Modeling infectious diseases

**Modeling infectious diseases using R:
Practical Session**

Static and Dynamic aspects of SIR model

What do we cover in this practical session ?

- Simple transmission models in R.
- SIR: static aspect (time homogeneity).
- SIR: dynamic aspects.
- Vaccination.

- Software: the deSolve package in R.

R requirements

- Basic knowledge in R.
- Programming of a user defined simple function.

- Why R ?
1. Free.
2. Fast (not in our case).
3. Updated.
4. Documented.

Part 1:
time homogeneity

SIR model :time homogeneity

$$\frac{dS(a)}{da} = -\lambda S(a)$$

$$\frac{dI(a)}{da} = \lambda S(a) - \sigma I(a)$$

$$\frac{dR(a)}{da} = \sigma I(a)$$

The force of infection: the rate in which individuals are infected

The recovery rate: the rate in which individuals recovered and move to the immune class.
Assumption: life long immunity.

SIR model: time homogeneity

$$\frac{dS(a)}{da} = -\lambda S(a)$$

$$\frac{dI(a)}{da} = \lambda S(a) - \sigma I(a)$$

$$\frac{dR(a)}{da} = \sigma I(a)$$

The force of infection = 0.2.
On average: 5 years in the susceptible class.

The recovery rate: 10 days.

The unit of the parameters are in years

Transmission models in R

- We need to integrate the system of the ordinary differential equation.

- deSolve package in R.
- Numerical integration using of ODE system.

$$\frac{dS(a)}{da} = -\lambda S(a)$$
$$\frac{dI(a)}{da} = \lambda S(a) - \sigma I(a)$$
$$\frac{dR(a)}{da} = \sigma I(a)$$
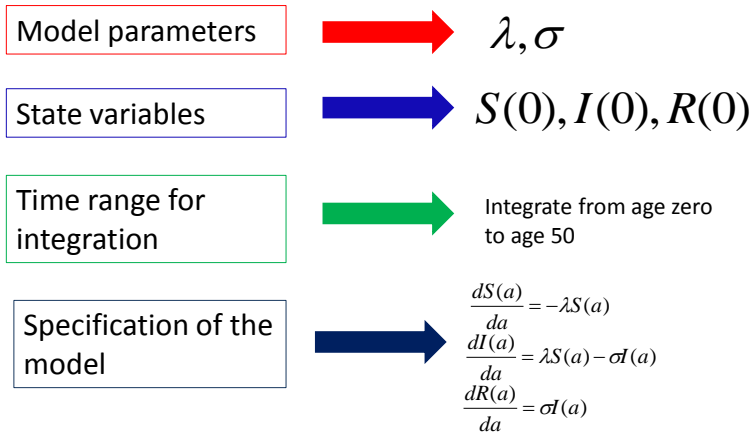
Transmission models in R

SIR model

$$\frac{dS(a)}{da} = -\lambda S(a)$$
$$\frac{dI(a)}{da} = \lambda S(a) - \sigma I(a)$$
$$\frac{dR(a)}{da} = \sigma I(a)$$

Specification in R

- Model parameters.
- State variables (the value of the parameters at age (time) zero.
- Time range (=age range) for integration.

Transmission models in R

R program

Model parameters	$\Longrightarrow$	λ, σ

State variables	$\Longrightarrow$	$S(0), I(0), R(0)$

Time range for integration	$\Longrightarrow$	Integrate from age zero to age 50

Specification of the model	$\Longrightarrow$	$\dfrac{dS(a)}{da} = -\lambda S(a)$ $\dfrac{dI(a)}{da} = \lambda S(a) - \sigma I(a)$ $\dfrac{dR(a)}{da} = \sigma I(a)$

Specification of the model parameters in R

```
> parameters <- c(lambda = 0.2, v=36.5)
> parameters
lambda      v
   0.2   36.5
```

The force of infection = 0.2 years.

$5^{-1} = 0.2$

Recovery rate 10 days.

$$\left(\frac{10}{365}\right)^{-1} = 36.5$$

The unit of the parameters are in years^{-1}

The state variables (initial values at age 0)

- Let us assume that the cohort size is 5000.
- At age=0:

$$S(0) = 4999$$
$$I(0) = 1$$
$$R(0) = 0$$

- Specification in R:

```
> state <- c(X=4999,Y=1,Z=0)
> state
  X    Y  Z
4999  1  0
```

Specification of the model in R

$$\frac{dS(a)}{da} = -\lambda S(a)$$
$$\frac{dI(a)}{da} = \lambda S(a) - \sigma I(a)$$
$$\frac{dR(a)}{da} = \sigma I(a)$$

```
SIR<-
function(t,state,parameters)
{
with(as.list(c(state,
parameters)),
{
dX <- -lambda*X
dY <- lambda*X - v*Y
dZ <- v*Y
list(c(dX, dY, dZ))
})
}
```

We ask from the function to
return the values of S, I and R

Specification of the time units for the integration

$$\frac{dS(a)}{da} = -\lambda S(a)$$

$$\frac{dI(a)}{da} = \lambda S(a) - \sigma I(a)$$

$$\frac{dR(a)}{da} = \sigma I(a)$$

- The solution of the model: numerical integration.
- Time units: age.
- Integration from age 0 to age 40 by unit of 0.01 years

```
> times<-seq(0,40,by=0.01)
> times
  [1]  0.00  0.01  0.02  0.03  0.04  0.05  0.06  0.07  0.08  0.09  0.10  0.11
 [13]  0.12  0.13  0.14  0.15  0.16  0.17  0.18  0.19  0.20  0.21  0.22  0.23
 [25]  0.24  0.25  0.26  0.27  0.28  0.29  0.30  0.31  0.32  0.33  0.34  0.35
 [37]  0.36  0.37
```

Running the model

```
require(deSolve)
out<-as.data.frame(ode(y=state,times=times,func=SIR,parms=parameters))
```

The state variables: the values at age 0.

The model parameters: force of infection (0.2) and recovery rate (10 dats)

Running the model

```
require(deSolve)
out<-as.data.frame(ode(y=state,times=times,func=SIR,parms=parameters))
```

Time range for
integration.

