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LETTER

A curve of thresholds governs plague epizootics in Central Asia

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Abstract

A core concept of infectious disease epidemiology is the abundance threshold, below which an infection is unable to invade or persist. There have been contrasting theoretical predictions regarding the nature of this threshold for vector-borne diseases, but for infections with an invertebrate vector, it is common to assume a threshold defined by the ratio of vector and host abundances. Here, we show in contrast, both from field data and model simulations, that for plague (*Yersinia pestis*) in Kazakhstan, the invasion threshold quantity is based on the *product* of its host (*Rhombomys opimus*) and vector (mainly *Xenopsylla* spp.) abundances, resulting in a combined threshold *curve* with hyperbolic shape. This shape implies compensation between host and vector abundances in permitting infection, which has important implications for disease control. Realistic joint thresholds, supported by data, should promote improved understanding, prediction and management of disease occurrence in this and other vector-borne disease systems.

Keywords

Flea, gerbil, infection ecology, plague, spatial epidemiology, threshold, vector-borne disease.

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INTRODUCTION

The idea that a sufficient abundance of hosts is necessary for an infectious agent to invade and/or persist – an abundance threshold or critical community size – is well established in epidemiology (Anderson & May 1991). Wildlife populations often exhibit large fluctuations in numbers compared with human populations. Hence, abundance thresholds may manifest themselves as intervals of time in which a pathogen can invade, spread and (temporarily) persist, interrupted by other periods in which the pathogen fails to invade, or successfully spread, and inevitably fades out. Thresholds generally have only rarely been demonstrated, but documented threshold phenomena over time have been especially scarce since long-term studies of infections in fluctuating wildlife populations are themselves rare (Lloyd-Smith *et al.* 2005).

One long-term dataset that has monitored the presence of a pathogen in a fluctuating population is that on plague in the PreBalkhash desert in Kazakhstan. There, the burrow-dwelling great gerbil (*Rhombomys opimus*) is the main host, and fleas (mainly *Xenopsylla* spp.) are the plague vectors, through which plague must pass for onward transmission. The total number of burrows is largely fixed, but the proportion occupied by extended family groups of gerbils (occupancy) varies and is an effective proxy for gerbil abundance (Davis *et al.* 2004). Gerbils have a 'home' burrow, but may visit other occupied burrows, especially during bouts of foraging (Goltzman 1977). Surveillance for gerbils, fleas and plague was initiated in 1949 to detect and control plague outbreaks in wildlife, so as to prevent plague transmission to humans. The resulting data reveal clear epizootics in the gerbils, interspersed by periods of 2–5 years in which plague is not detected in either fleas or rodents anywhere in the area (see Supporting Information, Appendix S1). The detectable presence of plague is well predicted by a threshold level of past-occupancy (1–2 years previously) (Davis *et al.* 2004, 2007a,b; Samia *et al.* 2007; see Fig. 1a). This appears to be a percolation threshold, where the fraction of burrows occupied needs to be large enough to ensure sufficient connectivity in the system for plague to spread (percolate) across the landscape, rather than the more familiar R_0-like threshold, based on random mixing between hosts (Davis *et al.* 2008).

As plague is vector-borne, flea abundance is expected to affect plague transmission dynamics (Stenseth *et al.* 2006; Samia *et al.* 2011). General models for vector-borne infections suggest that the invasion threshold is a ratio of vector to host abundance (in this case, the flea burden, see Fig. 1b and S1) when a fixed (host density-independent) biting rate of the vector is assumed, as it often is, for example, with mosquitoes (MacDonald 1957; May & Anderson 1979; Keeling & Rohani 2008). Alternatively, if the contact rate increases with the density of both host and vector, then the threshold should depend on the product of host and vector abundances, as is also conventionally assumed for macroparasites, like worms, with obligatory passage between, for example, both a vertebrate and an invertebrate host (May & Anderson 1979). The threshold then appears as a hyperbolic curve with limbs for each separate host/vector species (see Fig. 1c

