Interacting particle systems in population biology

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In these notes we propose to introduce the reader to some spatial stochastic models in population biology. Each model is motivated by a concrete biology hypothesis. After analyzing a model we come back to the initial biology hypothesis and use the mathematical results to discuss it.

These notes are based on a series of articles I have written, these last years, on the spread of infectious diseases, in particular on the spread of tuberculosis. The models are very simple minded and are not intended to make any type of quantitative prediction. However, I believe that they may be useful in testing qualitative hypotheses. All the models introduced here are *interacting particle systems.* That is, they are continuous time discrete space stochastic models that were first introduced to model physical systems (see for instance Liggett (1999) or Schinazi (1999)). In fact, the building blocks for each model is the so called *contact process*, a very simple, but quite interesting, interacting particle system. The main technique of proof is coupling. We prove most of the main results but try to explain the main ideas without getting too technical. Our models are rather intuitive and even the reader whose main interest is outside mathematics may have a good understanding of the behavior of the model.

I. The role of reinfection in the transmission of infectious diseases

We introduce a spatial stochastic model for the spread of tuberculosis. After a primary infection an individual may become sick (and infectious) through an endogenous reinfection or through an exogenous reinfection. We show that even in the absence of endogenous reinfection an epidemic is possible if the exogenous reinfection parameter is high enough. This is in sharp contrast with what happens for a mean field model introduced by Feng et al. (2001).

1. Introduction. Tuberculosis is usually acquired through airborne infection from someone with active TB. After a primary infection, a small proportion of infected individuals develop active TB but most die without ever developing active TB, see for instance Enarson and Rouillon (1998). In the medical literature there is still a debate on whether developing active TB is exclusively a consequence of a primary infection or whether it may come from re-exposure to TB through individuals with active TB, see Styblo (1991), Ziegler et al. (1985) and McMurray et al. (1989). This question is especially important for some parts of the world (in particular South-East Asia) where at least 50% of individuals have had a primary infection and there is bound to have many contacts between individuals with active and individuals with dormant TB, see Dye et al. (1999).

In this chapter we will analyze mathematical models with two types of reinfection. The first type is a reactivation of a dormant infection and is called an endogenous reinfection. The second type of reinfection is acquired from another individual and is called an exogenous reinfection. Both reinfections are assumed to make an individual with dormant TB develop active TB. Our aim is to examine the relative importance of the two types of reinfection in the spread of an infectious disease such as TB. We introduce a spatial stochastic model for which we show that even with no endogenous reinfection (in that case the only route to active TB is a primary infection followed by an exogenous reinfection) the infectious disease may spread provided the exogenous reinfection parameter is large enough. In contrast, following Feng et al. (2001), we show that for a mean field model (corresponding to our spatial stochastic model) with no endogenous reinfection the infectious disease cannot spread.

Our results seem interesting in at least two ways. By introducing a spatial stochastic model one sees that (at least in theory) exogenous reinfection may be crucial in the spread of an infectious disease. It is also interesting to note that this is one of the few cases for which a spatial stochastic model and its corresponding mean field model behave strikingly

differently.

2. A spatial stochastic model. We consider a continuous time spatial stochastic model on $\mathbf{Z}^d$ where each site may be in one of three states: 0, 1 or 2. There is always exactly one individual at each site. If the individual at site x is healthy then we say that site x is in state 0, if the individual at x is infected but not infectious we say that site x is in state 1, if the individual at x is infected and infectious then site x is said to be in state 2. In the case of tuberculosis it is thought that the vast majority of the people infected (in state 1) die without developping the disease so they never get to state 2.

If the model is in configuration η, let $n_1(x,\eta)$ and $n_2(x,\eta)$ be the number of nearest neighbors of x (among the $2d$ nearest neighbors of x) that are in state 1 and in state 2, respectively. Assume that the model is in configuration η, then the state at a given site x evolves as follows:

$$0 \to 1 \text{ at rate } \lambda_0 n_2(x,\eta)$$

$$1 \to 2 \text{ at rate } \gamma + \lambda_1 n_2(x,\eta)$$

$$1 \to 0 \text{ at rate } 1$$

$$2 \to 0 \text{ at rate } \delta$$

In words, infectious individuals infect nearest neighbors that are healthy at rate λ_0. Infected individuals that are not infectious may become infectious by two different routes: by an endogenous reinfection at rate γ and by an exogenous reinfection caused by an infectious nearest neighbor at rate λ_1. Infected individuals that are not infectious die at rate 1 and infectious individuals die at rate $\delta \geq 1$.

The model above is related to the contact process for which there are only two possible states, say 0 and 1, and that evolves according to

$$0 \to 1 \text{ at rate } \lambda n_1(x,\eta)$$

$$1 \to 0 \text{ at rate } 1$$

It is known that there is a critical value λ_c such that if $\lambda \leq \lambda_c$ then starting with any initial configuration the 1's die out while if $\lambda > \lambda_c$ then, for any configuration having 1's, there is a positive probability that there will always be 1's. For more on the contact process, see for instance Liggett (1999).

We also note that the special case $\lambda_1 = 0$ (no exogenous reinfection) was examined by Krone (1999).

We say that an epidemic is possible if starting with a single infectious individual there is a positive probability that there will be infectious individuals at all times. We are now ready to state our results.

Theorem. *We consider the spatial stochastic model on* $\mathbf{Z}^d$ *for any* $d \geq 1$.

(a) If $\lambda_0 \leq \lambda_c$ *(the critical value of the contact process) then no epidemic may take place for any* γ, λ_1 *in* $[0, \infty)$ *and* $\delta \geq 1$.

(b) If $\lambda_0 > \delta\lambda_c$ *and* $\delta \geq 1$, *for any* $\gamma \geq 0$ *there is a positive probability for an epidemic provided* λ_1 *is large enough.*

Not surprisingly, Theorem (a) states that it is enough to control primary infections in order to avoid an epidemic. More interestingly, Theorem (b) tells us that even with no endogenous reinfection (i.e. $\gamma = 0$) an epidemic is possible provided the exogenous reinfection parameter is high enough. We will see that Theorem (b) is not true for the mean field model corresponding to our spatial stochastic model.

3. The mean field equations. Let $u_i \geq 0$ be the density of individuals in state i, for $i = 0, 1, 2$, in particular $u_0 + u_1 + u_2 = 1$. Assuming total mixing of the population we get the following system of differential equations.

$$u_1' = \lambda_0 u_0 u_2 - \gamma u_1 - \lambda_1 u_1 u_2 - u_1$$
$$u_2' = \lambda_1 u_1 u_2 + \gamma u_1 - \delta u_2$$

Note that $(u_1, u_2) = (0, 0)$ is the disease free equilibrium. The equilibrium (0,0) is said to be stable if for every neighborhood U of (0,0) there is a neighborhood $U_1 \subset U$ of (0,0) such that every solution $(u_1(t), u_2(t))$ with $(u_1(0), u_2(0))$ in U_1 is defined and in U for all $t > 0$, see for instance 9.2 in Hirsch and Smale (1974). For this model, we will say that an epidemic is possible if $(0, 0)$ is not stable. Note that this is analogous to our definition of an epidemic for the spatial stochastic model, in both cases we say that an epidemic is possible if starting close to the disease free equilibrium the disease may grow.

We now investigate the stability of the disease free equilibrium. The Jacobian at (0,0) is

$$\begin{pmatrix} -\gamma - 1 & \lambda_0 \\ \gamma & -\delta \end{pmatrix}$$

By looking at the determinant and the trace of this matrix, one sees that it has at most one positive eigenvalue. The Jacobian has exactly one positive eigenvalue if and only if its determinant is negative. That is, if and only if

$$\lambda_0 \gamma > \delta(\gamma + 1) \tag{3.1}$$

The condition above is necessary and sufficient for an epidemic to be possible (see the Theorems p 181 and p 187 in Hirsh and Smale (1974)).

We now point to one property of the mean field model that is not true for the spatial stochastic model. Condition (3.1) cannot be met if $\gamma = 0$. That is, for the mean field model, if there is no endogenous reinfection then no epidemic is possible. In contrast Theorem (b) shows that an epidemic is possible for the spatial stochastic model even if $\gamma = 0$.

4. Discussion. Our Theorem (b) shows that even if γ is 0 then if λ_1 is large enough an epidemic is possible for the spatial stochastic model. In contrast if $\gamma = 0$ then no epidemic may take place in the mean field model. Thus, the exogenous reinfection parameter λ_1 may be crucial for the appearance of an epidemic in the spatial stochastic model while λ_1 does not even appear in condition (3.1). However, Feng et al. (2000) show for a mean field model similar to ours the existence of a non trivial equilibrium when (3.1) does not hold but λ_1 is large enough. Therefore, in the mean field model the exogenous parameter λ_1 is not relevant to the start of an epidemic but may be important in maintaining an epidemic.

We will now explain the difference in behavior between the two models by an intuitive argument. Assume $\gamma = 0$ and start the mean field model with a very low density of 2's and a high density of 0's (no 1's). Then the 2's are going to infect 0's and 1's are going to appear. Because of the constant mixing of the population in this model the 1's and 2's are likely to be separated and the 2's are not going to be able to reinfect the 1's. So the infected individuals are going to disappear. Our intuitive scenario is confirmed mathematically by the fact that if $\gamma = 0$

$$u_2' = \lambda_1 u_1 u_2 - \delta u_2.$$

For u_1 and u_2 small $\lambda_1 u_1 u_2$ is of smaller order than $-\delta u_2$ and the 2's die out.

In contrast to what happens for the mean field model there is little mixing in the population for the spatial stochastic model. If we put a 2 in a sea of 0's then the 2 will infect its neighbors. These neighbors are now 1's and if the exogenous reinfection rate λ_1 is large then it is likely that the 2 will reinfect its neighbors before dying. The neighbors of the original 2 are now 2's as well and the infection is spreading. We believe that our results hold for spatial stochastic models with finite range interaction. We have dealt here with nearest neighbor interaction only because it is simpler to analyze mathematically.

