Toward the unification of dilution effect theory for environmental and direct transmission pathogens OR How interspecific host competition and pathogen transmission mode influence dilution of disease

Michael H. Cortez*
Department of Biological Science
Florida State University
Tallahassee, FL 32306
(850) 645-8692
cortez@bio.fsu.edu

Meghan A. Duffy
Department of Ecology and Evolutionary Biology
University of Michigan
Ann Arbor, MI 48109
(734) 763-3658
duffymeg@umich.edu

January 21, 2020

Short title: Unifying dilution effect theory
Keywords: dilution effect; environmental transmission; direct transmission; density dependent; frequency dependent; competence; transmission mode; disease dynamics
Article submission
Word Counts: 5380 in main text; 143 in abstract. 1 Table; 4 Color figures
Supplementary Material: Online Appendix S1
*Corresponding author
Statement of Authorship: MHC and MAD designed the study; MHC did mathematical analysis and wrote first version of the paper; MAD contributed to writing.

ABSTRACT:

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) disease prevalence. In this study, we use a two-host-one-pathogen model to show how dilution effect theory for pathogens with environmental transmission and density and frequency dependent direct transmission can be unified. We use that unified framework to identify how the pathogen transmission mechanism and characteristics of an introduced host (disease competence and interspecific and intraspecific competitive abilities) influence disease prevalence in a focal host and under what conditions amplification or dilution is promoted. Our approach shows that there are general rules governing how specific biological mechanisms shape biodiversity-disease patterns, but the rules have context dependencies.

1 Introduction

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). Consequently, infection prevalence in a given host population can be influenced by the presence or absence of other host species, via the ways each host species interacts with the pathogen (e.g., the competence of the different host species) and the interspecific interactions between host species (e.g., resource competition and between species transmission). The dilution effect argues for a mechanistic link between increased host diversity and decreased disease (Keesing et al., 2006). However, when and whether increased host biodiversity reduces disease (dilution) or increases disease (amplification) in a focal host population has been vigorously 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 suggests that increased biodiversity likely has context-dependent effects (Salkeld et al., 2013), which has led to calls for theory that identifies which specific biological mechanisms promote 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 depends on how host species diversity affects host-pathogen encounter rates; transmission rates; host recovery rates; mortality rates of infected individuals; and susceptible host densities. In particular, many studies suggest that frequency dependent direct transmission promotes dilution whereas density dependent direct transmission and environmental transmission (e.g., spore-based 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 the specific outcome depends on interspecific resource competition (Ogden and Tsao, 2009; Strauss et al., 2015; O'Regan et al., 2015; Searle et al., 2016) and the relative rates of within and between-species transmission (Rudolf and Antonovics, 2005; O'Regan et al., 2015; Roberts and Heesterbeek, 2018). Accounting for these factors 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).

While this existing body of theory has provided some understanding about the drivers of amplification and dilution, it is limited in two key ways. First, current theory shows that the transmission mode and characteristics of the host species (e.g., competence and competitive ability) have context dependent effects on amplification and dilution. However, 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 fairly compare predictions across models and identify how the pathogen transmission mode influences patterns of amplification and dilution. Overall, there is a 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.

As a step towards addressing these limitations, we use a two-host-one-pathogen model to explore and identify which particular biological mechanisms promote amplification versus dilution. We first show how the theories for environmentally transmitted pathogens and pathogens with density dependent or frequency dependent direct transmission can be unified under a single framework. We use that framework to identify the conditions under which specific transmission modes and characteristics of the introduced host (specifically, disease competence and interspecific and intraspecific competitive abilities) promote higher versus lower disease prevalence in a focal host. We then interpret the conditions in terms of factors 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-two-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 model presentation and analysis, we assume there is no recovery from infection, i.e., infection is always lethal in both hosts. One empirical example is fungal infections of *Metschnikowia bicuspidata* in *Daphnia* (Searle et al., 2016). We refer to host species 1 as the 'focal host' and host species 2 as the 'introduced host'.

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 $f_i(S_1, S_2, I_1, I_2)$; infection occurs when susceptible hosts come in contact with infectious propagules at rate $\beta_i P$; infected hosts die at rate m_i and excrete infectious propagules into the environment at rate χ_i; and infectious propagules are lost due to uptake by all hosts ($u_{i1} S_i$ and $u_{i2} I_i$ terms) and degradation at rate μ. The total population size for each host is $N_i = S_i + I_i$.