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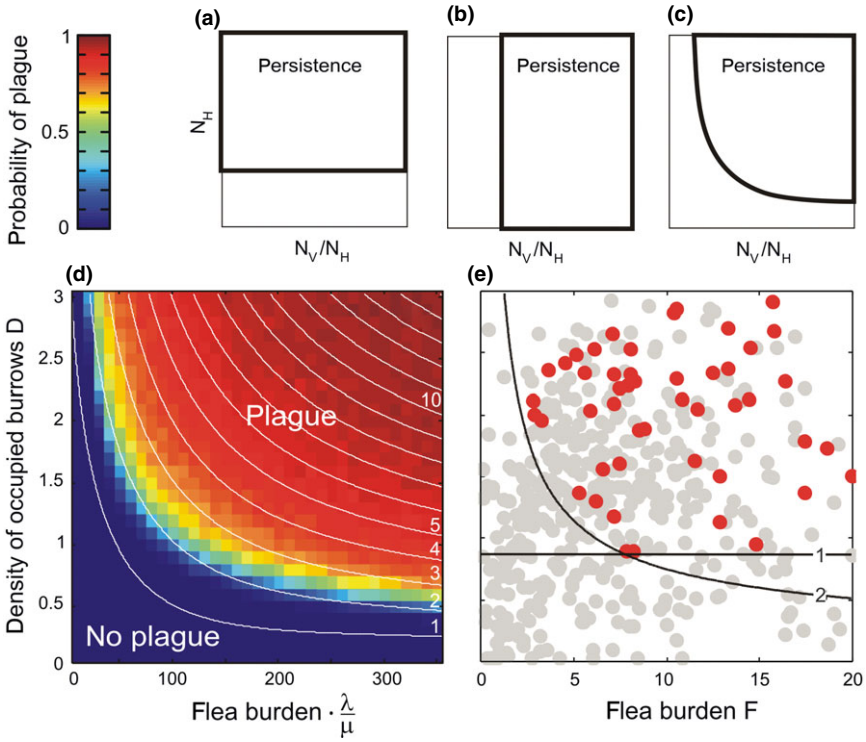

Figure 1 Cartoon of (a) a host density threshold, (b) a vector-to-host ratio threshold and (c) a hyperbolic vector/host threshold. (d) The results of the spatial SIR model simulations for plague epizootics: the fraction of simulated outbreaks that give rise to new infections at least 2 km from the site of the initial infection is plotted as a function of the occupied burrow density D and the flea burden F. The white lines correspond to different values of the connectivity proxy C, see text. (e) Field data on plague presence (red dots) or absence (grey dots) as a function of F and D. Different fitting models result in different threshold shapes (curves 1 and 2 refer to model (a) and (d) respectively).

and Holt *et al.* 2003 for a theoretical argument related to macroparasites).

Here, we assume no *a priori* knowledge on the nature of the threshold for the plague system in Kazakhstan, but do assume that transmission is a percolation (not a random mixing) process (Davis *et al.* 2008) and focus on the invasion of plague, see Appendix S1. We acknowledge further that flea movements are constrained by the mobility of their rodent hosts, which they use to move between burrows, and that the level of occupancy determines, in part, the connectivity between neighbouring occupied burrows. However, as each flea carried by a visiting infected gerbil may jump off and infect that burrow, and each flea in an infected burrow may jump onto a visiting susceptible gerbil, the connectivity between occupied burrows is also determined by the number of fleas carried by the gerbils (the flea burden).

Hence, in this article we elaborate on an earlier spatial epidemiological model (Davis *et al.* 2008) to include the flea burden in the force of infection between occupied burrows, and we simulate the probability of plague to spread throughout susceptible burrows, given the level of occupancy and the flea burden. This invasion probability allows us to define a proxy for the connectivity of the burrow network, which we then utilise to fit a threshold to the PreBalkhash field data in a similar way to that done in Davis *et al.* (2004). We then compare the explanatory power of this model to other models [with thresholds based on occupancy, on the vector-to-host ratio, on the product-of-abundances, and an earlier model of plague dynamics (Keeling & Gilligan 2000a, b)], and take into account spatial and temporal correlations in the dataset. Finally, we present a simplified mechanistic model, which allows us to relate the observed threshold to percolation theory.

