Exclusion of the fittest predicts microbial community diversity in fluctuating environments

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Abstract

Microorganisms live in environments that inevitably fluctuate between mild and harsh conditions. As harsh conditions may cause extinctions, the rate at which fluctuations occur can shape microbial communities and their diversity, but we still lack an intuition on how. Here, we build a mathematical model describing two microbial species living in an environment where substrate supplies randomly switch between abundant and scarce. We then vary the rate of switching as well as different properties of the interacting species, and measure the probability of the weaker species driving the stronger one extinct. We find that this probability increases with the strength of demographic noise, and peaks at either low, high, or intermediate switching rates depending on both species' ability to withstand the harsh environment. This complex relationship shows why finding patterns between environmental fluctuations and diversity has historically been difficult: response to fluctuations depends on species' properties. In parameter ranges where the fittest species was most likely to be excluded, however, the beta diversity in larger communities also peaked. In sum, while we find no simple rules on how the frequency of fluctuations shapes the diversity of a community, we show that their effect on interactions between two representative species predicts how diversity in the whole community will change.

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 microbiome 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) – or in the type of substrates taken up, which can be nutritious or harmful for the microbiota.

How environmental fluctuations (EFs) affect species diversity has been a highly contested topic in ecology. Here, EFs refer to changes that are not caused by the organisms themselves, but nevertheless affect their dynamics (e.g., abiotic resource supplies). The intermediate disturbance hypothesis argues that intermediate intensity and frequency of disturbances maximize species diversity (Connell, 1978; Grime, 1973) because highly competitive species dominate at a low level of disturbance, while only species that have adapted to the disturbance dominate at high 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).

Another framework that is used to predict species diversity under EFs is the modern coexistence theory (Chesson, 1994), which explains the maintenance of diversity through species' different responses to and preferences for environmental conditions, which can vary over spatial and/or temporal scales through fluctuations (Amarasekare, 2019; Chesson, 2000a,b; Letten et al., 2018b; Barabás et al., 2018; Ellner et al., 2019). The modern coexistence theory divides environmental factors into those that are independent of species abundances (e.g., temperature) and those that depend on them (e.g., amounts of resources). The latter environmental factors mediate the sign and/or magnitude of interspecific interactions (Hoek et al., 2016; Piccardi et al., 2019; Zuñiga et al., 2019), and whether species tend to cooperate or compete can, in turn, drive community diversity and stability (Mougi and Kondoh, 2012; Coyte et al., 2015). Microbial communities often experience extreme environmental fluctuations that can alter interactions between species and hence affect species diversity (Rodríguez-Verdugo et al., 2019; Nguyen et al., 2020).

Another important factor potentially influencing the outcome of interactions between species is demographic noise (DN) arising from randomness in birth and death events in finite populations. DN is negligible in large populations but strong in small ones, where it can lead to species extinction or fixation, and affect community composition (Roughgarden, 1979; Ewens, 2004). As EFs affect population sizes, they modulate the strength of demographic noise, leading to a coupling of EFs and DN. This interdependence has been understudied until recently, despite its potentially important consequences on eco-evolutionary dynamics (Wienand et al., 2017,

2018; West and Mobilia, 2020; Taitelbaum et al., 2020).

To understand how the interplay between EFs and DN affect community diversity, we set up a simple stochastic model of multiple species subject to a varying supply of nutrients and/or toxins. We include toxins in our model firstly as they are important in natural communities, but often missed in similar models. Secondly, toxins contribute to environmental harshness and reduce population sizes, which can modulate the strength of DN; and thirdly, we expect them to affect inter-species interactions, as species can absorb toxins and potentially facilitate the growth of others (Hoek et al., 2016; Piccardi et al., 2019; Zuñiga et al., 2019). Our model then allows us to ask: How do EFs, coupled to DN, affect species interactions and diversity?

The remainder of this paper starts with a description of our theoretical model, explaining how DN and EFs are implemented and how species interactions and diversity are measured (section 2). We first use it to explore how often one single species goes extinct due to environmental switching coupled with DN (section 3.1). We then add a second slower-growing species, still focusing on the behavior of the first, and ask how its extinction probability is affected by the slower-grower, and how different properties of the two species change the effects of the switching rate (section 3.2). We find that high sensitivity to the toxin increases the strength of DN because it decreases species abundances. Under strong DN, the probability of the faster-grower being driven extinct by its competitor peaks at either low, high, or intermediate switching rates depending on the two species' sensitivities to toxic substrates (sections 3.3 and 3.4). Finally, we expand our model to larger communities and show that our first analysis of the exclusion of the fittest species predicts beta diversity patterns in larger communities (section 3.5): community composition is the most diverse when strong species are most likely to be excluded. Section 4 discusses the importance of coupling EFs and DN on species interactions and diversity. Then, we compare our results with the intermediate disturbance hypothesis and the modern coexistence theory. Technical and computational details are given in a series of Appendices.

2 Model & Methods

In order to investigate the interdependence of EFs and DN on species interactions and diversity, we study an idealized chemostat model that combines DN and environmental switching (Fig. 1). We consider a well-mixed population consisting of N species of bacteria, and $N/2$ types of resources as well as $N/2$ types of toxins (without loss of generality, N is assumed to be even, except in the case mono-culture 3.1). Although many models ignore the role of toxins, they play two important roles in our model: first, sensitivities to toxin changes the strength of DN because population sizes of sensitive species are low. Second, toxins can enable a pair of species to facilitate each other (Piccardi et al., 2019) because toxin absorbance decreases the death rate of the other species. The community follows a continuous-time multi-variate birth-and-death process (see, e.g. Novozhilov et al. (2006); Allen (2010)) in a time-fluctuating binary environment (see, *e.g.*, Wienand et al. (2017, 2018); West and Mobilia (2020); Taitelbaum et al. (2020)). More specifically, we consider that at time σ the community consists of an amount $r_i(\sigma)$ of resources of type i ($i = 1, \ldots, N/2$), an amount $t_j(\sigma)$ of toxin of type j ($j = 1, \ldots, N/2$), and an abundance $s_k(\sigma)$ of microbial species k ($k = 1, \ldots, N$). Here, resources are assumed to be nutrients for all

species, allowing them to grow at different rates, while the toxins kill all species at different rates.

