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Anomalous percolation features in molecular evolution

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Self-replication underlies every species of living beings and simple physical intuition dictates that some sort of autocatalysis invariably constitutes a necessary ingredient for the emergence of molecular life. This led Worst *et al.* [E. G. Worst, P. Zimmer, E. Wollrab, K. Kruse, and A. Ott, New J. Phys. **18**, 103003 (2016)] to study a model of molecular evolution of self-replicating molecules where spontaneous ligation and simple autocatalysis are in competition for their building blocks. We revisit this model, where irreversible aggregation leads to a transition from a regime of small molecules to macromolecules, and find an array of anomalous percolation features, some of them predicted for very specific percolation processes [R. M. D'Souza and J. Nagler, Nat. Phys. **11**, 531 (2015)].

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I. INTRODUCTION

How early molecular life has begun from a primordial soup of small molecules is a fundamental question that penetrates many scientific disciplines. Experiments by Miller have shown that under conditions that probably prevailed on the early Earth essential biomolecules, in particular, amino acids, are spontaneously generated [1]. Recently, it has been found that among a wide variety of other molecules also ethylene glycol-based polymers were generated [2]. The presence of polymers is remarkable as amino acids need to be concatenated to form proteins and because it requires the presence of some catalyst. Consequently, the mixture meets essential requirements for molecular evolution.

Molecular systems based on RNA or DNA have been employed to understand possible mechanisms of early phases of the Earth's ecosystem [3–17]. Some of these systems combine autocatalytic molecular reproduction with some degree of spontaneous ligation, see Fig. 1, which have been identified as two key mechanisms for the emergence of life [9,18,19]. Autocatalytic reproduction is typically needed to overcome molecular decay [20], but also provides a mechanism by which acquired traits can be transmitted to future generations, whereas the spontaneous ligation of building blocks is the simplest form of noise in the system [21,22], which is necessary for generating mutations. How molecular evolution eventually generates living organisms, however, remains unclear. In studies where molecules self-reproduce without dedicated control, reproducing polymers typically end up competing for their building blocks and yield a molecule optimized for fast reproduction [5,9,23]. Similarly, in the theory of hypercycles that was established by Eigen and Schuster [19], eventually a single species wins and further evolution stops.

A step towards identifying conditions for continued molecular evolution that could eventually lead to an organism was made by introducing a system based on DNA strands, where molecular species are defined through their lengths [22]. Starting from building blocks of uniform length, new species emerge through spontaneous or through template-based ligation. As soon as the autocatalytic ligation rate is above a critical value, however, evolution can continue as long as building blocks are available and generates only specific molecular species out of the myriad of possible polymers.

In Ref. [22] a model was introduced to study the transition from uncontrolled proliferation of molecule lengths to a phase where only specific molecule lengths appear. Here, we revisit this model and analyze it from the point of view of percolation theory. Percolation describes the emergence of large-scale connectivity from the gradual addition of links on an underlying lattice or network. Polymerization processes can be naturally mapped onto percolation. In percolation processes, typically, a giant connected component emerges rapidly (but still smoothly) out of smaller components at a critical link density. The phase transition is of second order and exhibits self-averaging, that is, in the thermodynamic limit sample-to-sample fluctuations disappear everywhere except at the transition point, which shows prototypical critical behavior [24,25]. In past years, however, a number of percolation models have been found to exhibit anomalous features such as seemingly "explosive" but in the thermodynamic limit still continuous transitions [26,27], genuinely discontinuous transitions [28,29], or non-self-averaging behavior both before [30] and after the percolation transition [24,29,31]. The rich phenomenology of explosive percolation is presented in a number of reviews [32–34].

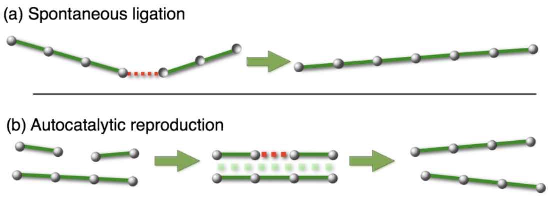

FIG. 1. Illustration of spontaneous ligation (a) and autocatalysis (b). The rate of the autocatalytic reaction depends on the template molecule concentration [see Eq. (1)].

