

# L01 Compartmental Models<sup>1</sup>

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Statistical Methods in Infectious Disease Epidemiology  
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# Outline

- 1 Reed-Frost model
- 2 Deterministic SIR model
- 3 Stochastic SIR model in continuous time

# Overview

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# The Reed-Frost epidemic model

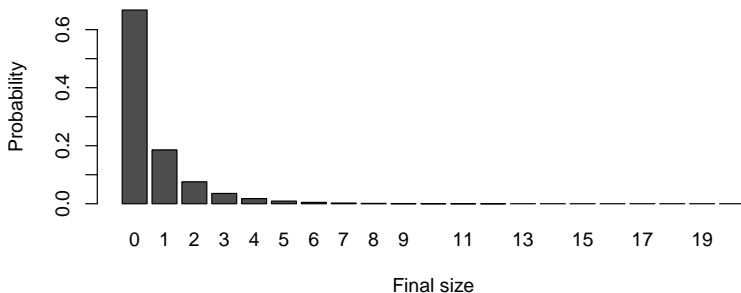
- Discrete-time SIR model, where individuals are either
  - Susceptible,
  - Infectious or
  - Recovered / Removed (dead, isolated or immune)
- Closed population with initially
  - $x_0 = n$  susceptible and
  - $y_0 = m$  infectious individuals
- Dynamics are described by a discrete-time Markov chain

$$Y_{t+1}|x_t, y_t \sim \text{Bin}(x_t, 1 - (1 - w)^{y_t}),$$
$$X_{t+1} = x_t - Y_{t+1},$$

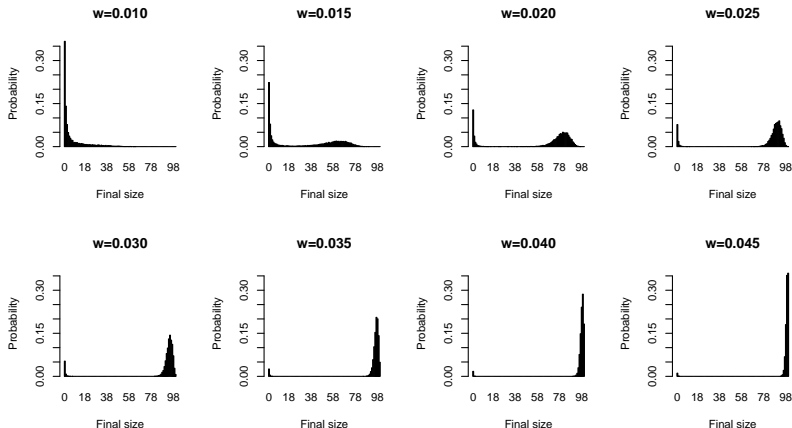
where  $w$  is the probability of an infectious contact between an infectious and a susceptible during one unit of time.

## Final size distribution

- The *final size* of the epidemic is  $Z = Y_1 + Y_2 + Y_3 + \dots$
- Final size distribution can be computed exactly for small  $n$ , say  $n \leq 30$ .
- Final size distribution for  $n = 20$ ,  $m = 1$  and  $w = 0.02$ :



# Simulated final size distribution for $n = 100$ and $m = 1$



# R Code for Simulation of the Reed-Frost Model

```
fsize.RF <-  
function(n, m, w, samples) {  
  #Initial susceptible  
  xj <- matrix(data=n, nrow=samples, ncol=1)  
  #Initial infectives  
  yj <- matrix(data=m, nrow=samples, ncol=1)  
  
  #Loop over all (samples) simulations until they all are ceased.  
  while (sum(yj>0) & sum(xj>0)) {  
    #Sample from all processes concurrently  
    yj <- ifelse(xj > 0, rbinom(samples, xj, 1-(1-w)^yj), 0)  
    #Update all xj  
    xj <- xj - yj  
  }  
  #Done  
  return(n-xj)  
}
```



