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Species dynamics and interactions via metabolically informed consumer-resource models

Mario E. Muscarella[1,*] & James P. O'Dwyer[1,2]
[1]Department of Plant Biology, University of Illinois
[2]Carl R. Woese Institute for Genomic Biology, University of Illinois
[*]corresponding author (mmuscar@illinois.edu)

Quantifying the strength, sign, and origin of species interactions, along with their dependence on environmental context, is at the heart of prediction and understanding in ecological communities. Pairwise interaction models like Lotka-Volterra provide an important and flexible foundation, but notably absent is an explicit mechanism mediating interactions. Consumer-resource models incorporate mechanism and the resource landscape dependency, but describing competitive and mutualistic interactions is more ambiguous. Here, we seek to bridge this gap by modeling a coarse-grained version of a species' true, cellular metabolism to describe resource consumption via uptake and conversion into biomass, energy, and byproducts. This approach does not require detailed chemical reaction information, but it provides a more explicit description of underlying mechanisms then pairwise interaction or consumer-resource models. Using a model system, we find that when metabolic reactions require two distinct resources we recover Liebig's Law and multiplicative co-limitation in particular limits. In between these limits, we derive a more general phenomenological form for consumer growth rate, and we find corresponding rates of secondary metabolite production, allowing us to model competitive and non-competitive interactions (e.g., mutualism). Using the more general form, we show how secondary metabolite production can support coexistence even when two species compete for a shared resource, and we show how differences in metabolic rates change species equilibria. Building on these findings, we make the case for incorporating metabolism to update the phenomenology we use to model species interactions.

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A central goal in ecology is to understand and predict the dynamics in communities of interacting species (Holt, 1977; Loreau, 2010; Vellend, 2010, 2016). Mathematical models allow us to generate and test theoretical predictions, and the development of such models leads to a hierarchy of challenges. The first challenge is determining an appropriate functional form describing species dynamics. A range of functional forms with increasing complexity has been used and each has strengths and weaknesses which are often context dependent (Holling, 1959; Abrams, 1982; DeAngelis *et al.*, 1989; Murdoch *et al.*, 2003; Mougi & Kondoh, 2012). Second, we need to parametrize these equations, for example by quantifying the strength and sign of species interactions in a given environmental context. While some attempts have been made to parametrize real-life systems, accurately fitting interaction strengths remains challenging in both empirical and theoretical work (Schoener, 1983; Tilman, 1987; Ives *et al.*, 2003; Carrara *et al.*, 2015; Terry *et al.*, 2017; Barner *et al.*, 2018). Finally, we may wish to determine how a change in the environmental context will modify species interactions, dynamics, and even coexistence. Integrating each of these goals will lead to the development of robust models which can predict the dynamics of complex communities, even when the environmental landscape changes within and across ecosystems.

The Lotka-Volterra equations provide an example of mathematical models which has been widely used for close to a century (Lotka, 1932; Volterra, 1926). These equations characterize species interactions in terms of the net, direct effect of one population on another's growth rate, so that in the case of two species with abundances N_1 and N_2:

$$\frac{dN_1}{dt} = r_1 N_1 - a_{11} N_1^2 - a_{21} N_1 N_2$$

$$\frac{dN_2}{dt} = r_2 N_2 - a_{22} N_2^2 - a_{12} N_1 N_2. \tag{1}$$

Here, r_1 and r_2 are per capita growth rates when species are rare, and the parameters a_{ij} (collectively called a community matrix) represent intra- and interspecific interactions. Empirically, it has been extremely difficult to reliably estimate these parameters (Schoener, 1983; Tilman, 1987). Even where it has

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been possible to infer or approximate pairwise interactions (Stein *et al.*, 2013; Marino *et al.*, 2013; Fisher & Mehta, 2014; Bucci *et al.*, 2016), it may be difficult to translate the inferred interactions in different environmental contexts. These models lack an explicit description of the mechanisms mediating interactions (Abrams, 1983; Grilli *et al.*, 2017). For example, if two species compete, it is often because consume common resources (Gause & Witt, 1935; MacArthur, 1970; Schoener, 1983). However, these models assume that resource dynamics can be safely ignored because resource dynamics are faster than consumer dynamics (MacArthur, 1970). This exposes an important context-dependence of Lotka-Volterra type equations: the strength and even the sign of a pairwise interaction may depend on what resources are present (Xiao *et al.*, 2017). As such, landscape variation can influence species composition due to differences in competitive ability and the context dependence of species interactions (Cadotte & Tucker, 2017).

An alternate approach is to model competitive interactions as the explicit result of shared resource consumption (Grover, 1990; Tilman, 1980; Tilman *et al.*, 1982; Litchman, 2003; Abrams, 2009). For example, in the case of two species with abundances N_1 and N_2 competing for a single shared resource, R, the prototypical consumer-resource model is:

$$\begin{aligned}
\frac{dR}{dt} &= \rho - a_i N_i R \\
\frac{dN_1}{dt} &= \epsilon_1 a_1 N_1 R - \mu_1 N_1 \\
\frac{dN_2}{dt} &= \epsilon_2 a_2 N_2 R - \mu_2 N_2,
\end{aligned} \tag{2}$$

where ρ describes the environmental input rate of an abiotic resource, a_i describes the resource uptake rates, ϵ_i describes the resource use efficiency, and μ_i are the species mortality rates. These models produce species interactions as an emergent property dependent on shared resource consumption, and so the issue of inferring species interactions is no longer quite the right question—though there is now a challenge in determining consumer feeding preferences. Assuming we can infer or otherwise estimate those preferences, one critical aspect of the environmental context is now explicitly characterized, via resource input rates like

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ρ. As such, species dynamics across resource landscapes can be understood better than in the case of Lotka-Volterra, where the effect of the environment is implicit (Tilman, 1977; Grover, 1990, 2011).

