Modelling pathogen transmission: the interrelationship between local and global approaches

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We describe two spatial (cellular automaton) host–pathogen models with contrasting types of transmission, where the biologically realistic transmission mechanisms are based entirely on ‘local’ interactions. The two models, fixed contact area (FCA) and fixed contact number (FCN), may be viewed as local ‘equivalents’ of commonly used global density- (and frequency-) dependent models. Their outputs are compared with each other and with the patterns generated by these global terms. In the FCN model, unoccupied cells are bypassed, but in the FCA model these impede pathogen spread, extending the period of the epidemic and reducing the prevalence of infection when the pathogen persists. Crucially, generalized linear modelling reveals that the global transmission terms βSI and $\beta' SI/N$ are equally good at describing transmission in both the FCA and FCN models when infected individuals are homogeneously distributed and N is approximately constant, as at the quasi-equilibrium. However, when N varies, the global frequency-dependent term $\beta' SI/N$ is better than the density-dependent one, βSI , at describing transmission in both the FCA and FCN models. Our approach may be used more generally to compare different local contact structures and select the most appropriate global transmission term.

Keywords: mathematical model; transmission; infection; density dependent; frequency dependent; cellular automata

1. INTRODUCTION

The practical reasons for studying infection dynamics are as varied as the host–pathogen systems investigated. For example, the desire to protect humans was the motivation for the investigation of rabies in the European fox (Anderson *et al.* 1981). Studies of BSE in cattle were also motivated by the desire to protect humans from disease, but also by the need to prevent economic losses and reduce animal suffering (Ferguson *et al.* 1997). By contrast, a study of feline panleucopenia virus in the feral cats of Marion Island was prompted by the desire to use disease as a form of pest control (Berthier *et al.* 2000). Despite the differences in motivation between these and other studies, a common goal is to learn more about the host–pathogen system through the construction of a model that captures the essential characteristics of the system, including pathogen transmission. To do this successfully, it is essential to base the transmission terms on known or hypothetical contact structures that capture the nature of the interactions between individuals.

The rate of transmission of infection has commonly been modelled using the terms βSI (density-dependent transmission) and $\beta' SI/N$ (frequency-dependent transmission). Here, S and I represent the number of susceptible and infected individuals in the population, N represents the total number of individuals and β and β' represent transmission parameters (which differ in dimen-

sion: see Begon *et al.* (2002)). These transmission terms are of the general form $\nu QSI/N$, where Q represents the expected number of contacts made by a susceptible per unit time and ν represents the probability of transmission per contact with an infected individual. In the case of density-dependent transmission, Q is proportional to the density of individuals in the population, N/A , which is typically simplified to N on the assumption that the area occupied by populations, A , is constant (i.e. $Q = kN$, where k is a constant of proportionality, and so $\beta = \nu k$) (Begon *et al.* 2002). In the case of frequency-dependent transmission, Q is constant (i.e. $\beta' = \nu Q$). Both of these terms have been widely used to model infectious diseases of both humans and other animals.

In the models that use these transmission terms, the population (or each of its subpopulations) is generally treated as a whole (i.e. the spatial location of particular individuals is not taken into account), and so local behaviour cannot be incorporated into the model. The spatial distribution of susceptible and infected individuals cannot be incorporated either. Instead, transmission depends purely on the total numbers of susceptible and infected individuals. Cellular automata models can take into consideration local behaviour and heterogeneity within the population (Durrett & Levin 1994; Keeling *et al.* 1997; McGlade 1999). The progress and state of each individual can be monitored and, as each individual has a unique location, local interactions can be specified.

