

SYNTHESIS

Microbiome influence on host community dynamics: Conceptual integration of microbiome feedback with classical host–microbe theory

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Abstract

Microbiomes have profound effects on host fitness, yet we struggle to understand the implications for host ecology. Microbiome influence on host ecology has been investigated using two independent frameworks. Classical ecological theory powerfully represents mechanistic interactions predicting environmental dependence of microbiome effects on host ecology, but these models are notoriously difficult to evaluate empirically. Alternatively, host–microbiome feedback theory represents impacts of microbiome dynamics on host fitness as simple net effects that are easily amenable to experimental evaluation. The feedback framework enabled rapid progress in understanding microbiomes' impacts on plant ecology, and can also be applied to animal hosts. We conceptually integrate these two frameworks by deriving expressions for net feedback in terms of mechanistic model parameters. This generates a precise mapping between net feedback theory and classic population modelling, thereby merging mechanistic understanding with experimental tractability, a necessary step for building a predictive understanding of microbiome influence on host ecology.

KEYWORDS

community ecology, host–pathogen interactions, microbiome, mutualism, plant–soil feedback, theory

INTRODUCTION

Microbiomes—the microbial communities associated with macroorganisms—are highly diverse, dynamic over time and variable across host species (David et al., 2014; Huttenhower et al., 2012; Muegge et al., 2011). Strong effects of microbiomes on both animal and plant host phenotype have generated optimism about their potential to mediate host health (Raaijmakers & Mazzola, 2016; Sonnenburg & Backhed, 2016) and acclimatisation to

perturbations (Jez et al., 2016; Mueller & Sachs, 2015). While the ecology of microbiomes within an individual host has been considered (Christian et al., 2015; Costello et al., 2012; Coyte et al., 2015; Joshi et al., 2018), the integration of microbiomes into basic aspects of host ecology, particularly within a multi-species context, remains a conceptual challenge (Morar & Bohannan, 2019).

Microbiomes have many potential effects on their hosts, ranging from negative effects of pathogenesis, to beneficial effects through pathogen suppression, digestion

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and nutrient uptake (Backhed et al., 2005; Friesen et al., 2011; Huttenhower et al., 2012). Given the breadth and magnitude of these effects, it is extremely difficult to assess the microbiome's net impact by studying the effects of individual taxa on host ecology. Effects of individual microbes on their hosts can depend upon the presence and density of other components of the microbiome, generating non-additive impacts on host fitness (Gerardo & Parker, 2014). The diversity of microbes within the microbiome combined with multiple sources of non-linearities means that some strategy for simplification is needed for practical study (Crawford et al., 2005).

Microbiome effects on host ecology have thus been investigated theoretically and empirically through two complementary, but largely independent, avenues. First, the effects of functional components, such as pathogens and mutualists, on plant and animal host ecology have been studied through the lens of classical population ecology (Hite et al., 2015; Jiang et al., 2020; Mordecai, 2013a; Umbanhowar & McCann, 2005). This approach allows detailed understanding of the transient and long-term effects of individual classes of microbes, but quickly becomes intractable with the inclusion of realistic microbiome diversity (Jiang et al., 2020). Second, investigations of the net feedback between microbiomes and host communities have become common for plant hosts (Bennett et al., 2017; Bever et al., 2012; van der Putten et al., 1993, 2013; Teste et al., 2017). This framework evaluates the net effect of the microbiome dynamics on host community structure and can be parameterised with straightforward experimentation (Bever et al., 1997). The feedback framework has been used to make strong statements on the effects of microbes on plant community structure (Bever et al., 2015), and could be constructively applied to animal hosts (Box 1) (Christian et al., 2015). Moreover, the simple modelling structure allows generalisation across multiple host species, allowing analytical prediction of coexistence and relative abundances of hosts (Eppinga et al., 2018; Mack et al., 2019). This simplicity, of course, comes at the expense of mechanistic detail.

Work from both of these approaches supports an argument that microbiomes play a major role in structuring host communities (Bever et al., 2015), but the lack of integration between them has impeded our ability to link specific mechanisms to total microbiome impacts at the host community level. The conceptual and theoretical unification of classical population dynamics theory with microbiome feedback theory could thus position the field for both empirical and theoretical advance. Here, we begin by outlining the theoretical and experimental microbiome feedback approach for assessing the net effect of microbial dynamics on host population and community dynamics. We compare the basic application of the feedback framework to the more standard approach of modelling populations of individual classes of microbial pathogens and mutualists. We then illustrate the benefits of connecting classical population dynamic models with the microbiome

Box 1 Microbiome feedback experimental framework adapted to animals

The microbiome feedback experimental approach involves two steps. A common microbiome inoculum is distributed to replicate mesocosms and different host species or genotypes are grown with this microbiome for a period of time. This microbiome training step allows host-specific differences in microbial fitness to generate differentiated microbiome compositions. Differentiation of the microbiome can be confirmed using morphological or environmental sequencing methods. The second step is to assay the fitness consequences of this potential differentiation on each of the host species or genotypes using a full factorial test experiment. Fitness estimates from this experiment can be used to estimate I_s (Bever et al., 1997). This approach was first applied to plant–soil microbiome interactions (Bever, 1994) and has since become a commonly used experimental approach in plant ecology to evaluate microbiome mediation of plant–plant interactions. This same approach could be used to test microbiome mediation of interactions of animal host species or genotypes.

We illustrate this approach for the study of interactions of zooplankton in Figure 2. In this case, the zooplankton species are grown on a common algal mix (small green circles) with a common inoculum of microbiome (other shapes) which could be acquired, for example, from a lake in which the zooplankton species co-occur. This training stage may involve regular replacement of a portion of the water volume with the algal mix to sustain the zooplankton populations while the microbiome may differentiate on host species. The fitness consequences of host-specific microbiome differentiation are evaluated by using the microbiomes from the training experiment as inocula in a separate test experiment (bottom panel) in which the algal food source is kept constant across all treatments. With aquatic animal hosts, the differentiated microbiomes could be applied repeatedly during the test experiment, potentially allowing assessment of the entire life cycle of the host in a relatively constant microbiome environment. This is a distinct advantage over the application of this approach to the study of plant–soil microbiome interactions, as soil microbiome can only be introduced at the beginning of the growth experiment. The potential for reversal of microbiome composition during the growth assay for plants constrains test experiments to short-term growth assays.

feedback framework to understand the role of microbial communities on host community ecology.

NET MICROBIOME FEEDBACKS IN HOST COMMUNITIES

The net feedback framework starts from the premise that the composition of microbiomes changes with host species or genotypic identity (Bever et al., 1997, 2012). These microbiome responses may be driven by host–symbiont compatibilities, trade-offs in overcoming host defences (Christian et al., 2015) and differential allocation by hosts (Vogelsang & Bever, 2009). Ensuing microbe–microbe competition or microbial trophic interactions have the potential to further differentiate the microbiomes of different host types. As new host individuals are likely to be colonised from other hosts with which they interact, the microbiome composition is also a function of closely interacting (e.g. neighbouring) hosts (Miller et al., 2018). In these ways, the composition of the microbiome is a function of host population and community diversity.

The feedback occurs when host diversity is in turn affected by microbiome composition through host-specific responses to microbial changes (e.g. Koziol & Bever, 2016). Changes in the microbiome composition can directly alter the fitness of conspecifics (in a community) or genetically similar individuals (in a population), as represented by α_{11} and α_{22} in Figure 1a, and can alter the fitness of competing host types (α_{12} and α_{21}).

The net microbiome feedback is the final outcome, summarising how changes in the host population or community will ultimately change host diversity as a result of these host–microbiome interactions. The long-term influence of microbiomes on host populations and communities will be determined by the sign of the net feedback (Bever et al., 1997). Should host-driven changes

in the microbiome decrease the relative fitness of conspecifics or genetically similar individuals, this negative microbiome feedback can promote species or genetic diversity. Alternatively, when host-specific changes in microbiome composition increase relative fitness of conspecifics or genetically similar individuals, this positive microbiome feedback can lead to monomorphism within the host community or population. Importantly, the sign of the effect of microbes on hosts (beneficial vs. detrimental) need not match the sign of the net feedback (Bever, 1999). For example, a mutualistic microbiome of one host type can nonetheless generate a negative net feedback if its mutualistic effect on the competing host type is even more strongly beneficial.

The basis for this result is a straightforward model (Bever et al., 1997) in which the presence of host type i promotes growth of its associated microbiome, collectively called M_i , that is characterised by the presences of particular microbial species in particular relative abundances. The variable M_i thus represents the microbiome of host species (or host genotype) i , and its magnitude represents the density of this particular microbiome in the environment. We note that $M_i = 0$ means the absence of influence of host i on the microbiomes, rather than an absence (density of 0) of individual microbes, and this difference in definition of the microbiome state variable is a critical difference between feedback models and classical theory in community ecology. With N_i representing the population density of host type i , out of n different host types,

$$\frac{dM_i}{dt} = \frac{v_i N_i}{\sum_{j=1}^n N_j} M_i, \quad (1a)$$

$$\frac{dN_i}{dt} = \sum_{j=1}^n \frac{G(i)_j M_j}{\sum_{k=1}^n M_k} N_i, \quad (1b)$$

