#### Mathematical Modelling of Infectious Diseases for Public Health

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#### **1** Revisiting Deterministic Epidemic Models

#### 2 Catching a Glimpse of Stochastic Epidemic Models

| Succeptible (8) | 351 | Infectious (1) | 36 | Beconcred | (8) |
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#### 1 Revisiting Deterministic Epidemic Models

#### 2 Catching a Glimpse of Stochastic Epidemic Models

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- (iii) Throughout the whole study period the population under consideration is fixed in size. There are no births, deaths, immmigration or emigration during the whole study period.

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These assumptions reflect the situation for many diseases, such as measles or influenza, and would seem to be reasonable for computers whose anti-virus software has been updated to recognise the virus.

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An immediate implication of the assumptions is that individuals can only make two moves: from S to I and from I to R. For this reason the model is said to be an SIR epidemic model.

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Moreover, in this model N = S + I + R does not change over time (by assumption!). The independent variable in the simple SIR Model is the time *t*, and the rates of transfer between compartments are mathematically expressed as derivatives with respect to time of the numbers *I* and *S* (each one viewed as a differentiable function of *t*). Hence, the simple SIR model is given by a system of 2 coupled non-linear ODEs:

$$\begin{aligned} \dot{S} &:= \frac{dS}{dt} &= f_1(S, I) := -\beta SI \\ \dot{I} &:= \frac{dI}{dt} &= f_2(S, I) := \beta SI - \gamma I = I(\beta S - \gamma) , \end{aligned}$$

where  $\beta, \gamma > 0$  are positive constants,  $S(t) \ge 0$  and  $I(t) \ge 0$  for all  $t \ge 0$ .

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By potentially substituting  $\beta$  through  $\beta N$  we may assume WLOG that S + I + R = 1. These ODEs, together with the initial conditions  $I(0) := I_0$  and  $S(0) := S_0 := 1 - I_0$  for some fixed  $0 < I_0 < 1$  define the model.

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#### Remark (Lotka-Volterra)

*Coupled non-linear ODE systems of this type are very similar to the Lotka-Volterra equations, also known as the predator-prey equations, given by* 

$$\dot{S} = \alpha S - \beta SI = S(\alpha - \beta I)$$
  
$$\dot{I} = \gamma SI - \delta I = I(\gamma S - \delta),$$

where  $\alpha, \beta, \gamma, \delta > 0$  and *S*, *I* are defined on  $[0, \infty)$ .

# Deterministic generalisations of simple SIR

Remark (Some deterministic generalisations of the simple SIR model)

One can add an inflow of newborns into the class *S* of susceptibles to the simple SIR model, at rate  $\mu N$ , and - the births balancing - deaths in the classes at rates  $-\mu S$ ,  $-\mu I$ ,  $-\mu R$  respectively, for some additional parameter  $\mu > 0$ . These models are known as classic endemic models.

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Observation

Since  $\dot{S} = -\beta SI$  on  $(0, \infty)$  and  $S, I : [0, \infty) \longrightarrow (0, \infty)$  it follows that  $\dot{S} < 0$  on  $(0, \infty)$ . Hence, in any case S is strictly decreasing on  $(0, \infty)$ .

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{ $t: t \ge 0$  and  $\beta S(t) - \gamma > 0$ }. Moreover,  $\frac{d}{dt}(S + I) = -\gamma I < 0$  on  $(0, \infty)$ , implying that - in any case - also the non-negative function S + I is strictly decreasing on  $(0, \infty)$ .

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Definition

 $R_0 := \frac{\beta}{\gamma} > 0$  is called basic reproduction ratio.

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Proposition

The initial value problem

$$\dot{I} = (\beta S(t) - \gamma) I, I(0) = I_0 \quad (I_0 \in (0, 1])$$

has an uniquely determined positive solution on  $[0,\infty).$  This solution is given by

$$I(t) := I_0 \exp\left(\beta \int_0^t S(u) \, du\right) \exp\left(-\gamma \, t\right) \qquad (t \ge 0) \, .$$

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Similarly, we can see that also S(t) > 0 for all  $t \ge 0$  (since  $S_0 > 0$  by assumption). Note that *in general* we don't know whether this unique solution *I* is bounded from above !
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The following statements are equivalent:

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Proof.