## Mathematical challenges

- Mathematical abstractions of real world phenomena → **equations**
- No outbreaks are similar → **stochasticity**
- Different modes of transmission: person-to-person, air-borne, water-borne, food-borne and vector-borne → **direct and indirect transmission**
- Population heterogeneity (e.g. different places of residence, contact behaviour, susceptibility) needs to be taken into account
- Conflict between observation frequency and speed of the epidemic → **time scale of a model**
- Not all relevant events for the course of the epidemic are observable → **partial observability**

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# The SIR model

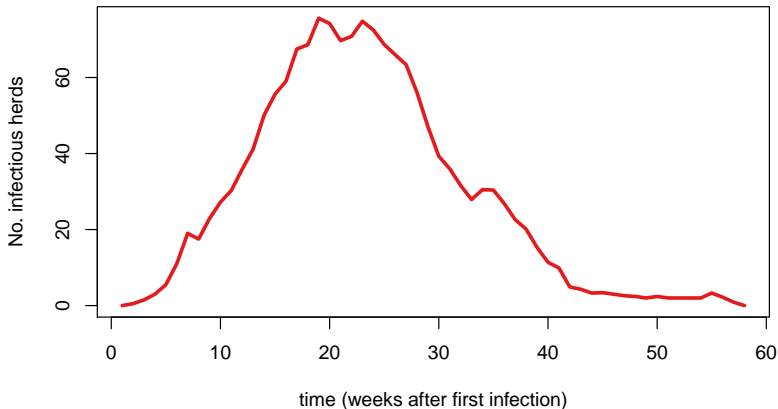
- When the population considered is large, it can be sufficient to disregard the stochasticity of the epidemic process and use deterministic models.
- Can formulate a continuous-time deterministic **SIR model** by using ordinary differential equations (ODEs).
- The deterministic system intends to model the mean behaviour of the underlying stochastic system.
- We assume a closed population (i.e. no demographics turnover) of size  $N$ .

## Example: CSFV in The Netherlands (1)

- Classical swine fever virus (CSFV) is a highly contagious disease of pigs and wild boar.
- Characteristics of the disease are
  - Symptoms after infection: dullness and anorexia.
  - Acute form: rapid mortality often without clinical symptoms.
  - Secondary symptoms: diarrhea or respiratory problems.
- A huge outbreak in the Netherlands took place between February 1997 and May 1998.
  - 429 infected herds detected and stamped out ( $\sim 700,000$  pigs)
  - 1286 herds pre-emptively slaughtered ( $\sim 1.1$  million pigs)
  - Note: Netherlands has approximately 21,500 pig herds

## Example: CSFV in the Netherlands (2)

- Stegeman, Elbers, Smak, and de Jong (1999) provide estimates on the weekly number of infectious herds from contact tracing and serological analysis:



## SIR differential equation system

- As before, divide population into three groups
  - Susceptible,
  - Infectious or
  - Recovered / Removed
- At all times  $S(t) + I(t) + R(t) = N$ , so  $S(0) + I(0) = N$ .
- Describe dynamics using an ordinary differential equation system

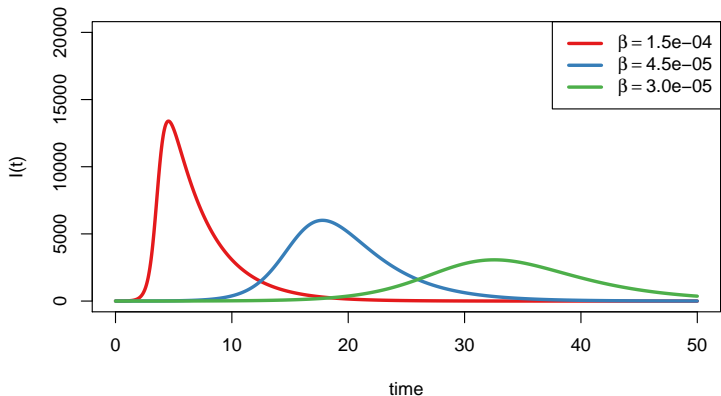
$$\begin{aligned}\frac{dS(t)}{dt} &= -\beta S(t)I(t) \\ \frac{dI(t)}{dt} &= \beta S(t)I(t) - \gamma I(t) \\ \frac{dR(t)}{dt} &= \gamma I(t)\end{aligned}$$

where  $\beta, \gamma > 0$ .