Through stochastic simulations, we show that the model of molecular evolution of Ref. [22] displays a wide variety of these anomalous percolation features [26,35–43]. By varying the ratio between the spontaneous and the autocatalytic ligation rates over 13 orders of magnitude, we find discontinuous percolation in the thermodynamic limit as well as non-self-averaging, stochastic staircases, and oscillations in the fluctuation function in finite-size systems. Phase transitions are usually defined in the thermodynamic limit only. Early molecular life, however, is a matter of the sustained emergence of large but finite molecules and its dynamics is governed by finite-size effects from the viewpoint of statistical physics. We thus conclude that anomalous percolation behavior was associated with early molecular life. Finally, we will discuss possible implications for the emergence of life.

II. THE SYSTEM

In the framework developed in Ref. [22], polymers consisting of indistinguishable monomers concatenate either spontaneously or autocatalytically. This dynamics describes the essential features of an experimental system, where the elementary building blocks are formed by DNA strands with a length of ten base pairs and where autocatalytic reproduction is realized by template-based ligation. In the model, however, any information on the base pair configurations, which is carried by the DNA strands, is neglected. Reactions occur spontaneously with a rate constant β or autocatalytically with a rate constant $\alpha[A_{n+m}]$,

$$A_n + A_m \xrightarrow[\alpha[A_{n+m}]+\beta]{} A_{n+m}, \tag{1}$$

where A_n represent polymers of length n. The brackets denote the corresponding densities (see Fig. 1).

We assume well-mixed molecule species in a fixed volume where the reactions are described in the mean-field limit by the Smoluchowsky equation

$$\frac{d}{dt}[A_{n+m}] = (\alpha[A_{n+m}] + \beta)[A_n][A_m] - \sum_{k\geqslant 1}(1+\delta_{n+m,k})(\alpha[A_{n+m+k}]+\beta)[A_{n+m}][A_k]. \tag{2}$$

Here $\delta_{n,m} = 1$ if $n = m$ and zero otherwise. The first term on the right-hand side describes production, whereas the second term covers all annihilation possibilities.

We start the simulations with N monomers, but no other polymers present. In the following, we will only consider the case that N is a power of 2, $N = 2^K$ for some natural number K. The simulations run until only one polymer of length N remains and no further reaction is possible anymore. We choose a normalized Monte Carlo time so that $\beta = 1$ and run the system using the Gillespie algorithm [44,45] and GNU Parallel [46]. Complementary to the physical time t we also study the system's progression with time as a function of the relative reaction number p, which is the number of reactions relative to the total monomer number N, $p =$ (number of reactions)$/N$ [40,47]. We characterize the system dynamics through the order parameter G, which is given by the size of the largest molecule S_1 relative to the total monomer number, $G = S_1/N$. In the course of a simulation with initially only monomers present, its value evolves from $G = 1/N$ to 1.

III. RESULTS

We will start our investigations with the analysis of the limiting cases of no or infinitely fast autocatalytic ligation and then move on to intermediate values.

A. The limiting cases $\alpha = 0$ and $\alpha \to \infty$

The two limiting cases of the above model, where either $\alpha = 0$ or $\alpha \to \infty$, have already been studied in different contexts. The case $\alpha = 0$ describes spontaneous assembly of polymers with two reactive ends [47]. In the thermodynamic limit $N \to \infty$, the order parameter G is known to exhibit a deterministic jump from zero to one at the end of the reaction process, where $p = 1$ [47]. For the present system, this property can already be guessed from finite-size systems that show a very steep increase of the order parameter in the last steps of the simulation [see Fig. 2(a)]. The end of the assembly process, which is given by the emergence of a single macromolecule and also called gelation [48], is fully described by percolation on a one-dimensional lattice. This process exhibits a simple discontinuous percolation transition at full link density $p = p_c = 1$ [49]. Note that we have used the same symbol p for the probability of having a link and for the relative reaction number as every reaction introduces exactly a single new link. Due to the lack of a supercritical regime, where $p > p_c$, this one-dimensional percolation transition is sometimes referred to as "trivial."

