

A spatially stochastic epidemic model with partial immunization shows in mean field approximation the reinfection threshold

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Recently, the notion of a reinfection threshold in epidemiological models of only partial immunity has been debated in the literature. We present a rigorous analysis of a model of reinfection which shows a clear threshold behaviour at the parameter point where the reinfection threshold was originally described. Furthermore, we demonstrate that this threshold is the mean field version of a transition in corresponding spatial models of immunization. The reinfection threshold corresponds to the transition between annular growth of an epidemics spreading into a susceptible area leaving recovered behind and compact growth of a susceptible-infected-susceptible region growing into a susceptible area. This transition between annular growth and compact growth was described in the physics literature long before the reinfection threshold debate broke out in the theoretical biology literature.

Keywords: SIRI model; critical threshold; compact growth; annular growth

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1. Introduction

In 1997, Grassberger, Chaté and Rousseau considered a model for the spreading of an agent in a medium whose susceptibility changes irreversibly at the first infection which, in their words, ‘can model epidemics with partial immunization’, where after a first infection the recovered host only have partial immunity against the pathogen or a genetically close mutant pathogen [18]. One driving question for looking at such models is the long going discussion in theoretical and computational physics about critical phenomena in models with absorbing states, especially with so-called frozen absorbing states.

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While the susceptible-infected-susceptible epidemics (SIS) has one unique absorbing state, hence clearly falls into the universality class of directed percolation (DP) with respect to its critical transition behaviour [17], the susceptible-infected-recovered epidemics (SIR) shows many frozen absorbing states of various configurations of recovered and susceptibles once the infection has died out, the universality class of the phase transition being ordinary percolation [16], or as nowadays also called dynamic percolation (DyP) when it comes to more than the static aspects. The spatial stochastic model of spreading in media with long-time memory [18] has the SIS and the SIR epidemics as special cases and interpolates between them. Below we will give a time continuous version of such a spatial SIRS epidemics, which shows, according to general knowledge of critical phenomena, the same universality as the originally considered time discrete model considered by Grassberger *et al.* [18].

Since partial immunity is a frequent feature of many pathogens, such as *Neisseria meningitidis*, *Streptococcus pneumoniae*, *Mycobacterium tuberculosis*, and especially those pathogens with pronounced multi-strain structure, in 2004, Gomes *et al.* [14] discussed various models of waning immunity as well as partial immunity and found in their ordinary differential equations (ODE) what they coined ‘a reinfection threshold’. In order to obtain non-trivial stationary solutions, where not all the population become recovered, they had to consider, in addition to the SIRS-model of spreading, also terms describing input into the susceptible class from other classes. They use natural birth and death for the hosts of the epidemics. In their stationary states analysis, they found a first threshold between a disease-free state and a non-trivial state with strictly positive endemic equilibrium. Besides this first threshold, they found a second threshold characterized by the ratio between the infection and reinfection rates. This second threshold they call the ‘reinfection threshold’.

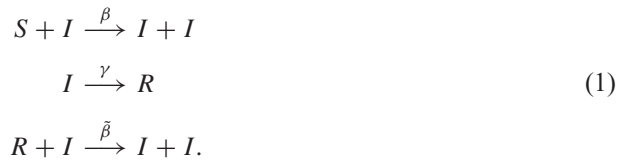
However, this notion of the reinfection threshold was questioned recently by Breban and Blower [4] in 2005, where they simply claim that ‘The reinfection threshold does not exist’. They do so on the basis that there would be nothing special going on in the stationary state solution at the point where the reinfection threshold was marked. An immediate reply by Gomes *et al.* [15] on the importance of the reinfection threshold emphasizes the epidemiological implications of vaccine efforts being successful below the threshold but not above. Beyond the reinfection threshold, the stationary solution is ruled by the secondary infections in the IRI sub-compartment of the SIRS model which cannot be further affected by vaccination. Vaccination only brings susceptibles directly into the recovered class by circumventing the infection class.

In the light of discussion in the above-mentioned physics literature, we construct a stochastic spatial epidemiological model for the SIRS-system, which has the same critical behaviour as the model considered by Grassberger *et al.* [18]. Especially, it shows transitions between phases of no growth below the DP or DyP critical points which are joined by a phase transition line, and another transition between annular growth and compact growth in two and higher spatial dimensions. We calculate the mean field approximation of this stochastic spatial epidemiological SIRS-model for the dynamics of the mean total numbers of susceptibles, infected and recovered. This mean field dynamics is the core of the ODE-models considered by Gomes *et al.* [14] for the reinfection mechanism. Instead of including the interactions of hosts birth and death, we just add to the spreading SIRS-model one more transition, namely from recovered to susceptibles with rate α , that ensures the existence of a non-trivial stationary solution and consider the limit of vanishing α . In that limit, we obtain a sharp threshold behaviour characterized by the parameter values of the reinfection threshold of Gomes *et al.* [14]. The threshold behaviour is in analogy to the Ising spin threshold, for example, in the limit of vanishing external magnetic field [2,19]. So we conclude that the reinfection threshold does exist in the sense that any other threshold in physical phase transitions exists or any bifurcation behaviour in mean field models exist. From the studies of spatial stochastic epidemics with partial immunization in two dimensions [18], we even know that the mean field threshold behaviour provides also a description of the threshold behaviour of spatial models, namely the transition between annular growth and compact growth.

Finally, we calculate the phase diagram for this mean field solution in the original parameters of first and secondary infection rates. The mean field phase diagram is in good agreement with phase diagrams of higher dimensional simulations of the stochastic partial immunization model as investigated by Dammer and Hinrichsen [6], in 2004. Hence, we find solid evidence that the reinfection threshold exists and is the mean field analogue of a well-studied phase transition line in spatial stochastic immunization models.