In this paper, we describe two cellular automata models with contrasting types of transmission. The transmission mechanisms are based entirely on the ‘local’ interactions

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between individual hosts and share characteristics with real biological systems. The outputs of the models—in terms of global host–pathogen dynamics—are compared with each other and with the patterns generated by commonly used global transmission terms. Of the two models examined, one reflects the fact that in some species, individuals tend to move within an ambit of approximately fixed area, and so the number of contacts they make per unit time varies with local population density. The second describes species where each individual has a roughly constant number of contacts per unit time. This could, for example, be a result of territory expansion and contraction in response to variations in the population density. Alternatively, it could be a consequence of seeking a mate, making the model suitable for describing the spread of a sexually transmitted disease. The two models may thus be viewed as local ‘equivalents’ of global density- and frequency-dependent models, but the correspondence between explicit local behaviour and implied global behaviour in host–pathogen models has been neglected in the past and it is an aim of this paper to examine this correspondence. This is important, as transmission terms should reflect local behaviour (because transmission is, generally, local) but are often cast in global terms (because most models themselves are framed globally).

2. MODEL COMPONENTS

The dynamics of the population are described in terms of cells. Each cell is either unoccupied or occupied by a single individual. They are grouped together to form a square lattice of cells (50×50 in our illustrations), in which all activity takes place. The lattice is not toroidal. In effect, the edge of the lattice represents the edge of suitable habitat. Consequently, an individual occupying a cell at the edge of the lattice has fewer neighbours. The cellular automata models consist of a series of steps relating to birth, death and transmission. The steps are executed for each individual in turn after each ‘time-step’. Several thousand time-steps make up any one simulation and the results from many simulations form a picture of the behaviour of the model.

Each individual is assigned a lifespan at the time it enters the lattice. After each time-step the age of the individual is increased until that individual completes its lifespan, at which time it is removed from the lattice. Lifespans are chosen at random from a negative exponential distribution with a fixed mean, simulating what is often observed in natural populations, namely that the majority of individuals only survive for a relatively short period of time.

The number of empty cells in the lattice is determined by a logistic birth rate. If the population level is less than the ‘carrying capacity’ κ , then newborn offspring are introduced. Because the number of deaths at each time-step varies, it is possible for the population to exceed κ . When this happens no new individuals are introduced at the next time-step and so the population falls, sometimes to a level below κ . If there is an insufficient number of vacant cells to accommodate all the offspring then the number added is equal to the number of vacant cells. Cells to which the offspring are assigned are chosen at random from all the unoccupied cells. Therefore, the empty cells move about

the lattice even when the population is in ‘equilibrium’ (i.e. when the number of individuals in the population is approximately constant).

(a) *Transmission of infection*

In the models considered here, an individual can either be susceptible, infected or recovered. ‘Infected’ individuals are also infectious and ‘recovered’ individuals have life-long immunity. A susceptible individual can only become infected if it has direct contact with an infectious individual. Therefore, each potentially infectious encounter (i.e. each encounter of a susceptible with another individual) is treated independently. Transmission only occurs when $\tilde{\beta} > q$, where $\tilde{\beta}$ is the strength of transmission (expressed as a number between 0 and 1) and q a random number uniformly distributed between 0 and 1. The number of infecteds in the ‘neighbourhood’ of the susceptible determines the number of times the test is repeated. Each time it is repeated, a different q is chosen at random. An infected individual remains infectious for period t_i , then recovers and becomes immune (unless it dies in the meantime).

(b) *Contact structure*

In the first model considered here, ‘fixed contact area’ (FCA), the neighbourhood consists of those individuals with whom the susceptible shares a boundary. Because the lattice is square, the maximum number of individuals that a susceptible can encounter is four. If one or more of the neighbouring cells is empty then the actual number encountered is less than four. Some or all of the individuals encountered may be infectious. In the second model, ‘fixed contact number’ (FCN), the neighbourhood is flexible: susceptibles ‘search’ for contacts (details below), the number of which is fixed at four (for comparison with the FCA model).

As explained previously, the difference between (globally) frequency-dependent and density-dependent transmission is in the form of Q , the number of individuals encountered per unit time. For frequency-dependent transmission, Q is constant; for density-dependent transmission, Q is directly proportional to the total host density. Unoccupied cells are introduced into the lattice in order to be able to incorporate similar (spatially explicit) types of transmission into the present models. Without them, the number of individuals encountered is inevitably constant (four) in both models; but with unoccupied cells, the number encountered becomes locally density-dependent in the FCA model, whereas in the FCN model, transmission is conceptually similar to frequency-dependent transmission (albeit local rather than global).