The more explicit mechanism gives an advantage, but there is a cost. Lotka-Volterra equations are extremely flexible and can straightforwardly incorporate a mixture of antagonistic and mutualistic interactions simply by altering the signs of entries in the community matrix, a_{ij} (Mougi & Kondoh, 2012; Allesina & Tang, 2012). But for consumer-resource models we have to be careful about how those mechanisms are formulated. Consumption can take a variety of forms depending, for example, on whether resources are substitutable or essential (Tilman, 1980), and mutualistic interactions can occur via resource production and exchange (Loreau, 2001; Freilich *et al.*, 2011; Zelezniak *et al.*, 2015). The latter in particular is under explored relative to consumption (Butler & O'Dwyer, 2018), and an open question is to what extent the precise form of exchange might affect community dynamics and species coexistence.

So how do we retain the advantages of consumer-resource models, but also incorporate the flexibility of models of direct species interactions? Current consumer-resource models are largely agnostic to what happens inside cells or organisms. For many systems, this approach may be valid especially when the resources (i.e., prey) belong to higher trophic levels, self-regulate, and/or closely match the stoichiometric requirements of the consumer (Sterner & Elser, 2002; Cherif & Loreau, 2007; Hall, 2009). However, most microorganisms consume abiotic resources which do not self-regulate. Second, any single resource consumed generally does not satisfy the full stoichiometric requirements. For example, heterotrophic microorganisms require organic carbon, but they still require nitrogen, phosphorus, and other resources to grow and reproduce. Because growth depends on multiple resources, dynamics may depend on a single limiting resource (e.g., Liebig's Law of the Minimum von Liebig & Gregory, 1842; Odum, 1959) or an interaction between resources (e.g., multiplicative co-limitation Harpole *et al.*, 2011). Likewise, the consumption and transformation of resources depends on how cells produce biomass, energy, and metabolic byproducts, and species interactions may therefore depend on metabolic rates and byproduct production. Furthermore, all of these processes may depend on environmental conditions like temperature, but it is not

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clear how to incorporate this information. Here, we propose that going one level deeper into cellular metabolism will allow us to generalize consumer-resource models in a meaningful way and give them the same flexibility to describe multiple interaction types as models of direct species interactions.

Results

The Metabolically Informed Consumer-Resource Model We know a substantial amount about the internal physiology of cells, and there have been large advancements in the development of flux balance models which use biochemistry and genomics to describe (to some level of approximation) every reaction that occurs within a cell (Kauffman *et al.*, 2003; Orth *et al.*, 2010). More recently, these models have been applied in the context of entire microbial communities and their interactions (Embree *et al.*, 2015; Zomorrodi & Segrè, 2016; Pacheco *et al.*, 2018). However, we propose that including a full description of a metabolic network may not be required to develop a useful ecological model. Here, we model the internal dynamics via simplified metabolic networks, which require less knowledge of the particular species' idiosyncrasies but still capture the major metabolic events transforming resources. Our simplified metabolic model is based on a basic fermentation reaction, homolactic fermentation, which uses glucose and phosphate and produces lactate (Fig. 1). If used strictly for energy production, one glucose and two phosphate molecules yields two molecules of lactate and generates chemical energy in the form of two ATP (Gottschalk, 1986). However, to produce biomass, some of the available glucose and phosphate must be used for anabolic metabolism—forming new biomass and maintaining cellular stoichiometry. In this reaction, the glucose is used to form new biomass and to produce chemical energy via fermentation. The energetic component results in the production of the byproduct, lactate, which is exported back into the environment (i.e., excretion); therefore, efficiency is emergent property determined by the balance between the biomass and energy production.

Here, we assume that cellular metabolism relies on the interaction of sugar and phosphate, producing new biomass and a byproduct (lactate). Given that we consider one phosphate molecule, this already

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simplifies the resource requirements relative to the true process. But we will see general principles emerge.

$$R_1 + R_2 \xrightarrow{\beta} \text{Biomass} + R_3 \tag{3}$$

R_1 here is the sugar, R_2 represents a source of phosphorus, and R_3 is the metabolic byproduct (lactate). We model this intracellular reaction as occurring at rate β. Next, we assume that our organism grows in a resource replete environment, such as a chemostat, and therefore resource inputs are constant. In addition, we assume that metabolic rates are not limited by any other factors and that resources do not inhibit growth. Therefore, we can balance fluxes for the internal cell densities of the three resources (labeled M_1, M_2 and M_3). This leads to:

$$\begin{aligned} \nu_{bio} &= \beta M_1 M_2 \\ \nu_1 &= k_1 - \beta M_1 M_2 \\ \nu_2 &= k_2 - \beta M_1 M_2 \\ \nu_3 &= \beta M_1 M_2, \end{aligned} \tag{4}$$

for uptake rates k_1 and k_2, which can depend in an arbitrary way on external resource concentrations R_1, R_2 and R_3, outflow (i.e., export) rates ν_1, ν_2 and ν_3, and biomass production ν_{bio}. We make a natural assumption that export of each resource is determined by passive excretion: i.e. that $\nu_\alpha = \lambda_\alpha M_\alpha$ for each metabolite, where $lambda_\alpha$ is a species and resource-specific constant.

We can now solve this system of polynomial equations for internal resource concentrations (see Methods). Using these equations, we built a set of generalized, co-limited consumer-resource equations using uptake rates and a simplified flux balance analysis as the only building blocks. For simplicity, we assume that resource uptake and export are passive processes. First, we focus on one species and model its uptake rate k_α of resource α as $C_{\alpha 1} R_\alpha$, where R_α is the *external* (environmental) concentration of this

