Microbial species interactions determine community diversity in fluctuating environments

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Abstract

Microorganisms often live in environments that fluctuate between mild and harsh conditions. Although such fluctuations are bound to cause local extinctions and affect species diversity, it is unknown how diversity changes at different fluctuation rates and how this relates to changes in species interactions. Here, we use a mathematical model describing the dynamics of resources, toxins, and microbial species in a chemostat where resource supplies switch. Over most of the explored parameter space, species competed, but the strength of competition peaked at either low, high or intermediate switching rates depending on the species' sensitivity to toxins. Importantly, however, the strength of competition in species pairs was a good predictor for how community diversity changed over the switching rate. In sum, predicting the effect of environmental switching on competition and community diversity is difficult, as species' properties matter. This may explain contradicting results of earlier studies on the intermediate disturbance hypothesis.

Key words: competitive exclusion, environmental switching, demographic noise, chemostat, beta diversity, intermediate disturbance hypothesis

1 Introduction

Natural environments are not static: temperature, pH, or availability of resources change over time. Many studies in microbiology, ecology and evolution have focused on responses to fluctuations in resource abundance in the regime of feast and famine periods (Hengge-Aronis, 1993; Vasi et al., 1994; Srinivasan and Kjelleberg, 1998; Xavier et al., 2005; Merritt and Kuehn, 2018; Himeoka and Mitarai, 2019). These models capture the dynamics within many natural ecosystems. For example, the gut microbiota of a host is exposed to fluctuating resources that depend on its host's feeding rhythm, which may affect microbiota diversity (Cignarella et al., 2018; Li et al., 2017; Thaiss et al., 2014). In addition to their magnitude, environmental fluctuations can also differ in their time scales: for the gut microbiota, a host's feeding rhythm may vary from hourly to daily, or even monthly if feeding depends on seasonal changes (Davenport et al., 2014; Smits et al., 2017).

How fluctuations affect species diversity has been a highly contested topic in ecology. The intermediate disturbance hypothesis argues that intermediate intensity and frequency maximize species diversity (Connell, 1978; Grime, 1973) because species with high competitive ability dominate at a low level of disturbance while species that adapted to the disturbance dominate at a high level of disturbance (Grime, 1977). This hypothesis is controversial (Fox, 2013) and other relationships between disturbance and species diversity have been reported both empirically and theoretically (Mackey and Currie, 2001; Miller et al., 2011). Theoretical studies also suggest that species interactions affect coexistence under fluctuating environments, resulting in changing species diversity. In competition-colonization models, for example, whether a species persists or not depends on other coexisting species, the disturbance and the focal species' traits (Hastings, 1980; Kinzig et al., 1999). Indeed, species coexistence requires a positive invasion growth rate of each species – the ability to grow when rare (Barabás et al., 2018; Chesson and Huntly, 1997; Fox, 2013; Yi and Dean, 2013). Because environmental conditions, especially amounts of resources and toxins, affect the sign and/or magnitude of species interactions (Hoek et al., 2016; Piccardi et al., 2019; Zuñiga et al., 2019), environmental fluctuations are expected to affect species interactions and invasion growth rates, which in turn should affect community diversity. Recently, Rodríguez-Verdugo et al. (2019) used theory and experiments to show that the rate of environmental fluctuations affects the coexistence of two species when the environment switches between two carbon sources that promote either exploitation or competition between the species. However, it is unclear whether and how environmental fluctuations in amounts of – rather than types of – resources affect species coexistence and diversity. More generally, can one predict patterns of diversity under fluctuating environments in larger communities composed of more than two species? And how do these relate to changes in inter-species interactions?

To shed light on these questions, we develop a mathematical model to investigate how the rate of environmental fluctuations affects species interactions and diversity. We start with a simple scenario with just two species in an environment that switches between scarce and abundant resource supplies. We focus on the faster grower and ask: (i) How often does this species go extinct due to the presence of a slower-growing competitor, and (ii) how does such extinction depend on the environmental switching rate and other properties of the environment? For most parameter values, the faster grower's extinction probability increases because of competitive

exclusion by the slower grower. To our surprise, we found that the competitive effect of the slower on the faster grower peaked at different switching rates depending on environmental toxicity. Without knowing how different species respond to varying environmental conditions, it may then be difficult to predict how they behave when subject to environmental fluctuations. Second, to verify whether these findings generalize to and predict the dynamics of larger community dynamics, we simulated communities of up to 10 species and found a similar pattern: beta diversity was highest at different switching rates in different environments. Although various forms of relationship between the disturbance and diversity have been previously reported (Mackey and Currie, 2001; Miller et al., 2011), our model successfully associates the strength of competition between two species with loss of beta diversity in a larger community under a fluctuating environment. In other words, to estimate how beta diversity changes over the environmental switching rate, it may be sufficient to analyze the sign and strength of interactions between two representative species under those same conditions.

2 Model

In this paper, we analyze how environmental switching rate ν affects species interactions and diversity in a chemostat model. For simplicity, we assume symmetric random switching (but see Taitelbaum et al. (2020) for asymmetric, random and periodic switching). This model combines two sources of noise: birth and death events occur randomly yielding demographic noise, while the environment randomly switches from being harsh to mild and vice versa and drives the population size (Wienand et al., 2017, 2018; West and Mobilia, 2020; Taitelbaum et al., 2020). When the environment becomes harsh (e.g., abundant toxins or scarce resources), the population shrinks and demographic noise can lead to extinction. As in previous work, a distinctive feature of this model is therefore the coupling of demographic and environmental noise: environmental switching changes the population size, which in turn modulates demographic fluctuations, which results in feedback loops. Here, we implement environmental switching by modeling time-varying resource and/or toxin supplies, as we are interested in how these environmental conditions mediate species interactions and diversity.

