Adaptive consumer-resource models can explain diauxic shifts and the violation of the Competitive Exclusion Principle

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(Dated: December 20, 2018)

Competitive ecosystems are most commonly described mathematically using MacArthur's consumer-resource model, leading to the "Competitive Exclusion Principle" which limits the number of coexisting competing species to the number of available resources. Nevertheless, several empirical evidences – such as bacterial community cultures – show that this principle is violated in real ecosystems. Another experimental evidence involving microbial populations that cannot be explained in this framework is the existence of diauxic (or polyauxic) shifts in microbial growth curves. By introducing adaptive metabolic strategies whose dynamics tends to maximize species' relative fitness, we are able to explain both these empirical evidences. Moreover, we show that adaptation and adaptation time scale play a fundamental role in how the species respond to external perturbations and volatile resources.

One of the most fascinating aspects of nature is biodiversity: from microbial to continental scales we observe complex communities of hundreds or thousands of species competing yet coexisting. The scientific community has long tried to explain such an amazing complexity, but this task requires the solution of many challenging problems. One of them is the violation of the so-called "Competitive Exclusion Principle" (CEP) [1], known in the literature with many other names like "Gause's law" or "niche-dimensionality hypothesis", which limits the number of coexisting competing species. In particular, the CEP states that if m consumers compete (with no predation between them) for p resources, then they may coexist only if $m \leq p$, otherwise at least $m - p$ of them will go to extinction. The CEP is indeed found in mathematical models [2–5], and yet there are many known cases in nature where the CEP is clearly violated [6, 7]. In particular, such violations have been recently observed in controlled bacterial community experiments [8–10], where many species can coexist in the presence of very few resources. It is clear, therefore, that we are missing something essential in order to explain the high biodiversity found in many ecological communities.

Competitive ecosystems are generally described mathematically using MacArthur's consumer-resource model [11–14], which prescribes that for a system of m species and p resources the population density $n_\sigma(t)$ of species σ and the concentration $c_i(t)$ of resource i evolve following:

$$\dot{n}_\sigma = n_\sigma \left(\sum_{i=1}^{p} v_i \alpha_{\sigma i} r_i(c_i) - \delta_\sigma \right) , \qquad (1)$$

$$\dot{c}_i = s_i - \sum_{\sigma=1}^{m} n_\sigma \alpha_{\sigma i} r_i(c_i) - \mu_i c_i \qquad (2)$$

(we omit for simplicity the time dependence of both n_σ and c_i). Here, δ_σ is the death rate of species σ, c_i represents the concentration of resource of type i, $r_i(c_i)$ is

the availability of resource i (which we assume, without loss of generality, to have the form of a Monod function, i.e. $r_i(c_i) = c_i/(K_i + c_i)$ with $K_i > 0$, and so $r_i(c_i) < 1 \; \forall c_i > 0$). The $\alpha_{\sigma i}$ are the "metabolic strategies", i.e. the rates at which species σ uptakes resource i; the parameters v_i are often called "resource values" and give a measure of how much efficiently a resource is converted into biomass: the larger v_i, the larger the population growth that is achieved for unit resource and thus the "more favorable" the resource i is. On the other hand, s_i is a constant nutrient supply rate, and the sum in Eq. (2) represents the action of consumers on resources, which of course depends on the metabolic strategies $\alpha_{\sigma i}$. Finally, μ_i is the degradation rate of resource i. Eqs. (1) and (2) lead to the aforementioned exclusion principle. This is easily seen to hold for Eq. (1): indeed a non-trivial stationary state is obtained if the m dimensional vector $\vec{\delta}$ (whose components are the death rates δ_σ) can be expressed as a suitable linear combination with non-negative coefficients of the p m-dimensional vectors $\vec{\alpha}_{\cdot i}$. If $m > p$ this does not happen unless the vector $\vec{\delta}$ lies in the subspace spanned by the p vectors $\vec{\alpha}_{\cdot i}$, which occurs with zero probability unless the metabolic strategies are somehow chosen *ad hoc* [15]. Many different mechanisms have been proposed in order to explain the violation of the CEP, ranging from non-equilibrium phenomena (species cannot reach an equilibrium because of spatio-temporal effects) [6], to the existence of additional limiting factors like the presence of predators [16, 17], cross-feeding relationships [18], toxin production [19–21], and complex or higher-order interactions [22, 23]; see [24] and [25] for comprehensive reviews. However, none of the current mathematical models used to describe consumer-resource population dynamics can explain the violation of the CEP without some fine tuning of the parameters [2–5, 15].

