Population viscosity suppresses disease emergence by preserving local herd immunity

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Abstract

Animal reservoirs for infectious diseases pose on-going risks to human populations. In the current theory of zoonoses, the introduction event that starts an epidemic is assumed to be independent of all preceding events. However, introductions are often concentrated in communities that bridge the ecological interfaces between reservoirs and the general population. In this paper, we explore how the risks of disease emergence are altered by the aggregation of introduction events within bridge communities. In viscous bridge communities, repeated introductions can elevate the local prevalence of immunity. This local herd immunity can form a barrier reducing the opportunities for disease emergence. In some situations, reducing exposure rates counter-intuitively increases the emergence hazards because of off-setting reductions in local immunity. Increases in population mixing can also increase emergence hazards, even when average contact rates are conserved. Our theory of bridge communities may help guide prevention and explain historical emergence events, where disruption of stable economic, political, or demographic processes reduced population viscosity at ecological interfaces.

Key words: infectious disease, local herd immunity, emergence hazard, bridge community, population viscosity, parochial vs proselyte transmission

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1 Introduction

Among the variety of low probability, high consequence risks that the human population of planet earth faces from nature, the emergence of new infectious diseases with high mortality is one that often captures the public imagination. Recent reports of Middle Easter Respiratory Syndrome (MERS) [1], Kyasanur Forest Disease Virus (KFDV) [2], and H7N9 influenza [3] are three of the most recent reminders that this is a real risk and that novel pathogens continue to emerge.

Animal reservoirs are believed to be the source of many of the infectious diseases that threaten human health [4, 5, 6, 7]. The smallpox virus, for example, is believed to have evolved from a rodent-borne virus between 10 and 100 thousand years ago [8], while the measles virus is believed to have evolved from the rinderpest virus only a thousand years ago [9]. A number of these recent zoonoses have been attributed to bats reservoirs (order Chiroptera) [10], with smaller contributions from pigs [11], birds [12], and primates [13].

In order to switch from transmission in an animal reservoir to transmission in the human population, germs must adapt to sustain themselves within a human host and to transmit themselves on to other humans. Antia–Regoes–Koella–Bergstrom (ARKB) theory [14], which is based on "branching process" mathematics [15, 16, 17], provides a widely used quantitative description of this emergence. ARKB theory captures a number of empirically observed patterns in disease emergence, including the randomness of the emergence process and the stochastic chattering of introductions of MERS [18]. It can been exploited to study the influence of factors including host type heterogeneity [19], adaptation pathways [20], spatial heterogeneity [21], on-going reservoir interaction [22], and surveillance conditions [23].

ARKB theory makes an important approximation. It assumes the probabilities of introduction and subsequent transmission are independent of all preceding introduction and transmission events. This approximation is best when the introduction events are rare and uniformly distributed across a large, well-mixed population, or when there is no memory of past events in the host population.

However, this only an approximation. The introduction and subsequent transmission events associated with disease reservoirs may not be uniformly distributed. Often only certain human sub-populations are directly at-risk through exposures to each disease reservoir. We call these sub-populations "bridge communities" because their contact networks connect reservoirs to the general human population.

Within bridge communities, people can be inoculated against zoonotic pathogens through exposure from disease reservoirs before mutations adapt the pathogens for human transmission. Studies within the Guangdong markets showed that 40% (8/20) of the wild animal traders and 20% (3/15) of the wild animal butchers were seropositive for SARS even though they had not reported the symptoms of the disease [24]. Bush hunters in Cameroon have been show to be seropositive for SIV, even though the virus is not transmissible person-to-person [25]. Rabies virus neutralizing antibodies have been found in Peruvian residents with

potential regular exposure to vampire bat bites despite the near-universal fatality rate of infection-sans-immunization [26]. 2% of poultry workers in parts of Asian have been shown to be seropositive for the H5N1 strain of influenza although the virus remains difficult to transmit between people [27]. And seropositive responses to Hantavirus have been found at high prevalences in some South American communities [28] even though human transmission of these viruses appears to be uncommon [29]. While seropositivity does not always imply immunity, it is generally accepted as an important correlate of protection [30, 31].

So we now arrive at the following question: If people in bridge communities can acquire immunity to zoonotic pathogens through exposure from animal reservoirs before mutations adapt the pathogens for human transmission, how does this affect the emergence process, relative to ARKB theory?

2 Simulations

Simulation methods like Bailey's lattice epidemic algorithm have been used in several studies to investigate pathogen evolution in spatially structured populations [32, 33, 34]. Here, we will describe related simulations of disease emergence through bridge communities. The simulations reveal that immunity in bridge communities can strongly diminish disease emergence.

Suppose the cells of a toroidal lattice represent a host population. Each cell is susceptible, infected, or immune. When a cell is infected, there is a constant chance each day that it will transmit the infection to each susceptible neighbor. The duration of infection is geometrically distributed, after which, infected cells recover and become immune. The duration of immunity is also geometrically distributed, after which cells return to the susceptible state.

At the center of the lattice, there is a square of cells representing a "bridge community". These cells are also exposed to a disease reservoir at a constant rate. When a cell in the bridge community is exposed to the reservoir, there is a small chance that it becomes infectious and can transmit infection to neighboring cells, possibly seeding an epidemic. Otherwise, the exposed cell gains immunity without ever becoming infectious. Subsequent transmission parameters in the bridge community are the same as outside the bridge community, and no special treatment is given to transmission across the bridge community's boundary.