(c) *The ‘searching’ mechanism*

In the FCN model, the number of contacts is always four, except in the rare cases when the population consists of four or fewer individuals. These contacts will be the four nearest neighbours, but to find them an individual may have to ‘seek’ beyond the first ‘ring’ of neighbouring cells. The rings are illustrated in figure 1. Cells labelled 0 are always searched and the order in which they are visited is unimportant. Cells labelled 1 form the first set of additional cells (ring 1). These are searched when at least one of the cells labelled 0 is unoccupied. If there are less

3	3	3	3	3	3	3
3	2	2	2	2	2	3
3	2	1	0	1	2	3
3	2	0	S	0	2	3
3	2	1	0	1	2	3
3	2	2	2	2	2	3
3	3	3	3	3	3	3

Figure 1. Illustration of the 'rings' involved in the 'searching' mechanism. Cells labelled 1 form ring 1, cells labelled 2 form ring 2, etc.

than four individuals in total in rings 0 and 1, then those in ring 2 are visited next, etc.

The contact mechanism can be modelled by cells within each ring being searched in a strict order, but this leads to directional bias. The cells could be searched at random, but this requires much computer time. Thus, to remove the possibility of directional bias, starting points and directions are chosen at random for each susceptible.

(d) Pathogen-induced mortality and reduced reproduction

To discover whether pathogen-induced extinction of the host is a possible outcome (as it is for global ordinary differential equation models with frequency-dependent (but not density-dependent) transmission (Zhou & Hethcote 1994)), pathogen-induced mortality is incorporated into the models by removing a proportion (α) of infected individuals at each time-step (results for $\alpha = 0$ are sometimes also given). The models also include a per capita intrinsic birth rate for infected individuals (a') which can be less than that for non-infected individuals (a).

3. RESULTS

(a) FCA transmission

There are two possible outcomes for the FCA model: host-pathogen coexistence (where the pathogen persists for at least 10 000 iterations) and 'low prevalence' pathogen extinction (either a deterministic approach to zero prevalence, 'burn-out', or stochastic extinction at low prevalence, 'fade-out'). Initially, there are no immune individuals, and so the infection moves steadily through the population. Susceptibles are 'consumed' by the pathogen and eventually replaced by recovered (immune) individuals. When the infectious period t_i is too short for a given β (figure 2a), the outcome is inevitable pathogen extinction. When it is sufficiently long, the pathogen can persist because enough infectious individuals remain to infect the new susceptibles that replace those that die (figure 2b). When the disease persists, the prevalence quickly settles to oscillating about an equilibrium level,

Figure 2. Prevalence plots for the FCA model with *ca.* 10% ($\kappa = 2250$) and 40% ($\kappa = 1500$) empty cells. Probabilities of extinction and coexistence are based on 100 simulations. (a) 'Low prevalence' pathogen extinction. 10% empty cells: probability of extinction within 150 iterations is 0.94 and within 1000 iterations is 1.00. 40% empty cells: probability of extinction within 150 iterations is 0.47, within 250 iterations is 0.96 and within 1000 iterations is 1.00 (mean lifespan = 129 weeks, $\beta = 0.5$, $t_i = 11$, $\alpha = 0$, $a = a' = 0.5$). (b) Host-pathogen coexistence. Probability of coexistence for at least 10 000 iterations is 1.00 in both cases (mean lifespan = 129 weeks, $\beta = 0.5$, $t_i = 61$, $\alpha = 0$, $a = a' = 0.5$).

though at the lowest prevalences, stochastic extinction may still occur. Thus, the boundary between host-pathogen coexistence and pathogen extinction is not exact, but rather a region of parameter space where either outcome is possible in any given run of the model. By averaging across several model runs, it is possible to obtain an approximate boundary (figure 3a). Examples of boundaries specific to a single model run can be found in Turner (2000).

