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Indirect effects in a planktonic disease system

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ABSTRACT

Indirect effects, both density- and trait-mediated, have been known to act in tandem with direct effects in the interactions of numerous species. They have been shown to affect populations embedded in competitive and mutualistic networks alike. In this work, we introduce a four-dimensional system of ordinary differential equations and investigate the interplay between direct density-effects and density- and trait-mediated indirect effects that take place in a yeast parasite–zooplankton host–incompetent competitor system embedded in a food web which also includes resources and predators. Among our main findings is the demonstration that indirect effects cause qualitative and quantitative changes almost indistinguishable from direct effects and the corroboration through our analysis of the fact that the effects of direct and indirect mechanisms cannot be disentangled. Our results underpin the conclusions of past studies calling for comprehensive models that incorporate both direct and indirect effects to better describe field data.

1. Introduction

In multi-species systems, interactions among focal species can be affected by peripheral species (Holt and Hochberg, 2001). For example, the complex web of ecological interactions in which hosts and their parasites are embedded has the potential to substantially alter patterns of infection (Cáceres et al., 2014; Duffy et al., 2011; Searle et al., 2016). In the past 15 years, there has been a growing call for host–parasite models to embrace this community context (Hatcher et al., 2006; Johnson et al., 2015; Keesing et al., 2006; Tompkins et al., 2011). In response, it has been demonstrated that introducing a predator into a host–parasite system can indirectly cause the parasite's extinction if the predator pushes host density below the minimum threshold for transmission (Hatcher et al., 2006; Hatcher and Dunn, 2011). These density-mediated indirect effects have also been exemplified in recent theoretical work on disease dilution, where species with low competence act as sinks for infections, thereby decreasing disease prevalence (proportion of population that is infected) in focal species (Keesing et al., 2006; Kopp and Jokela, 2007; Nelson et al., 2015; Telfer et al., 2005; Thieltges et al., 2009). Density-mediated indirect effects can also result in amplified disease in a focal species if the peripheral species serves as a reservoir or otherwise (Kelly et al., 2009; Mastitsky and Veres, 2010; Paterson et al., 2013; Power and Mitchell, 2004). Clearly, density-mediated effects can play important epidemiological roles by modulating the intensity of parasite exposure; however, a focus on density alone neglects the importance of the individual traits that also drive transmission, and how those may be altered by peripheral species (Bryden et al., 2013; Hatcher et al., 2006; Preisser et al., 2005; Werner and Peacor, 2003).

By affecting a focal species' traits, peripheral species can also indirectly affect the outcome of interactions (trait-mediated indirect effect; Fig. 1) (Ohgushi et al., 2012; Preisser et al., 2005; Werner and Peacor, 2003). A broad suite of morphological, physiological, and behavioral traits may be indirectly affected, and in host–parasite interactions, trait-mediated indirect effects are particularly important if they alter a host's exposure or susceptibility to infection (Johnson et al., 2008). Both density-mediated and trait-mediated indirect effects are thought to be important in natural host–parasite systems, but each form has been understudied due to their difficulty of measurement, as well as the potentially infinite array of possible indirect effects (Johnson et al., 2015). Questions include whether both types of effect act antagonistically, additively, or synergistically to alter patterns of

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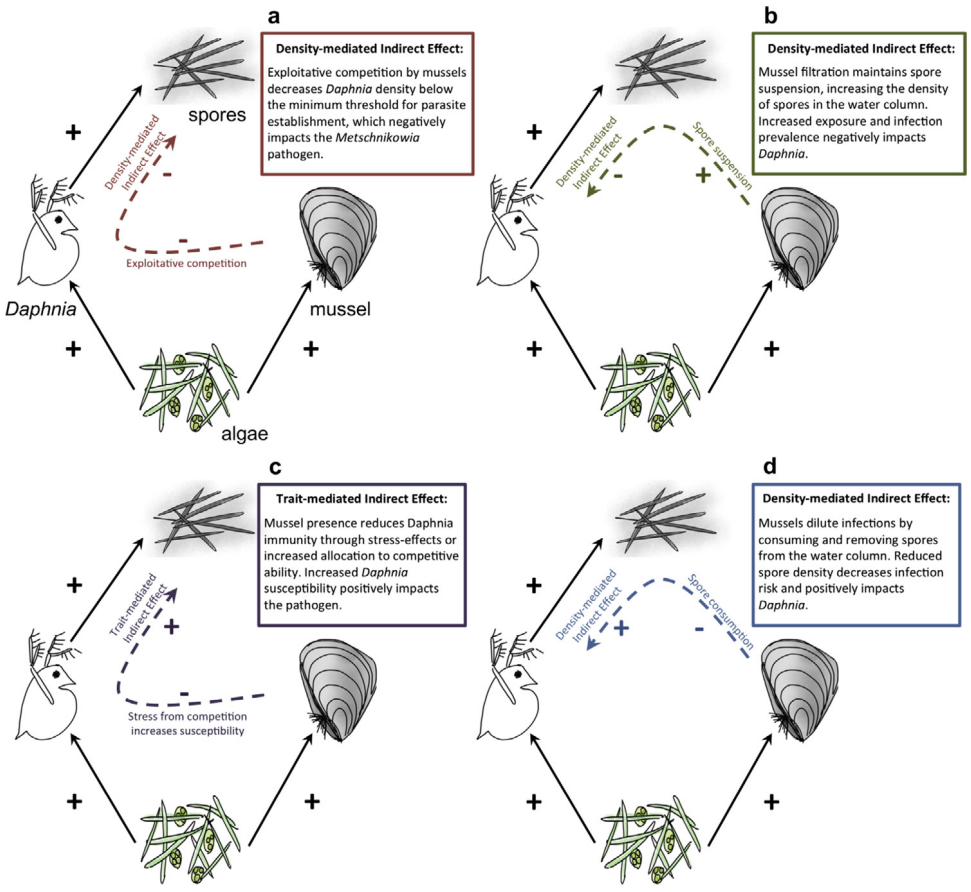

Fig. 1. A simplified food web is shown including only the *Daphnia* host, the mussel competitor *Dreissena*, algae and the free-living fungal spores. Four mechanisms (a–d) are outlined by which mussels may induce density- and trait-mediated indirect effects on the host and its pathogen. Solid arrows denote direct and dashed arrows indicate indirect effects. A $+/-$ sign is used to annotate the positive/negative effects.

disease, as well as what the relative impacts are of density-versus trait-mediated indirect effects.

Community modules provide a tractable method for isolating and examining the effects of multiple species (Holt and Hochberg, 2001), and we use them here to explore the importance of direct and indirect effects for parasite transmission in a multi-species planktonic system (Fig. 1). The focal host, *Daphnia*, is a cyclically parthenogenetic zooplankton that is widely distributed across the Midwestern United States. The focal parasite, *Metschnikowia*, is a common ascomycete fungal pathogen that produces environmentally transmitted spores that infect filter-feeding *Daphnia* (Ebert, 2005). Following ingestion, *Metschnikowia* achieve high intensity infections which ultimately kill the host, as is required for this parasite's transmission (Ebert, 2005). Here, we consider invasive *Dreissena* species (a mussel species) (Snyder et al., 1992) (*Dreissena polymorpha* and *Dreissena bugensis*) as the peripheral species in the *Daphnia*-fungus interaction. *Dreissena* can be a strong competitor with *Daphnia* (Wojtal-Frankiewicz et al., 2010), but is thought to be an incompetent (unsuitable) host for *Metschnikowia* (Kavouras et al.). We predict that the presence of *Dreissena* may alter disease dynamics in *Daphnia* through: competition with *Daphnia* for algal resources (Fig. 1a), the re-suspending (Fig. 1b) or consumption of spores (Fig. 1d), and an alteration of *Daphnia* susceptibility traits (Fig. 1c). This latter possibility is formulated as an increase in *Daphnia* susceptibility in response to mussel presence, which could occur through the immunosuppressive nature of stress (Adamo, 2012), or an allocation of energy away from *Daphnia* immune function to increased competitive ability. Using a four-dimensional nonlinear model based on ordinary differential equations, we investigated how the presence of *Dreissena* affects disease dynamics. We found that the introduction of invasive mussels to this host–parasite system has the potential to produce a variety of density-mediated and trait-mediated indirect effects (Fig. 1).