Our model includes the dynamics of the amount r_i of resource i ($i = 1, \ldots, N/2$, where N is an even number) that allows all species to grow, the amount t_j of toxic compound j ($j = 1, \ldots, N/2$) that kills all species, and the abundance s_k of species k ($k = 1, \ldots, N$). When $N = 2$ species, we recapitulate the environmentally mediated species interactions shown in the model of Piccardi et al. (2019), where species affect each other positively in toxic environments, with increasing competition in more benign environments. The dynamics are modelled in terms of a multivariate continuous-time birth-and-death process (see Novozhilov et al. (2006); Allen (2010) for

example) defined by the following "birth" and "death" reactions:

$$r_i \xrightarrow{\tau^+_{r_i}} r_i + 1, \tag{1a}$$

$$r_i \xrightarrow{\tau^-_{r_i}} r_i - 1, \tag{1b}$$

$$t_j \xrightarrow{\tau^+_{t_j}} t_j + 1, \tag{1c}$$

$$t_j \xrightarrow{\tau^-_{t_j}} t_j - 1, \tag{1d}$$

$$s_k \xrightarrow{\tau^+_{s_k}} s_k + 1, \tag{1e}$$

$$s_k \xrightarrow{\tau^-_{s_k}} s_k - 1, \tag{1f}$$

occurring with transition rates:

$$\tau^+_{r_i} = \alpha R_i\left(\xi\right), \tag{2a}$$

$$\tau^-_{r_i} = \sum_{k=1}^{N} \frac{\mu_{ik}}{Y^r_{ik}} \frac{r_i}{r_i + K^r_{ik}} s_k + \alpha r_i, \tag{2b}$$

$$\tau^+_{t_j} = \alpha T_j\left(\xi\right), \tag{2c}$$

$$\tau^-_{t_j} = \sum_{k=1}^{N} \frac{\delta_{jk}}{Y^t_{jk}} \frac{t_j}{t_j + K^t_{jk}} s_k + \alpha t_j, \tag{2d}$$

$$\tau^+_{s_k} = \sum_{i=1}^{N/2} \mu_{ik} \frac{r_i}{r_i + K^r_{ik}} s_k, \tag{2e}$$

$$\tau^-_{s_k} = \sum_{j=1}^{N/2} \delta_{jk} \frac{t_j}{t_j + K^t_{jk}} s_k + \alpha s_j, \tag{2f}$$

where α is the dilution rate of the chemostat, $\xi = \pm 1$ (see below) represents changing environmental conditions in terms of in-flowing resource and/or toxin concentration, $R_i(\xi)$ ($T_j(\xi)$) is resource i's (toxin j's) supply under the environmental condition ξ, Y^r_{ik} (Y^t_{jk}) is species k's biomass yield for resource i (toxin j), μ_{ik} is the maximum growth rate of species k by resource i, δ_{jk} is the maximum death rate of species k by toxin j (species k's sensitivity to toxin j), and K^r_{ik} (K^t_{jk}) is the amount of resource i (toxin j) that gives the half-maximum growth (death) rate of species k. In this model, we assume that growth and death rates depend on the amounts of resource and toxin in Monod function forms, respectively, and that the effects are additive.

Environmental switching changes resource and/or toxin supplies at rate ν according to

$$\xi \xrightarrow{\nu} -\xi, \tag{3}$$

where $\xi \in \{-1, +1\}$ is a coloured dichotomous (telegraph) noise assumed to be symmetric and stationary (Bena, 2006; Horsthemke and Lefever, 2006). Here, the mean of $\xi(t)$ is therefore always zero and its finite correlation time is $1/\nu$. One can imagine three environmental switching scenarios, where either or both resource and toxin supplies change (Table 1). In the main text, we analyze only scenario 1, but see Appendix 4 for the remaining

Table 1: Different scenarios of environmental switching

Scenario	$R_i(\xi=1)$	$R_i(\xi=-1)$	$T_j(\xi=1)$	$T_j(\xi=-1)$
1	R_i^+	R_i^-	$\langle T_j\rangle$	$\langle T_j\rangle$
2	$\langle R_i\rangle$	$\langle R_i\rangle$	T_j^-	T_j^+
3	R_i^+	R_i^-	T_j^-	T_j^+

scenarios. When environmental switching affects the resource supply R_i, it switches between abundant and scarce:

$$R_i(\xi) = \begin{cases} R_i^+ & \xi = 1 \text{ (abundant)} \\ R_i^- & \xi = -1 \text{ (scarce)} \end{cases} \quad \text{s.t. } R_i^+ > R_i^- > 0, \forall i. \tag{4}$$

It is clear that (2a)-(4) define a multivariate birth-and-death process *coupled* with environmental switching. As environmental switching does not affect toxin supply in this scenario, the mean amount of toxins is supplied $\langle T_j\rangle$, where $\langle\cdot\rangle$ represents the mean of abundant and scarce supplies of a focal resource or toxin (e.g., $\langle T_j\rangle \equiv \left(T_j^+ + T_j^-\right)/2$ such that $T_j^+ > T_j^- > 0, \forall j$).

Note that when demographic noise is ignored, the sole source of randomness stems from the dichotomous Markov noise, which clearly results in the waiting time between two environmental switches to be exponentially distributed with a mean $1/\nu$ (Bena, 2006). In the joint presence of demographic noise and environmental switching, see, e.g., (Hufton et al., 2016; West et al., 2018), the waiting time approximately follows the exponential distribution with mean $1/\nu$, with the larger the switching rate the shorter the sojourn in either of the environmental states.

The master equation for this model is defined by combining the dynamics of amount of resources and toxins, abundances of species, and environmental switching (Eqs (1a) - (3)):

$$\begin{aligned}
\dot{P}\left(\vec{r},\vec{t},\vec{s},\xi\right) = &\sum_{i=1}^{N/2}\left(\mathbb{E}_{r_i}^- - 1\right)\left\{\tau_{r_i}^+ P\left(\vec{r},\vec{t},\vec{s},\xi\right)\right\} \\
&+\sum_{i=1}^{N/2}\left(\mathbb{E}_{r_i}^+ - 1\right)\left\{\tau_{r_i}^- P\left(\vec{r},\vec{t},\vec{s},\xi\right)\right\} \\
&+\sum_{j=1}^{N/2}\left(\mathbb{E}_{t_j}^- - 1\right)\left\{\tau_{t_j}^+ P\left(\vec{r},\vec{t},\vec{s},\xi\right)\right\} \\
&+\sum_{j=1}^{N/2}\left(\mathbb{E}_{t_j}^+ - 1\right)\left\{\tau_{t_j}^- P\left(\vec{r},\vec{t},\vec{s},\xi\right)\right\} \\
&+\sum_{k=1}^{N}\left(\mathbb{E}_{s_k}^- - 1\right)\left\{\tau_{s_k}^+ P\left(\vec{r},\vec{t},\vec{s},\xi\right)\right\} \\
&+\sum_{k=1}^{N}\left(\mathbb{E}_{s_k}^+ - 1\right)\left\{\tau_{s_k}^- P\left(\vec{r},\vec{t},\vec{s},\xi\right)\right\} \\
&+\nu\left\{P\left(\vec{r},\vec{t},\vec{s},-\xi\right) - P\left(\vec{r},\vec{t},\vec{s},\xi\right)\right\}
\end{aligned} \tag{5}$$

