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On the exclusion of exponential autocatalysts by sub-exponential autocatalysts

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Selection among autocatalytic species fundamentally depends on their growth law: exponential species, whose number of copies grows exponentially, are mutually exclusive, while sub-exponential ones, whose number of copies grows polynomially, can coexist. Here we consider competitions between autocatalytic species with different growth laws and make the simple yet counterintuitive observation that sub-exponential species can exclude exponential ones while the reverse is, in principle, impossible. This observation has implications for scenarios pertaining to the emergence of natural selection.

I. INTRODUCTION

Autocatalysts are molecules that catalyze their own formation, leading to an auto-amplification process: the presence of more autocatalysts of a species leads to a decrease in the time required to produce additional autocatalysts of the same species [1]. This auto-amplification can cause the number of autocatalysts of a species to grow at a rate proportional to their concentration, a relationship mathematically described by $dA/dt = kA$, where A denotes the concentration of the autocatalytic species and k its replication rate. This model results in an exponential growth dynamics, $A(t) \sim e^{kt}$. This is not, however, the only dynamics that autocatalysts may follow. In fact, most non-enzymatic autocatalysts studied to date show a different behavior where their growth rate is sub-linear in their concentration and better described by $dA/dt = kA^n$ with $n < 1$ [1–5]. This corresponds to a slower, polynomial dynamics, of the form $A(t) \sim t^{1/(1-n)}$. The value $n \approx 1/2$ has most often been observed, leading to $A(t) \sim t^2$, also known as parabolic growth [6]. In autocatalysis through template replication, this value is understood as arising from product inhibition, the common rebinding of a product to a template [6]. As far as growth and selection are concerned, however, the underlying mechanisms are not essential.

Instead, past works have stressed that the value of n captures the most fundamental distinction, setting apart exponential ($n = 1$) from sub-exponential ($n < 1$) autocatalytic species [5, 7, 8]. While exponential species with different k are mutually exclusive, sub-exponential ones generally coexist, with exclusion taking place only in particular limiting cases [7, 9–11]. As a consequence of this result, the field of experimental abiogenesis and the broader community engaged in developing non-enzymatic autocatalysts have concentrated their efforts on creating autocatalysts that can achieve exponential growth [1, 6, 12–19]. However, the theoretical studies on which this conclusion is based have only considered autocatalytic species with different growth parameters k and the same exponent n , without exploring the possibility for n to differ between competitors. Yet, n is well-recognized to be,

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as much as k , an effective parameter that can vary between autocatalytic species and can therefore be subject to selection. Here, we extend previous analyses to study the selection of competing autocatalytic species with different exponents n , in addition to different parameters k . As we show, the results are counterintuitive and challenge the view that only exponential autocatalytic species can be excluding: sub-exponential autocatalytic species can exclude exponential ones, but not vice versa.

II. MODELS

The simplest setting to study autocatalysis under resource limitation is that of a continuous stirred-tank reactor, or chemostat [20], where the resource needed for reproduction is introduced and removed at a constant rate, such that its concentration R is coupled to the concentration A of the autocatalytic species by

$$\begin{aligned}\frac{dA}{dt} &= kRA^n - DA, \\ \frac{dR}{dt} &= D(R_0 - R) - kRA^n.\end{aligned}\tag{1}$$

In these equations, k denotes the species replication rate constant, n signifies its reaction order, and D serves a dual purpose: it represents both a common dilution or decay rate for the autocatalytic species and the resource, as well as the rate at which the resource is replenished from a reservoir with concentration R_0 . In what follows, we introduce $\tau = Dt$ and $\kappa = k/D$ to have effectively $D = 1$,

$$\begin{aligned}\frac{dA}{d\tau} &= \kappa RA^n - A, \\ \frac{dR}{d\tau} &= R_0 - R - \kappa RA^n.\end{aligned}\tag{2}$$

The minimal concentration of resource that allows an autocatalytic species to grow ($dA/d\tau > 0$) is $R = A^{1-n}/\kappa$. When growth is sub-exponential ($n < 1$), A therefore grows whenever it is small enough. More specifically, a stability analysis indicates that the boundary equilibrium $A = 0$ is always unstable when $n < 1$ ($\lim_{A \rightarrow 0} d^2A/d\tau^2 = +\infty$): this implies that sub-exponential autocatalytic species can never become extinct. When, instead, growth is exponential ($n = 1$), survival solely depends on the concentration of resource and is possible only if $R > 1/\kappa$; correspondingly, the boundary equilibrium $A = 0$ is unstable only if $R > 1/\kappa$ in this case. This fundamental difference is the key to understanding why sub-exponential autocatalytic species can coexist while exponential ones exclude each others but also, as we show below, why sub-exponential autocatalytic species can exclude exponential ones but not conversely.