The reproduction rates (f_i) account for intraspecific and interspecific host competition and for reproductive output from infected individuals. We use the general functions in order

to develop general theory that applies to any choice of functional forms for the reproduction rates. However, when presenting specific numerical examples we use the Lotka-Volterra competition functions, $f_i = r_i(S_i + c_i I_i)[1 - \alpha_{i1}(S_1 + e_{i1} I_1) - \alpha_{i2}(S_2 + e_{i2} I_2)]$ 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 than susceptible hosts, however it could occur for pathogens that cause gigantism, provided infection does not alter feeding rates.

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. We refer to p^* as the sympatric 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. We refer to $\hat{p}$ as allopatric equilibrium.

2.2 High and low competence hosts, sinks, and sources

Throughout, we describe the host species as being higher or lower competence and being small or large sinks or sources for infectious propagules. Host competence is defined by the pathogen basic reproduction number in an allopatric host population of infinite size, $\beta_i \chi_i / m_i u_{i1}$. Intuitively, higher competence hosts produce more new infections per infected individual because they have a combination of higher infection and infectious propagule release rates (larger β_i and χ_i), lower mortality rates (smaller m_i), and lower uptake rates by susceptible hosts (smaller u_{i1}).

Sink and source host 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 higher infectious propagule release rates (larger χ_i) and lower uptake rates (smaller u_{i2}).

Competence and sink/source are related, but not identical. For example, a high competence host can be a large source if β_i and χ_i are large and m_i, u_{i1}, and u_{i2} are small. In contrast, a high competence host with large β_i and small m_i can be a large sink if χ_i is small and u_{i2} is large.

2.3 Computing responses to characteristics of introduced host

Our metric of disease is the sympatric equilibrium disease prevalence of the focal host (I_1^*/N_1^*). Our approach is to compute how the parameters defining the competence (χ_2, β_2, m_2, and u_{2j}), the intraspecific competitive ability (e.g., α_{22} in a Lotka-Volterra model), and the interspecific competitive ability (e.g., α_{12} in a Lotka-Volterra model) of the introduced host influence the sympatric equilibrium prevalence of the focal host. Mathematically, this is done by computing how a small change in one parameter affects the sympatric equilibrium prevalence of the focal host. For example, the effect of the introduced host having a higher infection coefficient is computed using the derivative $\partial(I_1^*/N_1^*)/\partial\beta_2$; positive and negative values mean increased infection coefficients lead to higher or lower prevalence in the

focal host, respectively. The derivatives are computed using the Jacobian-based theory developed in (Bender et al., 1984; Yodzis, 1988; Novak et al., 2011; Cortez and Abrams, 2016); see appendix S1.2 for additional details. Due to their large size, all derivative equations are relegated to the appendices.

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 sympatric 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 promotes higher or lower sympatric prevalence allows us to make predictions about the factors that promote amplification (i.e., higher prevalence in sympatry than allopatry; $I_1^*/N_1^* > \hat{I}_1/\hat{N}_1$) versus dilution (i.e., lower prevalence in sympatry than allopatry; $I_1^*/N_1^* < \hat{I}_1/\hat{N}_1$), respectively.

3 Results

3.1 Unifying environmental and direct transmission models

We first extend prior work on single-host-single-pathogen models (Li et al., 2009; Eisenberg et al., 2013; Cortez and Weitz, 2013) by showing that environmental transmission, density dependent direct transmission, and frequency dependent direct transmission models with two host species can be unified under a single framework. We do this by identifying specific conditions under which our environmental transmission model reduces to a direct transmission model with density dependent or frequency dependent transmission.

In general, the environmental transmission model (1) reduces to a density dependent direct transmission model 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 environmental transmission model (1) reduces to a density dependent direct transmission model. Alternatively, if there is no degradation of infectious propagules ($\mu = 0$), then the environmental transmission model (1) reduces to a frequency dependent direct transmission model.