where $P\left(\vec{r},\vec{t},\vec{s},\xi\right)$ represents the probability density of $\vec{r} = (r_i)$, $\vec{t} = (t_j)$, $\vec{s} = (s_k)$, and ξ, the dot denotes the

time derivative, and $\mathbb{E}^{\pm}_{r_i}$ is a shift operator such that

$$\mathbb{E}^{\pm}_{r_i} P\left(\vec{r}, \vec{t}, \vec{s}, \xi\right) = P\left(r_1, \ldots, r_i \pm 1, \ldots, r_{N/2}, \vec{t}, \vec{s}, \xi\right), \tag{6}$$

and $\mathbb{E}^{\pm}_{t_j}$ and $\mathbb{E}^{\pm}_{s_k}$ are the equivalent shift operators for t_j and s_k, respectively. The last line on the right-hand-side of (5) accounts for the random switching reaction (3). The model given by Eq. (5) was implemented using the Gillespie algorithm (Gillespie, 1977) until, after a sufficiently large time T_{end}, the population size distribution converges to a quasi-stationary distribution (i.e., where distributions of species abundances appear to be stationary for a long time; the real equilibrium state corresponding to the extinction of all species being practically unobservable). For details on parameter values and the simulations, see Appendix 2. A schematic illustration of this model with $N = 2$ is summarized in Fig. 1.

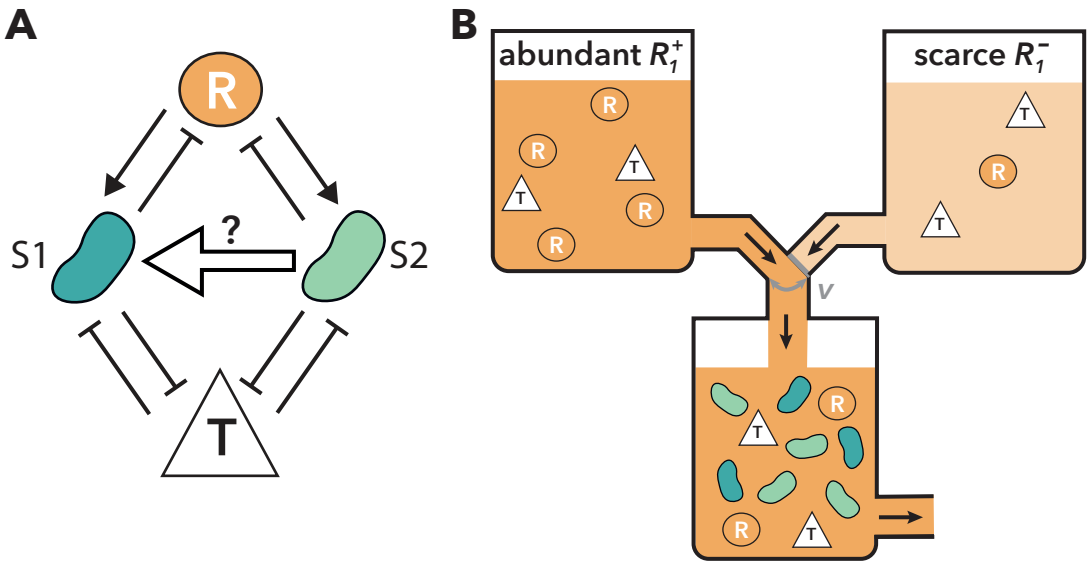

Figure 1: Schematic illustration of the model

A chemostat model with environmental switching. A: Interaction network when $N = 2$. A $\rightarrow$ B represents that A increases B while A $\dashv$ B represents that A decreases B. Two species compete for the same resource (R in a circle) but are killed by the same toxic compound (T in a triangle). As a proxy for species interactions, we follow the net effect of species 2 on species 1 (large arrow from species 2 to 1) – due to resource competition plus facilitation by detoxification – which can be environmentally mediated. B: An example of a chemostat model with environmental switching and $N = 2$. Environmental switching is realized by changing the media flowing into a chemostat. In this example, the current environmental condition is $\xi = 1$ (abundant resource supply R_1^+).

2.1 Evaluating species interactions

We begin by analyzing interactions between two species ($N = 2$) where the sign and magnitude of species interactions can change. We used parameter values such that species 1 always outcompetes species 2 in a deterministic and fixed environment setting (i.e., species 1 grows faster than species 2, see Appendix 1 for analysis and Table S.1 for exact parameter values) to clarify the effects of demographic noise. Under demographic noise coupled with environmental switching, either of the two species or both species tend to go extinct. As a proxy for interactions, we focus on the net effect of species 2 on species 1, which is defined by the extinction probability

of species 1 in mono-culture minus that in co-culture with species 2:

$$\Delta P\left(s_1(T_{end})=0\right) \equiv P\left(s_1(T_{end})=0; s_2(0)=0\right) - P\left(s_1(T_{end})=0; s_2(0)>0\right). \tag{7}$$

If $\Delta P\left(s_1(T_{end})=0\right)$ is < -0.01, we consider that species 2 increases the extinction probability of species 1 (negative effect), whereas $\Delta P\left(s_1(T_{end})=0\right) > 0.01$ implies that species 2 has a positive effect on species 1. We ignore small values of $|\Delta P\left(s_1(T_{end})=0\right)|$, as they are biologically meaningless and may be due to the finite number of simulations.

In the analysis of species diversity (see below) with $N=2$, we also analyzed the species interactions in 100 pairs of species that differ in $\mu_{ik}, K^r_{ik}, \delta_{jk}$, and K^t_{jk} in the presence of demographic noise and environmental switching. Since pairs of species may coexist depending on their parameter values in the diversity analysis, species 1 (or 2) is the one that has larger (or smaller) population size than the other in the absence of any noise. If both species go extinct in the absence of noise, species 1 is chosen randomly.

