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## "From individuals to epidemics"

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**These are preliminary lecture notes, intended only for distribution to participants.**

# From individuals to epidemics

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**Abstract**

Heterogeneous mixing fundamentally changes the dynamics of infectious diseases, and ways to incorporate it into models represent a fundamental 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, we describe attempts to achieve this transformation for a class of models where non-random mixing arises from the spatial localization of interactions. In general, we find that the epidemic threshold is larger due to spatial localization than for a homogeneous mixing population. We develop an improved estimate of the dynamics by 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, we investigate the connection with related partial differential equations.

**Index entries:** Epidemics; Spatial Models; Interacting Particle Systems; Cellular Automata; Heterogeneous Mixing; Scaling

## 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.* 1989b). The evolution of disease dynamics, the coevolution of hosts and parasites, and the beginnings of a community theory (see e.g. 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 (e.g., 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 behavior; a complementary approach (e.g., Hethcote & Yorke 1984; Schenzle 1985; Castillo-Chavez *et al.* 1989a) 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 behavior in terms of that of individual or local groupings, such as families.

## The Problem of Closure

To illustrate this point, consider the familiar $S - I - R$ system

$$\begin{aligned} \frac{dS}{dt} &= r\,(S + I + R) - \beta SI - \mu S \\ \frac{dI}{dt} &= \beta SI - \lambda I - \mu I \\ \frac{dR}{dt} &= \lambda I - \mu R, \end{aligned} \tag{1}$$

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; and $R$, the number of recovered or removed.

System (1) represents what physicists would call *mean field dynamics*. That is, these are the equations that arise in the limit as $N \to \infty$ of a homogeneously mixing population of $N$ individuals. Each infected individual is considered equally likely to infect each susceptible individual. Imagine instead that (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

$$\begin{aligned} S &= < S > + s \\ I &= < I > + i \end{aligned} \tag{2}$$

$$R = < R > + r$$

Here $< S >$, $< I >$ and $< R >$ 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 $< s >=< i >=< r >= 0$, system (1) leads to the system

$$\begin{aligned}
\frac{d < S >}{dt} &= r(< S > + < I > + < R >) - \mu < S > \\
&\quad -\beta < S >< I > -\beta < si > \\
\frac{d < I >}{dt} &= \beta < S >< I > +\beta < si > -\lambda < I > -\mu < I > \\
\frac{d < R >}{dt} &= \lambda < I > -\mu < R >,
\end{aligned} \tag{3}$$

in which $< si >$ is the metapopulation average of $si$. Except for the terms $< si >$, 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 $< si >$ in terms of the means (in the mean field approximation, one simply sets $< si >= 0$), or write equations for $d < si > /dt$ that will involve higher order correlations. At some point, the system must be

closed if one is to succeed in analyzing it by standard methods; compare, for example Adler & Brunet (1991). We illustrate approaches to such closure in the succeeding sections.

## 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 (1994a). Imagine a grid of cells, each either susceptible or infected. The only rules are that infected individuals (sites) recover at a rate $\delta$ (the interoccurrence times $t_i$ are independent and have an exponential distribution with mean $1/\delta$; i.e., $P(t_i > t) = e^{-\delta t}$), and that an infected individual can infect any of its 4 nearest neighbors at rate $\lambda$. Then the fraction of infected sites $p_t(1)$ satisfies the equation

$$\frac{dp_t(1)}{dt} = -\delta p_t(1) + 4\lambda p_t(01), \tag{4}$$

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, we have assumed that $P(\xi_t(x) = 0, \xi_t(x+z) = 1)$ is the same for $z = (1,0)$, $(0,1)$, $(-1,0)$, and $(0,-1)$. Due 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 $\lambda/\delta$, the infection will die out; but for $\lambda/\delta$ greater than a critical value ($\approx .41$), invasion will take place from low densities to an equilibrium configuration characterized by clustering of infectives (see figure 1). (**insert figure 1**).