The intuition is the following. Infectious propagules persist in the environment for short periods of time when the 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 of infectious propagules due to uptake by hosts 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 environmentally transmitted pathogen are essentially identical to those of a density dependent direct transmission 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 environmentally transmit-

ted pathogen are essentially identical to those of a frequency dependent direct transmission pathogen.

For the mathematical justification of the above, we assume the changes in infectious propagule density are much faster than changes in the host densities. This requires that the host excretion rates (χ_i) and infectious propagule degradation (μ) or uptake (u_{ij}) rates are large. Under these conditions, 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 equation yields

$$\frac{dI}{dt} = \underbrace{(\beta_i \chi_1 I_1 + \beta_i \chi_2 I_2)\frac{S_i}{U+\mu}}_{\text{infection}} \underbrace{-m_i I_i}_{\text{mortality}} . \tag{2}$$

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 rate simplifies to the infection rate for a density dependent direct transmission model, $\beta_i \chi_j I_j / \mu = \bar{\beta}_{ij} I_j S_i$. When there is no degradation ($\mu = 0$), the infection rate simplifies to that of a frequency dependent direct transmission 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 the assumption of fast infectious propagule dynamics is necessary for the dynamics of the environmental and direct transmission models to be identical, our results about equilibrium disease prevalence apply for any speed of the infectious propagule dynamics. This is because the equilibria of the environmental transmission model are always identical to those of a density dependent or frequency dependent direct transmission model when $U = 0$ or $\mu = 0$, respectively.

Altogether, this shows that by studying a single environmental transmission model, we can identify how the characteristics of the introduced host influence patterns of amplification and dilution for both environmentally and directly transmitted pathogens. In addition, this unified framework identifies how all three models sit in a two-dimensional space defined by the total uptake (U) and degradation (μ) rates of the infectious propagules, with environmental transmission lying intermediate between density dependent and frequency dependent direct transmission (see Figure 1A). In particular, the equilibrium densities of the environmental transmission model are identical to those of a density dependent direct transmission model when the uptake rates are negligible ($U = 0$; red horizontal axis) and identical to those of a frequency dependent direct transmission model when the degradation rate is zero ($\mu = 0$; blue vertical axis). When the uptake and degradation rates are both nonzero ($\mu > 0, U > 0$), the environmental transmission model behaves like a combination of the direct transmission models, 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 amplification and dilution by comparing prevalence in the focal host across the three models.

Our approach involves using a change of parameters, $f(q)$, to convert the environmental transmission model from a form that behaves like a density dependent transmission model

($U = 0$) to a form that behaves like a frequency dependent transmission model ($\mu = 0$) (black 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, our change of parameters holds constant the per capita total loss rate of infectious propagules at the allopatric 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 allopatric equilibrium densities being the same across models and only the sympatric equilibrium densities changing as the environmental transmission model is converted between forms. Thus, by identifying how the sympatric equilibrium prevalence changes with the transformation, we can determine how the pathogen transmission mode affects disease prevalence in the focal host. We note that our results are nearly identical if we use a change of parameters that holds the sympatric equilibrium densities constant and causes the allopatric equilibrium densities to change; see appendix S1.5.3 for details.

As shown in appendix S1.5.4, lower focal host prevalence under frequency dependent direct transmission 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 density dependent direct transmission is promoted by (i) stronger interspecific host competition, (ii) stronger intraspecific competition in the introduced host, and (iii) higher competence in the introduced host.

For example, in the absence of interspecific competition (Figure 1B), focal host prevalence is typically lower under frequency dependent direct transmission than density dependent direct transmission, 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 prevalence. For example, in the absence of interspecific competition, focal host prevalence is lower when transmission is frequency dependent 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 will cause greater prevalence than a lower competence host. That is, we expect disease

prevalence to be higher if the introduced host has larger values of $\beta_i\chi_i/m_i u_{1i}$. This pattern holds under many conditions. For example, prevalence declines with increased host mortality in Figure 2A (red and cyan curves) and prevalence increases with increased infection coefficients in Figure 2B (left side of red, magenta, and green curves). Intuitively, the mechanism is that higher competence hosts produce more infectious propagules per infectious propagule they are exposed to, which leads to more infections and higher prevalence in the focal host.