In the limit $\alpha \to \infty$, spontaneous concatenation is completely outcompeted by autocatalytic concatenation and restricted to phases when the latter process cannot occur due to a lack of templates. In this case, larger polymers assemble only by merging of two polymers of exactly the same size. This leads to a cascade of events in which the largest polymer doubles in size. As one can see in the example given in Fig. 2(b), close to $t = 1$, mergers are indeed of the type $A_{2^n} + A_{2^n} \to A_{2^{n+1}}$, n integer. This behavior is also present for smaller t, but cannot be seen directly on the curve in Fig. 2(b). In the last step, two equally large clusters merge, $A_{N/2} + A_{N/2} \to A_N$ (see inset). This dynamics is a special case of a network model, in which always the two smallest clusters merge and which appears as the deterministic limit of some random network models [24,28,29,37]. By definition, the last merger takes place at exactly $p = p_c = 1$. On the other hand, close to $p = 1$, the reaction rate becomes extremely low as the system

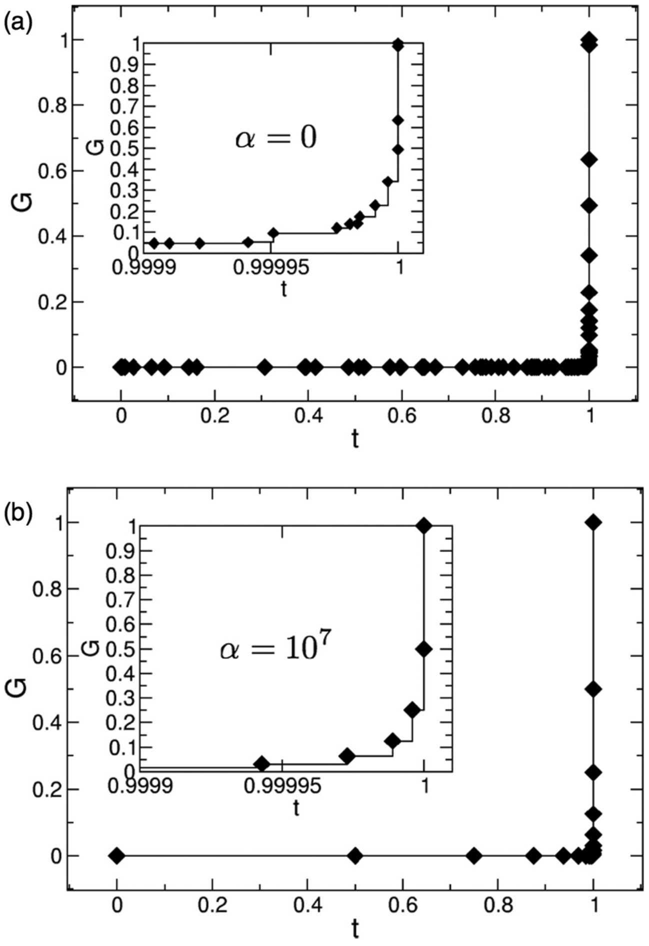

FIG. 2. Relative size of the largest cluster G as a function of time. Displayed are single realizations for the limiting cases $\alpha = 0$ (a) and $\alpha \gg \beta$, specifically $\alpha = 10^7$ (b). Independently of α, the model shows a strong increase at the end of the process with jumps of order 1 close to $t = 1$ (as $t \approx p_c = 1$, see text). Jumps of size $1/2, 1/4, \ldots$ in panel (b), for large system sizes N. Other parameters: $\beta = 1$ and $N = 2^{20}$.

encompasses only a few clusters in a finite volume. Thus, the final steps in the coalescence process consume most of the physical time t and the reactions end at about $t \approx p_c = 1$.

We conclude that the limiting cases $\alpha = 0$ and $\alpha \to \infty$ present discontinuous percolation in the thermodynamic limit. Also for any other value of α (and β), the percolation transition is discontinuous in the thermodynamic limit. Indeed, a continuous transition would require an acceleration of the growth of large polymers through merging small molecules [48,49]. Compared to the limiting case $\alpha \to \infty$, however, all other values of α lead to a slower autocatalytic merging of smaller molecules. Similarly, compared to the limiting case $\alpha = 0$, any other value of α is equivalent to reducing the value of β from the limit $\beta \to \infty$ to a finite value and thus a lower rate of spontaneous concatenation. As a consequence, the stochastic process Eq. (1) exhibits a discontinuous transition for any value of α/β.

We will now turn to the general case of intermediate autocatalytic reaction rates in greater detail. There we will focus our attention on finite system sizes.