The model

Numerical integration
using ordinary
differential equation

Solution

```
> require(deSolve)
> out <-
as.data.frame(ode(y=state,times=times,func=SIR,parms=
parameters))
> head(out)
  time          X           Y           Z
1 0.00 4999.000  1.000000   0.000000
2 0.01 4989.012  9.061818   1.926190
3 0.02 4979.044 14.641580   6.314481
4 0.03 4969.096 18.498345  12.405853
5 0.04 4959.168 21.159066  19.673391
6 0.05 4949.259 22.989501  27.751380
```

Graphical output

```
> plot (times,out$X ,type="l",main="X", xlab="time", ylab="-",lwd=2)
> lines(times,out$Z,col=3,lwd=2)
```
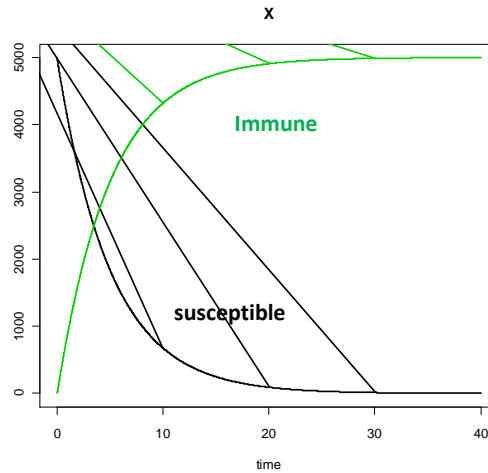

Graphical output

```
> plot (times,out$Y ,type="l",main="Y", xlab="time", ylab="-",lwd=2)
```

Graphical output

SIR model
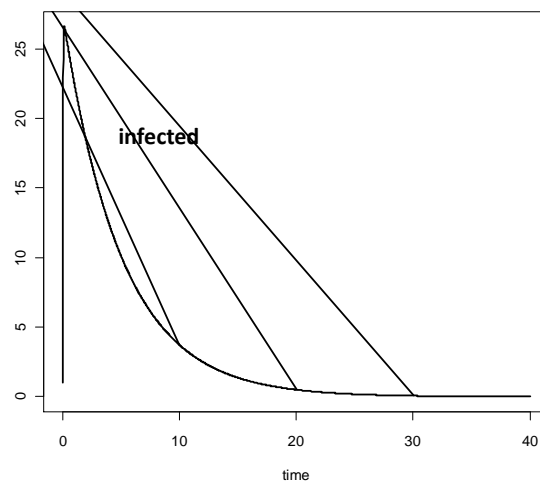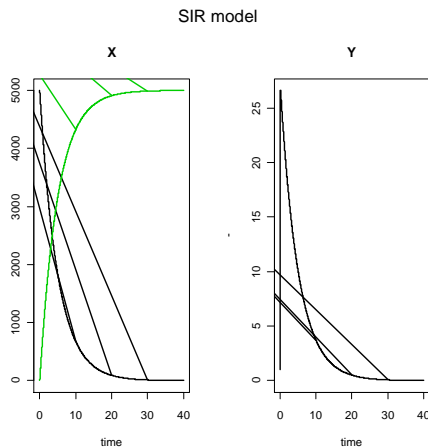
What do we see here ?

Number of infected
individuals at each age.

# Duration of stay in the different compartments of the models

Graphical output

SIR model
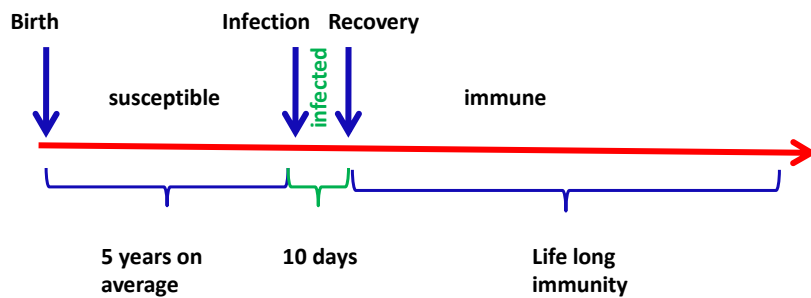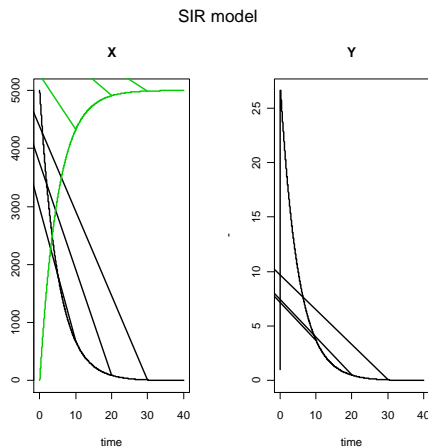
We expect to see only few infected individuals at each age (compared to the number of susceptible and immune).

Duration of stay in the different compartments of the models

Let us assume that the recovery rate is 2 months (i.e. individuals stay in the infected class 2 months)
What do we expect to see ?
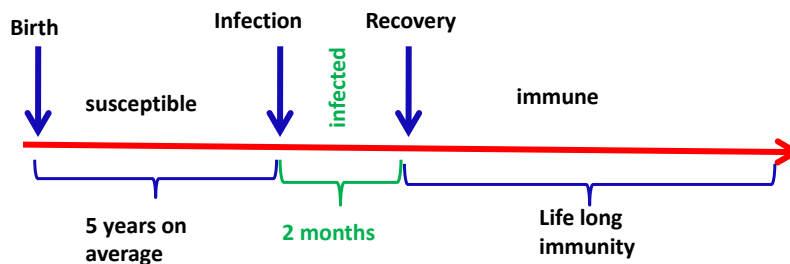
The model with recovery rate of 2 months

```
1/(60/365)
parameters <- c(lambda = 0.2, v=6.083333)
parameters

state <- c(X=4999,Y=1,Z=0)
state
SIR<-function(t,state,parameters)
{
with(as.list(c(state, parameters)),
{
dX <- -lambda*X
dY <- lambda*X - v*Y
dZ <- v*Y
list(c(dX, dY, dZ))
})
}
times<-seq(0,40,by=0.01)
times
require(deSolve)
out <- as.data.frame(ode(y=state,times=times,func=SIR,parms=parameters))
head(out)
par(mfrow=c(1,2), oma=c(0,0,3,0))
plot (times,out$X ,type="l",main="X", xlab="time", ylab="-",lwd=2)
lines(times,out$Z,col=3,lwd=2)
plot (times,out$Y ,type="l",main="Y", xlab="time", ylab="-",lwd=2)
mtext(outer=TRUE,side=3,"SIR model",cex=1.5)
```

$$\left(\frac{60}{365}\right)^{-1} = 6.08$$

Recover rate of 2 months
(60 days)