- Solve ODE with initial condition  $(S(0), I(0), 0)$  using numerical routines (R package `deSolve`).

## Example

- Number of infected  $I(t)$  for  $\gamma = 0.3$ ,  $N = 2 \times 10^4$ ,  $I(0) = 1$  and different values of  $\beta$ .



# Numerical Solution of the SIR ODE

- Defining the vector of derivatives for the SIR ODE

```
#####  
# Function to compute the derivative of the ODE system  
#  
# t - time  
# y - current state vector of the ODE at time t  
# parms - Parameter vector used by the ODE system  
#  
# Returns:  
# list containing dS(t)/dt and dI(t)/dt  
#####  
  
sir <- function(t,y, parms) {  
  beta <- parms[1]  
  gamma <- parms[2]  
  S <- y[1]  
  I <- y[2]  
  return(list(c(S=-beta*S*I,I=beta*S*I-gamma*I)))  
}
```

- Use deSolve::lsoda

```
sim <- lsoda(y=c(N-1,1), times=times, func=sir,parms=c(beta.grid[1],gamma))  
head(sim, n=3)  
##           time           1           2  
## [1,] 0.00000000 19999.00 1.000000  
## [2,] 0.05005005 19998.84 1.144682  
## [3,] 0.10010010 19998.66 1.310297
```



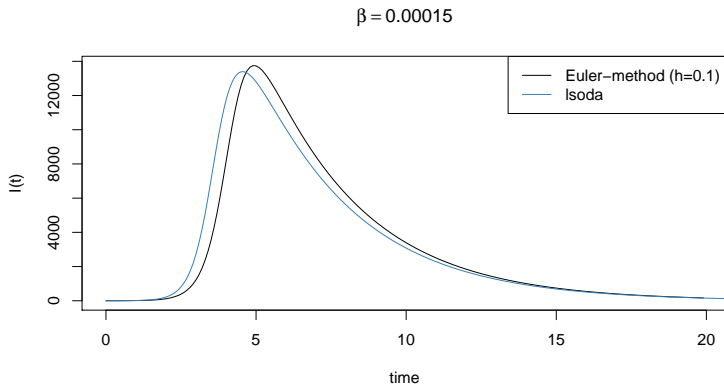
## Aside: Numerical Solution of ODEs (1)

- Simple method to solve an ODE system numerically given the initial condition: Euler-Method
- Example in R: Stepwidth  $h$  and initial value is  $S(0) = N - 1$  and  $I(0) = 1$

```
# Step width of the Euler method
h <- 0.1
y <- matrix(NA, nrow=ceiling(20/h), ncol=3, dimnames=list(NULL, c("t", "S", "I")))
# Initial value
y[1,] <- c(0, N-1, 1)
# Loop
for (i in 2:nrow(y)){
  y[i,] <- c(y[i-1, "t"]+h, y[i-1, c("S", "I")] +
    h * sir(y[i-1, "t"], y[i-1, c("S", "I")], parms=c(beta.grid[1], gamma))[[1]])
}
```

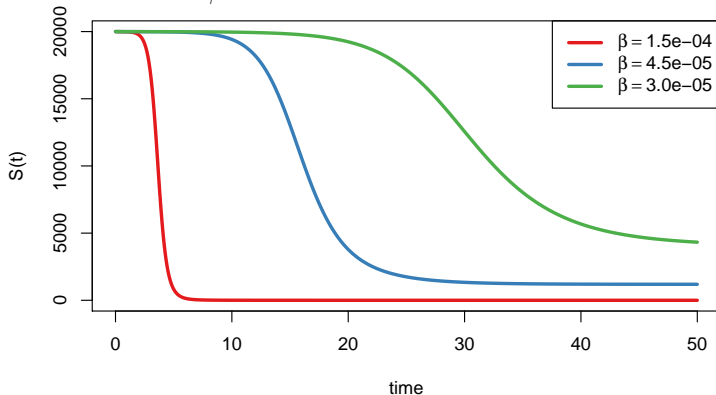
## Aside: Numerical Solution of ODEs (2)