 $\underbrace{(i) \Rightarrow (ii)}_{\exp \left(\beta \int_{0}^{t} S(u) \, du - \gamma \, t\right)} \leq I_0 \text{ for all } t \geq 0. \text{ Then} \\ \underbrace{\exp \left(\beta \int_{0}^{t} S(u) \, du - \gamma \, t\right)}_{\text{for all } t \geq 0. \text{ Hence, } \frac{1}{t} \int_{0}^{t} S(u) \, du \leq \frac{1}{R_0} \\ \text{for all } t \geq 0. \text{ Consequently, } S_0 = S(0) = \lim_{t \to 0} \frac{1}{t} \int_{0}^{t} S(u) \, du \leq \frac{1}{R_0}.$ 

## Discussion on the role of $\overline{R_0}$ II

#### Proof ctd.

 $\underline{(i) \Rightarrow (iii)}$ : Let  $S_0 \leq \frac{1}{R_0}$ . Since  $\dot{S} = -\beta IS$  on  $(0, \infty)$  and both, I and S are positive it follows that  $\dot{S} < 0$  on  $(0, \infty)$ , implying that S is a strictly decreasing function on  $(0, \infty)$ . Hence,  $S(t) < S(0) \leq \frac{1}{R_0}$  for all t > 0. In particular,  $\beta S - \gamma < 0$  on  $[0, \infty)$ . Consequently,  $\dot{I} = (\beta S - \gamma) I < 0$  on  $(0, \infty)$ , implying that I is strictly decreasing on  $(0, \infty)$ .

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 $\begin{array}{l} \underbrace{(i) \Rightarrow (iii)}{(iii)} : \operatorname{Let} S_0 \leq \frac{1}{R_0}. \ \text{Since} \ \dot{S} = -\beta IS \ \text{on} \ (0,\infty) \ \text{and both, } I \\ \hline \text{and } S \ \text{are positive it follows that} \ \dot{S} < 0 \ \text{on} \ (0,\infty), \ \text{implying that} \ S \\ \hline \text{is a strictly decreasing function on} \ (0,\infty). \ \text{Hence,} \\ S(t) < S(0) \leq \frac{1}{R_0} \ \text{for all} \ t > 0. \ \text{In particular,} \ \beta S - \gamma < 0 \ \text{on} \ [0,\infty). \\ \hline \text{Consequently,} \ \dot{I} = (\beta S - \gamma) \ I < 0 \ \text{on} \ (0,\infty), \ \text{implying that} \ I \ \text{is strictly decreasing on} \ (0,\infty). \ \text{Since} \ \beta S_0 - \gamma < 0 \ \text{(by assumption) it follows that} \\ \exp \left(\beta \ \int_0^t S(u) \ du\right) \exp \left(-\gamma t\right) \leq \exp \left(\beta S(0) t\right) \exp \left(-\gamma t\right) = \exp \left(-\alpha t\right), \\ \text{where } \alpha := - \left(\beta \ S_0 - \gamma\right) > 0. \ \text{Hence,} \ I(t) \ \text{decreases to } 0 \ \text{if } \end{array}$ 

 $t \to \infty$ .

#### Proof ctd.

 $(i) \Rightarrow (iii)$ : Let  $S_0 \leq \frac{1}{R_0}$ . Since  $\dot{S} = -\beta IS$  on  $(0,\infty)$  and both, I and *S* are positive it follows that  $\dot{S} < 0$  on  $(0, \infty)$ , implying that *S* is a strictly decreasing function on  $(0, \infty)$ . Hence,  $S(t) < S(0) \le \frac{1}{R_0}$  for all t > 0. In particular,  $\beta S - \gamma < 0$  on  $[0, \infty)$ . Consequently,  $I = (\beta S - \gamma) I < 0$  on  $(0, \infty)$ , implying that I is strictly decreasing on  $(0,\infty)$ . Since  $\beta S_0 - \gamma < 0$  (by assumption) it follows that  $\exp\left(\beta \int_0^t S(u) \, du\right) \exp\left(-\gamma t\right) \le \exp\left(\beta S(0) t\right) \exp\left(-\gamma t\right) = \exp\left(-\alpha t\right),$ where  $\alpha := -(\beta S_0 - \gamma) > 0$ . Hence, I(t) decreases to 0 if  $t \to \infty$ .  $(iii) \Rightarrow (i)$ : trivial.