The introduction of a spatial stochastic model has shown that (at least in theory) exogenous reinfection may be as important as endogenous reinfection in order to start an epidemic. Our results also illustrate the fact that mean field models do not always capture the whole picture. There are other examples in the mathematical biology literature of difference in qualitative behavior between mean field and low dimensional spatial models. See for instance Mollison (1977) and Schinazi (2000). However, note that in this chapter

we see a difference in behavior between a spatial model and the corresponding mean field model in all dimensions.

5. Proof of the Theorem We start by giving the graphical construction of our spatial stochastic process. Consider a collection of independent Poisson processes $\{N_0^{x,y}, N_1^{x,y}, D_x : x, y \in Z^d, ||x-y|| = 1\}$. For x and y in Z^d such that $||x-y|| = 1$ let the intensities of $N_0^{x,y}$, $N_1^{x,y}$ and D_x be λ_0, λ_1 and δ respectively. The graphical construction takes place in the space-time region $Z^d \times (0, \infty)$. At each arrival time t of $N_0^{x,y}$ if there is a 2 in x and a 0 in y we replace the 0 in y by a 1. At each arrival time t of $N_1^{x,y}$ if there is a 2 in x and a 1 in y we replace the 1 in y by a 2. At each arrival time of D_x if there is 2 at x we replace it by a 0, if there is a 1 at x we replace it by a 0 with probability $\frac{1}{\delta}$ (with probability $1 - 1/\delta$ we leave the 1 alone). In this way we construct a version of our spatial stochastic process. The process *restricted* to a space-time region $\mathcal{A}$ is constructed by using only the arrival times inside $\mathcal{A}$. For more on graphical constructions, see for instance Liggett (1999).

Proof of (a)

Consider the contact process ξ_t that evolves according to the following rules:

$$0 \to 2 \text{ at rate } \lambda_0 n_2(x, \xi)$$

$$2 \to 0 \text{ at rate } 1$$

We construct the tuberculosis model η_t and the contact process ξ_t simultaneously by using the Poisson processes defined above. The rules for η_t have been defined above. For ξ_t we use the following two rules. At each arrival time of $N_0^{x,y}$ if there is a 2 in x and a 0 in y we replace the 0 in y by a 2. At each arrival time of D_x if there is 2 at x we replace it by a 0 with probability $\frac{1}{\delta}$. We start ξ_t and η_t with the same initial configuration: a 2 at the origin of Z^d and 0's everywhere else. We claim that at every time t if there is 2 or a 1 at a certain site for η_t then there is a 2 at the same site for ξ_t. In order to check our claim it is enough to check that no transition in the graphical construction can make appear a 1 or a 2 for η_t without making appear a 2 for ξ_t. This is due to the fact that a 2 for the process ξ_t gives birth to a 2 while a 2 for the process η_t gives birth first to a 1 (which is not infectious). Note also that that death rates are higher for 2's in η_t than they are for 2's in ξ_t since $\delta \geq 1$.

Under the assumption $\lambda_0 \leq \lambda_c$ the 2's in ξ_t die out. Thanks to our coupling above the 2's in η_t must die out as well. This completes the proof of (a).

Proof of (b)

Let e_1 be the vector $(1, 0, \ldots, 0)$ in $\mathbf{Z}^d$

$$B = [-2L, 2L]^d \times [0, T] \qquad B_{m,n} = (4mLe_1, 50nT) + B$$

$$I = [-J, J]^d$$

$$\mathcal{L} = \{(m, n) \in \mathbf{Z}^2 : m + n \text{ is even}\}.$$

The process restricted to $(4Lme_1, 50Tn) + (-4L, 4L)^d \times R$ is the process constructed using only the Poisson processes $N_0^{x,y}, N_1^{x,y}, D_x$ for x and y in $4Lme_1 + (-4L, 4L)^d$. We define the following percolation process on $\mathcal{L}$. We declare $(m, n) \in \mathcal{L}$ wet if there is (x, t) in $B_{m,n}$ such that each site of the interval $x + I$ is occupied by a 2 at time t for the process restricted to $(4Lme_1, 50Tn) + (-4L, 4L)^d \times R$.

Set $\lambda_1 = \infty$ in the box $(-4L, 4L)^d \times R$. Note that if the initial configuration η_0 has no 1's then 1's do not appear at a further time in $(-4L, 4L)^d \times R$. In fact, with such an initial configuration, the process η_t with $\lambda_1 = \infty$ is a contact process that evolves according to the following rules:

$$0 \to 2 \text{ at rate } \lambda_0 n_2(x, \xi)$$

$$2 \to 0 \text{ at rate } \delta$$

Since we are assuming that $\lambda_0 > \delta\lambda_c$, this is a supercritical contact process. Bezuidenhout and Grimmett (1990) have shown that, for any $\epsilon > 0$, J, L and T can be chosen so that if $(0, 0)$ is wet then with probability $1 - \epsilon$, $(1, 1)$ and $(-1, 1)$ will also be wet. Here we are following the approach and notation of Durrett (1991). This shows that for any $\epsilon > 0$ we can pick J, L and T such that

$$P((1, 1) \text{ and } (-1, 1) \text{ are wet} | (0, 0) \text{ is wet}) > 1 - \epsilon \text{ for } \lambda_1 = \infty.$$

Since $(-4L, 4L)^d \times [0, 51T]$ is a finite space time box the total number of poisson occurrences inside this box has a Poisson distribution. For any $\epsilon > 0$, we can pick λ_1 large enough so that, with probability at least $1 - \epsilon$, every time a 1 appears inside the box (due to an infection of a nearest neighbor in state 2) then the 2 reinfects the 1 before the 1 or 2 dies. Thus, there is Λ so that

$$P((1, 1) \text{ and } (-1, 1) \text{ are wet} | (0, 0) \text{ is wet}) > 1 - \epsilon \text{ for } \lambda_1 > \Lambda.$$

We compare our set of wet sites to a simple oriented percolation model that we now define. Let $\zeta(z)$, $z \in \mathcal{L}$, be independent random variables with $P(\zeta(z) = 1) = 1 - \epsilon$ $P(\zeta(z) = 0) = \epsilon$. Site z is said to be open if $\zeta(z) = 1$, closed otherwise. At each $(m, n) \in \mathcal{L}$ we put an oriented arc from (m, n) to $(m - 1, n + 1)$ and one from (m, n) to $(m + 1, n + 1)$. Let $\mathcal{C}$ be the set of sites that can be reached from the origin $(0, 0) \in \mathcal{L}$, through oriented arcs, using only open sites. If ϵ is small enough then there is a positive probability that $\mathcal{C}$ has infinitely many sites and we say that percolation occurs (see Durrett (1991)).

It is not difficult to show that we may construct an oriented percolation model (in the same probability space the wet sites are defined on) ζ such that the set of wet sites of $\mathcal{L}$ contains the set of open sites of the oriented percolation (see Durrett (1991)). Thus, we may take $\epsilon > 0$ small enough so that there is an infinite cluster of wet sites in $\mathcal{L}$ with positive probability.

If we start the process η_t with at least one 2 then there is a positive probability of having a cube of side $2J+1$ in which each site is in state 2 somewhere at time 1. We then start the construction above and there is a positive probability of an infinite cluster of wet sites. This in turn guarantees that there will be sites in state 2 at all times and completes the proof of (b).

II. The role of social clusters in the transmission of infectious diseases

We introduce a spatial stochastic model for the spread of tuberculosis and HIV. We have three parameters: the size of the social cluster for each individual and the infection rates within and outside the social cluster. We show that when the infection rate from outside the cluster is low (this is presumably the case for tuberculosis and HIV) then an epidemic is possible only if the typical social cluster and the within infection rate are large enough. These results may be important in formulating new hypotheses for the transmission of TB and HIV.

1. Introduction. It is suspected that some infectious diseases can only spread in populations where people are grouped in clusters in which individuals have repeated and sustained contacts. This is the case for HIV and also for tuberculosis. In this paper we will concentrate on tuberculosis. This disease has been known for thousands of years and is associated with the emergence of urban civilizations and hence high concentration of population (see Ayvazian (1993)). Tuberculosis is a major world wide concern. This is due to the appearance of multi drug resistant strains and the fact that the HIV pandemic favors the appearance of TB; see the report of the Open Society Institute (1999). Transmission of tuberculosis is thought to occur mostly through sustained and repeated contact with an infected person. Many such cases have been documented, see for instance Lincoln (1965) and Raffalli et al. (1996). Several cases were documented in schools where a teacher or a student have infected other students. In most cases infection occurred after sustained and repeated contacts. In the case of tuberculosis we may think of individuals with whom we spend several hours a week in the same room (car or bus) as part of our social cluster. Most documented tuberculosis cases come from within the infected individuals' own clusters. However, it is clear that the infection needs to have originated somewhere else. That is, 'casual' transmission must be possible as well. There are a few documented cases of those as well. For instance, Raffalli et al. (1996) mentions a Dutch rock band that had two infected musicians and which is thought to have infected hundreds of people with tuberculosis during their concerts.

In this chapter we analyze mathematical models that incorporate social clusters. The idea of dividing a population in groups and consider different infection rates within and between groups goes back to at least Rushton and Mautner (1955). Sattenspiel (1989) reviews a number of such deterministic models and provides extensive references. We focus on different questions than the papers above. In particular we are interested in understanding the role and interplay of several parameters in the appearance of an epidemic.

We consider very simple minded models with only three parameters: the cluster size, the casual transmission rate and the within cluster transmission rate. We introduce a spatial stochastic model for which we have the following results. If the casual infection rate is high enough then there is a chance for an epidemic independently of the cluster size and the within cluster infection rate. In the case of tuberculosis the casual infection rate is probably not very high. For low or intermediate casual infection rate we show that an epidemic is possible only if the cluster size is large enough. However, in the case of low or intermediate casual infection rate, even if the cluster size is large enough the epidemic may occur only if the within cluster infection rate is large enough. We believe that these results shed some light about the interplay between the different parameters. In particular, the model suggests that given a low casual infection rate the cluster size and the within cluster infection rate are determinant.

