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The impact of resource quality on the evolution of virulence in spatially heterogeneous environments

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ABSTRACT

Understanding the drivers of parasite evolution and in particular disease virulence remains a major focus of evolutionary theory. Here, we examine the role of resource quality and in particular spatial environmental heterogeneity in the distribution of these resources on the evolution of virulence. There may be direct effects of resources on host susceptibility and pathogenicity alongside effects on reproduction that indirectly impact host-parasite population dynamics. Therefore, we assume that high resource quality may lead to both increased host reproduction and/or increased disease resistance. In completely mixed populations there is no effect of resource quality on the outcome of disease evolution. However, when there are local interactions higher resource quality generally selects for higher virulence/transmission for both linear and saturating transmission-virulence trade-off assumptions. The exception is that in castrators (i.e., infected hosts have no reproduction), higher virulence is selected for both low and high resource qualities at mixed local and global infection. Heterogeneity in the distribution of environment resources only has an effect on the outcome in castrators where random distributions generally select for higher virulence. Overall, our results further underline the importance of considering spatial structure in order to understand evolutionary processes.

1. INTRODUCTION

The evolution of parasites is of clear importance to human, agricultural and wildlife populations, and as a consequence the evolution of virulence theory is particularly well developed (Anderson and May, 1992; Best et al., 2011; Boots and Sasaki, 1999; Bremermann and Pickering, 1983; Dieckmann et al., 2002; Getz and Pickering, 1983; Laine, 2007; Rand et al., 1995). A key theoretical result is that host's spatial structure profoundly influences the evolution of parasites, with local infection selecting for lower virulence and rates of transmission (Boots and Sasaki, 2000; Boots and Mealor, 2007; Haraguchi and Sasaki, 2000; Kamo et al., 2007; Lion and Boots, 2010; Lion and Gandon, 2015; Rand et al., 1995). In these models, spatial structure arises naturally due to the local transmission and reproduction of hosts within a spatially homogenous environment. However, the environment in reality also typically varies in space and time, and this heterogeneity in environmental quality may directly impact host spatial structure and the outcome of the epidemic (Becks and Agrawal, 2010; de Roode et al., 2008; Mostowy and Engelstadter, 2011; Penczykowski et al., 2014; Restif and Kaltz, 2006; Wolinska and King, 2009). In addition, environmental quality may directly play an important role in host-parasite interactions, impacting host defence, parasite transmission and virulence (Cornet et al., 2014; Tack et al., 2014). One of the major theoretical challenges that remains therefore, is to explore how parasites adapt to hosts in environment with spatially heterogeneous resources.

Empirical and theoretical studies have shown that resource quality has the potential to impact host-parasite interactions in a number of ways. Resource quality can impact individual host immune function such that high resources lead to high resistance to infection (Boots, 2011; Forde et al., 2008; Hall et al., 2009; Lopez-Pascua and Buckling, 2008; Lopez-Pascua et al., 2014; Penczykowski et al., 2014). Generally, environmental stress should be associated with higher levels of virulence because decreased host immunity function in poor resources enhances pathogeniticity (Ferguson and Read, 2002; Hall et al., 2009; Jokela et al., 1999; Restif and Kaltz, 2006). However, it should also be noted that there might be indirect impacts of variation in host resource quality, where higher resources lead to higher host reproduction and abundance and then will further increase encounter rates between hosts and parasites (Anderson and May, 1992; Hall et al., 2009; Lopez-Pascua et al., 2014). Therefore, increased resource availability may transform benign microbial communities into virulent ones (Mckenzie

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and Townsend, 2007; Wedekind et al., 2010). As such, parasite fitness is likely to be directly and indirectly impacted by resource quality, and we therefore need a theoretical framework to tease apart the various roles of resources to the evolution of parasites.

Classic evolutionary epidemiology theory examines the evolutionary dynamics of parasites assuming well-mixed populations (Anderson and May, 1979, 1991; Boots and Haraguchi, 1999; Bowers et al., 1994). Theoretical models assuming completely mixed host populations ("mean-field" approximation) have predicted that parasites will evolve to infinite transmission and minimum virulence with no relationship between transmission and virulence (Anderson and May, 1992; Bremermann and Pickering, 1983; Dieckmann et al., 2002; Lenski and May, 1994; Lion and van Baalen, 2008). Recent theoretical works have shown the importance of spatially structured host populations on the evolution of parasites and indicated that an evolutionary stable transmission rate can exist despite no transmission-virulence trade-off (Haraguchi and Sasaki, 2000; Keeling, 1999; Lion and Boots, 2010; Messinger and Ostling, 2013; O'Keefe and Antonovics, 2002). Generally, parasites will evolve lower transmission rates and therefore potentially lower virulence when infections occur locally (Boots and Sasaki, 1999; Haraguchi and Sasaki, 2000; O'Keefe, 2005; Rand et al., 1995). Spatially heterogeneous environments are also fundamental for evolutionary dynamics and the maintenance of diversity in host-parasite interactions (Byers, 2005; Jousimo et al., 2014; Tack et al., 2014; Thrall and Burdon, 1997, 2002; Thrall et al., 2012). These previous works mainly assume homogenous environments in which the spatial heterogeneity emerges naturally from host-parasite interactions, but there is a lack of theoretical consideration for how parasite's evolution is expected to occur when the environment itself is heterogeneous (e.g., host resource quality varies spatially).