In consumer-resource models the metabolic strategies $\alpha_{\sigma i}$

are treated as fixed parameters instead of being considered as dynamic variables (see however [26] for a recent work where species can instantaneously switch from using one nutrient to another). There is however incontrovertible experimental evidence that microbes' metabolic strategies *can* and *do* change over time according to their surrounding environmental conditions. In fact, as early as the '40s Jacques Monod [27] observed for the first time that *Escherichia coli* and *Bacillus subtilis* exhibit a particular growth curve, which he called "diauxie", when exposed to an environment containing only two different sugars. In particular, instead of metabolizing the two sugars simultaneously, it turned out that bacteria consume them sequentially using first their "favorite" one (i.e. the one that ensures the highest growth rate) and once it has been depleted, after a lag phase, they start growing slower using their "least favorite" one (see the inset of figure 1). Since then diauxic growth has always been the subject of thorough empirical study [28–31] with experiments that generally involve the growth of one microbe on two resources, and has been observed to happen widely across different microbial species [32–34]. Many models have been proposed to describe this phenomenon, but all are focused on specific gene regulation and expression mechanisms (they generally involve *carbon catabolite repression* [35–37]), and sometimes are tailored in order to explain the growth of particular bacterial species on specific resources, involving also enzyme dynamics [38–41]. Furthermore, as highlighted by Chu and Barnes [41], it is generally said that the existence of diauxic shifts is "adaptive", and the central idea of related modeling frameworks is that regulatory processes behind diauxic shifts may be considered as the outcome of some optimization strategy [42]. Overall, it is clear that bacteria are able to change the gene expression of metabolic pathways through which they absorb energy from the environment, but a connection between this phenomenon and consumer-resource ecological modeling is still missing.

Besides to experiments of single species dynamics with multiple resources, in the last years there has been an increasing number of works studying microbial communities, both theoretically and experimentally [8–10, 18]. Some of these studies involved laboratory controlled microbial communities coming from different type of natural environments, and have confirmed that complex microbial communities with many species can be sustained in laboratory conditions even with few carbon sources, in apparent violation of the CEP.

It has been recently observed experimentally that the consumption of resources in an hierarchical order happens also when microbes live in diverse communities and that it maintains coexistence in competitive ecosystems [43]. However, form a theoretical point of view we completely lack a unifying framework that comprehends both the existence of diauxic shifts and the violation of the CEP. In this letter we show that they can be both ex-

plained by allowing the metabolic strategies $\alpha_{\sigma i}$ to be temporal variables evolving according to an appropriate dynamics that increases the relative fitness of each species. Using adaptive metabolic strategies allows also to give a theoretical explanation of the existence of diauxic shifts without relying on specific molecular details involved in the species' gene regulation and expression mechanisms.

Adaptive metabolic strategies. We now introduce our adaptive mechanism: we require that each metabolic strategy $\vec{\alpha}_\sigma$ evolves in order to maximize its own species' relative fitness, measured [44, 45] by the growth rate $g_\sigma = \sum_{i=1}^p v_i \alpha_{\sigma i} r_i(c_i)$. This can be achieved by requiring that metabolic strategies follow a simple "gradient ascent" equation:

$$\dot{\alpha}_{\sigma i} = \frac{1}{\tau_\sigma} \frac{\partial g_\sigma}{\partial \alpha_{\sigma i}} \ , \qquad (3)$$

where in general τ_σ is the characteristic timescale over which the metabolic strategy of species σ evolves. Since δ_σ is the only characteristic timescale of each species, a natural choice for τ_σ is to be proportional to the inverse of its corresponding death rate, i.e. $\tau_\sigma = (d\delta_\sigma)^{-1}$, where d regulates adaptation velocity.