Graphical output
(force of infection of 0.2 and recovery rate of 2 months)
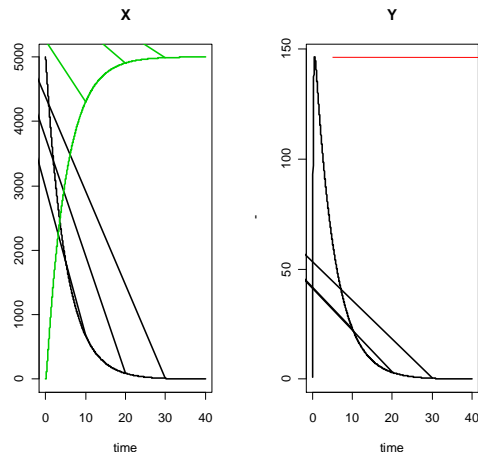
~ 150 infected
individuals at the
peak (compare with
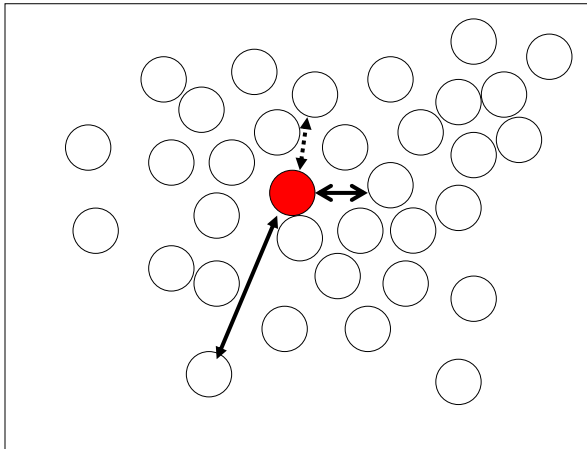~25 for recovery rate
of 10 days)

Part 2:
Mass action prenciple

The Mass-Action Principle
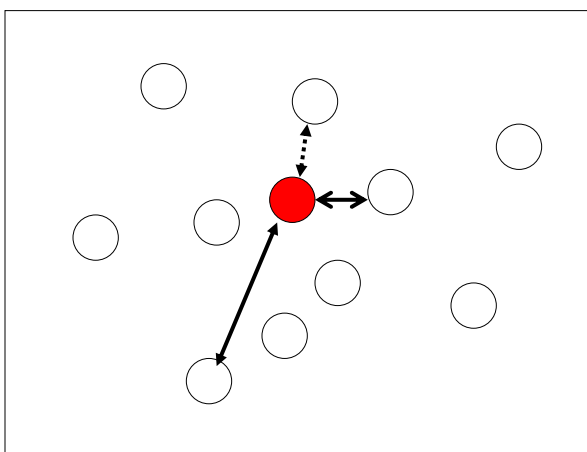
Contacts are made in random.
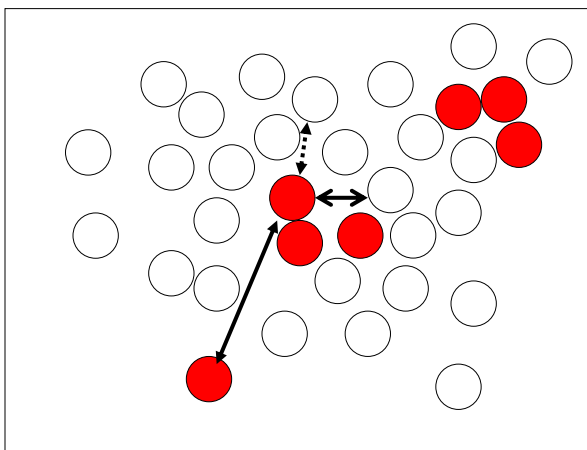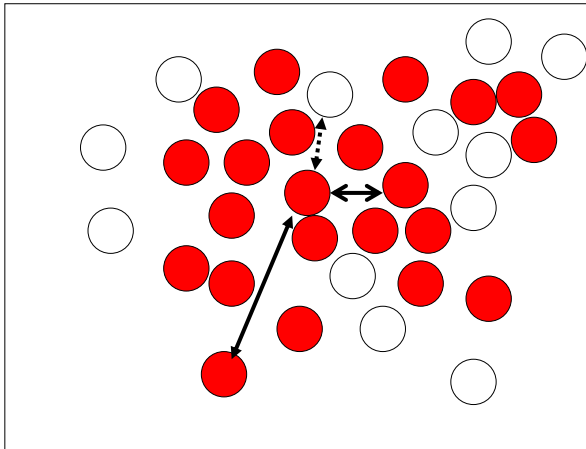
Number of new cases=P(transmission) X # of infectious X # of susceptible

The Mass-Action Principle

Contacts are made in random.

Number of new cases=P(transmission) X # of infectious X # of susceptible

The Mass-Action Principle

Contacts are made in random.

Number of new cases=P(transmission) X # of infectious X # of susceptible

The Mass-Action Principle

Contacts are made in random.

Number of new cases:

$$\beta \times I \times S$$

Transmission probability per contact

Number of new cases=P(transmission) X # of infectious X # of susceptible

The Mass-Action Principle

$$\frac{dS(a)}{da} = -\lambda S(a)$$

$$\frac{dI(a)}{da} = \lambda S(a) - \sigma I(a)$$

$$\frac{dR(a)}{da} = \sigma I(a)$$

$$\frac{dS(a)}{da} = -\beta \times I(a) \times S(a)$$

$$\frac{dI(a)}{da} = \beta \times I(a) \times S(a) - \sigma I(a)$$

$$\frac{dR(a)}{da} = \sigma I(a)$$

Age dependent force of infection

$$\frac{dS(a)}{da} = -\lambda(a)S(a)$$
$$\frac{dI(a)}{da} = \lambda(a)S(a) - \sigma I(a)$$
$$\frac{dR(a)}{da} = \sigma I(a)$$

$$\frac{dS(a)}{da} = -\beta \times I(a) \times S(a)$$
$$\frac{dI(a)}{da} = \beta \times I(a) \times S(a) - \sigma I(a)$$
$$\frac{dR(a)}{da} = \sigma I(a)$$

$$\lambda(a) = \beta \times I(a) \times S(a)$$

Age dependent   constant

Model parameters

$$\frac{dS(a)}{da} = -\beta \times I(a) \times S(a)$$
$$\frac{dI(a)}{da} = \beta \times I(a) \times S(a) - \sigma I(a)$$
$$\frac{dR(a)}{da} = \sigma I(a)$$

$\beta = 0.0085$

$\sigma = 36.5 \quad (10 \quad days)$

```
> parameters <- c(beta=0.0085, v=36.5)
> state <- c(X=4999,Y=1,Z=0)
> parameters
  beta      v
 0.0085 36.5000
> state
   X    Y    Z
4999    1    0
```