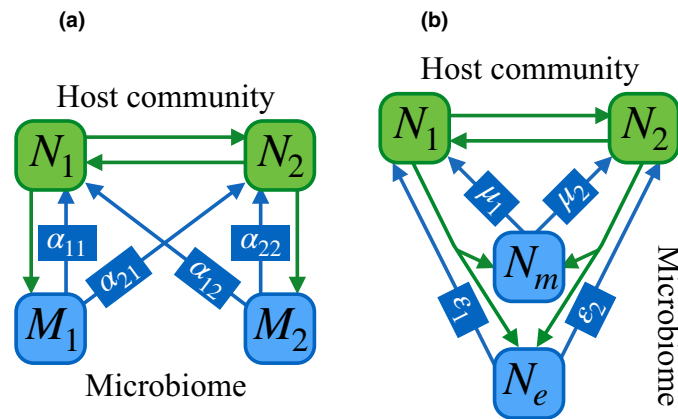


FIGURE 1 Two different representations of a two-host–microbiome community. (a) The plant–microbiome feedback framework, in which the net effect on host type i of host j 's microbiome is represented as α_{ij} . The density of host type i is N_i and the density of its microbiome is M_i . Each host type promotes the growth of its own microbiome at a rate proportional to its frequency in the host community (labels for the constants of proportionality, v_i , are omitted for clarity of presentation). (b) A more standard population ecology representation, in which the components of the microbiome are categorised as mutualists (N_m) or pathogens (N_e). The response of host type i to mutualists is μ_i , and to pathogens is ϵ_i

(Bever et al., 1997), where $G(i)_j$ is the fitness of host type i when exposed to host j 's microbiome. The first equation states that host i 's microbiome grows proportionately to the frequency of host type i relative to all other host types present, at proportional rate v_i . The second equation states that the per capita population growth rate of host i is the sum of its marginal fitness on each of the microbiomes present, weighted by the frequency of each microbiome. Considering a two-host system with $G(1)_1 = \alpha_{11}$, $G(1)_2 = \alpha_{12}$, $G(2)_1 = \alpha_{21}$ and $G(2)_2 = \alpha_{22}$ gives us the example illustrated in Figure 1a.

If this host-microbiome system is in a compositional equilibrium state of coexistence (both hosts and both microbes present and at constant frequencies), inter- and intraspecific feedbacks determine that all hosts have equal relative fitness (Eppinga et al., 2018) (Appendix A),

$$F_i = \sum_{j=1}^n \frac{G(i)_j M_j}{\sum_{k=1}^n M_k} = \hat{F} \quad \text{for } i = 1, 2, \dots, n, \quad (2)$$

where we note that host fitness at equilibrium only depends on microbiome community structure. Whether this equilibrium state is stable can then be determined by an interaction matrix (e.g. Novak et al., 2016), \mathbf{A} , which specifies the effects on each host of per capita changes in each microbiome,

$$\mathbf{A} = \begin{bmatrix} \frac{\partial F_1}{\partial M_1} & \dots & \dots & \frac{\partial F_1}{\partial M_n} \\ \dots & \dots & \dots & \dots \\ \dots & \dots & \dots & \dots \\ \frac{\partial F_n}{\partial M_1} & \dots & \dots & \frac{\partial F_n}{\partial M_n} \end{bmatrix} = \frac{1}{\sum_{k=1}^n M_k^*} \begin{bmatrix} \alpha_{11} & \dots & \dots & \alpha_{1n} \\ \dots & \dots & \dots & \dots \\ \dots & \dots & \dots & \dots \\ \alpha_{n1} & \dots & \dots & \alpha_{nn} \end{bmatrix}, \quad (3)$$

where M_k^* indicates the density of host k 's microbiome at compositional equilibrium and α_{ij} is the $G(i)_j$ evaluated at this equilibrium. As noted above, the feedback framework is focused on compositional changes in the microbiome, rather than changes in absolute densities, meaning that $\sum_{k=1}^n M_k^*$ can be considered constant. Under this assumption, the possibility for stable, long-term coexistence depends on the relative magnitude of the inter- and intraspecific feedbacks (Bever et al., 1997), and can be directly calculated from the interaction matrix (Eppinga et al., 2018). In a system with n different host types, the net microbiome feedback is summarised by the interaction coefficient,

$$I_s = (-1)^n \sum_{k=1}^n \mathbf{A}_k, \quad (4)$$

where \mathbf{A}_k is the interaction matrix \mathbf{A} with the k^{th} column replaced by a vector of ones (Eppinga et al., 2018). For example, in the two-host system in Figure 1a, scaled such that $\sum_{k=1}^n M_k^* = 1$, $\mathbf{A} = \begin{bmatrix} \alpha_{11} & \alpha_{12} \\ \alpha_{21} & \alpha_{22} \end{bmatrix}$, so $\mathbf{A}_1 = \begin{bmatrix} 1 & \alpha_{12} \\ \alpha_{21} & \alpha_{22} \end{bmatrix}$ and $\mathbf{A}_2 = \begin{bmatrix} \alpha_{11} & 1 \\ \alpha_{21} & 1 \end{bmatrix}$. Then, applying Equation (4),

$$I_s = \alpha_{11} - \alpha_{21} - \alpha_{12} + \alpha_{22}, \quad (5)$$

which is equivalent to the result presented in Bever et al. (1997), where I_s was obtained through linear stability analysis. This stability analysis of Equation (1) revealed that I_s is an important quantity governing host coexistence. When I_s is positive, the change in microbial composition increases the relative performance of the locally abundant host type generating a positive feedback. The result may be a loss of local diversity, as the system fixes on one of several alternative states dominated by the initially abundant host type and its microbiome. Conversely, competing host types can coexist through net negative feedback when the change in microbial composition decreases the relative performance of the locally abundant host. A negative I_s indicates net negative feedback, and $I_s < 0$ is a necessary (by describing stabilising mechanisms), though not sufficient (by omitting equalising mechanisms and higher order destabilising processes), condition for host-host coexistence (Bever et al., 1997; Eppinga et al., 2018). This simple condition for coexistence generally holds true with extension of the model to local-scale interaction and dispersal (Molofsky et al., 2002), though the conditions for extinction from positive feedback are modified (Molofsky & Bever, 2002). The $I_s < 0$ condition for coexistence also generally holds true, at least qualitatively, with addition of negative density dependence and variation in interspecific competition (Bever, 2003; Revilla et al., 2013).

Significance

The finding that the dynamics of competing host species depend on the sign and magnitude of the net microbiome feedback coefficient has important conceptual and empirical implications. Conceptually, the result identifies the paths through which negative intraspecific host-microbiome interactions ($\alpha_{11}, \alpha_{22} < 0$) can lead to positive net host community-level feedbacks ($I_s > 0$), and vice versa ($\alpha_{11}, \alpha_{22} > 0$ leading to $I_s < 0$). Empirically, the dependence of pairwise host dynamics on I_s provides an experimental approach to evaluating the role of the microbiome in host ecology. The net feedback coefficient can be estimated from full factorial experiments measuring the response of different host species to microbiomes trained by each of these respective host species (Bever et al., 1997). Specifically, a common initial microbial community is allowed to differentiate on multiple host types and then the fitness of these host types are evaluated when inoculated with each of the differentiated microbiomes (Bever, 1994) (Figure 2, Box 1). Net feedback coefficients can then be estimated using a priori contrasts within the interaction term of a single standard ANOVA model (Bever, 1994; Mangan et al., 2010).

Net feedback theory has been applied extensively to plant-soil microbiome interactions. Observed feedbacks are mostly negative, consistent with the idea that microbial dynamics contribute to plant coexistence

