Toward a unified dilution effect theory: How competence, competition, and the transmission mechanism influence disease-diversity relationships

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ABSTRACT:

Biodiversity in communities is changing globally, including the gain and loss of host species in host-pathogen communities. The dilution effect argues for a mechanistic link between increased host diversity and decreased disease in a focal host. However, we currently have a limited understanding of how the pathogen transmission mechanism and between-host interactions influence whether increased host diversity leads to increased (amplification) or decreased (dilution) infection prevalence. We use a two-host-one-pathogen model to unify dilution effect theory for pathogens with environmental transmission and density-dependent and frequency-dependent direct transmission. We use the unified framework to identify how the pathogen transmission mechanism and characteristics of an introduced host (disease competence and competitive ability) influence infection prevalence in a focal host and under what conditions amplification or dilution is promoted. Our approach identifies general rules governing how specific biological mechanisms shape host biodiversity-disease patterns.

1 Introduction

Biodiversity in communities is changing across the globe, with species introductions in some and extirpation in others. Altered biodiversity can influence patterns of infectious diseases because most pathogens can infect multiple host species and most communities are made up of multiple host species (Cleaveland et al., 2001; Pedersen et al., 2005; Rigaud et al., 2010). These effects of biodiversity on disease levels can occur both via the ways each host species interacts with the pathogen (e.g., within-species transmission) and as a result of interspecific interactions between host species (e.g., resource competition and between-species transmission).

The dilution effect argues that increased host biodiversity decreases disease prevalence (i.e., the proportion of infected hosts in a population) (Keesing et al., 2006). However, when and whether increased host biodiversity reduces disease prevalence (dilution) or increases disease prevalence (amplification) in a focal host population has been debated in the literature (e.g., Lafferty and Wood 2013; Ostfeld and Keesing 2013; Wood and Lafferty 2013 and reviewed in Rohr et al. 2019). Empirical evidence is mixed: a recent meta-analysis found general empirical support for dilution (Civitello et al., 2015), but amplification also occurs (Wood et al., 2014; Venesky et al., 2014; Searle et al., 2016). This implies that increased host biodiversity likely has context-dependent effects (Salkeld et al., 2013), motivating calls for theory that identifies specific biological mechanisms promoting amplification versus dilution (Buhnerkempe et al., 2015; Halsey, 2019; Rohr et al., 2019).

Current theory (Keesing et al., 2006, 2010) predicts that amplification versus dilution generally depends on how host biodiversity affects host-pathogen encounter rates, susceptible host densities, and transmission, mortality and recovery rates. Specific mechanisms affecting these factors include host competence (i.e., the host's ability to transmit infection), intraspecific and interspecific host competition, and the pathogen transmission mechanism. For the latter, some studies have focused on pathogens with frequency-dependent direct transmission (transmission via host-host contact that depends on the frequency of infected hosts),

density-dependent direct transmission (transmission via host-host contact that depends on the density of infected hosts), or environmental transmission (transmission via contact with infectious propagules, e.g., spores, excreted by infected hosts). Many of those studies suggest that frequency-dependent direct transmission promotes dilution whereas density-dependent direct transmission and environmental transmission promote amplification (Begon et al., 1992; Begon and Bowers, 1994; Dobson, 2004; Rudolf and Antonovics, 2005; Hatcher et al., 2006; Mihaljevic et al., 2014; Faust et al., 2017; Roberts and Heesterbeek, 2018). However, theoretical studies also show that accounting for interspecific host competition (Ogden and Tsao, 2009; Strauss et al., 2015; O'Regan et al., 2015; Searle et al., 2016) and host competence (Rudolf and Antonovics, 2005; O'Regan et al., 2015; Roberts and Heesterbeek, 2018) can qualitatively alter predictions. For example, introduction of a high competence host can cause dilution (i.e., *lower* prevalence) in a focal host, even when the pathogen utilizes density-dependent direct transmission (O'Regan et al., 2015; Roberts and Heesterbeek, 2018) or environmental transmission (Searle et al., 2016).

Current theory is limited in two key ways. First, while it shows that transmission mode and host species characteristics (e.g., competence and competitive ability) have context dependent effects on amplification and dilution, it is currently unclear what general rules govern these context dependencies and which biological mechanisms promote amplification versus dilution. Second, the theory for pathogens with different transmission modes has developed largely independently. This makes it difficult to compare predictions across models and to isolate the effects of pathogen transmission mode on disease prevalence. Overall, there is a clear need for new theory that can unify the existing bodies of theory and provide general predictions about how specific mechanisms shape host biodiversity-disease relationships.

To begin to address these limitations, we use a two-host-one-pathogen model to explore how the pathogen transmission mode and characteristics of the introduced host (specifically, disease competence and interspecific and intraspecific competitive abilities) influence infection prevalence in a focal host. We do this by developing and applying a framework that

unifies the theories for environmental transmission, density-dependent direct transmission and frequency-dependent direct transmission. We then interpret our conditions in terms of mechanisms that promote amplification and dilution. Our approach and results point the way forward for developing a unified theory for amplification and dilution of disease.

2 Models and Methods

2.1 Two-host-one-pathogen model with environmental transmission

We consider a system with two host species and an environmentally transmitted pathogen, where new infections arise when susceptible hosts come in contact with infectious propagules that were released by infected individuals. To simplify the presentation and analysis, we assume there is no recovery from infection (i.e., infection is always lethal). However, all of our results hold for models with recovery from infection; see appendix S2. We refer to host species 1 and 2 as the 'focal' and 'introduced' hosts, respectively.