16

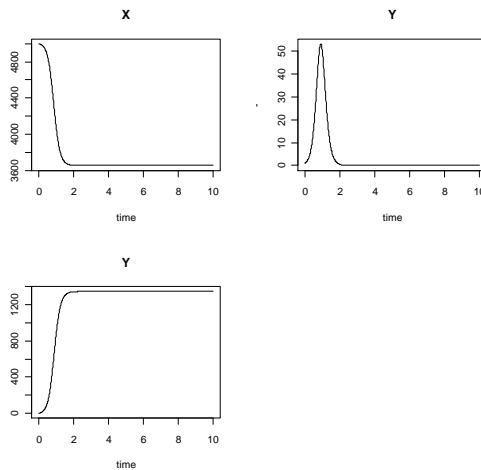## Specification of the model in R

$$\frac{dS(a)}{da} = -\beta \times I(a) \times S(a)$$

$$\frac{dI(a)}{da} = \beta \times I(a) \times S(a) - \sigma I(a)$$

$$\frac{dR(a)}{da} = \sigma I(a)$$

```
SIR<-function(t,state,parameters)
{
with(as.list(c(state, parameters)),
{
dX <- -beta*Y*X
dY <- beta*Y*X - v*Y
dZ <- v*Y
list(c(dX, dY, dZ))
})
}
```
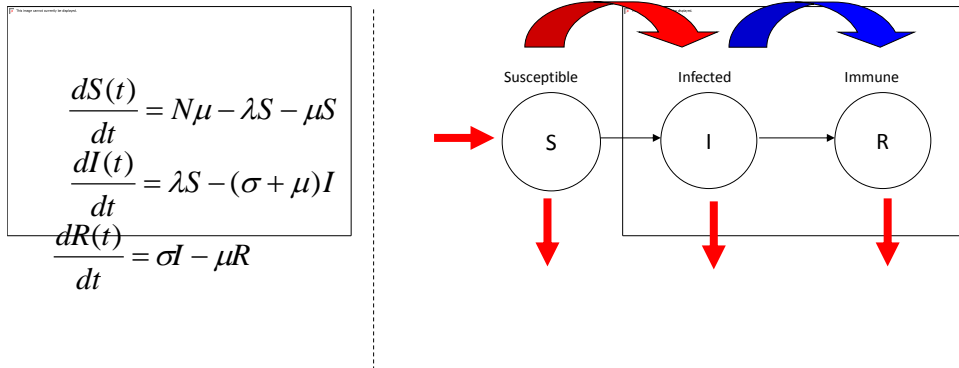
Numerical solution

SIR model

After ~ 2 years there are no infceted individuals.
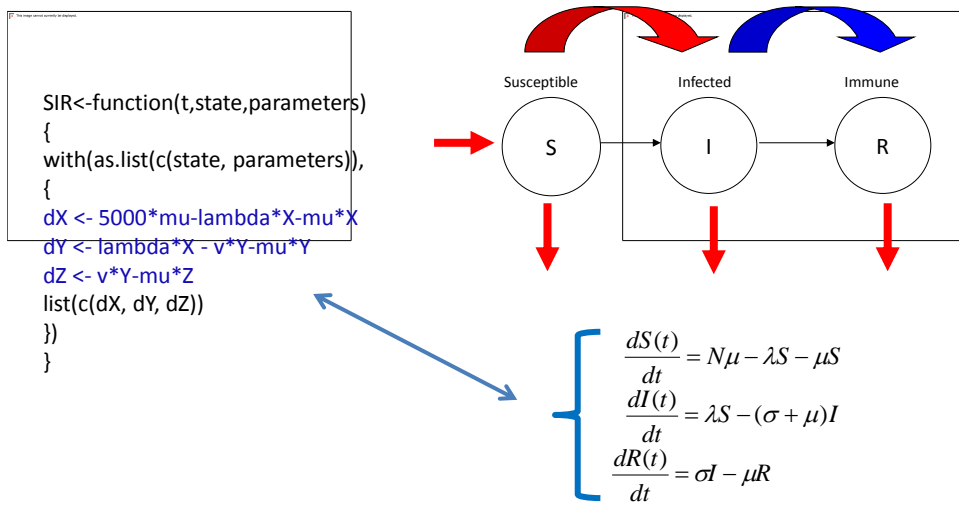
~3600 individuals will not be infection.

Equilibrium

SIR transmission model in open population

$$\frac{dS(t)}{dt} = N\mu - \lambda S - \mu S$$

$$\frac{dI(t)}{dt} = \lambda S - (\sigma + \mu)I$$

$$\frac{dR(t)}{dt} = \sigma I - \mu R$$

Susceptible   Infected   Immune

S   I   R

Birth and death rate are equal to μ (constant population size).

SIR transmission model in open population

```
SIR<-function(t,state,parameters)
{
with(as.list(c(state, parameters)),
{
dX <- 5000*mu-lambda*X-mu*X
dY <- lambda*X - v*Y-mu*Y
dZ <- v*Y-mu*Z
list(c(dX, dY, dZ))
})
}
```
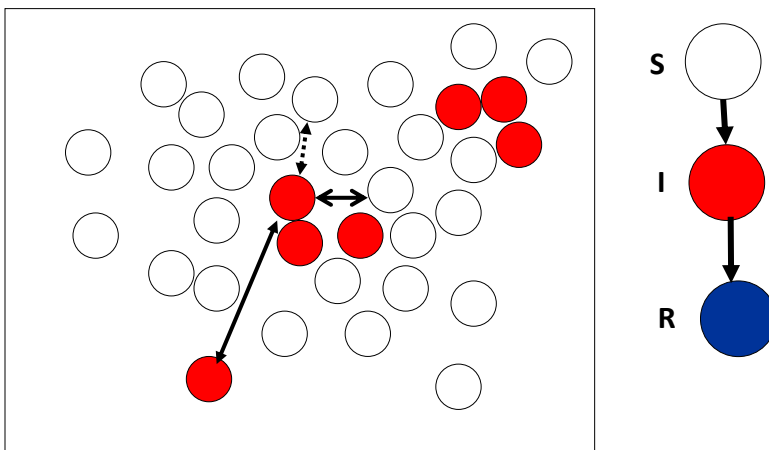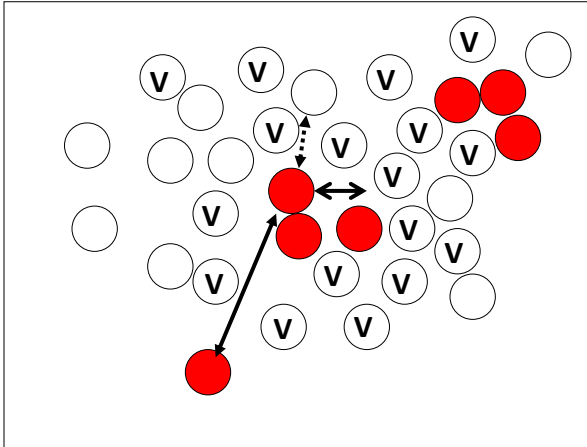
Susceptible   Infected   Immune