Increasing the number of empty cells significantly impedes the progress of the disease (figure 2a), and reduces the prevalence of infection where the pathogen persists (figure 2b). It also reduces the parameter space within which the pathogen can persist. So, for a given β , the infectious period required for host-pathogen coexistence becomes longer as the number of empty cells increases (figure 4a). These results presumably reflect the fact that opportunities for transmission decrease as the number of empty cells in the lattice increases.

Note that the invasion boundary (corresponding to $R_0 = 1$, where R_0 is the basic reproduction ratio of the pathogen) lies below the persistence (i.e. coexistence) boundary. Hence, in the region below the persistence boundary we observe either no invasion or invasion without persistence (e.g. figure 2a). Note also, longer infectious periods are needed for persistence when the expected lifespans are longer (immunes are replaced by susceptibles less often) and the pathogen is more likely to persist when

Figure 3. Regions of parameter space. Each boundary is the average of 10 simulations ($\kappa = 1500$ (i.e. 40% empty cells), $\alpha = 0.25$, $a = 0.5$ and $a' = 0.1$). (a) Boundaries between 'low prevalence' pathogen extinction and host-pathogen coexistence for the FCA model. (b) Boundaries between 'low prevalence' pathogen extinction, host-pathogen coexistence, 'low host' pathogen extinction and host extinction for the FCN model.

the host population is large. On a small lattice, the pool of susceptibles can quickly become exhausted leading to extinction of the infection.

Typical prevalence plots for the FCA model are included in figure 5a,b. Table 1a shows the average quasi-equilibrium prevalence (based on 100 simulations) for different combinations of α and a' . These results suggest that pathogen-induced mortality may substantially increase prevalence. By contrast, a pathogen-induced reduction in reproduction (i.e. $a' < a$) has little effect on the equilibrium prevalence level. Figure 6a illustrates more fully the effect of pathogen-induced mortality on persistence. It indicates that highly pathogenic organisms can effectively only persist when there is a fairly high level of transmission, whereas relatively non-pathogenic organisms can persist when there is a low level of transmission provided that the infectious period is long enough. The boundary of persistence is not affected by changes in a' (birth rate for infecteds).

(b) FCA versus FCN transmission

When every cell in the lattice is occupied, the FCA model coincides with the FCN one. But when, say, only 60% of the lattice is occupied, the difference between

Figure 4. Boundaries between 'low prevalence' pathogen extinction and host-pathogen coexistence (a) for FCA models, and (b) for FCN models. Each boundary is the average of five simulations (mean lifespan = 129 weeks, $\alpha = 0$, $a = a' = 0.5$).

FCA and FCN transmission is clear. For the parameter values in figure 5b, the observed equilibrium prevalence level for the FCA model is *ca.* 0.7, while that for the corresponding FCN model is *ca.* 0.8. The effect on the initial spread of infection is even more dramatic. The FCN model predicts that *ca.* 50% of the population will be infected after just 15 time-steps, while the FCA model predicts that only *ca.* 10% of the population will be infected.

Figure 4b shows boundaries of pathogen persistence (between 'low prevalence' pathogen extinction and host-pathogen coexistence) for the FCN model when 5%, 10% and 50% of the cells are unoccupied. Although the boundaries in figure 4b are not identical (the results are numerical), they are very similar. They all have a 'tail value' for t_i of *ca.* 19 weeks (the minimum infectious period necessary for pathogen persistence), presumably because empty cells in the lattice are simply bypassed. For the corresponding model with FCA transmission (figure 4a), the tail values clearly increase as the number of empty cells in the lattice increases. Indeed, the tail value in figure 4b is approximately the same as for the FCA model without empty cells. The tail value in the FCN model is not, however, independent of mean lifespan. A reduction in mean lifespan produces a boundary with a lower tail value and therefore makes pathogen persistence more likely, just as it does for the FCA model.