2. A model with partial immunization: SIRI

In the model with partial immunization, the SIRI-model, we have as transition rates the infection β as a transition from susceptible S to infected I , the recovery rate γ from I into the recovered R class, and as a special ingredient a rate of reinfection $\tilde{\beta}$ as effect of only partial immunization of the recovered. The reaction schemes for transitions of the SIRI system is given by



Let $p(S_1, I_1, R_1, S_2, I_2, R_2, \dots, R_N, t)$ be the probability of the state $S_1, I_1, R_1, S_2, I_2, R_2, \dots, R_N$ occur at time t . Let $J_{i,j} \in \{0, 1\}$ be the elements of the $N \times N$ adjacency matrix J , symmetric and with zero diagonal elements, describing the neighbouring structure of the individuals: if $J_{i,j} = 1$ then the individual i is a neighbour of j , and if $J_{i,j} = 0$ then the individual i is not a neighbour of j .

For the SIRI model, we have in the spatial set-up for the variables S_i, I_i and $R_i \in \{0, 1\}$ the constraint that an individual i belongs to one of the three classes

$$S_i + I_i + R_i = 1. \quad (2)$$

The master equation for the probability $p(S_1, I_1, R_1, S_2, I_2, R_2, \dots, R_N, t)$ of the spatial SIRI-system is for N individuals

$$\begin{aligned} &\frac{d}{dt} p(S_1, I_1, R_1, S_2, I_2, R_2, \dots, R_N, t) \\ &= \sum_{i=1}^N \beta \left(\sum_{j=1}^N J_{ij} I_j \right) (1 - S_i) p(S_1, I_1, R_1, \dots, 1 - S_i, 1 - I_i, R_i, \dots, R_N, t) \\ &\quad + \sum_{i=1}^N \gamma (1 - I_i) p(S_1, I_1, R_1, \dots, S_i, 1 - I_i, 1 - R_i, \dots, R_N, t) \\ &\quad + \sum_{i=1}^N \tilde{\beta} \left(\sum_{j=1}^N J_{ij} I_j \right) (1 - R_i) p(S_1, I_1, R_1, \dots, S_i, 1 - I_i, 1 - R_i, \dots, R_N, t) \\ &\quad - \sum_{i=1}^N \left[\beta \left(\sum_{j=1}^N J_{ij} I_j \right) S_i + \gamma I_i + \tilde{\beta} \left(\sum_{j=1}^N J_{ij} I_j \right) R_i \right] p(\dots S_i, I_i, R_i \dots). \end{aligned} \quad (3)$$

A first simulation of the model can be seen in Figure 1(a) and (b). For the simulation of the master equation, the so-called Gillespie algorithm was used, giving exponential waiting times

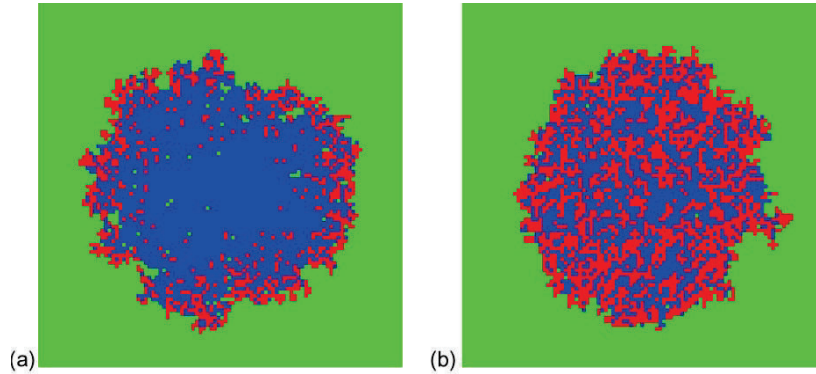


Figure 1. (Available in colour online) (a) Simulation of a two-dimensional SIRI spreading experiment. Green S , and initially one infected I (red) at the centre of the lattice spreads the infection, leaving mostly recovered R (blue) behind. Parameters of the simulation are $\beta = 2$, $\gamma = 1$ and $\tilde{\beta} = 0.1$. Lattice size is 100×100 . The annular growth of the infected is clearly visible for this parameter set. (b) Same as in Figure 1(a) but with a moderately higher $\tilde{\beta} = 0.5$. For this parameter set, the more compact like behaviour as opposed to the annular growth in Figure 1(a) is visible.

between transitions [10,11]. Hence, time is a real variable here, as opposed to discrete time processes considered previously [6,18].

To obtain expectation values, e.g. for the total number of infected hosts at a given time

$$\langle I \rangle(t) := \sum_{S_1=0}^1 \sum_{I_1=0}^1 \sum_{R_1=0}^1 \sum_{S_2=0}^1 \cdots \sum_{R_N=0}^1 \left(\sum_{i=1}^N I_i \right) \cdot p(S_1, I_1, R_1, S_2, \dots, R_N, t) \quad (4)$$

we can calculate the dynamics of such moments by taking its time derivative

$$\frac{d}{dt} \langle I \rangle(t) = \sum_{S_1=0}^1 \sum_{I_1=0}^1 \sum_{R_1=0}^1 \sum_{S_2=0}^1 \cdots \sum_{R_N=0}^1 \left(\sum_{i=1}^N I_i \right) \cdot \frac{d}{dt} p(S_1, I_1, R_1, S_2, \dots, R_N, t). \quad (5)$$

Now we have to insert the master equation (3) into Equation (5) for the expression $d/dt p(S_1, I_1, R_1, S_2, \dots, R_N, t)$ and after some calculation (for explicit calculations for the simpler SIS system see, e.g. [25]), we find in terms of all variables S , I and R

$$\begin{aligned} \frac{d}{dt} \langle S \rangle &= -\beta \langle SI \rangle_1 \\ \frac{d}{dt} \langle I \rangle &= \beta \langle SI \rangle_1 - \gamma \langle I \rangle + \tilde{\beta} \langle RI \rangle_1 \\ \frac{d}{dt} \langle R \rangle &= \gamma \langle I \rangle - \tilde{\beta} \langle RI \rangle_1 \end{aligned} \quad (6)$$

where, e.g.

$$\langle RI \rangle_1(t) := \sum_{S_1=0}^1 \sum_{I_1=0}^1 \cdots \sum_{R_N=0}^1 \left(\sum_{i=1}^N \sum_{j=1}^N (J^1)_{ij} R_i I_j \right) \cdot p(S_1, I_1, R_1, \dots, R_N, t)$$

is the mean number of pairs of recovered next to infected. In the equation for the dynamics of $\langle RI \rangle_1$ also an expression $\langle RI \rangle_2$ could show up. These are longer range correlations, formally given by a power of two of the adjacency matrix J^2 and then its elements $(J^2)_{ij} = \sum_{k=1}^N J_{ik} \cdot J_{kj}$.