2. The spatial stochastic model. Our model evolves on the square lattice $\mathbf{Z}^d$, typically $d = 2$ but our results hold in any dimension $d \geq 1$. At each site x in the square lattice $\mathbf{Z}^d$ there is a cluster of N individuals. We denote our stochastic process by η_t. For a site x in $\mathbf{Z}^d$ $\eta_t(x) = i$ means that there are i individuals (among the N individuals in the cluster at x) that are infected, i is an integer between 0 and N. Thus, each site has $N + 1$ possible states. We assume that an individual may get infected from within his cluster or from outside his cluster. The latter type of infection will also be called casual infection. The parameters λ and ϕ are the infection rates for infection from outside and from within the cluster, respectively. We use the notation $y \sim x$ to indicate that site y is one of the $2d$ nearest neighbors of site x. Assume that the model is in configuration η then the state at a given site x changes according to the following transition rates:

$$0 \to 1 \text{ at rate } \lambda \sum_{y \sim x} \eta(y)$$

$$i \to i + 1 \text{ at rate } i\phi \text{ for } 1 \leq i \leq N - 1$$

$$i \to 0 \text{ at rate } 1 \text{ for } 1 \leq i \leq N$$

In words, the model depends on three parameters λ, ϕ and N. We start the process with a single infected individual in the cluster at the origin of $\mathbf{Z}^d$. Infected individuals may infect individuals in their cluster at rate ϕ. Infected individuals may also infect individuals in one of the 2d neighboring sites at rate λ provided the target site has no infected individuals yet. The idea is that once a site is infected infections within the site are a lot more likely than additional infections from the outside so we neglect the latter. This hypothesis simplifies the mathematics and the model. Moreover, we have checked that allowing casual infections

in an already infected site does not change the qualitative behavior of the model. Finally, all the infected individuals in a cluster are simultaneously replaced by healthy individuals at rate 1. This applies in particular to places where there is a good tracking system of infectious diseases and once an infected individual is discovered its social cluster is rapidly tracked down.

We will start by stating a technical result that is crucial in our analysis.

Proposition 1. *Let η_t be our spatial stochastic process with parameters λ, ϕ and N and whose initial configuration is such that all the individuals are healthy except for one infected individual in the cluster at the origin of $\mathbf{Z}^d$. Let $|\eta_t|$ be the total number of infected individuals at time t. The probability*

$$P(|\eta_t| \geq 1, \text{ for all } t \geq 0)$$

is increasing in λ, ϕ and N.

That is, the probability that there will be infected individuals at all times increases the parameters λ, ϕ and N.

Given N and ϕ we define the critical value

$$\lambda_c(N, \phi) = \inf\{\lambda > 0 : P(|\eta_t| \geq 1, \text{ for all } t \geq 0) > 0\}.$$

By Proposition 1, one sees that if $\lambda < \lambda_c(N, \phi)$ then the infection eventually dies out in the population while if $\lambda > \lambda_c(N, \phi)$ there is a positive probability of an epidemic. That is, there is a positive probability that there will be infected individuals at all times.

The model with $N = 1$ is well known and is called the basic contact process. It is a model with just two states: 0 and 1 and it evolves as follows

$$0 \to 1 \text{ at rate } \lambda \sum_{y \sim x} \eta(y)$$
$$1 \to 0 \text{ at rate } 1$$

In the case $N = 1$ the value of ϕ is irrelevant, hence the critical value $\lambda_c(1, \phi)$ does not depend on ϕ and we will denote it by $\lambda_c(1)$. It is known that in any $d \geq 1$ the critical value $\lambda_c(1)$ is in $(\frac{1}{2d-1}, \frac{2}{d})$ but precise rigorous bounds are difficult to obtain. See, for instance, Liggett (1999) for more on the contact process. We now have enough notation to state our main result.

Theorem 1.

(a) if $\lambda > \lambda_c(1)$ then there is positive probability for an epidemic for models with parameters (λ, N, ϕ) for all $N \geq 1$ and all $\phi \geq 0$.

(b) if $N\lambda < \lambda_c(1)$ there can be no epidemic for models with parameters (λ, N, ϕ) for all $\phi \geq 0$.

(c) if $N\lambda > \lambda_c(1)$ but $\lambda < \lambda_c(1)$ then there is a critical value ϕ_c, in $(0, \infty)$, depending on λ and N such that if $\phi < \phi_c$ there is no epidemic for the model with parameters (λ, N, ϕ) while if $\phi > \phi_c$ there is a positive probability for an epidemic for the model with parameters (λ, N, ϕ).

Thus, (a) tells us that if the casual rate λ is large enough there is a positive probability for an epidemic independently of the cluster size N and the cluster infection rate ϕ. From (b) and (c) we see that if $\lambda < \lambda_c(1)$ there is critical cluster size: if $N > \lambda_c(1)/\lambda$ an epidemic is possible while if $N < \lambda_c(1)/\lambda$ no epidemic can take place. Finally, when $\lambda < \lambda_c(1)$ and N is above the critical cluster size $\lambda_c(1)/\lambda$ then an epidemic can happen only if the within cluster infection rate ϕ is large enough.

3. The mean field model

We now introduce the mean field model corresponding to our spatial stochastic model. Let u_i be the density of individuals whose cluster has i infected individuals for $0 \leq i \leq N$. In particular, $u_0 + u_1 + \ldots + u_N = 1$. Assuming that the contacts are through homogeneous mixing we get the following mean field model.

$$\begin{aligned}
u_0' &= \sum_{i=1}^{N} u_i - \sum_{i=1}^{N} i\lambda u_i u_0 \\
u_1' &= \lambda u_1 u_0 + 2\lambda u_2 u_0 + 3\lambda u_3 u_0 + \ldots + N\lambda u_N u_0 - u_1 - \phi u_1 \\
u_i' &= (i-1)\phi u_{i-1} - u_i - i\phi u_i \text{ for } 2 \leq i \leq N-1 \\
u_N' &= (N-1)\phi u_{N-1} - u_N
\end{aligned}$$

We have the disease free equilibrium $u_0 = 1$ and $u_i = 0$ for all $i \geq 1$. The first part of our analysis involves only the first differential equation. First note that

$$u_0' = \sum_{i=1}^{N} u_i - \sum_{i=1}^{N} i\lambda u_i u_0 \leq \sum_{i=1}^{N} u_i - \sum_{i=1}^{N} \lambda u_i u_0 = 1 - u_0 - \lambda u_0(1-u_0) = (1-u_0)(1-\lambda u_0).$$

Note that if $\lambda > 1$ and u_0 is in $(1/\lambda, 1)$ then $u_0' < 0$. That is, the disease free equilibrium is not stable and an epidemic is possible for all values of N and ϕ.

Next, observe that

$$u_0' = \sum_{i=1}^{N} u_i - \sum_{i=1}^{N} i\lambda u_i u_0 \geq \sum_{i=1}^{N} u_i - \sum_{i=1}^{N} N\lambda u_i u_0 = (1-u_0)(1-N\lambda u_0).$$

If $\lambda N < 1$ and $u_0 < 1$ then $u_0' > 0$. That is, the disease free equilibrium is stable and no epidemic can take place.

The analysis above shows that the behavior of the mean-field model is qualitatively the same as the behavior the spatial stochastic model as described in Theorem 1 (a) and (b).

We now turn to the case where $N\lambda > 1$. From the system of differential equations above we see that if $(u_0, u_1, \ldots, u_N)$ is an equilibrium then

$$u_i = \frac{(i-1)\phi}{i\phi+1} u_{i-1} \text{ for } 2 \leq i \leq N-1.$$

Hence,

$$u_i = \frac{(i-1)!\phi^{i-1}}{(i\phi+1)((i-1)\phi+1)\ldots(2\phi+1)} u_1 \text{ for } 2 \leq i \leq N-1. \tag{1}$$

From the last equation in the system of differential equations above we have

$$u_N = (N-1)\phi u_{N-1}.$$

Letting $i = N-1$ in (1) we get

$$u_N = \frac{(N-1)!\phi^{N-1}}{((N-1)\phi+1)\ldots(2\phi+1)} u_1.$$

We now use the last expression and (1) in the second equation of the system of differential equations above to get

$$u_0 = \frac{1+\phi}{\lambda} \frac{1}{1 + \sum_{i=2}^{N-1} \frac{i!\phi^{i-1}}{(i\phi+1)\ldots(2\phi+1)} + \frac{N!\phi^{N-1}}{((N-1)\phi+1)\ldots(2\phi+1)}}.$$

As we let ϕ go to infinity it is not difficult to see that u_0 converges to $\frac{1}{\lambda N}$. Thus, if $\lambda N > 1$ we can pick ϕ so that an equilibrium giving positive density to the infected states is possible. In other words, we have for the mean-field model a result similar to what we have for the spatial stochastic model in Theorem 1 (c).

4. Discussion. There has been interest in the recent literature on the relative importance of the cluster size, the within cluster infection rate and the casual infection rate in the transmission of infectious diseases, in particular for tuberculosis, see Aparicio et al. (2000) and Raffalli et al. (1996). In this chapter we obtain the following results for a spatial stochastic model. If the casual infection rate is above a certain threshold denoted by $\lambda_c(1)$ then there is a chance for an epidemic even for a cluster size of 1 and a within cluster infection rate of 0. If the casual infection rate is below $\lambda_c(1)$ then an epidemic is possible only if the cluster size is large enough. Even if the cluster size is large enough then an epidemic is possible only if the within cluster infection rate is large enough when the casual infection rate is below $\lambda_c(1)$. Note that some of the results just described (in particular, the existence of a critical cluster size) were already implicit for the deterministic model of Aparicio et al. (2000).

The main example we have in mind is the transmission of tuberculosis. However, we believe that this model is also interesting in the context of sexually transmitted diseases. It has been conjectured, for instance, that the transmission of HIV in the gay communities of the U.S.A is caused by a core of very sexually active individuals that are customers of bathhouses, see Thompson (1984) and Rotello (1997) for instance. One may think that such an individual is part of a huge cluster and even if the casual infection rate (that is, the infection rate from a very active cluster into another cluster) is low our results show that an epidemic may occur provided the within cluster infection rate is high enough. Of course, in reality all clusters have not the same size and it would be interesting to analyze a model with variable (maybe random) cluster size to see whether our results still hold.