To study exclusion and coexistence of species subject to a common limiting resource, we

extend the model to include two species dependent on the same resource,

$$\begin{aligned}\frac{dA_1}{d\tau} &= \kappa_1 R A_1^{n_1} - A_1, \\ \frac{dA_2}{d\tau} &= \kappa_2 R A_2^{n_2} - A_2, \\ \frac{dR}{d\tau} &= R_0 - R - \sum_{i=1}^2 \kappa_i R A_i^{n_i}.\end{aligned}\tag{3}$$

Here, we view the concentration R_0 of resource in the reservoir as an extrinsic or “environmental” parameter, but the parameters κ_i and n_i as parameters intrinsic to each autocatalytic species i and therefore potentially subject to selection. Our point is to identify the intrinsic and extrinsic conditions that lead to the exclusion of one species by another. To this end, we consider that a first, resident species has reached a steady state and analyze whether a second, invading species, can grow when introduced in infinitesimal quantity in the background of the resident one [8, 11, 21].

III. RESULTS

When the two autocatalytic species are exponential ($n_1 = n_2 = 1$), the invading species faces a concentration of resource \bar{R}_1 set by the resident autocatalysts with $\bar{R}_1 = 1/\kappa_1$ if $\kappa_1 > 1/R_0$ and $\bar{R}_1 = R_0$ otherwise, in which case the resident autocatalysts do not survive by themselves. If $\kappa_2 < \kappa_1$, the invading species cannot grow, while if $\kappa_2 > \kappa_1$ and $\kappa_2 > 1/R_0$ it grows to eventually exclude the resident species. This is the essence of the exclusion principle [5]: two exponential autocatalytic species cannot coexist if they depend on the same resource and have different replication rate constants.

If the resident species is exponential ($n_1 = 1$) but the invading one is sub-exponential ($n_2 < 1$), however, the situation is different since the sub-exponential species can always grow provided its concentration is low enough, i.e., provided $A_2 < (R/\kappa_2)^{1/(1-n_2)}$. There is therefore no way for the resident exponential autocatalytic species to exclude an invading sub-exponential species. If, on the other hand, the resident species is sub-exponential and the invading species is exponential, two scenarios are possible. If $\kappa_1 > 1/\bar{R}_2$, where \bar{R}_2 is the steady state concentration of resource in presence of the sub-exponential species alone, the exponential species can invade and come to coexist with the sub-exponential one. If, however, $\kappa_1 < 1/\bar{R}_2$, the exponential species cannot invade and is therefore excluded.

Beyond this invasion analysis, the condition for exclusion of a exponential ($n_1 = 1$) autocatalytic species by a sub-exponential ($n_2 < 1$) one is

$$R_0 < 1/\kappa_1 + (\kappa_2/\kappa_1)^{\frac{1}{1-n_2}}.\tag{4}$$

This includes, in particular, levels of resource R_0 where the exponential species would survive by itself but is excluded by the sub-exponential species, when $1/\kappa_1 < R_0 < 1/\kappa_1 + (\kappa_2/\kappa_1)^{\frac{1}{1-n_2}}$. This is illustrated in Fig. 1A with the case of an exponentially growing autocatalytic species ($n_1 = 1$) competing with a parabolically growing species ($n_2 = 1/2$).

Finally, when two sub-exponential species ($n_1 < 1$ and $n_2 < 1$) compete, they necessarily coexist. In the particular case where they have same exponent ($n_1 = n_2 = n$), their relative concentration at steady state only depends on their intrinsic parameters,