Let

$$\sum_{j=1}^N J_{ij} =: Q_i \quad (7)$$

be the number of neighbours of lattice site i . From now on we will only consider regular lattices where all sites has the same number of neighbours, hence $Q_i = Q$ for all i . The constant Q is often also called the coordination number.

In mean field approximation, we obtain

$$\langle RI \rangle_1(t) \approx \frac{Q}{N} \langle R \rangle \cdot \langle I \rangle \quad (8)$$

etc. such that the equation system Equation (6) gives a closed ODE system. Approximating the pairs in Equation (6), we obtain the following mean field equations for the SIRI model:

$$\begin{aligned} \frac{d}{dt} \langle S \rangle &= -\beta \frac{Q}{N} \langle S \rangle \langle I \rangle \\ \frac{d}{dt} \langle I \rangle &= \beta \frac{Q}{N} \langle S \rangle \langle I \rangle - \gamma \langle I \rangle + \tilde{\beta} \frac{Q}{N} \langle R \rangle \langle I \rangle \\ \frac{d}{dt} \langle R \rangle &= \gamma \langle I \rangle - \tilde{\beta} \frac{Q}{N} \langle R \rangle \langle I \rangle. \end{aligned} \quad (9)$$

In the ODE system Equation (9), one can study stationary solutions when including birth into the susceptible class and death from all classes. In the stochastic system even then the formal stationary solution only gives disease-free solutions as an absorbing state, since there is always a small probability of extinction in the I class. Hence, spreading experiments or steady import of infected from outside (and then considering the system in the limit of vanishing external import) can help to some extent [20]. See also [8] for another approach facing the problem of an absorbing boundary to obtain a quasi-stationary solution.

In the general system without the approximation of mean field behaviour Equation (6), one has to find a dynamic for the pairs $\langle SI \rangle_1$ and $\langle RI \rangle_1$, which will include triples $\langle SIS \rangle_{11}$ etc. for which in turn dynamics have to be found, including then even higher moments. Pair approximation is the next step after mean field to close the system. In the pair approximation, triples are approximated by an expression which only has means and pairs (for a detailed analysis of the present system in pair approximation see [21,27]). Beyond pair approximations, there are series expansions promising to gain further insights into the present models [22,24].

Taking the constraint $S_i + I_i + R_i = 1$ for local quantities into account (not to be confused with the relation for global quantities $\sum_{i=1}^N S_i + I_i + R_i = N$ giving the total number of host individuals) and thus replacing the set of variables S, I, R by the independent variables, e.g. I, R , hence $S_i = 1 - I_i - R_i$, we obtain for the pairs expectation value $\langle SI \rangle_1$

$$\begin{aligned} \langle SI \rangle_1 &= \left\langle \sum_{i=1}^N \sum_{j=1}^N J_{ij} S_i I_j \right\rangle = \left\langle \sum_{i=1}^N \sum_{j=1}^N J_{ij} (1 - I_i - R_i) I_j \right\rangle \\ &= \left\langle \sum_{j=1}^N I_j \sum_{i=1}^N J_{ij} \right\rangle - \langle II \rangle_1 - \langle RI \rangle_1. \end{aligned}$$

And for regular lattices, hence $\sum_{j=1}^N J_{ij} = Q$, we obtain

$$\langle SI \rangle_1 = Q \langle I \rangle - \langle II \rangle_1 - \langle RI \rangle_1. \quad (10)$$

Inserting Equation (10) into the dynamics for the mean values Equation (6), we obtain

$$\begin{aligned} \frac{d}{dt}\langle I \rangle &= (\beta Q - \gamma)\langle I \rangle - \beta\langle II \rangle_1 + (\tilde{\beta} - \beta)\langle RI \rangle_1 \\ \frac{d}{dt}\langle R \rangle &= \gamma\langle I \rangle - \tilde{\beta}\langle RI \rangle_1 \end{aligned} \tag{11}$$

and as a first result we recover for $\tilde{\beta} = \beta$, i.e. the reinfection being equal to the initial infection, the solution which one obtains in the SIS-system

$$\frac{d}{dt}\langle I \rangle = (\beta Q - \gamma)\langle I \rangle - \beta\langle II \rangle_1. \tag{12}$$

The other limit of the SIRI-model (the SIR limit $\tilde{\beta} = 0$) can, of course, be obtained directly from Equation (6) by inserting $\tilde{\beta} = 0$.

3. Local quantities

Considering local quantities like $\langle I_i \rangle(t)$, which in a continuous space model corresponds to the local density $\psi(x, t)$ with spatial variable x corresponding to i and lattice spacing a from our lattice model going to zero, we obtain

$$\frac{d}{dt}\langle I_i \rangle = \beta \sum_{j=1}^N J_{ij}\langle S_i I_j \rangle - \gamma\langle I_i \rangle + \tilde{\beta} \sum_{j=1}^N J_{ij}\langle R_i I_j \rangle. \tag{13}$$

Since $S_i + I_i + R_i = 1$, in the independent variables I_i and R_i we obtain

$$\frac{d}{dt}\langle I_i \rangle = \beta \nabla^2 \langle I_i \rangle + (\beta Q - \gamma)\langle I_i \rangle - \beta \sum_{j=1}^N J_{ij}\langle I_i I_j \rangle + (\tilde{\beta} - \beta) \sum_{j=1}^N J_{ij}\langle R_i I_j \rangle \tag{14}$$

where we use the discrete version of the diffusion operator

$$\nabla^2 \langle I_i \rangle = \sum_{j=1}^N J_{ij}(\langle I_j \rangle - \langle I_i \rangle). \tag{15}$$