However, Eq. (3) is missing an important biological constraint, related to intrinsic limitation of the species' resource uptake capabilities. Microbes, in fact, have limited amounts of energy that they can use to produce the metabolites necessary for resource uptake, so we must introduce such constraint in Eq. (3). We thus require that each species has a maximum amount of energy available for metabolism, i.e. $\sum_{i=1}^p w_i \alpha_{\sigma i}(t) := E_\sigma(t) \leq E_\sigma^*$ where E_σ^* is the maximum total resource uptake rate of species σ; the parameters w_i are called "resource costs" and take into account the fact that each resource could require more or less energy in order to be metabolized. Again, since E_σ^* is an uptake rate, it is reasonable to require that it is proportional to the death rate δ_σ, since it is the only characteristic timescale of each species (this is also in accordance to the metabolic theory of ecology [46]). We therefore set $E_\sigma^* = \mathcal{Q}\delta_\sigma$, with $\mathcal{Q}$ a positive real number. The constraint on the species uptake rate capacities introduces a trade-off between the use of different resources. In this case it can be shown that the maximization of each species' fitness explicitly depends on all species' metabolic strategies (see Supplemental Material [47]). In the Supplemental Material [47] we present a geometrical interpretation of the maximization problem given by Eq. (3), i.e. $\dot{\vec{\alpha}}_\sigma = \vec{\nabla}_{\vec{\alpha}_\sigma} g_\sigma$ where $\vec{\nabla}_{\vec{\alpha}_\sigma}$ is the gradient with respect to the components of $\vec{\alpha}_\sigma$. In particular, if we want $\vec{\alpha}_\sigma$ to evolve so that $\varphi(\vec{\alpha}_\sigma(t)) := \sum_{i=1}^p w_i \alpha_{\sigma i}(t) - \mathcal{Q}\delta_\sigma \leq 0$, it is sufficient to remove from $\vec{\nabla}_{\vec{\alpha}_\sigma} g_\sigma$ the component parallel to $\vec{\nabla}_{\vec{\alpha}_\sigma} \varphi(\vec{\alpha}_\sigma(t))$ as soon as $\varphi(\vec{\alpha}_\sigma(t)) = 0$. Moreover, we also want to prevent the metabolic strategies from becoming

negative. Eventually, the final equation for the metabolic strategies' dynamics is given by Eq. (4) (see Supplemental Material [47]), where Θ is Heaviside's step function, i.e. $\Theta(x) = 1$ when $x \geq 0$ and $\Theta(x) = 0$ otherwise.

$$\dot{\alpha}_{\sigma i} = \alpha_{\sigma i} d\delta_\sigma \left[v_i r_i - \Theta\left(\sum_{i=1}^{p} w_i \alpha_{\sigma i} - \mathcal{Q}\delta_\sigma \right) \frac{w_i}{\sum_{k=1}^{p} w_k^2 \alpha_{\sigma k}} \sum_{j=1}^{p} v_j r_j w_j \alpha_{\sigma j} \right] \tag{4}$$

For the moment we assume that all the degradation rates μ_i are null and for the sake of simplicity $d = 1$, but we will later discuss the more general case.

Diauxic shifts. If Eq. (4) is used alongside Eqs. (1) and (2), the simulations of the system's dynamics are capable of reproducing diauxic shifts when we expect such phenomena. Let us in fact consider the typical case studied in diauxic shift experiments, i.e. one species ($m = 1$) with two types of resources ($p = 2$) supplied only initially ($s_1 = s_2 = 0$ and $c_1(0), c_2(0) \neq 0$). Figure 1 shows the time evolution of the population density of our model in the case $c_1(0) > c_2(0)$ and $w_1/v_1 < w_2/v_2$: in this example, therefore, resource 2 is the "favorite" one and is scarce, while resource 1 is the "less preferred" one and is highly abundant. As we can see the population growth curve indeed exhibits a diauxic shift (for more information see figure S.2 in Supplemental Material [47]).