Initially, the 30×30 lattice consists of only susceptible cells. Epidemic dynamics progressed rapidly (with a generation time of 4 days) and were terminated when it was clear that a nascent epidemic had either fizzled or escaped stochastic extinction. The expected transmission rate is large enough that the basic reproductive ratio of our simulations is close to the number of neighbors of a lattice cell to make emergence easy to identify. The emergence hazard rate was calculated as the reciprocal of the average time between the start of the simulation and confirmation of the first epidemic.

When we perform some simulations, we find that for low exposure rates, the

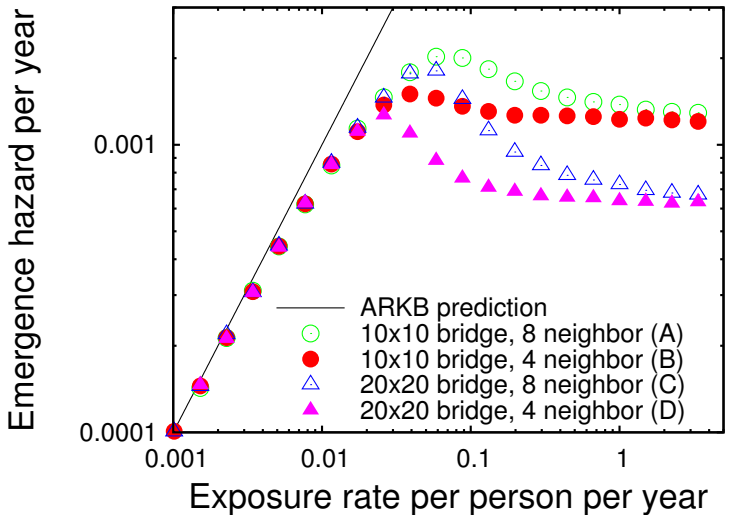

Figure 1: Plot of the risk of emergence of an epidemic in a lattice model under various conditions, all with the same predicted emergence hazard from the exposure rate ($\mathbb{E} = 0.1\lambda_0$), and basic reproduction ratio approximately equal to the neighborhood size, where exposed cells are immune for about 30 years: 10×10 bridge communities with adaptation probability $m = 0.001$ on an 8-neighbor lattice (A) or a 4-neighbor lattice (B), and 20×20 bridge community and adaptation probability $m = 0.00025$ on an 8-neighbor lattice (C) or a 4-neighbor lattice (D). Disease emergence is defined as an outbreak where more than 66% of the population becomes infected. More than 50 million years of time were cumulatively used for each data point. Naive ARKB theory predicts the emergence hazard well for low exposure rates, but turns over for large per-capita exposure rates. The more density connected the lattice (8 neighbors vs 4 neighbors), the weaker the turn. If the bridge community is enlarged and the adaptation probability is reduced proportionally, the turn becomes stronger because more introductions occur on the interior of the bridge community rather than the edges.

emergence hazard increases linearly as the exposure rate increases (see Figure 1 and Supplement S3). This matches the predictions of ARKB theory. However, for high exposure rates, we discover a point, beyond which emergence hazards decrease. The spot where the emergence hazard switches from increasing to decreasing is called a "turning point".

A little thought suggests one explanation – the accumulation of immunity in the bridge community at large exposure rates creates local herd immunity blocking introduction and transmission. This is confirmed by further exploration (see Supplement S3). Dimensional analysis and simulations show the emergence rate is inversely proportional to the duration of immunity when epidemics are fast. The effectiveness of local herd immunity depends on the process specifics. The less connected and clustered the population is, the more local herd immunity suppresses emergence. Conversely, the greater the perimeter-to-area ratio of the bridge community for comparable gross introduction rates, the greater the emergence rate. The details can be explicitly studied using percolation theory [35, 36, 37], which has previously shown that clustering in contact networks can strongly suppress transmission [38, 39].

The spectrum of behaviors between ARKB theory and our lattice simulations can be thought of in terms of "population viscosity". Population viscosity [40] was initially used in evolutionary biology to refer to the tendency of individuals in spatially-structured populations to have more in common with their neighbors than with the population as a whole. More generally, we can think of population viscosity as the tendency of the population to resist mixing and maintain clustering. The smaller the population viscosity, the more well-mixed the population is and the less information about an individual's state can be inferred from the past states of its neighbors. In a system with no population viscosity, mixing occurs faster than all other processes, and a particle's state is conditionally independent of its neighbors' states, given the population statistics. With infinite population viscosity, there is no mixing (the system is spatially frozen) and a particle's state is conditionally independent of the population statistics, given its neighbor's states.

Scaling the duration of immunity in our simulations is effectively scaling the population-viscosity by controlling the rate at which the bridge community mixes with the general population. The clustering in exposure preserved by slow turnover allows local herd immunity to build up and suffocate the emerging epidemic before it escapes to the rest of the population. However, this local herd immunity evaporates as the duration of immunity shortens. When mixing occurs rapidly in a large population, state-changes induced by past exposures are unlikely to be encountered by the next exposure, allowing the emergence hazard to increase linearly with exposure rate.

3 An emergence theory incorporating local herd immunity

To better understand how the over-all hazard rate for emergence of an infectious disease is influenced by population viscosity and immunity, we will use compartmental epidemic equations to augment a multi-type generalization of ARKB theory. We adopt a framework closely related to but slightly different from those previously proposed [5, 6, 7].