This article is structured as follows. In Section 2 we describe our model, in Section 3 we present bifurcation figures and other results that were obtained through analytical calculations, in Section 4 we summarize our findings, discuss their significance and offer future research directions. Details on our analytical calculations and additional figures resulting from the bifurcation analysis are contained in Appendices A through C.

2. Model

We divide the population of the focal host (*Daphnia*) into two classes: susceptible (S) and infected (I). We denote the free-living fungal spores by Z and algae by A. The invasive mussel competitor (*Dreissena*) appears in the model implicitly due to the slow timescale on which its dynamics operate. The average life-span of mussels is four years (Karatayev et al., 2006), whereas that of the *Daphnia* host (under laboratory) conditions is 50–150 days (Ebert, 2005). Then, the system of ordinary differential equations (ODEs) describing the dynamics is written as follows:

$$\frac{dS}{dt} = e_S f_S(A)(S + \rho I) - (d + p_S)S - \mu \frac{f_S(A)}{A} SZ \tag{1}$$

$$\frac{dI}{dt} = \mu \frac{f_S(A)}{A} SZ - (d + v + \theta_I p_S)I \tag{2}$$

$$\frac{dZ}{dt} = \sigma e_S f_S(A)[d+v]I - \lambda Z - \lambda_M Z - f_S(A)(S+I)\frac{Z}{A} \quad (3)$$

$$\frac{dA}{dt} = r(1-\frac{A}{K})A - f_S(A)(S+I) - f_M A \quad (4)$$

Variable units and parameter values and units are shown in Table 1 and follow our previous work (Cáceres et al., 2014; Rapti and Cáceres, 2016). This model is a synthesis of a consumer (S, focal host) — resource (A, algae) model which is a well studied classic model (Rosenzweig and MacArthur, 1963) with an equally seminal SI-model (Kermack and McKendrick, 1927) and a compartment for the free-living infectious propagules (Cáceres et al., 2009; Hall et al., 2009b, 2006). For other general models incorporating these or similar compartments see (Hilker and Schmitz, 2008; Hurtado et al., 2014). We now explain the terms used in the model (1)–(4).

In (1), the first term models the growth of the susceptible class, since both susceptible S and infected I hosts give birth to susceptible hosts, as there is no vertical transmission. However, infected hosts give birth at a reduced rate, denoted by $\rho e_S f_S(A)$, where $0 < \rho < 1$ (Duffy and Hall, 2008). The population growth rate is proportional to the feeding rate $f_S(A) = \frac{f_{S0}A}{h_S+A}$, which is a Holling type-II functional response with maximum feeding rate f_{S0} and half-saturation constant h_S. Here, e_S is the conversion efficiency of algal biomass to *Daphnia* biomass. Susceptible hosts die at a background rate of d and through predation at a constant rate p_S. Susceptible hosts are exposed to infectious propagules while filter-feeding and become infected at a per capita and per spore rate $\mu\frac{f_S(A)}{A}$. Here, μ denotes the host susceptibility to infectious propagules. The term $\frac{f_S(A)}{A}$ arises as follows. If one denotes the rate at which water is filtered by $w(A)$, then the functional response satisfies $f_S(A) = w(A) * A$. Since spores are ingested in the same manner as algae, the rate of ingesting spores then becomes $w(A) * Z = f_S(A)/A * Z$.

In (2), infected hosts experience an increase in their mortality based on direct effects of the pathogen (disease induced mortality at rate v), and selective predation at rate $\theta_I p_S$, where $\theta_I > 1$. The increased predation rate on I by visual predators, such as fish, occurs because infection with *Metschnikowia* renders the normally transparent *Daphnia* opaque and hence easier to detect (Duffy and Hall, 2008).

In (3), the density of free spores Z increases proportionally to the per capita death rate of infected hosts $d+v$; however, spores contained within living hosts are removed from the system if the infected host is consumed by a fish predator. Spore biomass within infected hosts depends on the host growth rate $e_S f_S(A)$ with a proportionality constant σ taking into account the conversion of host to spore biomass over the lifespan of the infected host (larger hosts harbor more spores on average). Hence, $\sigma e_S f_S(A)$ denotes the spore biomass contained in each dead infected *Daphnia* while $(d+v)I$ is the biomass of all dead *Daphnia* per unit time. Spores are lost due to sinking and other factors (Overholt et al., 2012) at a rate λ and when they are consumed by both host classes. They are also affected by mussels at a rate λ_M, where positive λ_M implies they are removed from the water column, while negative λ_M implies they are resuspended. We focus on parameter values such that $\lambda+\lambda_M \geq 0$, since mussels are unlikely to completely offset spore loss in the system.

In (4), algal resources are assumed to grow logistically at rate r with carrying capacity K and are lost due to consumption by *Daphnia* at rate $f_S(A)$ and *Dreissena* at rate f_M.

The above model resembles models from our previous work (Cáceres et al., 2014; Rapti and Cáceres, 2016), except for the introduction of two additional parameters that model the mussel contribution to spore removal/resuspension and algae removal:

- λ_M is the removal or addition (depending on its sign: positive for removal and negative for addition) of spores by *Dreissena* mussels;
- f_M is the feeding rate of *Dreissena* on algae.

We note that while adding λ_M is equivalent to varying λ, we introduce this additional parameter to distinguish between the different types of spore loss/resuspension and focus on the variations in spore densities explicitly due to the mussel presence. Similarly, adding f_M amounts to reducing the intrinsic growth rate r and carrying capacity K as can be seen with a simple rescaling.

We vary these two parameters λ_M and f_M as well as host susceptibility μ throughout this work to simulate the mechanisms (outlined in Fig. 1) by which the invasive mussels may affect the host-pathogen system. Also, the algal carrying capacity K and host half-saturation constant h_S are used as bifurcation parameters, due to the importance of resource competition and feeding in the infection process (Cáceres et al., 2014).

3. Analytical and numerical results

3.1. Density- and trait-mediated indirect effects

Dreissena mussels can indirectly affect *Daphnia* in at least three ways: (1) by competing for algal resources ($f_M > 0$), (2) by re-suspending infective spores in the water column through filter feeding ($\lambda_M < 0$), or (3) by removing infective spores through consumption ($\lambda_M > 0$). The first two cases represent negative density-mediated indirect effects to the *Daphnia* host from limited resource availability and higher exposure to infections, respectively, and the third case is representative of a positive density-mediated indirect effect to the *Daphnia* host from reduced exposure to infections. The mussels may also indirectly affect spore densities: through strong competition, mussels can decrease *Daphnia* density below the minimum threshold for parasite establishment (a density-mediated indirect effect) or competition-induced stress may increase host susceptibility to infections ($\mu >$ value in the absence of mussels) (Adamo, 2012), thus positively impacting the *Metschnikowia* pathogen (a trait-mediated indirect effect). These mechanisms are outlined in Fig. 1. In this section, we present analytical and numerical results related to the interplay between direct and indirect effects. This is achieved through the study of population dynamics and bifurcation analysis.