While our intuition is often correct, higher competence hosts can cause the focal host prevalence to decrease 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 very low excretion or very 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 underlying mechanism is that increasing the infection rate or decreasing the mortality rate of the sink host increases the number of infected hosts in the sink population. This results in greater rates of uptake of infectious propagules, which leads to decreased infectious propagule density and fewer infections 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 sources (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. A decrease in the density of a sink host results in more infectious propagules and consequently greater prevalence in the focal host. In contrast, a decrease in the density of a source host results in fewer infectious propagules and consequently 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. In particular, 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 a increase in focal host prevalence.

3.4 Predictions for factors promoting amplification versus dilution

Here, we interpret out conditions for increased and decreased infection prevalence of the focal host in terms of factors that promote whether introduction of the introduced host amplifies or dilutes disease 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 when compared to density dependent direct transmission 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 density dependent direct transmission under the opposite conditions.

It is important to note that our predictions focus on which factors promote amplification versus dilution and 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 frequency dependent direct transmission and amplification to occur under density dependent direct transmission (Figure 4A). In contrast, only when interspecific competition is sufficiently high is it possible for dilution to occur under density dependent direct transmission and amplification to occur under frequency dependent direct transmission. 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 density dependent direct transmission only when 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 coexistence of the two host species is pathogen-mediated.

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. Specifically, 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 in systems, 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). As an initial step toward addressing this need, we developed a framework that unifies environmental transmission models and direct transmission models with density or frequency dependent transmission and used that framework to identify general rules about which characteristics of an introduced host (specifically, competence and competitive ability) and the pathogen transmission mode promote higher versus lower prevalence in a focal host. Our resulting predictions about the factors that promote amplification versus 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, incorporating interspecific host competition can alter predictions (Ogden and Tsao, 2009; Strauss et al., 2015; O'Regan et al., 2015; Searle et al., 2016), including allowing for the possibility that dilution occurs under density dependent direct transmission, but not frequency dependent direct transmission (Figure 4B). Our results show that in general dilution in a focal host is promoted by increased interspecific competitive ability of another host, provided the other host is not a large source.

Our unified framework for environmental transmission and density dependent and fre-

quency dependent direct transmission models helps explain how differences in the transmission mechanism influence amplification and dilution. First, our framework shows that environmental transmission lies intermediate between the two types of direct transmission, with the relative rates of infectious propagule degradation and uptake by hosts determining 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 source hosts because the uptake rates are zero. This means that, all else being equal, a higher competence host will always amplify more than a lower competence host 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 imply greater amplification for frequency dependent direct transmission pathogens.

While our framework shows how the three types of models can be unified and identifies general rules governing the ways in which some mechanisms influence amplification and dilution, it also points towards areas where new theory is needed. First, our framework does not address correlations between traits, which could affect predictions about how host biodiversity affects amplification and dilution of disease. 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), suggesting that our results may apply. 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 different metrics to study how host biodiversity influences disease: the proportion of infected hosts (prevalence), the absolute number or 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 host and pathogen characteristics from having effects of different signs on the prevalence and density of infected

individuals. 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 reason for this disagreement is that the introduced host is a sufficiently large source to cause prevalence to decrease with increased intraspecific competitive ability, but an insufficiently large source to also cause the density of infected hosts to decrease. Similar kinds of disagreement 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 how host biodiversity affects levels of disease.

Overall, our work is step towards the development of a unified dilution theory for pathogens with environmental transmission and density dependent and frequency dependent direct transmission. While more work remains to be done, our framework provides a way forward toward the development of a general unified dilution theory.

5 Acknowledgments

We thank Patrick Clay for helpful comments on a previous version of the paper. MAD and MHC were supported by the National Science Foundation under Awards DEB-1748729 & DEB-1748848.

References

Begon, M., and R. G. Bowers. 1994. Host-host-pathogen models and microbial pest control: the effect of host self regulation. Journal of Theoretical Biology 169:275–287.

Begon, M., R. G. Bowers, N. Kadianakis, and D. E. Hodgkinson. 1992. Disease and community structure: the importance of host self-regulation in a host-host-pathogen model. American Naturalist 139:1131–1150.

Bender, E. A., T. J. Case, and M. E. Gilpin. 1984. Perturbation experiments in community ecology: theory and practice. Ecology 65:1–13.