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resource. Applying this assumption, we derive a general set of equations for the consumer and three resources:

$$
\begin{aligned}
\frac{dR_1}{dt} &= \rho_1 - \eta_1 R_1 - R_1 C_{11} N_1 + \nu_1 N_1 \\
&= \rho_1 - \eta_1 R_1 - N_1 \left(\frac{\lambda_1 \lambda_2}{2\beta} - \frac{F(\beta, C_{11}R_1, C_{21}R_2)}{2} + \frac{C_{11}R_1 + C_{21}R_2}{2} \right) \\
\frac{dR_2}{dt} &= \rho_2 - \eta_2 R_2 - R_2 C_{21} N_1 + \nu_2 N_1 \\
&= \rho_2 - \eta_2 R_2 - N_1 \left(\frac{\lambda_1 \lambda_2}{2\beta} - \frac{F(\beta, C_{11}R_1, C_{21}R_2)}{2} + \frac{C_{11}R_1 + C_{21}R_2}{2} \right) \\
\frac{dR_3}{dt} &= \rho_3 - \eta_3 R_3 + \nu_3 N_1 \\
&= \rho_3 - \eta_3 R_3 + N_1 \left(\frac{\lambda_1 \lambda_2}{2\beta} - \frac{F(\beta, C_{11}R_1, C_{21}R_2)}{2} + \frac{C_{11}R_1 + C_{21}R_2}{2} \right) \\
\frac{dN_1}{dt} &= \nu_{bio} N_1 - \mu_1 N_1 \\
&= N_1 \left(\frac{\lambda_1 \lambda_2}{2\beta} - \frac{F(\beta, C_{11}R_1, C_{21}R_2)}{2} + \frac{C_{11}R_1 + C_{21}R_2}{2} \right) - \mu_1 N_1,
\end{aligned} \tag{5}
$$

where ρ_α and η_α are inflow and outflow rates for each of the three resources, and μ_1 is the mortality rate of the consumer.

We now note two limits (see Methods). First, when β is large relative to the other rates the consumer-resource equations become:

$$
\begin{aligned}
\frac{dR_1}{dt} &= \rho_1 - \eta_1 R_1 - R_1 C_{11} N_1 \\
&\quad + \frac{N_1}{2} \left[R_1 C_{11} - R_2 C_{21} + |R_1 C_{11} - R_2 C_{21}| + \frac{\eta_1 \eta_2}{\beta} \left(\frac{R_1 C_{11} + R_2 C_{21}}{|R_1 C_{11} - R_2 C_{21}|} - 1 \right) \right] \\
\frac{dR_2}{dt} &= \rho_2 - \eta_2 R_2 - R_2 C_{21} N_1 \\
&\quad + \frac{N_1}{2} \left[R_2 C_{21} - R_1 C_{11} + |R_1 C_{11} - R_2 C_{21}| + \frac{\eta_1 \eta_2}{\beta} \left(\frac{R_1 C_{11} + R_2 C_{21}}{|R_1 C_{11} - R_2 C_{21}|} - 1 \right) \right] \\
\frac{dR_3}{dt} &= \rho_3 - \eta_3 R_3 + N_1 \min(R_1 C_{11}, R_2 C_{21}) \\
\frac{dN_1}{dt} &= N_1 \min(R_1 C_{11}, R_2 C_{21}) - \mu_1 N_1,
\end{aligned} \tag{6}
$$

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and therefore we recover Liebig's law (i.e. the net growth rate of the consumer is $\min(R_1C_{11}, R_2C_{21})$). Using these equations in numerical simulations, we observe that the consumer abundance saturates (Fig. 2A), and the final abundance depends on the inflow rate of the more limiting resource (Fig. 2B). As such, the model in this limit behaves similar to classical consumer-resource models. In addition, we generate novel terms for the byproduct production rate, which in this fast reaction rate limit is $\simeq N_1 \min(R_1C_{11}, R_2C_{21})$, and we find corresponding equations for the uptake and export of glucose and phosphate.

On the other hand, when β is small relative to the other rates the consumer-resource equations become:

$$\begin{aligned}
\frac{dR_1}{dt} &= \rho_1 - \eta_1 R_1 - R_1 C_{11} N_1 + N_1 \left(C_{11} R_1 - \frac{\beta C_{11} R_1 C_{21} R_2}{\lambda_1 \lambda_2} \right) \\
\frac{dR_2}{dt} &= \rho_2 - \eta_2 R_2 - R_2 C_{21} N_1 + N_1 \left(C_{21} R_2 - \frac{\beta C_{11} R_1 C_{21} R_2}{\lambda_1 \lambda_2} \right) \\
\frac{dR_3}{dt} &= \rho_3 - \eta_3 R_3 + N_1 \frac{\beta C_{11} R_1 C_{21} R_2}{\lambda_1 \lambda_2} \\
\frac{dN_1}{dt} &= N_1 \frac{\beta C_{11} R_1 C_{21} R_2}{\lambda_1 \lambda_2} - \mu_1 N_1.
\end{aligned} \tag{7}$$

Hence, we recover multiplicative co-limitation by the two resources (i.e., the net growth rate of the consumer is $\frac{\beta C_{11} R_1 C_{21} R_1}{\lambda_1 \lambda_2}$). Using numerical simulations, we observe that consumer abundance, N_1 saturates as expected but now includes a growth lag-phase (Fig. 2C). However, the final abundance depends on the inflow rate of both resources (Fig. 2D). An increase in the flux rate of either resource will yield a higher final population abundance.

In summary, from this coarse-grained representation, we recover two classic outcomes of consumer-resource theory by taking limits of the internal reaction rate β. We can also generalize these classic limits for intermediate β, in a way that is not currently used in consumer-resource models and falls neither into the category of Liebig's Law nor multiplicative co-limitation. Finally, we find functional forms

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for the production rate of lactate (and excretion of other resources) in each of these limits. Our model therefore demonstrates how we can generalize the functional form of consumer-resource models by considering realistic, simplified intracellular processes.

Two Species Model We now modify the model above to incorporate a second species. Here, both species use R_2 (phosphate), but the second species, N_2, uses a combination of R_2 and R_3 (lactate) to generate new biomass. While we are using this as a model with both competition (e.g., shared resources) and facilitation (e.g., metabolic cross feeding) interactions, it also represents the natural cross-feeding interaction between lactate producing and lactate consuming bacteria found in human and animal digestive systems (Duncan *et al.*, 2004). These metabolic cross-feeding interactions are common in microbial systems (Mee *et al.*, 2014; Tasoff *et al.*, 2015; Zelezniak *et al.*, 2015) and have industrial applications (Jiao *et al.*, 2012). As such, our model demonstrates how competition and facilitation mediate species dynamics and coexistence conditions and can be used to understand natural and engineered microbial systems.