The two-host-one-pathogen model describes the changes in the densities of susceptible (S_i) and infected (I_i) hosts in each population ($i = 1, 2$) and the density of infectious propagules (P) in the environment,

$$\begin{aligned}
\frac{dS_i}{dt} &= \underbrace{\left[f_i(S_1, S_2, I_1, I_2) \right]}_{\text{growth \& competition}} - \underbrace{\beta_i S_i P}_{\text{infection}} \\
\frac{dI_i}{dt} &= \underbrace{\beta_i S_i P}_{\text{infection}} \underbrace{-m_i I_i}_{\text{mortality}} \\
\frac{dP}{dt} &= \underbrace{\chi_1 I_1 + \chi_2 I_2}_{\text{propagule excretion}} - \underbrace{(u_{11} S_1 - u_{12} I_1 - u_{21} S_2 - u_{22} I_2) P}_{\text{propagule uptake}} \underbrace{-\mu P}_{\text{degradation}} .
\end{aligned} \tag{1}$$

In the model, susceptible hosts increase due to reproduction at rate $f_i(S_1, S_2, I_1, I_2)$ and

become infected when they come in contact with infectious propagules ($\beta_i S_i P$); infected hosts excrete infectious propagules into the environment ($\chi_i I_i$) and die ($m_i I_i$); and infectious propagules are lost due to uptake by all hosts ($u_{i1} S_i P$ and $u_{i2} I_i P$ terms) and degradation (μP). The total population size for each host is $N_i = S_i + I_i$. We assume model (1) has a stable endemic equilibrium, $p^* = (S_1^*, S_2^*, I_1^*, I_2^*, P^*)$, where both hosts coexist with the pathogen (hereafter, the 'multi-species equilibrium'). We also assume model (1) has a stable endemic equilibrium, $\hat{p} = (\hat{S}_1, 0, \hat{I}_1, 0, \hat{P})$, where only the focal host and pathogen coexist (hereafter, the 'single-species equilibrium').

The reproduction rates (f_i) account for reproductive output from both susceptible and infected individuals and the possibility of interspecific host competition. We use the general functions in order to develop theory that applies across systems. When presenting specific numerical examples we use the Lotka-Volterra competition functions,

$$f_i = r_i(S_i + c_i I_i)[1 - \alpha_{i1}(S_1 + e_{i1} I_1) - \alpha_{i2}(S_2 + e_{i2} I_2)] \tag{2}$$

where r_i and $c_i r_i$ are the maximum exponential growth rates of susceptible and infected individuals of species i, α_{ij} is the per capita competitive effect of host j on host i, and e_{ij} determines whether infected individuals of host j have weaker ($e_{ij} < 1$), equal ($e_{ij} = 1$), or stronger ($e_{ij} > 1$) competitive effects on host i than susceptible individuals of host j. In general, infected hosts are unlikely to be stronger competitors, however it could occur for pathogens that cause gigantism, provided infection does not alter feeding rates.

Our metric of disease is the infection prevalence of the focal host (I_1^*/N_1^*) at the multi-species equilibrium. Our approach is to compute how the parameters defining the competence and competitive ability of the introduced host influence infection prevalence of the focal host at the multi-species equilibrium. This is done using the Jacobian-based theory in Yodzis (1988); see Box 1 for additional details.

Box 1: Computing equilibrium density dependencies on model parameters

Infection prevalence of the focal host at the multi-species equilibrium (p^*) depends on the characteristics of the introduced host that define competence (χ_2, β_2, m_2, and u_{21}), sink/source (χ_2, u_{22}), intraspecific competitive ability (e.g., α_{22} in a Lotka-Volterra model), and interspecific competitive ability (e.g., α_{12} in a Lotka-Volterra model). We compute this dependence based on how a small change in one parameter affects the infection prevalence of the focal host at the multi-species equilibrium. Mathematically, this is done using partial derivatives. For example, the effect of the introduced host having a higher infection coefficient (β_2) is computed using the derivative $\partial(I_1^*/N_1^*)/\partial\beta_2$; positive and negative values mean larger infection coefficients lead to higher or lower prevalence in the focal host, respectively. Due to their large size, all derivative equations are relegated to the appendices.

The derivatives are computed using the Jacobian-based theory developed in Bender et al. (1984), Yodzis (1988), Novak et al. (2011), and Cortez and Abrams (2016); see appendix S1.2 for additional details. The Jacobian is a matrix of derivatives that accounts for all of the intraspecific and interspecific interactions of the system. The Jacobian for model (1) is

$$
\begin{aligned}
J\Big|_{p^*} &= \begin{pmatrix} J_{11} & J_{12} & J_{13} & J_{14} & J_{15} \\ J_{21} & J_{22} & J_{23} & J_{24} & J_{25} \\ J_{31} & 0 & J_{33} & 0 & J_{35} \\ 0 & J_{41} & 0 & J_{44} & J_{45} \\ J_{51} & J_{52} & J_{53} & J_{54} & J_{55} \end{pmatrix} \\
&= \begin{pmatrix} \frac{\partial f_1}{\partial S_1} - \beta_1 P & \frac{\partial f_1}{\partial S_2} & \frac{\partial f_1}{\partial I_1} & \frac{\partial f_1}{\partial I_2} & -\beta_1 S_1 \\ \frac{\partial f_2}{\partial S_1} & \frac{\partial f_2}{\partial S_2} - \beta_2 P & \frac{\partial f_2}{\partial I_1} & \frac{\partial f_2}{\partial I_2} & -\beta_2 S_2 \\ \beta_1 P & 0 & -m_1 & 0 & \beta_1 S_1 \\ 0 & \beta_2 P & 0 & -m_2 & \beta_2 S_2 \\ -u_{11} P & -u_{21} P & \chi_1 - u_{12} P & \chi_2 - u_{22} P & -U - \mu \end{pmatrix}\Bigg|_{p^*} .
\end{aligned}
\tag{3}
$$

