From individuals to epidemics

S. A. LEVIN[1] AND R. DURRETT[2]

[1] *Department of Ecology and Evolutionary Biology, Princeton University, Princeton, NJ 08544-1003, U.S.A.*
[2] *Department of Mathematics, Cornell University, Ithaca, NY 14853-7901, U.S.A.*

SUMMARY

Heterogeneous mixing fundamentally changes the dynamics of infectious diseases; finding ways to incorporate it into models represents a critical challenge. Phenomenological approaches are deficient in their lack of attention to underlying processes; individual-based models, on the other hand, may obscure the essential interactions in a sea of detail. The challenge then is to find ways to bridge these levels of description, starting from individual-based models and deriving macroscopic descriptions from them that retain essential detail, and filter out the rest.

In this paper, attempts to achieve this transformation are described for a class of models where non-random mixing arises from the spatial localization of interactions. In general, the epidemic threshold is found to be larger owing to spatial localization than for a homogeneously mixing population. An improved estimate of the dynamics is developed by the use of moment equations, and a simple estimate of the threshold in terms of a 'dyad heuristic'. For more general models in which local infection is not described by mass action, the connection with related partial differential equations is investigated.

1. INTRODUCTION

In recent years, the linkages between ecology and epidemiology have been made more explicit (Anderson & May 1991) through introduction of variable population sizes, interacting strains, and other ecological features into epidemiological models (see, for example, Castillo-Chavez *et al.* 1989*b*). The evolution of disease dynamics, the coevolution of hosts and parasites, and the beginnings of a community theory (see, for example, Levin *et al.* 1990) all have received attention.

One of the most important links between these disciplines is the way to represent heterogeneous mixing, acknowledged to be important in a wide range of diseases (see, for example, Hethcote & Yorke 1984). One approach (Hethcote & Yorke 1984; Liu *et al.* 1987; May & Anderson 1989; Anderson & May 1991) is to substitute phenomenological nonlinear terms representing aggregated behaviour; a complementary approach (see, for example, Hethcote & Yorke 1984; Schenzle 1985; Castillo-Chavez *et al.* 1989*a*) is to break the population into classes of individuals, each with its own dynamics and connections to other classes. Rarely, however, are these two approaches united. One goal of research in this area must be to relate dynamics on different scales by representing aggregate behaviour in terms of that of individual or local groupings, such as families.

2. THE PROBLEM OF CLOSURE

To illustrate this point, consider the familiar *S*–*I*–*R* system

$$\begin{aligned} \mathrm{d}S/\mathrm{d}t &= r(S+I+R)-\beta SI-\mu S,\\ \mathrm{d}I/\mathrm{d}t &= \beta SI-\lambda I-\mu I,\\ \mathrm{d}R/\mathrm{d}t &= \lambda I-\mu R, \end{aligned} \tag{1}$$

with or without the common assumption $r=\mu$ (note that without this assumption, the population grows or decays exponentially). Here, S refers to the number of susceptible individuals in the population; I, the number of infectious individuals; and R, the number of individuals recovered or removed.

System (1) represents what physicists would call mean field dynamics. That is, these are the equations that arise in the limit of $N\to\infty$ of a homogeneously mixing population of N individuals. Each infected individual is considered equally likely to infect each susceptible individual. Imagine instead that equation (1) represents the local dynamics within some subpopulation, and that many such subpopulations are linked together, through conservative dispersal (no loss), into a single 'metapopulation'. Write

$$\begin{aligned} S &= \langle S\rangle + s;\\ I &= \langle I\rangle + i;\\ R &= \langle R\rangle + r. \end{aligned} \tag{2}$$