A SPATIALLY EXPLICIT S-I-R MODEL

We take an approach similar to the spatial S-I-R-model of (Davis *et al.* 2008). Both time and space are continuous variables and interactions are local and stochastic. Individual burrows are classified as susceptible (S), infected (I) or recovered (R). They are located at discrete points in two-dimensional space. We consider a 5×5 km^2 area, where occupied burrows are distributed randomly with density D. Hence, we only take into account occupied burrows. As we are interested in rapid developments of epidemics, we do not consider colonisation of new burrows, nor the extirpation of inhabited burrows. Note that, because extirpation of inhabited burrows is not included, adding a latency period, which we do not do here (i.e. considering an S-E-I-R model) would slow down disease spread, but not affect the invasion probability. The burrow closest to the centre of the area is initially infected and can infect any susceptible burrow in the area. Infected burrows recover at a constant rate μ.

The rate at which a given susceptible burrow at position $\boldsymbol{r}$ becomes infected equals $\lambda F \Sigma_i K(||\boldsymbol{r} - \boldsymbol{r}_i||)$, where $\boldsymbol{r}_i$ are the locations of infected burrows, $K(r)$ is the dispersal kernel of a great gerbil (r being the distance from the centre of the burrow), and λF describes the rate at which infected fleas leave one burrow and infect other, susceptible burrows on arrival. This is proportional to the flea burden F, but also depends, like all transmission parameters, on the combination of a variety of other factors: the survival of fleas during dispersal, the fraction moving to burrow entrances to disperse, the survival of bacteria within a flea, and any other parameter that influences the effectiveness of bacterial transmission through flea bites. We assume that the number of fleas residing in the burrow to be proportional to

the flea burden (Krasnov *et al.* 2004). The flea burden changes dramatically throughout the years and will determine how many fleas are carried towards neighbouring burrows (see Section Plague Field Data, below). Hence, we also assume that, compared with the flea burden, the values of these other parameters change little between years, and can be contained within the single fitting parameter, λ.

The dispersal kernel was normalised, $\iint K(r) r dr d\theta = 1$, such that the resulting probability density function represents the probability per unit area that a plague bacterium released at location 0 travels a distance r. The two-dimensional dispersal kernel was modelled to be radially symmetric, using the half-logistic radial distribution which was fitted to observed movements of the great gerbils in the field (Davis *et al.* 2007a,b),

$$K(r) = \frac{c_2}{r} \frac{2e^{-c_1 r}}{(1 + e^{-c_1 r})^2},$$

with $c_1 = 0.0166$ a fitting parameter and c_2 a normalisation parameter. $\Sigma_i K(||\boldsymbol{r} - \boldsymbol{r}_i||)$ has to be calculated numerically. Note that we assume the number of gerbils per burrow to be independent of the gerbil density. Indeed, when the gerbil population increases, this will result in the colonisation of more burrows and hence this is accounted for by an increase in D. The simulation ends when there are no infected burrows left, or when the travelled distance from the initially infected burrow exceeds 2 km. Simulations (and model fitting) were done using Matlab.

The results of model simulations are displayed as a phase diagram in Fig. 1d. It shows the fraction of 1000 simulations in which an initial infection gives rise to new infections at least 2 km from the site of the initial infection, as a function of the density of occupied burrows, D, and $(\lambda/\mu)F$, where μ is the recovery rate of an infected burrow. This fraction can be taken to represent the probability that a sustained epizootic will occur following an initial infection, that is that plague can establish and spread in the governing host and vector population conditions. The model therefore shows an invasion threshold that is a hyperbolic-like curve in burrow density/flea burden-space, below which plague cannot invade the host population, but above which it can. The distribution of probabilities resembles the curved isocline proposed by Holt *et al.* (2003) in another context, and is implicit in other non-graphical models (May & Anderson 1979). As the flea burden decreases, the occupied burrow density threshold compensates by shifting to larger values. Equally, greater numbers of fleas being transported can compensate for lower occupancy levels that imply larger distances between neighbouring burrows. In theory, the threshold curve approaches each axis asymptotically. However, for low values of the occupied burrow density and with occupied burrows distributed evenly over the burrow population (i.e. not clustered), one expects that the hyperbolic curve will level off (compensation by a larger F will fail), because the distance between occupied burrows can become too large compared with the usual movement radius of gerbils.