where $U = u_{11}S_1 + u_{12}I_1 + u_{21}S_1 + u_{22}S_2$ is the total per spore uptake rate at equilibrium. The entries in the first and second rows represent combinations of effects of interspecific competition ($J_{12}, J_{14}, J_{21}, J_{23}$), infection ($J_{11}, J_{15}, J_{22}, J_{25}$), and intraspecific competition and

reproduction ($J_{11}, J_{13}, J_{22}, J_{24}$); the entries in the third and fourth rows represent the effects of infection (J_{31}, J_{35}, J_{42}, J_{45}) and mortality (J_{33}, J_{44}); and the entries in the fifth row represent the negative effects due to uptake by susceptible hosts (J_{51}, J_{52}) and degradation (J_{55}) and the combined effects of propagule release and uptake by infected hosts (J_{53}, J_{54}). With the Jacobian, we can predict how introduced hosts with higher or lower competence or competitive ability influence infection prevalence in the focal host. Roberts and Heesterbeek (2018) used a similar approach to explore how changes in introduced host density affected disease levels in a focal host. Our approach is distinct because we focus on how the characteristics (not the density) of the introduced host affects infected prevalence in the focal host.

There are two key advantages to our approach. First, it allows us to identify which specific characteristics of the introduced host promote higher versus lower multi-species prevalence in the focal host and if there are interactions between the characteristics (e.g., the effect of increased competence in the introduced host may depend on its interspecific competitive ability). Second, determining the factors that promote higher or lower multi-species prevalence allows us to make predictions about the factors that promote amplification (i.e., higher prevalence in the focal host at the multi-species equilibrium than the single-species equilibrium; $I_1^*/N_1^* > \hat{I}_1/\hat{N}_1$) versus dilution (i.e., lower prevalence in the focal host at the multi-species equilibrium than the single-species equilibrium; $I_1^*/N_1^* < \hat{I}_1/\hat{N}_1$), respectively.

The major limitation of this approach is that it is based on a linear approximation (the derivative). Consequently, it may not accurately capture how infection prevalence depends on a particular parameter if the dependence is sufficiently nonlinear. Nonetheless, because our approach only depends on the signs of the Jacobian entries, our general predictions will hold so long as the nonlinear dependence does not cause the Jacobian entries to change sign.

2.2 High and low competence hosts, sinks, and sources

Throughout, we describe the host species as being higher or lower competence and sinks or sources of infectious propagules. Host competence is defined by $\beta_i\chi_i/m_iu_{i1}$, which is the number of new infections produced by a single infected host when placed in a completely susceptible population of infinite size (i.e, R_0 when host density is arbitrarily large). Higher competence hosts produce more new infections per infected individual because they have a combination of larger infection coefficients (β_i), larger propagule release rates (χ_i), smaller mortality rates (m_i), and smaller uptake rates by susceptible hosts (u_{i1}).

Sink and source hosts are defined by the excretion (χ_i) and uptake (u_{i2}) rates of infected hosts. Source hosts excrete infectious propagules at rates faster than they take them up whereas sink hosts excrete infectious propagules at rates slower than they take them up. A host species is a larger source or a smaller sink if it has a larger propagule release rate (χ_i) and smaller uptake rates (u_{i2}).

Competence and sink/source are not identical because competence depends on the uptake rates of susceptible hosts whereas sink/source depends on the uptake rates of infected hosts. Thus, a high competence host can be a large sink if u_{i1} is small and u_{i2} is large.

3 Results

3.1 Unifying environmental and direct transmission models

We first show that by studying the environmental transmission model (1), we can identify how the characteristics of the introduced host influence patterns of amplification and dilution for both environmentally and directly transmitted pathogens. We do this by unifying environmental transmission (ET), density-dependent direct transmission (DDDT), and frequency-dependent direct transmission (FDDT) models with two host species under a single framework. This greatly extends prior work on single-host-single-pathogen models (Li

et al., 2009; Eisenberg et al., 2013; Cortez and Weitz, 2013).

Our approach involves identifying specific conditions under which our ET model reduces to a DDDT or FDDT model. In general, the ET model reduces to a model with direct transmission when the host excretion rates (χ_i) are large and the infectious propagule uptake (u_{ij}) or degradation (μ) rates are large. If the loss of infectious propagules due to uptake by hosts is negligible compared to loss due to degradation ($u_{ij} = 0$), then the ET model reduces to a DDDT model. Alternatively, if there is no degradation of infectious propagules ($\mu = 0$), then the ET model reduces to a FDDT model.

The intuition is the following. Infectious propagules persist in the environment for short periods of time when degradation or uptake rates are large. Consequently, susceptible hosts can only encounter infectious propagules immediately after the infectious propagules are excreted by an infectious host. This requires the susceptible hosts to be in close proximity to an infected individual, in effect implying infection only occurs when there are direct contacts between hosts. When loss due to uptake is negligible ($u_{ij} \approx 0$) compared to degradation, the rate of contact between susceptible hosts and infectious propagules is proportional to the density of infected hosts. In this case, the dynamics of the ET pathogen are essentially identical to those of a DDDT pathogen. In contrast, when there is no degradation ($\mu = 0$), the rate of contact between susceptible hosts and infectious propagules is proportional to the weighted frequency of susceptible hosts in the community, where the weights are the uptake rates of each host class. In this case, the dynamics of the ET pathogen are essentially identical to those of a FDDT pathogen.

