HETEROGENEITY FACILITATES PERSISTENT INFECTION

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Abstract

In this paper we review some recent results obtained in our research group, on the general question of the emergence of persistent infection in a closed region [Agrawal, Moitra & Sinha (2017)]. Specifically, the disease progression of the individuals is given by the Susceptible-Infected-Refractory-Susceptible (SIRS) cycle, and we investigate different degrees of heterogeneity in the initial population by considering varying fractions of the initial population in different disease compartments, and by varying the spread in the phases of disease progression among the individuals. Our central observation is that when the initial population is uniform, consisting of individuals at the same stage of disease progression, infection arising from a contagious seed does not persist. However when the initial population consists of randomly distributed refractory and susceptible individuals, a single source of infection can lead to sustained infection in the population, as heterogeneity facilitates the desynchronization of the phases in the disease cycle of the individuals. In particular, we show that the infection eventually dies out when the entire initial population is susceptible, while even a few susceptibles among an heterogeneous refractory population gives rise to a large persistent infected set.

Key words

SIRS Model, Cellular automata, Persistence, Heterogeneity

1 Introduction

How a disease spreads in a population is a question of considerable interest and practical relevance, and consequently has seen extensive research interest over the years [Heathcote (1976); Cliff & Haggett (1984)]. Attempts to understand the various dynamical aspects of disease spreading has led to the exploration of various classes of models with features of infectious dynamics [Rhodes & Anderson (1996); Earn *et al.* (2000); Kuperman & Abramson (2001); Gade and Sinha (2005); Kohar & Sinha (2013)].

In this work we will explore the following crucial question, that has not seen much focus yet: *what population compositions are conducive to the emergence of long-term persistence of infection in a population?* In order to address this question we will consider cellular-automata based descriptions of infection spreading, for a disease that has temporary immunity [Kuperman & Abramson (2001); Gade and Sinha (2005)]. We will consider initial populations with varying degrees of global heterogeneity, reflecting increasing diversity in the condition of the individuals comprising the population. Our attempt will be to ascertain the influence of this heterogeneity on the persistence of infection.

2 Model

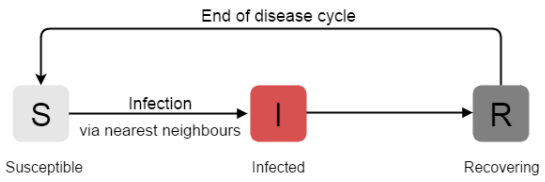

Figure 1. Schematic Representation of the SIRS cycle. The color scheme in all figures is as follows: black represents the refractory state (R); white represents the susceptible state (S); red represents the infected state (I).

In this work we will consider a well known model for non-fatal communicable disease progression is the Susceptible-Infected-Refractory-Susceptible (SIRS) cycle. This model appropriately describes the progression of diseases such as small pox, tetanus, influenza, typhoid fever, cholera and tuberculosis. Specifically, we consider a cellular automaton model

of the SIRS cycle, as shown in Fig. 1 [Kuperman & Abramson (2001); Gade and Sinha (2005); Kohar & Sinha (2013)]. In this model of disease progression, time t evolves in discrete steps, with each individual, indexed by (i, j) on a 2 dimensional lattice, characterized by a state variable $\tau_{i,j}$

$$\tau_{i,j}(t) = 0, 1, \ldots, \tau_I + \tau_R \tag{1}$$

describing its *phase* in the cycle of the disease [Kuperman & Abramson (2001)]. Here $\tau_I + \tau_R = \tau_0$, where τ_0 signifies the total length of the disease cycle.

The dynamics of the state $\tau_{i,j}(t)$ is given by the following transition rules:

$$\left.\begin{array}{ll} \tau_{i,j}(t+1) = \tau_{i,j}(t) + 1 & \text{if } 1 \leq \tau_{i,j}(t) < \tau_0 \\ = 0 & \text{if } \tau_{i,j}(t) = \tau_0 \end{array}\right\} \tag{2}$$

With no loss of generality we consider $\tau_I = 4$; $\tau_R = 9$; $\tau_0 = 13$ and a lattice of size 100×100.

Notice that there are two distinct features determining the local state of the individuals. The first is the transition from the susceptible to the infected state determined by the state of the immediate neighbourhood, which is *stochastic* in nature and dependent on the distribution of initial states of the individuals in the population. The second feature is the *deterministic* disease cycle: I $\rightarrow$ R $\rightarrow$ S. This interplay of a probabilistic feature and a deterministic cycle shapes the dynamics of disease in the population.