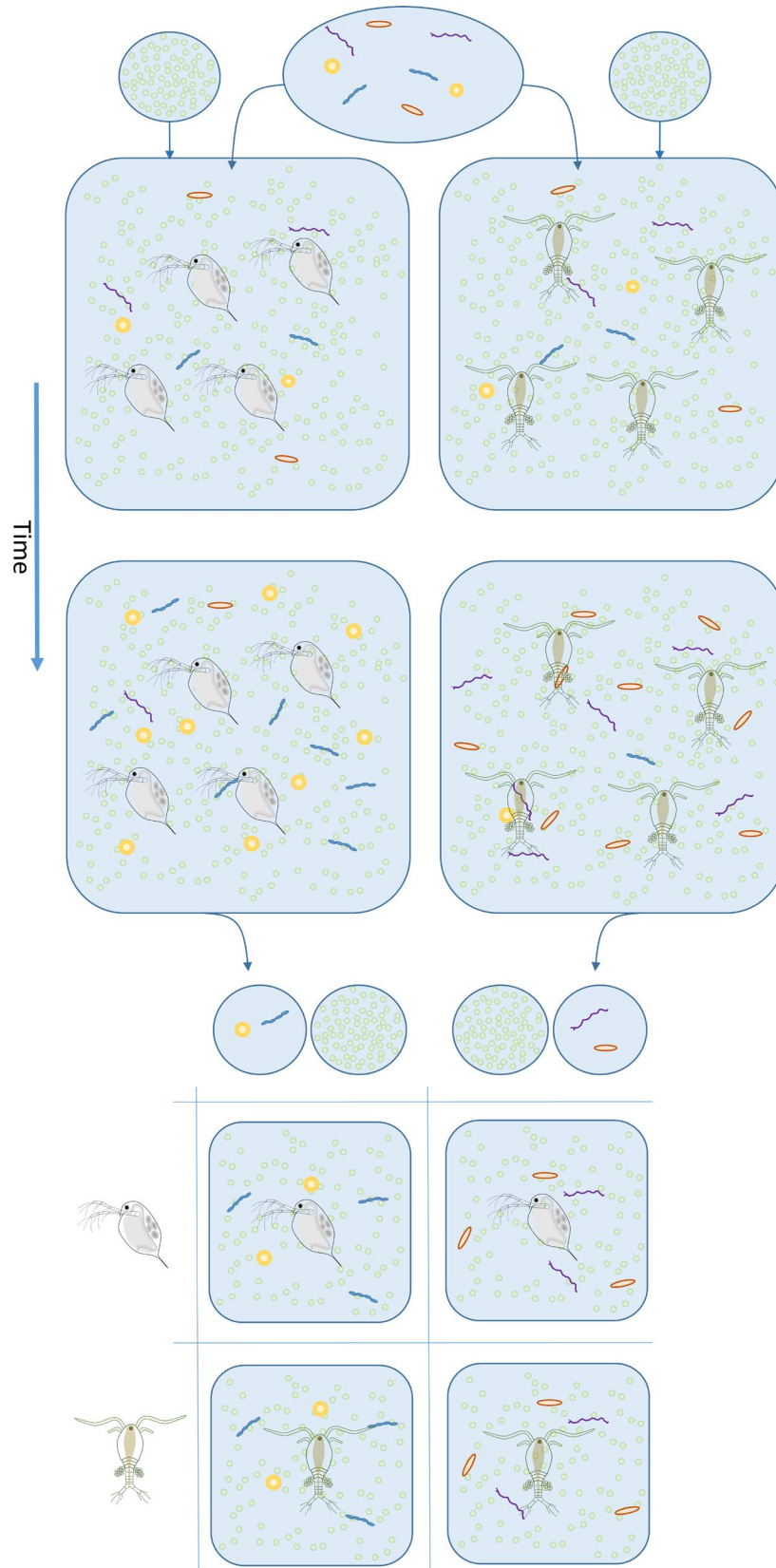


FIGURE 2 Depiction of an experimental protocol testing microbiome feedback on two species of zooplankton. In the training step, a common inoculum of microbiome (represented by the red, yellow, blue and purple shapes) is grown with two zooplankton species in media with an algal food source (small green circles). The fitness consequences of host-specific microbiome differentiation are evaluated by using the microbiomes from the training experiment as inocula in a separate test experiment (bottom panel) in which the algal food source is kept constant across all treatments. Feedback is measured as the differential response of zooplankton to their conspecific versus heterospecific microbiome, as described in Equation 5

(Bever, 1994; Crawford et al., 2019; Mangan et al., 2010; Peterman et al., 2008). While changes in abundance of many microbial groups act to generate feedbacks, including changes in the composition of mutualists (Bever, 2002), accumulation of host-specific pathogens is likely the most important mechanism generating negative feedbacks (Crawford et al., 2019).

While plant ecologists have embraced this framework, where, in addition to the many studies of soil microbiomes, it has also been applied to foliar microbiomes (Whitaker et al., 2017), we are unaware of its application to animal microbiomes. At least for animals that are easy to grow and manipulate in the lab, there is no reason this same approach cannot be successfully employed to understand the population and community-level effects of horizontally (i.e. within-generation) transferred animal microbiomes (Box 1). In fact, invertebrate microbiome feedback experiments may yield even more information than plant-soil feedback experiments when chemostats or similar approaches can be used to maintain a fixed microbiome environment during the testing phase. In vertebrate hosts, the host immune system will have a primary role in determining host-specific differentiation and impact of the microbiome. However, for both the gut and skin microbiomes, environmental and host-host transmission is common, both of which will have density dependence consistent with the feedback model. Vected or sexual transmission may differ, with corresponding differences in the microbial impact on host-host interactions (Rudolf & Antonovics, 2005). Experiments must adapt to the particular biology of the hosts and microbes to yield informative results.

BRIDGING FEEDBACK THEORY WITH CLASSICAL POPULATION ECOLOGY THEORY

While the net feedback framework divides up the microbial community into microbiomes characteristic of each host type, a more standard population and community ecology approach would be to divide the microbial community into functional groups, such as ‘mutualists’ or ‘pathogens’ (Jiang et al., 2020). This approach maintains closer links between the mechanisms through which microbiomes influence their hosts and the effects on host dynamics and diversity, but application of the models to evaluating microbiome influence on coexistence in any particular system is difficult because the direct connection to the net feedback coefficient, I_s , is lost. Therefore, to link I_s to explicit ecological mechanisms, rather than just the net effects of each microbiome on each host, we convert the feedback model, Equation (1), into a classical host-pathogen-mutualist population model and then derive I_s for this new model.

Each host type's microbiome contains a characteristic mix of microbial taxa. The number of functionally distinct microbial groups that need to be considered separately, as well as the potential of interactions between host effects on these groups, may increase with an increasing number of hosts and the phylogenetic distance between them (Crawford et al., 2019; Rinella & Reinhart, 2018). For simplicity in this proof-of-concept example, however, we assume that all influential members of the microbiome can be assigned to the mutualist or pathogen functional group, and that hosts independently stimulate the growth of these two groups. If the microbiome associated with host type i (M_i) is made up of a proportion γ_i mutualists (and thus $1-\gamma_i$ pathogens), the population density of mutualists is,

$$N_m = \sum_{i=1}^n \gamma_i M_i, \quad (6a)$$

and the density of pathogens (‘natural enemies’) is,

$$N_e = \sum_{i=1}^n (1-\gamma_i) M_i. \quad (6b)$$

If, as in feedback theory, the effect of each microbial type on hosts is proportional to its frequency, then we can define new parameters μ_i and ϵ_i , representing the effect on host type i of a unit increase in the frequency of mutualists and pathogens, respectively (Figure 1b). Then, host i 's population growth rate is,

$$\frac{dN_i}{dt} = \frac{\mu_i N_m + \epsilon_i N_e}{N_m + N_e} N_i, \quad i = 1, \dots, n. \quad (7a)$$

When host type i is very common, the frequency of mutualists in the environment will be close to γ_i and the frequency of pathogens will be close to $1-\gamma_i$, give or take small deviations due to the influence of less common host types. In a more evenly mixed host community, the frequency of each microbial group will represent a balance between each of the host type's γ values. We show how this balance comes about in a two-host example below.

In a system with two host types, with densities N_i , $i = 1, 2$, host dynamics are given by Equation (7a). We can derive expressions for the microbiome dynamics by recognising that Equation (6) imply $\frac{dN_m}{dt} = \sum_{i=1}^n \gamma_i \frac{dM_i}{dt}$ and $\frac{dN_e}{dt} = \sum_{i=1}^n (1-\gamma_i) \frac{dM_i}{dt}$. Obtaining $\frac{dM_i}{dt}$ from Eqn (1a) and rewriting in terms of our new variables N_m and N_e gives,

$$\frac{dN_m}{dt} = \sum_{i=1}^2 \frac{\gamma_i v_i N_i}{N_i + N_j} \left(\frac{\gamma_i (N_m + N_e) - N_m}{\gamma_j - \gamma_i} \right), \quad (7b)$$

$j \neq i$

$$\frac{dN_e}{dt} = \sum_{\substack{i=1 \\ j \neq i}}^2 \frac{(1-\gamma_i) v_i N_i}{N_i + N_j} \left(\frac{\gamma_j (N_m + N_e) - N_m}{\gamma_j - \gamma_i} \right). \quad (7c)$$

We recall that in the feedback framework the coefficients α_{ij} indicate the marginal fitness effect on host type i , as induced by the microbiome cultivated by host type j . We can now relate these coefficients mechanistically to the classical host–pathogen–mutualist population model. From Equation (6), it follows that host type j cultivates densities of $N_m = \gamma_j M_j$ and $N_e = (1 - \gamma_j) M_j$ of mutualists and pathogens, respectively. From Equation (7a) it then follows that these densities exert effects $\gamma_j \mu_i M_j$ and $(1 - \gamma_j) \varepsilon_i M_j$ on host type i . This shows that the term $G(i)_j M_j = \alpha_{ij} M_j$ in Equation (1) of the feedback framework corresponds to a term $(\gamma_j \mu_i + (1 - \gamma_j) \varepsilon_i) M_j$ in the classical host–pathogen–mutualist population model. Hence, if we define

$$\alpha_{ij} = \gamma_j \mu_i + (1 - \gamma_j) \varepsilon_i \quad \text{for } i, j = 1, 2, \quad (8)$$

the model in Equation (7) is exactly equivalent to the two-host version of Equation (1), just with the microbial community expressed in terms of functional groups rather than host-associated microbiomes. This equivalence allows us to derive an equivalent expression for the net feedback in terms of our new parameters,

$$\begin{aligned} I_s &= \alpha_{11} - \alpha_{21} - \alpha_{12} + \alpha_{22} \\ &= (\gamma_1 - \gamma_2)(\mu_1 - \mu_2 + \varepsilon_2 - \varepsilon_1) \\ &= \underbrace{(\gamma_1 - \gamma_2)}_{(m \text{ hosting ability})} \underbrace{(\mu_1 - \mu_2)}_{(\text{response to } m)} - \underbrace{((1 - \gamma_1) - (1 - \gamma_2))}_{(e \text{ hosting ability})} \underbrace{(|\varepsilon_1| - |\varepsilon_2|)}_{(\text{response to } e)} \end{aligned} \quad (9)$$

Although the second line in Equation (9) is more mathematically compact, the final line provides the most straightforward interpretation. The first parenthetical expression, $(\gamma_1 - \gamma_2)$, is the differential ability of host type 1 to promote growth of the mutualist, relative to host type 2. It will be negative if host 1 is a worse mutualist host. The second parenthetical expression, $(\mu_1 - \mu_2)$, is the difference in responsiveness to mutualists between the two host types. It will be positive if host 1's population growth is more strongly benefited by mutualists than is host 2's growth. Therefore, the entire first product, $(\gamma_1 - \gamma_2)(\mu_1 - \mu_2)$, will be negative if there is a negative relationship between a species' ability to host the mutualist and its responsiveness to mutualism.

The second product in Equation (9) is made up of similar parts: first, the differential ability of the two host types to promote pathogen growth $((1 - \gamma_1) - (1 - \gamma_2))$, followed by the differential effect of the pathogen on each type of host $(|\varepsilon_1| - |\varepsilon_2|)$. Note that because ε_i represents the effect of pathogens, it should be negative. Therefore, the absolute value signs make the last parenthetical expression positive if host type 1 is more susceptible to pathogens. The entire second product in Equation (9) is thus

positive if the same host is both a better host to, and is more strongly harmed by, pathogens.