2.2 Evaluating species diversity

To explore how species diversity changes over switching rates, we ran simulations at different community sizes ranging from $N=2$ to $N=10$ and different mean toxin sensitivities, from $\bar{\delta}=0.1$ to $\bar{\delta}=1$. For each condition (one community size and one $\bar{\delta}$), we sampled 100 sets of parameters $\mu_{ik}, K^r_{ik}, \delta_{jk}$, and K^t_{jk}, which represented 100 meta-communities composed of N species whose differences were reflected in the parameter values. For each set of parameter values and each environmental switching rate, we ran 100 simulations. In other words, each meta-community had 100 independent communities with independent environmental switching.

Because demographic noise and environmental switching affect species composition, at the end of each simulation run, we measured beta diversity (Jost, 2007; Chao et al., 2012) of each meta-community and species richness (number of surviving species) for each community at a quasi-stationary state (T_{end}):

$${}^1D_\beta\left(T_{end}\right) \equiv \frac{{}^1D_\gamma\left(T_{end}\right)}{{}^1D_\alpha\left(T_{end}\right)}, \tag{8}$$

with alpha and gamma diversities defined as below:

$${}^1D_\alpha\left(T_{end}\right) \equiv \exp\left(-\sum_{l=1}^{100}\sum_{k=1}^{N} w_l p_{lk}\left(T_{end}\right)\ln p_{ln}\left(T_{end}\right)\right), \tag{9}$$

$${}^1D_\gamma\left(T_{end}\right) \equiv \exp\left(-\sum_{k=1}^{N} \bar{p}_k \ln \bar{p}_k\left(T_{end}\right)\right). \tag{10}$$

w_l is a weight for community l calculated by size of community l (sum of species abundances in community l relative to the sum of community sizes over l), p_{lk} is the relative abundance of species k in community l (i.e., in community l, $p_{lk}\left(T_{end}\right) = s_k\left(T_{end}\right) / \sum_k s_k\left(T_{end}\right)$), and $\bar{p}_k = \sum_l w_l p_{lk}$ is the mean relative abundance of species k among communities $l = 1, \ldots, 100$. If all species go extinct in community l, it does not affect alpha, beta and gamma diversities as $w_l = 0$. If all species go extinct in all communities, beta diversity becomes

${}^{1}D_{\beta}\left(T_{end}\right) = 1$. For more detail, see Appendix 2.

2.3 Statistical analysis

Statistical analysis was performed with Python 3.7.6 and Scipy 1.4.1. For statistical tests of Spearman's rank-order correlation, scipy.stats.spearmanr was used.

3 Results

3.1 Toxin sensitivity changes how switching rate affects species interactions

Our aim is to investigate how species interactions and diversity change over the environmental switching rate. Rather than measuring interactions through the effect of each species on the other's biomass, we focus on a fast-growing species (that we call species 1) and analyze how its extinction probability is affected by the presence of a second slower-growing species (species 2). Our reasoning here is that in the absence of noise, species 1 should always out-compete species 2, so measuring any deviation from this outcome allows us to quantify the effect of coupled demographic and environmental fluctuations. We explored how this proxy for species interactions was affected by different environmental switching rates as well as different toxin sensitivities, which we varied simultaneously for both species, such that the species were always equally sensitive to the toxin.

When both species were highly sensitive to the toxin (large δ), species 2 has a positive effect on species 1. This occurs because species 2 also degrades the toxin, which outweighs the competition for nutrients (Piccardi et al., 2019). However, for most parameter values in Fig. 2A, species 2 has a negative effect on species 1 by increasing its extinction probability. We therefore focus on competitive interactions (i.e., $\Delta P\left(s_1(T_{end}) = 0\right) < 0$) for the remainder of the main part of the study and consider positive interactions in Appendix 5.

As we varied the switching rate, we observed that the strength of the competitive effect was highly dependent on the toxin sensitivity δ of the two species: monotonically increasing, monotonically decreasing, or non-monotonically changing with a minimum or maximum value at an intermediate switching rate (Fig. 2B). How our system behaves under the two extreme switching rates becomes clear if one considers what happens in the absence of environmental switching (Fig. S.3). At very low rate $\nu \to 0$, there are almost no switches: the environment remains either poor or rich in nutrient (probability 1/2) and microbes are as likely to experience either scarce or abundant resources from $t = 0$ until $t = T_{end}$. The outcome at this switching rate therefore corresponds to the mean outcome of those two environments. On the other hand, a very fast environmental switching rate ($\nu \to \infty$) corresponds to a scenario where the resource supply is at mean concentration (environmental noise self averages, see, e.g.,Wienand et al. (2017, 2018); West and Mobilia (2020); Taitelbaum et al. (2020)). How the strength of competition varies at an intermediate switching rate is, however, less intuitive. We explore this next.