First, we define two distinct internal metabolic processes, one for each consumer species:

$$\begin{aligned} R_1 + R_2 &\xrightarrow{\beta_1} \text{Biomass}_1 + R_3 \\ R_2 + R_3 &\xrightarrow{\beta_2} \text{Biomass}_2. \end{aligned} \tag{8}$$

Consumer N_2 may also produce a metabolic byproduct, but we have not included such a process here because we are focusing on competition for R_2 and facilitation through the production of R_3 by species N_1. Importantly, we now have two internal reaction rates, β_1 and β_2. Here we focus on how these rates, both relative to each other and also to the other rates in the model, affect species coexistence. This approach demonstrates the power of modeling coarse-grained metabolic processes as the mechanism underlying species interactions. Furthermore, it allows us to explore the potential for changes in species coexistence due to metabolic (i.e., reaction rates) and landscape (i.e., inflow rates) factors.

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Generalizing the approach in the previous section, we define the fluxes for an individual belonging to species N_1 as:

$$\begin{aligned}
\nu_{bio,1} &= \beta_1 M_1 M_2 \\
\nu_{11} &= k_{11} - \beta_1 M_1 M_2 \\
\nu_{21} &= k_{21} - \beta_1 M_1 M_2 \\
\nu_{31} &= \beta_1 M_1 M_2
\end{aligned} \tag{9}$$

for internal concentrations M_1 and M_2, and uptake rates k_{i1}. While for an individual of species N_2 we have:

$$\begin{aligned}
\nu_{bio,2} &= \beta_2 M_1 M_3 \\
\nu_{12} &= k_{12} - \beta_2 M_1 M_3 \\
\nu_{32} &= k_{32} - \beta_2 M_1 M_3.
\end{aligned} \tag{10}$$

We also assume that all resources can be secreted from both consumers, but to simplify the model slightly we will assume that the specific export rates are equal, λ, broadly consistent with passive diffusion across sufficiently similar cell wall types. With this assumption, we can solve for internal equilibrium in both cell types (see Methods). Finally, we can put all of this together to generate a set of equations for both species and all three resources.

To focus on the effects of internal reaction rates and the resource landscape, we will further simplify our model by making a few assumptions. We will assume that the outflow rates for each resource are the same, so that $\eta_i = \eta$, and that the per capita mortality rates for each consumer are equal, so that $\mu_i = \mu$. We will also again assume that the per capita uptake rate of resource i by species j can be written as $C_{ij} R_i$. We will then determine the effects of internal reaction rate by independently changing the value of

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β for each species. In addition, we will change the landscape conditions by exploring the inflow rates for each resource ρ_i. Given these assumptions, our two species consumer-resource model is:

$$
\begin{aligned}
\frac{dR_1}{dt} &= \rho - \eta R_1 - R_1 C_{11} N_1 + \nu_{11} N_1 - R_1 C_{12} N_2 + \nu_{12} N_2 \\
&= \rho - \eta R_1 \\
&\quad - N_1 \left(\frac{\lambda^2}{2\beta_1} - \frac{F(\beta_1, C_{11}R_1, C_{21}R_2)}{2} + \frac{C_{11}R_1 + C_{21}R_2}{2} \right) \\
&\quad - N_2 \left(\frac{\lambda^2}{2\beta_2} - \frac{F(\beta_2, C_{12}R_1, C_{32}R_3)}{2} + \frac{C_{12}R_1 + C_{32}R_3}{2} \right) \\
\frac{dR_2}{dt} &= \rho - \eta R_2 - R_2 C_{21} N_1 + \nu_{21} N_1 \\
&= \rho - \eta R_2 - N_1 \left(\frac{\lambda^2}{2\beta_1} - \frac{F(\beta_1, C_{11}R_1, C_{21}R_2)}{2} + \frac{C_{11}R_1 + C_{21}R_2}{2} \right) \\
\frac{dR_3}{dt} &= \rho - \eta R_3 + \nu_{31} N_1 - R_3 C_{31} N_3 + \nu_{32} N_2 \\
&= \rho - \eta R_3 \\
&\quad + N_1 \left(\frac{\lambda^2}{2\beta_1} - \frac{F(\beta_1, C_{11}R_1, C_{21}R_2)}{2} + \frac{C_{11}R_1 + C_{21}R_2}{2} \right) \\
&\quad - N_2 \left(\frac{\lambda^2}{2\beta_2} - \frac{F(\beta_2, C_{12}R_1, C_{32}R_3)}{2} + \frac{C_{12}R_1 + C_{32}R_3}{2} \right) \\
\frac{dN_1}{dt} &= N_1 \nu_{bio,1} - \mu N_1 \\
&= N_1 \left(\frac{\lambda^2}{2\beta_1} - \frac{F(\beta_1, C_{11}R_1, C_{21}R_2)}{2} + \frac{C_{11}R_1 + C_{21}R_2}{2} \right) - \mu N_1 \\
\frac{dN_2}{dt} &= N_2 \nu_{bio,2} - \mu N_2 \\
&= N_2 \left(\frac{\lambda^2}{2\beta_2} - \frac{F(\beta_2, C_{12}R_1, C_{32}R_3)}{2} + \frac{C_{12}R_1 + C_{32}R_3}{2} \right) - \mu N_2.
\end{aligned}
\tag{11}
$$

Using numerical simulations, we model the consumer dynamics to determine species dynamics and equilibrium conditions (Fig. 4). First we consider when the internal metabolic rates, β_i, are the same. When internal metabolic rates are both high, species coexist at a density determined by the shared resource inflow rate (i.e., ρ_2) until the inflow rate of the unshared resource, R_1, exceeds the inflow rate of the shared resource, R_2. When ρ_1 is greater than ρ_2 (i.e., $\rho_1/\rho_2 > 1$), species N_1 will outcompete species N_2 for R_2, and N_2 will become rare (Fig. 4A). These findings expand the expectations of Liebig's Law to

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two cross-feeding species and demonstrate both species dynamics and equilibrium abundances across various resource landscapes. In contrast, when internal metabolic rates are low, species relative abundances are determined by their respective required resources and both species have growth lag-phases. These findings expand the expectations of multiplicative co-limitation to two cross-feeding species. However, since species N_1 will not be resource limited when ρ_1 is greater than ρ_2, then species N_2 will maintain a higher relative abundance across wider resource landscape (Fig. 4B, see Eq. 7). Together, we find that if internal rates are the same but either high or low compared to the other rates in our model, then our results expand the expectations of Liebig's Law and multiplicative co-limitation to the two-species system with a metabolic dependency. In addition, we find that coexistence depends on both the internal metabolic rates and the resource inflow rates even when uptake rates are the same.