Our model is too simple to yield useful quantitative results. Transmission of infectious diseases depend on many more than 3 parameters. Transmission of tuberculosis is particularly challenging. It is believed that the vast majority of infected individuals never develop the disease and are never infectious. However, some do and some do more than once and the discussion is still on to decide whether the reinfection is usually exogenous or endogenous, see Feng et al. (2000) and Styblo (1991). These questions are now even more important with many people simultaneously infected by HIV and TB since HIV infected individuals are a lot more likely to develop TB. Models like ours are useful in getting a qualitative understanding of the basic transmission mechanisms. We believe that a lot must be understood about these basic transmission mechanisms before one can confidently look at models with more parameters.

In our spatial model there is very little mixing (individuals interact with their nearest neighbors only) while in the mean-field model every individual mixes with everybody else. The fact that the qualitative behavior is the same for both models shows that our results

are probably robust and do not depend on the specific mixing conditions of the models. In particular, we expect finite range spatial models to behave like our nearest neighbor spatial model.

5. Proofs

Proof of Proposition 1.

It is useful to have some idea on how to construct our process η_t. The construction we have in mind here is based on appropriate families of Poisson processes. Each site has Poisson processes corresponding to the different transition rates. For instance, each site x, for each integer i between 1 and $N-1$, has a Poisson process with rate $i\phi$. At each occurrence of the Poisson process with rate $i\phi$, if site x is in state i then it goes to state $i+1$. By defining appropriate families of Poisson processes we get a process with the prescribed transition rates. This type of construction is usually referred to as the graphical construction. For more details see p 32 in Liggett (1999), for instance. One of the nicest features of this construction is that it allows us to construct several processes on the same probability space. For instance, if we are interested in comparing two epidemic models η_t^1 with $\phi = \phi_1$ and η_t^2 with $\phi_2 > \phi_1$, then we may define at each site Poisson processes with rates $i\phi_2$ to construct η_t^2. We may use the same Poisson processes to get Poisson processes with rates $i\phi_1$ by doing the following. Every time there is an occurrence for η_t^2 it is an occurrence for η_t^1 with probability ϕ_1/ϕ_2. This gives us a process η_t^1 with the appropriate rates. Moreover, one sees that by constructing the two processes in the same probability space the process with ϕ_1 must have less infected individuals at every site than the process with ϕ_2. The same type of idea may be used to compare processes with different N and different λ. One only needs to check that no transition can make the process with the lower parameter have more infected individuals than the process with the higher parameter at any given site, provided one starts with the same configuration for both processes. A crucial feature of the model that ensures this monotonicity property is the constant transition rate for $i \to 0$ for all states $i \geq 1$ (actually, any transition rate which is decreasing in i would work). This completes the proof of Proposition 1.

Proof of Theorem 1. (a)

Due to Proposition 1 the critical parameter $\lambda_c(N,\phi)$ is decreasing in N and ϕ. Thus,

$$\lambda_c(N,\phi) \leq \lambda_c(1,\phi) = \lambda_c(1).$$

Since we assume that $\lambda > \lambda_c(1)$ we have $\lambda > \lambda_c(N,\phi)$ for any N and ϕ. By definition of $\lambda_c(N,\phi)$ we have that $P(|\eta_t| \geq 1, \text{ for all } t \geq 0) > 0$. Hence, there is a positive probability

of an epidemic for all models with parameters (λ, N, ϕ) such that $\lambda > \lambda_c(1)$. This completes the proof of Theorem 1 (a).

Proof of Theorem 1 (b)

Consider the model with $\phi = \infty$. In this case as soon there is one infected in the cluster all the cluster is infected. So each site has only two possible states: 0 and N. The transition rates are given by:

$$0 \to N \text{ at rate } \lambda \sum_{y \sim x} \eta(y)$$
$$N \to 0 \text{ at rate } 1$$

Observe that $\eta(y)$ can only be 0 or N. So the transition from 0 to N occurs at λN times the number of nearest sites that are infected. Therefore, the model above is a contact process with birth rate λN. If $\lambda N < \lambda_c(1)$ this contact process dies out. By Proposition 1 the model with parameters (λ, N, ∞) has more infected individuals than the model with parameters (λ, N, ϕ) for any $\phi \geq 0$. Since there can be no epidemic for the first model the same is true for the second model. This completes the proof of Theorem 1 (b).

Proof of Theorem 1 (c)

We are given λ and N such that $N\lambda > \lambda_c(1)$ and $\lambda < \lambda_c(1)$. We will proceed in two steps. Our first step will be to show that there is $\phi_1 > 0$ such that if $\phi < \phi_1$ then no epidemic can take place for the system with (λ, N, ϕ). In our second step we will show that there is $\phi_2 < \infty$ such that if $\phi > \phi_2$ then an epidemic may take place for the system with (λ, N, ϕ). Due to the monotonicity of this process this will imply the existence of a critical value $\phi_c(\lambda, N)$ in $[\phi_1, \phi_2]$ such that if $\phi < \phi_c$ no epidemic can happen while if $\phi > \phi_c$ an epidemic may happen.

Lemma 1. Assume that $\lambda < \lambda_c(1)$. There is ϕ_1 in $(0, \infty)$ such that if $\phi < \phi_1$ no epidemic is possible.

Proof of Lemma 1.

This proof is done under the assumption $d = 2$, in order to avoid more cumbersome notation.

We start the first step of the proof by defining two space–time regions:

$$\mathcal{A} = [-2L, 2L]^2 \times [0, 2L], \qquad \mathcal{B} = [-L, L]^2 \times [L, 2L]$$

where L is an integer to be chosen later. Define $\mathcal{C}$ to be part of the 'boundary' of the box $\mathcal{A}$:

$$\mathcal{C} = \Big\{(m, n, t) \in \mathcal{A} : |m| = 2L \text{ or } |n| = 2L \text{ or } t = 0\Big\}$$

We will compare the spatial stochastic model η_t to a certain dependent percolation process on the set $\mathcal{L} = \mathbf{Z}^2 \times \mathbf{Z}_+$, where $\mathbf{Z}_+ = \{0, 1, 2, \ldots\}$. We say that the site (k, m, n) in $\mathcal{L}$ is *wet* if there exist no infected sites in the (smaller) box $(kL, mL, nL) + \mathcal{B}$ *regardless of the states of sites in the boundary* $(kL, mL, nL) + \mathcal{C}$. In other words, we want no infection path going from the boundary of the larger box into the smaller box. Note that the event $\{(k, m, n) \text{ is wet}\}$ depends only on the existence (or not) of paths of infection within $\mathcal{A}$. We require this uniformity on the states of the boundary in order to ensure that the percolation process in $\mathcal{L}$ (to be defined below), although dependent, has an interaction with only finite range. Sites which are not wet are called *dry*.

Given $\lambda < \lambda_c(1)$ we will show that there is an integer L and a real number ϕ_1 such that

$$P\big((k, m, n) \text{ is wet}\big) \geq 1 - \epsilon \text{ if } \phi < \phi_1.$$

We start by showing the above property when $\phi = 0$. Then, using a continuity argument, we will deduce that the inequality remains true for small ϕ. By translation-invariance, it suffices to consider the site $(0, 0, 0) \in \mathcal{L}$.

Note that if $\phi = 0$ then each site may be in only 2 states: 0 and 1. The process η_t becomes a contact process with birth rate λ. If there is a 1 in $\mathcal{B}$ it must have originated in $[-2L, 2L]^2 \times 0$ or at a later time from one of the sides of the box $\mathcal{A}$. In the former case the infection must have survived at least L before it reaches $\mathcal{B}$ while in the latter case it must have a radius of at least L. Note that since $\lambda < \lambda_c(1)$ η_t is a subcritical contact process if $\phi = 0$. Bezuidenhout and Grimmett (1991) have shown, for the subcritical contact process, that the probability that an infection lasts L or more is less than $Ce^{-\gamma L}$ where C and γ are strictly positive constants and that the probability that an infection has a radius of L is less than $Ce^{-\gamma L}$. Therefore, we have

$$P\big((0, 0, 0) \text{ is wet}\big) \geq 1 - 8L(4L + 1)e^{-\gamma L} - (4L + 1)^2 e^{-\gamma L}.$$

By taking L large enough the probability above may be made larger than $1 - \epsilon/2$. We have

$$P\big((0, 0, 0) \text{ is wet}\big) \geq 1 - \epsilon/2 \text{ if } \phi = 0.$$

Since $\mathcal{A}$ is a finite box there is $\phi_1 > 0$ such that with probability at least $1 - \epsilon/2$ there are no occurrences of Poisson processes with rate ϕ_1 inside $\mathcal{A}$. Therefore, we get

$$P\big((0, 0, 0) \text{ is wet}\big) \geq 1 - \epsilon \text{ if } \phi < \phi_1.$$

This shows that even if all sites on the boundary of $\mathcal{A}$ are in state N by taking ϕ sufficiently small η_t will be a subcritical contact process inside $\mathcal{A}$ and with high probability there will

be no infected site in the smaller box $\mathcal{B}$. We now define a percolation process on $\mathcal{L}$. Let $\mathcal{A}(k,m,n) = (kL, mL, nL) + \mathcal{A}$. For each pair (k,m,n) and (x,y,z) in $\mathcal{L}$, we draw an oriented edge from (k,m,n) to (x,y,z) if (and only if) $n \leq z$ and $\mathcal{A}(k,m,n) \cap \mathcal{A}(x,y,z) \neq \emptyset$. The wet sites in the ensuing directed graph constitute a dependent percolation model. It is easy to see that there is a constant K such that if the distance between (k,m,n) and (x,y,z) is larger than K then the state of (k,m,n) is independent of the state of (x,y,z). Furthermore, there exists a positive finite constants δ such that the number of self-avoiding walks oriented paths on $\mathcal{L}$, having length r and any given endpoint is no larger than δ^r. There exists a constant ν such that any self-avoiding path of length r contains at least νr sites, the distance between any pair of which exceeds K.

Let T_0 be the supremum of all times t such that $\eta_t(0) \geq 1$. Suppose that $T_0 > LM$. Then there exists $m \geq M-1$ such that $(0,0,m)$ is is the endpoint of an oriented dry path of $\mathcal{L}$ whose other endpoint has the form $(x,y,0)$ for some (x,y) in $\mathbf{Z}^2$. By the remarks above

$$P(T_0 > LM) \leq \sum_{m \geq M-1} \sum_{r \geq m} \delta^r \epsilon^{\nu r}.$$

By taking $\epsilon > 0$ sufficiently small, the r.h.s. approaches 0 as $M \to \infty$. Thus, T_0 is almost surely finite. Since the same argument may be applied to any site x, Lemma 1 is proved.