3.2. Equilibrium points and their stability

The four-dimensional system (1)–(4) has a rich dynamical behavior and may reach one of many equilibrium points or undergo sustained oscillations. In this subsection we outline the main features of the equilibrium points and their stability. Additional mathematical details are provided in appendices A (existence) and B (stability).

The trivial equilibrium $E_0 = (0, 0, 0, 0)$, while it exists for all parameter values, is linearly unstable as long as $r > f_M$, namely when the algal intrinsic growth rate surpasses the mussel feeding rate. Since it is not biologically interesting, it will not be explored any further.

When only algae persists the equilibrium is $E_A = (0, 0, 0, A_A)$, where $A_A = \frac{(r-f_M)}{r}K$. The previous expression implies that it is biologically feasible as long as $r > f_M > 0$. When $r = f_M$ a transcritical bifurcation occurs and it coalesces with the trivial equilibrium E_0.

The disease free equilibrium $E_S = (S_S, 0, 0, A_S)$ is given by

$$A_S = \frac{(d+p_S)h_S}{e_S f_{S0} - (d+p_S)}, \quad S_S = \left((r-f_M) - \frac{rA_S}{K}\right)\frac{e_S A_S}{d+p_S} \quad (5)$$

Table 1
Variables and parameters.

Variable	Unit
S susceptible host	mg C/L
I infected host	mg C/L
Z fungal spores	mg C/L
A algae	mg C/L
t time	day
Parameter	**Value**
e_S: conversion efficiency	0.6 mg C/ mg C (Scheffer et al., 1997)
f_{S0}: maximal feeding rate	0.32 /day mg C/mg C (Scheffer et al., 1997)
h_S: half saturation constant (susceptible)	0.0–0.6 mg C/L (Scheffer et al., 1997)
ρ: reduced fecundity parameter	0.9 (Hall et al., 2010)
p_S: predation rate	0.1/day (Scheffer et al., 1997)
θ_I: predation selectivity	3
d: background mortality	0.03/day (Hall et al., 2009a)
μ: host susceptibility	10 mg C/mg C (Hall et al., 2010)
v: virulence	0.05/day (Hall et al., 2010)
σ: spore release parameter	31 days $\times$mg C/mg C (Hall et al., 2009a)
λ: spore loss rate	0.2/day (Hall et al., 2009a)
λ_M: spore removal/resuspension rate	-0.1 to 0.1/day
r: algal net maximal growth rate	0.2/day (Scheffer et al., 1997)
K: algal carrying capacity	0.0–6 mg C/L
f_M: mussel feeding rate	0–0.20/day

and is biologically feasible as long as

$$0 < A_S < \left(1 - \frac{f_M}{r}\right) K = A_A.$$

From this condition it follows that $A_S = A_A$ yields $S_S = 0$, hence this equilibrium coalesces with E_A through a transcritical bifurcation. It may also lose stability through a Hopf bifurcation, which is explored numerically in the next subsection or through another transcritical bifurcation, this time with the endemic equilibrium $E_E = (S_E, I_E, Z_E, A_E)$. The expressions for these equilibrium densities are too cumbersome to be presented here, and are instead given in Eqs. (11)–(14) (Appendix A). The endemic equilibrium may also lose stability through a Hopf bifurcation which is studied numerically.

3.3. Bifurcation analysis: Role of f_M, λ_M and μ

As a first step in the investigation of how the previous mechanisms affect disease dynamics and population densities, we study the bifurcations taking place in the system. Specifically, we vary key parameters that control the mechanisms outlined in Section 3.1. These parameters are the mussel feeding rate f_M, the mussel spore removal/resuspension rate λ_M (depending on its sign, which is positive for removal and negative for resuspension) and host susceptibility μ. In our bifurcation analysis, we vary the algal carrying capacity K and the half saturation constant for the feeding rate of the focal host h_S.

First, we consider the case when mussels are absent, namely when $f_M = 0 = \lambda_M$ and the focal host susceptibility parameter is set at its default value $\mu = 10$. The bifurcation curves are straight lines that can be solved explicitly and are provided in Eqs. (10) and (15) in appendices A and B, while figures are provided in Appendix C. Depending on the slope $\frac{h_S}{K}$, three outcomes are possible:

(a) only algae persists if $\frac{h_S}{K} > 0.4769$;

(b) the system reaches the disease-free steady state if $0.4132 < \frac{h_S}{K} < 0.4769$; and

(c) the system reaches the endemic steady-state if $\frac{h_S}{K} < 0.4132$.

We note that this finding generalizes the known result for the Rosenzweig–MacArthur model (Rosenzweig and MacArthur, 1963; Rosenzweig, 1971) on which our model is based.

Next, we consider the case when $f_M = 0.16$ and $\lambda_M = 0$, namely when mussels feed on algae ($f_M > 0$), but neither resuspend nor remove any spores ($\lambda_M = 0$). Also, it is assumed that host susceptibility is not altered ($\mu = 10$). The possible outcomes are

(a) only algae persists if $\frac{h_S}{K} > 0.0954$;

(b) the system reaches the disease-free steady state if $0.0385 < \frac{h_S}{K} < 0.0954$; and

(c) algae and the focal coexist and undergo oscillations if $\frac{h_S}{K} < 0.0385$.

This phenomenon is known as the paradox of enrichment (Rosenzweig, 1971). The destabilization can be explained as follows: given a certain value of h_S, if the carrying capacity K is large enough, the focal host population grows excessively large, which causes the algal population to crash. This is then followed by a decline in the host-consumer population which allows the algae to replenish. Lower values of K, restrain the host-consumer population, hence the dynamics are stable. Even with $\lambda_M = 0$, competition is enough to prevent the disease from persisting. We repeated the bifurcation analysis with positive λ_M ($\lambda_M = 0.1$) and the result did not change even though host susceptibility was set at $\mu = 15$. This case demonstrates the fact that the dilution effect of mussels overshadows any negative effect to the host due to stress-induced immunity reduction, manifested here by an increase in μ.

We also consider the case when $f_M = 0.16$, $\lambda_M = -0.1$ and $\mu = 10$, namely when mussels feed on algae ($f_M > 0$), resuspend spores ($\lambda_M < 0$), and do not affect host susceptibility ($\mu = 10$). The possible outcomes are the following.

(a) Only algae persists if $\frac{h_S}{K} > 0.0954$;

(b) the system reaches the disease-free steady state if $0.0635 < \frac{h_S}{K} < 0.0954$; and

(c) the system reaches the endemic steady state if $0.0455 < \frac{h_S}{K} < 0.0635$; and

(d) all four populations persist in an oscillatory manner if $\frac{h_S}{K} < 0.0455$.

Hence, the effect of spore resuspension is the expected one: disease reappears. Therefore, the previous positive effect to the *Daphnia* host of the competitor may be eclipsed if it resuspends spores, thus increasing the contact between spores and hosts.