S   I   R

$$\frac{dS(t)}{dt} = N\mu - \lambda S - \mu S$$

$$\frac{dI(t)}{dt} = \lambda S - (\sigma + \mu)I$$

$$\frac{dR(t)}{dt} = \sigma I - \mu R$$

Open population (1)

The model

SIR Model

$$\frac{dS(t)}{dt} = N\mu - \lambda S - \mu S$$

$$\frac{dI(t)}{dt} = \lambda S - (\sigma + \mu)I$$

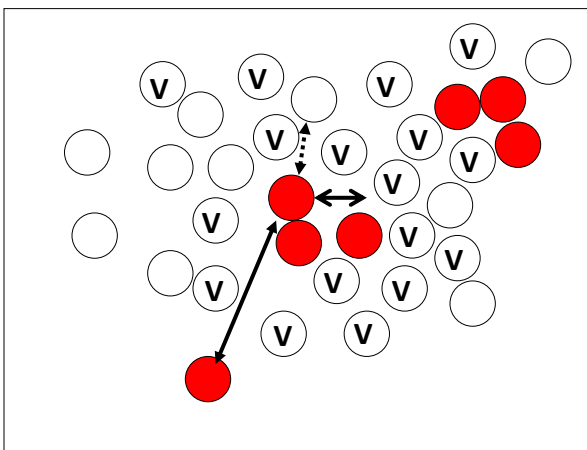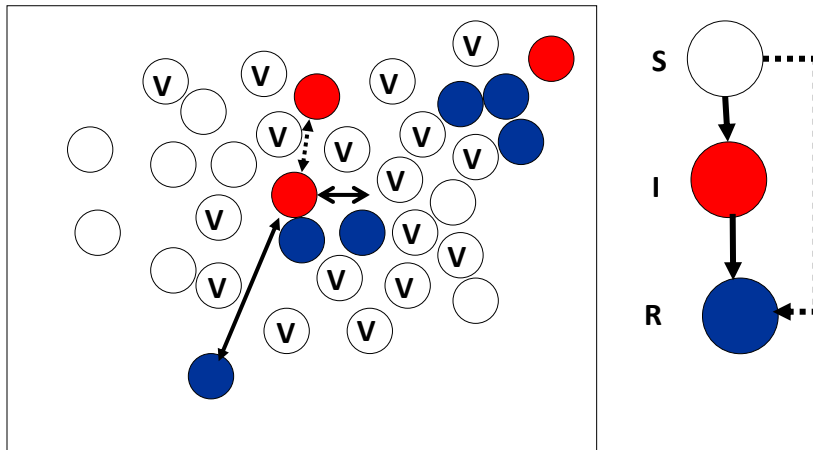$$\frac{dR(t)}{dt} = \sigma I - \mu R$$

Equilibrium values

Vaccination

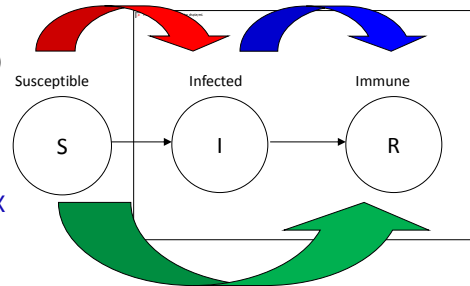S

I

R
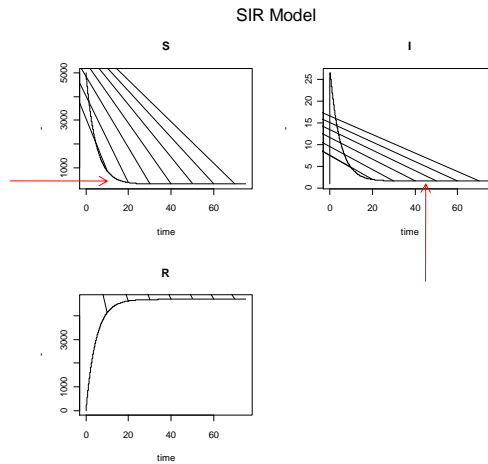
Vaccination

Vaccination

Vaccination

Part 3:
vaccination in SIR model

Transmission model with vaccination

$$\frac{dS(t)}{dt} = N\mu \times (1-P) - \lambda S - \mu S$$

$$\frac{dI(t)}{dt} = \lambda S - (\sigma + \mu)I$$

$$\frac{dR(t)}{dt} = \sigma I - \mu R + N\mu \times P$$

Susceptible   Infected   Immune

S   I   R

Vaccination: proportion P individuals are vaccinated at birth (i.e transfer to the immune class)

SIR transmission Model with vaccination

Model parameters:

1. Life expectancy: 75 years
2. Force of infection 0.2
3. Recovery rate 10 days.
4. ~~Vaccination 70% at birth.~~

Susceptible   Infected   Immune

S   I   R

vaccination

```
> parameters <- c(mu=1/75,lambda=0.2, v=36.5,P=0.7)
> parameters
        mu      lambda           v           P
 0.01333333  0.20000000 36.50000000  0.70000000
```
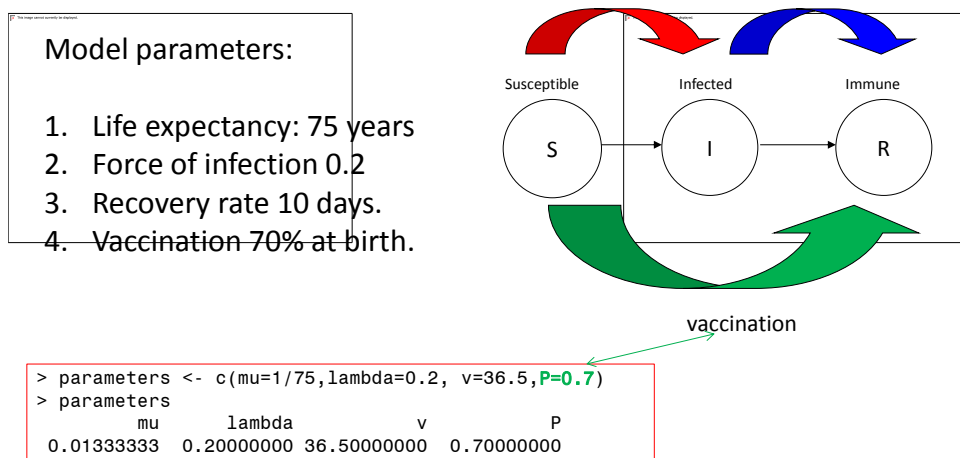
SIR transmission model with vaccination

```
SIR<-function(t,state,parameters)
{
with(as.list(c(state,
parameters)),
{
dX <- 5000*mu*(1-P)-lambda*X-mu*X
dY <- lambda*X - v*Y-mu*Y
dZ <- v*Y-mu*Z+5000*mu*P
list(c(dX, dY, dZ))
})
}
```
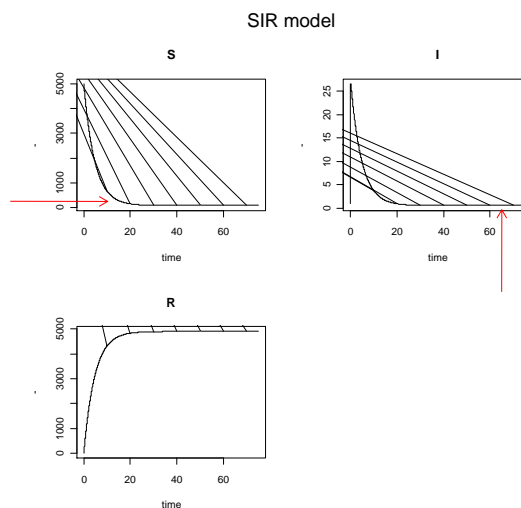

Susceptible   Infected   Immune

S   I   R

$$\frac{dS(t)}{dt} = N\mu \times (1-P) - \lambda S - \mu S$$

$$\frac{dI(t)}{dt} = \lambda S - (\sigma + \mu)I$$

$$\frac{dR(t)}{dt} = \sigma I - \mu R + N\mu \times P$$

SIR transmission Model with vaccination

Equilibrium values

SIR model

<div align="center" style="color:red">

Part 4:
Dymamic

</div>

SIR model in open population: Dynamic aspects

- In order to understand the dynamic of the SIR model we need to allow for time dependent force of infection.
- Open population.
- Mass action principle.

$$\lambda(t) = \beta \times I(t) \times S(t)$$
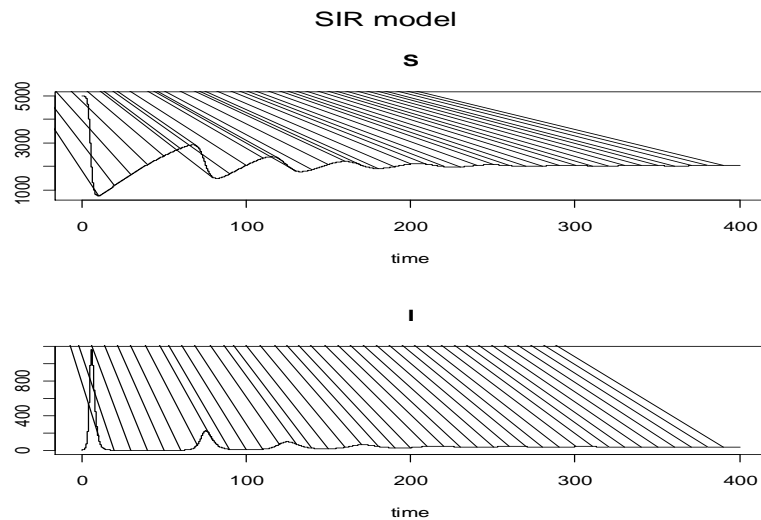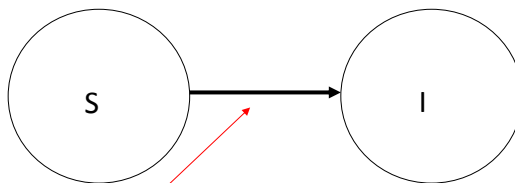
SIR transmission model in open population
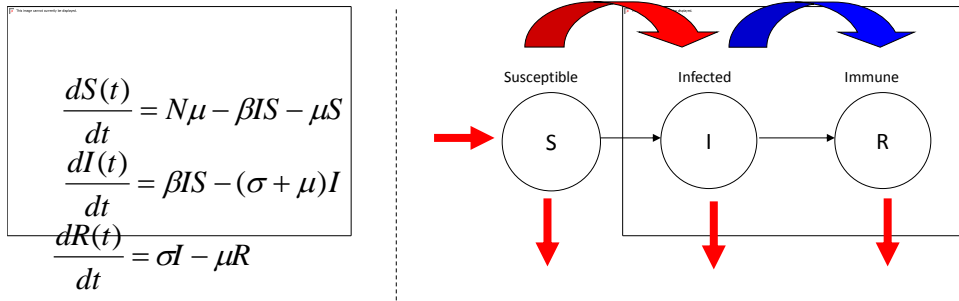
$$\frac{dS(t)}{dt} = N\mu - \beta IS - \mu S$$

$$\frac{dI(t)}{dt} = \beta IS - (\sigma + \mu)I$$

$$\frac{dR(t)}{dt} = \sigma I - \mu R$$

Susceptible   Infected   Immune

S   I   R

SIR transmission model in open population

$$\frac{dS(t)}{dt} = N\mu - \beta IS - \mu S$$

$$\frac{dI(t)}{dt} = \beta IS - (\sigma + \mu)I$$

$$\frac{dR(t)}{dt} = \sigma I - \mu R$$

```
SIR<-function(t,state,parameters)
{
with(as.list(c(state,
parameters)),
{
dX <- 5000*mu-beta*Y*X - mu*X
dY <- beta*Y*X - v*Y - mu*Y
dZ <- v*Y -mu*Z
list(c(dX, dY, dZ))
})
}
```

