_v years, after which the fact susceptible is reduced by a factor p_v which are instantaneously added to the recovered class.

To plot the output we first create a new time vector and then proceed as before. This figure also shows the change in susceptibles over time, showing how the pulsed vaccination is working.

```
> data$time <- seq(50, Tmax+50, by=tau)
> par(mar=c(5,4,4,4)+0.1)
> plot(data$time[1:500], data$I[1:500], type='l', xlab='Time', ylab='', col='red', axes=FALSE)
> axis(2, col.axis='red')
> mtext(side=2, line=2.5, 'Infected', col='red')
> box()
> axis(1)
> par(new=TRUE)
> plot(data$time[1:500], data$S[1:500], type='l', xlab='', ylab='', axes=FALSE, col='black')
> axis(4)
> mtext(side=4, line=2.5, 'Susceptibles')
```





Interestingly, pulsed vaccination gives rise in a change to the stable dynamics. Whereas continuous vaccination less than the critical level required for elimination yields a stable endemic equilibrium, pulsed vaccination generates period oscillations.

Exercise 1. Why might this periodicity be of interest? What might be the consequences of "peaks" and "troughs" for public health?

Exercise 2. By modifying the value of p_v, see if you can locate the vaccination threshold. Does this agree with the analytically predicted threshold?

***Exercise 3.** One thing we might be interested in knowing is how our vaccination strategy affects mean disease prevalance. Devise a strategy to study this question and produce a plot illustrating the result.

4 Homework

In this exercise we have developed an approach to studying the SIR model with pulsed vaccination. For homework, study how increasing the fraction of susceptibles vaccinated in each pulse affects disease prevalence. Assume $R_0 = 10$, $1/\gamma = 10$, the per capita birth rate is 2%, that the mean life span is 50 years, and that the time between pulses is 4 years. If you integrate the SIR model for 50 years before introducing vaccination and then plot mean prevalence for 100 years you should get something like this.

The red line (y-axis on right) shows the theoretical eradication criterion presented in class. Notice that if you increase p_v by different increments than used here (0.01 then your figure may look slightly different.

Exercise 4. By thinking about analytical results shown in class, explain what the crossing of the red and green lines means. Is this conclusion confirmed by the blue line?

***Exercise 5.** By studying specific values of p_v around 0.15-0.18, investigate why there is a rise in mean prevalence as you pulse vaccination. Can you provide an intuitive explanation of this phenomenon?

***Exercise 6.** Do we see this rise in mean prevalence is we pulse vaccination more frequently (e.g. $T_v = 3$) or less frequently (e.g. $T_v = 5$)?