Finally, we consider the dynamics and equilibria when the internal metabolic rates, β_i, are the different. We find that, when the rates differ the outcome depends on which species has the higher metabolic rate. When the byproduct producer, N_1, has the higher rate, then the results are similar to when both species have high internal metabolic rates (Fig. 4C). We do note, however, two important differences: 1) species N_2 exhibits a growth lag-phase, and 2) both R_1 and R_2 are depleted as the species reach an equilibrium. However, when species N_2, has the higher rate, then the coexistence conditions and high relative abundances for both species are greatly expanded. In fact, we find coexistence with moderate abundances along all inflow rates tested and the final abundances of both species are determined only by the shared resource, R_2 (Fig. 4D). In addition, we find that both species exhibit growth lag-phases and that R_2 and R_3 are now the depleted resources. These findings highlight how variation in both the internal metabolic reaction rates and in the environmental conditions can influence species interactions and change expectations for coexistence.

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Discussion

Classic formulations for pairwise interactions and consumer resource dynamics have each led to insights regarding species coexistence, community stability, population self-regulation (Schoener, 1983; Barabás *et al.*, 2017; Allesina & Tang, 2012; Leibold & McPeek, 2006). Here, we identify trade-offs with each approach. Lotka-Volterra (and related) equations provide a flexible approach to modeling a range of interactions between species but are unable to generalize across environmental variation because they do not provide an unambiguous way to include the resource landscape. While it may be possible to modify per capita growth rates to be a function of environmental conditions (e.g., temperature) and the resource landscape, it is not clear how information would be included the species interaction terms. However, these models allow positive and negative species interactions to be explored straighforwardly. Consumer-resource models explicitly include the interaction between the resource landscape and consumers, but at the expense of introducing more explicit mechanism, and therefore more choices in the way interactions are implemented. Including positive interactions through the production of resources has led to new predictions regarding the stability of communities (Butler & O'Dwyer, 2018), indicating that incorporating resource exchange may be important for understanding the dynamics of real communities. However, we don't know how sensitive these results may be to the precise way consumption and exchange are formulated. Here, we argue that incorporating metabolism more explicitly into consumer-resource dynamics will allow us to explain a broader range of community dynamics and natural phenomena, with less ambiguity in the functional form of interactions, and these metabolic rates may also reveal how environmental conditions like temperature which can change metabolic rates contribute to species dynamics.

In including these processes, we reformulated the classical consumer-resource model to independently include resource uptake, internal metabolic rates, and byproduct export. As such, our model is more complex than the Lotka-Volterra equations but not as complex as a full multi-species flux balance analysis. We found that when internal metabolic dynamics are included in addition to uptake two common models of resource limitation (Liebig's Law and multiplicative co-limitation) appear in particular limits of the

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internal reaction rates. In this model, we also make predictions for the functional form of the production of metabolic byproducts, and we balance the requirements for growth, energy, storage, and export. We further expand our model to include a second species which uses the metabolic byproduct of the first species. In this metabolically-informed approach to consumer-resource models both species interactions (competitive and mutualistic) and resource use efficiency are emergent properties of the system. In addition, we show how internal metabolic reaction rates and the resource landscape determine species dynamics and equilibria. We find that the metabolic rates can change when resources are *metabolically* limiting, and therefore our model shows how how metabolic rates and the resource landscape change the interactions between cross-feeding species. We further show that, if interacting species have different metabolic rates, species and resource equilibria can change while maintaining the competitive and facilitative interactions among species. We propose that when extended more broadly, this approach will lead to mechanistic predictions for the role of positive interactions along stress gradients (Callaway & Walker, 1997; Brooker & Callaghan, 1998), the ability of species interactions to stabilize or de-stabilize communities (Butler & O'Dwyer, 2018; Allesina & Tang, 2012), and the mechanisms underlying biodiversity ecosystem function relationships (Duffy *et al.*, 2007; Flynn *et al.*, 2011; Cardinale *et al.*, 2012). In short, we propose that metabolically-informed consumer-resource dynamics will provide a platform to explore the consequences of cooperative and competitive interactions across environmental contexts.

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Methods

Solution for Polynomial Equations We can solve the single-species polynomial equations (Eq. 4) for internal resource concentrations to obtain:

$$\begin{aligned} M_1 &= \frac{k_1 - k_2}{2\lambda_1} - \frac{\lambda_2}{2\beta} + \frac{1}{2\lambda_1} F(\beta, k_1, k_2) \\ M_2 &= \frac{k_2 - k_1}{2\lambda_2} - \frac{\lambda_1}{2\beta} + \frac{1}{2\lambda_2} F(\beta, k_1, k_2), \end{aligned} \tag{12}$$

while biomass production is given by

$$\nu_{bio} = \frac{\lambda_1 \lambda_2}{2\beta} - \frac{F(\beta, k_1, k_2)}{2} + \frac{k_1 + k_2}{2}, \tag{13}$$

where $F(\beta, k_1, k_2) = \sqrt{\left(k_1 + k_2 + \frac{\lambda_1 \lambda_2}{\beta}\right)^2 - 4k_1 k_2}$ depends on uptake, export, and reaction rates.