As in the previous example, (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

$$\begin{aligned} \frac{dp_t(1)}{dt} &= -\delta p_t(1) + 4\lambda p_t(1)[1 - p_t(1)] \\ &= p_t(1)[(4\lambda - \delta) - 4\lambda p_t(1)] \end{aligned} \tag{6}$$

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

$$\frac{\lambda}{\delta} \leq \frac{1}{4}, \tag{7}$$

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

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

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 ($\approx .41$) seen in the contact process, since 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

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

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 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 *et al.* 1987a,b, 1992; Harada & Iwasa 1994; Sato *et al.* 1994; Harada *et al.* 1995), we make the approximation

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

and similarly

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

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

$$\begin{aligned} p_t(11) &= p_t(1) - p_t(01) \\ p_t(00) &= p_t(0) - p_t(01) \\ p_t(1) &= 1 - p_t(0) \end{aligned} \tag{12}$$

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

$$\begin{aligned} \dot{u} &= -\delta u + 4\lambda v \\ \dot{v} &= -(\lambda + \delta)v + \delta(u - v) - 3\lambda v(2v + u - 1)/(1 - u), \end{aligned} \tag{13}$$

where superdots denote time derivatives.

To find the equilibria for the system in (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 $\lambda$ 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 we have set the birth rate $\lambda = 1$ and varied the death rate $\delta$ 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 performs the same comparisons for the probability of a 01 pair, i.e., the probability a site $x$ will be vacant but its right neighbor $x + (1, 0)$ 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. **Place figure 2 and 3 here.**

It is important to note that (13) is a dynamic approximation, describing system dynamics during the transient stages. Comparison of results in terms of equilibrium behavior is one convenient measure of the success of the approach, but (13) may yield improvement as well in the description of transient dynamics. Nonetheless, 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.

## The Generalized Contact Process

Consider now a more general contact process with neighborhood set $\mathcal{N}$. Here $\mathcal{N}$ represents the neighbors of the origin $(0,0)$, i.e., the set of sites it can infect, and the neighbors of a general site $x$ are $x+\mathcal{N} = \{x+y : y \in \mathcal{N}\}$. Because we want the relationship that $x$ is a neighbor of $y$ to be symmetric, we will assume that if $z \in \mathcal{N}$ then $-z \in \mathcal{N}$.

The dynamics for the more general model are, except for the choice of neighborhood, identical to the nearest neighbor case: infected individuals recover at a rate $\delta$, while an infected individual can infect any of its neighbors at rate $\lambda$. 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 (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 (4) in the current situation is

$$\frac{d}{dt}P(\xi_t(x)=1) = -\delta P(\xi_t(x)=1) + \lambda \sum_{z\in\mathcal{N}} P(\xi_t(x)=0, \xi_t(x+z)=1) \tag{14}$$

If we were to assume that neighboring 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

$$\frac{du}{dt} = -\delta u + N\lambda u(1-u) \tag{15}$$

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 $N\lambda \leq \delta$ and that a globally stable endemic equilibrium $1 - \delta/N\lambda$ exists if $N\lambda > \delta$. Since $R = N\lambda/\delta$ is the expected number of contacts made by an infected individual in its lifetime, this is the familiar threshold result of epidemic theory. It, however, again underestimates the true threshold of the contact process.

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

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

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

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

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

Note that since 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 (17) we have

$$P(\xi_t(x) = 0, \xi_t(x+z_i) = 0, \xi_t(x+z_i+z_j) = 1) \approx \frac{(1-u-v_i)v_j}{1-u} \tag{18}$$

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

$$\frac{du}{dt} = -\delta u + \lambda \sum_i v_i \tag{19}$$

$$\frac{dv_i}{dt} = -(\lambda+\delta)v_i + \delta(u - v_i) \tag{20}$$
$$-\lambda \sum_{j \neq i} \frac{v_i v_j}{1-u} + \lambda \sum_{j: z_i + z_j \neq 0} \frac{(1-u-v_i)v_j}{1-u}$$

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

$$\delta u = \lambda \sum_i v_i \tag{21}$$

In the nearest neighbor 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 we instead note that if $u$ is small, which will be true when $\lambda/\delta$ is close to the critical value, then $1 - u \approx 1$ and $v_i \leq u$ so $v_i v_j$ and $u v_j$ are much smaller than $u$. Thus

$$\frac{dv_i}{dt} \approx -(\lambda + 2\delta)v_i + \delta u + \lambda \sum_{j: z_i + z_j \neq 0} v_j \tag{22}$$

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

$$0 = -(\lambda + 2\delta) \sum_i v_i + N\delta u + (N-1)\lambda \sum_i v_i \tag{23}$$

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

$$\lambda/\delta > 1/(N-1) \tag{24}$$

generalizing the result already achieved for $N = 4$. Note that (22) represents the linearization of the equation (20) around 0, which is why a threshold condition on $\lambda/\mu$ emerges. When $\lambda/\delta$ is large enough, the original system (19), (20) has a nontrivial equilibrium and the linearized system grows exponentially. Thus the critical value $\lambda/\delta$, 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 (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, using the methods described on pages 36–37 of Griffeath (1978), that the approximation in (24) always underestimates the true critical value. Thus, it is a step in the right direction.