Solution for the model

SIR model

Incidence data : Measles in UK

The weekly number of individuals who move from the susceptible to the infected class
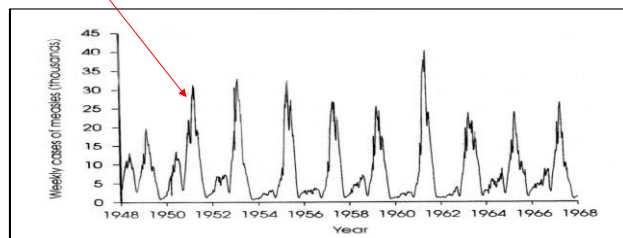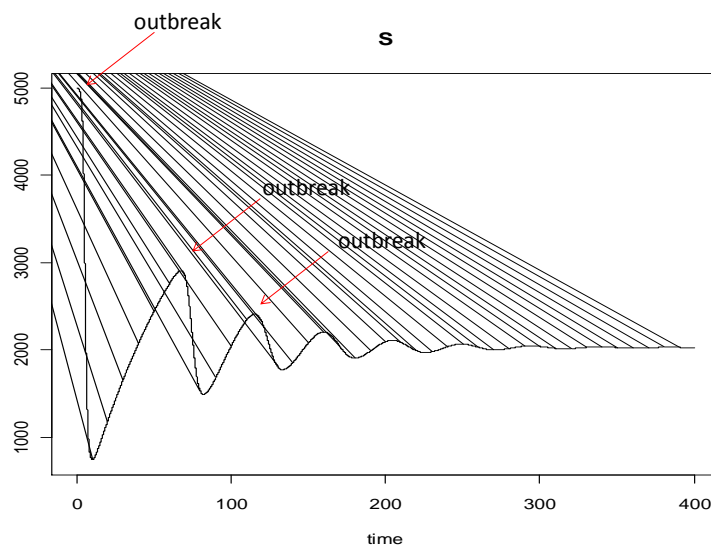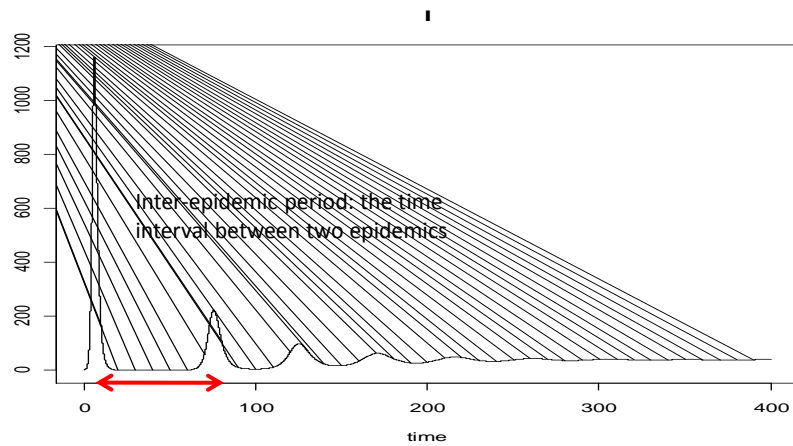

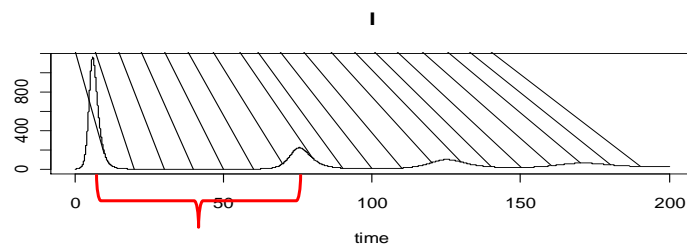*Time unit=week*

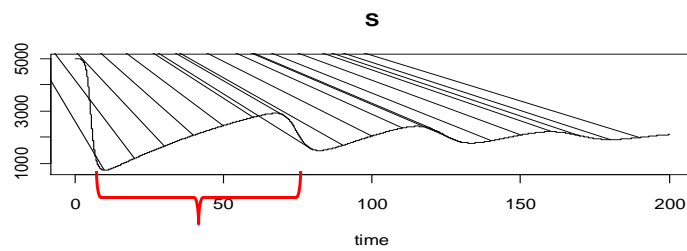15

Observed outbreak and predicted outbreak
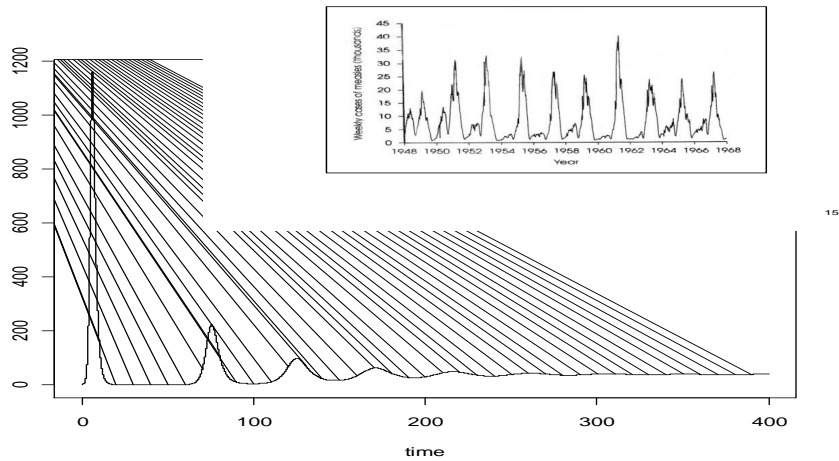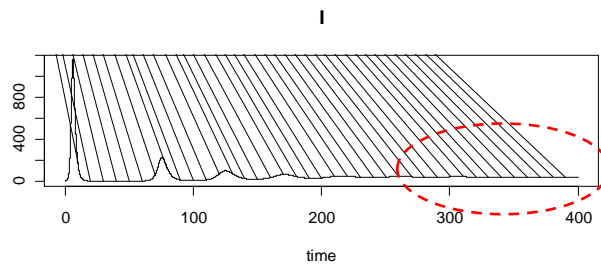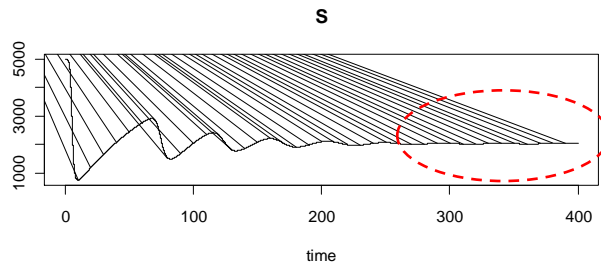

The susceptible class

The infected class

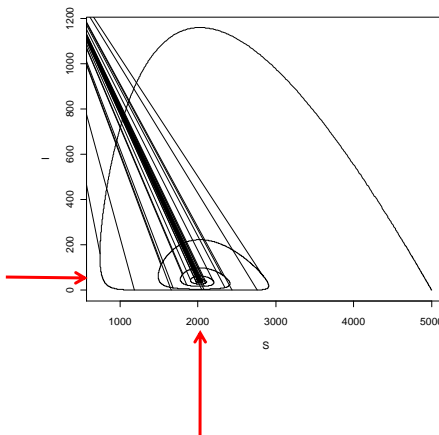Inter-epidemic period: the time interval between two epidemics