We now deal with the second step of our proof. The crucial observation is that the process η_t with $\phi = \infty$ is a contact process with birth rate λN. Each site may be in one of 2 states: 0 and N. Since we are assuming that $\lambda N > \lambda_c(1)$, this is a supercritical contact process. As mentioned in Chapter I (see the proof of Theorem (b) there), a supercritical contact process dominates a (very) supercritical percolation model. By following the same steps as in the proof of Theorem (b) (Chapter I) one sees that there is $\phi_2 \in (0, \infty)$ such that if $\phi > \phi_2$ then there is a positive probability to have sites in state N at all times. This completes the second step of our proof and the proof of Theorem (c).

III. A model for the spread of drug resistant diseases

We introduce an interacting particle system to model the emergence of drug resistant diseases, one of the most serious health problems in modern society. We are interested in diseases for which a natural strain may mutate into a drug resistant strain. This happens, for instance, when antibiotics are misused. The main result of our analysis is that with an efficient drug against the natural strain, if there is even a small chance that the natural strain mutates into the drug resistant one, then there will eventually be an outbreak of the drug resistant strain throughout the population. In that case the natural strain disappears and is replaced by the drug resistant strain. The disturbing part of this is that an efficient treatment of the natural strain gives an edge to the drug resistant strain.

1. Introduction. One of the most serious health problems today is the emergence of drug resistant diseases, see for instance Blower, Small and Hopewell (1996) and Castillo-Chavez and Feng (1997) and the references there for an account of the situation for tuberculosis. In this chapter we will introduce a very simple stochastic model for the spread of a drug resistant strain of a given disease. We are interested in drug resistant strains that appear by mutation of the natural (or wild type) strain. This is the case when antibiotics are misused: incomplete treatment in the case of TB or overuse in many other cases. Our model will show that (at least in theory) for a large range of parameters it is possible for the drug resistant strain to replace the natural strain. One case is of particular interest: if the rate of successful treatment for the natural strain is high enough then, even if the rate at which the natural strain mutates into the drug resistant strain is very low, the drug resistant strain will eventually sweep through the population. This possibility is somehow disturbing: it shows that an efficient treatment of the natural strain may give an edge to the drug resistant one!

We now introduce our model. We think of our population as being spatially distributed on the square lattice $\mathbf{Z}^d$. Each site of $\mathbf{Z}^d$ is empty or occupied by at most one individual. We think of 0 as being the empty state, 1 being healthy, 2 infected with the natural strain, 3 infected with the drug resistant strain. The state of the particle system at time t is denoted by η_t and is in $\{0,1,2,3\}^{\mathbf{Z}^d}$. If the process is in state η and $x \in \mathbf{Z}^d$ then $\eta(x) = 0$ if site x is empty, $\eta(x) = 1$ if x is occupied by a healthy individual, $\eta(x) = 2$ if x is occupied by an individual infected with the natural strain of the disease and $\eta(x) = 3$ if x is occupied by an individual infected with the drug resistant strain of the disease.

Denote by $||.||$ the Euclidean norm and for $x \in Z^d$, $\eta \in \{0,1\}^{\mathbf{Z}^d}$, let for $i = 1, 2, 3$

$$n_i(x,\eta) = card(\{y \in \mathbf{Z}^d : ||y - x|| = 1, \text{ and } \eta(y) = i\})$$

That is, $n_i(x,\eta)$ is the number of nearest neighbors of x that are in state i. A site x changes its state in the configuration η according to the following transition rates:

$$0 \to 1 \text{ at rate } \beta_1$$

$$1 \to 2 \text{ at rate } \beta_2 n_2(x,\eta)$$

$$1 \to 3 \text{ at rate } \beta_3 n_3(x,\eta)$$

$$2 \to 3 \text{ at rate } \phi$$

$$2 \to 1 \text{ at rate } r$$

$$3 \to 0 \text{ at rate } 1$$

In words, there is birth of healthy individuals at rate β_1. Healthy individuals get infected by contact at rate β_2 and β_3 by infected individuals with natural and drug resistant strains, respectively. An individual infected with the natural strain has two possible outcomes: either his strain mutates into the drug resistant strain at rate ϕ or he recovers at rate r. Finally, an individual with the drug resistant strain dies at rate 1.

We now turn to a model for the disease without treatment. With no treatment, only strain 2 is present and we could have the following rules for the model ζ_t.

$$0 \to 1 \text{ at rate } \beta_1$$

$$1 \to 2 \text{ at rate } \beta_2 n_2(x,\zeta)$$

$$2 \to 0 \text{ at rate } 1$$

The particular case with $\beta_1 = 0$ has been studied under the names "spatial epidemic" and "forest fire" by Mollison (1977), Kuulasmaa (1982), Cox and Durrett (1988). Kuuslasmaa has shown the existence of a critical parameter β_c (depending on the spatial dimension $d \geq 2$) such that if $\beta_2 > \beta_c$, starting with a single 2 at the origin and 1's everywhere else, there is a positive probability of having 2's at all times. Durrett and Neuhauser (1991) have studied the model with the additional parameter β_1. They have shown that if $\beta_2 > \beta_c$ and $\beta_1 > 0$ there exists a stationary distribution for ζ_t that concentrates on configurations with infinitely many 2's. See also Andjel and Schinazi (1996) and Berg, Grimmett and Schinazi (1998). With our interpretation, this means that in the absence of treatment, if β_2 is high enough, then strain 2 may be endemic in the population.

We also need to introduce the contact process in order to formulate our results. The contact process ξ_t has only two possible states per site, say 1 and 2, and evolves according to the following rules:

$$1 \to 2 \text{ at rate } \lambda n_2(x,\xi)$$

$$2 \to 1 \text{ at rate } 1$$

Moreover, there is a critical parameter λ_c (depending on the spatial dimension d) such that if $\lambda > \lambda_c$ there is a stationary distribution for the contact process that concentrates on configurations with infinitely many 2's. If $\lambda \leq \lambda_c$ the unique stationary distribution is the trivial one: the all 1's configuration, see Bezuidenhout and Grimmett (1990) for more on the contact process.

We are now ready to state the main result of this paper:

Theorem 1. *Assume that* $\frac{\beta_2}{\phi+r} < \lambda_c$, $\phi > 0$, $\beta_1 > 0$ *and* $\beta_3 > \beta_c$. *Then, there is an epidemic of the drug resistant strain in the following sense. If the initial configuration has infinitely many 2's then, with probability 1, there is a spatial region with no 2's and with 3's in it that grows through the whole space* $\mathbf{Z}^2$.

In an ideal scenario the treatment rate of the natural strain r is much higher than the mutation rate from the natural strain to the drug resistant strain ϕ. Theorem 1 shows that even in this ideal scenario an epidemic of the drug resistant strain will eventually happen, if $\phi + r$ (which is essentially r in this case) is high enough. This poses the question of the ultimate effectiveness of any drug that may provoke the appearance of a mutated drug resistant strain.

In reality, we are far from the ideal scenario described above. As noted by Blower, Small and Hopewell (1996) the treatment rate for tuberculosis can be rather low (r and ϕ could then be of the same order of magnitude) and then the perverse effects of treatment may make the treatment an undesirable option.

Theorem 1 is proved assuming that we have infinitely many individuals infected with the natural strain to start with. This is, of course, an approximation of an endemic state. The proof works if we start with only finitely many infected individuals but then the conclusion is that there is a strictly positive probability (instead of probability 1) of an epidemic of the drug resistant strain. It seems intuitively clear, but might be difficult to prove, that the probability of an epidemic increases rapidly with the number of infected individuals we start with.

We may think of the two strains as competing for the same susceptibles. Under the conditions $\frac{\beta_2}{\phi+r} < \lambda_c$ and $\beta_3 > \beta_c$, the natural strain is out competed by the resistant strain. The mean-field analysis of the next section will show that there are probably other conditions under which the natural strain is out competed by the resistant strain. The paradoxical result of our analysis is that it is when the treatment is most effective, and r is large, that the population is more at risk of a major outbreak of the drug resistant strain. It is when the treatment is effective and the natural strain is rapidly disappearing that we will have an epidemic of the drug resistant strain.

The following is another possible application of our model. It has been observed that after a few weeks of lamivudine treatment, HIV infected patients are subjected to a large increase in lamivudine resistant virus. This is analogous to the large epidemic of drug resistant strain our model predicts when the treatment of the natural strain is efficient. See Bonhoeffer, Coffin and Nowak (1997), in particular Figure 2 there.

Our other result is that if $\phi + r$ is low enough then coexistence of strains 2 and 3 is possible.

Theorem 2. *If $\phi + r$ is low enough and $\phi > 0$, coexistence is possible. That is, there is a stationary distribution for η_t on $\mathbf{Z}^d$ ($d \geq 1$) that concentrates on configurations with infinitely many 2's and 3's.*

Note that if $\beta_2 > \beta_c$ and $\frac{\beta_2}{\phi+r} < \lambda_c$ then the 2's would persist in the process ζ_t (the model with no treatment) and would die out in the process η_t (the model with treatment). In other words, for this range of parameters, strain 2 would survive in the absence of treatment but would be eliminated by strain 3 as a consequence of the treatment. However, Theorem 2 shows that coexistence is possible for $\phi + r$ small in the model with treatment, confirming the results that Castillo-Chavez and Feng (1997) obtained for their deterministic non-spatial model.