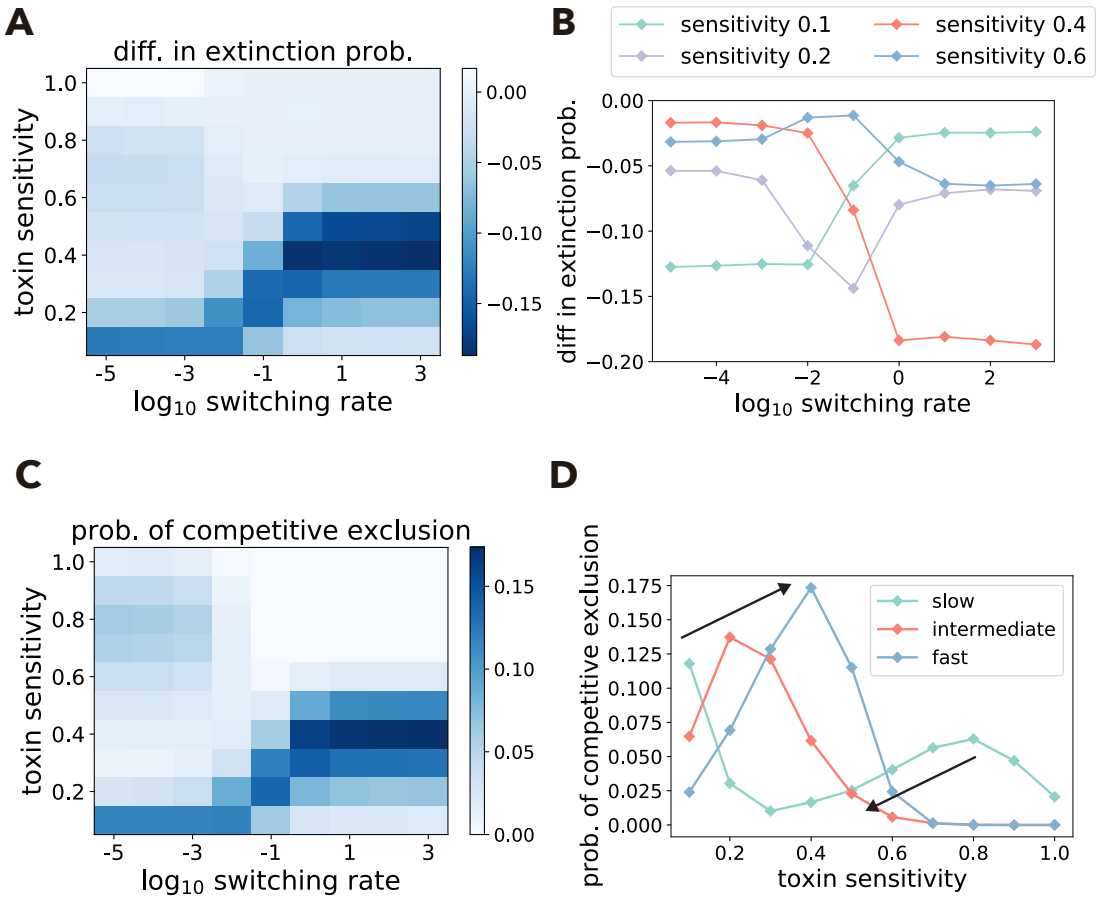

Figure 2: Species interaction strength changes differently over the switching rate

A: The effect of species 2 on species 1's extinction probability $\Delta P\left(s_1(T_{end})=0\right)$ (Eq 7) changes over the switching rate ν and the toxin sensitivity $\delta=\delta_{11}=\delta_{21}$. In most of the parameter space, species 2 has a negative effect on species 1. B: Some illustrative examples from panel A plotted differently to show how ΔP changes over the switching rate at given toxin sensitivities. The difference in extinction probability can monotonically increase ($\delta=0.1$, green), monotonically decrease ($\delta=0.4$, red), or non-monotonically change with a minimum ($\delta=0.2$, purple) or a maximum ($\delta=0.6$, blue) value at an intermediate switching rate. C: Probability that species 2 persists but species 1 goes extinct (i.e., competitive exclusion) over switching rate and toxin sensitivity. D: competitive exclusion probabilities over the toxin sensitivity, when the environmental switching rate is slow ($\nu=10^{-5}$), intermediate ($\nu=10^{-1}$), or fast ($\nu=10^{3}$).

3.2 Competitive exclusion explains negative species interactions

To better understand the unexpected changes in the effect of species 2 on species 1 (Fig. 2B), we analyse our proxy for species interactions in more detail. $\Delta P\left(s_1(T_{end})=0\right)$ represents the difference between the probability of species 1 going extinct in mono-culture ($P\left(s_1(T_{end})=0; s_2(0)=0\right)$) versus in co-culture with species 2 ($P\left(s_1(T_{end})=0; s_2(0)>0\right)$) (Eq. 7). By decomposing the co-culture component into two probabilities depending on whether species 2 persists or not and rearranging the equation, we obtain:

$$\begin{aligned}\Delta P\left(s_1(T_{end})=0\right) = &-\underbrace{P\left(s_1(T_{end})=0, s_2(T_{end})>0; s_2(0)>0\right)}_{\text{competitive exclusion}} \\ &+\left\{\underbrace{P\left(s_1(T_{end})=0; s_2(0)=0\right)}_{\text{sp 1 goes extinct in mono-culture}} - \underbrace{P\left(s_1(T_{end})=0, s_2(T_{end})=0; s_2(0)>0\right)}_{\text{both species go extinct}}\right\}.\end{aligned} \tag{11}$$

The first line of Eq (11) represents the probability that species 2 excludes species 1 and survives (competitive exclusion), while the second line is species 1's extinction probability in mono-culture minus the probability of both species going extinct.

Fig. S.2 shows that the overall interaction strength is not affected much by the second line of Eq (11), and that the competitive exclusion probability explains the variation in species interaction strength in most cases (compare Fig. 2A and C). Intuitively, this is because under the environmental conditions where both species are likely to go extinct (i.e., small resource supplies and high toxin sensitivity), species 1 is also likely to go extinct in mono-culture, resulting in a small magnitude of the second line of Eq (11). For this reason, the competitive exclusion probability changes similarly to the effect of species 2 on species 1 over environmental switching rates and toxin sensitivities (Fig. 2C). In other words, we can assume that the second line of Eq (11) is negligible and focus instead on the competitive exclusion probability.

3.3 Competitive exclusion explains non-monotonic changes in species interactions

Following the logic outlined above, we now use the competitive exclusion probability to investigate why the strength of negative interactions changes over the switching rate in various ways, depending on toxin sensitivity.

In the absence of environmental switching, the competitive exclusion probability is uni-modal over toxin sensitivity δ, regardless of the resource supply (Fig. 3A). As a reminder, competitive exclusion implies the extinction of species 1 and the survival of species 2. Since toxin sensitivity is identical for both species, when toxin sensitivity is too high, both species are likely to go extinct (Fig. S.4), which does not count as competitive exclusion. Instead, competitive exclusion is most likely at lower toxin sensitivities whose value depends on the amount of resource supply: when more resources are supplied, the peak moves to a higher toxin sensitivity because species are more likely to survive (Fig. 3A). Hereafter, we refer to the toxin sensitivity that maximizes the competitive exclusion probability in the absence of environmental switching as the "critical toxin sensitivity".

This analysis clarifies what happens at the two extreme switching rates. At a very slow switching rate ($\nu \to 0$), the environment remains for a long time with either scarce or abundant resources. Accordingly, competitive exclusion has two peaks over the toxin sensitivity (at $\delta = 0.1$ and 0.8 in Figs. 2C and D) corresponding to the critical toxin sensitivities under the scarce and abundant resource supplies in Fig. 3A, respectively. On the other hand, at very fast switching rates ($\nu \to \infty$), where resources remain at mean abundance, competitive exclusion has one peak (at $\delta = 0.4$ in Figs. 2C and D) corresponding to the critical toxin sensitivity under the mean resource supply in Fig. 3A. In sum, the form of the competitive exclusion probability in Fig. 2C changes from bi-modal to uni-modal by increasing the switching rate.