## The Dyad Heuristic

While the use of moment equations as described above is not new, we provide here a novel and simple viewpoint from which the threshold results can be derived very simply and more generally. To set the stage, we observe that the mean field answer can be derived by noting that a single infected in isolation recovers at rate $\delta$ but gives rise to a new infection at rate $N\lambda$. So the infection is doomed to extinction when $N\lambda \leq \delta$, 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 neighbor 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? Thus assume we have two infected sites that are neighbors. New infections arising from these occur at rate $2(N-1)\lambda$ while recovery occurs at rate $2\delta$. The infection rate is larger than the recovery rate when $\lambda/\delta > 1/(N-1)$, the condition in (24).

The last calcuation, 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 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 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 neighbors at time $n$ and count the number of 1's 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 1's and 2's we suppose $p_{5-k} = 1 - p_k$ for $k = 0, 1, 2$. We also suppose that all 1's and all 2's are absorbing states, i.e. $p_5 = 1$ and $p_0 = 0$. This leaves our 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 one will competitively exclude the other.

Following traditional reasoning we expect coexistence if 1's can invade 2's: 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 1's will have an average 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 behavior of the spatial model, although there are differences that would only become apparent in a higher order approximation.

## 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 $I$. 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 qualitiative dynamics (see for example Hassell *et al.* 1991). In particular, let the state of the system at time $t$ be

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

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 centered at the point. For purposes of illustration, no recovereds are considered, but the approach can be extended easily to include these.

The model we describe 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 (1994a) 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 neighborhood $\mathcal{N}_1$, susceptibles 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 neighborhood $\mathcal{N}_1$ and $P_t$ is the proportion of neighbors that are infected.

Births: Occur at rate $\alpha$ 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 neighborhood $\mathcal{N}_2$.

Migration: Occurs at rate $\gamma$ to any cell on a neighborhood $\mathcal{N}_3$; 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 neighborhoods in question are the whole grid, one obtains the mean-field dynamics

$$\begin{aligned} \frac{dS}{dt} &= S\left[\alpha - \beta\frac{I}{S+I} - (\mu + K(S+I))\right], \\ \frac{dI}{dt} &= I\left[\beta\frac{S}{S+I} - (\mu + K(S+I))\right]. \end{aligned} \tag{27}$$

A variety of behaviors are possible for (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

$$\frac{d}{dt}(S/I) = \frac{1}{I}\frac{dS}{dt} - \frac{S}{I^2}\frac{dI}{dt} = (\alpha - \beta)S/I \tag{28}$$

Thus $S/I = e^{(\alpha-\beta)t}S_0/I_0$ 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 (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 decimate the population but leave isolated susceptibles to rebuild the population before the next epidemic wave. For more on this, see Durrett & Levin (1994a).

Adding diffusion terms to (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 (1994a), allowing cell sizes to shrink to zero and scaling parameters appropriately leads to the limit

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

in which

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

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

## 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 susceptibles, infectives, and recovereds, adjusting the rate of infection via phenomenologically-derived terms reflecting the influence of the heterogeneous distribution of individuals. This is not entirely satisfactory, since it confounds attempts to extrapolate beyond the particular situation.

An alternative, especially given the increased ease of highspeed 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—e.g., schools—provide more natural starting points. We argue, however, that the individual-based approach, though still not easily parameterized, 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; and the most powerful analytic methods will be ones that focus attention on determing 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 neighbor correlations to the full spatial covariance function (see also Levin & Pacala 1996; Mollison 1977); but 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, representing 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 (e.g. Liu *et al.* 1987); but, since 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 behavior to the desired macroscopic dynamics. It is, indeed, only a beginning.