2.1 Heterogeneity

In the present study, we consider heterogeneity to be non-uniformity in the states of the individuals. This may be characterized in different ways. Consider a generic initial population patch comprised of a random admixture of susceptible, infected and refractory individuals, given by initial fractions S_0, I_0 and R_0. So, if either S_0, I_0 or R_0 tends to one, we have a homogeneous situation where almost all individuals are in the same state, namely almost all susceptible ($S_0 \rightarrow 1$), or almost all infected ($I_0 \rightarrow 1$), or almost all recovered ($R_0 \rightarrow 1$). Increasing deviations from this reflects increasing heterogeneity in the population, as it implies an increasing spread among different disease compartments. Further, a source of heterogeneity arises from non-uniform stages of disease within a disease compartment. We therefore study the influence of heterogeneity in individual phases within the refractory subpopulation on the persistence of infection in the population as well.

3 Observations

Having described the dynamics of the model, and having defined heterogeneity in the context of the present study, we first focus on infection spreading patterns.

3.1 Non-persistent Infection in a Homogeneous Susceptible Population

We observe that starting from a homogeneous initial condition, such as all susceptible (Fig. 2), the system simply undergoes a relaxation oscillation, and infection does not persist.

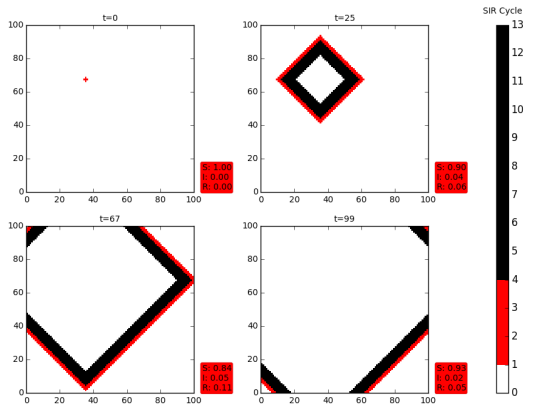

Figure 2. Snapshots at times $t = 0, 25, 67, 99$, showing the spread of infection from one infected individual at $t = 0$, in a homogeneous susceptible initial population (i.e. $S_0 \sim 1$, $R_0 = 0$, $I_0 \sim 0$). The color bar bar shows the relative lengths of the susceptible (S), infected (I) and refractory (R) stages in the disease cycle, where $\tau_I = 4$, $\tau_R = 9$ and the total disease cycle τ_0 is 13 (see text). The red box shows the fraction of S, I and R individuals in the population at that instant of time [Agrawal, Moitra & Sinha (2017)].

The key factor in infection spreading is the contact of susceptible individuals with infected ones. It is clear that such an interaction takes place only at the outer edge of the wave of infection, while the inner boundary of the infected zone is contiguous only to refractory individuals. So the infection only spreads outwards, and does not move back into the interior of the lattice again.

3.2 Persistent infection in Heterogeneous Populations

Next we investigate the infection spread in the more realistic scenario where both refractory ($\tau_{i,j} > \tau_I$) and susceptible individuals ($\tau_{i,j} = 0$) are present in the initial population, and are randomly distributed spatially. We first consider the case where the refractory individuals have phases $\tau_{i,j} = \tau_I + 1$, namely, they are at the start of the refractory stage of the disease cycle. We investigate the persistence of infection in heterogeneous populations, with the initial state having (a) a single seed of infection (Fig. 3) and (b) varying initial fractions of infected individuals (I_0) (Fig. 4). In both scenarios, we analyze the effect of varying S_0 and R_0 on the persistence of infection.

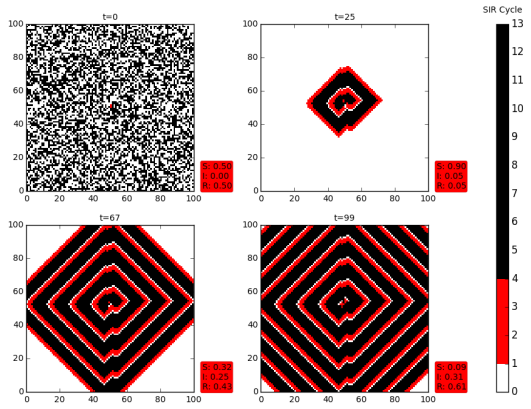

Figure 3. Snapshots of the infection spreading pattern in a heterogeneous population comprising initially of a random mixture of equal numbers of susceptible and refractory individuals ($S_0 \sim 0.5$, $R_0 \sim 0.5$ and $I_0 \sim 0$), with one infected individual at $t = 0$. Here the refractory individuals have phases $\tau_{i,j} = \tau_I + 1$ (namely, they are at the start of the refractory stage of the disease cycle). Interestingly, the spatially random population evolves into a more regular pattern after a short transient time [Agrawal, Moitra & Sinha (2017)].