Taken together, I_s is guaranteed to be negative—indicating a net negative feedback—when the species that is a worse host to the mutualist (if this is host 1, e.g. $\gamma_1 < \gamma_2$) and a better host to the pathogen ($1 - \gamma_1 > 1 - \gamma_2$) is also most responsive to both microbial groups ($\mu_1 > \mu_2$, indicating a stronger benefit from mutualists, and $|\varepsilon_1| > |\varepsilon_2|$, indicating greater susceptibility to pathogens). This analysis makes rigorous the mechanisms underlying the result in Bever et al. (1997).

A convenient way to remember this result is that a net negative feedback results when there is a negative correlation between ‘hostiness’ (a species' relative ability to host a particular microbiome functional group) and ‘happiness’ (a larger gain (mutualists) or smaller loss (pathogens) from interacting with that functional group). Examples of positive and negative hostiness-happiness relationships have been documented for both mutualists and pathogens (Figure 3), illustrating a diversity of net microbiome effects in nature. While pathogen-driven net negative hostiness–happiness relationships were the most common type seen in plant–soil systems (Crawford et al., 2019), whether this is generally true across taxa and across different types of (eco)systems is an open question.

The examples in Figure 3 come from studies on a single microbial functional group (just pathogens, or just mutualists). Measuring microbial effect on, and response to, each host becomes much more complicated when multiple microbial types coexist. Indeed, this is the problem for which feedback theory provides the workaround, by allowing I_s to be estimated without knowledge of the individual α_{ij} values. Just as with feedback theory, breaking an empirical estimate of I_s into its components—here, the ‘happiness’ and ‘hostiness’ terms in Equation (9)—requires additional, non-trivial work. The proportion of the microbiome that is mutualistic (γ_i) may for some systems be estimable from sequencing approaches, for example, and the individual microbial effects (μ_i and ε_i) may be measurable where the microbiome can be sorted into functional groups (e.g. by size or through differential biocides) during the test phase of the feedback experiment. Even rough estimates of any of these quantities can be combined with the I_s measured from a standard feedback experiment to constrain the range of possibilities for the remaining terms in Equation (9), and thus the range of viable hypotheses for which feedbacks are structuring the community.

ADVANCING MICROBIOME THEORY: THE UTILITY OF LOOP ANALYSIS FOR COMPLEX HOST–MICROBIOME INTERACTIONS

The results discussed so far have been extended to models that add host–host resource competition and host self-limitation (Bever, 2003; Revilla et al., 2013). The general

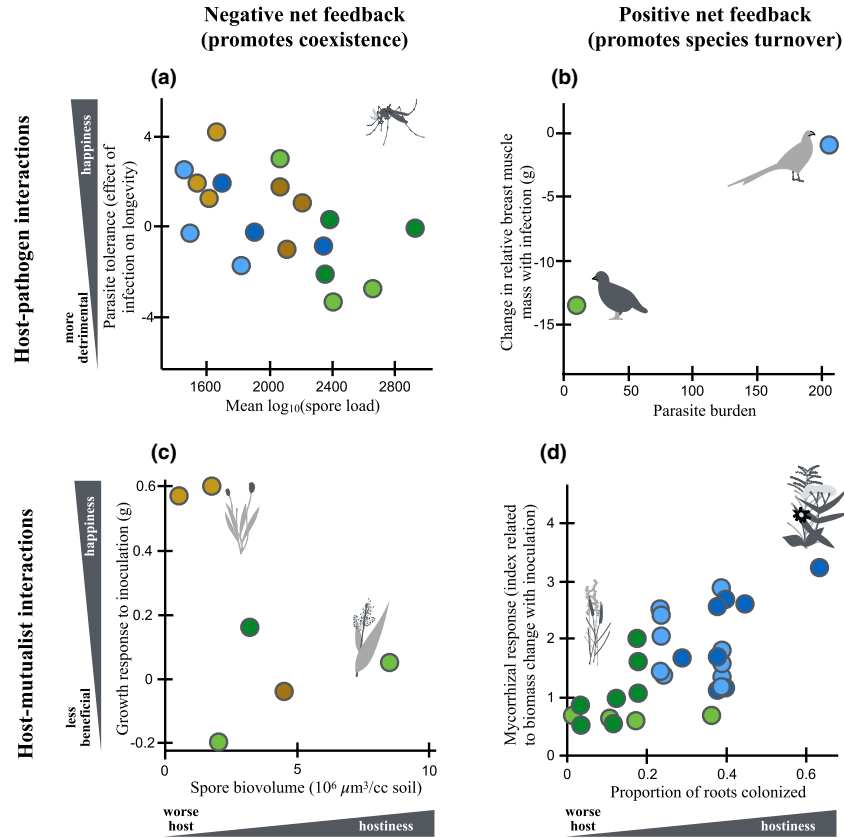


FIGURE 3 Examples of positive and negative ‘hostiness-happiness’ relationships between hosts and their pathogens or mutualists. (a) From Zeller and Koella (2017): *Aedes aegypti* mosquito lineages with different evolutionary histories (different colours) and their microsporidian parasite *Vavraia culicis* show evidence of a negative feedback. Lineages that can host higher parasite loads (more hosty) have lower tolerance to infection (less happy). Tolerance was measured as the slope of the longevity–parasite load relationship. (b) From Thompkins et al. (2000, 2001): differential impacts of the parasitic nematode *Heterakis gallinarum* promotes competitive exclusion of grey partridges (*Perdix perdix*, green) by ring-necked pheasants (*Phasianus colchicus*, blue). Pheasants have better body condition when infected relative to control (more happy), yet they host many more worms per year (more hosty). (c) From Bever (2002): *Plantago lanceolata* (brown) benefits more (more happy) from arbuscular mycorrhizal fungal (AMF) species (*Acaulospora morrowiae* and *Archaeospora trappei*, plotted in lighter shades) for which it is a poorer host (less hosty) relative to its competitor, *Panicum sphaerocarpon* (green). *Plantago* also benefits less from AMF, that it hosts better (*Scutellospora calospora*, dark shades). (d) From Koziol and Bever (2015): for 30 prairie plant species from across successional stages (earliest to latest: light green, dark green, light blue, dark blue), the mycorrhizal response ratio of the mass of AMF-inoculated plants tends to be lower in earlier successional plants that are also worse AMF hosts. This generates a positive feedback that may contribute to successional turnover. All figures have been redrawn for display on hostiness–happiness axes using data presented in figures or tables in the original references

feature that there is an analogue to I_s that describes net feedback and provides information on expected host diversity extends to these more complex cases.

Loop analysis (Levins, 1974; Puccia & Levins, 1991) provides a convenient means to gain insight into the feedbacks structuring more complicated models, at a somewhat aggregated level. In this context, a loop refers to a configuration in which each component of the community exerts an effect on a component and receives an effect from a component. For example, the net feedback generated in a two-host system with host density dependence (Figure 4a) is determined by the sum of four different feedback loops (Figure 4b; see Box 2 for a mathematical description). Two of these loops (loops 1 and 4) involve the direct feedback between one host and its microbiome (Figure 4b). Following the convention of loop analysis, in which each loop involves exactly one effect imposed on and imposed by each variable, this direct feedback is

multiplied by the strength of intraspecific competition experienced by the host not involved in the direct feedback (Figure 4b; Puccia & Levins, 1991). The other two feedback loops (loops 2 and 3) involve an indirect feedback, in which one focal host manipulates the composition of the microbiome, which affects the density of the competing host, and this change in competitor density feeds back to the focal host via interspecific competition (Figure 4b). If the two hosts did not differ in terms of intra- and interspecific competition strength, the net feedback generated in the system would exactly equal I_s (Box 2).

This approach can be generalised to any density-dependent interactions between and within the hosts, and within mutualists and pathogens. Without specifying the functions for relative fitness ($F_1 = \frac{1}{N_1} \frac{dN_1}{dt}$, $F_2 = \frac{1}{N_2} \frac{dN_2}{dt}$, $F_m = \frac{1}{N_m} \frac{dN_m}{dt}$, $F_e = \frac{1}{N_e} \frac{dN_e}{dt}$), we can write the interaction matrix as,

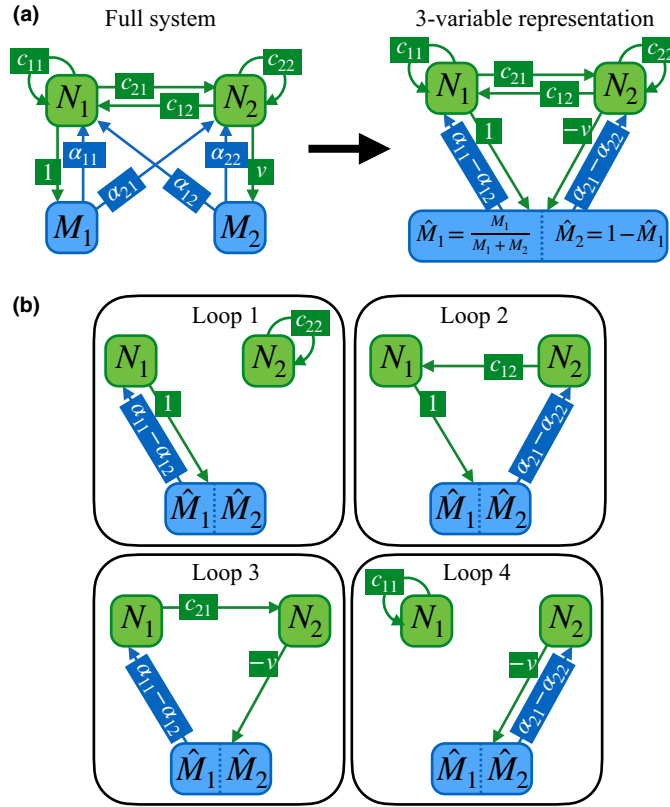


FIGURE 4 Loop analysis for a two-host–microbiome community model with density-dependent resource competition within and between host types. (a) Combining information about the microbiome into a single variable representing the frequency of host 1’s microbiome, \hat{M}_1 . (b) The four loops that make up the 3-variable model. Each loop (which need not form a closed path; see e.g. Loops 1 and 4) consists of a set of interactions in which each variable has exactly one arrow pointing towards it and exactly one arrow pointing away. See Box 2 for a full mathematical description

$$\mathbf{A} = \begin{bmatrix} \frac{\partial F_1}{\partial N_1} & \frac{\partial F_1}{\partial N_2} & \frac{\partial F_1}{\partial N_m} & \frac{\partial F_1}{\partial N_e} \\ \frac{\partial F_2}{\partial N_1} & \frac{\partial F_2}{\partial N_2} & \frac{\partial F_2}{\partial N_m} & \frac{\partial F_2}{\partial N_e} \\ \frac{\partial F_m}{\partial N_1} & \frac{\partial F_m}{\partial N_2} & \frac{\partial F_m}{\partial N_m} & \frac{\partial F_m}{\partial N_e} \\ \frac{\partial F_e}{\partial N_1} & \frac{\partial F_e}{\partial N_2} & \frac{\partial F_e}{\partial N_m} & \frac{\partial F_e}{\partial N_e} \end{bmatrix}. \quad (10)$$