Here $\langle S\rangle$, $\langle I\rangle$ and $\langle R\rangle$ represent the average values of S, I and R for the entire metapopulation, where S, I and R are the numbers of each type within a subpopulation, and s, i and r are the deviations from the population means. Then, because $\langle s\rangle=\langle i\rangle=\langle r\rangle=0$, system (1) leads to the system

$$\begin{aligned} \mathrm{d}\langle S\rangle/\mathrm{d}t &= r(\langle S\rangle+\langle I\rangle+\langle R\rangle)-\mu\langle S\rangle\\ &\quad -\beta\langle S\rangle\langle I\rangle-\beta\langle si\rangle,\\ \mathrm{d}\langle I\rangle/\mathrm{d}t &= \beta\langle S\rangle\langle I\rangle+\beta\langle si\rangle-\lambda\langle I\rangle-\mu\langle I\rangle,\\ \mathrm{d}\langle R\rangle/\mathrm{d}t &= \lambda\langle I\rangle-\mu\langle R\rangle, \end{aligned} \tag{3}$$

in which $\langle si\rangle$ is the metapopulation average of si. Except for the terms $\langle si\rangle$, the system looks identical to the mean field equations. Note that the parameters

have been assumed to be identical for all subpopulations. Furthermore the assumption that dispersal is conservative assures that there is no net contribution to the terms for the means.

System (3) represents a second-order correction to the mean field dynamics. The difficulty is that the system is not closed: one must either assume some form for $\langle si \rangle$ in terms of the means (in the mean field approximation, one simply sets $\langle si \rangle = 0$), or write equations for $\mathrm{d}\langle si \rangle / \mathrm{d}t$ that will involve higher-order correlations. At some point, the system must be closed if one is to succeed in analysing it by standard methods; compare, for example, Adler & Brunet (1991). Approaches to such closure are illustrated in the succeeding sections.

3. THE BASIC CONTACT PROCESS

The model of the preceding section is deterministic, but the methods can be applied equally to stochastic processes. In particular, for spatial stochastic processes, ensemble averages may be taken over the set of all realizations of the process, as well as over space.

The challenge of closure then can be illustrated effectively with another, even simpler model of epidemic spread: the contact process. This model has been studied by mathematicians for more than twenty years. For references and more information see Durrett & Levin (1994*a*). Imagine a grid of cells, each either susceptible or infected. The only rules are that infected individuals (sites) recover at a rate δ (the inter-occurrence times t_{i} are independent and have an exponential distribution with mean $1/\delta$; i.e. $P(t_{\mathrm{i}} > t) = \mathrm{e}^{-\delta t}$), and that an infected individual can infect any of its four nearest neighbours at rate λ. Then the fraction of infected sites $p_t(1)$ satisfies the equation

$$\mathrm{d}p_t(1)/\mathrm{d}t = -\delta p_t(1) + 4\lambda p_t(01), \tag{4}$$

where $p_t(01)$ is the probability that an ordered pair of adjacent sites will be in the configuration (susceptible–infected). Here, to simplify the description, it is assumed that $P(\xi_t(x) = 0, \xi_t(x+z) = 1)$ is the same for $z = (1,0)$, $(0,1)$, $(-1,0)$, and $(0,-1)$. Owing to the symmetries of the model, if this is true in the initial distribution at time $t = 0$ it will be true at all times $t > 0$. For small values of λ/δ, the infection will die out; however, for λ/δ greater than a critical value ($\lambda/\delta \approx 0.41$), invasion will take place from low densities to an equilibrium configuration characterized by clustering of infectives (see figure 1).

Figure 1. The basic contact-process equilibrium when $\lambda = 0.25$ and $\delta = 0.35$. Reprinted from Durrett & Levin (1994*b*).

As in the previous example, equation (4) does not represent a closed system. The simplest (mean-field) assumption, that adjacent sites are independent, yields the approximation

$$p_t(01) = p_t(0)\,p_t(1) = [1 - p_t(1)]\,p_t(1), \tag{5}$$

and hence

$$\begin{aligned}\mathrm{d}p_t(1)/\mathrm{d}t &= -\delta p_t(1) + 4\lambda p_t(1)\,[1 - p_t(1)] \\ &= p_t(1)\,[(4\lambda - \delta) - 4\lambda p_t(1)].\end{aligned} \tag{6}$$