The discretized diffusion operator [5] for any local function f_i is defined as

$$\nabla^2 f_i := \sum_{j=1}^N J_{ij}(f_j - f_i) \tag{16}$$

which in one dimension, e.g. simply gives the well-known expression

$$\begin{aligned} \nabla^2 f_i &= J_{i,i-1}(f_{i-1} - f_i) + J_{i,i+1}(f_{i+1} - f_i) \\ &= f_{i+1} - 2 \cdot f_i + f_{i-1} \end{aligned} \tag{17}$$

for the second derivative. Thus, the dynamics for both mean values is given by

$$\begin{aligned} \frac{d}{dt}\langle I_i \rangle &= \beta \nabla^2 \langle I_i \rangle + (\beta Q - \gamma)\langle I_i \rangle - \beta \sum_{j=1}^N J_{ij}\langle I_i I_j \rangle + (\tilde{\beta} - \beta) \sum_{j=1}^N J_{ij}\langle R_i I_j \rangle \\ \frac{d}{dt}\langle R_i \rangle &= \gamma\langle I_i \rangle - \tilde{\beta} \sum_{j=1}^N J_{ij}\langle R_i I_j \rangle. \end{aligned} \tag{18}$$

Further equations for $d/dt \langle I_i I_j \rangle$ and $d/dt \langle R_i I_j \rangle$ have to be calculated explicitly from the master equation.

In Equation (18) the drift and diffusion terms, well known from partial differential equations (PDEs), are recovered as well as the expected reaction terms. Of course, creation from one particle at one site to a neighbouring site and subsequent annihilation on the original site can be interpreted as diffusion (remark in [17]).

Ignoring local correlations, or equivalently looking at a coarse grained version of Equation (18), we can, e.g. approximate

$$\langle R_i I_j \rangle \approx \langle R_i \rangle \cdot \langle I_i \rangle \quad (19)$$

then leaving the summation over the adjacency matrix elements $\sum_{j=1}^N J_{ij} = Q$ gives a closed equation system for the local dynamics

$$\begin{aligned} \frac{d}{dt} \langle I_i \rangle &= \beta \nabla^2 \langle I_i \rangle + (\beta Q - \gamma) \langle I_i \rangle - \beta Q \langle I_i \rangle \langle I_i \rangle + (\tilde{\beta} - \beta) Q \langle R_i \rangle \langle I_i \rangle \\ \frac{d}{dt} \langle R_i \rangle &= \gamma \langle I_i \rangle - \tilde{\beta} Q \langle R_i \rangle \langle I_i \rangle. \end{aligned} \quad (20)$$

This system can be interpreted as a discretized version of a PDE system

$$\begin{aligned} \frac{\partial}{\partial t} \psi(\underline{x}, t) &= \beta \nabla^2 \psi + (\beta Q - \gamma) \psi - \beta Q \psi^2 + (\tilde{\beta} - \beta) \phi \psi \\ \frac{\partial}{\partial t} \phi(\underline{x}, t) &= \gamma \psi - \tilde{\beta} Q \phi \psi. \end{aligned} \quad (21)$$

and simulated as such, see Figure 2(a) and (b) in good comparison with Figure 1(a) and (b). Remember that we are analysing diffusive spreading, hence relations like $I_i + S_j \xrightarrow{\beta} I_i + I_j$ and $I_i + R_j \xrightarrow{\tilde{\beta}} I_i + I_j$ for neighbouring lattice sites i and j and single site transitions like $I_i \xrightarrow{\gamma} S_i$, etc. so that the lattice neighbourhood describes contacts between host individuals and not physical movement of such individuals on an otherwise empty lattice. Hence only the infectives spread due to infecting other lattice sites and only this gives a diffusion term in the PDE for the infected, whereas none appears for the recovered class or the susceptibles.

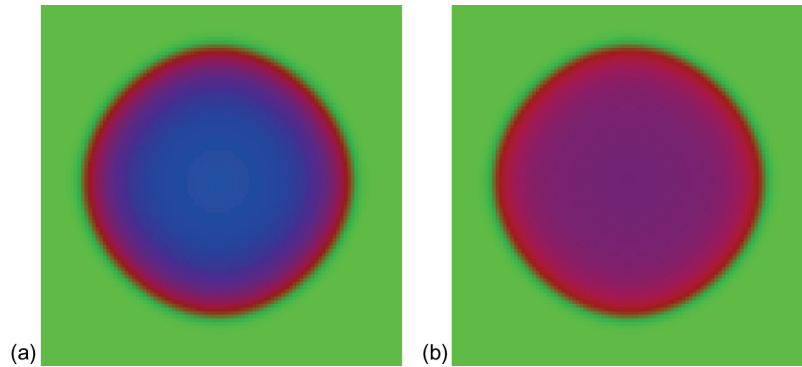


Figure 2. (Available in colour online) (a) Simulation of the PDE system with parameters as previously used in Figure 1(a) for the stochastic system, i.e. $\beta = 2$, $\gamma = 1$ and $\tilde{\beta} = 0.1$. The colour code is comparable as in Figure 1, but now ratios between the classes are possible, so that, e.g. a proportion of recovered (blue) in an area mainly occupied by infected (red) results in a violet colour. The annular growth again is well visible. (b) Simulation of the PDE system, this time with parameters as previously used in Figure 1(b) for the stochastic system, hence $\beta = 0.1$. Now the compact like growth is observed.

The mean field type approximation Equation (19) is a good approximation whenever the covariance is smaller than the product of means ($\langle R_i I_j \rangle - \langle R_i \rangle \cdot \langle I_j \rangle < \langle R_i \rangle \cdot \langle I_j \rangle$), a version of the Ginzburg criterium for the region of validity of the mean field approximation. Outside the critical region of the phase transitions or above the upper critical dimension (for DP that is dimension 4, for DyP it is 6) the mean field approximation is appropriate. Since we are interested in the qualitative picture of the phase diagram (rather than the critical behaviour at the phase boundaries, as also show our simulation parameters), the mean field approximation is sufficient here.

In the spatial system, we have, in two and higher dimensions, annular growth near the SIR-limit of the SIRI-system and compact growth for supercritical values around the SIS-limit [18]. Grassberger *et al.* [18] considered a two-dimensional spatial system (and briefly mention the degenerate one-dimensional case), whereas Dammer and Hinrichsen [6] in 2004 investigate the partial immunization system for three to six spatial dimensions, including the phase diagrams.