Because our interest is in microbiome interactions driving host dynamics, we can simplify the interaction matrix by assuming that intraspecific and interspecific competition coefficients for the two hosts are equal,

$$\rho = \frac{\partial F_1}{\partial N_1} = \frac{\partial F_1}{\partial N_2} = \frac{\partial F_2}{\partial N_1} = \frac{\partial F_2}{\partial N_2}. \quad (11)$$

Using loop analysis to calculate the net feedback shows some familiar elements:

Specifically, we see that the first two terms again describe the equivalent of I_s . Furthermore, the third term comprises the set of direct and indirect feedbacks previously described by the loops in Figure 4. Thus, dynamics are still governed by the hostiness-happiness relationships, where the importance of the mutualist feedback and pathogen feedback are mediated by the strength of intraspecific and interspecific density dependence of the hosts, and intraspecific density dependence in pathogens and mutualists (Equation (12)). There is also an interaction between the mutualist- and pathogen-driven feedbacks, which can be disentangled into a set of direct and indirect feedbacks that only involve host–microbiome effects (Figure 5).

$$\underbrace{\rho \frac{\partial F_e}{\partial N_e}}_{\text{(self-limitation of } e\text{)}} + \underbrace{\left(\frac{\partial F_1}{\partial N_m} - \frac{\partial F_2}{\partial N_m} \right)}_{\text{response to } m} \underbrace{\left(\frac{\partial F_m}{\partial N_2} - \frac{\partial F_m}{\partial N_1} \right)}_{m \text{ hosting ability}} + \underbrace{\rho \frac{\partial F_m}{\partial N_m}}_{\text{(self-limitation of } m\text{)}} + \underbrace{\left(\frac{\partial F_1}{\partial N_e} - \frac{\partial F_2}{\partial N_e} \right)}_{\text{response to } e} \underbrace{\left(\frac{\partial F_e}{\partial N_2} - \frac{\partial F_e}{\partial N_1} \right)}_{e \text{ hosting ability}} + \underbrace{\left(\frac{\partial F_1}{\partial N_e} \frac{\partial F_2}{\partial N_m} - \frac{\partial F_1}{\partial N_m} \frac{\partial F_2}{\partial N_e} \right)}_{\text{within and between host community feedbacks – see Fig. 5}} \underbrace{\left(\frac{\partial F_e}{\partial N_1} \frac{\partial F_m}{\partial N_2} - \frac{\partial F_e}{\partial N_2} \frac{\partial F_m}{\partial N_1} \right)}_{\text{within and between host community feedbacks – see Fig. 5}}. \quad (12)$$

Box 2 Loop analysis of a combined Lotka–Volterra competition–feedback model

Density-dependent resource competition within and between host types can be considered by combining the feedback model (Equation (1)) with the Lotka–Volterra competition model (Bever, 2003). Considering two hosts and their associated microbiomes, we write

$$\frac{dN_i}{dt} = r_i N_i \left(1 + \alpha_{ii} \widehat{M}_i + \alpha_{ij} \widehat{M}_j \right) - c_{ii} N_i^2 - c_{ij} N_i N_j \quad i, j = 1, 2, \quad (\text{B2.1a})$$

$$\frac{d\widehat{M}_1}{dt} = \frac{\widehat{M}_1 \widehat{M}_2}{N_1 + N_2} (N_1 - v N_2), \quad (\text{B2.1b})$$

where r_i is the host i 's intrinsic population growth rate, \widehat{M}_i is the frequency of its microbiome in the shared environment ($\widehat{M}_i = \frac{M_i}{M_1 + M_2}$), and $c_{ij} > 0$ is the competitive effect of host type j on host type i . All other notations follow the main text, except that we set microbiome i 's response to host type i , v_i in Equation (1a), to 1 for $i = 1$ and write it simply as v for $i = 2$, for consistency with (Bever, 2003). By representing the microbiome in terms of frequencies, we only need one microbiome equation (Figure 4a). Loop analysis can be performed on the interaction matrix of the system described by Equation (B2.1), which can be written as follows:

$$\tilde{\mathbf{A}} = \begin{bmatrix} \frac{\partial F_{N_1}}{\partial N_1} & \frac{\partial F_{N_1}}{\partial N_2} & \frac{\partial F_{N_1}}{\partial \widehat{M}_1} \\ \frac{\partial F_{N_2}}{\partial N_1} & \frac{\partial F_{N_2}}{\partial N_2} & \frac{\partial F_{N_2}}{\partial \widehat{M}_1} \\ \frac{\partial F_{M_1}}{\partial N_1} & \frac{\partial F_{M_1}}{\partial N_2} & \frac{\partial F_{M_1}}{\partial \widehat{M}_1} \end{bmatrix} = \begin{bmatrix} \frac{\partial \left(\frac{1}{N_1} \frac{dN_1}{dt} \right)}{\partial N_1} & \frac{\partial \left(\frac{1}{N_1} \frac{dN_1}{dt} \right)}{\partial N_2} & \frac{\partial \left(\frac{1}{N_1} \frac{dN_1}{dt} \right)}{\partial \widehat{M}_1} \\ \frac{\partial \left(\frac{1}{N_2} \frac{dN_2}{dt} \right)}{\partial N_1} & \frac{\partial \left(\frac{1}{N_2} \frac{dN_2}{dt} \right)}{\partial N_2} & \frac{\partial \left(\frac{1}{N_2} \frac{dN_2}{dt} \right)}{\partial \widehat{M}_1} \\ \frac{\partial \left(\frac{1}{\widehat{M}_1} \frac{d\widehat{M}_1}{dt} \right)}{\partial N_1} & \frac{\partial \left(\frac{1}{\widehat{M}_1} \frac{d\widehat{M}_1}{dt} \right)}{\partial N_2} & \frac{\partial \left(\frac{1}{\widehat{M}_1} \frac{d\widehat{M}_1}{dt} \right)}{\partial \widehat{M}_1} \end{bmatrix} = \begin{bmatrix} -c_{11} & -c_{12} & r_1 (\alpha_{11} - \alpha_{12}) \\ -c_{21} & -c_{22} & r_2 (\alpha_{21} - \alpha_{22}) \\ \varphi & -v\varphi & 0 \end{bmatrix}, \quad (\text{B2.2})$$

where $\varphi = \frac{\widehat{M}_2^*}{N_1^* + N_2^*}$ with the asterisks representing equilibria. Since φ is always positive, it does not affect the sign of the net feedback in the system. Therefore, the net feedback of the system can be inferred from the matrix

$$\mathbf{A} = \begin{bmatrix} -c_{11} & -c_{12} & r_1 (\alpha_{11} - \alpha_{12}) \\ -c_{21} & -c_{22} & r_2 (\alpha_{21} - \alpha_{22}) \\ 1 & -v & 0 \end{bmatrix},$$

whose determinant is

$$\det \tilde{\mathbf{A}} = \frac{\det \mathbf{A}}{\varphi} = r_1 (c_{22} + v c_{21}) (\alpha_{11} - \alpha_{12}) + r_2 (c_{12} + v c_{11}) (\alpha_{22} - \alpha_{21}). \quad (\text{B2.3})$$

Expanding Equation (B2.3) yields the four feedback loops described in the main text and shown in Figure 3. In the absence of competitive differences between hosts (i.e. $r_1 = r_2 = r$, $c_{11} = c_{22} = c_{\text{Intra}}$, $c_{12} = c_{21} = c_{\text{Inter}}$, $v = 1$), the net feedback of the system reduces to,

$$\det \tilde{\mathbf{A}} = \varphi \det \mathbf{A} = r \varphi (c_{\text{Intra}} + c_{\text{Inter}}) I_s. \quad (\text{B2.4})$$

Because $r \varphi (c_{\text{Intra}} + c_{\text{Inter}})$ is a positive constant, the sign of the net feedback in the system is described by I_s (Equation 5) in this case.

The structure of Equation (B2.3) reveals several different processes that are important in generating the system-level host–microbiome feedback. The first factor in the first term, $(c_{22} + v c_{21})$, quantifies the ability of host 1 to indirectly manipulate the microbiomes through its competitive effect on host 2. This ability increases not only with the degree of interspecific competition exerted on host 2 (c_{21}), but also with the degree of

Box 2 (Continued)

intraspecific competition experienced by host 2 (c_{22}), and the per capita effect of host 2 on microbiome composition (ν). The second factor in the first term quantifies the ability of both microbiomes to manipulate the density of host 1, as it describes how the net microbiome effect on this host changes when it increases in relative abundance ($\alpha_{11} - \alpha_{12}$). The multiplication by r_1 accounts for the rate at which these latter effects develop. By symmetry, the second term of Equation (B2.3) quantifies these impacts for host 2.