To mathematically justify the above, we assume the changes in infectious propagule density are much faster than changes in the host densities, i.e., the host excretion rates (χ_i) and infectious propagule degradation (μ) or uptake (u_{ij}) rates are large. Under this condition, the infectious propagule densities reach a quasi-steady state defined by $dP/dt = 0$. Solving

for the quasi-steady density and substituting into the infected host equations yields

$$\frac{dI_i}{dt} = \underbrace{(\beta_i\chi_1 I_1 + \beta_i\chi_2 I_2)\frac{S_i}{U+\mu}}_{\text{infection}} \underbrace{-m_i I_i}_{\text{mortality}}. \tag{4}$$

where $U = u_{11}S_1 - u_{12}I_1 - u_{21}S_2 - u_{22}I_2$ is the total uptake of infectious propagules by all host classes. When loss due to uptake is negligible relative to degradation ($U + \mu \approx \mu$), the infection rates simplify to the infection rates of a DDDT model, $\beta_i\chi_j I_j/\mu = \bar{\beta}_{ij} I_j S_i$. When there is no degradation ($\mu = 0$), the infection rates simplify to the infection rates of a FDDT model with weighted frequencies, $\beta_i\chi_j I_j S_i/U = \bar{\beta}_i I_j S_i/(u_{11}S_1 - u_{12}I_1 - u_{21}S_2 - u_{22}I_2)$. While fast infectious propagule dynamics are necessary for the dynamics of the environmental and direct transmission models to be identical, our results about equilibrium infection prevalence apply for any speed of the infectious propagule dynamics. This is because the equilibria of the ET model are always identical to those of a DDDT or FDDT model when $U = 0$ or $\mu = 0$, respectively.

This unified framework shows that the three transmission modes sit in a two-dimensional space defined by the total uptake (U) and degradation (μ) rates of the infectious propagules, with ET lying intermediate between DDDT and FDDT (see Figure 1A). In particular, the equilibrium densities of the ET model are identical to those of a FDDT model when the degradation rate is zero ($\mu = 0$; blue vertical axis) and identical to those of a DDDT model when the uptake rates are negligible ($U = 0$; red horizontal axis). When the uptake and degradation rates are both nonzero ($\mu > 0$, $U > 0$; white), ET behaves like a combination of DDDT and FDDT, determined by the magnitudes of the uptake and degradation rates.

3.2 How transmission mode affects amplification and dilution

The previous section showed that environmental transmission sits intermediate between density-dependent and frequency-dependent direct transmission. Here, we use that to identify how the pathogen transmission mode influences prevalence in the focal host.

Our approach involves using a change of parameters to convert the ET model from a form that behaves like a DDDT model ($U = 0$) to a form that behaves like a FDDT model ($\mu = 0$) (gray line in Figure 1A). To make a fair comparison between models, our change of parameters satisfies two constraints. First, all parameters are kept constant except the uptake (u_{ij}) and degradation (μ) rates, which must necessarily differ between the models. Second, we hold constant the per capita total loss rate of infectious propagules at the single-species equilibrium ($\hat{U}+\mu = u_{11}\hat{S}_1 - u_{12}\hat{I}_1 - u_{21}\hat{S}_2 - u_{22}\hat{I}_2 + \mu$); see appendix S1.5.4 for details. This results in the single-species equilibrium densities being the same across models and only the multi-species equilibrium densities changing as the environmental transmission model is converted between forms. Thus, by identifying host densities at the multi-species equilibrium change with the transformation, we can determine how the pathogen transmission mode affects infection prevalence in the focal host. We note that our results are nearly identical if we use a change of parameters that instead holds the multi-species equilibrium densities constant and causes the single-species equilibrium densities to change; see appendix S1.5.3 for details.

As shown in appendix S1.5.4, lower focal host prevalence under FDDT is promoted by (i) weaker interspecific host competition, (ii) weak intraspecific competition in the introduced host, and (iii) lower competence in the introduced host. Conversely, lower focal host prevalence under DDDT is promoted by (i) stronger interspecific host competition, (ii) stronger intraspecific competition in the introduced host, and (iii) higher competence in the introduced host. Prevalence in the focal host under ET always sits between FDDT and DDDT.

For example, in the absence of interspecific competition (Figure 1B), focal host prevalence is typically lower under FDDT than DDDT, but the opposite can occur if the introduced host is a strong intraspecific competitor and a high competence host (purple curve). When interspecific host competition is stronger (Figure 1C), lower focal host prevalence under density-dependent direct transmission is more common. Moreover, increased interspecific competition can reverse the relationship between transmission mode and focal host preva-

lence. For example, in the absence of interspecific competition, focal host prevalence is lower under FDDT for introduced hosts in Figure 1B that are low competence, strong intraspecific competitors (vermilion "Low, Strong" curve) and high competence, weak intraspecific competitors (blue-green "High, Weak" curve). However, the pattern reverses when interspecific competition is sufficiently strong (vermilion and blue-green curves are decreasing in Figure 1C). In our numerical simulations, transmission mode only had a modest effect on focal host prevalence in all cases where the introduced host was a high competence, weak intraspecific competitor and increased interspecific competition reversed the relationship between transmission mode and focal host prevalence (blue-green curves in Figure 1 have small slopes).

3.3 How host competence and competitive ability affect amplification and dilution

We now explore how the competence and intraspecific and interspecific competitive abilities of the introduced host affect prevalence in the focal host. Details are provided in appendix S1.4.

Competence of the introduced host: Intuition suggests that a higher competence host (larger $\beta_i\chi_i/m_iu_{1i}$) will cause greater prevalence than a lower competence host. This pattern holds under many conditions. For example, prevalence declines with increased host mortality in Figure 2A (red and magenta curves) and prevalence increases with increased infection coefficients in Figure 2B (left side of red, magenta, and green curves). The mechanism is that higher competence hosts produce more infectious propagules per infectious propagule they are exposed to, which leads to more infectious propagules and consequently, higher prevalence in the focal host.