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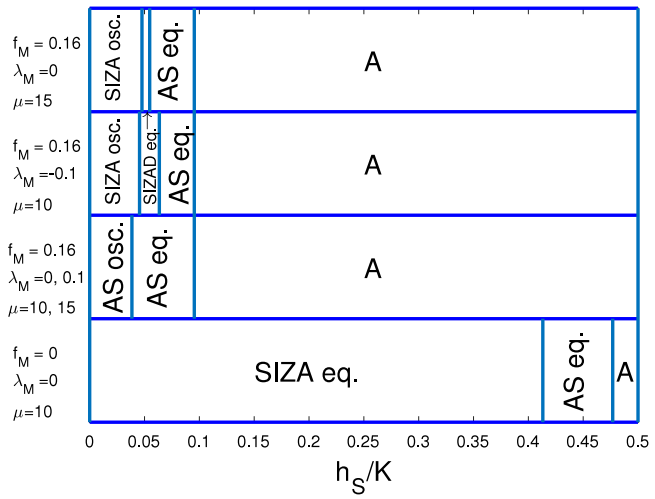

Fig. 2. The system dynamics are summarized as a function of the ratio of host half-saturation constant h_S over algal carrying capacity K for different values of mussel feeding rate f_M, spore removal/resuspension rate by the mussels $\lambda_M = 0$, and host susceptibility parameter μ. A denotes the equilibrium where only algae is present, AS eq. denotes the disease free equilibrium, AS osc. denotes oscillations of the focal host and algae, SIZA eq. denotes the endemic equilibrium, and SIZA osc. denotes endemic oscillations. All other parameters are at their default values and follow Table 1.

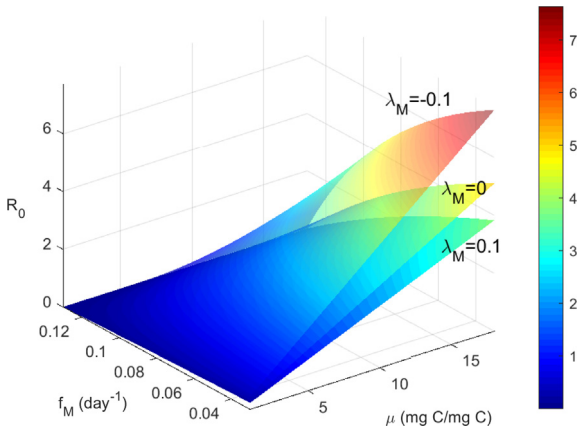

Fig. 3. The basic reproductive number R_0 as a function of host susceptibility μ and mussel feeding rate f_M. As the spore resuspension/removal rate by the mussels λ_M is varied from $\lambda_M = -0.1$ (resuspension), to $\lambda_M = 0$ (neither resuspension, nor removal) and then to $\lambda_M = 0.1$ (removal), R_0 decreases. However, the value of R_0 also depends nonlinearly on f_M and linearly on μ, which may vary due to mussel presence. Carrying capacity is set at $K = 3$ and the host's half-saturation constant is $h_S = 0.5$. All other parameters are at their default values and follow Table 1.

The final case we considered is when $f_M = 0.16$, $\lambda_M = 0$ and $\mu = 15$, namely when mussels feed on algae ($f_M > 0$), neither resuspend nor remove spores ($\lambda_M = 0$), but increase the susceptibility of the focal host $\mu = 15$. The possible outcomes are identical to the preceding case, but occur at different values of the slope when the transcritical bifurcation from the disease-free to the endemic steady state ($\frac{h_S}{K} = 0.0547$) and the Hopf bifurcation of the endemic steady state ($\frac{h_S}{K} = 0.0477$) take place. Hence, the effect of a stress-induced increase in host susceptibility is the expected one: disease reappears. Therefore, the previous positive effect to the focal host of the competitor may be reversed by its effect on modifying the host's traits.

This analysis demonstrates that it may be hard to disentangle indirect from direct effects even in relatively simple disease systems. This feature is not limited to the location of bifurcation curves. As we show later in this section, different combinations of direct and indirect effects produce quantitatively similar population densities, as well. All results are summarized in Fig. 2. It must be noted that several bifurcation slopes were obtained numerically.

3.4. Prevalence and density: Role of f_M and μ

Next, we study the role of f_M and μ on the basic reproductive ratio R_0 as well as population densities and disease prevalence $\frac{I}{S+I}$ at equilibrium. R_0 is defined as the average number of secondary infections produced by a single infectious host in a population of entirely susceptible hosts (Hethcote, 2000). It is a threshold that describes when a disease can invade a susceptible host population. In our system, it is obtained through a linear stability analysis of the disease-free equilibrium point, the details of which are presented in Appendix B. The exact expression for our model is

$$R_0 = \frac{\sigma e_S f_S(A_S)(d+v)}{(d+v+\theta_I p_S)\left(\lambda+\lambda_M+\frac{f_S(A_S)}{A_S}S_S\right)}\mu\frac{f_S(A_S)}{A_S}S_S, \tag{6}$$

where the densities at the disease-free equilibrium state for the host S_S and the algae A_S are given in Eq. (5). Its various components have the following biological interpretation. The term $\sigma e_S f_S(A_S)(d+v)$ denotes the release rate of spore biomass per unit host biomass, while $\mu\frac{f_S(A_S)}{A_S}S_S$ denotes the infection rate per unit spore biomass. R_0 is proportional to the lifespan of infected hosts $(d+v+\theta_I p_S)^{-1}$ as well as the lifespan of the spores $\left(\lambda+\lambda_M+\frac{f_S(A_S)}{A_S}S_S\right)^{-1}$.

In Fig. 3 we plot R_0 as a function of μ, which varies from 1 to 18 and f_M, which varies from 0.03 to 0.13 for three different values of λ_M, namely $\lambda_M = -0.1$ (spore resuspension), $\lambda_M = 0$ (neither removal, nor resuspension) and $\lambda_M = 0.1$ (spore removal). One observes that for large enough f_M it holds $R_0 < 1$, while as f_M decreases, high values of μ result in $R_0 > 1$. Therefore, when the competitor removes algae at a high rate f_M, no matter how high host susceptibility μ is, the disease cannot persist. On the other hand, for lower values of f_M, high enough μ allows the disease to persist. We notice that the behavior of R_0 is qualitative similar in all three surface plots, regardless of the value of λ_M. As the spore removal rate λ_M decreases, R_0 increases monotonically, but in a nonlinear fashion. For this figure, the values $K = 3$ and $hs = 0.5$ were chosen.

In Fig. 4 we plot the equilibrium densities for algae, the susceptible and infected hosts, the spores and disease prevalence as f_M varies. We used the value $\mu = 15$, while the other parameters are at their default values. We observe that as the feeding rate of the mussels f_M increases, algal density decreases monotonically in the endemic (SIZA region), stays constant in the disease-free (AS) region and decreases monotonically in the region where no hosts are present (panel a). Similarly, the susceptible host density decreases monotonically in the endemic (SIZA) and the disease-free (AS) regions, until it reaches the zero value in the only algae (A) region (panel b). In the endemic region, the density of the infected hosts and fungal spores (panel c) and disease prevalence (panel d) decrease monotonically with f_M. Hence, as competition for resources becomes more intensive, algal density decreases, as do the densities of the focal hosts and fungal spores. This figure highlights the unexpected effect on an invasive species on population densities of indigenous species and their pathogens, namely as competition increases the disease is eliminated but at a cost to the focal host in terms of decreased population density.