In a static environment (no EFs), this chemostat model evolves according to the birth-and-death process 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:

$$\tau^+_{r_i} = \alpha R_i, \tag{2a}$$

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

$$\tau^+_{t_j} = \alpha T_j, \tag{2c}$$

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

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

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

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 amount. $R_i(\xi)$ ($T_j(\xi)$) 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 for species k (see also Table A.1). These transition rates hence reflect that (i) the amounts of resources and toxins increase depending on the product of their in-flow concentrations and dilution rate, (ii) the amounts of resources and toxins decrease with the dilution rate and with the consumption/absorption by species, (iii) the growth and death rates depend in Monod functional forms on the amounts of resources and toxins, respectively, and (iv) all effects are additive. When R_i and T_j are constant, the environment is static and the birth-and-death process defined by Eqs (1a) – (2f) naturally accounts for the DN arising in the population,

which is the sole source of noise.

We model EFs by considering a time-fluctuating binary environment resulting in R_i and/or T_j to be *dichotomous random variables*, i.e., $R_i = R_i(\xi(\sigma))$ and/or $T_j(\xi(\sigma))$, where $\xi(\sigma) = \pm 1$ represents the binary state of the environment ($\xi = 1$ represents a mild environment while $\xi = -1$ represent a harsh environment). We hence assume that R_i and/or T_j switch between two values at a rate ν, according to a time-continuous colored dichotomous Markov noise (random telegraph noise) (Bena, 2006; Horsthemke and Lefever, 2006)

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

We call ν a "switching rate" because we implement a symmetrically switching environment as a simple example of EFs (but see Appendix 5 for other forms of EFs). We investigate three environmental switching scenarios, where either or both resource and toxin supplies fluctuate over time, see Table 1. In the main text, we focus on the scenario where only resource supplies switch between abundant and scarce supplies (R_i^+ and R_i^-, respectively, such that $R_i^+ > R_i^- > 0$) while the amounts of toxins supplies remain constant over time ($\langle T_j \rangle \equiv (T_j^+ + T_j^-)/2$); see Appendix 3 for the remaining scenarios. The initial resource supply in the main text is $R_i(\xi(0)) = R_i^+$ with probability 0.5 and otherwise $R_i(\xi(0)) = R_i^-$.

We assume that ξ switches symmetrically between the states ± 1 (see Taitelbaum et al. (2020) and Appendix 5 for the cases of asymmetric switching). In all our simulations, ξ is at stationary and thus ξ has zero mean, $\langle \xi(\sigma) \rangle = 0$, autocorrelation $\langle \xi(\sigma)\xi(\sigma') \rangle = \exp(-2\nu|\sigma - \sigma'|)$, where $\langle \cdot \rangle$ denotes the ensemble average over the environmental noise, and finite correlation time $1/(2\nu)$. A great advantage of dichotomous noise is its simplicity: ξ is bounded (R_i and T_j are always well defined) and straightforward to simulate. This choice allows us to model suddenly changing environmental conditions, which reflect situations in microbial life such as exposure to resource or toxin oscillations that can be reproduced in lab-controlled experiments (Sunya et al., 2013). Other forms of EFs are also possible, e.g. ξ could be a Gaussian random variable, but then R_i and T_j would be unbounded and vary continuously and could take unrealistic values. Modeling EFs with Eq (3) is arguably the simplest biologically-motivated choice to couple fluctuations in resource/toxin supplies with demographic noise, and allows us to investigate questions that are not specific to dichotomous noise.

The master equation for this model is defined by combining the dynamics of the amounts of resources and

toxins, abundances of species, with the environmental switching (Eqs (1a) - (3)):

$$\begin{aligned}\frac{d}{d\sigma}P\left(\vec{r},\vec{t},\vec{s},\xi,\sigma\right) = &\sum_{i=1}^{N/2}\left(\mathbb{E}_{r_i}^{-}-1\right)\left\{\tau_{r_i}^{+}P\left(\vec{r},\vec{t},\vec{s},\xi,\sigma\right)\right\}\\ &+\sum_{i=1}^{N/2}\left(\mathbb{E}_{r_i}^{+}-1\right)\left\{\tau_{r_i}^{-}P\left(\vec{r},\vec{t},\vec{s},\xi,\sigma\right)\right\}\\ &+\sum_{j=1}^{N/2}\left(\mathbb{E}_{t_j}^{-}-1\right)\left\{\tau_{t_j}^{+}P\left(\vec{r},\vec{t},\vec{s},\xi,\sigma\right)\right\}\\ &+\sum_{j=1}^{N/2}\left(\mathbb{E}_{t_j}^{+}-1\right)\left\{\tau_{t_j}^{-}P\left(\vec{r},\vec{t},\vec{s},\xi,\sigma\right)\right\}\\ &+\sum_{k=1}^{N}\left(\mathbb{E}_{s_k}^{-}-1\right)\left\{\tau_{s_k}^{+}P\left(\vec{r},\vec{t},\vec{s},\xi,\sigma\right)\right\}\\ &+\sum_{k=1}^{N}\left(\mathbb{E}_{s_k}^{+}-1\right)\left\{\tau_{s_k}^{-}P\left(\vec{r},\vec{t},\vec{s},\xi,\sigma\right)\right\}\\ &+\nu\left\{P\left(\vec{r},\vec{t},\vec{s},-\xi,\sigma\right)-P\left(\vec{r},\vec{t},\vec{s},\xi,\sigma\right)\right\} \qquad (4)\end{aligned}$$

where $P\left(\vec{r},\vec{t},\vec{s},\xi,\sigma\right)$ gives the probability to find the population in state $\left(\vec{r},\vec{t},\vec{s},\xi\right)$ at time σ, with $\vec{r}=(r_i)$, $\vec{t}=(t_j)$, $\vec{s}=(s_k)$. Here, $\mathbb{E}_{r_i}^{\pm}$ is a shift operator such that

$$\mathbb{E}_{r_i}^{\pm}P\left(\vec{r},\vec{t},\vec{s},\xi,\sigma\right) = P\left(r_1,\ldots,r_i\pm 1,\ldots,r_{N/2},\vec{t},\vec{s},\xi,\sigma\right), \qquad (5)$$

and $\mathbb{E}_{t_j}^{\pm}$ and $\mathbb{E}_{s_k}^{\pm}$ are the equivalent shift operators for t_j and s_k, respectively. Note that $P\left(\vec{r},\vec{t},\vec{s},\xi,\sigma\right)=0$ whenever any of $r_i, t_j, s_k < 0$. The first to sixth lines on the right-hand-side of Eq (4) represent the birth-and-death processes (1), while the last line accounts for environmental switching.