Buhnerkempe, M. G., M. G. Roberts, A. P. Dobson, H. Heesterbeek, P. J. Hudson, and J. O. Lloyd-Smith. 2015. Eight challenges in modelling disease ecology in multi-host, multi-agent systems. Epidemics .

Civitello, D. J., J. Cohen, H. Fatima, N. T. Halstead, J. Liriano, T. A. McMahon, C. N. Ortega, E. L. Sauer, T. Sehgal, S. Young, and J. R. Rohr. 2015. Biodiversity inhibits parasites: Broad evidence for the dilution effect. PNAS 112:8667–8671.

Cleaveland, S., M. K. Laurenson, and L. H. Taylor. 2001. Diseases of humans and their domestic mammals: pathogen characteristics, host range and the risk of emergence. Philosophical Transactions of the Royal Society of London B 356:991–999.

Cortez, M. H., and P. A. Abrams. 2016. Hydra effects in stable communities and their implications for system dynamics. Ecology 97:1135–1145.

Cortez, M. H., and J. S. Weitz. 2013. Distinguishing between indirect and direct modes of transmission using epidemiological time series. American Naturalist 181:E43–E52.

Dallas, T., R. J. Hall, and J. M. Drake. 2016. Competition-mediated feedbacks in experimental multispecies epizootics. Ecology 97:661–670.

Dobson, A. 2004. Population dynamics of pathogens with multiple host species. American Naturalist 164:S64–S78.

Eisenberg, M. C., S. L. Robertson, and J. H. Tien. 2013. Identifiability and estimation of multiple transmission pathways in cholera and waterborne disease. Journal of Theoretical Biology 324:84–102.

Evans, H., and P. Entwistle. 1987. Viral diseases, in" epizootiology of insect diseases",(fuxa, jr and tanada, y., eds.).

Faust, C. L., A. P. Dobson, N. Gottdenker, L. S. Bloomfield, H. I. McCallum, T. R. Gillespie, M. Diuk-Wasser, and R. K. Plowright. 2017. Null expectations for disease dynamics in shrinking habitat: dilution or amplification? Philosophical Transactions of the Royal Society B: Biological Sciences 372:20160173.

Hall, S. R., L. Sivars-Becker, C. Becker, M. A. Duffy, A. J. Tessier, and C. E. Cáceres. 2007. Eating yourself sick: transmission of disease as a function of foraging ecology. Ecology Letters 10:207–218.

Halsey, S. 2019. Defuse the dilution effect debate. Nature ecology & evolution 3:145.

Hatcher, M. J., J. T. A. Dick, and A. M. Dunn. 2006. How parasites affect interactions between competitors and predators. Ecology Letters 9:1253–1271.

Keesing, F., L. K. Belden, P. Daszak, A. Dobson, and C. D. Harvell et al. 2010. Impacts of biodiversity on the emergence and transmission of infectious diseases. Nature 468:647–652.

Keesing, F., R. D. Holt, and R. S. Ostfeld. 2006. Effects of species diversity on disease risk. Ecology Letters 9:485–498.

Lafferty, K. D. 1993. Effects of parasitic castration on growth, reproduction and population dynamics of the marine snail cerithidea californica. Marine Ecology-Progress Series 96:229–229.

Lafferty, K. D., and C. L. Wood. 2013. It's a myth that protection against disease is a strong and general service of biodiversity conservation: Response to Ostfeld and Keesing. Trends in Ecology and Evolution 28:503–504.

Li, S., J. N. Eisenberg, I. H. Spicknall, and J. S. Koopman. 2009. Dynamics and control of infections transmitted from person to person through the environment. American journal of epidemiology 170:257–265.

Mihaljevic, J. R., M. B. Joseph, S. A. Orlofske, and S. H. Paull. 2014. The scaling of host density with richness affects the direction, shape, and detectability of diversity-disease relationships. PloS one 9:e97812.

Miller, E., and A. Huppert. 2013. The effects of host diversity on vector-borne disease: the conditions under which diversity will amplify or dilute the disease risk. PLoS One 8:e80279.

Miura, O., A. M. Kuris, M. E. Torchin, R. F. Hechinger, and S. Chiba. 2006. Parasites alter host phenotype and may create a new ecological niche for snail hosts. Proceedings of the Royal Society B: Biological Sciences 273:1323–1328.