In Fig. 5 we plot the endemic equilibrium densities as a function of f_M for three combinations of values for μ and λ_M. Specifically, we consider the following cases (i) $\mu = 10$, $\lambda_M = -0.05$

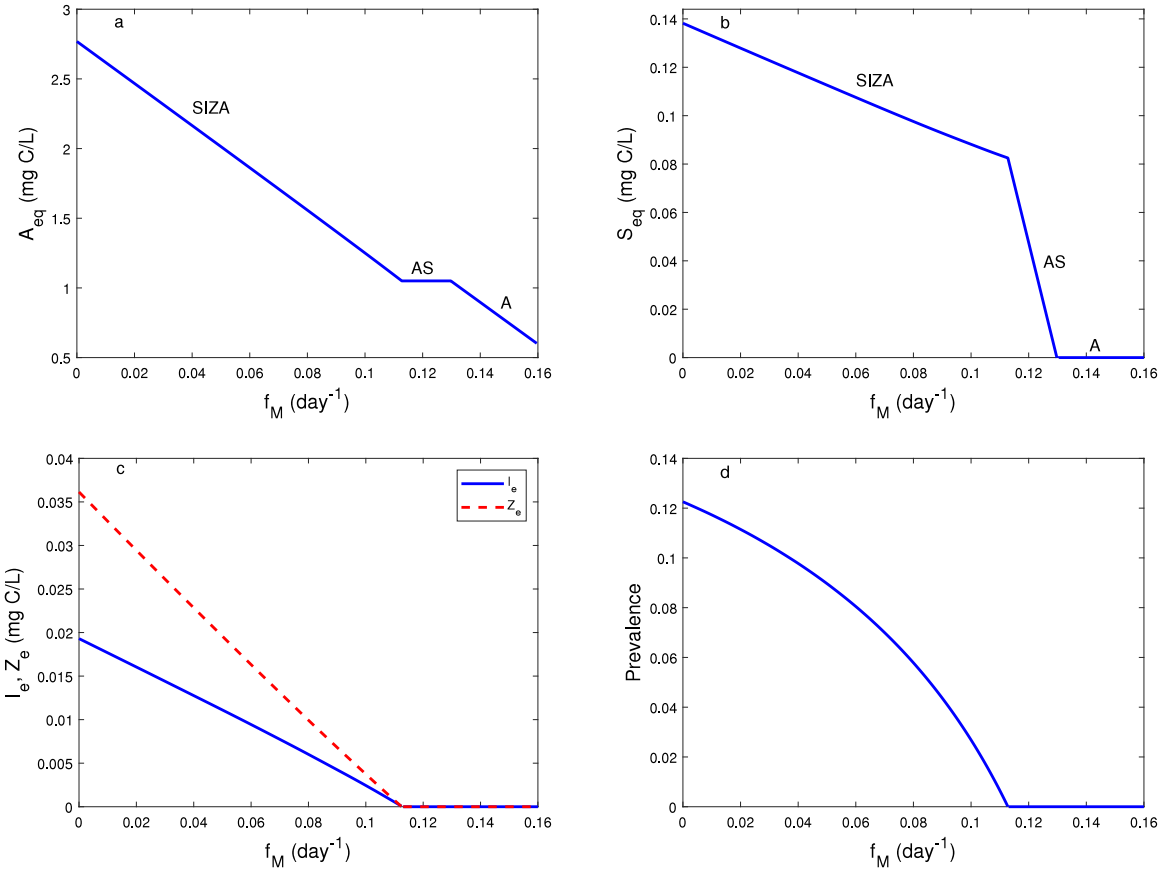

Fig. 4. The equilibrium densities of algae A (panel a), susceptible hosts S (panel b) infected hosts I and fungal spores Z (panel c) and disease prevalence (panel d) as the feeding rate f_M of mussels varies. The annotations SIZA (endemic equilibrium), AS (disease-free equilibrium) and A (algae only) refer to the equilibrium at which the system is. Here, host susceptibility is set at $\mu = 15$, mussel feeding rate is $\lambda_M = 0$, carrying capacity is $K = 3$ and the host's half-saturation constant is $h_S = 0.5$.

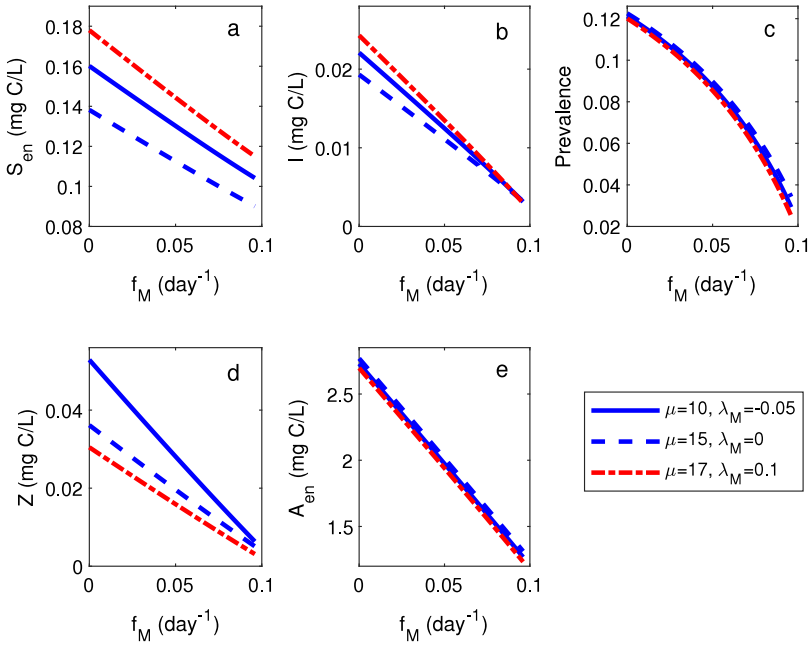

Fig. 5. The equilibrium densities of the susceptible (S_{en}, panel a) and infected (I, panel b) hosts, spores (Z, panel d), and algae (A_{en}, panel e), as well as prevalence (panel c) as a function of mussel feeding rate f_M. In all panels, $K = 3$ and $h_S = 0.5$ and three cases are considered: $\mu = 10$, $\lambda_M = -0.05$ (solid blue line), $\mu = 15$, $\lambda_M = 0$ (dashed blue line), $\mu = 17$, $\lambda_M = 0.1$ (dashed–dotted red line). All other parameters are at their default values and follow Table 1. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

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where the mussels resuspend spores, but do not induce stress-related immunological changes in the host; (ii) $\mu = 15$, $\lambda_M = 0$ where the mussels increase the host's susceptibility (by 50%) due to competition stress, but neither remove nor resuspend spores; and finally, (iii) $\mu = 17$, $\lambda_M = 0.1$ where the mussels remove spores, and cause an increase in the host's susceptibility due to stress. As expected, since the mussels consume more algae as f_M increases, all equilibrium population densities decrease. However, this result yet again highlights the fact that different combinations of direct and indirect effects yield practically indistinguishable disease prevalence (panel c) and algal population densities (panel e). Moreover, densities for the infected class (panel b) and spores (panel d) are close, at least for some combinations of parameter values. Finally, the density of the susceptible host decreases to no less than 77% of the maximum among the three parameter choices (panel a). Hence, if one is faced with the question to disentangle, based on available data, direct from indirect effects, this might not be possible due to practical parameter identifiability issues. As one sees in these model simulations, this phenomenon persists for a wide range of mussel feeding rate values: from the mussels being absent ($f_M = 0$) until the endemic equilibrium becomes zero ($f_M \approx 0.1$).

4. Discussion

Holt & Hochberg in Holt and Hochberg (2001) first introduced the community module as a closed system within which the implications of indirect effects could be explored. Indirect effects are predicted to result in novel outcomes by influencing a focal species' population density, in addition to its individuals' traits (Preisser et al., 2005; Werner and Peacor, 2003). While indirect effects have been well explored for predator–prey interactions (Bertram et al., 2013; McCoy and Bolker, 2008; Orlofske et al., 2012; Pangle et al., 2007; Preisser et al., 2005), as well as interactions with non-native and invasive species (Holt and Hochberg, 2001; Pangle et al., 2007), host–parasite interactions remain one area that can benefit through incorporating density- and trait-mediated indirect effects (Hatcher et al., 2006; Hatcher and Dunn, 2011; Johnson et al., 2008). Using the *Daphnia-Metschnikowia* system as a theoretical model, we have demonstrated that an invasive species can destabilize host–parasite dynamics through its indirect competitive effects. Specifically, strong competition by the invasive *Dreissena* mussel results in the suppression or exclusion of the native parasite, alongside substantial decreases in *Daphnia* density (Fig. 4).