The master equation (4) fully describes the model dynamics and can be simulated exactly with the Gillespie algorithm (Gillespie, 1977). It is worth noting that owing to the stochastic nature of the model, after a time that diverges exponentially with the community size, DN will cause the eventual collapse of the population (Spalding et al., 2017; Assaf and Meerson, 2017). This phenomenon is practically unobservable when resource levels remain sufficiently large, i.e. if $R_i^{-} \gg 1$, and the population settles in a long-lived quasi-stationary distribution. Here we focus on the quasi-stationary regime that is attained when distributions of species abundances appear to be stationary for a long time (estimated from our simulations for our choice of parameters) (see supplementary video): the distributions of two species' abundances change little from time $\sigma = 130$ onward, which allows us to set $\sigma_{end} = 200$.

2.1 Evaluating species interactions

First, we analyze species interactions by measuring the extinction probabilities in the presence or absence of another species (see Appendix 1.1 for details). We begin with two species ($N = 2$) where the sign and magnitude of species interactions can change because the amounts of resources and toxins can change the net

effect of resource competition and facilitation via detoxification (Piccardi et al., 2019). We used parameter values such that species 1, if it persists, always outcompetes species 2 in the absence of DN (i.e., species 1 grows faster than species 2, see Appendix 2 for analysis and Table A.1 for exact parameter values) to identify the effects of DN. Under DN coupled with EFs in our chosen parameter range, 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 (Eq (A.1)): species 2 has a negative (positive) effect on species 1 if species 1's extinction probability in mono-culture is smaller (larger) than in co-culture with species 2. We performed 10^5 simulations for each switching rate and toxin sensitivity in mono- and co-cultures. We calculated 95% of highest posterior density intervals (HPDI) to measure the uncertainty of species 1's extinction probabilities (see Appendix 1.1) but they are too small to see.

2.2 Evaluating species diversity

To explore how species diversity changes with the switching rate, we ran simulations at different numbers of species ranging from $N = 2$ (2 species) to $N = 10$ (10 species) and different mean toxin sensitivities (see Appendix 1.2 for details). For each condition (one number of species and one mean toxin sensitivity), we sampled 100 sets of parameters from certain probability distributions. These sets of parameters represented 100 communities composed of N species.

The dynamics of each community were independently simulated 100 times to see whether the species composition was robust against DN and EFs. These 100 replicate runs can be seen as 100 independent "patches"that initially consist of the same species set, but no species migrate from one to another. We measured the beta diversity of each community (Jost, 2007; Chao et al., 2012) and species richness (number of surviving species) as functions of the environmental switching rate in the quasi-stationary distribution (at time σ_{end}). Beta diversity accounts for the heterogeneity of each community within 100 replicates (or "patches") and thus is convenient for analyzing species diversity in our stochastic dynamics.

In the analysis of species diversity with $N = 2$, species 1 (or 2) is the one that has larger (or smaller) species abundance in the absence of any noise. In the species interaction analysis, we use parameter values such that species 1 always grows faster than species 2: their long term coexistence is impossible in the absence of noise. In the diversity analysis, two species' parameter values are sampled from certain probability distributions: the two species may coexist depending on their parameter values. For this reason, we labeled the dominant species as species 1 in the diversity analysis. If both species go extinct in the absence of noise, either of the two species is randomly labeled as species 1. This enables us to generalize the results of species interaction analysis in the two-species community and to compare the species interaction with beta diversity over the stitching rate and toxin sensitivity.

2.3 Statistical analysis

Statistical analysis was performed with Python 3.7.6 incorporating Scipy 1.4.1. and pymc3 3.10.0. For statistical tests of Spearman's rank-order correlation, scipy.stats.spearmanr was used. For calculation of HPDIs, pymc3.stats.hpd was used.

3 Results

3.1 Toxin sensitivity determines single species' response to EFs coupled with DN

To establish our intuition on how the coupling of EFs and DN affects the dynamics, we first analyse the extinction probabilities of a single species (species 1) in mono-culture with one type of resource and toxin (Fig. 2A). As the switching rate decreases, the duration of the harsh or mild environments become longer. In the presence of DN, this duration determines whether or not the species goes extinct, together with its sensitivity to toxins in the environment, which can be seen to modulate environmental harshness. When the switching rate is very low ($\nu \to 0$), the species is exposed to the static environment with either abundant or scarce resources (with probability 0.5, respectively) depending on the initial environmental condition $\xi(0)$: it mostly goes extinct under scarce resource supplies even when their sensitivity to toxin is low (Fig. 2B). On the other hand, abundant resource supplies maintain species 1 with some probability even if it is very sensitive to the toxin (Fig. 2D). Over many simulations, low fluctuation rates therefore result in a bimodal distribution of the species' abundance (e.g., Fig. 2B). At the other extreme, very high switching rates ($\nu \to \infty$) expose the bacteria to an environment with mean abundance of resources (Wienand et al., 2017, 2018; West and Mobilia, 2020; Taitelbaum et al., 2020). This is enough to rescue the species with a low toxin sensitivity (Fig. 2B) but not with a high sensitivity (Fig. 2D). At an intermediate toxin sensitivity (Fig. 2C), the worst situation lies in the intermediate fluctuation rate: the duration of the harsh environment is long enough to drive them extinct, but the time with abundant resource supply is not long enough to rescue them fully. In sum, even when only a single species is present, we see non-trivial patterns in its response to EFs coupled with DN, which depends on its sensitivity to toxins.