It is worth noticing that some of these spreading patterns are reminiscent of coalescing and interacting spiral waves initiated by local inhomogeneity in a uniform background.

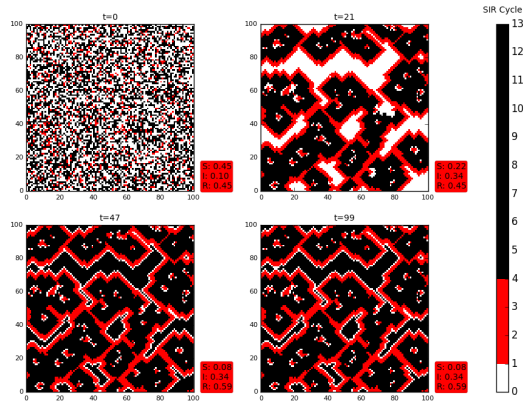

Figure 4. Snapshots of the infection spreading pattern in a heterogeneous population comprising initially of a random mixture of individuals, with $S_0 = R_0$ and $I_0 = 0.1$ [Agrawal, Moitra & Sinha (2017)].

Next we focus on the time evolution of an initial population consisting of a random mixture of S, I and R states. A typical random initial condition is shown in Fig. 4, with the initial fraction of infected sites I_0 being one-tenth and the initial fraction of susceptibile and refractory individuals being equal (i.e. $S_0 = R_0$).

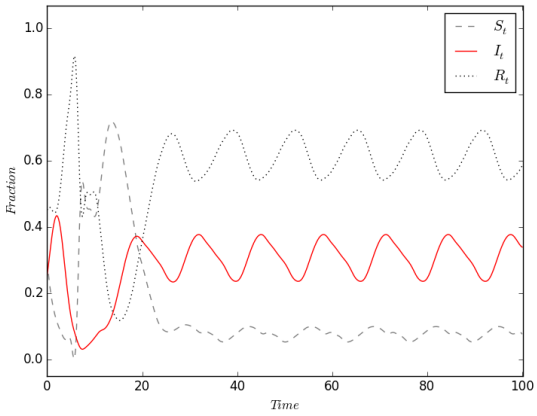

Figure 5. Time evolution of I_t, S_t, R_t, in a heterogeneous population comprising initially of a random mixture of individuals, with $S_0 = R_0$ and $I_0 = 0.1$.

Here too we find that infection is sustained. Further, interestingly, it is clear that there is an *approximate recurrence of the fractions (Fig. 5) and the complex patterns of infected individuals in the population*.

4 Results

We now attempt to gauge the statistically significant trends in I_t, by averaging the fraction of infected individuals at asymptotic time t, arising from a wide range of random initial configurations at time $t = 0$. We denote this by $\langle I_t \rangle$. In terms of this quantity, persistent infection is indicated by a non-zero value. However, after sufficient transient timesteps, if $\langle I_t \rangle$ is zero, it indicates that the infection has died out. So $\langle I_t \rangle$ can serve as an order parameter for the transition to sustained infection in a population.

4.1 Dependence of persistence of infection on the initial fraction of susceptibles

For fixed τ_I and τ_0 we have calculated $\langle I_t \rangle$, for different initial fractions of susceptible individuals S_0, and a *single* infectious seed. We explore the full possible range of $S_0 \in [0, 1]$, where $S_0 = 0$ signifies a population comprised entirely of refractory individuals who are immune to infection initially, and $S_0 = 1$ implies an initial population comprised entirely of individuals susceptible to infection.

The results obtained from a large sample of initial states is shown in Fig. 6, and it is evident from there that $\langle I_t \rangle$ is *very low for both high and low* S_0, peaking around $S_0 \sim 0.65 - 0.75$. Namely, homogeneous initial populations where all individuals are immune ($S_0 = 0$), or all are susceptible to disease ($S_0 = 1$),