2. Mean-Field Analysis

We do a mean-field analysis of our model in order to get a more complete picture of what the phase diagram of the spatial model might be. Let us start at time 0 with a translation invariant distribution, with a positive density of 1's, 2's and 3's. Then at all times t, the distribution of $\eta_t(x)$ is translation invariant, and $u_i(t) = P(\eta_t(x) = i)$ does not depend on x, for $i = 1, 2, 3$. From the dynamics and the approximation that the states at different sites are independent it is straightforward to derive the system of differential equations

$$\begin{aligned} u_1'(t) =& \beta_1(1 - u_1 - u_2 - u_3) - \beta_2 u_1 u_2 - \beta_3 u_1 u_3 + r u_2 \\ u_2'(t) =& \beta_2 u_1 u_2 - r u_2 - \phi u_2 \\ u_3'(t) =& \beta_3 u_1 u_3 + \phi u_2 - u_3. \end{aligned}$$

We now look for an equilibrium that concentrates on 1's, 2's and 3's. Using that $u_i' = 0$ for $i = 1, 2, 3$, we get from the second equation that

$$u_1 = \frac{r + \phi}{\beta_2}.$$

The third equation yields

$$u_2 = \frac{\phi}{1 - \beta_3 u_1} u_3.$$

Plugging the expressions for u_1 and u_2 in the first equation yields u_3. In order to have u_i in (0,1) for $i = 1, 2, 3$ it is easy to check that it is necessary and sufficient to have the following conditions:

$$\phi > 0 \qquad \beta_2 > r + \phi \qquad \frac{\beta_2}{r+\phi} > \beta_3.$$

As for the spatial model we get that if $\frac{\beta_2}{r+\phi}$ is not large enough then the 2's do not survive. We also get a new interesting condition: if β_3 is larger than $\frac{\beta_2}{r+\phi}$ then the 2's die out. This makes us conjecture that in the spatial model too strain 3 is going to out compete strain 2 if $\frac{\beta_2}{r+\phi} < \beta_3$.

Since it is so easy to derive results for the mean-field model the reader may wonder at this point what is gained in terms of biological insight by the analysis of the interacting particle system. Spatial and mean-field models have different advantages and drawbacks. A Mean-field model is usually simple to analyze and in this case it gives precise conditions for coexistence. On the other hand spatial models are usually more difficult to analyze and computations of precise critical values are very difficult. However, in this particular case the analysis of the interacting particle system gives a precise pathwise analysis of how 2's that are endemic, in the initial configuration, will be driven out by 3's under certain conditions, see Theorem 1. Moreover, space seems quite important in the spread of epidemics and is completely ignored by mean-field models. Of course, our spatial model is a caricature of reality but we believe it is a first step in incorporating space into the model.

3. Proof of Theorem 1

Throughout this paper, we think of the epidemic process as being generated by Harris' graphical representation. That is to say, we are given appropriate families of independent Poisson processes which may be used to couple together different processes. Such constructions are standard; see for instance Durrett (1995).

Note that in the absence of 2's the process of 3's behaves like a forest fire model (i.e. the process ζ_t) introduced above. That is,

$$0 \to 1 \text{ at rate } \beta_1$$
$$1 \to 3 \text{ at rate } \beta_3 n_3(x, \eta)$$
$$3 \to 0 \text{ at rate } 1$$

Durrett and Neuhauser (1991) have proved that for $\beta_3 > \beta_c$ and $\beta_1 > 0$ there is a stationary distribution that concentrates on configurations with infinitely many 3's, for the forest fire model in dimension 2. The crucial point of their proof is that starting with at least one 3

there is a positive probability that 3's will persist forever in a growing spatial region (see Lemma 1.1 in their paper). Their proof is rather difficult and technical. However, if one observes, as in Andjel and Schinazi (1996), that if $\beta_1 = \infty$ the forest fire becomes a contact process then one can use the method in Section 5 Chapter I to prove that, for large β_1 and β_2 above the critical value of the contact process, the forest fire model dominates a supercritical percolation model.

Here we have to show that the forest fire model result still holds in the presence of 2's. In order to control the influence of the 2's, consider the following contact process

$$1 \to 2 \text{ at rate } \beta_2 n_2(x, \xi)$$
$$2 \to 1 \text{ at rate } \phi + r$$

We say that configuration ξ has more i's ($i = 1$ or $i = 2$) than configuration η if $\eta(x) = i$ implies that $\xi(x) = i$ for every x in $\mathbf{Z}^2$. Using the graphical construction, one can couple (that is, construct on the same probability space) η_t to ξ_t in such a way that if ξ_0 has more 1's and 2's than η_0 then ξ_t has more 1's and 2's than η_t at all times $t > 0$. But if

$$\frac{\beta_2}{r + \phi} < \lambda_c,$$

the 2's die out in the process ξ_t and therefore in the process η_t as well. Moreover, the 2's die out exponentially fast, see Bezuidenhout and Grimmett (1991). The exponential decay of the 2's implies the following. Let $B(r)$ be the closed Euclidean ball centered at the origin and with radius r.

Lemma 1. *Consider the contact process ξ_t under the condition $\frac{\beta_2}{r+\phi} < \lambda_c$. For any $a > 0$ and any $\epsilon > 0$ there is N such that if there are no 2's in $B(2N)$ at time 0 then there are no 2's in $B(at)$ at all times $t > 0$, with probability at least $1 - \epsilon$.*

Proof of Lemma 1.

Let a be a real number and N an integer to be chosen later. We consider small and large times. Let $b > 0$ such that $ab < 1$. Let ξ_t^N be the contact process, with birth rates $\beta_2 n_2(x, \xi)$ and death rates $\phi + r$, starting with no 2's in $B(2N)$ and 2's everywhere else.

$$\begin{aligned} &P(\exists t \le bN, \xi_t^N(x) = 2 \text{ for some } x \in B(at)) \le \\ &P(\exists x \in B(abN) : \xi_t^N(x) = 2 \text{ for some } t) \end{aligned} \tag{1}$$

But the contact process is an additive process: if $\xi_t^N(x) = 2$ then there must be some $y \in Z^d$ such that $\xi_t^y(x) = 2$ where ξ_t^y is the contact process starting with a single 2 at y

and 1's everywhere else, moreover we need to have $\xi_0^N(y) = 2$ so y must belong to $B(N)^c$. The r.h.s. of (1) is therefore less than

$$\sum_{x \in B(abN), y \in B(N)^c} P(\xi_t^y(x) = 2 \text{ for some } t) \tag{2}$$

Since ξ_t is a subcritical contact process we know by Bezuidenhout and Grimmett (1991) that there is a $c > 0$ such that

$$P(\xi_t^y(x) = 2 \text{ for some } t) \leq e^{-c||x-y||} \tag{3}$$

So the sum in (2) goes to zero exponentially fast as N goes to infinity if we pick b such that $ab < 1$. So for $N > N_1$, (2) is less than ϵ.

We now take care of the large times. By additivity again we get

$$P(\exists t \geq bN, \xi_t^N(x) = 2 \text{ for some } x \in B(at)) \leq$$

$$\sum_{k \geq bN} P(\exists t \in [k, k+1), \exists y \in Z^d, \xi_t^y(x) = 2 \text{ for some } x \in B(at))$$

We now consider large and small y. Define the survival time of the process ξ_t^y by

$$\tau^y = \inf\{t : \xi_t^y(x) = 1 \text{ for all } x \in Z^d\}$$

Then

$$\begin{aligned} &\sum_{k \geq bN} P(\exists t \in [k, k+1), \exists y \in B(2ak), \xi_t^y(x) = 2 \text{ for some } x \in B(at)) \leq \\ &\sum_{k \geq bN} P(\exists y \in B(2ak), \tau^y > k) \leq \sum_{k \geq bN} (4ak+1)^d P(\tau^0 > k) \end{aligned} \tag{4}$$

But again thanks to Bezuidenhout and Grimmett (1991) we know that

$$P(\tau^0 > k) \leq e^{-ck}$$

Therefore the r.h.s. of (4) goes to zero exponentially fast as N goes to infinity and for $N > N_2$ it is less than ϵ. We finally consider what happens for large y.

$$\sum_{k \geq bN} P(\exists t \in [k, k+1), \exists y \in B^c(2ak), \xi_t^y(x) = 2 \text{ for some } x \in B(at)) \leq$$

$$\sum_{k \geq bN} P(\exists y \in B^c(2ak), \exists x \in B(a(k+1)) \text{ such that } \xi_t^y(x) = 2 \text{ for some } t)$$

But this last sum is less than

$$\sum_{k\geq bN} \quad \sum_{x\in B(a(k+1))} \quad \sum_{y\in B^c(2ak)} P(\xi_t^y(x) = 2 \text{ for some } t)$$

Using (3) again we see that this term is less than

$$\sum_{k\geq bN} \quad \sum_{l\leq a(k+1)} \quad \sum_{m\geq 2ak} (2l+1)^d (2m+1)^d e^{-c(m-l)}$$

But this sum goes to zero as N goes to infinity, therefore for $N > N_3$ this sum is less than ϵ. This completes the proof of Lemma 1.

Recall that η_0 has infinitely many 2's. Since the mutation rate ϕ is strictly positive there is, with probability one at time 1, a site z in state 3. We start, at time 1, the construction of Durrett and Neuhauser (1991). There is a positive probability that the 3 will generate a spatial growing region, B_t, that will take over the whole space. To be more precise, we may think of B_t as being the smallest Euclidean ball that contains all the 3's, at time t, whose line of infection goes back to z. Moreover, it is not difficult to see that B_t grows at most linearly, see for instance p17-18 in Durrett (1988). More precisely, for any $\epsilon > 0$ there is an $R_1 > 0$ such that the event

$$\mathcal{A} = \{B_t \subset [-R_1 t, R_1 t]^2 \text{ for all } t \geq 1\}$$

has probability at least 1-ϵ. On the other hand, by Lemma 1.1 we have that the event

$$\mathcal{B} = \{ \text{ there are no 2's in } [-R_2 t, R_2 t]^2 \text{ for all } t \geq 1\}$$

has probability at least 1-ϵ, for R_2 large enough. Take $R_2 > R_1$. Observe that that $\mathcal{A} \cap \mathcal{B}$ has probability at least $1 - 2\epsilon$. Therefore, the probability that the construction succeeds, that is, that B_t grows forever and that $\mathcal{A}$ and $\mathcal{B}$ occur has a strictly positive probability. If the construction fails, i.e., the 3's die out or come into contact with the 2's we can try this construction again. Since the trials are independent and the probability of success of each trial is bounded below by the same constant, the construction will eventually succeed. This proves Theorem 1.

4. Proof of Theorem 2.

It is enough to work in $d = 1$ because the construction that follows may be embedded in higher dimensional spaces.