B. Doubling cascades

Let us consider the time evolution of the abundances of small molecules for different values of the autocatalytic rate constant α. For $\alpha = 10^{-9}$, molecules of all possible sizes are produced. They emerge in a sequence of increasing molecule length. Initially, they grow algebraically in number, reach a maximum, and eventually vanish algebraically [see Fig. 3(a)]. The exponent for the growth phase is roughly 1 for A_2 and initially increases for larger molecules, whereas the exponent for the decay is essentially independent of the molecule size.

From the autocatalytic reproduction of molecules one might have expected an exponential increase in molecule numbers. However, spontaneous production of molecules largely outcompetes autocatalytic reproduction for this small value of α. Explicitly,

$$\frac{d}{dt}[A_2] \approx \beta[A_1]^2 - \beta[A_1][A_2] + \alpha[A_2][A_1]^2 \qquad (3)$$

$$\approx \beta[A_1]^2, \qquad (4)$$

where we have only kept terms that are lowest order in t. In this regime, the number of dimers increases roughly linearly, $[A_2] \approx \beta[A_1]^2 t$, showing that autocatalytic reproduction of dimers is negligible in the initial phase. In addition, the consumption of A_2 for the formation of larger molecules prevents a potential exponential proliferation of dimers.

For molecules of larger size, given the low abundance of building blocks, for example, A_2 for the formation of A_3, the rate of their spontaneous formation is limited. Again, the spontaneous formation of even larger molecules suppresses an exponential growth. In the case of A_3 we have explicitly

$$\frac{d}{dt}[A_3] \approx \beta[A_1][A_2] \qquad (5)$$

and thus

$$[A_3] \approx \beta^2 [A_1]^3 t^2/2. \qquad (6)$$

For a somewhat larger autocatalytic rate constant of $\alpha = 10^{-1}$, the overall dynamics changes dramatically [see Fig. 3(b)]. Now, molecules of sizes that are a power of 2 vastly dominate the distribution up to the size 64. In this doubling cascade, the growth phase of the concentration of a species is initially exponential and then crosses over into algebraic growth. This reflects the autocatalytic contribution. The growth phase is followed by a plateau phase. Eventually, the molecules of a species are used to form even larger molecules and their concentration decays. At some point also molecules of length other than a power of 2 gain a significant concentration, i.e., a concentration larger than molecules of the doubling cascade. From that time on, the doubling cascade ceases to exist and the distribution of molecular species widens.

For very large autocatalytic rate constants $\alpha \gg \beta$, there are abrupt transitions between phases, in which molecules of only one size are present [see Fig. 3(c)]. The sizes are subsequent powers of 2. After the spontaneous formation of a molecule of size 2^n, the very fast autocatalytic process leads to an almost instantaneous transformation of all molecules of size 2^{n-1} into pairs and thus into molecules of size 2^n. The times between two transitions are distributed exponentially, which reflects the Poissonian character of spontaneous concatenation