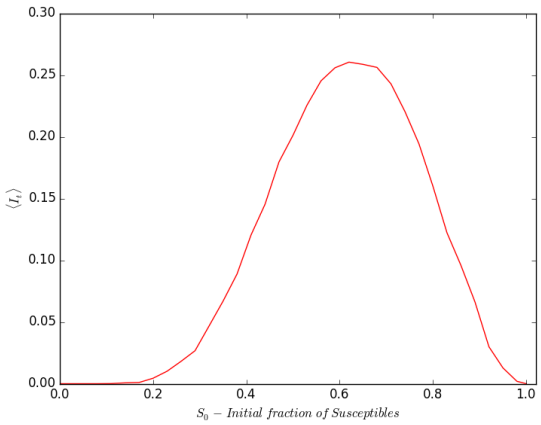

Figure 6. Variation of $\langle I_t \rangle$ (after transience) with respect to the fraction of susceptible individuals in the initial population S_0, arising from the presence of a single infected individual at time $t = 0$. Here I_t is averaged over 10^3 realizations of the initial population on the lattice. The specific case of a 100×100 lattice is displayed. However note that different lattice sizes yield the same result [Agrawal, Moitra & Sinha (2017)].

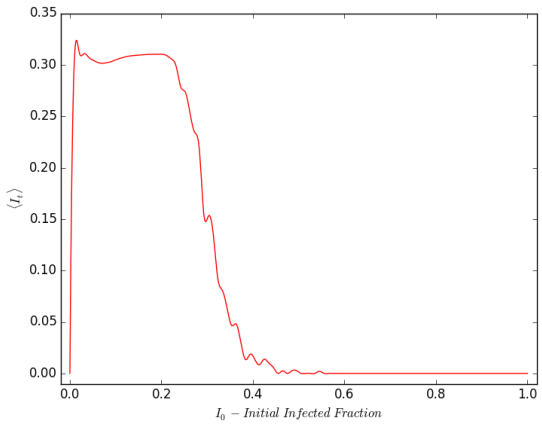

Figure 7. Variation of $\langle I_t \rangle$ (after transience) with respect to the initial fraction of infected individuals I_0 in the population, and $S_0 = R_0$. I_t is averaged over 10^3 initial realizations. The specific case of a 100×100 lattice is displayed. However note that different lattices sizes yield the same result [Agrawal, Moitra & Sinha (2017)].

do not yield persistent infection. Rather, mixed populations lead to most sustained infection, with persistently high numbers of infected individuals.

4.2 Dependence of persistence of infection on the initial fraction of infecteds

We consider an ensemble of initial conditions, with specific $I_0 \in [0, 1]$, S_0 and R_0 and find the time averaged I_t, after long transience for each realization. The ensemble average of this quantity is displayed in Fig. 7. Notably, we find that there is a definite *window of persistence* over the range of I_0, where the infection never dies down and the fraction of infected individuals in the population is reasonably high on an average.

The transition to persistent infection is sharp and occurs at $I_0 \to 0$. This implies that *the infection can spread and persist even when there is only a single infected individual in the initial population*. This is consistent with the results we presented earlier (cf. Fig. 6) on infection spreading from a single infected individual.

4.3 Effect of varying degrees of non-uniformity in the refractory sub-population on the persistence of infection

The effect of initializing the refractory sub-population with a spread in their phases $\tau_{i,j} \in [\tau_I + 1, \tau_0]$ was found to enhance persistence in general. We employ two ways of interpolating between completely uniform and completely heterogeneous states within the R_0 sub-population:

1. A fraction f_{rand} of the R_0 is initialized with phases in the range $[\tau_I + 1, \tau_0]$, and $1 - f_{rand}$ is initialized with a fixed phase $\tau_I + 1$.
2. The phases of R_0 are selected from a range of phases R_{rand}, which varies from $[\tau_I + 1, \tau_I + 1]$ to $[\tau_I + 1, \tau_0]$. The range $[\tau_I + 1, \tau_I + 1]$ implies all R_0 individuals are initialized at $\tau_I + 1$, and $[\tau_I + 1, \tau_0]$ implies the initial phases are spread over the entire range.

In the following results, I_t is averaged over 10^3 realizations, lattice size is 100×100, and the disease cycle parameters are $\tau_I = 4$, $\tau_0 = 13$.

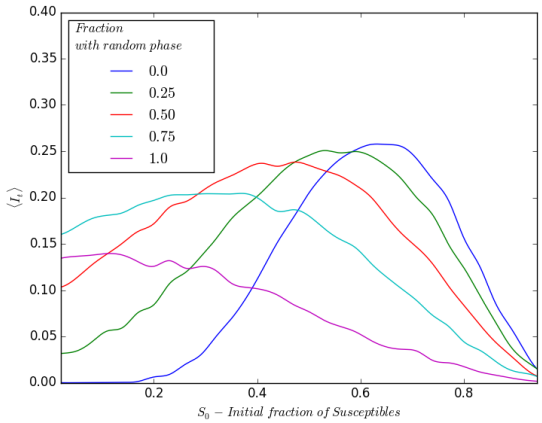

Figure 8. Variation of $\langle I_t \rangle$ (after transience) with respect to initial fraction of susceptible individuals S_0, for different fractions f_{rand} of the initial refractory sub-population having randomly distributed phases (see key).