In this framework it is also possible to estimate the instant at which the diauxic shift occurs. In particular from Eq. (4), in the case $m = 1$ and with initial conditions such that $\sum_{i=1}^{p} w_i \alpha_i < \mathcal{Q}\delta$ we can approximate the initial growth of the metabolic strategies as $\alpha_i(t) \sim \alpha_i(0) \exp(\delta v_i r_i t)$, where we are assuming that r_i remain constant in this time interval (see figure S.3c in Supplemental Material [47]). We then call $\bar{t}$ the solution of $\sum_{i=1,2} w_i \alpha_i(0) \exp(\delta v_i r_i t) = \mathcal{Q}\delta$ with respect to t, i.e. the instant at which $\varphi(\vec{\alpha}(\bar{t})) = 0$. In figure 1 we have also added a vertical grey line at $\bar{t}$ to show where this instant lies with respect to population growth curve; as we can see, it is indeed a good estimate of the instant at which the species starts growing on the second resource.

Competitive exclusion principle. We now show that incorporating adaptive strategies in our consumer-resource model is also a key factor that allows the coexistence of multiple species in violation of the CEP.

Recently, Posfai et al. [15] have studied MacArthur's consumer-resource model with static metabolic strategies and the "hard" constraint $\sum_{i=1}^{p} w_i \alpha_{\sigma i} = E_\sigma$. They found that an arbitrary number of species can coexist only if $E_\sigma/\delta_\sigma = $ const. and the rescaled nutrient supply rate vector $\hat{s}_i := v_i s_i / \sum_{j=1}^{p} v_j s_j$ belongs to the convex hull of the rescaled metabolic strategies $\hat{\alpha}_{\sigma i} := w_i \alpha_{\sigma i} / \sum_{j=1}^{p} w_j \alpha_{\sigma j}$ (see Supplemental Material [47]). In general, any broader constraint (like $\sum_{i=1}^{p} w_i \alpha_{\sigma i} \leq E_\sigma$) will lead to the extinction of at least $m - p$ species, i.e. the system will
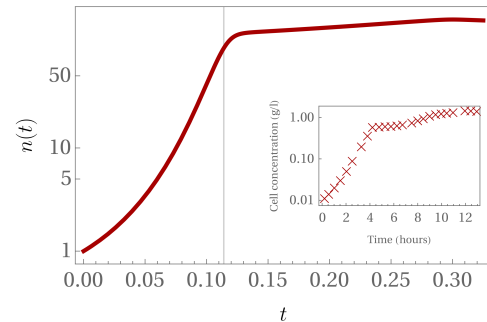

FIG. 1: Growth of the population over time using (4) for the time evolution of the metabolic strategies. In this case we have used $n(0) = 1$, $\vec{c}(0) = (40, 5)$, $\vec{s} = (0, 0)$, $\vec{v} = (2, 25)$, $\vec{w} = (1, 4)$, $\vec{\alpha}(0) = (1, 1)$, $\vec{K} = (1, 3)$, $\mathcal{Q} = 25$ and $\delta = 1$; time is in arbitrary units. The grey vertical line corresponds to $\bar{t}$, the estimate of the instant at which the diauxic shift occurs (in this case we have $\bar{t} \approx 0.114$, see the discussion for more details). **Inset**: Data of experimental measurements of the growth of *Klebsiella oxytoca* on glucose and lactose, taken from [28, figure 11] for comparison only (the parameters have *not* been set in order to reproduce the data.