For the system described by Equation (B2.1), the net feedback determines the position of the one equilibrium point in which the hosts and their microbiomes coexist,

$$N_1^* = \frac{r_1 r_2 \nu J_S}{\det \mathbf{A}}, \quad (\text{B2.5a})$$

$$N_2^* = \frac{r_1 r_2 J_S}{\det \mathbf{A}}, \quad (\text{B2.5b})$$

$$\widehat{M}_1^* = \frac{\det \mathbf{A}_{C1}}{\det \mathbf{A}} = \frac{\det \mathbf{A}_{C1}}{\det \mathbf{A}_{C1} + \det \mathbf{A}_{C2}}, \quad (\text{B2.5c})$$

in which

$$J_S = \alpha_{11} - \alpha_{12} - \alpha_{21} + \alpha_{22} + \alpha_{11}\alpha_{22} - \alpha_{12}\alpha_{21} = I_S + \alpha_{11}\alpha_{22} - \alpha_{12}\alpha_{21}, \quad (\text{B2.5d})$$

and matrices \mathbf{A}_{C1} and \mathbf{A}_{C2} are defined below. We derive the equilibrium by setting the equations (B2.1) to zero. In this case, the microbiome would maintain both hosts at equilibrium if microbiome effects cancel out the density-independent and density-dependent effects on fitness resulting from host–host interactions. As per capita effects on fitness are constant (Equation B2.2), and $\widehat{M}_2 = (1 - \widehat{M}_1)$, we can infer from this equilibrium requirement that the following equation needs to be fulfilled:

$$\begin{bmatrix} -c_{11} & -c_{12} & r_1(\alpha_{11} - \alpha_{12}) \\ -c_{21} & -c_{22} & r_2(\alpha_{21} - \alpha_{22}) \\ 1 & -\nu & 0 \end{bmatrix} \begin{bmatrix} N_1 \\ N_2 \\ \widehat{M}_1 \end{bmatrix} = \begin{bmatrix} -r_1(1 + \alpha_{12}) \\ -r_2(1 + \alpha_{22}) \\ 0 \end{bmatrix}. \quad (\text{B2.6})$$

Using Cramer's rule, we obtain \widehat{M}_1^* (and $\det \mathbf{A}_{C1}$) by substituting the right-hand side of Equation (B2.6) into the third column of the interaction matrix, to obtain the host-specific feedback exerted on \widehat{M}_1 (and N_1):

$$\det \mathbf{A}_{C1} = \det \begin{bmatrix} -c_{11} & -c_{12} & -r_1(1 + \alpha_{12}) \\ -c_{21} & -c_{22} & -r_2(1 + \alpha_{22}) \\ 1 & -\nu & 0 \end{bmatrix} = r_2(c_{12} + \nu c_{11})(1 + \alpha_{22}) - r_1(c_{22} + \nu c_{21})(1 + \alpha_{12}). \quad (\text{B2.7})$$

By symmetry, obtaining the host-specific feedback exerted on \widehat{M}_2^* (and N_2) then requires solving the matrix equation:

$$\begin{bmatrix} -c_{11} & -c_{12} & r_1(\alpha_{11} - \alpha_{12}) \\ -c_{21} & -c_{22} & r_2(\alpha_{21} - \alpha_{22}) \\ -1 & \nu & 0 \end{bmatrix} \begin{bmatrix} N_1 \\ N_2 \\ \widehat{M}_2 \end{bmatrix} = \begin{bmatrix} -r_1(1 + \alpha_{11}) \\ -r_2(1 + \alpha_{21}) \\ 0 \end{bmatrix}, \quad (\text{B2.8})$$

which then yields:

$$\det \mathbf{A}_{C2} = \det \begin{bmatrix} -c_{11} & -c_{12} & -r_1(1 + \alpha_{11}) \\ -c_{21} & -c_{22} & -r_2(1 + \alpha_{21}) \\ -1 & \nu & 0 \end{bmatrix} = r_1(c_{22} + \nu c_{21})(1 + \alpha_{11}) - r_2(c_{12} + \nu c_{11})(1 + \alpha_{21}). \quad (\text{B2.9})$$

Box 2 (Continued)

A feasible equilibrium point requires that all equilibrium densities be positive, meaning

$$\text{sign}(J_S) = \text{sign}(\det \mathbf{A}) = \text{sign}(\det \mathbf{A}_{C1}) = \text{sign}(\det \mathbf{A}_{C2}); \quad (\text{B2.10})$$

thus, either all signs in Equation (B2.10) are positive, or they are all negative. To assess which of these two cases is stable, we can solve the determinant of the Jacobian matrix of the system described by Equation (B2.1), evaluated at the coexistence equilibrium point. As the determinant is the product of the system's three eigenvalues, a negative determinant is necessary (though not sufficient) for stability. The determinant of the Jacobian matrix, \mathbf{U} , can be written as follows:

$$\det \mathbf{U} \Big|_{\substack{N_i = N_i^* \\ \widehat{M}_1 = \widehat{M}_1^*}} = r_1 r_2 \frac{v}{1+v} \widehat{M}_1^* (1 - \widehat{M}_1^*) J_S = r_1 r_2 \frac{v}{1+v} \frac{\det \mathbf{A}_{C1} \det \mathbf{A}_{C2}}{(\det \mathbf{A})^2} J_S. \quad (\text{B2.11})$$

The parameters r_1, r_2 and v must be positive for biological realism, and if Equation (B2.10) holds, then the fraction in Equation (B2.11) is also positive. Hence, stable coexistence of both plant hosts and their microbiomes requires $J_S < 0$, corresponding to negative host–microbiome feedback, thereby obtaining a result of (Revilla et al., 2013), who used a graphical approach.

$$\begin{aligned} & \left(\frac{\partial F_1}{\partial N_e} \frac{\partial F_2}{\partial N_m} - \frac{\partial F_1}{\partial N_m} \frac{\partial F_2}{\partial N_e} \right) \left(\frac{\partial F_e}{\partial N_1} \frac{\partial F_m}{\partial N_2} - \frac{\partial F_e}{\partial N_2} \frac{\partial F_m}{\partial N_1} \right) \\ &= \left(\begin{array}{cc} N_1 & N_2 \\ N_e & N_m \end{array} \begin{array}{cc} N_1 & N_2 \\ N_m & N_e \end{array} \right) - \left(\begin{array}{cc} N_1 & N_2 \\ N_m & N_e \end{array} \begin{array}{cc} N_1 & N_2 \\ N_e & N_m \end{array} \right) \\ &= \underbrace{\left(\begin{array}{cc} N_1 & N_2 \\ N_m & N_e \end{array} \begin{array}{cc} N_1 & N_2 \\ N_m & N_e \end{array} \right) - \left(\begin{array}{cc} N_1 & N_2 \\ N_e & N_m \end{array} \begin{array}{cc} N_1 & N_2 \\ N_m & N_e \end{array} \right)}_{\text{direct (within-host) community feedbacks}} + \underbrace{\left(\begin{array}{cc} N_1 & N_2 \\ N_m & N_e \end{array} \begin{array}{cc} N_1 & N_2 \\ N_e & N_m \end{array} \right) - \left(\begin{array}{cc} N_1 & N_2 \\ N_e & N_m \end{array} \begin{array}{cc} N_1 & N_2 \\ N_m & N_e \end{array} \right)}_{\text{indirect (between-host) community feedbacks}} \end{aligned}$$

FIGURE 5 Graphical representation of the second row of Equation (12). Arrows pointing from species or functional group j to species or group i represent the fitness effect of j on i 's population growth rate. This is the i,j^{th} element of the interaction matrix (Equation (10)). In the final row, products are depicted as multiple arrows drawn together

THE UTILITY OF SIMPLE THEORY FOR UNDERSTANDING COMPLEX SYSTEMS

The loop analysis discussed above and illustrated in Box 2 shows that many of the insights gained from models (1) and (7) transfer well to more realistic settings. This is notable, since the basic models lack density dependence and equilibrate only in terms of the frequencies of each community member. Nevertheless, the key roles of hosting ability and benefits derived from the microbiome in determining net community outcome are robust to inclusion of the myriad sources of density dependence (Equation (12)). We are therefore interested in knowing how far simple feedback theory can get us. Even in the

simplest host–microbiome feedback model (Bever et al., 1997), $I_s < 0$ is a necessary but not sufficient condition for host coexistence. We do not expect I_s to provide complete information on community-level outcomes because there are multiple system characteristics and mechanisms that may prevent species coexistence even when $I_s < 0$. Most obviously, the theoretical coexistence state that would be maintained by negative feedback may include negative densities of hosts and/or microbiome populations (Kandlikar et al., 2019). Second, the negative feedback generated by $I_s < 0$ may or may not be sufficient to constrain a system with complex eigenvalues to a stable limit cycle (Eppinga et al., 2018). An interesting difference between the dominant eigenvalue of the Jacobian matrix and I_s is that the former only informs about the fate of

small perturbations around the coexistence equilibrium, while the latter informs about the attraction of the coexistence equilibrium when one host is rare (Eppinga et al., 2018). Hence, $I_s < 0$ is a necessary condition for species persistence, while a negative dominant eigenvalue is not (Eppinga et al., 2018). The reason $I_s < 0$ is not sufficient is that it does not consider that multiple hosts and their microbiomes can simultaneously become rare, after which one or more hosts and their microbiomes may get excluded (Eppinga et al., 2018). In future analyses, Floquet theory (e.g. Klausmeier, 2008) may provide further insights into the connection between I_s and the ability of a community to persist while fluctuating.