Because this is the familiar logistic equation, it is clear that equation (6) has a globally stable disease-free equilibrium at $u_t(1) = 0$ if

$$\lambda/\delta \leqslant 1/4, \tag{7}$$

and a globally stable endemic equilibrium $u_t(1) = (1-\delta)/4\lambda$ provided

$$\lambda/\delta > 1/4. \tag{8}$$

The problem with this approximation is that it ignores the clustering that is characteristic of the contact process. Hence, the threshold at $1/4$ is less than the true threshold ($\lambda/\delta \approx 0.41$) seen in the contact process, because in the latter case clustering of infected individuals causes a higher fraction of the potentially infectious contacts to be wasted than if the sites were independent. An improvement on the mean field dynamics is possible by introduction of the second equation

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t} p_t(01) = &-(\lambda + \delta)\,p_t(01) + \delta p_t(11) \\ &- 2\lambda p_t\begin{pmatrix}1 & \\ 0 & 1\end{pmatrix} - \lambda p_t(101) \\ &+ 2\lambda p_t\begin{pmatrix} & 1 \\ 0 & 0\end{pmatrix} + \lambda p_t(001),\end{aligned} \tag{9}$$

where, for example, $p_t(101)$ is the probability that three successive sites are in the configuration infected-susceptible-infected. This equation is derived in a straightforward manner by considering the ways in which a 01 pair can be created or destroyed, and the rates at which the corresponding transitions occur.

Taking a clue from the physics literature and applications in biology (see, for example, Dickman 1986, 1988; Matsuda 1987; Matsuda *et al.* 1987, 1992; Harada & Iwasa 1994; Sato *et al.* 1994; Harada *et al.* 1995), we make the approximation

$$p_t(001) = p_t(01)\frac{p_t(001)}{p_t(01)} \approx p_t(01)\frac{p_t(00)}{p_t(0)} \tag{10}$$

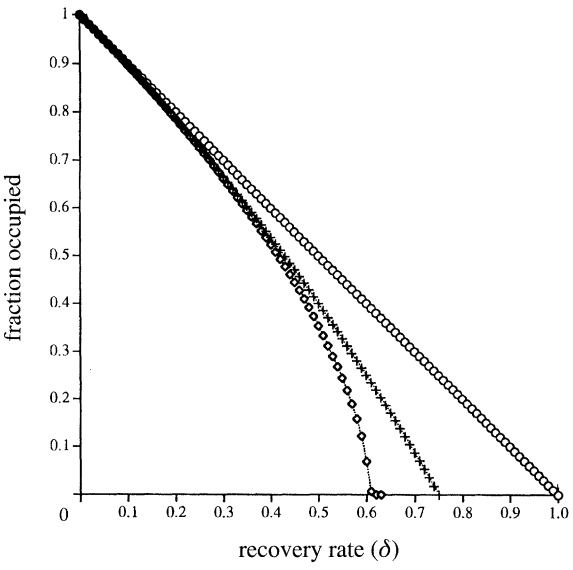

Figure 2. Fraction of occupied sites as a function of the recovery rate δ. The lowest curve (diamonds) denotes a simulation result, the upper curve (circles) the mean field approximation, and the middle curve (pluses) the improved agreement possible via second-order approximation.

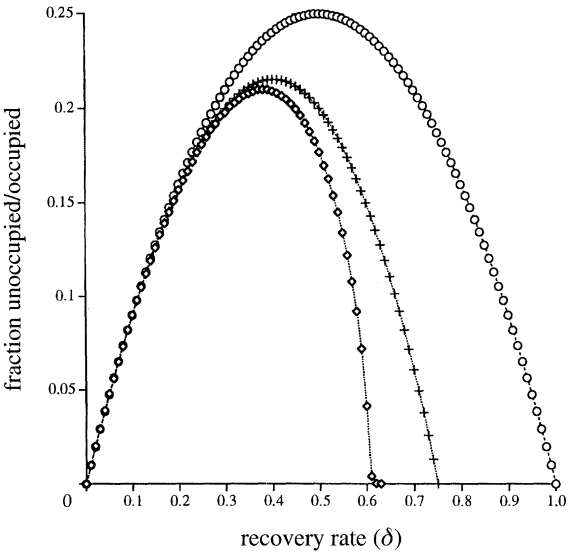

Figure 3. Fraction of contiguous pairs of (unoccupied/occupied) cells in the configuration as a function of the recovery rate δ. Symbols are as in figure 2. Again, the lowest curve demonstrates a simulation, the upper curve the mean field, and the middle curve the second-order approximation.