We have also recently studied the phase transition lines for the spatially stochastic SIRI model in continuous time (see forthcoming article [18]), and obtain qualitatively similar results as found in the time discrete version by Grassberger *et al.* [18].

4. Mean field model: SIRI with reintroduced susceptibles

To obtain any useful insight into the mean field stationary state behaviour of the SIRI model, we investigate the model with the additional reintroduction of susceptibles. This can be done in various ways, e.g. with death from all classes S , I and R and reintroduction to the S class, i.e. birth into susceptibility [14] or by just taking the original SIR transition α from recovered to susceptibles.

So we consider the following reaction scheme:



with the additional transition from R to S with rate α .

The reaction scheme results in the master equation of the following form:

$$\begin{aligned}
 &\frac{d}{dt} p(S_1, I_1, R_1, S_2, I_2, R_2, \dots, R_N, t) \\
 &= \sum_{i=1}^N \beta \left(\sum_{j=1}^N J_{ij} I_j \right) (1 - S_i) p(S_1, I_1, R_1, \dots, 1 - S_i, 1 - I_i, R_i \dots, R_N, t) \\
 &+ \sum_{i=1}^N \gamma (1 - I_i) p(S_1, I_1, R_1, \dots, S_i, 1 - I_i, 1 - R_i \dots, R_N, t) \\
 &+ \sum_{i=1}^N \tilde{\beta} \left(\sum_{j=1}^N J_{ij} I_j \right) (1 - R_i) p(S_1, I_1, R_1, \dots, S_i, 1 - I_i, 1 - R_i \dots, R_N, t)
 \end{aligned}$$

$$\begin{aligned}
& + \sum_{i=1}^N \alpha(1 - R_i) p(S_1, I_1, R_1, \dots, 1 - S_i, I_i, 1 - R_i, \dots, R_N, t) \\
& - \sum_{i=1}^N \left[\beta \left(\sum_{j=1}^N J_{ij} I_j \right) S_i + \gamma I_i + \tilde{\beta} \left(\sum_{j=1}^N J_{ij} I_j \right) R_i + \alpha R_i \right] \cdot p(\dots S_i, I_i, R_i \dots). \quad (23)
\end{aligned}$$

For the mean total number of susceptible, infected and recovered hosts, we obtain (for explicit calculations, see [21])

$$\begin{aligned}
\frac{d}{dt} \langle S \rangle &= \alpha \langle R \rangle - \beta \langle SI \rangle_1 \\
\frac{d}{dt} \langle I \rangle &= \beta \langle SI \rangle_1 - \gamma \langle I \rangle + \tilde{\beta} \langle RI \rangle_1 \\
\frac{d}{dt} \langle R \rangle &= \gamma \langle I \rangle - \alpha \langle R \rangle - \tilde{\beta} \langle RI \rangle_1
\end{aligned} \quad (24)$$

again involving pairs of infected and susceptibles or pairs of infected and recovered. Either additional dynamic equations for these pairs have to be derived from the master-equation or being approximated with the mean field assumption.

The mean field approximation is

$$\begin{aligned}
\frac{d}{dt} \langle S \rangle &= \alpha \langle R \rangle - \beta \frac{Q}{N} \langle S \rangle \langle I \rangle \\
\frac{d}{dt} \langle I \rangle &= \beta \frac{Q}{N} \langle S \rangle \langle I \rangle - \gamma \langle I \rangle + \tilde{\beta} \frac{Q}{N} \langle R \rangle \langle I \rangle \\
\frac{d}{dt} \langle R \rangle &= \gamma \langle I \rangle - \alpha \langle R \rangle - \tilde{\beta} \frac{Q}{N} \langle R \rangle \langle I \rangle.
\end{aligned} \quad (25)$$

This ODE system can be studied in the scaled quantities, time changed to $\tau := t/\gamma$ and consequently

$$\rho := \beta Q/\gamma, \quad \varepsilon := \alpha/\gamma \quad (26)$$

and the ratio of infectivities given by

$$\sigma := \tilde{\beta}/\beta. \quad (27)$$

Further, we consider densities of susceptibles, infected, and recovered, hence $s := \langle S \rangle/N$, $i := \langle I \rangle/N$. Then with $\langle R \rangle/N = 1 - s - i$, we obtain the two-dimensional ODE system

$$\begin{aligned}
\frac{d}{d\tau} s &= \varepsilon(1 - s - i) - \rho s i \\
\frac{d}{d\tau} i &= \rho i(s + \sigma(1 - s - i)) - i
\end{aligned} \quad (28)$$

to compare with the formulation in [14]. The stationary solution is either $i_1^* := 0$ or

$$i_2^* := -\frac{r}{2} + \sqrt{\frac{r^2}{4} - q} \quad (29)$$

with

$$r := \frac{1}{\rho\sigma}(1 - \rho\sigma + \varepsilon) \quad \text{and} \quad q := \frac{\varepsilon}{\rho^2\sigma}(1 - \rho) \quad (30)$$

In original coordinates this gives $\langle I \rangle_1^* = 0$ and $(\langle I \rangle_2^*/N)^2 + r \cdot (\langle I \rangle_2^*/N) + q = 0$ with

$$r = \left(\frac{\gamma + \alpha}{\tilde{\beta}Q} - 1 \right) \quad \text{and} \quad q = \frac{\alpha}{\tilde{\beta}Q} \left(\frac{\gamma}{\beta Q} - 1 \right). \quad (31)$$

At $\rho = 1$, which is the classical epidemiological threshold quantity and also known as the basic reproduction number R_0 [3], the solutions i_1^* and i_2^* meet each other, i.e. $i_2^* = 0$, coinciding with $q = 0$. And at $\varepsilon = 0$, we obtain another change of regime with $r = 0$, which is slightly more subtle in the first inspection. This change of regime is the reinfection threshold. The whole concept of this second threshold behaviour was questioned in [4] as a comment to [14]. They in turn justified the concept of the reinfection threshold by looking at the behaviour of the basic mean field model under vaccination, showing that the first threshold can be shifted towards larger ρ values by the introduction of vaccination, but cannot be shifted beyond the second threshold by any means of vaccination [15]. Here we demonstrate that in the SIRI model with reintroduced susceptibles (in our version of the transition from recovered to susceptibles with rate α), the reinfection threshold appears in the limit of α decreasing to zero as a sharp threshold.