3.2 Toxin sensitivity changes how switching rate affects two-species competition

Next, we add another species (species 2) that grows slower than species 1 into the environment and ask how it interacts with species 1 in our model. Rather than measuring interactions through the effect of each species on the other's abundances, we focus on species 1 and analyze how its extinction probability is affected by the presence of species 2, compared to mono-culture (Fig. 2). Our reasoning is that (i) species 1 should always out-compete species 2 in the absence of EFs and DN, and that (ii) we already know the extinction probability of species 1 under EFs and DN in mono-culture; measuring any deviation from these outcomes allows us to quantify how likely it is for strong species to be lost in a given community. Such species loss events can be seen as ecological drift. We again explore changes in the species' toxin sensitivity, as we learned above that it affects

species abundances via DN (Fig. 2), but also because we expect it to affect species interactions (Piccardi et al., 2019). We varied sensitivity to toxins simultaneously for both species.

When both species were highly sensitive to the toxin, species 2 has a positive effect on species 1, reducing its extinction probability. This occurs because both species degrade the toxin, which outweighs the competition for nutrients (Piccardi et al., 2019). However, for most parameter values in Fig. 3A, species 2 has a negative effect on species 1 by increasing its extinction probability. We therefore focus on competitive interactions in the main text and consider positive interactions in Appendix 4.

As in the single species case (Fig. 2), the extinction of species 1 was highly dependent on the toxin sensitivity of the two species, as we varied the fluctuation rate: monotonically increasing, monotonically decreasing, or non-monotonically changing with a minimum or maximum value at an intermediate switching rate (Fig. 3B). Interestingly, this pattern does not match the single-species behavior (compare Fig. 2A and 3B).

3.3 Behavior at extreme switching rates explains non-monotonic changes in exclusion of the fittest

To better understand why the faster-grower goes extinct in the observed parameter ranges (Fig. 3B), we decompose species 2's effect on species 1 into the probability that species 2 persists but species 1 goes extinct (hereafter, called probability of exclusion of the fittest) and the probability of any other outcome (Eq (A.2)). Fig. A.2 shows that the probability of exclusion of the fittest explains the variation in species interaction strength in most cases (compare Fig. 3A and C). Based on this, we now use this probability to investigate how the strength of negative interactions changes over the switching rate and depends on toxin sensitivity.

We again let the two extreme switching rates guide our intuition (Fig. A.4). At a very slow rate ($\nu \to 0$), the resource supply remains either scarce or abundant, while a very fast environmental switching rate ($\nu \to \infty$) drives resource supply to the mean concentration. We explore system behavior at these three constant resource supplies (scarce, abundant or mean) and different toxin sensitivities, which together represent how harsh the environment is. When the environment is harsh (toxin sensitivity is high and/or resources are low), both species are most likely to go extinct rather than to outcompete each other (Figs. 4A – C). As toxin sensitivity goes down and species survival becomes more likely, DN becomes more important and we see a higher probability that even the fitter species (species 1) will be excluded. The more resources are available, the more likely it is that species survive – in particular, that species 1 out-competes species 2, and the peak of competitive exclusion moves to a higher toxin sensitivity (see arrows in Figs.4A – C). When it is easy for both species to survive (toxin sensitivity is low and/or resources are abundant), DN no longer plays an important role and the faster-growing species 1 is unlikely to be excluded. Hereafter, we refer to the toxin sensitivity that maximizes the probability of exclusion of the fittest in the absence of environmental switching as the "critical toxin sensitivity" (arrows in Figs.4A – C).

This analysis clarifies what happens at the two extreme switching rates. We see two critical toxin sensitivities (at 0.1 and 0.8 in Figs. 3C and D, Figs. 4A and C) at $\nu \to 0$ that correspond to the long time spent with

either scarce or abundant resources, while at $\nu \to \infty$, where resources remain at mean abundance, there is a single critical toxin sensitivity (at 0.4 in Figs. 3C and D) where competitive exclusion is most likely (Fig. 4B). As the switching rate increases from one extreme to the other, the form of the probability of exclusion of the fittest in Fig. 3C changes from bi-modal to uni-modal. We now see that the landscape of competitive exclusion in Fig. 3C contains two "mountain ranges". The first includes two peaks corresponding to the critical toxin sensitivities under scarce and mean resources $(0.1, 0.4$, respectively). The peak at toxin sensitivity 0.1 converges to the peak at 0.4 (Fig. 3D) with increasing environmental switching. The second mountain range has a single peak corresponding to the critical toxin sensitivity under abundant resources (0.8), which vanishes by increasing the switching rate (Fig. 3D). At toxin sensitivities between the critical values under scarce and mean resource supplies ($\delta = 0.2, 0.3$), the probability of exclusion of the fittest changes in a humped shape over the switching rate (species interactions change in a U shape, see Fig. 3B), as it passes over the first mountain range. When the toxin sensitivity is between the critical values under mean and abundant resources (e.g. $\delta = 0.6$), the probability of exclusion of the fittest instead has a "valley" over the switching rate (species interactions change in a humped shape, see Fig. 3B). At toxin sensitivities larger than the abundant resource critical value ($\delta > 0.8$), exclusion of the fittest is very unlikely because both species frequently go extinct (Fig. 4C).

In summary, the transition between the two extreme switching rates results in a highly rugged landscape. This means that the stochastic exclusion of the stronger species can be very high or very low at an intermediate switching rate (either in agreement or in contradiction with the intermediate disturbance hypothesis), depending on species' toxin sensitivities, our proxy for environmental harshness. This makes predicting the outcome at a given switching rate very difficult, as it is dependent on precise parameter values.

3.4 Competition strength changes non-monotonically under different scenarios

We have shown that using a given set of parameters, the rugged landscape shown in Fig. 3C causes the competitive exclusion of a faster-growing species to either increase, decrease or vary non-monotonically across switching rates, depending on toxin sensitivity. We next explore the generality of this finding. 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 3), or where (iii) we change the amounts of scarce and abundant resource supplies (Appendix 4).

In all these scenarios, the landscapes of the probability of exclusion of the fittest also contain two "mountain ranges" (Figs. A.5, A.7), leading, as before, to a variety of patterns as switching rates and toxin sensitivities change. The shape of these landscapes is in part dependent on the distances between the three critical toxin sensitivities (mild, mean and harsh, e.g. black arrows in Figs. 4A–C). Accordingly, we asked whether these distances might predict the probability of observing non-monotonic behavior. In Table A.2 and Fig. A.12 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. A.12, 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. A.12, 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 other words, we find non-monotonic behavior under many different scenarios, with no easily observable pattern for when they occur. Once again, 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 exclusion of the fittest

In the previous sections, we focused on interactions between two species and the conditions under which one may drive the other extinct. Ultimately, however, our interest is to predict how whole communities comprised of tens, hundreds or even thousands of species are affected by fluctuations in the environment.