- Plot for Euler solve for SIR system



## Example cont.

- Number of susceptibles  $S(t)$  for  $\gamma = 0.3$ ,  $N = 2 \times 10^4$ ,  $I(0) = 1$  and different values of  $\beta$ .



# The basic reproduction number $R_0$

## Basic reproduction number $R_0$

$R_0$  is the number of new infections produced by one infected in a fully susceptible population

- If  $R_0 < 1$  the number of infected is expected to fade out right after introduction. If  $R_0 > 1$  an epidemic will result.
- In a simple SIR model

$$R_0 = \frac{\beta N}{\gamma}.$$

- In the previous example we thus have  $R_0 = 10, 3$  and  $2$ .

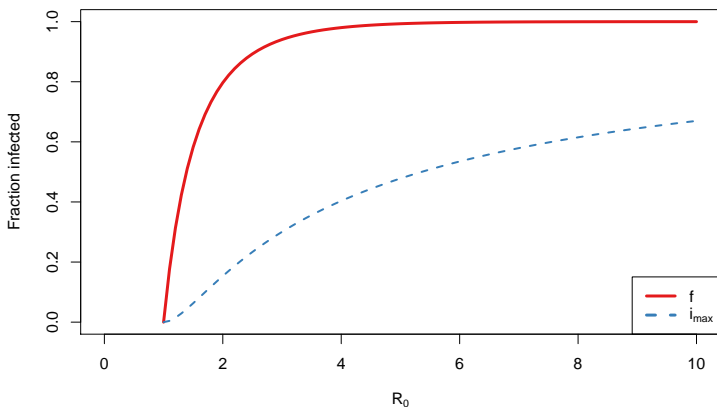
## The final size of an epidemic (1)

- In a closed population the number of susceptibles can only decrease, hence it must have a limit for  $t \rightarrow \infty$ .
- Is the limit zero? Or will some fraction of the population escape from ever getting infected?
- Let  $f$  be the fraction of the (initially susceptible) population that got infected. This is also called the *final size* of the epidemic.
- It can be found as the solution to the equation

$$1 - f = \exp(-R_0 f).$$

## The final size of an epidemic (2)

- For fixed  $R_0$  the final size equation can be solved numerically
- Plot of  $f$  as a function of  $R_0$  together with  $i_{\max} = \max_{0 \leq t \leq \infty} (I(t)/N)$ :



- In the example we thus have  $f = 1, 0.94$  and  $0.8$ .

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## Stochastic SIR model in continuous time (1)

- If the population under study is large enough, deterministic approximations are reasonably valid to obtain an understanding of the disease.
- In small populations, however, stochasticity plays an important role for extinction, which cannot be ignored.
- Stochastic epidemic modeling is described in Becker (1989), Daley and Gani (1999) and Andersson and Britton (2000), who all rely heavily on the theory of stochastic processes.



## Stochastic SIR model in continuous time (2)

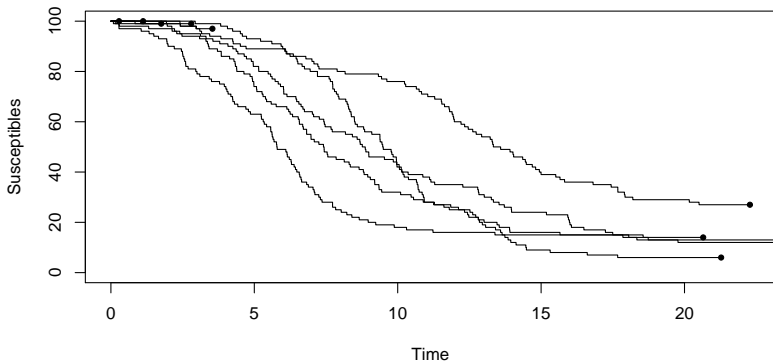
- The *stochastic SIR model* can be described as a continuous-time Markov process, where the event rates for infection and removal are:

Event	Transition	Rate
Infection:	$(S(t), I(t)) \rightarrow (S(t) - 1, I(t) + 1)$	$\beta \cdot S(t) \cdot I(t)$
Removal:	$(S(t), I(t)) \rightarrow (S(t), I(t) - 1)$	$\gamma \cdot I(t)$

- Again,  $R(t)$  is implicitly given, because a fixed population of size  $S(0) + I(0)$  is assumed.
- The integer size of the population is now taken into account: Once  $I(t) = 0$ , the epidemic ceases.
- Point process viewpoint: piecewise constant rates, while the length of the infective period is exponentially distributed.

## Stochastic SIR model in continuous time (3)

10 SIR simulations with  $S(0) = 100$ ,  $I(0) = 1$ ,  $\beta = 0.01$  and  $\gamma = 0.5$ :

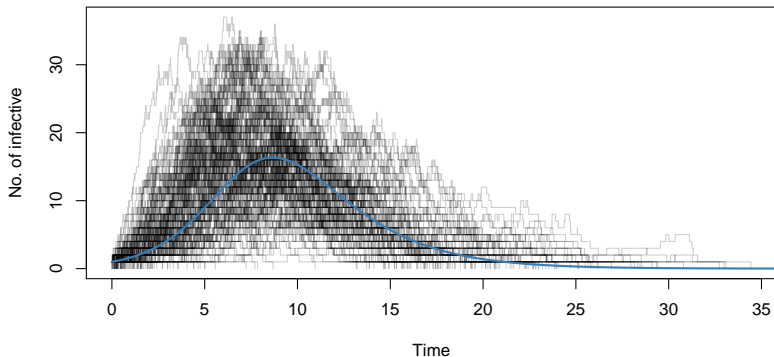


# R Code for Simulation of the Stochastic SIR Model

```
rSIR <-  
function(T, beta, gamma, n, m) {  
  #Initialize (x= number of susceptibles)  
  t <- 0  
  x <- n  
  y <- m  
  
  #Possible events  
  eventLevels <- c("S->I", "I->R")  
  #Initialize result  
  events <- data.frame(t=t, x=x, y=y, event=NA)  
  #Loop until we are past time T  
  while (t < T & (y>0)) {  
    #Draw the waiting type for each possible event  
    wait <- rexp(2, c("S->I"=beta*x*y, "I->R"=gamma*y))  
    #Which event occurs first  
    i <- which.min(wait)  
    #Advance Time  
    t <- t+wait[i]  
    #Update population according to the event type  
    if (eventLevels[i]=="S->I") { x <- x-1 ; y <- y+1}  
    if (eventLevels[i]=="I->R") { y <- y-1 }  
    #Store result  
    events <- rbind(events, c(t, x, y, i))  
  }  
  #Recode event type and return  
  events$event <- factor(eventLevels[events$event], levels=eventLevels)  
  return(events)  
}
```

# Stochastic SIR vs. deterministic SIR model

Same parameters as previously - 250 trajectories vs. the ODE solution:



## Literature I



Andersson, H., and T. Britton. 2000.

Stochastic Epidemic Models and their Statistical Analysis. Vol. 151.  
Springer Lectures Notes in Statistics. Springer-Verlag.



Becker, N. G. 1989. Analysis of Infectious Disease Data. Chapman & Hall/CRC.



Daley, D. J., and J. Gani. 1999. Epidemic Modelling: An introduction.  
Cambridge University Press.



Stegeman, A., et al. 1999. "Quantification of the transmission of classical swine fever virus between herds during the 1997- 1998 epidemic in The Netherlands". Preventive Veterinary Medicine 42:219–234.