and similarly

$$p_t\begin{pmatrix}0 & 1\\ 1 & \end{pmatrix} = p_t\begin{pmatrix}1 & \\ 0 & 1\end{pmatrix} = p_t(101) \approx p_t(10)\frac{p_t(01)}{p_t(0)}. \quad (11)$$

The symmetry $p_t(10) = p_t(01)$ and the identities

$$p_t(11) = p_t(1) - p_t(01),$$
$$p_t(00) = p_t(0) - p_t(01),$$
$$p_t(1) = 1 - p_t(0) \quad (12)$$

with the changes of variable $u = p_t(1)$ and $v = p_t(01)$ then transform equation (9) to the pair

$$\dot{u} = -\delta u + 4\lambda v;$$
$$\dot{v} = -(\lambda+\delta)v + \delta(u-v) - 3\lambda v(2v+u-1)/(1-u), \quad (13)$$

where superdots denote time derivatives.

To find the equilibria for the system in equations (13), one notes that the first equation implies $u = (4\lambda/\delta)v$ and then inserts this into the second to get a quadratic equation. Solving that equation one finds that there is an equilibrium $u = (12\lambda - 4\delta)/(12\lambda - \delta)$ with $u, v > 0$ if and only if $\lambda/\delta > 1/3$, closer by half to the correct threshold of 0.41. The equilibrium u is identical in form to that of the mean field model, but with the birth rate λ diminished by $\delta/12$; to a first approximation, the effect of spatial localization is to reduce the growth rate.

The location of the threshold is only one way to compare the various approximations with the true dynamics. In figure 2 the birth rate is set to $\lambda = 1$ and the death rate δ is varied to compare the equilibrium density of infected sites in the contact process as determined by simulation (diamonds), with the predictions of mean field theory (circles) and our second-order approximation (pluses). Figure 3 shows the same comparisons for the probability of a 01 pair, i.e. the probability that a site x will be vacant but its right neighbour $x + (1, 0)$ will be occupied. In each case, the second-order approximation is not very accurate in the range 0.5–0.75 but represents a considerable improvement over mean-field theory.

It is important to note that system (13) is a dynamic approximation, describing system dynamics during the transient stages. Comparison of results in terms of equilibrium behaviour is one convenient measure of the success of the approach, but system (13) may also yield improvement in the description of transient dynamics. None the less, it must be recognized that moment equations are likely to be less effective in dealing with the initial stages of invasion, when the invading population is limited to a small area of space.

4. THE GENERALIZED CONTACT PROCESS

Consider now a more general contact process with neighbourhood set $\mathcal{N}$. Here $\mathcal{N}$ represents the neighbours of the origin $(0, 0)$, i.e. the set of sites it can infect, and the neighbours of a general site x are $x + \mathcal{N} = \{x + y : y \in \mathcal{N}\}$. Because the relation that x is a neighbour of y is required to be symmetric, the assumption is made that if $z \in \mathcal{N}$ then $-z \in \mathcal{N}$.

The dynamics for the more general model are, except for the choice of neighbourhood, identical to the nearest-neighbour case: infected individuals recover at a rate δ, and an infected individual can infect any of its neighbours at a rate λ. The new level of generality forces us to adopt different notation, but otherwise the mean field reasoning is the same. The reader who is not interested in the details can skip ahead to equation (24).