However, higher competence can decrease focal host prevalence in two instances. First, focal host prevalence can increase with higher introduced host mortality rates (m_2) (blue curve in 2A) if the introduced host is a large sink (i.e., the introduced host has low excretion

or high uptake rates). Second, focal host prevalence can decrease with higher infection coefficients (β_2) if the introduced host is a large sink (left side of cyan and blue curves in Figure 2B). The mechanism is that increasing the infection rate or decreasing the mortality rate of a sink host increases the number of infected hosts in the sink population. This results in greater rates of uptake of infectious propagules, decreased infectious propagule density, and consequently, lower prevalence in the focal host.

Intraspecific competitive ability of the introduced host: Stronger intraspecific competition in the introduced host leads to increased focal host prevalence, unless the introduced host is a sufficiently large source (i.e., the introduced host has very high excretion or very low uptake rates). In addition, the threshold for being a sufficiently large source increases with increased interspecific competition between the hosts. For example, in the absence of interspecific competition (Figure 3A), stronger intraspecific competition leads to greater focal host prevalence when the introduced hosts are sinks (blue curve) and lower prevalence when the introduced hosts are sources (cyan and red curves). However, when interspecific competition is higher (Figure 3B), stronger intraspecific competition causes lower prevalence only if the introduced host is a sufficiently strong source (cyan curve switches from decreasing in Figure 3A to increasing in Figure 3B).

The mechanism is the following. In the absence of interspecific competition, increased intraspecific competitive ability causes the density of the introduced host to decrease. If the introduced host is a sink, the decrease in density results in more infectious propagules and greater prevalence in the focal host. In contrast, if the introduced host is a source, the decrease in density results in fewer infectious propagules and lower prevalence in the focal host. In the presence of interspecific competition, the decrease in density of the introduced host also reduces competition with the focal host. This causes an increase in the number of susceptible hosts in the focal population, which leads to more infections and greater prevalence in the focal host. Because of this positive effect on focal host prevalence, the introduced host must be a very large source of infectious propagules in order for increases

in its intraspecific competitive ability to have an overall negative effect on prevalence in the focal host.

Interspecific competitive ability of the introduced host: Stronger interspecific competitive ability of the introduced host causes a decrease in focal host prevalence, unless the introduced host is a large source. Specifically, when the introduced host is an equal or smaller source than the focal host, stronger interspecific competition leads to decreased focal host prevalence (blue and cyan curves in Figure 3C). In contrast, when the introduced host is a sufficiently larger source than the focal host, stronger interspecific competition leads to greater prevalence (magenta and red curves in Figure 3C).

The mechanism is that increased interspecific competitive ability of the introduced host has two effects. First, increased interspecific competitive ability decreases susceptible focal host density, which in turn decreases the focal host transmission rate. Second, the decrease in focal host density causes an increase in introduced host density (through reduced interspecific competition from the focal host). This results in an increased density of infected introduced hosts, which leads to greater infectious propagule densities and an increase in the focal host transmission rate. If the introduced host is not a large source of infectious propagules, then the decrease in focal host infection rates (effect 1) is greater than the increase (effect 2), resulting in a decrease in focal host prevalence. However, if the introduced host is a large source of infectious propagules, then the increase in focal host infection rates (effect 1) is greater, resulting in increased focal host prevalence.

3.4 Predictions for factors promoting amplification versus dilution

Here, we interpret the conditions for increased and decreased infection prevalence in terms of factors promoting amplification or dilution in the focal host. Our predictions are summarized in Table 1.

We predict higher competence introduced hosts promote amplification, unless the introduced host is a large sink; introduced hosts that are stronger intraspecific competitors

promote amplification, unless the introduced host is a large source; and introduced hosts that are stronger interspecific competitors promote dilution, unless the introduced host is a large source. We also predict that greater dilution and less amplification will occur under frequency-dependent direct transmission (FDDT) when compared to density-dependent direct transmission (DDDT) when interspecific host competition is weak, the introduced host has lower competence, and the introduced host experiences weaker intraspecific competition. Greater dilution and less amplification occurs under DDDT under the opposite conditions.

Our predictions focus on which factors promote amplification versus dilution, but do not necessarily indicate which one will occur in a given system. However, in some cases, we can place restrictions on which outcome can occur. Specifically, for any level of interspecific competition, it is possible for dilution to occur under FDDT and amplification to occur under DDDT (Figure 4A). In contrast, only when interspecific competition is sufficiently high can dilution occur under DDDT and amplification occur under FDDT. For example, in Figure 4B, amplification occurs for both transmission mechanisms when interspecific competition is absent or low (dashed curves are above dotted line) whereas dilution can occur for DDDT if interspecific competition is sufficiently strong (solid line passes through dotted line).

There are three conditions under which some or all of our predictions can be reversed. First, all of the predictions can be reversed if the effects of interspecific host competition are greater than the effects of intraspecific competition. This can occur, e.g., in systems where there is pathogen-mediated coexistence of the two host species.

Second, all of the predictions can be reversed if one or both hosts are experiencing sufficiently large positive density dependence (at equilibrium). This occurs when the pathogen reduces the density of one host to the point where the growth rate of that host is an increasing function of its own density. This is analogous to positive density dependence of a prey species in a predator-prey system, which occurs when the predator reduces the prey density to levels below the hump in the predator nullcline. The filled circles in Figure 2BC denote the minimum parameter values at which one host is experiencing positive density

dependence. When the positive density dependence is sufficiently large, all of the curves reverse direction.

Third, the predictions about host competence can be reversed if infected hosts are sufficiently stronger interspecific competitors than susceptible hosts. For example, if infected hosts are stronger interspecific competitors, then higher competence hosts can amplify disease less (decreasing portions of magenta and red curves left of the filled circles in Figure 2C). We do not expect this scenario to arise frequently, but it can occur, e.g., in systems where pathogens cause gigantism in the host, provided infection does not also decrease feeding rates.