Figure 5. Prevalence plots for the FCA and the FCN models. Probabilities of extinction and coexistence are based on 100 simulations. (a) 'Low prevalence' pathogen extinction. FCA model: probability of extinction within 250 iterations is 0.91 and within 1000 iterations is 1.00. FCN model: probability of extinction within 250 iterations is 0.39, within 1000 iterations is 0.73 and within 3000 iterations is 1.00 (mean lifespan = 129 weeks, $\kappa = 1500$ (i.e. 40% empty cells), $\beta = 0.5$, $t_i = 11$, $\alpha = 0.05$, $a = 0.5$ and $a' = 0.3$). (b) Host-pathogen coexistence. Probability of coexistence for at least 10 000 iterations is 1.00 for both models (mean lifespan = 129 weeks, $\kappa = 1500$ (i.e. 40% empty cells), $\beta = 0.5$, $t_i = 61$, $\alpha = 0.05$, $a = 0.5$ and $a' = 0.3$).

Table 1. Average quasi-equilibrium prevalence (based on 100 simulations) for different values of α (pathogen-induced mortality rate) and a' (birth rate for infected individuals), (a) for the FCA model, and (b) for the FCN model. Birth rate for uninfected individuals (a) is 0.5 throughout.

	$\alpha = 0$	$\alpha = 0.05$
(a) FCA model		
$a' = 0.3$	0.266 404	0.701 067
$a' = 0.5$ (i.e. $a' = a$)	0.265 962	0.710 030
(b) FCN model		
$a' = 0.3$	0.360 812	0.772 785
$a' = 0.5$ (i.e. $a' = a$)	0.360 625	0.772 772

Average quasi-equilibrium prevalence levels for the FCN model with different combinations of α and a' are given in table 1b. Results are very similar to those for the FCA model. The effect of α on the coexistence boundary is demonstrated in figure 6b, which indicates that highly pathogenic organisms can persist at relatively low levels of transmission, unlike in the FCA model.

For the FCN model, an additional type of pathogen extinction is possible when α is relatively large, namely 'low host' pathogen extinction (figure 3b). Typically, the pathogen spreads through the whole population, causing

Figure 6. Boundaries between 'low prevalence' pathogen extinction and host-pathogen coexistence (a) for FCA models, and (b) for FCN models. Each boundary is the average of five simulations. In all the models $\kappa = 1500$ (i.e. 40% empty cells), $a = 0.5$ and $a' = 0.5$.

host numbers to fall dramatically. The host and pathogen then coexist in low numbers until a stochastic event causes the pathogen to go extinct, at which time the host population is released from the grip of the pathogen and is free to grow in size until it reaches the 'carrying capacity'. If the birth rate for uninfected individuals is too low, however, the host is unable to recover and becomes extinct also. These outcomes occur when α is relatively large and the transmission parameter and/or the infectious period are also relatively high. Their existence makes host-pathogen coexistence less likely for the FCN model with relatively large α . The region of host-pathogen coexistence also becomes smaller as a' decreases. Note also that, as is the case for the boundary between 'low prevalence' pathogen extinction and host-pathogen coexistence in figure 3a, the boundary between 'low host' pathogen extinction and host extinction in figure 3b is a gradient of probabilities rather than having exact demarcations. Pathogen extinction is most likely close to the boundary with coexistence and host extinction is most likely further away.

4. COMPARISON OF SPATIALLY EXPLICIT AND GLOBAL TRANSMISSION TERMS

Generalized linear modelling (Becker 1989) was performed using S-PLUS (MathSoft, Inc.) to determine the extent to which the global outputs from the cellular automata models, defined by their contact structure to be either locally frequency dependent (FCN) or locally density dependent (FCA), can be described by globally fre-

Figure 7. Plots showing observed and predicted numbers of newly infected individuals for data series where N is approximately constant (mean lifespan = 129 weeks, $\kappa = 1500$ (i.e. 40% empty cells), $\beta = 0.5$, $t_i = 61$, $\alpha = 0.05$, $a = 0.5$ and $a' = 0.3$, initial population size = 1500, initial number of infecteds = 1), (a) for FCA models, and (b) for FCN models. Solid line, observed values; long dashes, number predicted by the global density-dependent term βSI ; short dashes, number predicted by the global frequency-dependent term $\beta' SI/N$.