The non-monotonic change of competitive exclusion probability over the switching rate can happen at toxin sensitivities between the critical toxin sensitivities under scarce (or abundant) and mean resource supplies (Fig. 2C). This phenomenon can be explained by considering that the landscape of competitive exclusion depicted in Fig. 2C contains two "mountain ranges". The first "mountain range" includes two peaks corresponding to the critical toxin sensitivities under the scarce and mean resource supplies ($\delta = 0.1, 0.4$, respectively). By increasing environmental switching from a very slow rate, the peak at $\delta = 0.1$ converges to the peak at $\delta = 0.4$ (Fig. 2D). The second "mountain range" consists of the peak corresponding to the critical toxin sensitivity under the abundant resource supply ($\delta = 0.8$). This peak vanishes by increasing the switching rate (Fig. 2D).

At toxin sensitivities between critical values under scarce and mean resource supplies ($\delta = 0.2, 0.3$), the competitive exclusion probability changes in a humped shape over the switching rate (species interactions change in a U shape, see Fig. 2B). This is because an intermediate switching rate has a peak of competitive exclusion probability belonging to the first mountain range. When the toxin sensitivity is $\delta = 0.6$, the environmental switching rate also non-monotonically affects the competitive exclusion probability, but for a different reason. Toxin sensitivities between the critical values under mean and abundant resource supplies can have a "valley" over the switching rate: at such toxin sensitivities, competitive exclusion probability changes in a U shape over the switching rate (species interactions change in a humped shape, see Fig. 2B). At toxin sensitivities larger than the critical value under the abundant resource supply, competitive exclusion probability is very small and does not change non-monotonically over the switching rate because both species frequently go extinct (Fig S.4).

3.4 Non-monotonic changes in species interactions happen under different scenarios of environmental differences

We have shown that using a given set of parameters, the rugged landscape shown in Fig. 2C causes competition to either increase, decrease or vary non-monotonically across switching rates, depending on toxin sensitivity. We next explore the generality of this finding and ask whether it will hold under different scenarios. In the appendix, we explore scenarios where (i) switching occurs in toxin rather than resource supplies, where (ii) both resource and toxin supplies switch (Table 1, see Appendix 4), or where (iii) we change the amounts of scarce and abundant resource supplies (Appendix 5).

In all these scenarios, the landscapes of competitive exclusion probability also contain two "mountain ranges"

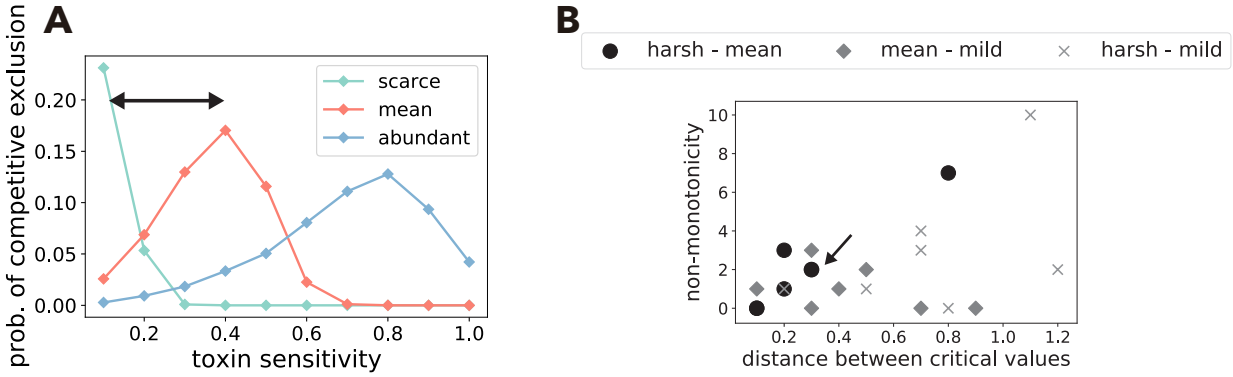

Figure 3: Competitive exclusion explains changes in species interactions

Analysis on competitive exclusion predicts at which toxin sensitivity the species interaction can change non-monotonically. A: In the absence of environmental switching, the competitive exclusion probability (i.e., probability that species 2 excludes species 1) is uni-modal over the switching rate. The toxin sensitivities giving the peak values (critical toxin sensitivities) depend on the resource supply: scarce $R_1 = R_1^-$ (green), mean $R_1 = \langle R_1 \rangle$ (red), or abundant $R_1 = R_1^+$ (blue). B: The number of times we observe non-monotonic species interactions across the explored parameter range changes with the distance between the two critical toxin sensitivities, depending on where distances are measured (between harsh and mean environments: dots, between mean and mild: environment diamonds, and between harsh and mild environments: crosses). These three distances were measured in each of the following seven scenarios: three different scenarios of environmental switching (Table 1 and Appendix 4) and four environmental switching scenario 1s with changing amounts of resource supplies (Appendix 5). The correlation is only significantly positive for the distance between scarce resource or abundant toxin supplies (i.e., harsh environments) and mean resource/toxin supplies (Spearman's $\rho = 0.77$, P-value: 0.043). The distance corresponding to the scenario analyzed in the main text is shown by the black arrow in panel A, where scarce resources are considered to be a harsh environment (dot indicated by the arrow in panel B).

(Figs. S.5, S.7), leading, as before, to a variety of patterns as switching rates and toxin sensitivities change. In each scenario, the distances between the three critical toxin sensitivities (mild, mean and harsh, e.g. black arrow in Fig. 3A) change (see Table S.2). Do these distances predict the shape of the landscape and the probability of observing non-monotonic behavior? In Table S.2 and Fig. 3B we show that the distance between critical sensitivities under harsh and mean environments (i.e., very fast environmental switching) correlates positively with the likelihood of observing non-monotonic effects of the switching rate on competition (Fig. 3B, black circles; Spearman's $\rho = 0.77$, P-value: 0.043), but no significant correlation was found with the distance between the critical toxin sensitivities under the mean and mild, or the harsh and mild environments (Fig. 3B, grey diamonds and cross marks; Spearman's $\rho = -0.22$, P-value: 0.64, and $\rho = 0.42$, P-value: 0.35, respectively). These differences can be explained by changes in the shape of the landscape (see subsection 3.3). In sum, we find non-monotonic behavior under many different scenarios, with no easily observable pattern for when they occur. Overall, this makes it challenging to predict how the strength of interspecific interactions will change over environmental switching rates.