Naug, D. 2014. Infected honeybee foragers incur a higher loss in efficiency than in the rate of energetic gain. Biology letters 10:20140731.

Normal, R., R. G. Bowers, M. Begon, and P. J. Hudson. 1999. Persistence of tick-borne virus in the presence of multiple host species: Tick reservoirs and parasite mediated competition. Journal of Theoretical Biology 200:111–118.

Novak, M., J. T. Wootton, D. F. Doak, M. Emmerson, J. A. Estes, and M. T. Tinker. 2011. Predicting community responses to perturbations in the face of imperfect knowledge and network complexity. Ecology 92:836–846.

Ogden, N. H., and J. I. Tsao. 2009. Biodiversity and lyme disease: Dilution or amplification? Epidemics 1:196–206.

O'Regan, S. M., J. E. Vinson, and A. W. Park. 2015. Interspecific contact and competition may affect the strength and direction of disease-diversity relationships for directly transmitted microparasites. The American Naturalist 186:480–494.

Ostfeld, R. S., and F. Keesing. 2013. Straw men don't get lyme disease: response to Wood and Lafferty. Trends in Ecology and Evolution 28:502–503.

Pedersen, A. B., S. Altizer, M. Poss, A. A. Cunningham, and C. L. Nunn. 2005. Patterns of host specificity and transmission among parasites of wild primates. International Journal of Parasitology 35:647–657.

Rigaud, T., M. Perrot-Minnot, and R. J. F. Brown. 2010. Parasite and host assemblages: embracing the reality will improve our knowledge of parasite transmission and virulence. Proceeding of the Royal Society B 277:3693–3702.

Roberts, M., and J. Heesterbeek. 2018. Quantifying the dilution effect for models in ecological epidemiology. Journal of The Royal Society Interface 15:20170791.

Rohr, J. R., D. J. Civitello, F. W. Halliday, P. J. Hudson, K. D. Lafferty, C. L. Wood, and E. A. Mordecai. 2019. Towards common ground in the biodiversity–disease debate. Nature Ecology & Evolution pages 1–10.

Rudolf, V. H. W., and J. Antonovics. 2005. Species coexistence and pathogens with frequency-dependent transmission. American Naturalist 166:112–118.

Salkeld, D. J., K. A. Padgett, and J. H. Jones. 2013. A meta-analysis suggesting that the relationship between biodiversity and risk of zoonotic pathogen transmission is idiosyncratic. Ecology Letters 16:679–686.

Searle, C. L., M. H. Cortez, K. K. Hunsberger, D. C. Grippi, I. A. Oleksy, C. L. Shaw, S. B. de la Serna, C. L. Lash, K. L. Dhir, and M. A. Duffy. 2016. Population density, not host competence, drives patterns of disease in an invaded community. American Naturalist 188:554–566.

Strauss, A. T., D. J. Civitello, C. E. Cáceres, and S. R. Hall. 2015. Success, failure and ambiguity of the dilution effect among competitors. Ecology letters 18:916–926.

Venesky, M. D., X. Liu, E. L. Sauer, and J. R. Rohr. 2014. Linking manipulative experiments to field data to test the dilution effect. Journal of Animal Ecology 83:557–565.

Williams, E. S., and I. K. Barker. 2008. Infectious diseases of wild mammals. John Wiley & Sons.

Wobeser, G. A. 2013. Essentials of disease in wild animals. John Wiley & Sons.

Wood, C. L., and K. D. Lafferty. 2013. Biodiversity and disease: a synthesis of ecological perspectives on lyme disease transmission. Trends in Ecology and Evolution 28:239–247.

Wood, C. L., K. D. Lafferty, G. De Leo, H. S. Young, P. J. Hudson, and A. M. Kuris. 2014. Does biodiversity protect humans against infectious disease? Ecology 95:817–832.

Yodzis, P. 1988. The indeterminacy of ecological interactions. Ecology 69:508–515.