Zoonotic disease emergence and invasion has four facets: compatibility, opportunity, adaptation, and percolation (see Figure 2). The compatibility between a host and pathogen is determined by the molecular biology and physiological configurations of host and parasite, and best studied observationally and experimentally. Theoretical biology studies can better address the features that govern the opportunity, adaptation, and percolation. For novel pathogens compatible with human physiology, we may define the emergence hazard rate $\mathbb{E}$ as the probability per unit time that an epidemic is started by a zoonotic transmission along each pathway, summed over all independent pathways, or

$$\mathbb{E} := \sum_{x \in \text{pathways}} \Lambda(x)\mathcal{C}(x)\mathcal{M}(x)\mathcal{P}(x) \tag{1}$$

where $\Lambda(x)$ is the exposure rate along pathway x, $\mathcal{C}(x)$ is the probability that an exposed individual is susceptible, $\mathcal{M}(x)$ is the probability that the pathogen successfully adapts to be transmissible along path x after introduction, and $\mathcal{P}(x)$ is the probability of percolation of the transmission chains emerging into an epidemic given introduction and adaptation.

Let us suppose we have a bridge community of size N in contact with an animal reservoir along a single emergence pathway, and individuals in this bridge community are exposed to infection at a rate λ_0 per person. Subscripts 1 and 2 will refer to a bridge community and the larger surrounding general population, respectively. Let c_1 and c_2 be the probabilities that contacts inside and outside the bridge community are susceptible, and let m be the small probability that the pathogen adapts to be human-transmissible. We use this simple scenario for pathogen adaptation because it is a parsimonious way to account for the specifics of a potentially complicated mutation process. Then we propose to estimate the emergence hazard rate along a single pathway using

$$\mathbb{E} = N\lambda_0 c_1 m \mathcal{P}_{12}, \tag{2}$$

where $\mathcal{P}_{12}$ is the probability that an adapted introduction in the bridge community percolates and leads to an epidemic in the larger population. Note that the basic reproduction number $\mathscr{R}_0$ ubiquitous in other areas of theoretical epidemiology does not appear in Equation (2) – while the basic reproduction number and the percolation probability are often positively correlated, they are in general independent quantities, which precludes the use of $\mathscr{R}_0$ in general formulas for emergence hazards.

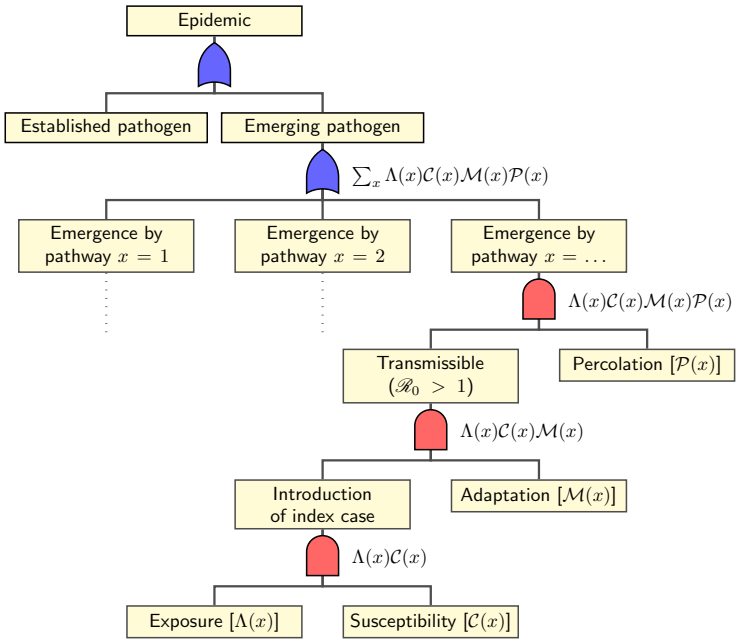

Figure 2: Illustrative fault tree for an epidemic caused by the emergence of a novel infectious pathogen from a zoonotic reservoir. Fault trees like this are used in probabilistic risk assessment [41]. "Or" gates are blue, while "and" gates are red.

Because of acquired immunity and the maintenance of clustering, the terms in Eq. (2) are interdependent, and must be modelled jointly. Using a compartmental model of zoonotic exposure, we can calculate the steady-state susceptibility c_1 in terms of the exposure rate (λ_0), the probability of acquiring immunity (r), and the basic demographic rates (η and μ) (see Supplement S1). The percolation probability ($\mathcal{P}_{12}$) is then calculated using a two-type branching-process generalization of ARKB theory (see Supplement S2). The branching process depends on the expected number of transmission events per infected person inside the bridge community (ζ_1) and outside the bridge community (ζ_2), as well as the fractions f and g of these transmissions that are confined to their respective populations. We find that the emergence hazard

$$\mathbb{E} = \frac{\eta}{\mu} \times \frac{\lambda_0}{1 + r\lambda_0/\mu} \times m\,\mathcal{P}_{12}\left(\frac{r\lambda_0}{\mu}, \zeta_1, \zeta_2, f, g\right), \tag{3}$$

where η is entry rate of susceptible individuals into the bridge community, μ is the turnover rate of the bridge community, and $r\lambda_0/\mu$ is the odds ratio of immune to susceptible members of the bridge community.