4 Discussion

Whether increased host biodiversity leads to greater or less disease has been contested in the literature (Lafferty and Wood, 2013; Ostfeld and Keesing, 2013; Wood and Lafferty, 2013), leading to calls for new theory explaining how particular mechanisms influence amplification and dilution (Buhnerkempe et al., 2015; Halsey, 2019; Rohr et al., 2019). To begin to address this need, we developed a framework that unifies environmental transmission and direct transmission models and used that framework to identify general rules about how host competence and competitive ability and the pathogen transmission mode promote higher versus lower prevalence in a focal host. Our resulting predictions about factors promoting amplification and dilution (Table 1) help unify and extend the existing bodies of dilution theory and point the way forward for developing a unified theory for amplification and dilution of disease.

Our approach shows that there are general rules governing how specific biological mechanisms shape biodiversity-disease patterns, but the rules have context dependencies (Table 1). This in turn helps explain some of the differing predictions made in previous studies. For example, in agreement with previous studies that did not include interspecific host

competition (Dobson 2004; Rudolf and Antonovics 2005; Hatcher et al. 2006; Faust et al. 2017), in the absence of interspecific competition, dilution occurs more frequently under frequency-dependent direct transmission and amplification occurs more frequently under density-dependent direct transmission and environmental transmission (Figure 4). However, as found in other studies (Ogden and Tsao, 2009; Strauss et al., 2015; O'Regan et al., 2015; Searle et al., 2016), incorporating interspecific host competition can alter predictions, including the possibility that dilution occurs under density-dependent direct transmission, but not frequency-dependent direct transmission (Figure 4B). Our results show that in general increased interspecific competitive ability of the introduced host promotes dilution in a focal host, unless the introduced host is a large source of infectious propagules.

Our unified framework helps explain how differences in the transmission mechanism influence amplification and dilution. First, our framework shows that environmental transmission lies intermediate between density-dependent and frequency-dependent direct transmission, with the relative rates of infectious propagule degradation and uptake by hosts dictating whether an environmental transmission system behaves more like a density-dependent or frequency-dependent direct transmission system (Figure 1A). Second, while our general rules (Table 1) hold for all three transmission types, their implications can differ for density-dependent and frequency-dependent direct transmission pathogen. For example, under density-dependent direct transmission, all hosts are necessarily sources of infectious propagules because the uptake rates are zero. This means that, all else being equal, a higher competence of the introduced host promotes amplification when there is density-dependent-direct transmission. In contrast, under frequency-dependent direct transmission, a host can be a sink or a source. An introduced host is more likely to be sink if (i) the introduced host has a lower transmission coefficient; (ii) the introduced host has lower density, which can arise via the introduced host being a strong intraspecific competitor or the focal host be a strong interspecific competitor; and (iii) the focal host spends more time per encounter interacting with heterospecifics than conspecifics (e.g., focal hosts spend more time defending territory

against heterospecifics than conspecifics). Because hosts can be sinks, higher competence of an introduced host does not necessarily promote amplification for frequency-dependent direct transmission pathogens.

Our framework identifies additional areas where new theory is needed. First, our framework does not address correlations between traits, which could potentially affect predictions about biodiversity-disease relationships. For example, the diluting effects of *Daphnia* species are influenced by propagule uptake rates and resource consumption rates, both of which are affected by the host filtering rate (Hall et al., 2007; Dallas et al., 2016). Similar correlations may also be present in insects (Evans and Entwistle, 1987; Naug, 2014), snails (Lafferty, 1993; Miura et al., 2006), and grazing mammals (Williams and Barker, 2008; Wobeser, 2013) that consume their environmentally transmitted pathogens or encounter them while foraging (Hall et al., 2007).

Second, new theory is needed to understand if our predictions also hold for vector-borne pathogens. Vector transmission and frequency-dependent direct transmission are thought to be similar (Rudolf and Antonovics, 2005). However, patterns of amplification and dilution can be influenced by how host biodiversity affects the abundance and biting behavior of the vector (Miller and Huppert, 2013; Normal et al., 1999). An important area of future work is exploring if our unified framework for environmental and direct transmission can be extended to include vector-borne transmission.

Finally, previous studies have used three metrics to study biodiversity-disease relationships: the proportion of infected hosts (prevalence), the density of infected hosts, and the pathogen basic reproductive number (R_0). Predictions can disagree between metrics (Roberts and Heesterbeek, 2018). For our model, all of our general predictions about focal host prevalence (Table 1) also hold for focal host infected density; see appendices for details. However, this does not preclude disagreement between the metrics. For example, in Figure 3B, increased intraspecific competitive ability of the introduced host causes higher infected density in all cases, even though prevalence decreases when the introduced host

has the largest excretion rate (red curve). The disagreement is due to the introduced host being a sufficiently large source to cause prevalence to decrease with increased intraspecific competitive ability, but an insufficiently large source to also cause the infected host density to decrease. Similar disagreements can occur with other host characteristics or the pathogen transmission mode. Thus, new theory is needed to determine when and why predictions differ between the three metrics and how that affects our understanding of biodiversity-disease relationships.

Overall, our work helps unify dilution theory for pathogens with environmental or direct transmission and provides a way forward toward the development of a general unified dilution theory.