We examined four indirect effect pathways, three density-mediated and one trait-mediated (Fig. 1), and found that *Metschnikowia* is fully excluded in half of these scenarios. In these two cases, strong exploitative competition by *Dreissena* results in *Daphnia* densities that fall below the threshold density for transmission, where R_0 is less than one. This is a similar finding as that of Searle et al. (2016), which documented that interspecific competition can reduce disease by decreasing both native and invasive host density. Searle et al. (2016) focused on two *Daphnia* species with only slight variation in competitive ability, and our results magnify this competitive asymmetry by focusing on competitors with broad differences in body size, lifespan, and feeding rates. These results seem to be true for more general models: while our model uses a Holling type-II functional response and incorporates feeding dependent spore removal, numerical simulations suggest that the dynamics and major qualitative results are not changed substantially if these are replaced by simpler expressions. At first glance, the loss of the *Metschnikowia* pathogen might be considered a benefit for the *Daphnia* host. However, *Metschnikowia* exclusion comes at a cost for the host: *Daphnia* suffered lower host densities in competition than when alone with the pathogen (Searle et al., 2016), and we find that *Daphnia* density is also higher in the presence of the endemic *Metschnikowia* pathogen than it is in the presence of the invasive mussel competitor (Fig. 4 and also supported by data Kavouras et al.). Hence, the population-level costs of an introduced competitor can well exceed those of a native parasite.

The first departure from parasite exclusion occurred when we incorporated a trait-mediated indirect effect. Even in the presence of strong mussel competition, *Metschnikowia* is able to remain in the system if host susceptibility is sufficiently increased. In this instance, two indirect effects act antagonistically: the parasite is suppressed through a density-mediated indirect effect, but simultaneously amplified through a trait-mediated indirect effect (Fig. 1). Ultimately, the trait-mediated effect dominates, and this finding supports a recently advanced idea that trait-mediated indirect effects can be as strong if not stronger than density-mediated indirect effects (Preisser et al., 2005; Werner and Peacor, 2003). We have a limited understanding of the mechanisms that underlie and shape *Daphnia* susceptibility, but an increase in susceptibility in response to competition is feasible. First, stress is generally considered to be immunosuppressive (Adamo, 2012), and mussel competitors could produce a stress response in *Daphnia* that reduces their ability to resist or clear infections. Second, mussel competition could increase *Daphnia* susceptibility through trade-offs if *Daphnia* shunt energy from immune defenses to allocate toward competitive traits. Direct evidence for trait-mediated indirect effects affecting host susceptibility has been provided in the monarch-*Ophriocystis* system. De Roode et al. (de Roode et al., 2011) demonstrated that aphids can indirectly reduce monarch parasite resistance through their feeding interactions with milkweed, and this has knock-on effects for both the prevalence and virulence of the *Ophriocystis* pathogen. How trait-mediated indirect effects amplify or suppress parasite transmission remains an exciting area in invertebrate systems, and one that will certainly grow as we gain information about the sensitivity and plasticity of invertebrate immune responses.

We have so far demonstrated that the invasive *Dreissena* mussel can indirectly affect the *Metschnikowia* parasite through its effects on host density and traits. However, the opposite path is also possible, wherein the mussel directly affects the parasite which then indirectly affects the host. Because *Dreissena* is a filter feeder, it may interact with infectious spores in the water column, and we allowed it to consume (positive λ_M) or re-suspend (negative λ_M) *Metschnikowia* spores (Fig. 1 bottom panels). *Dreissena* can hence be evaluated as a spore diluter or as an amplifier to determine the relative strength of these indirect effects. Interestingly, the competition only scenario is similar to the dilution scenario, that is, the diluting effects of *Dreissena* on the parasite are strongly overwhelmed by those of strong competition. This is also evident in Fig. 5, where it is shown that besides producing qualitatively equivalent bifurcation figures, these effects also produce quantitatively almost identical equilibrium population densities. This finding should signal caution for those studying biodiversity–disease relationships; while dilution in the strict sense is certainly occurring, the actual reduction in parasite density is accomplished entirely through low host density, with dilution through consumption being an incidental occurrence. For density-dependent transmission, decreased disease is predicted to occur when the addition of a species reduces the density of the focal host (Rudolf and Antonovics, 2005).

Only within limited parameter space did *Dreissena* presence result in *Metschnikowia* endemicity, a result driven by elevation in *Daphnia* susceptibility rather than *Dreissena* susceptibility. However, *Dreissena* can and do amplify native disease when they serve as alternative hosts for parasites (Mastitsky and Veres, 2010). In the interplay among natives, invasives, and parasites, predicting

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which species will decline becomes exceedingly complicated as we factor in each host's susceptibility and capacity to transmit infection (termed "competence"). For example, Mordecai (2013) documented coexistence of all three players (e.g. native bunchgrass host, invasive cheatgrass host, and exotic fungal pathogen) that appeared to be promoted by the pathogen's negative effects on the invasive, and more susceptible, host. Alternatively, haemoparasites of native wood mice in Ireland decreased following the introduction of voles, which acted as low-competence sinks for the parasite (Telfer et al., 2005). Native hosts, too, have declined in response to parasite spillover (e.g. squirrels; Tompkins et al., 2003) and parasite spillback (e.g. fish; Paterson et al., 2013) from introduced hosts. These outcomes seem as diverse as the systems they span, and require a careful consideration of how host density and competence operate together to influence the performance of competing hosts and their parasites.

Finally, we found that *Metschnikowia* was able to persist when mussels re-suspended spores. This amplification could theoretically occur via the mussel filtration process, since *Dreissena* are important players in the movement and circulation of aquatic particles (Fanslow et al., 1995). Interestingly, spore re-suspension by *Dreissena* produced similar outcomes as the trait-mediated indirect effect. This finding highlights the importance of both host exposure and susceptibility in this system, as increased *Daphnia* susceptibility produced almost equivalent results as increased spore density. The past decade of research has revealed numerous ecological factors that influence *Metschnikowia* epidemics through directly affecting spore density and rates of host exposure (Cáceres et al., 2006, 2009; Duffy et al., 2011; Hall et al., 2007). *Daphnia* can recover from infection with *Metschnikowia* and show considerable variation in their immunological defenses (Stewart Merrill and Cáceres, 2018; Stewart Merrill et al., 2019); however, the contribution of immunological processes to these dynamics is unknown. Further research into the mechanisms of *Daphnia* susceptibility will reveal the extent to which host defenses contribute to infection dynamics.

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Appendix A. Existence of equilibrium points

The trivial equilibrium $E_0 = (0, 0, 0, 0)$ exists for all parameter values. Biologically this means that neither the focal host and the competing mussels, nor any algae is left in the water column.

The equilibrium where only algae persists $E_A = (0, 0, 0, A_A)$ is given by

$$A_A = \frac{(r - f_M)}{r} K \tag{7}$$

and is biologically feasible (positive) as long as

$$r > f_M > 0.$$

This has the following significance. In the absence of the focal host, in order algae to persist, its intrinsic growth rate r must be larger than the loss rate f_M due to the mussels. When $r = f_M$ a bifurcation occurs and this equilibrium coalesces with the trivial equilibrium E_0.