We set up a model of 100 communities composed of between 2 and 10 species each. Species within each community were defined by parameter values that were randomly sampled from the same distributions with the exception of toxin sensitivity δ, which was sampled from normal distributions with different means, ranging from $\bar{\delta} = 0.1$ to 1. We generated a new set of 100 communities with different numbers of species and different fluctuation rates as above, and ran 100 replicate simulations for each of the 100 communities in each set. We then measured beta diversity across the 100 replicate simulations per community and final species richness (number of surviving species) over all 100 runs for the 100 communities (total: 10'000). In this model design, the 100 replicate runs represent independent "patches" without migration. Their beta diversity then indicates how different the species compositions were across all patches in a given environment (e.g. a given fluctuation rate), and we repeat the exercise 100 times with different species sampled from the same distributions to see generality of the results. This choice reduces computational cost (as opposed to simulating a community with 1000s of species), while also remaining realistic, as species in a spatially-structured natural environment are likely to only interact with few neighbouring ones. Our meta-communities of non-interacting patches can be seen as a crude first approximation of spatially-structured natural environment where species interact within each patch.

In two-species communities, beta diversity changes over the environmental switching rate similarly to the probability of exclusion of the fittest for four out of the five tested mean toxin sensitivities (columns A and B in Fig. 5): 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 the probability of exclusion of the fittest and beta diversity over the switching rate do not match. At this toxin sensitivity, beta diversity remains high at low switching rates ($\nu = 10^{-5}, 10^{-4} 10^{-3}$) because both species go extinct in 50% of the runs but they can coexist in about 7%, as illustrated by our measure of final species richness (column C in Fig. 5). Beta diversity ignores the cases of both-species extinction but increases in cases of coexistence, see Eq (A.6). Overall, looking at final species richness (Fig. 5, column C), we see that complete extinction is more likely to occur as sensitivity increases. At the highest toxin sensitivity, the

only way a species can survive is if the switching rate is really low and they can benefit from abundant resources for a long time, while at lower toxin sensitivity, extinctions only occur at low switching rates, because there is long term exposure to scarce resources.

In communities with 10 species (see also Figs. A.13 and A.14), we observe similar patterns between beta diversity (column D in Fig. 5) and the probability of exclusion of the fittest. Although variation in species richness (column E in Fig. 5) increases beta diversity, the inverse is not always true: beta diversity can be large when only one species survives if different species persist in each run (see $\bar{\delta} = 0.4$ and 0.6 at switching rate larger than 10^1 in D and E columns in Fig. 5). In sum, estimating the probability of exclusion of the fittest between two species (section 3.3) is a good predictor for the beta diversity of larger communities under those same environmental conditions. This similarity is not coincidental: as for the probability of exclusion of the fittest, beta diversity is also maximized when DN is the strongest, such that different species survive in each patch.

4 Discussion

Understanding how species diversity in microbial communities arises and is maintained is a central question in microbial ecology and evolution. While many theoretical and experimental studies have addressed this question in static environments, community diversity is expected to respond to fluctuations between benign and harsh environmental conditions, which can alter the abundance of different species and the interactions between them (see e.g., Rodríguez-Verdugo et al. (2019)). Strong drops in population sizes caused by harsh conditions can increase the strength of DN, which, coupled with EFs may lead to non-trivial outcomes (Wienand et al., 2017, 2018; West and Mobilia, 2020; Taitelbaum et al., 2020). Here we have used a mathematical model to explore how community diversity – mediated by inter-specific interactions and DN – changes with environmental fluctuation rates.

Our study is centred on two main findings. First, we show that the rate at which resource supplies switch changes the ability of a slower-growing species to drive a fast-growing one extinct (Fig. 3). While the fitter species will never be excluded in the absence of DN, in a fluctuating environment with DN, harsh conditions (e.g. scarce resources) strengthen DN to sometimes drive species extinction in spite of their greater fitness. We see this as a form of ecological drift, wherein selection by the environment is not strong enough to maintain the fittest species and thus the fittest species may go extinct due to DN. By changing the length of time spent in the harsh environment, the environmental switching rate affects such competitive exclusion. In addition, the species' own properties, in this case their toxin sensitivities, can also strengthen DN and lead to stronger ecological drift. We confirmed the generality of these results by exploring various forms of EFs (e.g., asymmetric switching environments and cyclically changing environments in Appendix 5). In larger, spatially structured communities, this increased stochasticity means that which species go extinct under these harsh conditions is less dependent on their relative competitiveness, and species composition will be more random, leading to greater beta diversity. Recent studies corroborate this finding: smaller communities show larger varieties in

species composition due to DN (Gilbert and Levine, 2017), while species composition is robust against EFs when species are insensitive to EFs (Dedrick et al., 2021).

Although we now understand that beta diversity increases when the probability of exclusion of the fittest is high, precisely when such ecological drift is maximized will be difficult to predict in practice, as it is a function of multiple factors: the form of the EFs (Appendix 3 and Appendix 5), the magnitude of EFs (Appendix 4), the rate of EFs and the sensitivity of species to environmental harshness. Our second main finding is that a good way to find maximum beta diversity is to measure the probability of exclusion of the fittest in two representative species across fluctuation rates and use it as an indicator for how the beta diversity of the whole community will behave with environmental switching (Fig. 5). In two species communities, the similarity between the probability of exclusion of the fittest and beta diversity is straightforward: beta diversity accounts for the probabilities that both or either of the two species persist. In larger communities, the similarity is not straightforward but our first main finding helps to understand this result. EFs affecting DN strength could exclude species that would persist in a community without noise. If the "fittest" species goes extinct with some probability due to DN, community compositions at time σ_{end} are heterogeneous and beta diversity increases. Therefore, our two findings emphasize the importance of coupling EFs and DN: competition results can reverse from those in static environments and this affects beta diversity.