5 Acknowledgments

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6 Tables & Figures

Table 1: Predictions for how the characteristics of an introduced host and the pathogen transmission mode affect amplification and dilution in a focal host

Characteristic	Predicted effects
Competence	Higher competence promotes amplification, unless the host is a sufficiently large sink for infectious propagules
Competitive ability	Stronger intraspecific competition promotes amplification, unless the host is a sufficiently large source of infectious propagules Stronger interspecific competitors promotes dilution, unless the host is a sufficiently large source of infectious propagules
Transmission mode	Frequency-dependent direct transmission promotes dilution more than density-dependent direct transmission when (i) weak interspecific host competition (ii) introduced host is a weaker intraspecific competitor (iii) introduced host is a lower competence host Density-dependent direct transmission promotes dilution more than frequency-dependent direct transmission when (i) strong interspecific host competition (ii) introduced host is a stronger intraspecific competitor (iii) introduced host is a higher competence host
Conditions that can reverse predictions	Sufficiently strong positive density dependence in either host Interspecific competition greater than intraspecific competition Infected hosts are stronger interspecific competitors than susceptible hosts

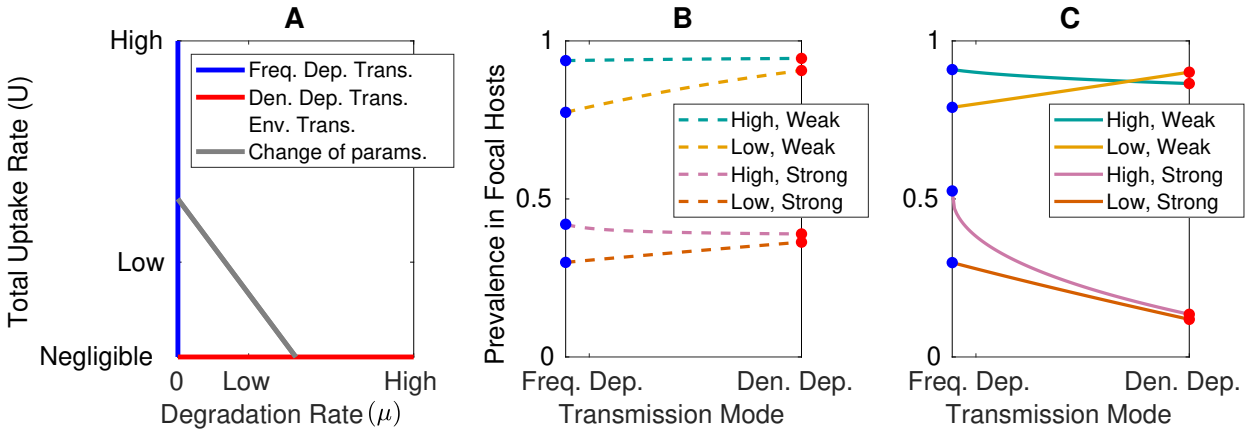

Figure 1: Environmental transmission models and density-dependent and frequency-dependent direct transmission models can be unified, which helps identify how the transmission mechanism influences infection prevalence in a focal host. (A) Environmental transmission sits intermediate between density-dependent and frequency-dependent direct transmission, with environmental transmission models (white) being identical to density-dependent direct transmission models when loss of infectious propagules due to uptake by hosts is negligible ($U = 0$, red) and identical to frequency-dependent direct transmission models when there is no infectious propagule degradation ($\mu = 0$, blue). Gray line illustrates a change of parameters that transforms a particular parameterization of the environmental transmission model from a frequency-dependent form to a density-dependent form while holding the single-species equilibrium densities constant; see text for details. Effect of transmission mode on focal host prevalence in the (B; dashed) absence and (C; solid) presence of interspecific host competition for introduced hosts that are low or high competence and weak or strong intraspecific competitors. Panels show equilibrium prevalence in the focal host as the environmental transmission model is transformed from a frequency-dependent form (blue dots) to a density-dependent form (red dots) while holding the single-species equilibrium densities constant. See appendix S1.6 for models and parameters.

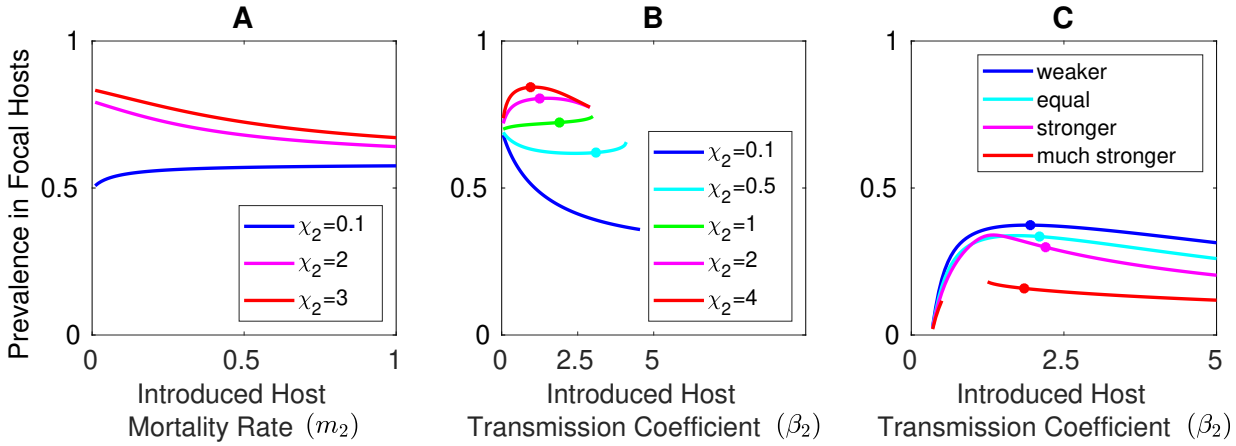

Figure 2: Increased competence of an introduced host leads to greater infection prevalence in a focal host, unless the introduced host is a sufficiently large sink for infectious propagules, one or both hosts experience strong positive density dependence at equilibrium, or infected hosts are stronger interspecific competitors than susceptible hosts. All panels show equilibrium prevalence in the focal host as components defining the competence of the introduced host are varied; filled circles in panels B and C denote parameter values above which at least one host experiences positive density dependence. (A) Response to increased disease-induced mortality when the introduced host is a (blue) large sink, (magenta) small source, or (red) large source. (B) Response to increased transmission rates when the introduced host is a (blue) large sink, (cyan) small sink, (green) equal source, (magenta) large source, or (red) very large source. (C) Response to increased transmission rates when infected hosts are (blue) weaker, (cyan) equal, (magenta) stronger, or (red) much stronger interspecific competitors than susceptible hosts. Break in red curve is due to coexistence being impossible for intermediate transmission coefficients. See appendix S1.6 for equations and parameters.