From a percolation perspective, the ability to spread successfully is equivalent to the emergence of long-range connectivity in the contact network (Grimmett 1999). In this view, the probability contours in Fig. 1d join (F, D) combinations with the same network connectivity. Due to the complex nature of the burrow network – its random nature, patterns in gerbil movement, variations in the flea burden, the infectious period, etc. – it is difficult to assess connectivity exactly. A possible proxy for the network connectivity, although, is C, which has an R_0-like interpretation at the burrow level and which we define here as the expected number of new infected burrows arising from a single infectious burrow in a network of susceptible burrows. Note that C has analogies to R_*, which is essentially R_0, but rescaled at the level of households and metapopulations (Ball & Neal 2002). We have denoted our quantity as C to avoid confusion with R_0 and R_* which have their threshold values at 1, and characterise growth in the number of infected hosts/households, when contacts are subject to random mixing or socially stratified random mixing. When there are strong spatial constraints on transmission between hosts, and hosts have a fixed position in space, as is the case here, then C has neither of these properties. The C is calculated from the S-I-R model simulations, by counting the number of secondary infections caused by the initial infection, and this value is averaged over 10000 simulation runs. The contour lines of C, plotted in Fig. 1d (white lines), appear to have indeed the same shape as the plague probability distribution (colour coded). In the analysis below, we will use this connectivity proxy as an explanatory variable for plague presence.

PLAGUE FIELD DATA

To test the validity of the phase diagram predicted by our spatially explicit model (Fig. 1d), we used data from the PreBalkhash focus to compute the density of occupied burrows, D, the flea burden, F and the plague occurrence. Each spring and autumn between 1949 and 1995, the proportion of burrows inhabited and the average number of gerbils per burrow were estimated at a variable number of locations in the PreBalkhash focus by the Kazakh Anti-Plague Authorities. Gerbils and fleas were trapped and tested for *Y. pestis* infection, and the samples pooled at the 10×10 km^2 sector level. The PreBalkhash focus consists of approximately 352 such sectors. We did not restrict ourselves to areas with long and continuous time series (see Appendix S2), but started from the data set comprising the whole of the PreBalkhash focus, including only those samples for which for plague had been tested at year t (plague detected or undetected), and the burrow occupancy, the number of trapped rodents and their fleas had been measured during at least one season in the current and/or the previous 2 years, (t, t–1, t–2). If these had been measured more than once, the average was used (except for plague occurrence). The density of occupied burrows, D, was computed as the product of the occupancy and the burrow density. The burrow density changes little over time, and is measured and up-dated only rarely. The flea burden, F, was calculated as the ratio of the number of rodent fleas that were found on the trapped rodents, divided by the number of rodents examined each season. These ratios are available in the data from 1975 onwards. Plague occurrence was determined for the trapped great gerbils, which were tested for plague by plating rodent samples (blood, liver and spleen) on Hottinger's agar containing 1% haemolysed sheep erythrocytes. Note that a positive bacteriological test is usually only obtained from rodents with acute plague, which may considerably underestimate the number of rodents that carry the infection.

Filtering of the field data (as described above) generates 461 observation points, for 49 of which plague was detected. The field data (Fig. 1e) suggest a threshold density of occupied burrows, but also suggest that this threshold shifts to lower densities as the flea burden increases, and that at the lowest flea burdens high burrow density is not sufficient to sustain plague.

MODEL FITTING AND COMPARISON

To compare the explanatory power of the connectivity proxy C, derived from our spatial S-I-R model, with quantities suggested by other models or by theoretical predictions in the literature, we fit the same functional form for a threshold curve as in Davis *et al.* (2004). For the different models, the plague data (see above) are projected onto a single independent variable: respectively, C (our model), D (density of occupied burrows), F (vector-to-host ratio), FD^2 (product-of-abundances), $F[1-\exp(-aD)]$ (Keeling and Gilligan model). The resulting distributions are then fitted to the cumulative Weibull distribution function (see Davis *et al.* 2004)

$$p(x) = \begin{cases} 0 & x \leq \gamma \\ 1 - exp\left[-\left(\frac{x-\gamma}{\eta}\right)^{\beta}\right] & x \geq \gamma \end{cases},$$