Limits of the general set of equations

We now solve Eq. 5 for two limits. The first limit is where β is large relative to the other rates,

$$\begin{aligned} M_1 &\simeq \frac{k_1 - k_2 + |k_1 - k_2|}{2\lambda_1} + \frac{\lambda_2}{2\beta}\left(\frac{k_1 + k_2}{|k_1 - k_2|} - 1\right) + O(1/\beta^2) \\ M_2 &\simeq \frac{k_2 - k_1 + |k_1 - k_2|}{2\lambda_2} + \frac{\lambda_1}{2\beta}\left(\frac{k_1 + k_2}{|k_1 - k_2|} - 1\right) + O(1/\beta^2) \\ \nu_1 &= \lambda_1 M_1 \\ \nu_2 &= \lambda_2 M_2 \\ \nu_3 = \nu_{bio} &\simeq \min(k_1, k_2) + O(1/\beta) \end{aligned} \tag{14}$$

Note that we have to keep the $O(1/\beta)$ terms for M_1 and M_2, because for at least one of the two

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(depending on whether $k_1 > k_2$ or $k_1 < k_2$) the O(1) term vanishes in this limit of fast reaction rate β.

The second limit is where β is small relative to the other rates,

$$
\begin{aligned}
M_1 &\simeq \frac{k_1}{\lambda_1} - \frac{\beta k_1 k_2}{\lambda_1^2 \lambda_2} + O(\beta^2) \\
M_2 &\simeq \frac{k_2}{\lambda_2} - \frac{\beta k_1 k_2}{\lambda_1 \lambda_2^2} + O(\beta^2) \\
\nu_1 &= \lambda_1 M_1 \\
\nu_2 &= \lambda_2 M_2 \\
\nu_3 = \nu_{bio} &\simeq \beta \frac{k_1 k_2}{\lambda_1 \lambda_2} + O(\beta^2)
\end{aligned} \tag{15}
$$

0.1 Internal Equilibrium in Two-Species Model

For the two-species model (Eqs. 9 & 10), we assume that all resources can be secreted from both consumers, but to simplify the model slightly we will assume that the specific export rates are equal, λ, broadly consistent with passive diffusion across sufficiently similar cell wall types. Based on these assumptions, we can solve for internal equilibrium in both cell types to obtain:

$$
\begin{aligned}
\nu_{bio,1} &= \frac{\lambda^2}{2\beta_1} - \frac{F(\beta_1, k_{11}, k_{21})}{2} + \frac{k_{11} + k_{21}}{2} \\
\nu_{bio,2} &= \frac{\lambda^2}{2\beta_2} - \frac{F(\beta_2, k_{12}, k_{32})}{2} + \frac{k_{12} + k_{32}}{2},
\end{aligned} \tag{16}
$$

where, similarly to the one species case, the function $F(x, a, b) = \sqrt{\left(a + b + \frac{\lambda^2}{x}\right)^2 - 4ab}$.

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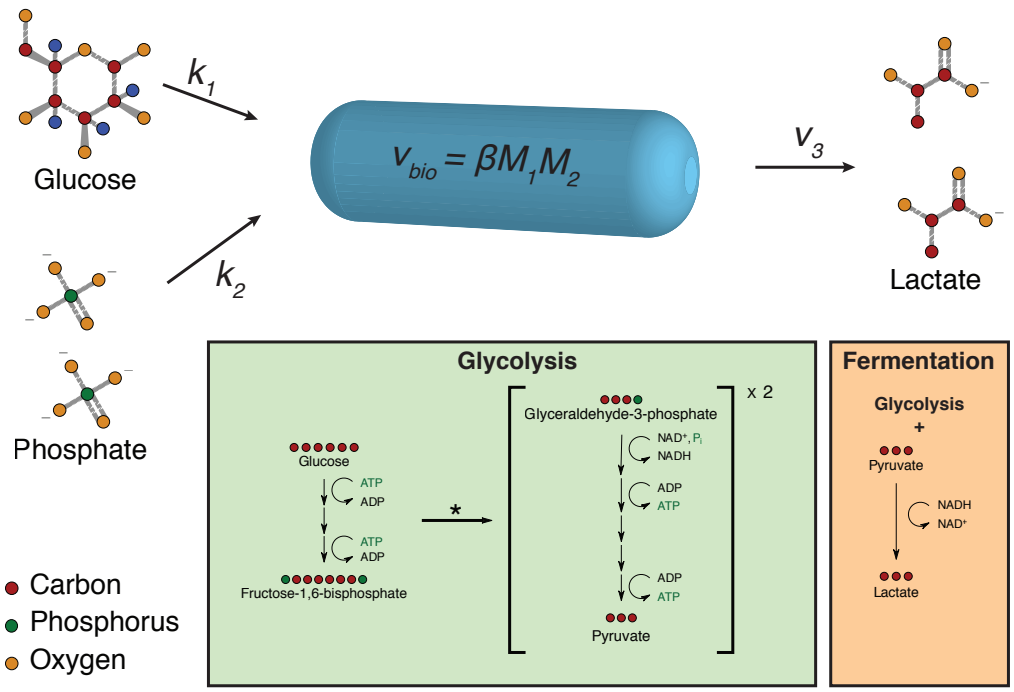

Figure 1: **Conceptual Model**. To demonstrate our metabolically informed consumer-resource model we used fermentation as a prototype. Fermentation is an anaerobic—usually sugar consuming—metabolic lifestyle, and is the primary anaerobic energy-producing reaction for many microorganisms (Gottschalk, 1986). A signature of fermentation is that it results in byproducts such as organic acids, alcohols, and/or gases, which are produced due to the incomplete resource oxidation during the energy producing reactions. Homolactic fermentation, the simplest type of fermentation, results in the incomplete oxidation of glucose. The inputs are one glucose and two phosphate molecules, and the products are two lactate molecules. This energy producing reaction yields a net two ATP per glucose. Here, we show the detailed chemical reactions involved with homolactic fermentation. First, glycolysis is used to turn one molecule of glucose into two pyruvate molecules. At this stage, the pyruvate can either be used for biomass, or it can be fermented into lactate. In our model, glucose and phosphate enter the cell at uptake rates k_i, biomass is generated at rate $\beta M_1 M_2$, and the metabolic byproduct, lactate, is exported from the cell at rate ν_3.