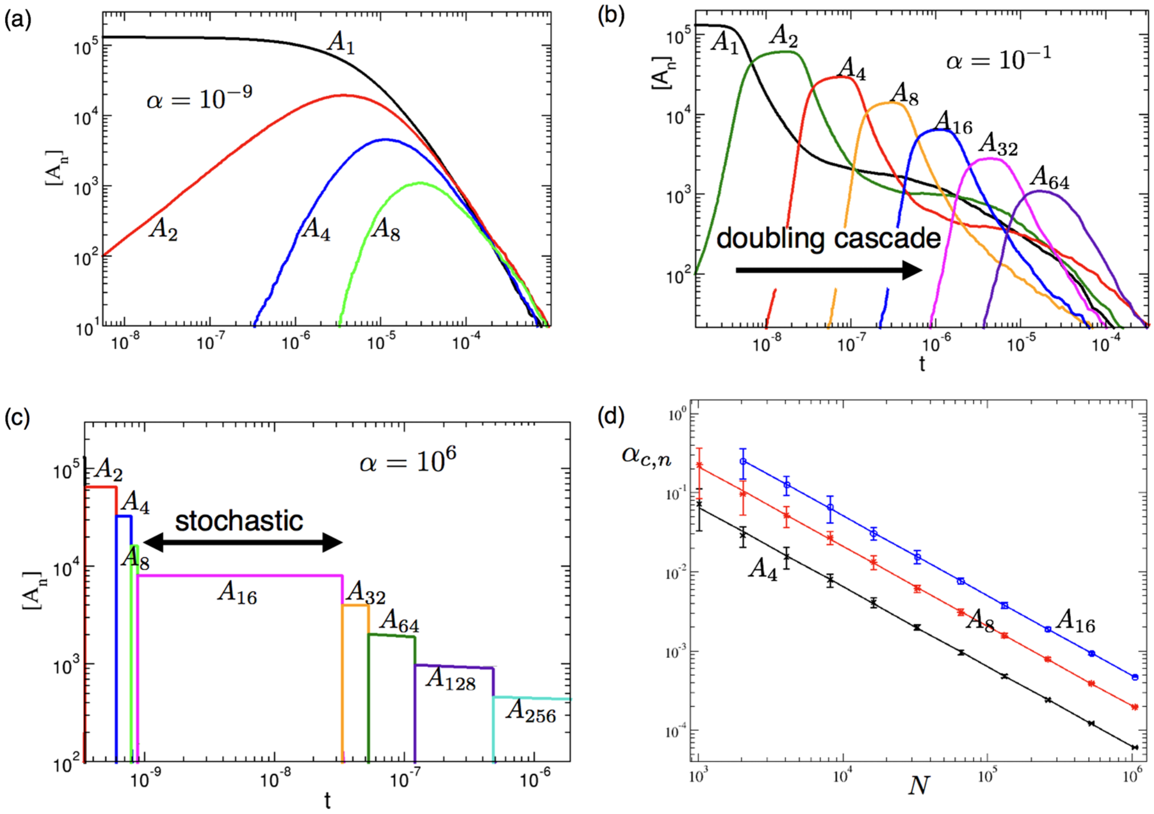

FIG. 3. Time course of molecule concentrations. Single realization for $\alpha = 10^{-9}$ (a), $\alpha = 0.1$ (b), and $\alpha = 10^6$ (c). Other parameters: $\beta = 1$ and $N = 2^{17}$. Note that only the concentrations for molecules of size of powers of 2 are displayed as otherwise the curves would be too close together. (d) Critical value $\alpha_{c,n}$ of the autocatalytic rate for selection up to species A_n (for $n = 4,8,16$) as a function of the initial monomer concentration N.

in a background of molecules of only one size that occurs at rate β.

These observations suggest that there is a critical value α_c of the autocatalytic rate above which molecular doubling outcompetes the spontaneous generation of molecules of length that are not powers of 2. For $\alpha > \alpha_c$ molecules of length 2^n for some n are the dominant length in the system. This critical value depends on the initial monomer number N. To see this, let us define a critical value that depends on n, $\alpha_{c,n}$, such that for $\alpha > \alpha_{c,n}$ molecules that are shorter than 2^n have a length that is equal to a power of 2. We plot this critical value for $n = 2,3,$ and 4 in Fig. 3(d). Clearly, $\alpha_{c,n} \sim N^{-1}$ and $\alpha_{c,n} < \alpha_{c,n+1}$, where $\alpha_{c,n+1}/\alpha_{c,n}$ decays with n. Further details can be found in Ref. [22].

The transition between the doubling cascade and unrestricted growth is also visible in the system's entropy, to which we turn now.

Entropy oscillations

We define the entropy through the polymer densities as $S = -\sum_n [A_n] \log[A_n]$. At the beginning but also at the end of a simulation, we clearly have $S = 0$ as only one molecular species is present at these times. For early times the entropy has a general tendency to increase (see Fig. 4). However, the overall increase is modulated by oscillations, such that periods of decreasing entropy recurrently appear. The time interval between such two periods as well as their duration increases exponentially with time. At some point, these "oscillations" cease, reflecting the transition between the doubling cascade and the unrestricted appearance of new molecule lengths. Eventually, the now monotonically increasing entropy reaches