Observation (Shape of the function *I* if  $R_0 > 1$ ) Let  $R_0 > 1$  and  $0 < t^*$  such that  $S(t^*) = \frac{1}{R_0}$ . Then *I* is strictly increasing on  $(0, t^*)$ . *I* attains its single maximum at  $t^*$ . *I* is strictly decreasing on  $(t^*, \infty)$ .

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### Proof.

Elementary differentiation and a bit of elementary algebra induced by the structure of the SIR ODE system shows us that  $\dot{I}(t) = 0$  if and only if  $t = t^*$  and

$$\ddot{I} \stackrel{\checkmark}{=} I \left(\frac{\beta S}{\beta - \gamma}\right)^2 - \beta^2 I^2 S - \gamma I$$

on  $(0, \infty)$ . Consequently, at  $t^*$  *I* attains its single (and hence global) maximum.

Proof ctd. Let  $0 < t < t^*$ . Then  $\frac{1}{R_0} = S(t^*) < S(t)$ , implying that in fact *I* is strictly increasing on  $(0, t^*)$ . Now let  $t^* < t$ . Then  $S(t) < S(t^*) = \frac{1}{R_0}$ . Hence, *I* is strictly decreasing on  $(t^*, \infty)$ .

#### Susceptible (3) (SI Infectious (1) (Figure Recovered (8)

# Shape of the functions S, I and R in the case $R_0 > 1$

Here, N := 500 and  $S, I, R : [0, \infty) \longrightarrow (0, N]$  (not the percentages!).



time

Even if the basic reproduction ratio  $R_0$  is not known to us the number of susceptibles today (i.e.,  $S_0$ ) and the percentage of remaining susceptibles  $S_{\infty} := \lim_{t \to \infty} S(t) \le 1$  when the epidemic is over already allows us to retrieve  $R_0$  at least if  $S_0 \le \frac{1}{R_0}$ , since:

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Proposition Let  $S_0 \leq \frac{1}{R_0}$  and S(0) + I(0) = 1. Then  $\ln \left( \begin{array}{c} S_0 \end{array} \right) = R_0 \left( 1 - S_0 \right)$ 

$$\ln\left(\frac{S_0}{S_\infty}\right) = R_0 \left(1 - S_\infty\right) \,.$$

Proof. Since  $\dot{S}(t) = -\beta S(t)I(t)$  for all  $t \in (0, \infty)$  and  $S(0) = S_0 = 1 - I_0$  we have

$$S(t) = S_0 \exp\left(-\beta \int_0^t I(u) \, du\right) \quad (t \ge 0) \, .$$

Hence,

$$S(t) \stackrel{(!)}{=} S_0 \exp\left(R_0 \int_0^t (-\gamma I(u)) \, du\right)$$

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=  $S_0 \exp\left(R_0 \left(I(t) + S(t) - 1\right)\right)$  (why?).

Proof ctd. Equivalently written:

$$\ln\left(\frac{S(0)}{S(t)}\right) = \mathbf{R}_0 \left(1 - S(t) - I(t)\right) \,.$$

Now we take limits on both sides of the latter equation (as  $t \to \infty$ ). Since  $S_0 \le \frac{1}{R_0}$  by assumption we know that  $I_{\infty} = \lim_{t \to \infty} I(t) = 0$  - and the claim follows.

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### 1 Revisiting Deterministic Epidemic Models





## A glimpse of the continuous time Markov chain SIR model I

View the class of susceptibles, respectively the class of infected as stochastic random variables, changing randomly in time.



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## A glimpse of the continuous time Markov chain SIR model I

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In addition, given the current state of the  $S \times S$ -valued process  $(S_t, I_t)_{t \ge 0}$  at time *t*, we assume that the future state of this process at time  $t + \Delta t$ , for any  $\Delta t > 0$ , does not depend on times prior to *t* (known as Markov property).

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## A glimpse of the continuous time Markov chain SIR model I

View the class of susceptibles, respectively the class of infected as stochastic random variables, changing randomly in time. Think e.g. at nodes in a random graph which change colour according to their state. A bit more formally, fix an arbitrary probability space  $(\Omega, \mathcal{F}, \mathbb{P})$  and consider the mappings  $\Omega \times [0, \infty) \ni (\omega, t) \mapsto S_t(\omega)$ , respectively  $\Omega \times [0, \infty) \ni (\omega, t) \mapsto I_t(\omega)$ , where  $I_t(\omega), S_t(\omega) \in S := \{0, 1, 2, ..., N\}$  for all  $\omega \in \Omega$  and  $t \in [0, \infty)$ .