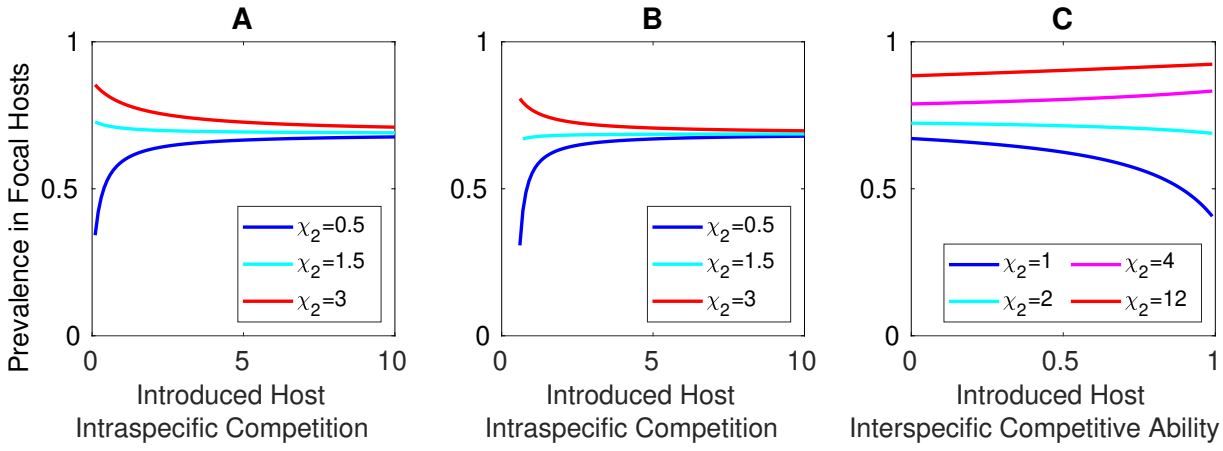

Figure 3: Increased intraspecific competitive ability of the introduced host leads to greater infection prevalence in the focal host and increased interspecific competitive ability of the introduced host leads to lower infection prevalence in a focal host, unless the introduced host is a sufficiently large source of infectious propagules. All panels show equilibrium infection prevalence in the focal host as the (A,B) intraspecific or (C) interspecific competitive ability of the introduced host is varied. Response to increased intraspecific competitive ability of the introduced host in the (A) absence and (B) presence of interspecific competition when the introduced host is a (blue) large sink, (cyan) small source, or (red) large source. (C) Response to increased interspecific competitive ability of the introduced host when the introduced host that is a (blue) large sink, (cyan) equal source, (magenta) large source, or (red) very large source. See appendix S1.6 for equations and parameters.

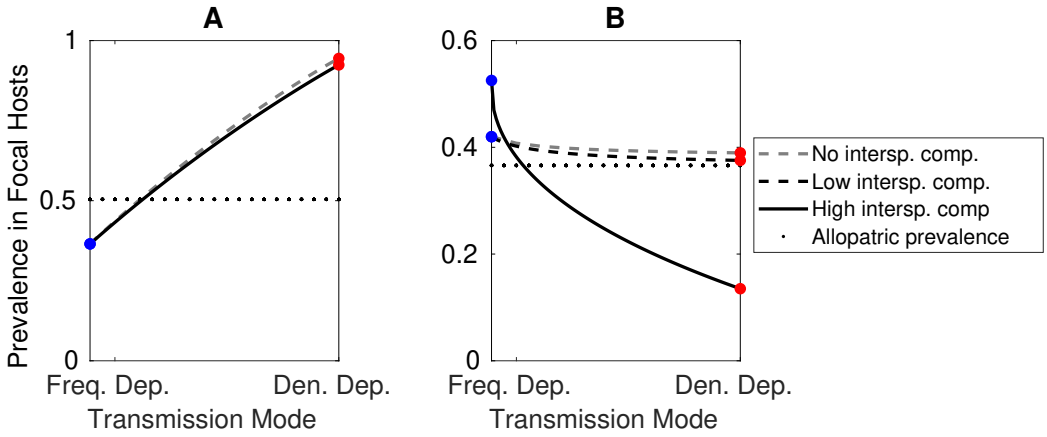

Figure 4: Interspecific host competition influences whether frequency-dependent and density-dependent direct transmission lead to different predictions about amplification and dilution in a focal host. (A) Frequency-dependent direct transmission can cause dilution when density-dependent direct transmission causes amplification in the (dashed gray) absence or (solid black) presence of interspecific competition. (B) Less amplification can occur under density-dependent direct transmission than frequency-dependent direct transmission when interspecific host competition is absent (dashed gray) or low (dashed black). However, density-dependent direct transmission can cause dilution when frequency-dependent direct transmission causes amplification only if (solid black) interspecific host competition is sufficiently strong. In both panels, dotted horizontal lines denote the prevalence in the focal host in allopatry. Dashed and solid curves show multi-species equilibrium prevalence in the focal host as the environmental transmission model is transformed from a frequency-dependent form (blue dots) to a density-dependent form (red dots) while holding the single-species equilibrium densities for the focal host constant; see text for details. See appendix S1.6 for models and parameters.