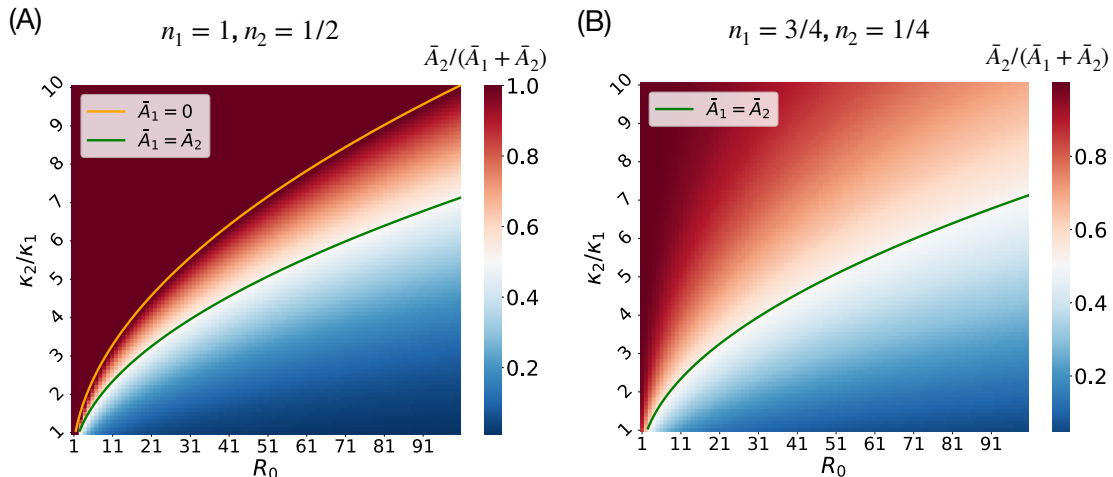


FIG. 1: Exclusion and coexistence in competitions of autocatalytic species with different growth laws, i.e., different exponents n . **A.** Mixture of an exponential and a sub-exponential autocatalytic species: $n_1 = 1$ and $n_2 = 1/2$. **B.** Mixture of two sub-exponential species: $n_1 = 3/4$ and $n_2 = 1/4$. The graphs show the relative concentration at steady state of one of two species, $\bar{A}_2/(\bar{A}_2 + \bar{A}_1)$, as a function of the total concentration of resource R_0 and of the ratio κ_2/κ_1 , when $\kappa_1 = 1$. The steady-state concentrations are obtained by numerical integration of the kinetic equations, Eq. (3). In A, the orange line indicates the total concentration of resource R_0 below which the exponential autocatalytic species is excluded ($\bar{A}_1 = 0$). The green lines indicate the total concentration R_0 for which the two species are in same proportion, $\bar{A}_1 = \bar{A}_2$.

$\bar{A}_1/\bar{A}_2 = (\kappa_1/\kappa_2)^{1/(1-n)}$. More generally, however, their relative concentration is controlled by the amount of resource R_0 . In this case again, when R_0 is low, the most abundant one can be, somewhat counterintuitively, the one with lowest exponent n (Fig. 1B).

The analysis can be extended to investigate the conditions under which a sub-exponential autocatalytic species ($n < 1$) can exclude a super-exponential one ($n > 1$). The minimal concentration of resource that allows super-exponential species to grow ($dA/d\tau > 0$) increases as their concentration decreases, $R = 1/(A^{n-1}\kappa)$. Therefore, in a situation where the resident species is sub-exponential, an autocatalytic species introduced in infinitesimal quantity is less advantaged when it is super-exponential than when it is exponential. However, a resident species requires a smaller concentration of resource when it is super-exponential than when it is exponential, and it is therefore more difficult to displace. The results of the competition of a super-exponential species with another species therefore depends strongly on the initial conditions. This has been referred to as the “survival of the first” in previous studies [22]. Autocatalytic species growing super-exponentially have, however, not been demonstrated experimentally so far, even though theoretical models that include hypercycles could result in it [23–26].

IV. DISCUSSION

The primary aim of this paper is to highlight that a sub-exponential autocatalytic species can exclude an exponential autocatalytic species and, more generally, that a sub-exponential species can dominate one of higher replication order, i.e., following a growth law $dA/dt = kA^n$ with a larger exponent n . This selection for autocatalytic species of lower

order occurs because autocatalytic dynamics depends not only on the growth order n , but also on the replication rate constant k : a species with a lower reaction order can outcompete another with a higher reaction order if it has a greater replication rate constant.

Our results rely on the phenomenological equation $dA/dt = kA^n$, which is widely employed to model the competitive dynamics of autocatalysts dependent on a common limiting resource [1, 5, 8–11]. In practice, the parameters k and n may be either inferred from experimental data [2, 3, 13, 15, 27], or derived from mechanistic models [6]. Derivations from mechanistic models bring an important nuance by showing that sub-exponential growth typically arises as an approximation of a more general relationship $dA/dt = f(A)$, where $f(A) \sim A^n$ with $n < 1$ for sufficiently high concentrations of A [6, 7, 11]. At low concentration, however, this sub-exponential growth typically turns into an exponential growth, since $dA/dt \approx f'(0)A$ for small values of A . The presence of these two regimes is well understood when sub-exponential growth stems from product inhibition [3, 6], which is necessarily negligible at low autocatalyst concentration. This dependence of the growth rate on the concentration of autocatalyst is generic and, in the absence of mechanistic details, autocatalytic growth can typically be captured through logistic or similarly shaped functions, for which the growth of an autocatalyst is exponential at low concentration and decreases at higher concentration [28, 29]. In any case, this implies that a sub-exponential autocatalytic species following a growth law with these two regimes becomes extinct below a certain concentration, which opens the possibility for an exponential one to exclude it. This does not affect, however, the possibility for the same sub-exponential species to exclude an exponential species, as we have noted.

Current research on autocatalysis is geared towards the experimental design of exponential autocatalytic species, motivated by the desire to observe exclusion, which is viewed as a key step towards achieving evolution by natural selection [7, 15, 30, 31]. The exclusion principle, first formulated by Gause in an ecological context [32], states that among two exponential species, the one with the higher replication rate will outcompete the other, irrespective of the magnitude of the difference between the rates [5]. Yet, our findings indicate that sub-exponential autocatalytic species can outperform their exponential and even super-exponential counterparts, and can therefore also cause selection by exclusion. As such, sub-exponential autocatalytic species set constraints on the evolutionary emergence of the first exponential ones. The issue takes on particular importance when we recognize the interrelated nature of the parameters k and n arising from mechanistic models. These parameters are indeed influenced by shared physical factors like reaction volume and autocatalyst-substrate interaction strength, resulting in a trade-off between them. Given that we have shown that k can be the primary determinant of autocatalyst dominance, this type of physical correlation further calls into question an exclusive emphasis on exponential autocatalysts.

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