A complete discussion is presented in [Agrawal, Moitra & Sinha (2017)].

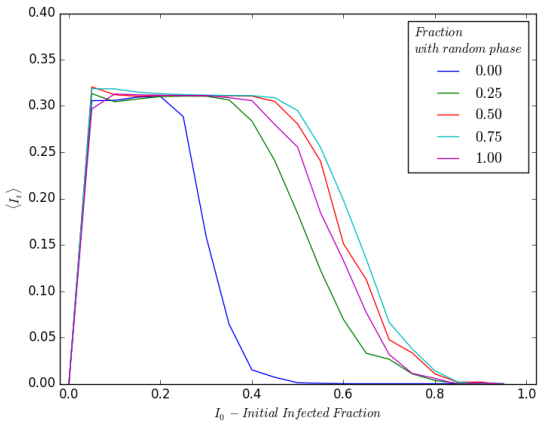

Figure 9. Variation of $\langle I_t \rangle$ (after transience) with respect to the initial fraction of infected individuals I_0 in the population, and $S_0 = R_0$. The initial refractory sub-population consists of different fractions f_{rand} with randomly distributed phases (see key).

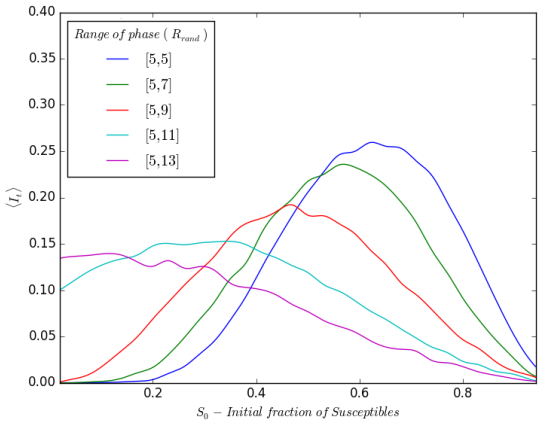

Figure 10. Variation of $\langle I_t \rangle$ (after transience) with respect to initial fraction of susceptible individuals S_0, for the case where there is a ***single*** infected individual in the population at the outset, and the refractory individuals in the population have phases τ randomly distributed over different ranges R_{rand} in the refractory stage : [5,5]; [5,7]; [5,9]; [5,11]; [5,13].

5 Discussion

In summary, we have explored infection spreading qualitatively and quantitatively in a patch of population, where the disease progression of the individuals was given by the SIRS model. We have focused on the emergence of persistent infection in the patch, under varying degrees of heterogeneity in the initial population.

We consider varying fractions of the initial population in different disease compartments. Our central result is the following: we find that an infectious seed does not give rise to persistent infection in a homogeneous population consisting of individuals at the same stage

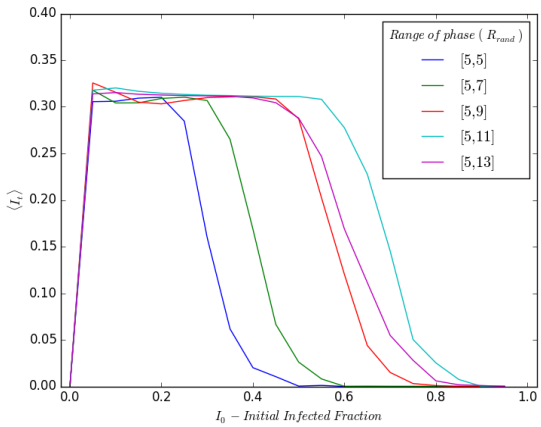

Figure 11. Variation of $\langle I_t \rangle$ (after transience) with respect to initial fraction of infected individuals I_0, for the refractory individuals having phases τ randomly distributed over different ranges R_{rand} in the refractory stage : [5,5]; [5,7]; [5,9]; [5,11]; [5,13].

of disease progression. Rather, when the population consists of randomly distributed individuals at various stages of the disease, infection becomes persistent in the population patch.

The key to persistent infection is found to be the random admixture of refractory and susceptible individuals, leading to de-synchronization of the phases in the disease cycle of the individuals. So we have demonstrated that when the entire population is susceptible to infection, the infection eventually dies out, while even a few susceptibles among a heterogeneous refractory population gives rise to a large persistent infected subpopulation.

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