Here, our aim is to understand the evolutionary behavior of parasites in hosts on spatially structured heterogeneous resource environments. For generality, we consider a simple host-pathogen/parasite model, with resource-mediated host reproduction and parasite transmission. We start by examining the evolutionary dynamics of parasites in non-spatially structured host population ("mean-field" approximation), in comparison with the spatial models. Second, we use pair approximation (i.e., constructing ordinary differential equations for global and local densities of single and neighbouring pairs of habitat patches that change over time) to explore how the virulence evolution changes with resource quality in spatially homogeneous environments. Pair approximation has been successfully applied in a wide range of ecological, epidemiological, and evolutionary systems (Hiebeler, 2000; Hui and MeGeoch, 2007; Iwasa, 2000; Matsuda et al., 1992; Su et al., 2009b; Webb et al., 2013). We finally build a spatially explicit stochastic model to examine how spatial heterogeneity of habitat resources drives the outcome of virulence evolution.

2. Methods

We explore a classical host-parasite interaction in a lattice-structured environment where each patch can be either empty (denoted by O) or occupied by a susceptible (S) or infected (I) individual. Individuals consume the resources of patches where each patch k has a fixed resource quality R_k ($k = 1, \ldots, N \times N$). In a homogenous resource environment, all patches have the same value of R, with variations in R resulting in a heterogeneous environment (Okuyama, 2008). For homogenous resource environments, mean-field and pair approximations can work well for describing host-parasite evolutionary dynamics accurately. The heterogeneous model makes the mathematical analysis complex and therefore we rely on spatially stochastic simulations to analyze these cases.

Susceptible host individuals reproduce at rate r (which depends on their resource consumption) into neighbouring empty patches (Boots and Sasaki, 1999; Kamo et al., 2007; Webb et al., 2013). As in many species (e.g., *Daphnia*), reproduction rate increases with resource quality but then slows as resource quality becomes high (Hall et al., 2007). Then, we assume that the rate of host reproduction depends on the resource quality according to an exponential function: $r = r_{\max}(1 - \exp(-\eta_r R))$, where parameter $r_{\max}$ is the maximum reproduction rate with available abundant resource, η_r is a constant that controls the efficiency of resource used by the host population. Disease-associated reductions in fecundity can occur with reproduction from infected individuals taking place at a fractional rate, denoted by rf ($f \in [0, 1]$), where castrator ($f = 0$) indicates parasites prevent the infected hosts reproduction. Changes in resource quality can modify the condition of hosts, which may in term affect their susceptibility for parasites (Anderson and May, 1992; Daniels et al., 2013; Hall et al., 2009; Penczykowski et al., 2014). High-quality resources may reduce susceptibility through direct effects on immunity or general improved condition (Babin et al., 2010; Boots, 2010; Penczykowski et al., 2014; Venesky et al., 2012). Then, we further assume another similar form as resource-mediated reproduction rate, between transmission rate and resource quality,$\beta = \beta_{\max} \exp(-\eta_\beta R)$, where $\beta_{\max}$ is the maximum infection rate with available abundant resource, η_β is a constant reflecting the efficiency of the feedback process. The natural death rate of host individuals is d, and infected hosts have an increased mortality due to parasitic infection (virulence α).

Parasitic infection happens through the contact of infected and susceptible host individuals locally at neighbouring patches ($z = 4$) and globally at patches chosen at random (G denotes the proportion of global infection where $0 \le G \le 1$, Fig. 1). We assume that virulence is a cost to parasite transmission since higher within host growth rate leads to both higher transmission and more damage leading to a higher host death rate (Best et al., 2011; Boots and Sasaki, 1999; Haraguchi and Sasaki, 2000; Messinger and Ostling, 2013). Thus, in the case that infected host can reproduce ($0 < f \le 1$), increasing transmission rate is probably relatively more costly than in the case with castrator ($f = 0$). Here, the functional forms of the transmission-virulence trade-off are either taken as linear for $\beta_{\max} = 3\alpha$ or saturating for $\beta_{\max} = 5\log(\alpha + 1)$ (Kamo et al., 2007; Webb et al., 2013). There are a number of parasite's strains ($t = 1, \ldots, n$) that differ in their intrinsic transmission rate ($\beta_{\max}$) (the rate of causing infection) and have correlated changes in the virulence. Evolution occurs through small mutations (in any single time-step mutation to the neighbourhood strain with the next high or next low transmission rate can occur, Appendix S1, S2).

2.1. Mean-field approximation

Before analyzing the viscous system, we first consider the equiva-

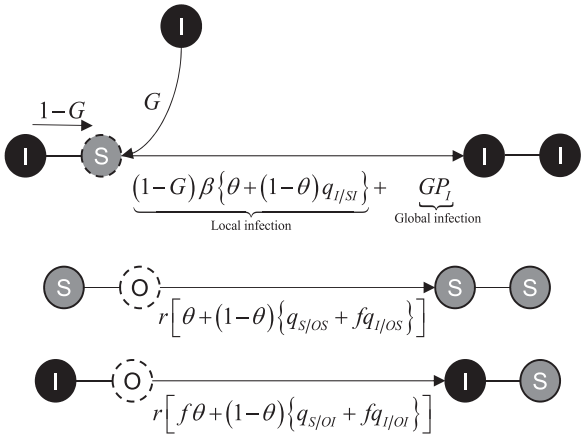

Fig. 1. Diagram for host reproduction and parasite infection process with possible pair state and their transition probability. A susceptible individual can be infected from a nearest-neighbor ($z = 4$) at probability $1 - G$ and globally from a distant patch at G. β, r, and f represents the transmission rate, reproduction rate and infected fecundity, respectively.