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

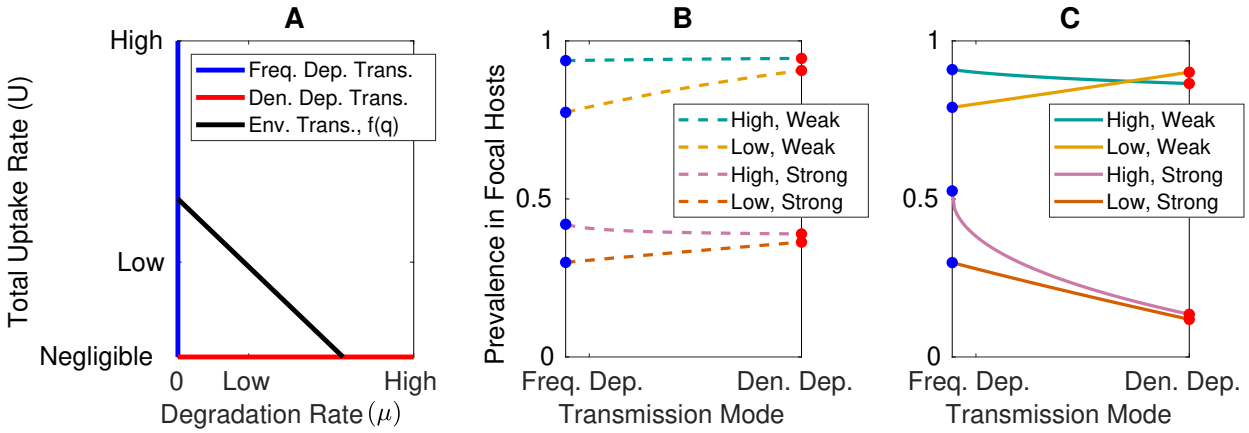

Figure 1: Environmental transmission models and density dependent and frequency dependent direct transmission models can be unified, which helps identify how the transmission mechanism influences infection prevalence in the focal host. (A) Environmental transmission sits intermediate between density dependent and frequency dependent direct transmission, with environmental transmission models 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). 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 function $f(q)$ is used to transform the environmental transmission model from a frequency dependent form (red dots) to a density dependent form (blue dots) while holding the allopatric equilibrium densities constant; see text for details. See appendix S1.6 for models and parameters.

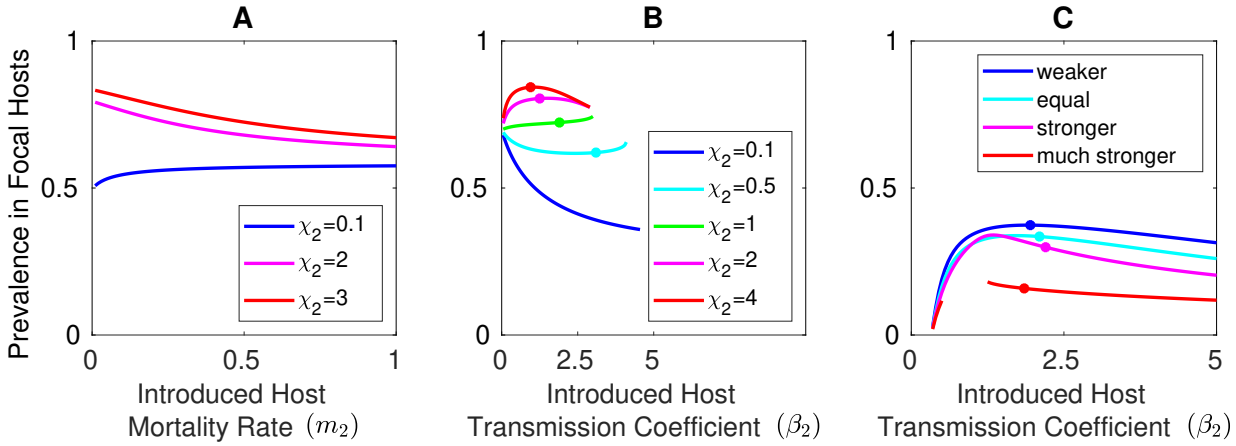

Figure 2: Increased competence of an introduced host leads to greater infection prevalence in a focal host, unless the introduced host is a sufficiently large sink for infectious propagules, one or both host experience strong positive density dependence at equilibrium, or infected hosts are stronger 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.