Equation (3) is a nonlinear algebraic equation that encodes our theory of how changes in a number of factors alter emergence hazards. First, the greater the rate of immigration of naive individuals (η) into the bridge community, the greater the emergence hazard rate. For a fixed population size ($N = \eta/\mu$ is constant), faster turnover of the bridge community increases the emergence rate. On the other hand, the greater the probability of exposure inducing immunity (r), the lower the emergence rate. Population viscosity controls the evaporation rate of immunity acquired from pre-emergent exposures within the bridge community (μ). The percolation probability $\mathcal{P}_{12}$ is a decreasing function of the odds ratio of immunity in the bridge community ($r\lambda_0/\mu$). An upper bound is obtained when there is no acquired immunity ($r = 0$) or turnover of the bridge community is very fast ($\mu \to \infty$, N constant), in which case the emergence hazard rate increases linearly with exposure rate ($\mathbb{E} = N\lambda_0 m\mathcal{P}_{12}(0)$) as predicted by ARKB theory. For large exposure rates, the risk of emergence saturates and $\mathbb{E} \sim \frac{\eta m}{r}\mathcal{P}_{12}(\infty)$ where $\mathcal{P}_{12}(\infty)$ is calculated using Lambert's W function (see Supplement S2).

More importantly, Eq. (3) also captures two competing effects of the exposure rate λ_0 under strong immunization ($r \approx 1$). As exposures become more frequent, the number of susceptible people decreases, reducing both the percentage of exposures becoming successful introductions and the percolation probability. The balance of these effects depends on the structure of transmission, and specifically the ease with which a transmission chain can escape from the bridge community into the broader population. In our theory, this is controlled by a parameter f (Supplement S2), which balances transmission between purely parochial ($f = 1$, all transmission by bridge individuals is within the bridge community) to purely proselyte ($f = 0$, all transmission by bridge individuals is to people outside the bridge community). So, $\zeta_1 f$ is the expected number of transmissions from a person in the bridge community to other people in the

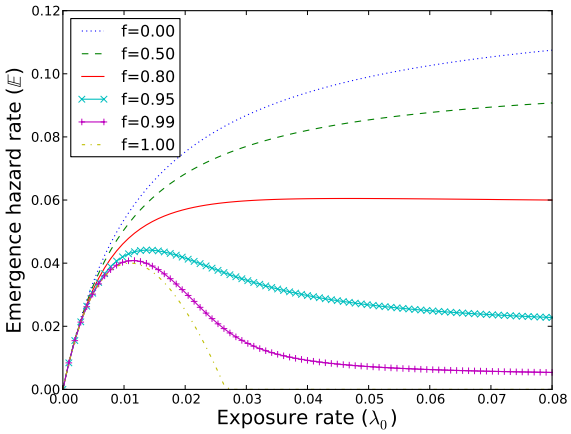

Figure 3: Plot of emergence hazard rate for various relative contact allocations within the bridge population (f) when there is no back-transmission to the bridge community ($g = 1$). If contacts are completely parochial ($f = 1$), then emergence becomes impossible for large λ_0. If contacts are completely proselyte ($f = 0$), then the emergence rate increases monotonely with the exposure rate. The turning-point falls out of the system after moderate relaxation of parochial transmission ($f \approx 0.8$). Parameter values: $\zeta_1 = \zeta_2 = 3$, $\mu = 1/75$, $N = \eta/\mu = 100$, $r = 1$, $m = 1/10$.

bridge community, and $\zeta_1(1-f)$ is the expected number of transmissions from a person in the bridge community to people outside bridge community. Changing the value of f is like tuning the surface-volume ratio effects observed in our lattice simulations. A second value, g, indicates the frequency of parochial transmission outside the bridge community: $\zeta_2 g$ is the expected number of transmissions from a person outside the bridge community to other people outside the bridge community, and $\zeta_2(1-g)$ is the expected number of transmissions from a person outside the bridge community to people in the bridge community. Strong population viscosity corresponds to a strong clustering of exposure and transmission. Parametrically, strong population viscosity implies parochial transmission ($f \approx 1$) in the bridge community. Weak population viscosity, when exposure and transmission are independent and the bridge community is small, has proselyte transmission ($f \approx 0$).

In situations where the bridge community makes up a very small fraction of the total population, transmission outside the bridge community will be parochial ($g = 1$) and the impact of accumulated immunity on the emergence hazard will chiefly depend on the frequency of parochial transmission inside the bridge community (see Figure 3). We find that for sufficiently strong parochial transmission within the bridge community, a turning point appears in the response of the emergence hazard to increases in exposure rate. Similar results can be found in other cases (see Supplement S1 and Figure 4).

Figures 3 and 4 both demonstrate the same unimodal behavior observed in Figure 1 for stochastic simulations – clustering between exposure and transmission mediated by immunity can suppress transmission to such a degree that emergence hazard rates eventually decline as exposure rate is increased past a turning point. In general, the turning point condition depends on the distribution of contacts, and occurs when the reductions in the percolation probability perfectly balance increases in the number of exposures:

$$-\frac{\lambda_0}{\mathcal{P}_{12}}\frac{\mathrm{d}\mathcal{P}_{12}}{\mathrm{d}\lambda_0} = \frac{\mu}{\mu + r\lambda_0}. \tag{4}$$

4 Applications

Does local herd immunity impact emergence risk in real-world situations? The exact nature of local herd immunity will depend on the specifics of the contact distribution structure and mixing patterns, so sensitivity is hard to assess in general. However, we can make some estimates of lower bounds under high population viscosity when bridge community transmission is purely parochial and the post-mutation transmission rate ζ_1 in the general population is close to the critical threshold. We find (see Supplement S2) that the turning point hazard rate λ_0^τ that maximizes the emergence hazard as a function of the exposure rate satisfies the inequality

$$\lambda_0^\tau \geq \frac{\mu}{r}\frac{(\zeta_1 - 1)}{2}. \tag{5}$$

Based on ball-park estimates of $1/\mu = 50$ years residence in the bridge community, $\zeta_1 = 2$ new cases per case on average, and easily acquired immunity ($r = 1/2$), exposure rates comparable to rates of bridge-population turnover (*e.g.* once every 50 years per person, $\lambda_0 > 0.02$) are large enough that local herd immunity begins to suppress emergence. While this is only a lower bound, it is a level of exposure that seems likely to occur in some real-world scenarios. We conclude that there may be situations where emergence has been suppressed by acquired immunity in the past and currently.