3.5 Beta diversity changes similarly to competitive exclusion

In the previous sections, we have focused on interactions between two species and the conditions under which they may drive each other extinct. Ultimately, however, our interest is to predict how species diversity is affected

by the environment in communities comprised of tens, hundreds or even thousands of species. In this section, we ask whether the same rules that we have uncovered between two species apply for larger communities of up to 10 species. Will the diversity of a community similarly depend on environmental switching rates and toxin sensitivities?

We address this question by extending our model to simulate communities of between 2 and 10 species. Simulating larger communities with this model would be too computationally expensive. As our model includes stochastic environmental switching and demographic noise, we ran 10'000 simulations for each community size and for each of 5 different mean toxin sensitivities (here species in a community could differ in their toxin sensitivity) ranging from $\bar{\delta} = 0.1$ to $\bar{\delta} = 1$ (see Methods). At the end of each simulation run, we measured the beta diversity and species richness (number of surviving species). These 10'000 (100×100) simulations were composed of 100 replicate runs for one of 100 randomly sampled sets of parameter values (see Methods).

In two-species communities, beta diversity changes over the environmental switching rate similarly to the competitive exclusion probability for four out of five mean toxin sensitivities (columns A and B in Fig. 4): both monotonically decrease (mean toxin sensitivity $\bar{\delta} = 0.1$ or 1.0), or non-monotonically change with maximum ($\bar{\delta} = 0.2$) or minimum ($\bar{\delta} = 0.6$) values at intermediate switching rates. At one mean toxin sensitivity $\bar{\delta} = 0.4$, the patterns of competitive exclusion and beta diversity over the switching rate do not match. Our measure of final species richness (column C in Fig. 4) shows that at low switching rates and $\bar{\delta} = 0.4$, both species can sometimes co-exist, which keeps beta-diversity high. Although two species can also coexist when $\bar{\delta} = 0.1$ or 0.2, the probability of coexistence changes over the switching rate similarly to the competitive exclusion probability, leading to similar patterns in both measures.

We next increase the number of species in community to 10 (Figs. S.10 and S.11) to see whether the same patterns of beta diversity are observed. The similarity remains in 10-species communities (columns D and E in Fig. 4). Although variation in species richness increases beta diversity, the inverse is not true: beta diversity can be large when species richness is likely to be one (see $\bar{\delta} = 0.4$ and 0.6 at switching rate larger than 10^1 in fourth and fifth columns in Fig. 4). In such cases, different species fixate in each simulation by competitive exclusion. In sum, estimating the competitive exclusion probability in two species in a given environment is a good predictor for the beta diversity of larger communities under those same environmental conditions.

4 Discussion

Understanding how species diversity in microbial communities arises and is maintained is a central question in microbial ecology and evolution. Diversity is affected by biotic interactions between species, but also by abiotic properties of the environment, such as its harshness (availability of nutrients and/or toxicity), and how conditions fluctuate over time. Here we have used a mathematical model to explore the relationship between these three factors and how they affect the diversity of small communities.

Our study is centred on two main findings. First, we show that the rate at which resource abundance fluctuates in the environment changes the strength of negative interactions (competition) – quantified as the