obey the CEP; in this sense the system allows coexistence only when fine-tuned. However, if we allow $\alpha_{\sigma i}$ to evolve following Eq. (4) the system gains additional degrees of freedom which make it possible to find steady states where an *arbitrary* number of species can coexist, even when initial conditions are such that $\vec{s}$ does not lie in the convex hull of the rescaled metabolic strategies $\vec{\alpha}_{\sigma \cdot}$, i.e. the system violates the CEP without having fine-tuned parameters (see Supplemental Material [47]). In figure 2 we show the initial and final states of a time evolution (for more information see figure S.3 in Supplemental Material [47]) in the final state $\vec{\hat{s}}$ lies inside of the rescaled strategies' convex hull: it is therefore clear that our model is capable of *self-organization*, because the metabolic strategies change in order to put the system in the right conditions for coexistence even when they are initially not satisfied.

An interesting feature of our model is that it predicts that if one of the available resources, e.g. resource j, is too "expensive" then adaptation will bring all the j-th components of the metabolic strategies to zero, i.e. species will stop using that resource. In fact, the "expensiveness" of resource i can be measured by w_i/v_i, i.e.
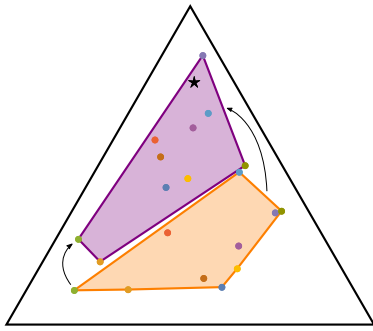
FIG. 2: Comparison between the initial (orange) and final (purple) convex hull of the rescaled metabolic strategies (colored dots) when they are allowed to evolve, using (4) for the time evolution of $\alpha_{\sigma i}$. These results have been obtained for a system with $m = 10$ and $p = 3$, so the rescaled metabolic strategies and nutrient supply rate vector (black star) all lie on a 2-dimensional simplex (i.e. the triangle in the figure), where each vertex corresponds to one of the resources; for more information on the parameters used, and for the plots of the time evolution of the population densities and metabolic strategies see figure S.3 in Supplemental Material [47]. As we can see, in the final state $\hat{\alpha}_{\sigma i}$ have "incorporated" $\vec{\tilde{s}}$ in their convex hull.

FIG. 3: Comparison between the evolution of the population of species $\sigma = 1$ with fixed and adaptive metabolic strategies, when $\vec{s}$ changes in time. We have considered a system with $m = 20$, $p = 3$, and the nutrient supply rate vector switches at regular intervals between two values, in particular we have $\vec{s}(t) = \vec{s}_{\text{in}}$ for a time interval of length $\tau_{\text{in}} = 20$, then $\vec{s}(t) = \vec{s}_{\text{out}}$ for a time interval of length $\tau_{\text{out}} = 20$ and then back again to $\vec{s}_{\text{in}}$, where $\vec{s}_{\text{in}}$ is drawn inside of the convex hull of the rescaled metabolic strategies and $\vec{s}_{\text{out}}$ is drawn outside it. For more information on the parameters used and how $\vec{s}(t)$ is defined, see figure S.7 in Supplemental Material [47]. **Inset:** Evolution of the population of the same species, with the same parameters and initial conditions, but with $\tau_{\text{in}} = 20$ and $\tau_{\text{out}} = 5$.

the ratio between its cost and its value, and an analytical analysis of our model with fixed metabolic strategies leads to the conclusion that in order to have a nontrivial stationary state we must have $w_i/v_i < Q \; \forall i$ (see Supplemental Material [47]). However, when Eq. (4) is used the system behaves interestingly even when there is at least one j for which $w_j/v_j > Q$: in this case, in fact, resource j becomes too "expensive", and it is possible to show that the system "decouples" from that resource, i.e. the j-th components of *all* the metabolic strategies become null (see Supplemental Material and figure S.4 [47]).