5 Discussion

In this paper, we have pointed out that the ARKB theory of infectious disease emergence makes an important approximating assumption on the independence of introduction events. Using math and simulation, we've identified circumstances created by acquired immunity and contact-network clustering that can reduce emergence hazard rates relative to the predictions of ARKB theory. Our study shows that in cases of frequent exposure, decreasing exposure rates may counter-intuitively increase the risk of disease emergence. These results can be interpreted in terms of population viscosity – stronger population viscosity

preserves local herd immunity in bridge communities and impedes emerging epidemics.

Our mathematical and simulation models are based on a variety of hypotheses, including compartmental epidemic dynamics, exponentially distributed event-times, the simplest possible scenario for pathogen evolution, and planar or patch-mixing contact patterns. These assumptions are made primarily for convenience and to facilitate the comparative analysis of theories, and deserver to be revisited in the future. For example, evolutionary change of a pathogen within its natural reservoir was not considered explicitly and may be interpreted as accelerating the rate of immunity lose, but evolutionary changes in transmission and morbidity following an introduction may depend on local immunity.

We have assumed each term in Eq. (1) is stationary over time. But transient dynamics are important in some situations. For example, when a bridge community first comes into contact with a new reservoir in our lattice simulations, there will be a burn-in phase, during which exposure events are independent because there is no standing pool of exposed individuals who have acquired immunity. When adaptation is likely, the burn-in phase could be a window of greater risk. In cases where the exposure rates are large relative to population turnover rates and adaptation is unlikely, this burn-in phase will not contribute much to long-term risk.

Eq. (1) also assumes that each exposure event seeds a distinct epidemic and epidemics can be treated independently. In cases where the duration of infection is so long that multiple nascent epidemics overlap, transmission chains may interfere with each other. Careful consideration will be needed parse the consequences of this interference. But the longer the epidemic generation time for a given $\mathscr{R}_0$, the less life-long immunity can suppress emergence.

To mitigate the risks of disease emergence, several activities can be considered. Surveillance for seroconversion could be used more pro-actively identify particular bridge communities where risks are concentrated. Forecasting models could then incorporate the specifics of the pathogen and the community, allowing for proactive responses to changes in demographic or movement patterns in bridge communities. Bridge populations may be identified as priority targets from preventive vaccination programs, since this is certain to reduce transmission hazards. An immunity barrier requires good immune responses, so improvements in health, through improved nutrition or reductions in disease burden from other parasites, can increase the strength of the immunity barrier and reduce emergence risk. And from an economist's stand point, taxes or other monetary interventions might be imposed on industries or organizations that support bridge communities to offset some of the excess infection risk in ways similar to those proposed for antibiotics [46, 47].

Researchers have enumerated many ways in which globalization and disruption of social structures, from ancient [4] to historical [42, 43] and modern times [44], interacts with disease transmission. The potential evaporation of local herd-immunity barriers is yet another example of the connectivity. Any social, economic, environmental, or demographic disturbance which enlarges or mixes the structure of bridge communities creates greater opportunity for emergence.

In fact, the emergence of HIV, dengue, Lassa fever, and Hanta virus have all been associated with social or ecological disruptions that have altered bridge communities [45]. While in these cases, the emergence events have not been directly linked to the specific mechanism modelled here, the possibility seems worth further consideration and research.

Finally, we feel it is important to acknowledge that the collective risk to the human population differs from the risks and interests of individual members of the population. Members of a bridge community are by definition at greater risk from zoonotic reservoirs, and changes like an increase in the relative degree of parochial transmission that reduce the overall risk of the general population may increase the risk to the bridge community. Immune individuals in a bridge community are providing protection to the general population but also bearing a cost for which they may not be compensated. While bridge communities may offer some unique opportunities for prophylactic interventions, we should consider other possible social, economic, and health correlates that distinguish bridge communities from the general population and how these correlates may further alter the potential for disease emergence.

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Electronic Supplementary Information

S1 Compartmental model of immunity in the bridge community

Table 1: Model parameters and their definitions.

Symbol	Definition
η	Birth/immigration rate into the bridge community
μ	Death/removal rate in bridge community
r	probability of acquiring immunity per exposure
m	probability of adapting for human-to-human transmission
c_1	probability that a bridge individual is susceptible
c_2	probability that an individual outside the bridge is susceptible
λ_0	rate of per-capital exposure in the bridge community
ζ_1	expected number of transmissions by a person in the bridge community.
ζ_2	expected number of transmissions by a person outside the bridge community.
f	parochial contact fraction in the bridge community.
$1-f$	proselyte contact fraction in the bridge community.
g	parochial contact fraction outside the bridge community.
$1-g$	proselyte contact fraction outside the bridge community.