This brings us to a hypothesis that has been debated at length in ecology: the intermediate disturbance hypothesis (Connell, 1978; Grime, 1973), which states that intermediate intensity and frequency of disturbance maximize species diversity. Fox (2013) argues that the intermediate disturbance hypothesis should be abandoned because many examples disagree with it (Mackey and Currie, 2001; Miller et al., 2011). In our model, fluctuations in resource and toxin can be regarded as disturbances. In agreement with Mackey and Currie (2001) and Miller et al. (2011) then, an intermediate intensity (i.e., toxin sensitivity) or disturbance frequency (environmental switching rate) does not always maximize beta diversity: our analysis shows that intermediate frequencies of disturbance maximize beta diversity only when mean toxin sensitivity is within a certain range. Mean toxin sensitivities at the two thresholds of this range show that beta diversity monotonically decreases or increases over the switching rate. These thresholds depend on scenarios of environmental switching and amounts of resource supplies because these parameters change the probability of competitive exclusion (see Appendix 3 and Appendix 4). High beta diversity at intermediate disturbances is then a consequence of a change in environmental conditions and not expected to apply generally.

The relationship between EFs and species diversity is also an important question in the modern coexistence theory, which predicts that fluctuations will affect species coexistence by changing species growth rates when rare (Chesson, 2000a,b; Barabás et al., 2018; Ellner et al., 2019; Letten et al., 2018a). Compared to the approach taken in this study – where we ask how many and which species persist at the end of a long but fixed time frame (i.e., for a quasi-stationary distribution, Fig. 5) – the modern coexistence theory allows one to analyze whether or for how long a set of species will all coexist (Schreiber et al., 2020). An interesting future direction would be to apply the modern coexistence theory to investigate how environmental fluctuation rates and toxin sensitivities affect the duration of all-species coexistence. This approach would help to propose biological mechanisms behind

species coexistence in our setup.

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 environmental switching from a daily to an hourly scale, for example, would show different species compositions or diversity. Second, 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 increases its partner species' extinction probability (Dunn et al., 2009; Goldberg and Friedman, 2020). 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 fluctuations changes the importance of species fitness for survival and thus community beta diversity. This occurs in our model when EFs affect the strength of DN, leading to the occasional exclusion of strong species. Predicting how the strength of DN changes is not simple because it is affected by both environmental and species' parameters (resource and/or toxin supplies and toxin sensitivities in our model). This may be one explanation why the intermediate disturbance hypothesis does not always hold, but rather there are many relations between diversity and disturbance (Mackey and Currie, 2001; Miller et al., 2011). Nevertheless, we found similarities between how competitive exclusion plays out between two species and beta diversity at the community level. In the event that we would like to predict how the diversity of a given ecosystem, such as a soil community or a bioremediation ecosystem, responds to environmental fluctuations, it may be sufficient to isolate two culturable species and analyze their interactions over different fluctuation rates. This approach promises to greatly facilitate our ability to study large and complex natural communities and their response to harsh conditions.

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Data accessibility

The programming codes and simulation data in csv files for this manuscript are available in Github.

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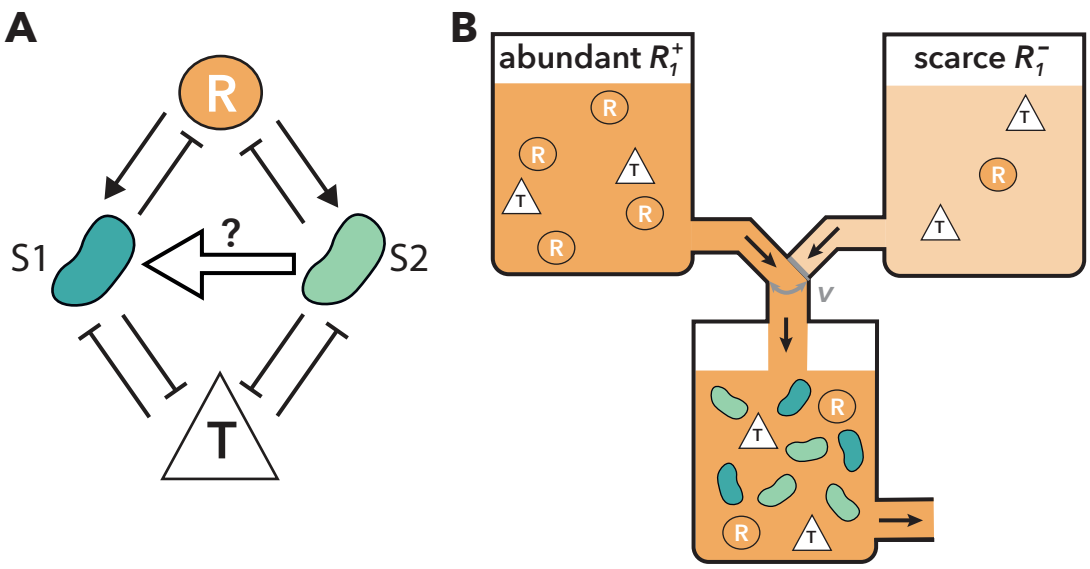

Figure 1: Schematic illustration of the model

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 the slower-growing species 2 on species 1 (large arrow from species 2 to 1). 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 abundant resource supply R_1^+.