Let $\xi_t(x) = 1$ denote that x is infected at time t, and

$\xi_t(x) = 0$ denote that it is susceptible. The analogue of equation (4) in the current situation is

$$\frac{\mathrm{d}}{\mathrm{d}t}P(\xi_t(x) = 1) = -\delta P(\xi_t(x) = 1)$$

$$+\delta \sum_{z\in\mathcal{N}} P(\xi_t(x) = 0,\ \xi_t(x+z) = 1). \quad (14)$$

If we were to assume that neighbouring sites were independent and write $u(t) = P(\xi_t x) = 1$ then we would arrive at a close relative of equation (6), the mean field approximation

$$\mathrm{d}u/\mathrm{d}t = -\delta u + N\lambda u(1-u), \quad (15)$$

where N is the number of points in $\mathcal{N}$. Repeating the previous argument, we see that the disease-free equilibrium is globally stable if $N\lambda \leqslant \delta$ and that a globally stable endemic equilibrium $(1-\delta)/N\lambda$ exists if $N\lambda > \delta$. Because $R = N\lambda/\delta$ is the expected number of contacts made by an infected individual in its lifetime, this is the familiar threshold result of epidemic theory. However, it again underestimates the true threshold of the contact process.

Turning to the second-order approximation, we find that the analogue of equation (9) is

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}&P(\xi_t(x) = 0,\ \xi_t(x+z) = 1)\\ &= -(\lambda+\delta)\,P(\xi_t(x) = 0,\ \xi_t(x+z) = 1)\\ &\quad +\delta P(\xi_t(x) = 1,\ \xi_t(x+z) = 1)\\ &\quad -\lambda \sum_{w\neq z} P(\xi_t(x) = 0,\ \xi_t(x+z) = 1,\ \xi_t(x+w) = 1)\\ &\quad +\lambda \sum_{w+z\neq 0} P(\xi_t(x) = 0,\ \xi_t(x+z)\\ &= 0,\ \xi_t(x+z+w) = 1). \end{aligned} \quad (16)$$

Here $z\in\mathcal{N}$ is a fixed neighbour and the sums are over all $w\in\mathcal{N}$ with the indicated properties.

If we enumerate the points in the neighbourhood $\mathcal{N} = \{z_1, \ldots, z_n\}$, and let $v_i(t) = P(\xi_t(x) = 0,\ \xi_t(x+z_i) = 1)$ then we can approximate

$$\begin{aligned}&P(\xi_t(x) = 0,\ \xi_t(x+z_i) = 1,\ \xi_t(x+z_j) = 1)\\ &\approx \frac{P(\xi_t(x) = 0, \xi_t(x+z_i) = 1)\,P(\xi_t(x) = 0, \xi_t(x+z_j) = 1)}{P(\xi_t(x) = 0)}\\ &= v_i v_j/(1-u). \end{aligned} \quad (17)$$

Note that, because correlations will depend on distance, it is no longer reasonable to expect that $v_j = v$ for all j.

Using $P(\xi_t(x) = 0,\ \xi_t(x+z) = 0) = \{1-P(\xi_t(x) = 1)\} - P(\xi_t(x) = 0,\ \xi_t(x+z) = 1)$ and reasoning as in equation (17), we have

$$\begin{aligned}&P(\xi_t(x) = 0,\ \xi_t(x+z_i) = 0,\ \xi_t(x+z_i+z_j) = 1)\\ &\quad \approx (1-u-v_i)\,v_j/(1-u). \end{aligned} \quad (18)$$

Combining equation (14) with equations (16)–(18) and the observation $P(\xi_t(x) = 1,\ \xi_t(x+z_i) = 1) = u - v_i$ we have

$$\frac{\mathrm{d}u}{\mathrm{d}t} = -\delta u + \lambda \sum_i v_i; \quad (19)$$

$$\begin{aligned}\frac{\mathrm{d}v_i}{\mathrm{d}t} &= -(\lambda+\delta)\,v_i + \delta(u-v_i)\\ &\quad -\lambda \sum_{j\neq i} \frac{v_i v_j}{1-u} + \lambda \sum_{j:\,z_i+z_j\neq 0} \frac{(1-u-v_i)\,v_j}{1-u}. \end{aligned} \quad (20).$$