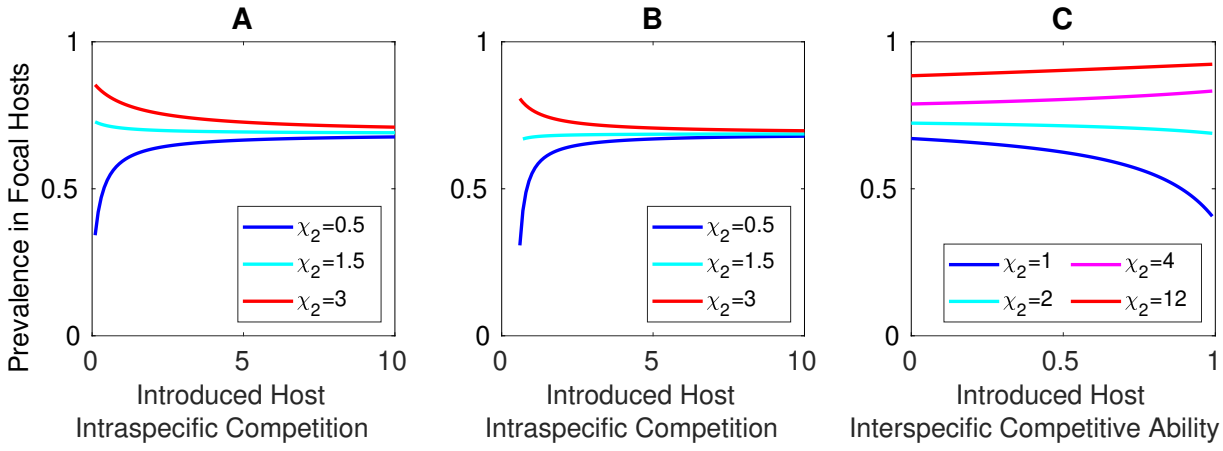

Figure 3: Increased intraspecific competitive ability of the introduced host leads to greater infection prevalence in the focal host and increased interspecific competitive ability of the introduced host leads to lower infection prevalence in a focal host, unless the introduced host is a sufficiently 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) larger source, or (red) much larger source. See appendix S1.6 for equations and parameters.

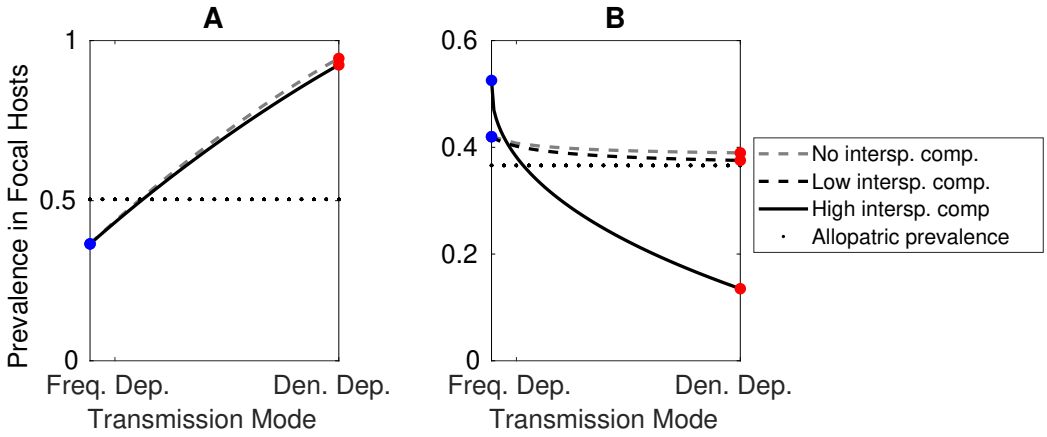

Figure 4: Interspecific host competition influences whether frequency dependent and density dependent direct transmission lead to different predictions about amplification and dilution in a focal host. (A) Frequency dependent direct transmission can cause dilution when density dependent direct transmission causes amplification in the (dashed gray) absence or (solid black) presence of interspecific competition. (C) 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 sympatric equilibrium prevalence in the focal host as the function $f(q)$ is used to transform the environmental transmission model from a frequency dependent form (red dots) to a density dependent form (blue dots) while holding the allopatric equilibrium densities for the focal host constant; see text for details. See appendix S1.6 for models and parameters.