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## Figure Legends

Figure 1: The basic contact process equilibrum when $\lambda = 0.25$ and $\delta = 0.35$. Reprinted from Durrett & Levin 1994b.

Figure 2: Fraction of occupied sites as a function of the recovery rate $\delta$. Lowest curve ($\diamond$) denotes a simulation result, upper curve ($\circ$) the mean field approximation, and middle curve ($+$) 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 $\delta$. Symbols are as in Figure 2. Again, lowest curve demonstrates simulation, upper curve mean field, and middle curve the second-order approximation.

Figure 1

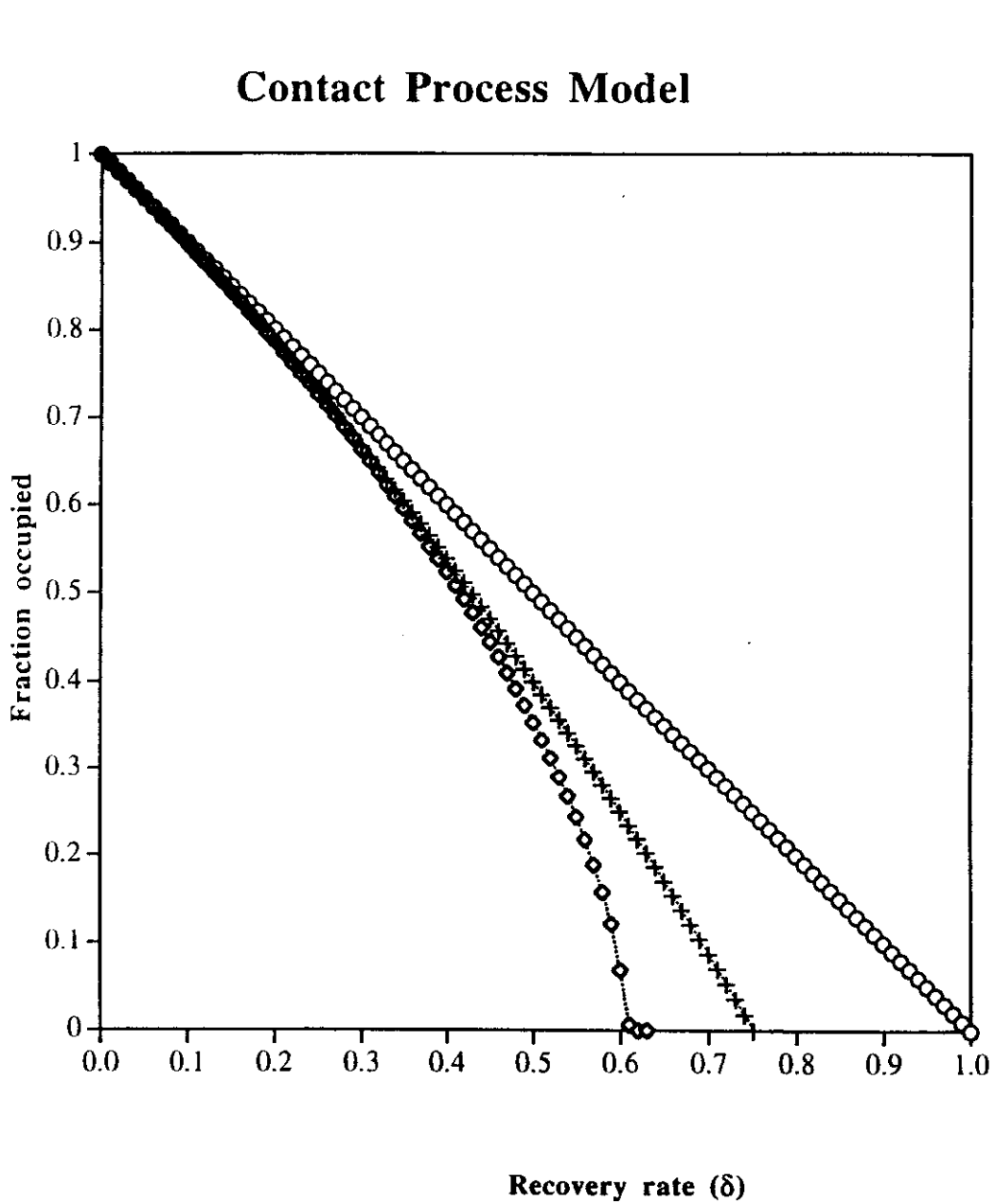
Contact Process Model
Fraction occupied
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
Recovery rate (δ)