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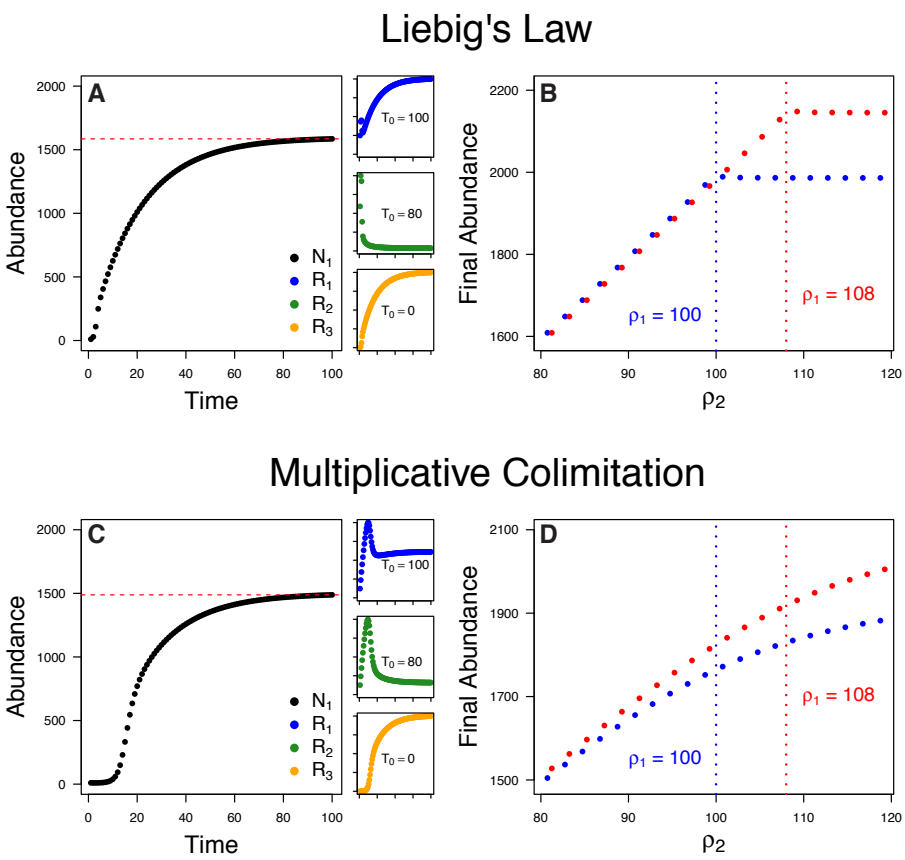

Figure 2: **Single Species Simulation**. We used numerical simulations of our single-species model to determine how the resource landscape changes population dynamics. **A & B**: In the limit where β is high relative to other rates (Eq. 6), we recover Liebig's Law of the Minimum. Consumer abundance saturates, but the final abundance depends on the inflow rate, ρ_i, of the more limiting resource. When the inflow of R_2 (ρ_2) is lower than the inflow of R_1 (ρ_1), R_2 becomes depleted. At saturation, R_1 is in excess while R_2 is limiting (**A**). Changes in the inflow rates alters the final abundance (**B**), but the final abundance will always be determined by the more limiting resource. When $\rho_1 = 100$ (blue) the final abundance will increase until $\rho_2 = 100$, and when $\rho_1 = 108$ (red) the final abundance will increase until $\rho_2 = 108$. In contrast, in the limit where β is low relative to other rates (Eq. 7), we recover multiplicative co-limitation. Consumer abundance still saturates, albite at a lower final abundance given the same resource inflow rates and with a growth lag-phase (**C**). As consumer abundance increases, both R_1 and R_2 are depleted. In addition, the final abundance increases as inflow rates increase (**D**). When $\rho_1 = 100$ (blue) the final abundance will continue to increase past $\rho_2 = 100$, and when $\rho_1 = 108$ (red) the final abundance will continue to increase past $\rho_2 = 108$.

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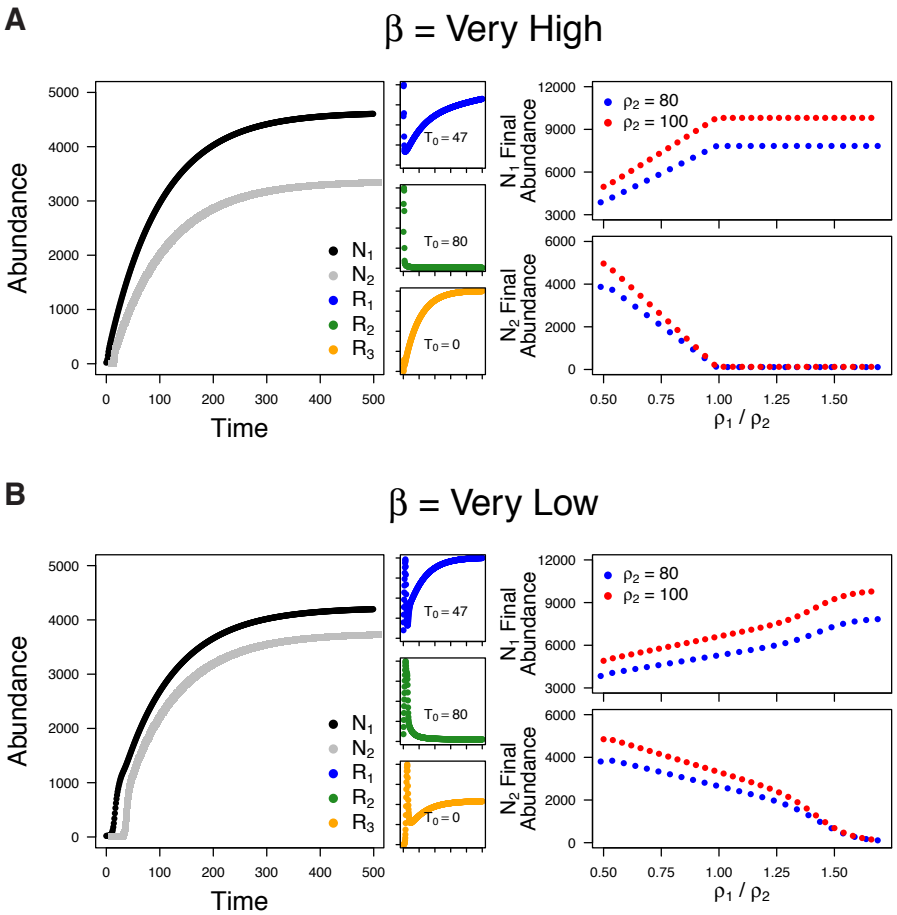