Consider the process η_t with $\phi = r = 0$ restricted to some finite box $[-4L, 4L]$ and with 2's on every site of the interval $[-L, L]$. In the case $\phi = r = 0$ the 2's do not die and

the rightmost 2, denoted by r_t, can only go to the right. We now describe one of the ways r_t may jump at least one unit to the right. Assume that $r_t = x$ and that there is a death with rate 1 at $x+1$ (so that if there is 3 at $x+1$ it is killed), followed by a birth of a 1 at $x+1$ and finally an infection from x to $x+1$ before anything else happens. After this succession of events $r_t = x+1$. This shows that we may couple r_t to a renewal process in such a way that r_t is always larger than the renewal process. Thus, by the Renewal Theorem we see that

$$\liminf_{t\to\infty} \frac{r_t}{t} \geq \frac{1}{1+\frac{1}{\beta_1}+\frac{\beta_2}{(\beta_2+\beta_3)^2}}. \tag{5}$$

Let

$$B = [-4L, 4L] \times [0, T] \qquad B_{m,n} = (2mL, nT) + B$$

$$\mathcal{L} = \{(m,n) \in \mathbf{Z}^2 : m+n \text{ is even}\}.$$

We define the following percolation process on $\mathcal{L}$. We declare $(m,n) \in \mathcal{L}$ wet if each site of the interval $2mL + [-L, L]$ is occupied by a 2 at time nT for the process restricted to $(2Lm, Tn) + (-4L, 4L) \times [0, T]$.

By (5), for every $\epsilon > 0$ there are L and $T = cL$ (where c depends on the edge speed) such that

$$P((1,1) \text{ and } (-1,1) \text{ are wet} | (0,0) \text{ is wet}) > 1 - \epsilon \text{ for } \phi = r = 0.$$

Since we are dealing with the process restricted to a finite space time region, we have by continuity that

$$P((1,1) \text{ and } (-1,1) \text{ are wet} | (0,0) \text{ is wet}) > 1 - \epsilon \text{ for } \phi + r > 0.$$

This is enough to show that the 2's in η_t dominate a supercritical oriented percolation model. See the last step in the proof of Theorem (b) in Chapter I.

Starting with 2's on every site of Z, standard arguments (see Liggett (1985)) show that a subsequence of the Cesaro average of the distributions converges to a stationary distribution that concentrates on configurations with infinitely many 2's. Since $\phi > 0$, this stationary distribution must concentrate on configurations with infinitely many 3's as well. There is coexistence for $\phi + r$ small enough and this proves Theorem 2.

IV A model for HIV/TB interaction

It is known that an HIV infection when concomitant with another disease such as tuberculosis or pneumonia is a lot more lethal than HIV alone. We introduce two mathematical models for which if the concomitant diseases are prevalent enough in a given population and if double infections are lethal enough then HIV cannot take hold in this population. This provides an alternative (or a complement) to the theory that what determines whether a population will suffer an HIV epidemic is its sexual behavior. Our point of view may be relevant to the situation in Southeast Asia.

1. Introduction. There are many infectious diseases that plague the poorest populations: tuberculosis, pneumonia, sexually transmitted diseases. The combination of one of these infectious diseases with HIV is known to be more lethal than HIV alone. For instance, it is thought that today at least one billion people are infected with tuberculosis. Of these, if they are not also infected with HIV, only a fraction (between 5% and 15%) will develop the disease during their lifetime, see Enarson and Rouillon (1998). The appearance of HIV in an individual infected with TB disrupts the balance between the tubercle bacillus and its human host. It is believed that more than 30% of people infected with both HIV and TB develop TB during their lifetime. Moreover, the response to TB treatment is much better in people who are HIV negative than in people who are HIV positive, see Enarson and Rouillon (1998), Rieder et al. (1989) and Chum et al. (1996).

The HIV pandemic has hit very hard some populations (in particular in Africa) while it has largely spared some other populations (in particular in some parts of Asia). A widely accepted explanation for that is the difference in sexual behavior in different populations (see UNAIDS (1998) and (1999)). In this chapter we propose an alternative theory. If the double infection by HIV and a given concomitant infection is lethal enough and if a given population has a high enough density of the concomitant infection then HIV cannot take hold in the population. It is known that if a given disease is too virulent (such as Ebola, for instance) then it cannot spread. Our hypothesis is that many double infections such as TB/HIV are too virulent to spread. We are in particular interested in Southeast Asia where TB is highly prevalent (more than 50% of the population is infected in some countries) and which has been somewhat spared by the HIV pandemic so far, see Dye et al. (1999). We will use two simple mathematical models to make our point more precise. In the first model we will assume that all individuals mix together. In the second model there will be a spatial structure and the individuals will be able to mix only with their nearest neighbors. Our results will show that the two models have the same qualitative

behavior. Since these two models are at opposite ends in terms of mixing and they show the same qualitative behavior we think this is a good indication that our results hold for a rather general class of models. The models used below are variations of models used in Schinazi (2001) for another question.

2. A model with total mixing. We consider a population for which there is at least one endemic disease such as TB, pneumonia or a sexually transmitted disease which is not HIV. An individual taken at random in the population is infected with the endemic disease with probability p. For each individual in the population there are three possible states: 0 (HIV negative), 1 (HIV positive, no concomitant infection) or 2 (HIV positive, concomitant infection). Our (very) simple minded model evolves as follows. An individual in state 0 is infected by HIV at a rate proportional to the density of HIV infected individuals in the population. A newly HIV infected individual is in state 2 with probability p or in state 1 with probability $1-p$, depending whether he was already infected by something else or not. Individuals in states 1 and 2 die at rate δ_1 and δ_2, respectively. We will assume the biologically meaningful hypothesis that

$$\delta_1 < \delta_2.$$

Let u_i, $i = 0, 1, 2$, be the density of individuals in state i. In particular, $u_0 + u_1 + u_2 = 1$. Assuming that all individuals mix with each other we get the following system of differential equations:

$$\begin{aligned}\frac{du_1}{dt} =& \lambda(1-p)u_0(u_1+u_2) - \delta_1 u_1\\ \frac{du_2}{dt} =& \lambda p u_0(u_1+u_2) - \delta_2 u_2\end{aligned}$$

where λ is the infection rate. It is clear that $(u_1, u_2) = (0, 0)$ is an equilibrium for the system above. This is the HIV free equilibrium. If this equilibrium is unstable we will say that an HIV epidemic is possible. If (0,0) is stable then we will say that an HIV epidemic is not possible. We know that an equilibrium is stable if and only if all eigenvalues of the Jacobian matrix have strictly negative real parts. For an elementary introduction to stability see for instance Boyce and DiPrima (1992). The Jacobian of the system of differential equations at (0,0) is

$$\begin{pmatrix} \lambda(1-p) - \delta_1 & \lambda(1-p) \\ \lambda p & \lambda p - \delta_2 \end{pmatrix}.$$

The determinant of this matrix is

$$Det = \lambda p(\delta_2 - \delta_1) - \delta_2(\lambda - \delta_1)$$

and its trace is

$$Tr = \lambda - (\delta_1 + \delta_2).$$

There are three cases to consider.

(a) Assume that $\lambda < \delta_1 < \delta_2$. In this case the determinant is positive and the trace is negative for any p in [0,1] and $\delta_2 > \delta_1$. Thus, the eigenvalues of the Jacobian have negative real parts. The equilibrium (0,0) is stable and no epidemic can take place.

(b) Assume that $\delta_1 < \lambda < \delta_2$. Note that the determinant is negative if and only if

$$p < p_c$$

where

$$p_c = \frac{\delta_2}{\delta_2 - \delta_1}(1 - \delta_1/\lambda).$$

Observe that under the assumption $\delta_1 < \lambda < \delta_2$ the critical value p_c is strictly between 0 and 1.

If

$$p > p_c$$

then the determinant is positive and the trace is negative. Thus, no epidemic is possible.

In conclusion, under the assumption $\delta_1 < \lambda < \delta_2$ an epidemic is possible if and only if p is smaller than p_c.

(c) Assume that $\delta_1 < \delta_2 < \lambda$. In this case the determinant is negative for all p in [0,1]. For, using that $p \leq 1$ we get

$$Det = \lambda p(\delta_2 - \delta_1) - \delta_2(\lambda - \delta_1) \leq \lambda(\delta_2 - \delta_1) - \delta_2(\lambda - \delta_1) = \delta_1(-\lambda + \delta_2) < 0.$$

Thus, in this case an epidemic is always possible.

Case (b) is the most interesting one. There, we assume that $\delta_1 < \lambda < \delta_2$. That is, an HIV epidemic is possible in the absence of concomitant diseases ($p = 0$ and $\delta_1 < \lambda$) but is not possible in the case where the whole population is infected by a concomitant disease ($p = 1$ and $\lambda < \delta_2$). We have shown that an HIV epidemic is possible if and only if the proportion p of the population infected with a concomitant infection is above a certain threshold p_c. So, at least in theory, if the double infection is lethal enough (mathematically this is translated by $\lambda < \delta_2$) then an HIV epidemic is not possible in a population where other infections are highly prevalent (that is, if $p > p_c$).

3. A model with little mixing

We now consider a continuous time spatial stochastic model η_t on $\mathbf{Z}^d$ where each site may be in one of three states: 0, 1 or 2. If the model is in configuration η, let $n_1(x,\eta)$ and $n_2(x,\eta)$ be the number of nearest neighbors of x (among the $2d$ nearest neighbors of x) that are in state 1 and in state 2, respectively. Assume that the model is in configuration η, then the state at a given site x evolves as follows:

$$0 \to 1 \text{ at rate } \lambda(1-p)(n_1(x,\eta)+n_2(x,\eta))$$
$$0 \to 2 \text{ at rate } \lambda p(n_1(x,\eta)+n_2(x,\eta))$$
$$1 \to 0 \text{ at rate } \delta_1$$
$$2 \to 0 \text{ at rate } \delta_2$$

In words, 1's and 2's infect nearest neighbors that are in state 0 at rate λ. Newly infected individuals are 1 with probability $1-p$ or 2 with probability p. Infected individuals in state 1 and 2 die at rates δ_1 and δ_2, respectively. For this model we will say that an HIV epidemic is possible if there is a positive probability that the process never hits the configuration where all sites are in state 0.