which is a nonlinear regression function that assumes the existence of a threshold γ. Parameters η and β are shape parameters and x is the independent variable considered. In the current analysis, $p(x)$ is the binomial model function which expresses the probability that plague successfully invaded (was detected), given the explanatory variable has the value x. To fit $p(x)$ to the field data, we minimised the Akaike's Information Criterion value (AIC) (Sakamoto *et al.* 1986), which is given by AIC = $2K-2\ln[L(p(x)|x,y)]$, where $L(p(x)|x,y)$ is the binomial likelihood function

$$L(p(x)|x_i, y_i) = \Pi_i p(x_i)^{y_i}[1 - p(x_i)]^{1-y_i},$$

where y_i is plague presence (1) or absence (0) at the field data points described by their independent variable x_i.

For the spatially explicit model, when fitting C as the independent variable, we have an extra fitting parameter, λ/μ. Nevertheless, in this case too, the fit only involves three fitting parameters, (λ/μ, η, β), as for this model the threshold value occurs within a limited interval, $1.5 < \gamma < 2.5$, as can be inferred from Fig. 1d. See the Appendix S3 for more details.

The resulting probability of detecting plague in the case of the spatially explicit model ($x = C$) is shown in Fig. 2: there is a non-zero threshold value above which the probability of plague increases almost linearly as a function of C (Fig. 2a). The probability is shown in the two-dimensional (F, D) phase plane in Fig. 2b. The simulated probability of plague in Fig. 1d is larger and increases more rapidly with increasing C, compared with the probability of detecting plague from the field data, see Fig. 2b. This can be understood by realising that in the field data, a sector may show no signs of plague, not because the necessary conditions are not met, but because there was no initial infection with plague or because it was not detected due to the sparse sampling. The simulated probability does not suffer these constraints, as it presupposes an initial infection and infallible plague detection.

If we use the same fitting procedure for the other models, and compare their respective AIC-values, then the spatially explicit model including flea burden ($x = C$, Fig. 2a and b) significantly outperforms the model based only on the occupied burrow density ($x = D$, Fig. 2c and d) and the vector-to-host ratio model ($x = F$, Fig. 2e and f), but it performs similarly to the product-of-abundances model ($x = D^2F$, Fig. 2g and h). Indeed, the probability distribution resulting from our spatially explicit model (Fig. 2b) is very similar to that corresponding to the product-of-abundances model (Fig. 2h), both having a hyperbolic threshold (see also Appendix S4). Finally, we have also considered the model of Keeling & Gilligan (see Appendix S5) which performed significantly worse than the other hyperbolic models.

Note that, in the above analysis, we have used (t, $t-1$, $t-2$) as input data for the models. To investigate the sensitivity of the different models to the choice of the input range, in Appendix S6 we have