From (19) it follows that in equilibrium we must have

$$\delta u = \lambda \sum_i v_i. \quad (21)$$

In the nearest-neighbour case we used symmetry to conclude that all the v_i are equal and reduce the system to two equations in two unknowns. That device is not available here, so instead note that if u is small, as will be true when λ/δ is close to the critical value, then $1-u \approx 1$ and $v_i \leqslant u$ so $v_i v_j$ and uv_j are much smaller than u. Thus

$$\frac{\mathrm{d}v_i}{\mathrm{d}t} \approx -(\lambda+2\delta)\,v_i + \delta u + \lambda \sum_{j:\,z_i+z_j\neq 0} v_j. \quad (22)$$

Setting the last quantity to 0, summing over i, and noting that the condition $z_i + z_j \neq 0$ excludes each of the v_j exactly once we have

$$0 = -(\lambda+2\delta) \sum_i v_i + N\delta u + (N-1)\,\lambda \sum_i v_i. \quad (23)$$

Combining equations (21) and (23) now, we have $0 = \{-(\lambda+2\delta) + N\lambda + (N-1)\,\lambda\} \Sigma_i v_i$ for the threshold. Thus, there is a non-trivial equilibrium if and only if

$$\lambda/\delta > 1/(N-1); \quad (24)$$

this equation generalizes the result already achieved for $N = 4$. Note that equation (22) represents the linearization of the equation (20) around 0, and this is why a threshold condition on λ/μ emerges. When λ/δ is large enough, the original system (19), (20) has a non-trivial equilibrium and the linearized system grows exponentially. Thus the critical value λ/δ, i.e. the threshold for survival, is characterized by the existence of a zero eigenvalue for the linearized system.

The reader should note that the second-order approximation in equation (24) is always larger than the mean field approximation of the critical value $\lambda/\delta = 1/N$. On the other hand, it can be shown, by the methods described on pp. 36–37 of Griffeath (1978), that the approximation in equation (24) always underestimates the true critical value. Thus, it is a step in the right direction.

5. THE DYAD HEURISTIC

Although the use of moment equations as described above is not new, what is provided here is a novel and simple viewpoint from which the threshold results can be derived very simply and more generally. To set the

stage, observe that the mean field answer can be derived by noting that a single infected individual in isolation recovers at rate δ but gives rise to a new infection at rate $N\lambda$. So the infection is doomed to extinction when $N\lambda \leqslant \delta$, and if no infections were lost onto already infected sites it would prosper when $N\lambda > \delta$.

The reasoning in the previous paragraph leads to the mean field critical value, but ignores clustering. Clustering means that any invasion will typically find that an occupied site is more likely to have a neighbour occupied than would a randomly chosen site. Thus, it is natural to ask what happens beyond the first successful 'infection' event; that is, will a pair of adjacent occupied sites successfully spread? Let us therefore assume we have two infected sites that are neighbours. New infections arising from these occur at rate $2(N-1)\lambda$ and recovery occurs at rate 2δ. The infection rate is larger than the recovery rate when $\lambda/\delta > 1/(N-1)$, the condition in equation (24).

The last calculation, which we term the 'dyad heuristic', can not only often easily reproduce the result of second-order approximations as above, but can also be used in a variety of more complicated situations (see, for example, Altmann 1995, who considers the full dynamics of all dyads), including those where we do not know how to perform the second-order approximation. As an example of the latter, consider the nonlinear voter model. In this system each lattice point can be in state 1 or state 2. The name comes from thinking of the states as representing two opinions, but one could equally well think of two competing species or, more relevant to this paper, susceptible and infected individuals.

In the nonlinear voter model, time is discrete: $n = 0, 1, 2, \ldots$. To compute the state of a site x at time $n+1$ we look at the state of x and its four nearest neighbours at time n and count the number of 1s we see. If that number is k then the site will be 1 with probability p_k and 2 with probability $1-p_k$, with the choices for different sites being decided by independent random events. This allows consideration of a range of nonlinear local infection dynamics.

To have a model that is symmetric under interchange of 1s and 2s, suppose $p_{5-k} = 1-p_k$ for $k = 0, 1, 2$. Suppose also that all 1s and all 2s are absorbing states, i.e. $p_5 = 1$ and $p_0 = 0$. This leaves the model with two parameters: p_1 and p_2. Our task is to determine as a function of p_1 and p_2 whether the two types coexist or whether one will competitively exclude the other. (Molofsky, unpublished.)