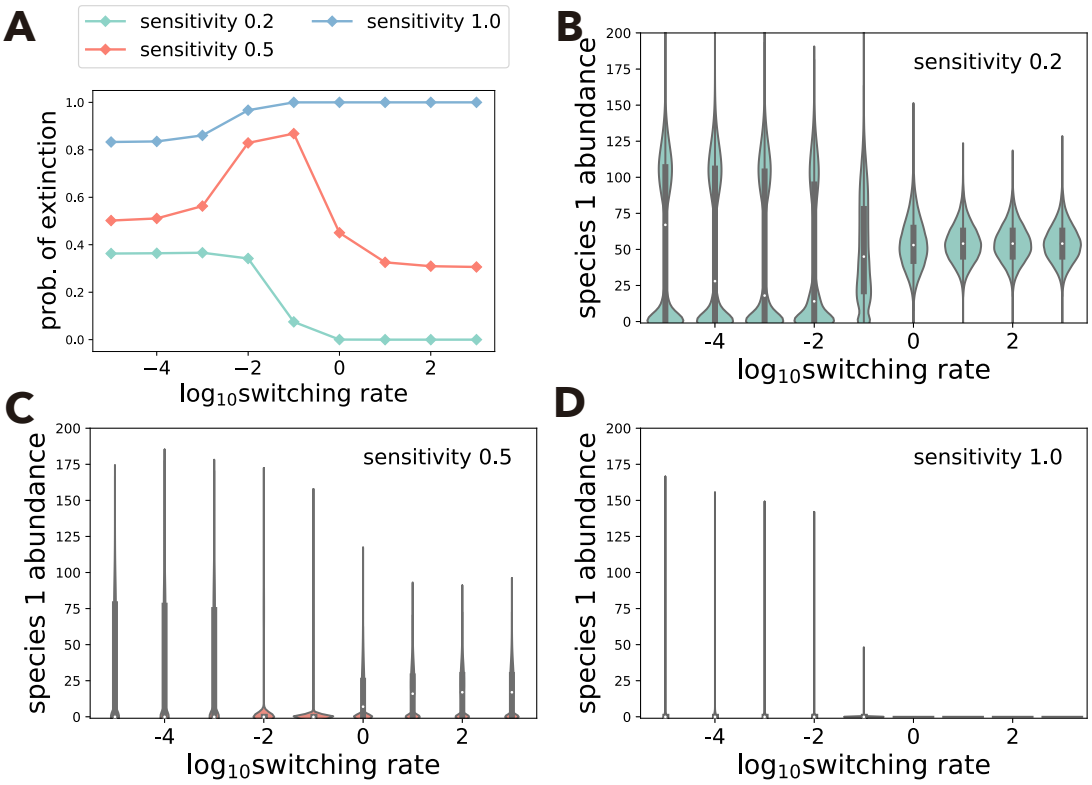

Figure 2: Extinction probability and species abundance in mono-culture

A: Extinction probability of species 1 in mono-culture when the toxin sensitivity is low (green), moderate (orange), or high (blue). 95% HDPIs are too small to see. B–D: violin plots of species 1's abundance at the end of 10^5 simulations with a low (B), moderate (C), or high (D) toxin sensitivity. White dots and black bars represent median values of the abundances and their interquartile ranges, respectively.

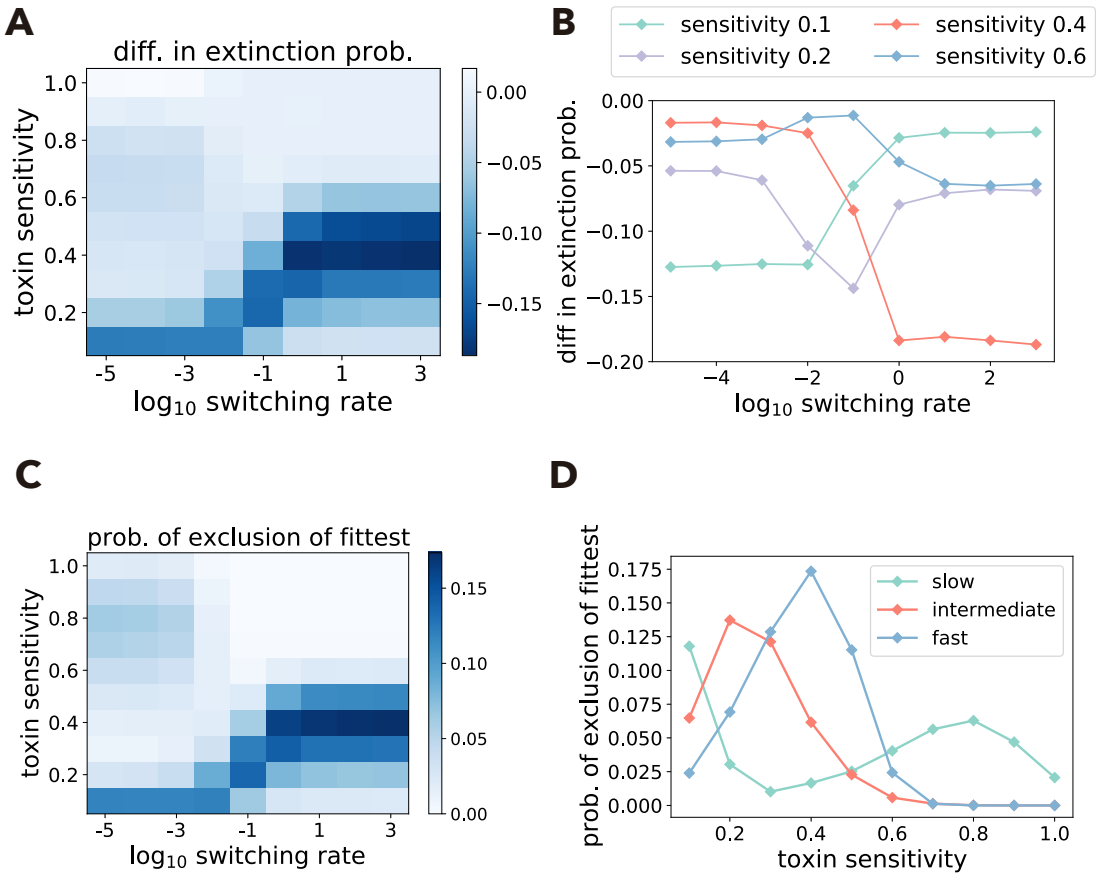

Figure 3: Species interaction strength changes differently over the switching rate

A: The effect of species 2 on species 1's extinction probability (Eq A.1) changes over the switching rate ν and the toxin sensitivity. 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 species 2's effect on species 1 changes over the switching rate at given toxin sensitivities. The difference in extinction probability can monotonically increase (toxin sensitivity 0.1, green), monotonically decrease (toxin sensitivity 0.4, red), or non-monotonically change with a minimum (toxin sensitivity 0.2, purple) or a maximum (toxin sensitivity 0.6, blue) value at an intermediate switching rate. C: Probability that species 2 persists but species 1 goes extinct (i.e., exclusion of the fittest) over the switching rate and the toxin sensitivity. D: probabilities of exclusion of the fittest over the toxin sensitivity, when the environmental switching rate is slow ($\nu = 10^{-5}$), intermediate ($\nu = 10^{-1}$), or fast ($\nu = 10^{3}$). In panels B and D, 95% HDPIs are too small to see.