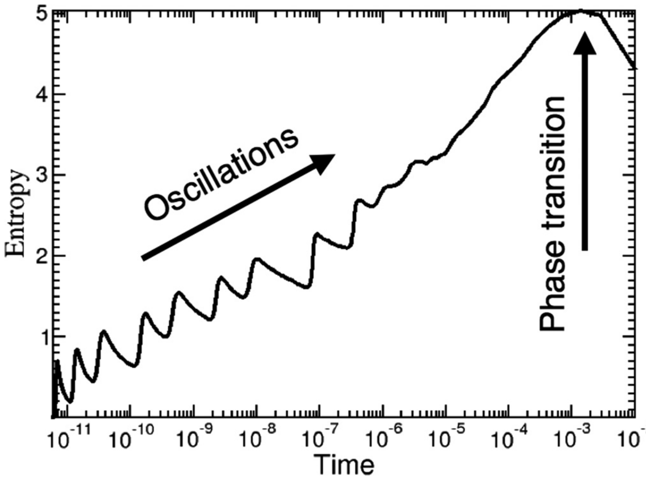

FIG. 4. Entropy as a function of time. Single realization for $\alpha = 10$, $\beta = 1$, and $N = 2^{20}$. The entropy necessarily vanishes in the beginning (N "clusters" of size $1/N$) and in the end of the process (one cluster of size N).

a maximum and decays to zero. The maximum in the entropy signals another transition. At this point the broadest distribution in molecule sizes is reached. Afterwards the finite number of monomers in the system restricts a further broadening and it collapses eventually onto the molecule of the maximal size. During this collapse, the entropy decreases.

The occurrence of oscillations in $S = -\sum_n [A_n] \log[A_n]$ as a function of time necessarily implies oscillations in the relative variance of the percolation order parameter, because both observables describe the degree of the system's disorder. More generally, the evolution of molecule sizes can be interpreted in terms of standard percolation observables, as we demonstrate next.

C. Dynamics of the order parameter

We now analyze the dynamics of the order parameter G. As we recall, G is the size of the largest molecule relative to the maximally possible size N. As a function of time, the order parameter is a stochastic quantity. For sufficiently large values of the autocatalytic rate constant α our data suggest that it remains stochastic even in the thermodynamic limit [see Fig. 5(a)]. In fact, the maximum and the minimum value of the order parameter increase exponentially as a function of time until they eventually collapse after the maximum of G has inevitably reached the value 1.

In contrast, as a function of the relative reaction number p and for $\alpha \to \infty$, the doubling cascade becomes deterministic in the thermodynamic limit. This is suggested by simulations for $N = 2^{20}$ [see Fig. 5(b)]. Up to some value of p, the maximum and the minimum of the order parameter coincide. For larger values of the relative reaction number, the maximum and minimum values of G separate. This difference reflects the nonzero fraction of spontaneous concatenations, which only vanishes for $\beta/\alpha = 0$.

1. Non-self-averaging

To quantify the variations in the order parameter between different realizations, we consider the relative variance in G, which is given by

$$R_v = \frac{\langle G - \langle G\rangle\rangle^2}{\langle G\rangle^2}. \tag{7}$$

In this expression, brackets denote ensemble averaging. In case $R_v \to 0$ for $N \to \infty$, the system is said to be self-averaging as sample-to-sample fluctuations vanish and the order parameter becomes sharp. In the opposite case, the system is said to be non-self-averaging. Recall that in the thermodynamic limit the order parameter G jumps from zero to one at $p = p_c = 1$, that is, at the end of the process. As a consequence, at $p = 1$ the dynamics defined by Eq. (2) is necessarily self-averaging in the thermodynamic limit, $R_v \to 0$ for $N \to \infty$, except for a singular peak exactly at $p = p_c$ [24,25]. This limit can, however, be approached very slowly [50,51]. Only very recently a number of percolation processes have been proven to exhibit genuine peaks in the relative variance R_v, which do not disappear in the thermodynamic limit. Still, the width of any peak in the subcritical regime must approach zero in the thermodynamic limit [30].