The threshold behaviour is in analogy to the Ising spin threshold for example in the limit of vanishing external magnetic field. So we conclude that the reinfection threshold does exist in the sense that any other threshold in physical phase transitions exists or any bifurcation behaviour in mean field models exist. From the studies of spatial stochastic epidemics with partial immunization [6,18], we even know that the mean field threshold behaviour is qualitatively describing also the threshold behaviour of spatial models, namely the transition between annular growth and compact growth.

In the following, we just analyse the mean field behaviour of the SIRI-model with α -interaction and investigate the limiting behaviour of vanishing α , finding a sharp transition at $1/\sigma$, the reinfection threshold.

In Figure 3(b) the solution $i_2^* = -r/2 + \sqrt{(r^2/4) - q}$, full line, is plotted against the curves $-r$ and its modulus $|r|$. For non-zero values of ε , the solution i_2^* changes from negative to positive at $\rho = 1$, while in the limit of ε tends to zero the curves for $-r$ and $|r|$ change at $\rho = 1/\sigma$. Therefore, in this limiting case, the solution i_2^* given by

$$i_2^* = \frac{-r + |r|}{2}$$

also changes from negative to positive. This qualitative change at $\rho = 1/\sigma$ is the reinfection threshold as predicted by Gomes *et al.* [14].

When plotting the stationary state solution as function of both independent parameters ρ and ε (Figure 4), the threshold behaviour for vanishing $\varepsilon = 0$ is clearly visible, whereas for finite ε the curves for $I^*(\rho)$ are smoothed out around the reinfection threshold.

This behaviour is qualitatively very similar to what happens in magnetic models. The Figure 4, which we have just discussed, can be well compared with the mean field solution of the Ising model, where the magnetization $m(V, h)$, as function of the coupling strength V between spins (analogue to infectivity β in epidemiology) and external magnetic field h (analogue to waning immunity α), shows a similar threshold behaviour for positive but vanishing external magnetic field $h \rightarrow 0$ as shown in Figure 5 (see, e.g. [2] or [26] for a detailed description). Hence, the bifurcation point for vanishing waning immunity α or vanishing external magnetic field h extends qualitatively into the region for small parameter values of these quantities and remains as a qualitative jump in dynamic behaviour. In nature you never find any magnetic system with exactly zero external magnetic field, but of course the phase transition can be studied experimentally because of the extension into the small h region. In the epidemiological system we have, in addition, another threshold between extinction of disease and persistence which is a bifurcation point for non-vanishing α . Hence from

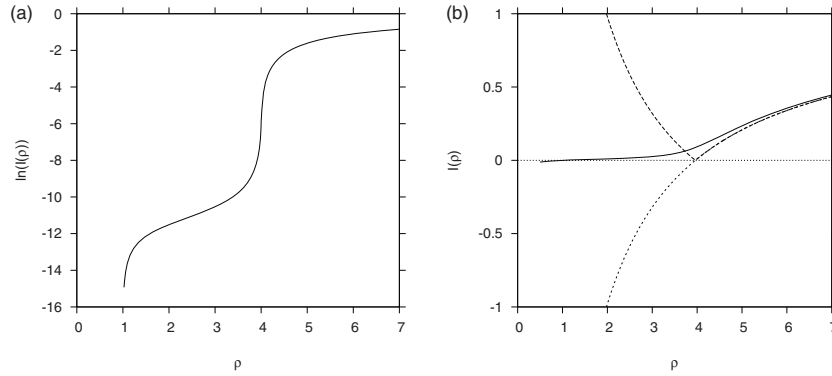


Figure 3. (a) The conventional picture of the reinfection threshold, in semi-logarithmic plot [14]. We just use the parameter α instead of the death out of all classes and birth into susceptibles. The value for $\sigma = 1/4$ will also be used in Figure 3(b), and $\varepsilon = 0.00001$ to demonstrate a clear threshold behaviour around $\rho = 1/\sigma$. (b) The solution $i_2^* = -r/2 + \sqrt{(r^2/4) - q}$, full line is plotted against the curves $-r$ and its modulus $|r|$. While i_2^* changes from negative to positive at $\rho = 1$, the curves for $-r$ and $|r|$ change at $\rho = 1/\sigma$ for vanishing or small ε . This qualitative change at $\rho = 1/\sigma$ is the reinfection threshold. Parameters are $\sigma = 1/4 = 0.25$ and $\varepsilon = 0.01$.

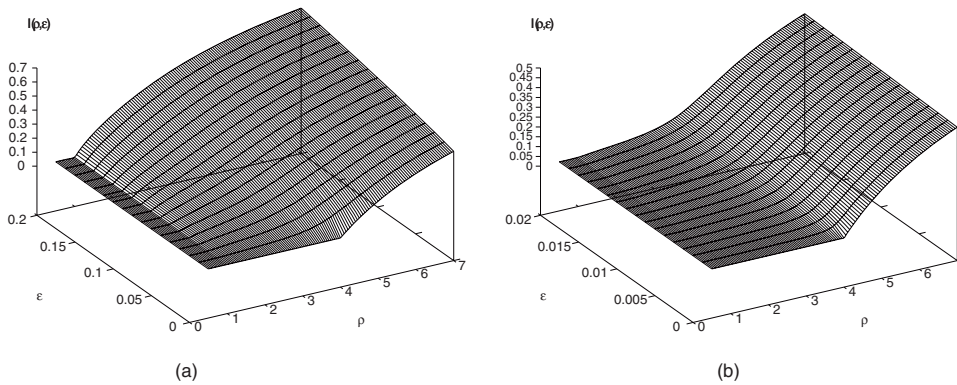


Figure 4. (a) The stationary value of the number of infected individuals with both parameters ρ and ε shows for high values of ε , here up to $\varepsilon = 0.2$, just a threshold behaviour at $\rho = 1$ and for vanishing ε the threshold at $\rho = 1/\sigma = 4$ (better seen in (b)), since σ was fixed to be $\sigma := 1/4$. The continuous change from behaviour dominated by the first threshold $\rho = 1$ for $\varepsilon = 0.2$ to the behaviour around the second threshold $\rho = 1/\sigma$ for $\varepsilon = 0$ can be seen here. (b) The enlargement of the graphic in (a) for small values of ε , here increasing only up to $\varepsilon = 0.02$.

an operational point, we have clearly two thresholds in the reinfection model for small waning immunity, as observed in Figure 4.