Figure 2

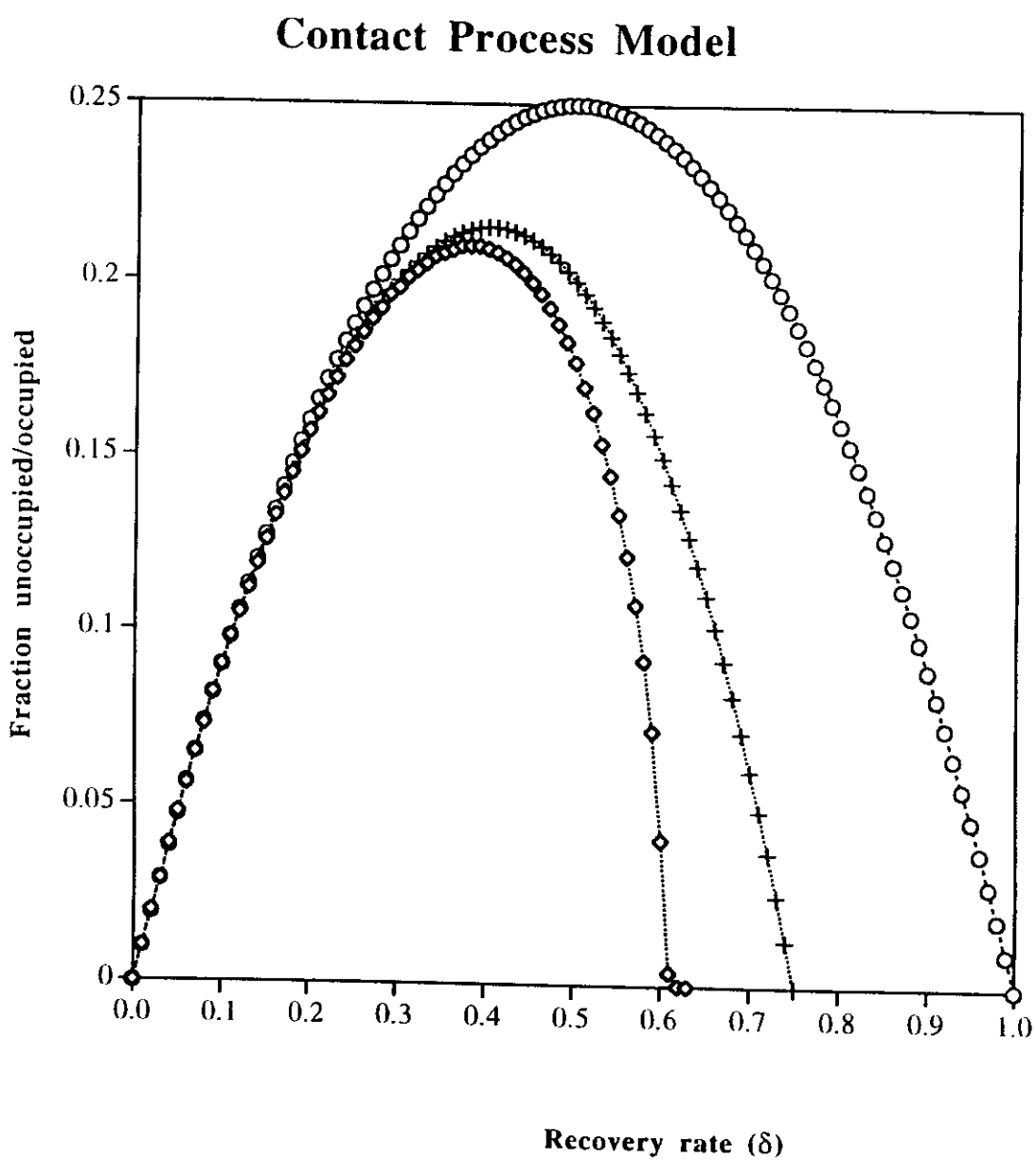
Contact Process Model
Fraction unoccupied/occupied
0.25
0.2
0.15
0.1
0.05
0
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
Recovery rate (δ)

Figure 3