Following traditional reasoning, we expect coexistence if 1s can invade 2s, i.e. if when their initial density is small it will tend to increase. The first-order or mean field approximation is to note that a single 1 will on the average have $5p_1$ offspring in the first generation, so coexistence will occur if $p_1 > 0.2$. The second-order, or dyad, approximation is to note that a pair of adjacent 1s will have a mean of $2p_2+6p_1$ offspring in the next generation, so coexistence occurs if $2p_2+6p_1 > 2$. Unpublished results of simulations performed separately by J. Molofsky and D. Griffeath indicate that this approximation is remarkably close to the behaviour of the spatial model, although there are differences that would only become apparent in a higher-order approximation.

6. SPATIALLY STRUCTURED POPULATIONS

The model of the preceding section assumes that each site is either infected or not. That means either that sites and individuals are identical, or that sites represent subpopulations that are either disease-free or fully infected. A more general formulation identifies each site by a number of susceptible individuals, S, and a number of infected ones, I. This approach has been used for a wide variety of applications in biology, in which it is shown that spatial localization can again fundamentally change the qualitative dynamics (see, for example, Hassell *et al.* 1991). In particular, let the state of the system at time t be

$$(S_t\, I_t) : Z^2 \{0, 1, \ldots\}, \tag{25}$$

where Z is the set of all integers, $S_t = S_t(x)$ is the number of susceptible individuals at time t and $I_t = I_t(x)$ is the number of infected individuals at time t in a square of side 1 centred at the point. For the purposes of illustration, no recovered individuals are considered, but the approach can easily be extended to include these.

The model described in this section is termed an interacting particle system. We have considered this system earlier as a spatial version of Maynard Smith's evolutionary game: see Durrett and Levin (1994*a*), which has references to earlier work on these models. Let the state of the system change (in continuous time) according to the following rules.

Infection: On an interaction neighbourhood $\mathcal{N}_1$, susceptible individuals become infected at rate

$$\beta P_t(x) = \beta \frac{\bar{I}_t(x)}{\bar{S}_t(x) + \bar{I}_t(x)}, \tag{26}$$

where the superbars indicate that averages are computed over the neighbourhood $\mathcal{N}_1$ and P_t is the proportion of neighbours that are infected.

Births: Occur at rate α per susceptible individual, and remain in the cell of the parent; infected individuals do not give birth.

Deaths: Occur at rate $\mu + K(\hat{S}_t + \hat{I}_t)$, where superhats indicate density dependence operating over a neighbourhood $\mathcal{N}_2$.

Migration: Occurs at rate γ to any cell on a neighbourhood $\mathcal{N}_3$; more general movement kernels are easily accommodated.

Note that infection is determined by the *proportion* of contacts that are infectious.

In the limit when all neighbourhoods in question are the whole grid, one obtains the mean-field dynamics

$$\frac{\mathrm{d}S}{\mathrm{d}t} = S\left[\alpha - \beta\frac{I}{S+I} - (\mu + K(S+I))\right],$$

$$\frac{\mathrm{d}I}{\mathrm{d}t} = I\left[\beta\frac{S}{S+I} - (\mu + K(S+I))\right]. \tag{27}$$

A variety of behaviours are possible for equation (27). If $\alpha > \mu$, a disease-free equilibrium, $\bar{S} = (\alpha-\mu)/K$, exists and is stable in the absence of the disease; but if $\beta > \alpha$ it is unstable to invasion by the disease. To see this, note that

$$\frac{\mathrm{d}}{\mathrm{d}t}(S/I) = \frac{1}{I}\frac{\mathrm{d}S}{\mathrm{d}t} - \frac{S}{I^2}\frac{\mathrm{d}I}{\mathrm{d}t} = (\alpha-\beta)S/I. \tag{28}$$

Thus $S/I = \mathrm{e}^{(\alpha-\beta)t}S_0/I_0$ and hence, if $\alpha < \beta$, S and hence I must both tend asymptotically to 0.