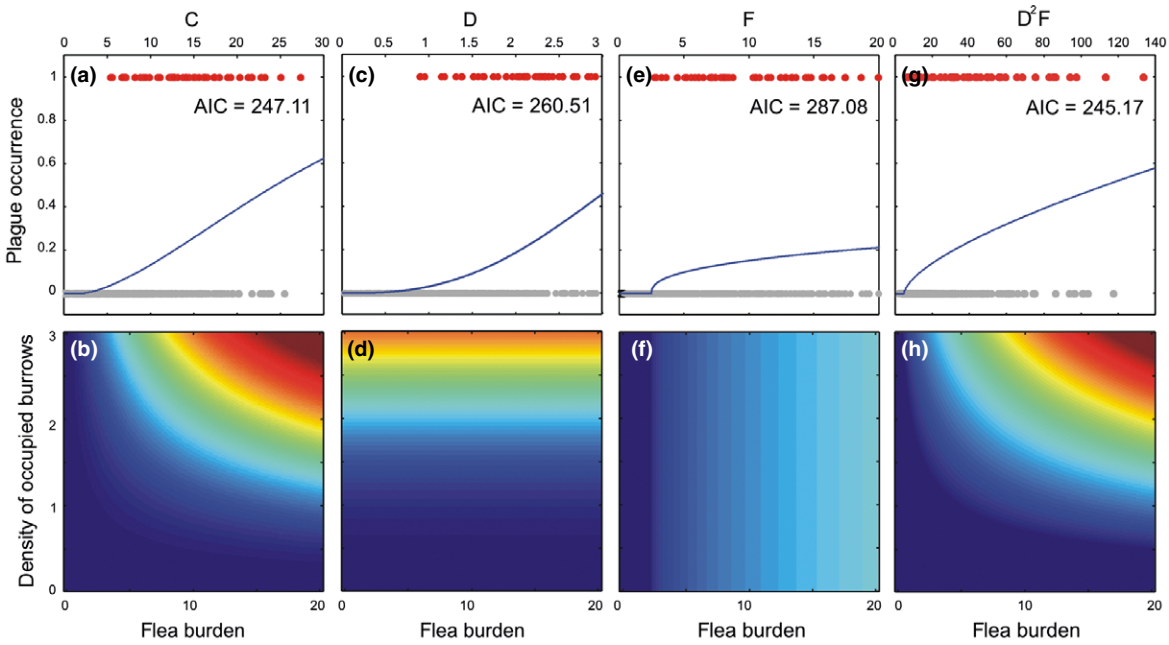

Figure 2 Plague presence (red dots) or absence (grey dots) when field data are projected, respectively, on (a) the simulated connectivity C, (c) the occupied burrow density D, (e) the flea burden F and (g) the product-of-abundances D^2F. Assuming the cumulative Weibull distribution function as the functional form (see text) along this dimension, the probability to detect plague is shown (solid line). In (b), (d), (f) and (h), for the different models, the probability is shown as function of the flea burden and the density of occupied burrows, as in Fig. 1e. Note that the probability of plague for the spatially explicit model (b) is very similar to that of the product-of-abundances model (h).

tested the performance of each model for a range of different input data. From these analyses, it follows that the spatially explicit and the product-of-abundances model perform best over a wide range of input years, as long as the concurrent information (t) on the flea burden and the occupied burrow density are included. The best results are obtained when combining data from t, $t-1$ and $t-2$, as was considered above.

REDUCING TEMPORAL AND SPATIAL CORRELATIONS

In the analysis above, possible spatial and/or temporal correlations between individual sample points are neglected. In Fig. 3 we plot the autocorrelation of the three relevant parameters in the data: the density of occupied burrows D, the flea burden F and also plague occurrence, a binary variable that gives insight into the dynamics of plague spread. On the x-axis is the time difference between the samples, and on the y-axis is the distance between the sectors where the samples were taken. Note that the temporal autocorrelations of the occupied burrow density and the flea burden were partly introduced by averaging the input data over the past 2 years (which is not the case for plague occurrence, as this is only evaluated at time t). Occupied burrow density is mainly correlated in time, with a correlation time of about 2 years. The correlation with distance axis drops very quickly, suggesting a minor correlation covering approximately 40 km. For the flea burden, both the correlation time and correlation length are shorter. Lastly, plague occurrence seems to be mainly correlated along the spatial dimension, indicating that plague spread is indeed a spatial phenomenon where neighbouring sectors are more likely to infect each other (Heier *et al.* 2011). The limited temporal correlation between samples (1 year) indicates that changes happen at a rather short time scale, and that plague may invade and disappear rather abruptly.

To account for these temporal and spatial correlations, we subsampled our original dataset randomly, using only samples separated both in time and space such that the correlations were small, and hence generating less correlated subsets of the dataset shown in Fig. 1e. This is the case when the time lag exceeds 2 years and the distance is larger than 10 km (Fig. 3). The subsampling was carried out as follows: from the total data set, we randomly selected one data point and removed all the data points within the correlation time and correlation length. From this reduced set, a second data point was randomly selected and correlated samples were again removed, and this procedure was repeated until there were no data points left. We used these data subsets to fit the models in the same way as before, generating an increasing ensemble of different subsets and calculating the $\langle\Delta\text{AIC}\rangle$. The averages of these converge for large ensemble sizes, and this ensemble average shows that the proposed joint threshold model is significantly better than the model based on occupancy only ($\langle\Delta\text{AIC}\rangle = 7.27$), the model proposed by Keeling & Gilligan (2000a,b) ($\langle\Delta\text{AIC}\rangle = 3.29$), and the vector-to-host ratio model ($\langle\Delta\text{AIC}\rangle = 13.81$). The difference from the product-of-abundances model is much smaller ($\langle\Delta\text{AIC}\rangle = -0.1$). Hence, reducing temporal and spatial correlations, by selectively removing possibly correlated samples, decreases the difference between the models, but does not change the basic result.