The disease free equilibrium $E_S = (S_S, 0, 0, A_S)$ is given by

$$A_S = \frac{(d + p_S)h_S}{e_S f_{S0} - (d + p_S)} \tag{8}$$

$$S_S = \left((r - f_M) - \frac{rA_S}{K}\right) \frac{e_S A_S}{d + p_S} \tag{9}$$

and is biologically feasible as long as

$$0 < A_S < \left(1 - \frac{f_M}{r}\right) K = A_A,$$

which practically states that the resource requirement A_S of the focal host must be smaller than the density A_A of the equilibrium where only algae persists. When $A_S = A_A$, Eq. (9) implies that $S_S = 0$, hence this equilibrium coalesces with E_A. Using (7) and (8), the condition $A_S = A_A$ can be written equivalently as

$$h_S = \frac{e_S f_{S0} - (d + p_S)}{d + p_S} \frac{r - f_M}{r} K. \tag{10}$$

The endemic equilibrium $E_E = (S_E, I_E, Z_E, A_E)$ satisfies the following algebraic equations

$$\frac{S_E}{I_E} = \frac{d + v + \theta_I p_S - \rho e_S f_S(A_E)}{e_S f_S(A_E) - (d + p_S)} \tag{11}$$

$$Z_E = \frac{(d + v + \theta_I p_S)A_E}{\mu f_S(A_E)} \frac{e_S f_S(A_E) - (d + p_S)}{d + v + \theta_I p_S - \rho e_S f_S(A_E)} \tag{12}$$

$$I_E = \frac{\lambda + \lambda_M + r(1 - \frac{A_E}{K}) - f_M}{\sigma e_S f_S(A_E)(d + v)} \frac{d + v + \theta_I p_S}{\mu f_S(A_E)} \frac{(e_S f_S(A_E) - (d + p_S))A_E}{d + v + \theta_I p_S - \rho e_S f_S(A_E)} \tag{13}$$

$$S_E = \frac{\lambda + \lambda_M + r(1 - \frac{A_E}{K}) - f_M}{\sigma e_S f_S(A_E)(d + v)} \frac{(d + v + \theta_I p_S)A_E}{\mu f_S(A_E)} \tag{14}$$

It also follows from (4) that

$$S_E + I_E = \left(rA_E\left(1 - \frac{A_E}{K}\right) - f_M A_E\right) \frac{1}{f_S(A_E)}.$$

This yields the following cubic polynomial for A_E:

$$\begin{aligned}
&[r(d + v + \theta_I p_S)(v + (\theta_I - 1)p_S + e_S f_{S0}(1 - \rho)) - \\
&\ r\mu\sigma e_S f_{S0}(d + v)((d + v + \theta_I p_S) - \rho e_S f_{S0})](A_E)^3 + \\
&[\mu\sigma e_S f_{S0}(d + v)[(d + v + \theta_I p_S - \rho e_S f_{S0})K(r - f_M) \\
&\ - (d + v + \theta_I p_S)h_S r] + \\
&rh_S(d + v + \theta_I p_S)(v + (\theta_I - 1)p_S) - \\
&((v + (\theta_I - 1)p_S) + e_S f_{S0}(1 - \rho))((\lambda + r + \lambda_M - f_M)K \\
&\ - rh_S)(d + v + \theta_I p_S)](A_E)^2 + \\
&(d + v + \theta_I p_S)[(r - f_M)\mu\sigma e_S f_{S0}(d + v)Kh_S - \\
&((\lambda + \lambda_M - f_M + r)K - rh_S)(v + (\theta_I - 1)p_S)h_S \\
&\ - (\lambda + \lambda_M - f_M + r)Kh_S[v + (\theta_I - 1)p_S + e_S f_{S0}(1 - \rho)]]A_E \\
&\ - (d + v + \theta_I p_S)(\lambda + \lambda_M - f_M + r)Kh_S^2(v + (\theta_I - 1)p_S) = 0.
\end{aligned}$$

One can observe that when $A_E = A_S$, then $I_E = Z_E = 0$ and the endemic equilibrium coalesces with the disease free one. This is expected, since $A_E = A_S$ implies that the resource requirements for the focal hosts in the endemic state equal those in the disease free state.

Appendix B. Stability of equilibrium points

Next, we present the analytically tractable stability results used to generate the bifurcation figures and to obtain the basic reproductive number R_0.

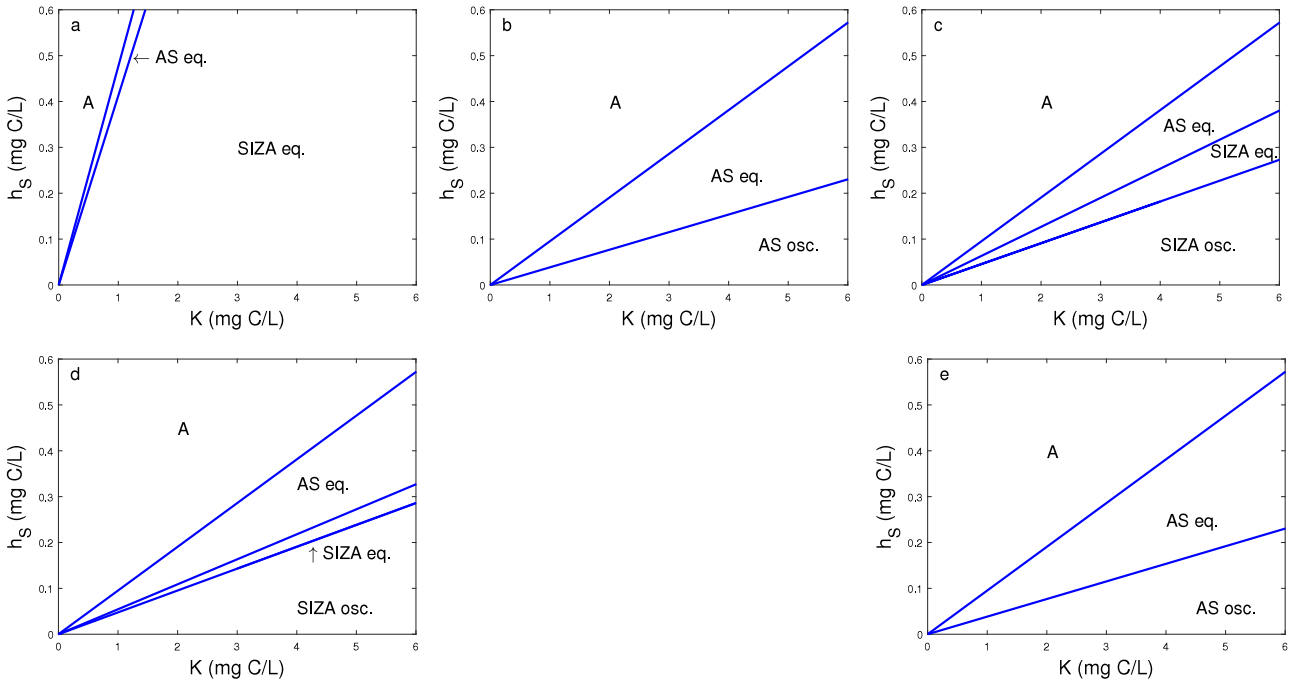

Fig. 6. Using as bifurcation parameters the host half saturation h_S and algal carrying capacity K, we demonstrate different mechanisms in which mussel presence may affect *Daphnia*. In panel a, no mussels are present and the susceptibility parameter is set at its default value $\mu = 10$. In panel b, mussel feeding rate is set at $f_M = 0.16$ and spore removal/resuspension is set at $\lambda_M = 0$). In panel c, $f_M = 0.16$ and $\lambda_M = -0.1$, namely mussels feed on algae and resuspend spores. In panel d, $f_M = 0.16$ and $\lambda_M = 0$, namely mussels feed on algae, neither resuspend nor release spores, but increase the host's susceptibility ($\mu = 15$). In panel e, $f_M = 0.16$, $\lambda_M = 0.1$ and $\mu = 15$. Namely, mussels feed on algae, remove spores and increase host susceptibility. *A* denotes the equilibrium where only algae is present, AS eq. denotes the disease free equilibrium, AS osc. denotes oscillations of the focal host and algae, SIZA eq. denotes the endemic equilibrium, and SIZA osc. denotes endemic oscillations. All other parameters are at their default values and follow Table 1.