It is interesting to see that for large values of, e.g. $\varepsilon = 0.2$, the behaviour of I^* is completely dominated by the simple threshold behaviour around $\rho = 1$, the reinfection threshold not visible even qualitatively (Figure 4(a)). In contrast, for vanishing $\varepsilon = 0$, there is only the qualitative behaviour left from the behaviour around the second threshold $\rho = 1/\sigma$. The change between these two extremes is quite continuous, as can be seen in Figure 4(a). However, close to the reinfection threshold $\rho = 1/\sigma$, the solutions for I^* for small ε are a smoothed out version of that threshold, as better seen in Figure 4(b).

Finally, we look at the phase diagram in the original coordinates, β and $\tilde{\beta}$, as opposed to the scaled variables ρ and ε , remembering the definitions for these, Equation (26). The phase diagram for the mean field model for the two-dimensional case, $Q = 4$ neighbours is shown in Figure 6. This phase diagram can be compared with the phase diagrams of the epidemic process with partial immunization on a d -dimensional cubic lattice investigated by Dammer and Hinrichsen [6], where

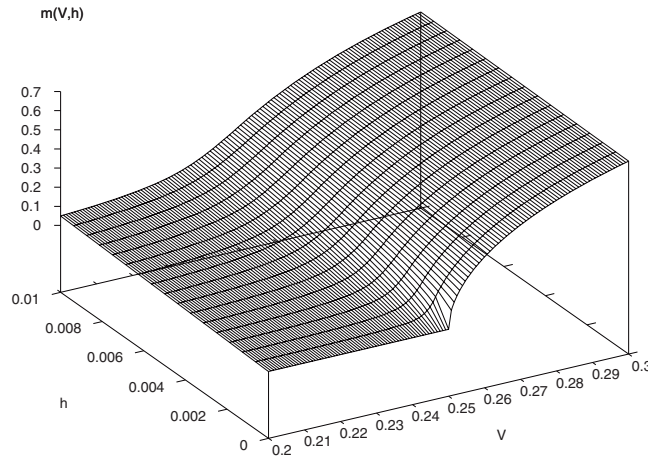


Figure 5. The state equation in its natural variables $m(V, H)$ as function of V and h as the independent variables. The magnetization m is obtained via Newton's method from $\text{artanh}(m) - 2 \cdot QVm - h =: f(m) = 0$. The critical threshold for vanishing external magnetic field is clearly visible, whereas positive external field results in a smoothing of the curves around the threshold.

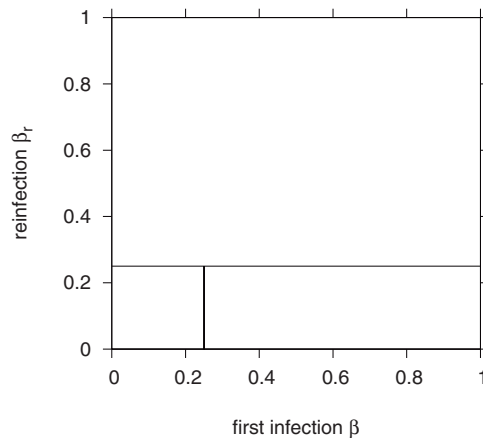


Figure 6. Mean field phase diagram for the SIRS model with reintroduced susceptibles. It comprises three different phases, the no-growth, annular growth and compact growth, and is in good agreement with the phase diagrams presented in [6], obtained with higher dimensional spatial stochastic simulations. For consistency with the previously investigated two-dimensional case, we set $Q = 4$ neighbours.

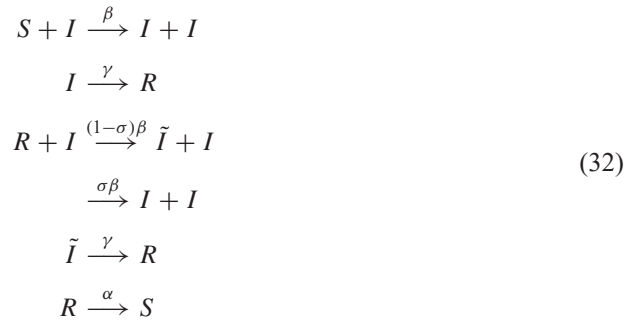
the mean field behaviour is approached by spatial stochastic simulations for $d = 3, 4, 5, 6$. The threshold at $\rho = 1$ gives the critical value for β with $\beta = \gamma/Q$, the vertical line corresponding to the transition between no-growth and annular growth. The threshold for $\rho = 1/\sigma$ gives the critical value for $\tilde{\beta}$ with $\tilde{\beta} = \gamma/Q$, the horizontal line corresponding to the transition between annular growth and compact growth. In the limit of vanishing ε , this line defines the reinfection threshold.

5. Generic appearance of the concept of reinfection threshold

The concept of the reinfection threshold turns out to be quite generically appearing in various models of multi-strain dynamic epidemiological models (generic in the sense of wider appearance than just appearing in the above-mentioned model).

Here we look at a simplified version of existing influenza models, namely where reinfection of the R class can happen, but mostly only leads to a boost in immunity without creating enough pathogens to be infectious, a class we label with \tilde{I} , with transition rate $(1 - \sigma)\beta$, whereas only in few cases a new infected I is caused, with rate $\sigma\beta$. On first inspection it is not obvious that the reinfection threshold also appear in this more complicated model. But the analysis shows that the reinfection threshold is not only present in this model, but does not even change the position where it appears.