quency-dependent and globally density-dependent transmission terms. In each time-series, the output variable was the number of newly infected individuals at a particular time-step. This number was compared with the numbers of newly infected individuals predicted by the global density-dependent and global frequency-dependent transmission terms βSI and $\beta' SI/N$, where S and I were the numbers of susceptible and infected individuals at the previous time-step and N was the total number of individuals at the previous time-step. An identity link function was used and Poisson errors were assumed (Becker 1989; Begon *et al.* 1999). How well a particular model fits the data is expressed by the scaled deviance (residual deviance). This is given in table 2 along with the corresponding coefficient, which is the estimate of β or β' as appropriate.

Neither the global density-dependent nor the global frequency-dependent transmission terms were able to capture the dynamics of new infections at the beginning of a time-series generated by either the FCA or the FCN model, where the time-series represented the outcome of invasion by a few infecteds (results not shown). This is not surprising given that at the beginning all infection is concentrated in small portions of the lattice, whereas both

global models assume that it is homogeneously spread over the lattice. Hence, to allow such transient behaviour to die away, points corresponding to the interval 1000–1099 iterations were selected. As shown in table 2a and illustrated in figure 7, both global transmission models fit the data from the FCA and FCN models equally well. This is because, in both cases, a quasi-equilibrium has been achieved. Consequently, over this interval, N is approximately constant and hence βSI and $\beta' SI/N$ are essentially proportional to one another.

A second pair of time-series was therefore examined, where the initial total population was 500 (sufficiently far from the 'carrying capacity' κ of 1500), the starting prevalence was approximately equal to the equilibrium prevalence (rather than being close to zero as for invasion) and the interval was restricted to the first 20 points (so as to preclude quasi-equilibrium behaviour but still yield an interval comparable in length to many ecological data-series (e.g. Begon *et al.* 1998, 1999)). The first and third conditions ensure that N increases over the interval and hence βSI and $\beta' SI/N$ are not simply proportional to one another; the second that infecteds are distributed throughout the lattice at the start so that atypical local effects, such as occur with invasion, are minimized. The results (table 2b and figure 8) show that data from both the FCA and FCN models are far better described by the global frequency-dependent term than by the global density-dependent term.

5. DISCUSSION

We set out to investigate the relationship between local behaviour (contacts) and global transmission terms. Global models (and the transmission terms therein) effectively assume that all individuals make the same number of contacts per unit time and that the proportion of these that are infectious is equal to the overall proportion of infected individuals in the population. Cellular automata models, by contrast, treat each individual separately and take into account local variations in the number of infecteds. The FCA model in this paper also takes into account local variations in the number of neighbouring individuals, and hence the number of contacts. Indeed, this is the crucial difference between the FCA and FCN models.

The results for the FCN model show clearly that the unoccupied cells are largely bypassed by the contact mechanism. Therefore, the number of empty cells in the lattice does not greatly affect the outcome. In the FCA case, however, the empty cells impede the spread of the pathogen, extending the period of the epidemic and, in the case of persistence, reducing the prevalence of infection. These results are intuitive and indicate that the cellular automata models, although simple, capture the essence of transmission within real systems. It is worth noting that in addition to 'low prevalence' pathogen extinction and host–pathogen coexistence, two other outcomes are possible for the FCN model when α is relatively large. These are 'low host' pathogen extinction and host extinction. The possibility of the latter is expected because equivalent behaviour is found for global models with frequency-dependent transmission (Zhou & Hethcote 1994). However, the existence of the former is somewhat surprising as conventionally frequency-dependent transmission is

Table 2. Results of fitting generalized linear models to data generated by the cellular automata models. (a) For data points corresponding to the time interval 1000–1099, where N is approximately constant (parameter values and initial conditions as for figure 7). (b) For data points corresponding to the time interval 1–20, where N increases (parameter values and initial conditions as for figure 8).