Figure 3: **Two Species with the Same Metabolic Rates**. We simulated species dynamics in the two-species model with equal internal metabolic rates, β_i. In this model, two species compete for a shared resource (R_2), but species N_1 also consumes R_1 and produces R_3 as a metabolic byproduct which is consumed by species N_2. When metabolic rates are high, species abundances saturate and species can coexist provided the appropriate resource conditions (**A**). When the shared resource inflow rate (ρ_2) is higher than the inflow rate of R_1 (ρ_2), then the two species can coexist at a relatively high abundance because N_1 is more limited by its exclusive resource (R_1). However, when ρ_1 is higher than ρ_2 (i.e., $\rho_1/\rho_2 > 1$), then N_1 can outcompete N_2 for the shared resource (R_2) and the final abundance of N_2 will be greatly reduced. Even when the inflow rate of the shared resource is increased ($\rho_2 = 100 vs 80$), the final abundance of N_2 does not increase when $\rho_1/\rho_2 > 1$. When metabolic rates are low, species still coexistence, but the range of coexistence is greatly expanded (**B**). While the final abundance of N_2 still decreases as the resource inflow ratio (ρ_1/ρ_2) approaches 1, it does not decrease at the same rate and the final abundance remains relatively high even when the resource inflow ratio is 1. In this simulation, the resource inflow ratio needs to be greater than 1.5 before N_1 outcompetes N_2 and N_2 becomes rare.

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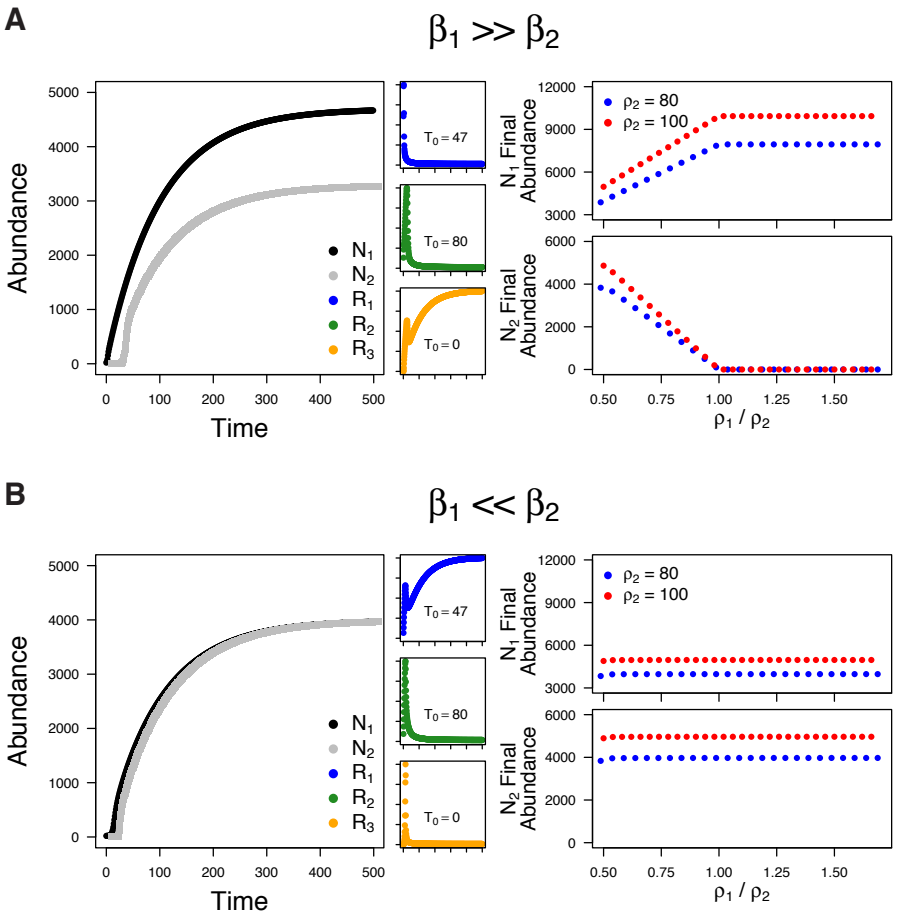

Figure 4: **Two Species with Different Metabolic Rates**. We simulated species dynamics in the two-species model where the species have different internal metabolic rates, β_i. In this model, one of the species has high and the other low metabolic rates compared to the other rates in the model. The species compete for R_2, and species N_1 consumes R_1 and produces R_3 which is used by species N_2. When N_1 has the higher metabolic rate, the species dynamics are similar and the coexistence conditions are identical to the model where both species have high metabolic rates (**A**). However, there are now two important differences. First, N_2 (gray line) has a growth lag-phase. Second, both R_1 and R_2 are now depleted as the population abundance saturates. When N_2 has the higher metabolic rates, the coexistence conditions are drastically different (**B**). N_1 and N_2 have growth lag-phases, and R_2 and R_3 are now the depleted resources. In addition, both species coexist at a final abundance determined only by the shared resource inflow rate (ρ_2) across all resource inflow rates (ρ_1/ρ_2) tested.