The reaction scheme for the simplified influenza model is



with the reaction between R and I has two reaction channels, the one to $\tilde{I} + I$ and the other to $2I$. The mean field equations hence is

$$\begin{aligned}
 \frac{d}{dt}\langle S \rangle &= \alpha\langle R \rangle - \beta\frac{Q}{N}\langle S \rangle\langle I \rangle \\
 \frac{d}{dt}\langle I \rangle &= \beta\frac{Q}{N}\langle S \rangle\langle I \rangle - \gamma\langle I \rangle + \sigma\beta\frac{Q}{N}\langle R \rangle\langle I \rangle \\
 \frac{d}{dt}\langle R \rangle &= \gamma\langle I \rangle - \alpha\langle R \rangle - \sigma\beta\frac{Q}{N}\langle R \rangle\langle I \rangle - \omega\beta\frac{Q}{N}\langle R \rangle\langle I \rangle + \psi\langle \tilde{I} \rangle \\
 \frac{d}{dt}\langle \tilde{I} \rangle &= \omega\beta\frac{Q}{N}\langle S \rangle\langle I \rangle - \psi\langle \tilde{I} \rangle
 \end{aligned} \tag{33}$$

where, for reasons of easier analysis, we have replaced $(1 - \sigma)$ by ω and the recovery rate γ from the sub-infective infected \tilde{I} by ψ .

Again we find solutions $\langle I \rangle_1^* = 0$ and a quadratic equation $(\langle I \rangle_2^*/N)^2 + r \cdot (\langle I \rangle_2^*/N) + q = 0$ with in this case

$$r = \left(\frac{\gamma + \alpha}{\beta Q \left(\sigma + \omega \frac{\gamma}{\psi} \right)} - \frac{\sigma}{\sigma + \omega \frac{\gamma}{\psi}} \right) \tag{34}$$

and

$$q = \frac{\alpha}{\sigma\beta Q} \left(\frac{\sigma}{\sigma + \omega \frac{\gamma}{\psi}} \right) \cdot \left(\frac{\gamma}{\beta Q} - 1 \right) \tag{35}$$

which comes back to Equation (31) when setting the transition ω to zero, as expected.

But also when setting $\omega := (1 - \sigma)$ and $\psi := \gamma$, as given in the reaction scheme, we obtain

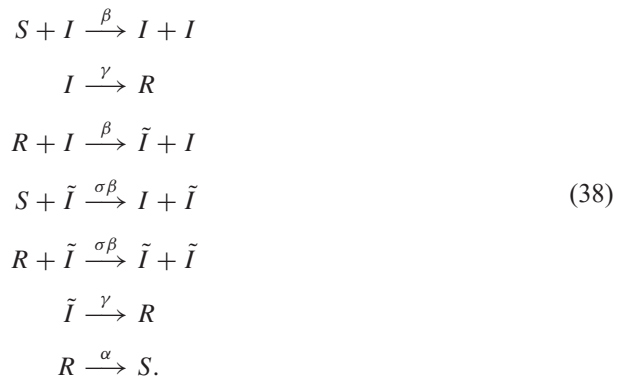
$$\sigma + \omega \frac{\gamma}{\psi} = 1 \tag{36}$$

and hence very similarly to Equation (31)

$$r = \left(\frac{\gamma + \alpha}{\beta Q} - \sigma \right), \quad q = \frac{\alpha}{\beta Q} \left(\frac{\gamma}{\beta Q} - 1 \right) \tag{37}$$

with surprisingly the thresholds at the same positions as in the original model, namely from $q = 0$ at $((\beta Q)/\gamma) = 1$ and for vanishing $\alpha = 0$ from $r = 0$ the reinfection threshold at $((\beta Q)/\gamma) = 1/\sigma$.

Partial immunization is implemented in this and previous papers [14,15] as a reduction in the susceptibility to reinfection applying to individuals who have been previously infected (or vaccinated). However, we could think of partial immunization acting in slightly different ways. As we will see, the reinfection threshold is robust to some changes in model structure but not to all, emphasizing the importance of awareness of the associated effects before settling on a specific model for a given disease. Suppose that rather than preventing infection, partial immunization modulates the infectious load of affected individuals making them less infectious to others. This mechanism is implemented by the following model structure:



This model also exhibits a reinfection threshold and associated effects when $\rho = 1/\sigma$. The formulations of reduced susceptibility and reduced infectivity have been used interchangeably in more elaborate models describing the transmission dynamics of multi-strain pathogens and demonstrated to lead to similar behaviour [9].

If, however, we assume that the effect of immunization is to provide an all-or-nothing protection (i.e. randomly protects a fraction $(1 - \sigma)$ of exposed individuals, while the remaining σ have no protection at all) then no reinfection threshold is observed. The basic model structure is



This mechanism has also been extended to model multi-strain pathogens showing significant differences in behaviour when compared with the previous two alternatives [7].

Besides the alternative formulations of partial immunization and the extension to multi-strain pathogens, these models have been combined with processes that are specific to different diseases leading to a variety of effects. In tuberculosis, the inclusion of a latency class does not significantly alter the results present here. This is, perhaps, the prime application of the results concerning variable efficacy of vaccination programmes [13]. In pertussis, besides reducing susceptibility to (re)infection, partial immunization has the additional effect of reducing disease symptoms. In this case, we observe that maximum levels of severe disease incidence are expected at intermediate levels of transmission [1]. This is because high transmission settings sustain higher levels of immunity through repeated boosting, which ultimately leads to lower levels of severe disease. In influenza, we investigate the possible effects of reinfection thresholds in the processes of drift and shift evolution [12] and investigate the robustness of the results to varying the contact structure between hosts [23].

6. Summary

We have considered a spatial stochastic epidemiological model with partial immunization. For the classical SIRI model, where the individuals can be susceptibles, infecteds, recovered and again infected, we include one more transition from recovered to susceptibles. We present a rigorous analysis for this SIRI model in the mean field approximation and observe two different threshold regions. In the limiting case when no transitions from recovered to susceptibles occur, the second region becomes a sharp threshold, as predicted by Gomes *et al.* [14]. We further support the existence of the reinfection threshold showing the appearance of this phenomena in different epidemiological models with partial immunization. We expect that the reinfection threshold plays a fundamental role in the epidemiology of many infectious diseases and should be further explored both theoretically and in practical applications. In essence, it is a powerful source of variability explaining discrepancies between data collected in populations with different transmission intensities. Moreover, it brings out the need to carefully consider the characteristics of specific population when designing control programmes.

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