The Inter epidemic period
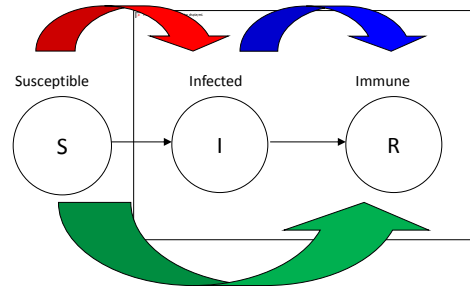
Equilibrium

Equilibrium

At the long run, the infection reach the endemic equilibrium state in which at each time unit there are the same number of susceptible and infected individuals in the population.

Transmission Model with vaccination

$$\frac{dS(t)}{dt} = N\mu \times (1-P) - \beta IS - \mu S$$

$$\frac{dI(t)}{dt} = \beta IS - (\sigma + \mu)I$$

$$\frac{dR(t)}{dt} = \sigma I - \mu R + N\mu \times P$$

Susceptible	Infected	Immune
S	I	R

```
SIR<-function(t,state,parameters)
{
with(as.list(c(state, parameters)),
{
dX <- 5000*mu*(1-P)-beta*Y*X - mu*X
dY <- beta*Y*X - v*Y - mu*Y
dZ <- v*Y -mu*Z+5000*mu*P
list(c(dX, dY, dZ))
})
}
```
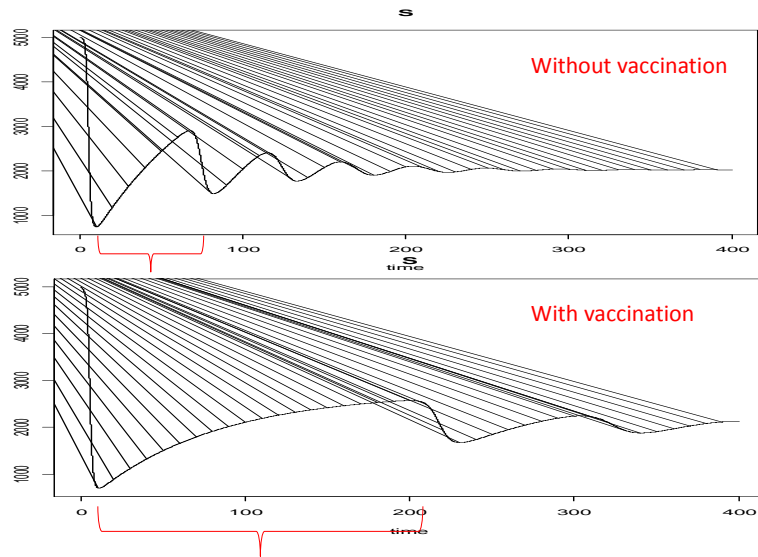
SIR model with vaccination at birth

45% are vaccinated at birth.
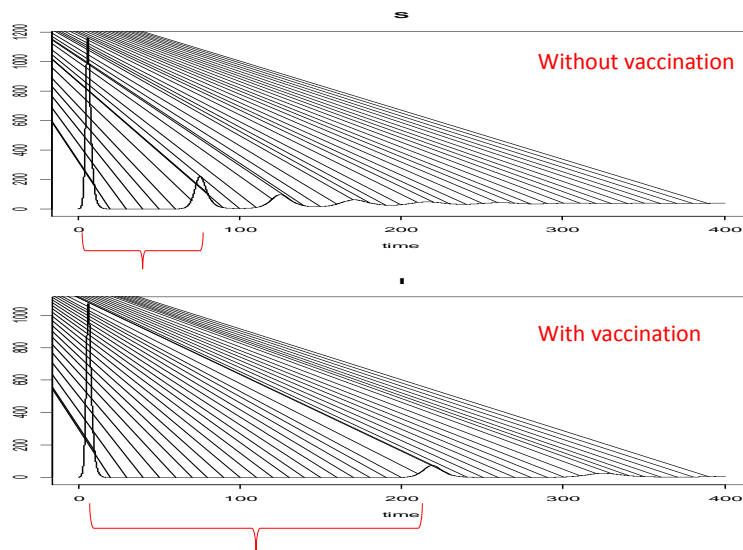
```
> parameters <- c(mu=1/75,beta=0.001/2, v=1, P=0.45)
> parameters
     mu       beta      v          P
0.01333333 0.00050000 1.00000000 0.45000000
```
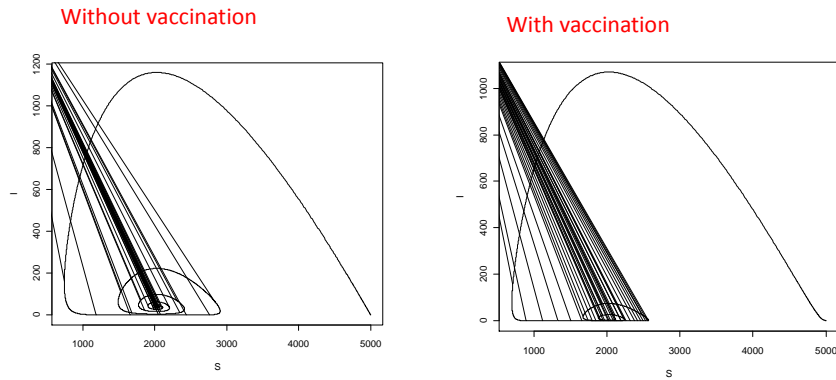
Susceptible: inter epidemic period

Without vaccination

With vaccination

Infected class: inter epidemic period

Without vaccination

With vaccination

Equilibrium

Without vaccination

With vaccination

Equilibrium

Without vaccination

```
> out[39998:40001,]
        time         X        Y         Z
39998 399.97 2024.816 39.54316 2935.641
39999 399.98 2024.812 39.54280 2935.645
40000 399.99 2024.809 39.54243 2935.649
40001 400.00 2024.805 39.54206 2935.653
```

With vaccination

```
> out[39998:40001,]
        time         X        Y         Z
39998 399.97 2117.341 9.663568 2872.995
39999 399.98 2117.323 9.667949 2873.009
40000 399.99 2117.305 9.672332 2873.023
40001 400.00 2117.287 9.676716 2873.036
```