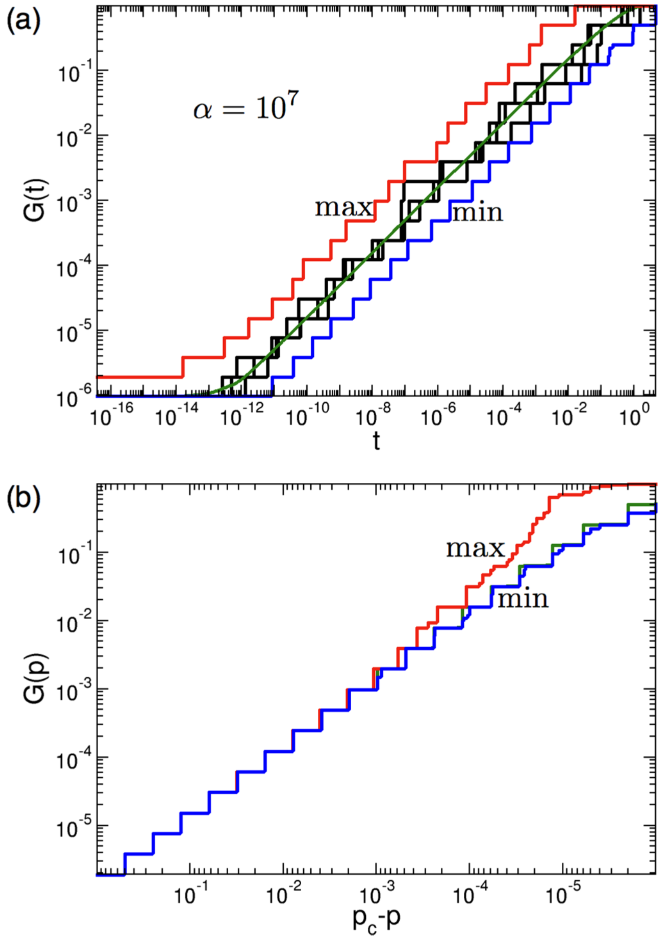

FIG. 5. Relative size of the largest molecule as a function of the reaction time t (a) and of the reaction number p (b). Shown are the maximum, minimum, average (curve in between in green/gray), and three realizations [black, displayed only in panel (a)]. Parameters: $\alpha = 10^7$, $\beta = 1$, and $N = 2^{20}$. The maximum, minimum, and average have been obtained from 10 000 realizations.

Peaks in the relative variance of the order parameter can be observed for our system if the distribution of molecule lengths exhibits a doubling cascade (see Fig. 6). The width of the peaks decreases with increasing α and with increasing N. The heights of the peaks increases with increasing N, but for the same N they decrease with increasing α. Furthermore, the maximum shifts towards p_c with increasing N.

The peaks in the relative variance correspond to molecule length doubling events. Consequently, the distance between two peaks decreases exponentially as p increases.

2. Discrete scale invariance

Discrete scale invariance (DSI) arises when the scale invariance of an observable $\mathcal{O}(x) \sim x^\alpha$ obeying $\mathcal{O}(\lambda x) = \lambda^\alpha \mathcal{O}(x)$ is broken such that the scaling relation does not hold for all λ, but only for a countable set $\lambda_1, \lambda_2, \ldots$. These discrete values are linked through $\lambda_n = \lambda^n$, where λ is the fundamental scaling ratio of the system [52,53].

Doubling cascades in explosive percolation have been shown to follow DSI [30]. Figure 6 suggests that the peaks