DISCUSSION

Host–microbiome feedback theory has proven useful for understanding net effects of interactions between plants and their soil microbes on plant communities, and we contend that the framework translates readily to other host taxa. While the combination of the theory with empirical tests is powerful, it treats the feedbacks as a ‘black box’, whereby host and microbial responses to one another are input and output but the mechanisms underlying these responses are not addressed. Classic ecological theory for how hosts interact with shared mutualists and pathogens allows us to study these mechanisms, but has previously been unconnected with net community-level feedbacks. In this paper, we have synthesised feedback theory with classic modelling approaches. By merging these two research directions, we can now link net feedback theory, with its readily measurable and highly informative net feedback coefficient, with mechanistic theory that opens the black box.

The central constructs of microbiome feedback theory are state variables that represent the direction of change in microbiome composition due to association with a particular host (Bever et al., 1997). These state variables are qualitatively different from common state variables, such as density, that can be directly measured. While host-specific microbiome divergence, a critical step in microbiome feedback, could be quantified through amplicon sequencing or other tools, feedback theory measures host-specific divergence through microbiome impacts on host fitness. This framework has the advantage of constructing theory around a workable experimental test of microbiome influence on fitness (Figure 2, Box 1), but it has been difficult to represent the meaning of the parameters of the feedback model. By explicitly bridging these two theoretical frameworks, we show that feedback parameters correspond to integrative measures of host effects on microbes and host responses to microbes. Microbiome feedback then corresponds to the product of the differential ability to host microbes and the differential host fitness response to those microbes. A negative ‘hostiness-happiness’ correlation generates

negative microbiome feedback that can stabilise coexistence of host species, while positive microbiome feedbacks generated by a positive correlation can drive host turnover or alternative stable states (Figure 3).

Our analyses show that microbiome feedback theory and classic ecological theory are complementary approaches to understanding the influence of the microbiome on host communities. Considering disease dynamics as an example, classic theory explicitly models disease spread separately from disease impacts and this modelling approach has motivated a general prediction that disease incidence will decline with host diversity (Keesing et al., 2006). This prediction, called the dilution effect, became very controversial because of the dependence on specific modelling assumptions and questions of correspondence to empirical systems (Randolph & Dobson, 2012). Microbiome feedback theory does not monitor disease incidence, and therefore does not inform questions of disease incidence per se. However, by representing the net consequence of disease dynamics on host fitness, feedback theory does predict that when negative feedback predominates, increases in host diversity will result in reduced impact of pathogens on host fitness. Given evidence that root pathogens drive negative microbiome feedback in plant communities (Crawford et al., 2019), some have argued that impacts of root pathogens will generally be diluted by increasing plant diversity (Collins et al., 2020). Moreover, a general argument on the importance of pathogens in structuring plant communities can be constructed by combining inference from the few tests of classic host–pathogen models parameterised to particular systems (Mordecai, 2013b, a) with the much broader data available on patterns of plant–soil microbiome feedback (Bever et al., 2015).

We argue that integrating work under the classical and microbiome feedback frameworks is necessary to build a predictive understanding of how environmental change may alter host–microbiome interactions and thereby host community structure. For example, when the signs of feedback loops through various components differ (e.g. simultaneous positive feedback through mutualists and negative feedback through pathogens), changes in environmental factors like climate or nutrient availability may readily reverse the sign of the net feedback. While building and parameterising models that incorporate environmental dependence of host–microbe interactions is a priority, prospects for broad application of this approach are limited given the fantastic diversity of host–microbe interactions. Rapid progress may be possible by using illustrative examples from classic ecology theory to generate predictions that can then be tested using the host–microbiome feedback approach. The microbiome feedback approach provides tests of the potential for the microbiome to mediate host–host interactions, and inference from these tests is constrained to the test's microbiome source (Crawford et al., 2019; Diez et al., 2010)

and environmental context (Smith-Ramesh & Reynolds, 2017). However, the environmental dependence of microbiome feedback can provide tests of general tendencies of these systems. For example, a recent test of plant–soil microbiome feedback found that consistency of environment generated more stabilising negative feedbacks than did fluctuating environments (Duell et al., 2019).

Peter Chesson's partitioning of interspecific interactions into stabilising and equalising effect (Chesson, 2000), often called ‘modern coexistence theory’, has been embraced as a useful guide to bridge theory and empirical studies (e.g. Ellner et al., 2019; HilleRisLambers et al., 2012). The aim of the feedback framework is to evaluate the stabilising potential of microbiome dynamics. The quantity I_s represents the stabilising potential of microbiome dynamics near the coexistence equilibrium: the more strongly negative, the greater the stabilising potential. Full application of modern coexistence theory to the feedback model (i.e. determining if the internal equilibrium exists and estimating the equalising effect of the microbiome; Kandlikar et al., 2019; Ke & Wan, 2020) is difficult because it requires estimation of individual feedback parameters (α_{ij}). These parameters represent the difference between host fitness with differentiated microbiomes and host fitness with a naïve microbiome (i.e. upon initiation of the training step of the feedback experiment). Because microbiomes are not static, and because relative fitness effects are best estimated in a randomised common environment, the fitness effect of a naïve microbiome is empirically challenging to estimate. Host fitness in a naïve environment should not, despite the suggestion of Ke and Wan (2020), be conflated with fitness in a sterile environment, as this would confound the effects of microbiome dynamics with the effects of microbiome presence. As such, practical challenges remain for the unification of modern coexistence theory with feedback experiments.

As both empirical and theoretical investigations of host–microbiome feedbacks are extended to include more taxa and more processes, we expect linkages between net feedbacks and underlying mechanisms will be important for building understanding and prediction. Many patterns in community ecology are context-dependent, making generalisation a challenge (Lawton, 1999). The type of synthesis we promote here elucidates the origins of ‘microbial context-dependence’, where the potential for positive feedbacks and alternative stable states creates a situation in which the final community-level outcome depends (predictably, once one knows how to look) on initial microbiome composition (Jiang et al., 2020) and/or initial host densities (Bever, 1999).

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AUTHORSHIP

KCA and JDB motivated the study; KCA, MBE, JU and MB performed mathematical analyses; KCA, JDB and MBE wrote the first draft, and all authors contributed substantially to revisions.

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No new data are presented.

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REFERENCES

- Backhed, F., Ley, R.E., Sonnenburg, J.L., Peterson, D.A. & Gordon, J.I. (2005) Host-bacterial mutualism in the human intestines. *Science*, 307, 1915–1920.
- Bennett, J.A., Maherali, H., Reinhart, K.O., Lekberg, Y., Hart, M.M. & Klironomos, J. (2017) Plant-soil feedbacks and mycorrhizal type influence temperate forest population dynamics. *Science*, 355(6321), 181–184. <https://doi.org/10.1126/science.aai8212>.
- Bever, J.D. (1994) Feedback between plants and their soil communities in an old field community. *Ecology*, 75, 1965–1977.
- Bever, J.D. (1999) Dynamics within mutualism and the maintenance of diversity: inference from a model of interguild frequency dependence. *Ecology Letters*, 2, 52–61.
- Bever, J.D. (2002) Negative feedback within a mutualism: host-specific growth of mycorrhizal fungi reduces plant benefit. *Proceedings of the Royal Society of London. Series B: Biological Sciences*, 269, 2595–2601.
- Bever, J.D. (2003) Soil community feedback and the coexistence of competitors: conceptual frameworks and empirical tests. *New Phytologist*, 157, 465–473.
- Bever, J.D., Mangan, S.A. & Alexander, H.M. (2015) Maintenance of plant species diversity by pathogens. *Annual Review of Ecology, Evolution, and Systematics*, 46, 305–325.
- Bever, J.D., Platt, T.G. & Morton, E.R. (2012) Microbial population and community dynamics on plant roots and their feedbacks on plant communities. *Annual Review of Microbiology*, 66, 265–283.
- Bever, J.D., Westover, K.M. & Antonovics, J. (1997) Incorporating the soil community into plant population dynamics: the utility of the feedback approach. *Journal of Ecology*, 85(5), 561–573.
- Chesson, P.L. (2000) Mechanisms of maintenance of species diversity. *Annual Review of Ecology and Systematics*, 31, 343–366.
- Christian, N., Whitaker, B.K. & Clay, K. (2015) Microbiomes: unifying animal and plant systems through the lens of community ecology theory. *Frontiers in Microbiology*, 6, 100.
- Collins, C.D., Bever, J.D. & Hersh, M.H. (2020) Community context for mechanisms of disease dilution: insights from linking epidemiology and plant-soil feedback theory. *Annals of the New York Academy of Sciences*, 1469, 65–85.
- Costello, E.K., Stagaman, K., Dethlefsen, L., Bohannan, B.J.M. & Relman, D.A. (2012) The application of ecological theory