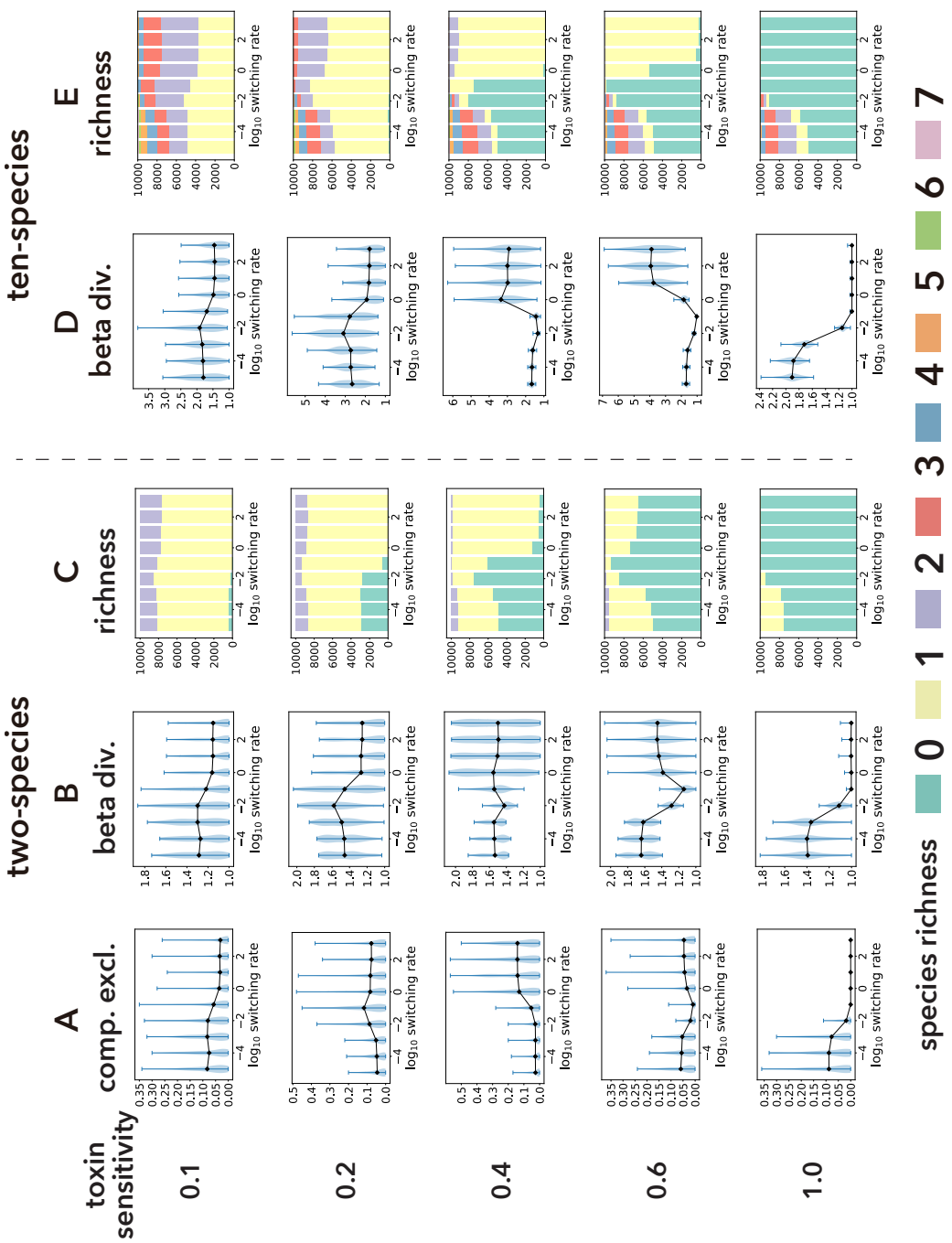

Figure 4: Comparison of competitive exclusion and beta diversity

Competitive exclusion probabilities (column A), beta diversities (column B), and species richness (column C) over the switching rate in two-species communities. Here, competitive exclusion refers the event where the slower-growing species excludes the faster-growing species. Columns D and E show the beta diversity and species richness in ten-species communities, respectively. In the plots of competitive exclusion probability and beta diversity, the black lines show the means and blue areas represent the probability distributions calculated from 10'000 simulations (100 beta diversity and each of them from 100 replicate runs). Each color in the species richness plots represents the proportion of 10'000 runs where at the end of the run there were that number of species surviving. Each row represents the mean toxin sensitivity $\bar{\delta}$ of communities in those runs.

ability of a slower-growing species to drive a fast-growing one extinct –, but that these changes depend strongly on how toxic the two species perceive their environment to be. As the switching rate increases, competition can be: monotonically increasing, monotonically decreasing, or changing non-monotonically (Fig. 2B), depending on the toxin sensitivity. These negative interactions mostly manifest as competitive exclusion, rather than the extinction of both species (Figs. 2C and S.2). By calculating the critical toxin sensitivities that maximize competitive exclusion in the absence of environmental switching, one can predict how the switching rate will affect the strength of competition at a given toxin sensitivity. Our second main finding is that studying changes in the probability of two species competitively excluding one another is a good indicator for how the beta diversity of a community composed of up to 10 species will change with environmental switching (Fig. 4). In that sense, species interactions are closely associated with species diversity and each can be inferred from the other.

This brings us to a hypothesis that has been debated at length in ecology: the intermediate disturbance hypothesis (IDH) (Connell, 1978; Grime, 1973), which states that "diversity of competing species is, or should be expected to be, maximized at intermediate frequencies and/or intensities of disturbance or environmental change" (Fox, 2013). Fox (2013) argues that the IDH is lacking in empirical and theoretical support, and should be abandoned. Although our model does not specifically model disturbances, fluctuations in resource supplies (and/or abundant toxin supplies) can here be regarded as disturbances, and we can thus offer additional evidence regarding the IDH. A variety of forms of diversity are reported over the frequency and intensity of disturbance (Mackey and Currie, 2001; Miller et al., 2011), which matches our observation of the patterns of beta diversity varying over environmental switching rates and toxin sensitivities. Indeed, in agreement with Mackey and Currie (2001) and Miller et al. (2011), an intermediate intensity or disturbance frequency does not always maximize beta diversity. Rather, our analysis shows that this occurs in a transition from a benign environment of low toxin sensitivity where a linear relationship exists to a harsh environment of high toxin sensitivity where the opposite linear relationship is observed. The hump-shape is then a consequence of a change in environmental conditions and not expected to apply generally.

Of course, our model makes some simplifying assumptions and has some limitations. First, we used arbitrary time units, which in practice can be considered to be hours, corresponding to typical bacterial growth rates in relevant experiments (Novick and Szilard, 1950; Lin et al., 2002; Zhao and Lin, 2003). This implies that species interactions and beta diversity will vary when environmental switching ranges from hourly ($\nu = 10^0$) to about once every four days ($\nu = 10^{-2}$) on average, which is shorter than in some experimental studies (Benneir and Lenski, 1999; Rodríguez-Verdugo et al., 2019; Chen and Zhang, 2020) but not impractical. That said, under this assumption, changing an hourly to a monthly scale, for example, would have different effects on ecological dynamics. Second, the switching rate is assumed to be symmetric between abundant and scarce resources (and/or toxin supplies, see Appendix 4). One may include more than two environmental conditions or assume asymmetric environmental switching, as in work by Taitelbaum et al. (2020), who show that asymmetric switching can non-trivially change the effects of environmental switching. Third, our model focuses on competitive exclusion but other types of interactions can also affect diversity (Rodríguez-Verdugo et al., 2019). Positive interactions

between pairs of species (e.g., cross-feeding), for example, might increase alpha and gamma diversities, because such interactions enable species to coexist (Sun et al., 2019). This could result in an increase in beta diversity because the extinction of one species by demographic noise, for example, increases its partner species' extinction probability. Finally, our community analysis considers up to ten microbial species, which is orders of magnitude below the size of natural microbial communities, according to genomic sampling (Gans, 2005; Roesch et al., 2007). However, it may also be reasonable to assume that species live in structured environments where they cannot possibly interact with more than a handful of other genotypes (Tecon et al., 2019). This suggests that a 10-species community may already be biologically meaningful.

In conclusion, the time scale of environmental switching affects the strength of species interactions, resulting in changing beta diversity via competitive exclusion. In addition, how species interactions and beta diversity change over the environmental switching rate varies depending on how sensitive species are to environmental toxicity. This may be one mechanism by which the intermediate disturbance hypothesis does not always hold. The variety with which species interactions and beta diversity change over the switching rate means that it will be very difficult for a given scenario to predict how an ecosystem, such as the gut microbiome, will behave under environmental fluctuations. Nevertheless, the similarity between how competitive exclusion plays out between two species and beta diversity at the community level means that analysing how the former changes over switching rates (as in Rodríguez-Verdugo et al. (2019), for example) may be sufficient to predict the latter. More generally, our study, along with others (Mackey and Currie, 2001; Miller et al., 2011) show that predicting how the environment shapes diversity in ecology remains a challenging problem.

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