PERCOLATION ISOCLINES

Noting that the product-of-abundances model performs as well our customised spatially explicit model, and that the product-of-abundances model was originally derived on the assumption of random mixing, we here examine whether a very general model of percolation can generate an output that is similar to the product of abundances. We consider simple bond percolation on a lattice-like arrangement of burrow systems, where bonds are only allowed between nearest neighbours.

Suppose occupied burrows have a regular spatial arrangement such that the distance between nearest neighbours is a constant $d = 1/\sqrt{D}$, where D is the density of occupied burrows. Furthermore, for each pair of nearest neighbours (i, j) let $p_{ij} = p$ be the probability that if burrow i were to become infected then j would also become infected, i.e. there is a directed edge between i and j. This is an example of directed, short-range bond percolation on a lattice, and hence, in the case of an infinite lattice, there exists a threshold p^*, such that when $p \geq p^*$ there is a positive probability that an arbitrary node belongs to an infinite cluster. In percolation models for infectious disease transmission in a spatial setting, p^* is the invasion threshold for the pathogen (see Davis *et al.* 2008).

Now suppose that the *rate* at which infectious fleas are transported from a burrow to a neighbouring burrow is proportional to the mean flea burden (F) of the gerbil population and depends on the distance, d, between occupied burrows. The relationship between the rate of transport of fleas and the distance between two burrows is given by $K(r)$ but in this simplified scenario, where only nearest-neighbours are considered, we suppose that the rate of transport of fleas is proportional to $H(d)$.

For the plague system, p is the probability that at least one infectious flea is transported from the infectious burrow to its neighbour, where

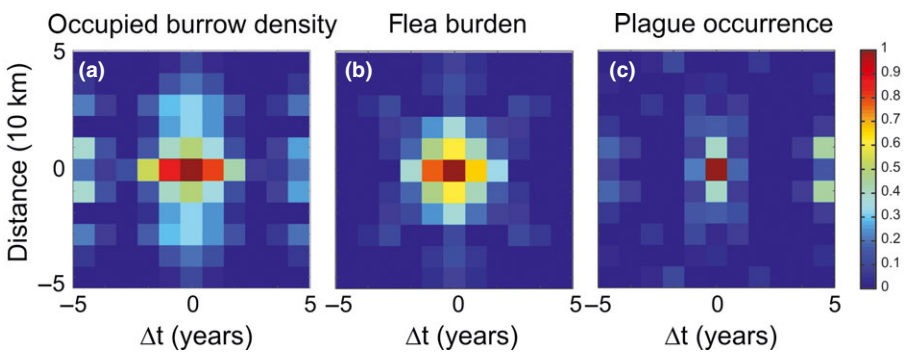

Figure 3 The autocorrelation of (a) the density of occupied burrows, (b) the flea burden and (c) the plague occurrence as function of the distance between the sample sectors and the time difference between the samples.

we have assumed that this is guaranteed to lead to a newly infected burrow. Now let the number of transported infectious fleas between two neighbouring burrow systems have a Poisson distribution with mean $cFH(d)$, where the constant c takes into account the mean infectious period of a burrow as well as two constants of proportionality. From the Poisson assumption, we can write,

$$p = 1 - \exp[-cFH(d)],$$

which, provided $cFH(d)$ is small, can be approximated by

$$p \approx 1 - [1 - cFH(d)] = cFH(d).$$

The function $H(d)$ remains unknown. However, we know that it at least ought to be a positive, monotonically decreasing function of d to represent our qualitative knowledge of the spatial constraints on flea movements, and in the absence of further biological information, a reasonable suggestion is $H(r) \sim 1/r^{\alpha}$. Finally, then, we note that for, the threshold quantity p has the same form as the product-of-abundances threshold for R_0. That is, inserting $H(d) \sim 1/d^4$ into the above equation yields

$$p \sim FD^2 \sim N_v N_h,$$

which is exactly the product-of-abundance model. This is an artificial scenario, in that in reality, fleas will be transported beyond the nearest neighbouring burrows and occupied burrows are not arranged on a regular grid, and consequently we arrive at a kernel $H(d)$ that is different from the one considered in the rest of the article. However, this nevertheless shows that it is possible to arrive at the product-of-abundances model by a route that is entirely consistent with percolation of plague through the transport of fleas.