The Jacobian matrix for the dynamical system (1)–(4) is the following:

$$\left(\begin{array}{c|c|c|c} e_S f_S(A) - (d + p_S) - \mu \frac{f_S(A)}{A} Z & \rho e_S f_S(A) & -\mu \frac{f_S(A)}{A} S & e_S(S+\rho I)\frac{df_S(A)}{dA} - \mu \frac{d}{dA}\left(\frac{f_S(A)}{A}\right) SZ \\ \hline \mu \frac{f_S(A)}{A} Z & -(d+v+\theta_I p_S) & \mu \frac{f_S(A)}{A} S & \mu \frac{d}{dA}\left(\frac{f_S(A)}{A}\right) SZ \\ \hline -\frac{f_S(A)}{A} Z & \sigma e_S f_S(A)(d+v) - \frac{f_S(A)}{A} Z & -\lambda - \lambda_M - \frac{f_S(A)}{A}(S+I) & \sigma e_S \frac{df_S(A)}{dA}(d+v) I - \frac{d}{dA}\left(\frac{f_S(A)}{A}\right)(S+I) Z \\ \hline -f_S(A) & -f_S(A) & 0 & r(1-\frac{2A}{K}) - \frac{df_S(A)}{dA}(S+I) - f_M \end{array}\right)$$

For the trivial equilibrium E_0 the Jacobian matrix is diagonal. The eigenvalues are $-(d+p_S) < 0$, $-(d+v+\theta_I p_S) < 0$, $-\lambda - \lambda_M$, $r - f_M$. The trivial equilibrium is unstable as long as $r - f_M > 0$. This makes biological sense for the following reason: $r > f_M$ implies that the feeding rate of the mussels on the algae is lower than the algal intrinsic growth rate (hence algae can sustain itself).

For the equilibrium E_A, the eigenvalues are $e_S[f_S(A_A) - f_S(A_S)]$, $-(d + v + \theta_I p_S) < 0$, $-\lambda - \lambda_M$, and $r\left(1 - 2\frac{A_A}{K}\right) - f_M$. The equilibrium is linearly stable when $A_A < A_S$, $-\lambda - \lambda_M < 0$ and $r > f_M$.

For the equilibrium E_S, the four eigenvalues satisfy

$$\Lambda^2 - [r(1 - \frac{2A_S}{K}) - f_S'(A_S)S_S - f_M]\Lambda + e_S S_S f_S'(A_S) f_S(A_S) = 0$$

$$\Lambda^2 + (d + v + \theta_I p_S + \lambda + \lambda_M + \frac{f_S(A_S)}{A_S} S_S)\Lambda$$

$$+(d + v + \theta_I p_S)(\lambda + \lambda_M + \frac{f_S(A_S)}{A_S} S_S) -$$

$$\mu \sigma e_S (d + v) \frac{f_S^2(A_S)}{A_S} S_S = 0.$$

Equivalently, by defining

$$a_1 = r(1 - \frac{2A_S}{K}) - f_S'(A_S)S_S - f_M$$

$$b_1 = e_S S_S f_S'(A_S) f_S(A_S) > 0$$

$$a_2 = d + v + \theta_I p_S + \lambda + \lambda_M + \frac{f_S(A_S)}{A_S} S_S$$

$$b_2 = (d + v + \theta_I p_S)(\lambda + \lambda_M + \frac{f_S(A_S)}{A_S} S_S) - \mu \sigma e_S (d + v) \frac{f_S^2(A_S)}{A_S} S_S,$$

it holds

$$\Lambda^2 - a_1 \Lambda + b_1 = 0 \Leftrightarrow \Lambda = \frac{a_1 \pm \sqrt{a_1^2 - 4b_1}}{2}$$

$$\Lambda^2 + a_2 \Lambda + b_2 = 0 \Leftrightarrow \Lambda = \frac{-a_2 \pm \sqrt{a_2^2 - 4b_2}}{2}.$$

From this, it follows that the eigenvalues are real negative and/or are complex conjugate with negative real part if and only if $a_1 < 0$, $a_2 > 0$ and $b_2 > 0$.

It can be shown that

$$a_1 = \frac{rA_S}{K(h_S + A_S)}(K - h_S - 2A_S) - \frac{f_M A_S}{h_S + A_S}$$

$$= \frac{rA_S}{K(h_S + A_S)}\left(\frac{r - f_M}{r} K - h_S - 2A_S\right).$$

Hence we obtain two eigenvalues that are negative or have negative real part if $\frac{r - f_M}{r} K - h_S - 2A_S < 0$. It follows that

$$b_2 = (d + v + \theta_I p_S)\left(\lambda + \lambda_M + \frac{f_S(A_S)}{A_S} S_S\right)(1 - R_0),$$

where

$$R_0 = \frac{\sigma e_S f_S(A_S)(d+v)}{(d+v+\theta_I p_S)\left(\lambda+\lambda_M+\frac{f_S(A_S)}{A_S}S_S\right)}\mu\frac{f_S(A_S)}{A_S}S_S$$

or equivalently

$$R_0 = \frac{\mu\sigma(d+p_S)(d+v)}{d+v+\theta_I p_S}\times \frac{(r-f_M)K(e_S f_{S0}-(d+p_S))-rh_S(d+p_S)}{(\lambda+\lambda_M+r-f_M)K(e_S f_{S0}-(d+p_S))-rh_S(d+p_S)}.$$

From the above conditions it follows that the disease-free equilibrium is linearly asymptotically stable when

$$\frac{r-f_M}{r}K-h_S-2A_S<0,\quad d+v+\theta_I p_S+\lambda+\lambda_M+(A_A-A_S)\frac{r}{K}>0\quad\text{and}\quad R_0<1.$$

The transcritical bifurcation condition $R_0=1$ can be written as

$$h_S = \frac{e_S f_{S0}-(d+p_S)}{r(d+p_S)}\,\frac{\mu\sigma(d+v)(d+p_S)(r-f_M)-(d+v+\theta_I p_S)(\lambda+\lambda_M+r-f_M)}{\mu\sigma(d+v)(d+p_S)-(d+v+\theta_I p_S)}K. \tag{15}$$

Appendix C. Bifurcation figures

We show the bifurcations obtained with bifurcation parameters:

- the algal carrying capacity K (placed on the horizontal axis), and
- the half saturation constant for the feeding rate of the focal host h_S (placed on the vertical axis).

We vary h_S from 0 to 0.6 and K from 0 to 6. These figures are then created for various combinations of values for the mussel feeding rate f_M, the mussel spore removal/resuspension rate λ_M, and host susceptibility μ. (See Fig. 6.)

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