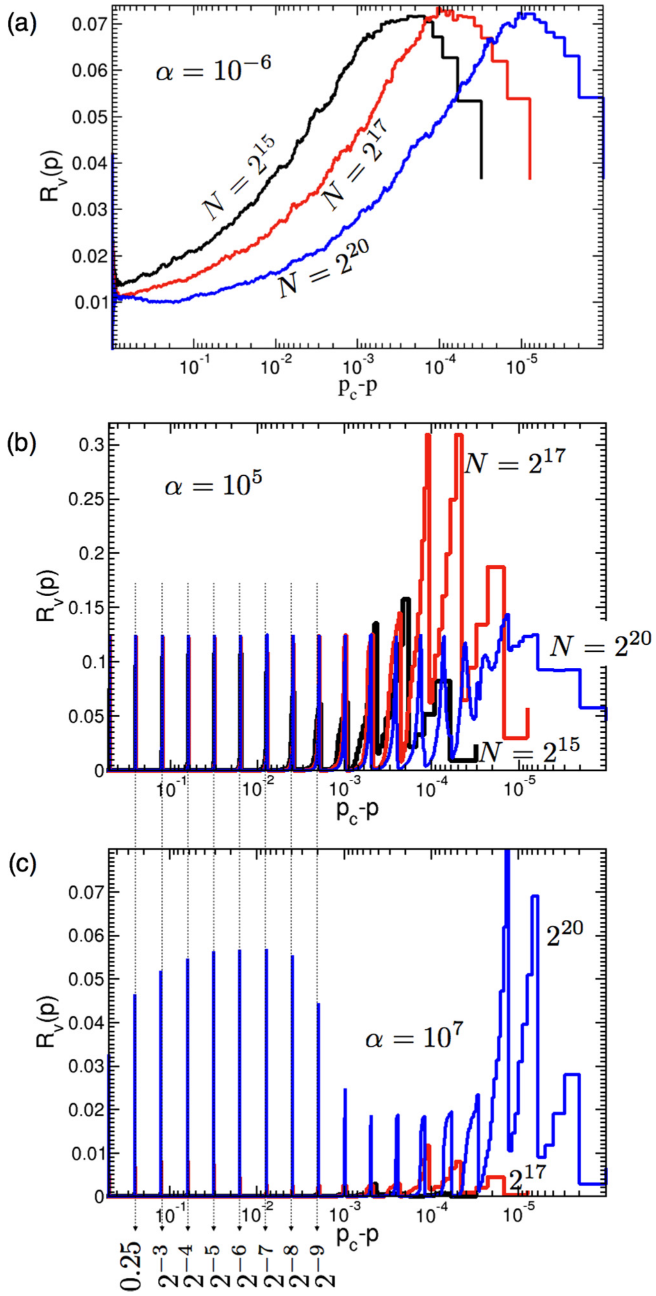

FIG. 6. Non-self-averaging and discrete scale invariance. Relative variance R_v of the order parameter G as a function of the distance to the phase transition in the relative reaction number $p - p_c$ for $\alpha = 10^{-6}$ (a), $\alpha = 10^5$ (b), and $\alpha = 10^7$ (c). Other parameters $\beta = 1$ and system sizes $N = 2^{15}$, 2^{17}, and 2^{20} in comparison.

in R_v occur at $p_n = p_c - 2^{-n}$ with $n \geqslant 0$. At these positions, the value of the order parameter G doubles. Consequently,

$$\frac{p_c - p_{n+1}}{p_c - p_n} = 1/\lambda \tag{8}$$

and

$$G(p_{n+1}) = \lambda G(p_n) \tag{9}$$

with $\lambda = 2$ [30,52,53]. This prediction for large α is in good agreement with Figs. 6(b) and 6(c).

IV. FINAL REMARKS

We have studied a model which adopts the minimal ingredients of molecular evolution: self-replicating molecules in presence of spontaneous ligation [22], which are molecular forms of proliferation and mutation. We analyzed the model in terms of a dynamic percolation process, where the percolated state corresponds to the final state, when all monomers are incorporated in a single polymer. Since we neglect any breakup of molecules, percolation is inevitable in this model. Our study revealed, however, that the percolation transition shows various features that are uncommon.

First of all, for any choice of the ratio between the spontaneous concatenation rate and the autocatalytic rate constant, β/α, the percolation phase transition, defined in the thermodynamic limit, is discontinuous, with a deterministic jump of the order parameter at the end of the process. Then, for small molecules in a finite system, we find large sample-to-sample fluctuations and the order parameter is non-self-averaging (Fig. 6). This situation characterizes the early stage of molecular life where small molecules necessarily dominate the reaction process. The emergence of large molecules is then announced by stochastic staircases. This is reminiscent of discontinuous phase transitions, which have been observed in models of digital life where the fitness exhibits first-order phase transitions [14,54]. As our model incorporates a somewhat limited form of mutation and does not involve an explicit fitness landscape one might argue that this is a mere coincidence. Still, it is exactly mutation in the form of spontaneous ligation, which allows the system to explore "species" beyond those that can be reached by variations of letters in an alphabet, as well as the autocatalytic proliferation rate, which can be viewed as a state-dependent fitness function, that make this model special: these features allow the system to avoid evolutionary dead ends. In this way, it might fall into the same class of models of digital life exhibiting discontinuous phase transitions. Probably more importantly, since the relative variance is a monotonous function of the entropy associated with the cluster size distribution, our results explain why evolution of (molecular) life is necessarily linked to oscillations of the fluctuation function and entropy [55].

To conclude, an array of anomalous percolation features is inherent to the emergence of molecular life: anomalous behaviors of the molecule concentrations, stochastic staircases, and finite-size non-self-averaging. Future research must establish how our results are affected quantitatively or even qualitatively by more complex processes in the emergence of molecular life, in particular, if the polymer species contain information beyond their length and if the information contained in the polymers is used in functional processes like reproduction. Even more ambitiously, one could consider the case when molecule reproduction is tightly linked to compartmentalization [21].

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