To incorporate the immunity induced by regular exposure within the bridge community into ARKB theory, we make use of a deterministic compartmental model. Table 1 is provided for easy reference to our principle parameter definitions. Inside the bridge community, some fraction of individuals gain immunity from exposure. Suppose new people enter the bridge community at rate η per year, and leave the community through death or emigration at rate μ per person per year. While in the bridge community, individuals are exposed at rate λ_0. If the pathogen fails to adapt, there is a probability r that the exposed individual gains immunity against infection on future exposures, and a probability $1-r$ that they remain susceptible. Since adaptive mutation (m) is assumed to be rare ($m \approx 0$), we approximate the population-scale dynamics for human-to-human transmission assuming $m = 0$. However, an adaptive mutation might arise once a disease is introduced into the bridge community, and thus we assume $0 < m \ll 1$ when calculating the emergence hazard (see S2).

If $S(t)$ is the number of susceptible individuals in the bridge community and $R(t)$ is the number of immune individuals in the bridge community in year t, then

$$\frac{\mathrm{d}S}{\mathrm{d}t} = \eta - \mu S - \lambda_0 S + (1-r)\lambda_0 S \tag{6a}$$

$$\frac{\mathrm{d}R}{\mathrm{d}t} = r\lambda_0 S - \mu R \tag{6b}$$

The equilibrium number of susceptible (S^*) and immune (R^*) individuals under

these dynamics is

$$S^* := \frac{\eta}{\mu + r\lambda_0}, \quad \text{and} \quad R^* := \left(\frac{\eta}{\mu + r\lambda_0}\right)\left(\frac{r\lambda_0}{\mu}\right). \tag{7}$$

The total size of the bridge community $N = S^* + R^* = \eta/\mu$. The fraction of people in the bridge community who are susceptible to infection at any given time is then

$$c_1 = \frac{S^*}{S^* + R^*} = \frac{\mu}{\mu + r\lambda_0} \tag{8}$$

S2 Emergence hazard calculations

When the pathogen successfully adapts to its introduction to a bridge community, the infected member of the bridge community expects to transmit to ζ_1 individuals, although the actual number is a random draw from a Poisson distribution. A fraction f of these transmissions will be parochial and confined to the bridge community, while the remainder $1 - f$ will be proselyte to individuals outside the bridge community. Outside the bridge community, we assume a similar transmission law, with ζ_2 expected transmissions, of which a fraction g are parochial and the remainder $1 - g$ are proselyte. The parameters ζ_1 and ζ_2 can be thought of as local reproduction numbers. Based on the assumption that bridge communities are rural rather than urban, we will assume that $\zeta_1 \leq \zeta_2$.

Under these specifications, we define single-generation probability generating functions to represent the distribution of transmission events inside and outside the bridge community. Let

$$\tilde{y}_1(s_1, s_2) = \sum_{i=0}^{\infty}\sum_{j=0}^{\infty} p_1(i,j) s_1^i s_2^j, \tag{9}$$

where $p_1(i, j)$ is the probability that an infected individual in the bridge community transmits to i other individuals in bridge community and j individuals outside the bridge community. Let

$$\tilde{y}_2(s_1, s_2) = \sum_{i=0}^{\infty}\sum_{j=0}^{\infty} p_2(i,j) s_1^i s_2^j, \tag{10}$$

where $p_2(i, j)$ is the probability that an infected individual outside the bridge community transmits to i other individuals in bridge community and j individuals outside the bridge community. Using standard methods [15], we may show that, under the assumption of Poisson-distributed contacts,

$$\begin{bmatrix} \ln \tilde{y}_1(s_1, s_2) \\ \ln \tilde{y}_2(s_1, s_2) \end{bmatrix} = \begin{bmatrix} \zeta_1 f c_1 & \zeta_1(1-f)c_2 \\ \zeta_2(1-g)c_1 & \zeta_2 g c_2 \end{bmatrix} \begin{bmatrix} s_1 - 1 \\ s_2 - 1 \end{bmatrix} \tag{11}$$

The probabilities that a random contact inside the bridge community is susceptible (c_1) is given by Eq. (8), while outside the bridge community, there is no regular exposure, so we assume $c_2 = 1$ without loss of generality.

Our probability generating functions from Eq. (11) are then

$$\begin{bmatrix} \ln \tilde{y}_1(s_1, s_2) \\ \ln \tilde{y}_2(s_1, s_2) \end{bmatrix} = \begin{bmatrix} \dfrac{\zeta_1 f \mu}{(\mu + r\lambda_0)} & \zeta_1(1-f) \\ \dfrac{\zeta_2(1-g)\mu}{(\mu + r\lambda_0)} & \zeta_2 g \end{bmatrix} \begin{bmatrix} s_1 - 1 \\ s_2 - 1 \end{bmatrix} \tag{12}$$

Iteration of the generating function represents successive generations of transmission, so the basic reproduction number can be calculated as the dominate eigenvalue of the expectation matrix, or

$$\mathscr{R}_0 = \rho \left(\begin{bmatrix} \dfrac{\zeta_1 f \mu}{(\mu + r\lambda_0)} & \zeta_1(1-f) \\ \dfrac{\zeta_2(1-g)\mu}{(\mu + r\lambda_0)} & \zeta_2 g \end{bmatrix} \right) \tag{13}$$

When we define $\mathcal{P}_{ij}$ as the probability that a single infected person in population type i starts an epidemic with a large number of cases in population j, mathematicians have shown [48, 22] that

$$\begin{bmatrix} 1 - \mathcal{P}_{11} \\ 1 - \mathcal{P}_{12} \end{bmatrix} = \begin{bmatrix} \tilde{y}_1(1 - \mathcal{P}_{11}, 1 - \mathcal{P}_{12}) \\ \tilde{y}_2(1 - \mathcal{P}_{11}, 1 - \mathcal{P}_{12}) \end{bmatrix}. \tag{14}$$