In the absence of concomitant infection, i.e. $p = 0$, we have a population of 0's and 1's only. In this particular case, the system evolves as

$$0 \to 1 \text{ at rate } \lambda n_1(x,\eta)$$
$$1 \to 0 \text{ at rate } \delta_1$$

The model above is called a contact process. It is known that there is a critical value λ_c (that depends on the dimension d of the grid $\mathbf{Z}^d$) such that if $\lambda \le \lambda_c$ then an epidemic is not possible (the 1's die out) while if $\lambda > \lambda_c$ then an epidemic is possible. For more on the contact process, see for instance Liggett (1999). We are now ready to state our result.

Theorem. *(a) If $\frac{\lambda}{\delta_1} < \lambda_c$ then no HIV epidemic can take place for any p in [0,1] and any $\delta_2 > \delta_1$.*

(b) If $\frac{\lambda}{\delta_2} < \lambda_c$ then for any $\delta_1 < \delta_2$ there is a $p_c(\lambda,\delta_1,\delta_2)$ in (0,1) such that no HIV epidemic can take place for any $p > p_c$.

(c) If $\frac{\lambda}{\delta_2} > \lambda_c$ then for any $\delta_1 < \delta_2$ and any p in [0,1] an epidemic is possible.

Observe that the spatial stochastic model has the same qualitative behavior as the mean field model. We see again in (b) that if a large proportion of a population is already sick and if the double infection with HIV is lethal enough then HIV will not be able to invade this population. This might be one explanation why Southeast Asia has been

largely spared (so far) by the HIV pandemic: this is one of the regions in the world where TB prevalence is the highest (see Dye et al. (1999)). However, there are certainly other explanations why some populations have been hit harder than others by the HIV pandemic. In particular, sexual practices such as the number of partners per individual seem to play a pivotal role, see Rotello (1997), UNAIDS (1998) and (1999). It might be the case that the proportion in the population of concomitant infection is useful as a secondary explanatory variable (after sexual practices) to predict whether HIV will invade a given population.

4. Proof of the Theorem. We now give the explicit graphical construction for the process η_t. The graphical construction takes place in the space-time region $\mathbf{Z}^d \times (0, \infty)$. Consider a collection of independent Poisson processes: $\{N^{x,y}, D^x : x, y \in \mathbf{Z}^d, ||x-y|| = 1\}$. For x and y in $\mathbf{Z}^d$ such that $||x - y|| = 1$ let the intensities of $N^{x,y}$, D^x be λ and δ_2, respectively. For each x in $\mathbf{Z}^d$, at each arrival time of the Poisson process D^x, if there is a 2 at x it is replaced by a 0. If there is a 1 at x then it is replaced by a 0 with probability δ_1/δ_2. With this recipe deaths of 2's occur at rate δ_2 and deaths of 1's occur at rate δ_1. Moreover, the deaths are coupled in a way that will be useful in our proof. At an arrival time of $N^{x,y}$ if there is a 1 or a 2 at x and a 0 at y we put a 1 at y with probability $1 - p$ or a 2 at y with probability p. In this way we obtain a version of our spatial stochastic process. We construct the process *restricted* to a space-time region $\mathcal{A}$ if we only use the arrival times of the Poisson processes $N^{x,y}$ and D^x for x and y inside $\mathcal{A}$. For more on graphical constructions, see p 32 in Liggett (1999).

Proofs of Theorem (a) and (c)

Consider the contact process ξ_t with only states 0 and 1 and rates:

$$0 \to 1 \text{ at rate } \lambda n_1(x, \xi)$$
$$1 \to 0 \text{ at rate } \delta_1$$

We construct the process ξ_t with the same Poisson processes $N^{x,y}$ and D^x that we use for η_t. However, for ξ_t we take $p = 0$ in this construction. It is easy to check that if we take initial configurations ξ_0 and η_0 such that if there is a 1 or 2 at x for the configuration η_0 then there is a 1 at x for the configuration ξ_0 then the same is true at any time t for configurations η_t and ξ_t. This is due to the fact that birth rates for ξ_t and η_t are the same but death rates are lower for ξ_t than for η_t. Under the assumption $\frac{\lambda}{\delta_1} < \lambda_c$, the 1's in ξ_t die out for any initial configuration thus the 1's and 2's in η_t must die out as well. An epidemic is not possible. This completes the proof of (a).

The proof of (c) is quite similar to the proof of (a). We consider a contact process ζ_t

that evolves according to the following rates:

$$0 \to 2 \text{ at rate } \lambda n_2(x,\zeta)$$
$$2 \to 0 \text{ at rate } \delta_2$$

We also construct ζ_t in the same probability space as η_t by using the same Poisson processes to construct both processes. However, for ζ_t we take $p = 1$ in this construction. This time ζ_t is below η_t in the following sense. If we take initial configurations ζ_0 and η_0 such that if there is a 2 at x for the configuration ζ_0 then there is a 1 or a 2 at x for the configuration η_0 then the same is true at any time t for configurations ζ_t and η_t. This is due to the fact that birth rates are the same for both processes but death rates are higher for ζ_t than for η_t. Under the assumption $\frac{\lambda}{\delta_2} > \lambda_c$, starting with at least one 2, the 2's in ζ_t have a positive probability of surviving forever. The same must be true for η_t. An epidemic is possible. This completes the proof of (c).

Proof of Theorem (b)

We prove (b) under the assumption $d = 2$, in order to avoid more cumbersome notation. The same ideas work in any $d \geq 1$.

We define two space–time regions:

$$\mathcal{A} = [-2L, 2L]^2 \times [0, 2L], \qquad \mathcal{B} = [-L, L]^2 \times [L, 2L]$$

where L is an integer to be chosen later. Define $\mathcal{C}$ to be part of the 'boundary' of the box $\mathcal{A}$:

$$\mathcal{C} = \Big\{(m,n,t) \in \mathcal{A} : |m| = 2L \text{ or } |n| = 2L \text{ or } t = 0\Big\}$$

We will compare our spatial stochastic model to a certain dependent percolation process on the set $\mathcal{L} = \mathbf{Z}^2 \times \mathbf{Z}_+$, where $\mathbf{Z}_+ = \{0, 1, 2, \ldots\}$. We say that the site (k, m, n) in $\mathcal{L}$ is *wet* if there are no 1's and no 2's in $(kL, mL, nL) + \mathcal{B}$ whatever the configuration in $(kL, mL, nL) + \mathcal{C}$ is for the process restricted to $(kL, mL, nL) + \mathcal{A}$. Sites which are not wet are called *dry*.

For any $\epsilon > 0$, given $\frac{\lambda}{\delta_2} < \lambda_c$ and $\delta_1 < \delta_2$ we will show that there is an integer L and a proportion p_c such that:

$$P\big((k,m,n) \text{ is wet}\big) \geq 1 - \epsilon \text{ if } p > p_c.$$

We start by showing the above property when $p = 1$. Then, using a continuity argument, we will deduce that the inequality remains true for p close to but smaller than 1. By translation-invariance, it suffices to consider the site $(0, 0, 0) \in \mathcal{L}$. Note that if $p = 1$ then

1's and 2's do not give birth to 1's in the space-time region $\mathcal{A}$ and the 1's that are in $[-2L, 2L]^2$ at time 0 will rapidly disappear. Let E be the event that there are no 1's left at time $L/2$ in $[-2L, 2L]^2$. Because there are $(4L+1)^2$ sites in $\mathcal{A}$ and since the death rate of 1's is δ_1 we have that

$$P(E) \geq (1 - e^{-\delta_1 L/2})^{(4L+1)^2}.$$

By taking L large enough, the r.h.s. may be made larger than $1 - \epsilon/4$ for an arbitrarily small $\epsilon > 0$.

On E there are only 0's and 2's left in $[-2L, 2L]^2$ by time $L/2$. Thereafter the 2's evolve as a subcritical contact process in $\mathcal{A}$. Let F be the event that there are no 2's in the space time region $\mathcal{B}$. On E, if there is a 2 in $\mathcal{B}$ there must be an infection path from $[-2L, 2L]^2 \times L/2$ into $\mathcal{B}$ or from one of the sides of the box $\mathcal{A}$ into $\mathcal{B}$. Let $\mathcal{D}$ be

$$\mathcal{D} = \{(m, n) \in \mathbf{Z}^2 : |m| = 2L \text{ or } |n| = 2L\}.$$

Let $\{(x, t) \to \mathcal{B}\}$ denote the event that there is an infection path from (x, t) to $\mathcal{B}$ inside $\mathcal{A}$. An infection path from x in $\mathcal{D}$ to $\mathcal{B}$ has length at least L. Bezuidenhout and Grimmett (1991) have shown, for the subcritical contact process, that the probability that an infection path is at least L long is less than $Ce^{-\gamma L}$ where C and γ are strictly positive constants. Thus,

$$P(\exists x \in \mathcal{D}, \exists t \in [0, 2L] : (x, t) \to \mathcal{B}) \leq 2L \times 4(4L+1)Ce^{-\gamma L}.$$

Similarly the probability of an infection path from $[-2L, 2L]^2 \times L/2$ to $\mathcal{B}$ is less than $(4L+1)^2 Ce^{-\gamma L/2}$. Therefore, we have

$$P(F|E) \geq 1 - 8L(4L+1)Ce^{-\gamma L} - (4L+1)^2 Ce^{-\gamma L/2}.$$

By taking L large enough the probability above may be made larger than $1 - \epsilon/4$. We have

$$P\big((0,0,0) \text{ is wet}\big) \geq P(EF) = P(E)P(F|E) \geq 1 - \epsilon/2 \text{ if } p = 1.$$

Since $\mathcal{A}$ is a finite box there is $p_c < 1$ such that with probability at least $1 - \epsilon/2$ there are no arrivals inside $\mathcal{A}$ of Poisson processes with rate $\lambda(1-p)$. That is, by picking p close enough to one there will be no birth of 1 inside $\mathcal{A}$, with high probability. Therefore, we get

$$P\big((0,0,0) \text{ is wet}\big) \geq 1 - \epsilon \text{ if } p > p_c.$$

With the preceding result in hand to complete the proof of Theorem (b) one can use exactly the same arguments as the ones in the proof of Lemma 1 (Chapter II). In particular, if T_0 is the supremum of the times for which there is a 1 or a 2 at the origin, the probability that T_0 is larger than t goes to 0 exponentially fast.

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