- toward an understanding of the human microbiome. *Science*, 336, 1255–1262.
- Coyte, K.Z., Schluter, J. & Foster, K.R. (2015) The ecology of the microbiome: networks, competition, and stability. *Science*, 350, 663–666.
- Crawford, J., Harris, J., Ritz, K. & Young, I. (2005) Towards an evolutionary ecology of life in soil. *Trends in Ecology & Evolution*, 20, 81–87.
- Crawford, K.M., Bauer, J.T., Comita, L.S., Eppinga, M.B., Johnson, D.J., Mangan, S.A. et al. (2019) When and where plant-soil feedback may promote plant coexistence: a meta-analysis. *Ecology Letters*, 17, 1613.
- David, L.A., Maurice, C.F., Carmody, R.N., Gootenberg, D.B., Button, J.E., Wolfe, B.E. et al. (2014) Diet rapidly and reproducibly alters the human gut microbiome. *Nature*, 505, 559–563.
- Diez, J.M., Dickie, I., Edwards, G., Hulme, P.E., Sullivan, J.J. & Duncan, R.P. (2010) Negative soil feedbacks accumulate over time for non-native plant species. *Ecology Letters*, 13, 803–809.
- Duell, E., Bever, J.D. & Wilson, G.T. (2019) Climate affects plant-soil feedbacks of native and invasive grasses: negative feedbacks in stable but not variable environments. *Frontiers in Ecology and Evolution*, 7, 419.
- Ellner, S.P., Snyder, R.E., Adler, P.B. & Hooker, G. (2019) An expanded modern coexistence theory for empirical applications. *Ecology Letters*, 22, 3–18.
- Eppinga, M.B., Baudena, M., Johnson, D.J., Jiang, J., Mack, K.M.L., Strand, A.E. et al. (2018) Frequency-dependent feedback constrains plant community coexistence. *Nature Ecology & Evolution*, 2(9), 1–8.
- Friesen, M.L., Porter, S.S., Stark, S.C., von Wettberg, E.J., Sachs, J.L. & Martinez-Romero, E. (2011) Microbially mediated plant functional traits. *Annual Review of Ecology, Evolution, and Systematics*, 42, 23–46.
- Gerardo, N.M. & Parker, B.J. (2014) Mechanisms of symbiont-conferred protection against natural enemies: an ecological and evolutionary framework. *Current Opinion in Insect Science*, 4, 8–14.
- HilleRisLambers, J., Adler, P.B., Harpole, W.S., Levine, J.M. & Mayfield, M.M. (2012) Rethinking community assembly through the lens of coexistence theory. *Annual Review of Ecology, Evolution, and Systematics*, 43, 227–248.
- Hite, J.L., Penczykowski, R.M., Shocket, M.S. & Strauss, A.T. (2015) Parasites destabilize host populations by shifting stage-structured interactions. *Ecology*, 97, 439–449.
- Huttenhower, C. & The Human Microbiome Project Consortium (2012) Structure, function and diversity of the healthy human microbiome. *Nature*, 486, 207–214.
- Jez, J., Lee, S.G. & Sherp, A.M. (2016) The next green movement: plant biology for the environment and sustainability. *Science*, 353, 1241–1244.
- Jiang, J., Abbott, K.C., Baudena, M., Eppinga, M.B., Umbanhowar, J. & Bever, J.D. (2020) Pathogens and mutualists as joint drivers of host species coexistence and turnover: implications for plant competition and succession. *American Naturalist*, 195, 591–602.
- Joshi, T., Elder, B.D. & Abbott, K.C. (2018) No appendix necessary: fecal transplants and antibiotics can resolve *Clostridium difficile* infection. *Journal of Theoretical Biology*, 442, 139–148.
- Kandlikar, G.S., Johnson, C.A., Yan, X., Kraft, N.J.B. & Levine, J.M. (2019) Winning and losing with microbes: how microbially mediated fitness differences influence plant diversity. *Ecology Letters*, 108, 5638.
- Ke, P.-J. & Wan, J. (2020) Effects of soil microbes on plant competition: a perspective from modern coexistence theory. *Ecological Monographs*, 90, e01391.
- Keesing, F., Holt, R.D. & Ostfeld, R.S. (2006) Effects of species diversity on disease risk. *Ecology Letters*, 9, 485–498.
- Klausmeier, C.A. (2008) Floquet theory: a useful tool for understanding nonequilibrium dynamics. *Theoretical Ecology*, 1, 153–161.
- Koziol, L. & Bever, J.D. (2015) Mycorrhizal response trades off with plant growth rate and increases with plant successional status. *Ecology*, 96(7), 1768–1774. <https://doi.org/10.1890/14-2208.1>.
- Koziol, L. & Bever, J.D. (2016) AMF, phylogeny and succession: specificity of plant response to arbuscular mycorrhizal fungal species increases with succession. *Ecosphere*, 7, e01555.
- Lawton, J.H. (1999) Are there general laws in ecology? *Oikos*, 84(2), 177–192.
- Levins, R. (1974) The qualitative analysis of partially specified systems. *Annals of the New York Academy of Sciences*, 321, 123–138.
- Mack, K.M.L., Eppinga, M.B. & Bever, J.D. (2019) Keystone competitors stabilize plant communities structured by biotic feedbacks: invasion, coexistence, and robustness in multi-species models. *PLoS One*, 14, e0211572.
- Mangan, S.A., Schnitzer, S.A., Herre, E.A., Mack, K.M.L., Valencia, M.C., Sanchez, E.I. et al. (2010) Negative plant-soil feedback predicts tree-species relative abundance in a tropical forest. *Nature*, 466, 752–755.
- Miller, E.T., Svanbäck, R. & Bohannan, B.J.M. (2018) Microbiomes as metacommunities: understanding host-associated microbes through metacommunity ecology. *Trends in Ecology & Evolution*, 33, 926–935.
- Molofsky, J. & Bever, J.D. (2002) A novel theory to explain species diversity in landscapes: positive frequency dependence and habitat suitability. *Proceedings of the Royal Society of London. Series B: Biological Sciences*, 269, 2389–2393.
- Molofsky, J., Bever, J.D., Antonovics, J. & Newman, T.J. (2002) Negative frequency dependence and the importance of spatial scale. *Ecology*, 83, 21–27.
- Morar, N. & Bohannan, B.J.M. (2019) The conceptual ecology of the human microbiome. *The Quarterly Review of Biology*, 94, 149–175.
- Mordecai, E.A. (2013a) Consequences of pathogen spillover for cheatgrass-invaded grasslands: coexistence, competitive exclusion, or priority effects. *American Naturalist*, 181, 737–747.
- Mordecai, E.A. (2013b) Despite spillover, a shared pathogen promotes native plant persistence in a cheatgrass-invaded grassland. *Ecology*, 94, 2744–2753.
- Muegge, B.D., Kuczynski, J., Knights, D., Clemente, J.C., Gonzalez, A., Fontana, L. et al. (2011) Diet drives convergence in gut microbiome functions across mammalian phylogeny and within humans. *Science*, 332, 970–974.
- Mueller, U.G. & Sachs, J.L. (2015) Engineering microbiomes to improve plant and animal health. *Trends in Microbiology*, 23, 606–607.
- Novak, M., Yeakel, J.D., Noble, A.E., Doak, D.F., Emmerson, M., Estes, J.A. et al. (2016) Characterizing species interactions to understand press perturbations: what is the community matrix? *Annual Review of Ecology, Evolution, and Systematics*, 47, 409–432.
- Peterman, J.S., Fergus, A.J.F., Turnbull, L.A. & Schmid, B. (2008) Janzen-Connell effects are widespread and strong enough to maintain diversity in grasslands. *Ecology*, 89, 2399–2406.
- Puccia, C.J. & Levins, R. (1991) Qualitative modeling in ecology: loop analysis, signed digraphs, and time averaging. In: Fishwick, P.A. & Luker, P.A. (Eds.) *Qualitative Simulation Modeling and Analysis*. York: Springer, New, pp. 119–143.
- Raaijmakers, J.M. & Mazzola, M. (2016) Soil immune responses. *Science*, 352, 1392–1393.
- Randolph, S.E. & Dobson, A.P. (2012) Pangloss revisited: A critique of the dilution effect and the biodiversity-buffers-disease paradigm. *Parasitology*, 139, 847–863.
- Revilla, T.A., Veen, G.F., Eppinga, M.B. & Weissing, F.J. (2013) Plant-soil feedbacks and the coexistence of competing plants. *Theoretical Ecology*, 6, 99–113.
- Rinella, M.J. & Reinhart, K.O. (2018) Toward more robust plant-soil feedback research. *Ecology*, 99, 550–556.
- Rudolf, V.H.W. & Antonovics, J. (2005) Species coexistence and pathogens with frequency-dependent transmission. *American Naturalist*, 166, 112–118.

- Smith-Ramesh, L.M. & Reynolds, H.L. (2017) The next frontier of plant-soil feedback research: unraveling context dependence across biotic and abiotic gradients. *Journal of Vegetation Science*, 28, 484–494.
- Sonnenburg, J.L. & Backhed, F. (2016) Diet-microbiota interactions as moderators of human metabolism. *Nature*, 535, 56–64.
- Teste, F.P., Kardol, P., Turner, B.L., Wardle, D.A., Zemunik, G., Renton, M. et al. (2017) Plant-soil feedback and the maintenance of diversity in Mediterranean-climate shrublands. *Australian Journal of Zoology*, 355(6321), 173–176.
- Thompkins, D.M., Greenman, J.V. & Hudson, P.J. (2001) Differential impact of a shared nematode parasite on two gamebird hosts: implications for apparent competition. *Parasitology*, 122(02), 1–7. <https://doi.org/10.1017/S0031182001007247>.
- Thompkins, D.M., Greenman, J.V., Robertson, P.A. & Hudson, P.J. (2000) The role of shared parasites in the exclusion of wildlife hosts: *Heterakis gallinarum* in the ring-necked pheasant and the grey partridge. *Journal of Animal Ecology*, 69, 829–840.
- Umbanhowar, J. & McCann, K. (2005) Simple rules for the coexistence and competitive dominance of plants mediated by mycorrhizal fungi. *Ecology Letters*, 8, 247–252.
- van der Putten, W.H., Bardgett, R.D., Bever, J.D., Bezemer, T.M., Casper, B.B., Fukami, T. et al. (2013) Plant-soil feedbacks: the past, the present and future challenges. *Journal of Ecology*, 101, 265–276.
- van der Putten, W.H., van Dijk, C. & Peters, B.A.M. (1993) Plant-specific soil-borne diseases contribute to succession in fore-dune vegetation. *Nature*, 362, 53–56.
- Vogelsang, K.M. & Bever, J.D. (2009) Mycorrhizal densities decline in association with nonnative plants and contribute to plant invasion. *Ecology*, 90, 399–407.
- Whitaker, B.K., Bauer, J.T., Bever, J.D. & Clay, K. (2017) Negative plant-phylosphere feedbacks in native Asteraceae hosts – a novel extension of the plant-soil feedback framework. *Ecology Letters*, 20, 1064–1073.
- Zeller, M. & Koella, J.C. (2017) The role of the environment in the evolution of tolerance and resistance to a pathogen. *American Naturalist*, 190, 389–397.

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