Surprisingly, perhaps, spatial localization makes a huge difference in the dynamics. That is, the interacting-particle version of equation (27) need not go extinct. For generic initial conditions, the system on the infinite lattice will persist indefinitely. Because it is a stochastic system, it will ultimately go extinct on any finite lattice; but even for moderate size systems the time required is the computer equivalent of millions of years. The explanation for persistence is simple. In the spatial model, severe epidemics reduce the population but leave isolated susceptibles to rebuild the population before the next epidemic wave. For more on this, see Durrett & Levin (1994*a*).

Adding diffusion terms to equation (27) does not help. With diffusion at identical rates for both species, the system still goes extinct. However, a proper diffusion limit can be derived from the interacting-particle version. As shown in Durrett & Levin (1994*a*), allowing cell sizes to shrink to zero and scaling parameters appropriately leads to the limit

$$\frac{\partial u}{\partial t} = \sigma\Delta u + u\{(\alpha-\mu) - \beta g\frac{v}{u+v} - K(u+v)\}$$

$$\frac{\partial v}{\partial t} = \sigma\Delta v + v\{-\mu + \beta g\frac{u}{u+v} - K(u+v)\} \tag{29}$$

in which

$$g = 1-\exp(-N_1(u+v))$$

and N_1 is the number of sites in the neighbourhood $\mathcal{N}_1$. In the extreme ($g = 1$), system (29) is the mean field system with diffusion added, and cannot support persistence. For intermediate N_1, however, persistence is possible in system (29), because susceptible individuals stay isolated long enough to build up their numbers.

7. CONCLUSION

In recent years, it has become increasingly clear that the assumption of homogeneous mixing is a poor one for the dynamics of many diseases. The simplest approach, rooted in the classical methods, is to modify the usual dynamical system for susceptible, infective and recovered individuals, adjusting the rate of infection via phenomenologically derived terms that reflect the influence of the heterogeneous distribution of individuals. This is not entirely satisfactory, because it confounds attempts to extrapolate beyond the particular situation.

An alternative, especially given the increased ease of high-speed computations, is to develop individual-based models, in which rules are given for every individual in a population. (In other situations, intermediate levels of heterogeneity, such as schools, provide more natural starting points. We argue, however, that the individual-based approach, though still not easily parametrized, provides an invaluable dual to the macroscopic view.) Such an approach cannot be an end in itself, however. For a variety of statistical and methodological reasons, the most reliable and useful models will be ones that assume some level of generality; the most powerful analytic methods will be ones that focus attention on determining how much or how little detail at the individual level is essential for understanding the macroscopic dynamics.

In this paper, we have introduced approaches that seek to bridge the gap between individual-based models and macroscopic descriptions for epidemic systems. Moment-closure methods, such as those described for the contact process and related models, provide a first step towards renormalization. These methods can be expanded, as in the work of Bolker & Pacala (1996) for forest growth models, beyond neighbour correlations to the full spatial covariance function (see also Levin & Pacala 1996; Mollison 1977); however, such approaches have not yet been applied to epidemiological problems.

Contact-process models are the simplest of all spatial epidemic models. More generally, space may be divided up into cells, which represent highly mixing subpopulations that exchange individuals less frequently with other subpopulations. The epidemiological dynamics of such spatially structured populations can differ qualitatively from other formulations. For such models, diffusion approximations may mimic the behavior of the interacting-particle systems under appropriate conditions. To derive such approximations requires that, mimicking techniques used in deriving diffusion approximations for random walks, we develop finer and finer lattices in which cell size is shrunk to zero, and moment rates scaled appropriately.

Heterogeneous mixing is a fact for many epidemiological systems, and can qualitatively change dynamics. It is attractive to represent the effects of nonlinearity through appropriate nonlinear terms (see, for example, Liu *et al.* 1987); however, because those terms cannot be derived from first principles, confidence in them must be limited. In this paper, we point the way to some useful techniques for making the transition from assumptions about individual behaviour to the desired macroscopic dynamics. It is, indeed, only a beginning.

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