Using these calculations, we express an emergence hazard rate ($\mathbb{E}$) as the probability per unit time that an epidemic is started by the given zoonotic transmission,

$$\mathbb{E} = \left(\frac{\eta}{\mu} \right) \lambda_0 m \left(\frac{\mu}{\mu + r\lambda_0} \right) \mathcal{P}_{12}(r\lambda_0/\mu, \zeta_1, \zeta_2, f, g) \tag{15}$$

Note this assumes emergence dynamics are very fast in E_{12}, compared to the exposure rate λ_0. We can now solve System (14) to determine $\mathcal{P}_{12}$, the probability that an exposure in the bridge population starts a large epidemic emerges in the general population. For the general model specified by System (12), we note that there are qualitative changes in the emergence hazard when the bridge community transitions from a sink to a source population ($\zeta_1 f \mu/(\mu + r\lambda_0) > 1$) and when the general population transitions from a sink to a source population ($\zeta_2 g > 1$).

In the limit of independent exposures and strong mixing, almost all transmissions by the bridge population will be proselyte ($f = 0$) while almost all other transmissions will be parochial ($g = 1$), so

$$\begin{bmatrix} \ln \tilde{y}_1(s) \\ \ln \tilde{y}_2(s) \end{bmatrix} = \begin{bmatrix} 0 & \zeta_1 \\ 0 & \zeta_2 \end{bmatrix} \begin{bmatrix} s_1 - 1 \\ s_2 - 1 \end{bmatrix} \tag{16}$$

Then the log of the percolation probability,

$$\mathcal{P}_{12} = 1 - e^{-\zeta_1 \operatorname{Lm}(\zeta_2)} \tag{17}$$

where $\mathrm{Lm}(z) = 1 + \mathrm{W}(-ze^{-z})/z)$ and W() represents Lambert's W function. The emergence hazard rate is a strictly increasing function of the exposure rate λ_0, with an upper bound $\mathbb{E} < m(\eta/r)\mathcal{P}_{12}(\zeta_1, \zeta_2)$.

On the other hand, if contact patterns are exchangeable, so that $\zeta_1 = \zeta_2$ and $g = 1 - f$,

$$\mathcal{P}_{12} = \mathrm{Lm}\left(\frac{\zeta_1 f\mu}{\mu + r\lambda_0} + \zeta_1(1-f)\right) \tag{18}$$

Using the series-based approximation

$$\mathrm{Lm}(z+1) \approx H(z)\left[2z - 8/3z^2 + 28/9z^3 + O(z^4)\right] \tag{19}$$

where $H(z)$ is the Heaviside function, we can show that when $f = 1$, $g = 0$, $\zeta_1 \approx 1$ and $\lambda_0 \approx 0$, the turning point

$$\lambda_0^\tau \approx \frac{d}{r}\left[\frac{(\zeta_1 - 1)}{2} - \frac{1}{9}(\zeta_1 - 1)^2\right] \tag{20}$$

The effects of heterogeneity in contact rates can be inferred from the work on the use of negative-binomial distributions to capture super-spreading in place of our Poisson distributions [49].

When population viscosity preserves local herd immunity within the bridge community but allows rapid mixing of contacts across the population, then contact frequencies inside and outside the bridge community will be exchangable ($f = 1 - g$). The basic results under an "exchangable" contact pattern are similar (see Figure 4). When secondary transmissions are proselyte, faster exposure rates accelerate the emergence rate. When secondary transmissions are parochial, faster exposure rates induce greater herd immunity, and can suppress emergence. But under the exchangable contacts hypothesis, the bridge community composes a fixed fraction of transmissions, and high prevalences of immunity in the bridge community can bestow herd immunity on the general population.

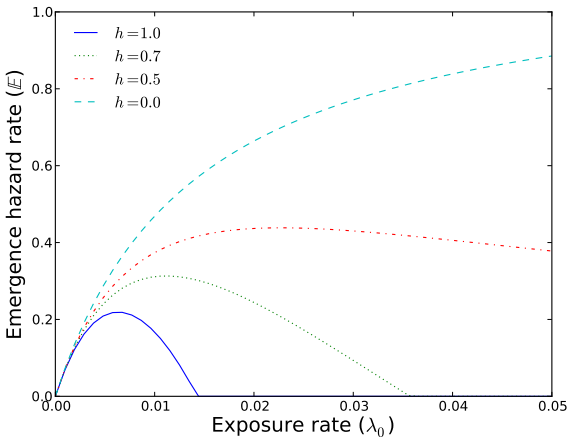

Figure 4: Emergence hazards under exchangeable mixing where individuals inside and outside the bridge community have the same contact patterns ($h = g = 1 - f$) also exhibit a turning point as the exposure rate λ_0 increases. This turning point moves to smaller exposure rates as transmission shifts from favoring contacts outside the bridge community ($h = 0$) to favoring contacts inside the bridge community ($h = 1$). Parameter values: $\mu = 1/70$, $\zeta_1 = \zeta_2 = 2$, $r = 1$, $m = 1/10$, $N = \eta/\mu = 1000$.

S3 Extra simulation results

In this section, we supply some additional figures supporting our simulation results.