	FCA model		FCN model	
	residual deviance	coefficient	residual deviance	coefficient
(a) N constant				
model G1: SI	97.0644	0.0003175	13.4545	0.0008418
model G2: SI/N	94.8049	0.4214	13.4336	1.0997
(b) N increasing				
model G1: SI	127.3572	0.0002664	183.8641	0.001094
model G2: SI/N	12.2197	0.3153	6.2605	1.0490

Figure 8. Plots showing observed and predicted numbers of newly infected individuals for data series where N is increasing (mean lifespan = 129 weeks, $\kappa = 1500$ (i.e. 40% empty cells), $\beta = 0.5$, $t_i = 61$, $\alpha = 0.05$, $a = 0.5$ and $a' = 0.3$, initial population size = 500, starting prevalence $\approx$ quasi-equilibrium prevalence). (a) for FCA models, and (b) for FCN models. Solid line, observed values; long dashes, number predicted by the global density-dependent term βSI ; short dashes, number predicted by the global frequency-dependent term $\beta' SI/N$.

associated with pathogen persistence at low host densities. It is presumed that the occurrence of 'low host' pathogen extinction is due in part to stochastic variation within the cellular automata model.

To discover which global transmission terms could approximate the transmission occurring on the lattice, we

used generalized linear modelling to compare the actual number of newly infected individuals at each time-step with the number predicted by each global term. Not surprisingly, neither global term is a good descriptor of the epidemic behaviour following invasion by a small number of infected individuals. This is because the infected individuals are not even approximately homogeneously distributed throughout the lattice. When they are homogeneously distributed and N is approximately constant (and hence I/N is approximately proportional to I/A) as at the quasi-equilibrium, the global transmission terms βSI and $\beta' SI/N$ are equally good at describing transmission in both the FCA and FCN models. This emphasizes that ultimately it is the global relationship between I/N and I/A , rather than the underlying transmission patterns, that determines whether density- or frequency-dependent transmission terms can be distinguished as descriptors of global host–pathogen dynamics.

Most importantly, however, when N varies (and atypical local transmission effects are minimized), the global frequency-dependent term emerges as the better descriptor irrespective of local transmission behaviour. Even when the contact rate is *locally* density dependent as in the FCA model, the host–pathogen dynamics of the whole system can be modelled satisfactorily as though transmission were *globally* frequency dependent. It seems that the slight clustering of infected individuals (that is an inevitable consequence of local transmission) causes the probability of a cell being occupied by an infected individual to be closer to I/N than I/A .

Begon *et al.* (1998, 1999) used the approach of comparing different generalized linear models in their investigation of cowpox in bank voles and wood mice (indeed, that work suggested the approach used here). Their results indicated that the global frequency-dependent term was better than the density-dependent one at describing the cowpox–rodent system, and they speculated that this may be instructive as to the nature of the (local) transmission. The present results, on the contrary, indicate that such findings may simply reflect the fact that transmission is local, and may say nothing about the nature of that local transmission. The results do show, though, that the relatively simple global term $\beta' SI/N$, which may be criticized as being unrealistic because it takes no explicit account of local distribution and behaviour, can none the less

approximate different types of transmission. However, as transmission is typically local, the results suggest that the commonly adopted global transmission term, βSI , may be of somewhat restricted applicability.

None of the results presented here contradict any assertion that there may be other, more complex global transmission terms that would do the job better. Thus, it may be useful more generally to use biological knowledge of contact behaviour to construct a cellular automata model that can then be used to suggest an appropriate global transmission term. This approach would be more justifiable than opting to use a simple term for simplicity's sake, or using a more complex one such as $\beta[S^p I^q]SI$ (Hochberg 1991) which has flexibility but little basis in biology. Complex terms that include a contact function (e.g. $\lambda(N)SI/N$; Zhou & Hethcote (1994)) are more realistic, but it is difficult to know *a priori* what the function should look like. Using cellular automata models and generalized linear modelling (as here) would be one way to compare different contact functions and select the most appropriate.

Future attempts to improve our understanding of the relationship between global transmission terms and local behaviour in cellular automata, as advocated above, may suggest alternative global terms that can be tested against real datasets, such as that for the rodent–cowpox system. This could refine further our understanding of the type of local behaviour consistent with the observed global dynamics.

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