Something analogous happens also when we let $\mu_i > 0$: in this case at stationarity the convex hull of the rescaled metabolic strategies will include the vector with components $\tilde{s}_i := v_i(s_i - \mu_i c_i^*)/\sum_{j=1}^{p} v_j(s_j - \mu_j c_j^*)$ (see Supplemental Material [47]), and if one of the μ_i is sufficiently large this vector will lie on one of the sides of the $p - 1$-dimensional simplex where our system can be represented. This means that if the degradation rate μ_j of resource j becomes too large then again all the j-th components of the metabolic strategies will become null (see figures S.5 and S.6 in Supplemental Material [47]). Therefore, we have that in our model the species will not waste energy metabolizing resources that are "unfavorable" (either because they are too "expensive" or volatile) and will focus their efforts on the more "convenient" ones.

Variable environmental conditions. Having adaptive metabolic strategies has positive effects when the environmental conditions of our system are variable, i.e. when $\vec{s}$ is a function of time $\vec{s}(t)$. Let us consider a sce-
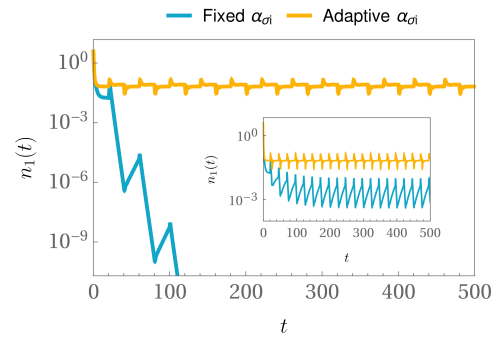
nario where the nutrient supply rates change periodically; this can be implemented by shifting $\vec{s}$ between two different values at regular time intervals: one inside the convex hull of the initial (rescaled) metabolic strategies and one outside of it. We found that when $\vec{\alpha}_\sigma$ are allowed to evolve, then the species' populations oscillate between two values and manage to coexist, while when the metabolic strategies are fixed in time species go extinct (see figure 3) and the CEP is recovered. Only when we let $\vec{s}(t)$ lie outside of the convex hull for a short period of time coexistence is possible. Figure 3 shows an example of such a case (for more details see figure S.7 in Supplemental Material [47]). Also in this case, when we introduce non-null resource degradation rates we find again that if μ_i is sufficiently large with respect to w_i/v_i, then all the i-th components of the metabolic strategies will vanish (see figure S.8 in Supplemental Material [47]). Therefore, adaptive metabolic strategies allow the species to efficiently deal with variable environmental conditions, typical of most natural systems.

Adaptation velocity. A physically relevant parameter characterizing the capacity of the species to adapt to new environments is d, which as already discussed regulates the species' adaptation velocity of the metabolic strategies. Increasing the value of d leads to metabolic strategies that evolve more rapidly, and as a consequence the species' growth rates will be optimized for a longer period of time; this means that when d has larger values the species' stationary populations will be higher (see figure S.9 in Supplemental Material [47]), and less variable

when $\vec{s}(t)$ changes in time (see figure S.10 in Supplemental Material [47]). On the other hand, if d tends to zero we recover the case of fixed metabolic strategies and thus the CEP will be recovered. This means that for different adaptation velocities the distribution of the stationary species' populations can change sensibly and if d is small enough, for a given extinction threshold, then we can have that some species go extinct. In other words, if the adaptation velocity is small enough we can recover the CEP with our model.

Conclusions. In conclusion, introducing adaptive metabolic strategies in a MacArthur's consumer-resource model evolving so that each species' growth rate is maximized allows us to explain phenomena observed experimentally from the single-species to the community level. Furthermore, with this hypothesis we can naturally violate the CEP without any strong assumption on the parameters of the model, but at the same time we can explain why competitive exclusion still happens in some cases. We have therefore shown that having adaptive metabolic strategies is indeed a determining factor in microbial communities. Recently, an increasing amount of attention is being drawn on the study of cross-feeding relationships between microbial species [18, 48, 49]. A future development is to generalize our approach to include also cross-feeding strategies in the model.

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