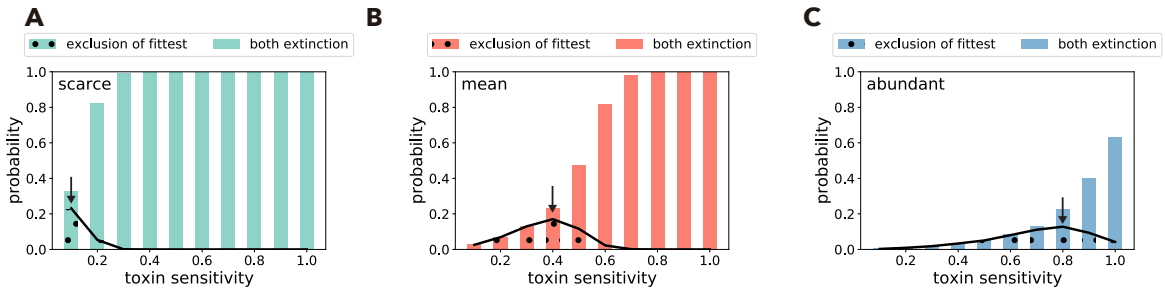

Figure 4: Exclusion of the fittest explains how DN changes with toxin sensitivity and resource supply

Analysis of exclusion of the fittest predicts at which toxin sensitivity DN is strongest. A – C: In the absence of environmental switching, the probability of exclusion of the fittest (i.e., probability that species 2 excludes species 1 and survives) is uni-modal over the toxin sensitivity while the probability of both species extinction monotonically increases. The toxin sensitivities giving the peak values of probabilities of exclusion of the fittest (critical toxin sensitivities, pointed by black arrows) depend on the resource supply: scarce $R_1 = R_1^-$ (A), mean $R_1 = \langle R_1 \rangle$ (B), or abundant $R_1 = R_1^+$ (C). 95% HDPIs are not observable as they are very small.

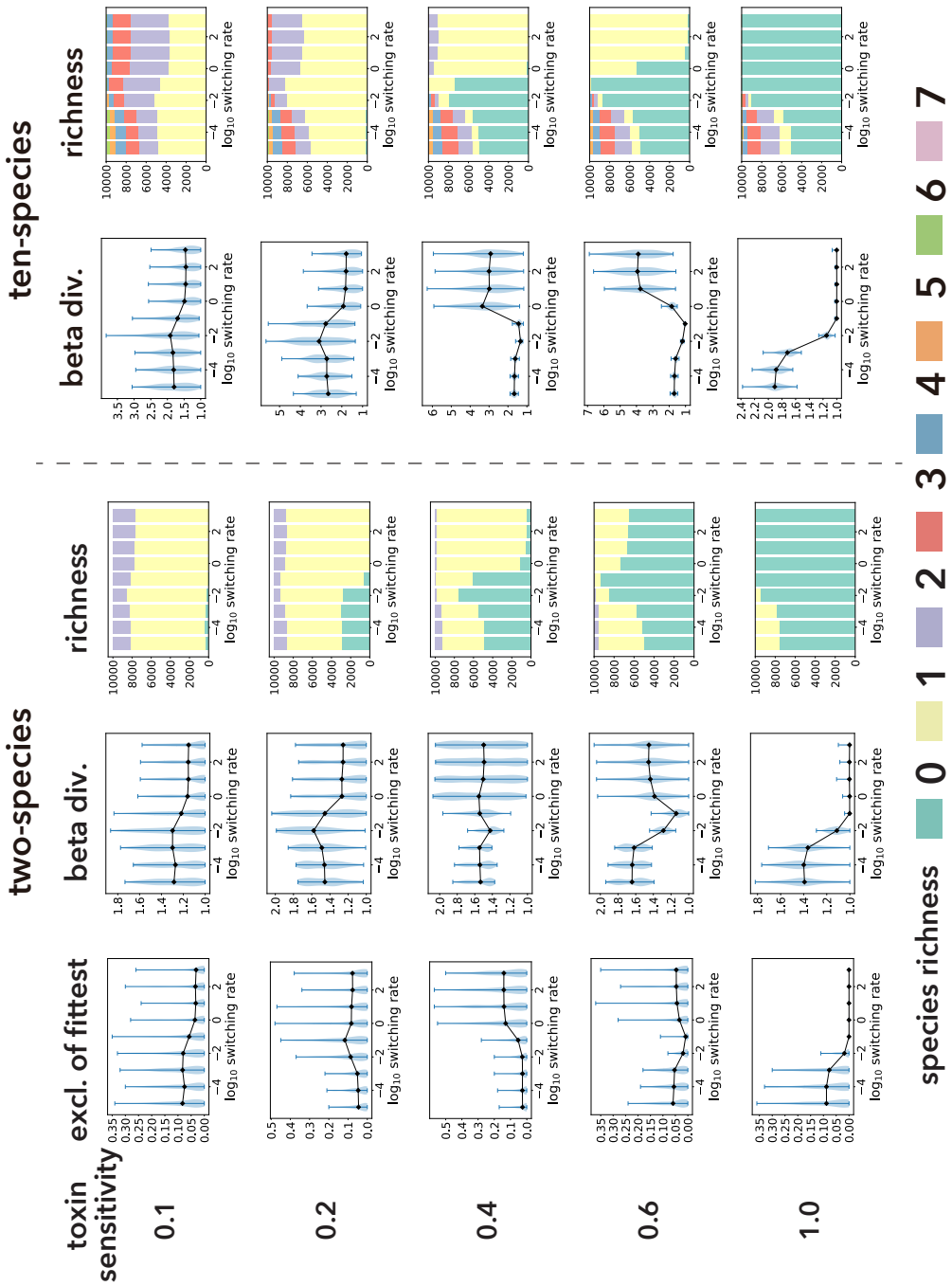

Figure 5: Comparison of exclusion of the fittest and diversity

Probabilities of exclusion of the fittest (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 probability of exclusion of the fittest 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 of communities in those runs.

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^+

$R_i^+ > R_i^-$ and $\langle R_i\rangle = \left(R_i^+ + R_i^-\right)/2$ for $i = 1, \ldots, N/2$. Similar relations hold for T_j.