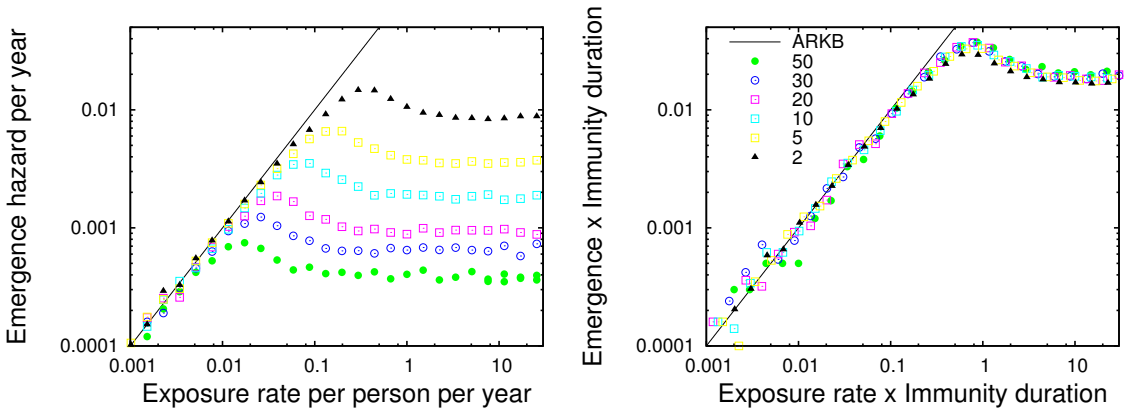

Figure 5: Simulation results showing how emergence rate depends on the duration of acquired immunity. Immunity may be lost from the bridge community through waning or population turnover. As the duration of immunity increases from 2 to 50 years, the emergence hazard decreases uniformly for all exposure rates (left). If the emergence rate and exposure rate are both scaled linearly by the duration of immunity (right), we see that all the curves overlap.

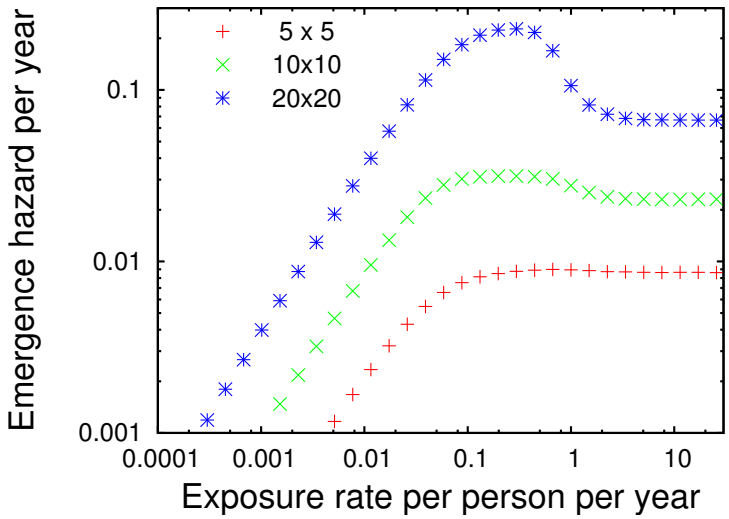

Figure 6: Plots of annual emergence hazard as a function of exposure rate for successively larger bridge communities in our lattice epidemic simulations, with all other parameters fixed. Enlarging the bridge community increases the annual emergence hazard because the total number people being exposed each year is increased. At low exposure rates, this increase is linear, but at large exposure rates, local herd immunity has a larger impact in larger bridge communities. Simulations were performed on 60x60 lattices with von Neumann neighborhoods with $\mathscr{R}_0 \approx 4$, a generation time of 4 days, adaptation probability 0.01 and immunity lasting 20 years.

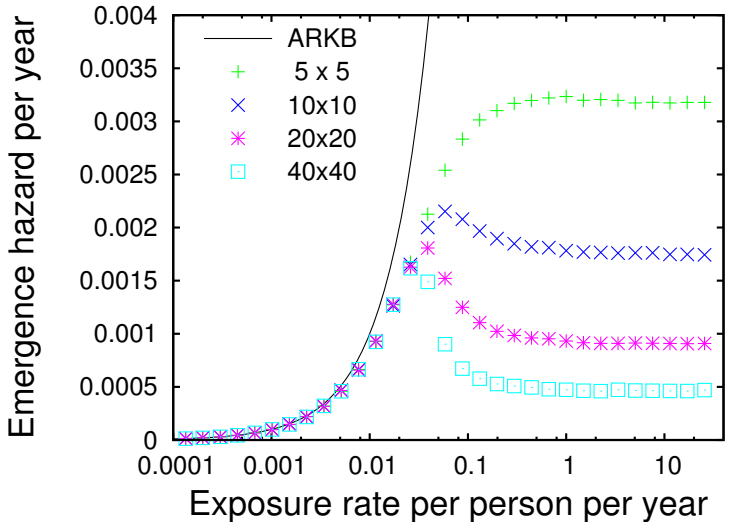

Figure 7: Plots of annual emergence hazard as a function of exposure rate for successively larger bridge communities in our lattice epidemic simulations. For this figure, the adaptation probability is decreased in proportion to the increase in bridge community size ($Nr = 0.1$). With the community-size effect scaled out to facilitate comparison, we find that the annual emergence hazard scales like ARKB theory predicts at low exposure rates for all the simulations. At high exposure rates, the effects of local herd immunity become more pronounced as the bridge community gets larger. Simulations were performed on 60x60 lattices with von Neumann neighborhoods with $\mathscr{R}_0 \approx 4$, a generation time of 4 days, adaptation probability 0.01 and immunity lasting 20 years.