In addition, given the current state of the  $S \times S$ -valued process  $(S_t, I_t)_{t \ge 0}$  at time t, we assume that the future state of this process at time  $t + \Delta t$ , for any  $\Delta t > 0$ , does not depend on times prior to t (known as Markov property). "The stochastic system has no memory!"

Succeptible (8) (SI Infectious (3) (1) Becorered (8)

## A glimpse of the continuous time Markov chain SIR model II

Let  $s, i, k, j \in S$  and  $t \in [0, \infty)$ . Then the associated time-homogeneous transition probabilities

$$p_{(s,i),(s+k,i+j)}(\Delta t) := \mathbb{P}\left((S_{t+\Delta t}, I_{t+\Delta t}) = (s+k, i+j) \mid (S_t, I_t) = (s, i)\right)$$
are modelled as

$$p_{(s,i),(s+k,i+j)}\left(\Delta t\right) := \begin{cases} \beta s \, i \, \Delta t + o(\Delta t) & \text{if } (k,j) = (-1,1) \\ \gamma i \, \Delta t + o(\Delta t) & \text{if } (k,j) = (0,-1) \\ 1 - (\beta s \, i - \gamma i) \, \Delta t + o(\Delta t) & \text{if } (k,j) = (0,0) \\ o(\Delta t) & \text{else} \end{cases}$$

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Unfolding the powerful machinery of Chapman-Kolmogorov equations, respectively time-homogeneous Markov semigroups one can then start to calculate transition probabilities and derived probabilities (think at multiple life insurance mathematics...).

# A glimpse of the SDE SIR model of Allen I

### Coupled SDE SIR Model of Allen Let $\beta > 0$ , $\gamma > 0$ and $W^{(1)}$ and $W^{(2)}$ be two independent standard Brownian motions.

$$dS_t = -\beta S_t I_t dt - \sqrt{\beta S_t I_t} dW_t^{(1)}$$
  

$$dI_t = (\beta S_t I_t - \gamma I_t) dt + \sqrt{\beta S_t I_t} dW_t^{(1)} - \sqrt{\gamma I_t} dW_t^{(2)}$$

Moreover, the initial conditions are given by  $I(0) := I_0$ ,  $S(0) := S_0 := 1 - I_0$ ,  $0 < I_0 < 1$  (as in the simple deterministic case).

## A glimpse of the SDE SIR model of Allen II

One equivalent formulation of the SDE SIR model of Allen is the following one:

## A glimpse of the SDE SIR model of Allen II

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Coupled SDE SIR Model of Allen in Vector Notation Let  $\beta > 0$ ,  $\gamma > 0$  and  $W^{(1)}$  and  $W^{(2)}$  be two independent standard Brownian motions.

$$d\begin{pmatrix} S\\I \end{pmatrix} = \begin{pmatrix} -\beta I & 0\\ \beta I & -\gamma \end{pmatrix} \begin{pmatrix} S\\I \end{pmatrix} dt + \begin{pmatrix} -\sqrt{\beta S I} & 0\\ \sqrt{\beta S I} & -\sqrt{\gamma I} \end{pmatrix} d\begin{pmatrix} W^{(1)}\\W^{(2)} \end{pmatrix}$$

Moreover, the initial conditions are given by  $\binom{S(0)}{I(0)} := \binom{S_0}{I_0}$ , where  $S_0 := 1 - I_0$ ,  $0 < I_0 < 1$  (as in the simple deterministic case).

## A glimpse of the SDE SIR model of Allen III

#### Problem

Is the SDE SIR model of Allen well-defined? To answer this non-trivial question we need the whole machinery of (multidimensional) Itô calculus including theory and application of the (vector-valued stochastic) Itô integral ! Actually, SDEs are stochastic integral equations. Brownian motion paths are nowhere differentiable with probability 1!

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| Succeptible (8) | 357 | Infectious (1) | 10 | Becorered ( | 8) |
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## Thank you for your attention!

## Are there any questions, comments or remarks?