DISCUSSION

A hyperbolic threshold curve emerges here both from our spatially explicit model and from our analysis of field data (Fig. 1c), and arises too from a general mechanistic model of the probability of a connection between two occupied burrows. The hyperbolic threshold curve is also implicit in models that relax the assumption of a fixed vector biting rate (Keeling & Rohani 2008) and in more general, product-of-abundances models with alternating hosts (May & Anderson 1979). Indeed, the performance of the latter is similar to that of our spatially explicit model, and can be seen, therefore, to capture, in a non-specific way, the joint dependence suggested by our customised model and supported by our analysis of field data. It is clear from our results, however, that a general dependence of transmission on the abundance of both host and vector may arise for a variety of reasons, not considered in conventional derivations, depending on the system concerned.

In the present case, this arises because maintenance of plague in the population requires transport of fleas between infectious and susceptible burrows. Our results suggest that the rate at which fleas are transported between burrow systems increases with both the density of occupied burrows and the flea burden. In contrast, a recent study of a relatively small data set on plague in prairie dogs (*Cynomys* spp.) in North America (Brinkerhoff *et al.* 2010) failed to find any causal association between flea burden and plague outbreaks. This, although, is reasonable for that system, as plague spreads rapidly through prairie dog towns, fleas do not play the same 'connecting' role between sub-populations, and the role of conventional flea-borne transmission has itself been questioned (Webb *et al.* 2006). In fact, a recent model has suggested the feasibility of a second host species, the grasshopper mouse (*Onychomys leucogaster*) providing the percolation vehicle for plague in prairie dog populations (Salkeld *et al.* 2010). Perhaps, if data were collected on both prairie dog and grasshopper mouse abundance, a hyperbolic-like threshold would emerge here, too, in the two-host phase plane.

Biologically different, but nevertheless related processes (in the sense of invalidating the assumption of fixed biting rates) are also likely to pertain in other host-vector systems. For example, the midges that transmit bluetongue virus amongst ruminants are more likely to approach a trap (proxy host) if there are more hosts (sheep) in the vicinity (Garcia-Saenz *et al.* 2011), and will also waste an increasing proportion of bites on hosts not competent for bluetongue as the proportion (abundance) of competent, ruminant hosts declines [an example of the 'dilution effect' (Norman *et al.* 1999), which also applies to a number of other vector-, especially tick-borne infections (Keesing *et al.* 2010)]. Bluetongue transmission seems likely to increase, therefore, both with midge and with ruminant abundance.

Previous studies of this system were focused on prediction (Davis *et al.* 2004, 2007a), but we have now shown that plague presences and absences are far better accounted for by including flea burden at t. Furthermore, the manner in which we have done so (a hyperbolic threshold curve), while consistent with a number of biological scenarios, is demonstrably consistent (our spatially explicit model) with the threshold being a percolation threshold, as proposed previously (Davis *et al.* 2008), albeit by other means and in a density-only context. A particular benefit could be the elimination, through the monitoring of flea burden, of many of the large number of 'false positive' predictions (occupancy above the threshold but plague nevertheless absent; see Fig. 1e), which characterise previous threshold models of the system, and undermine the utility of the model to public health practitioners in practice (Klassovskaya *et al.* 2007). Hopefully, similar refinements to canonical threshold models, tailored to the details of particular vector-borne disease systems, will improve our ability to predict and ultimately manage these threats to human and veterinary health.

AUTHOR CONTRIBUTIONS

HL, SD and JR initiated the question how the threshold will vary under different conditions. JR wrote code, ran the model and analysed the output data, relating these to the historical data set, made available by VSA. HL, MB and JAPH framed the results in a broader epidemiological context. SD related the results to percolation theory. JR, MB, SD, HL and JAPH wrote the article.

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