

Self-organized criticality of a catalytic reaction network under flow

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Self-organized critical behavior in a catalytic reaction network system induced by smallness in the molecule number is reported. The system under a flow of chemicals is shown to undergo a transition from a stationary to an intermittent reaction phase when the flow rate is decreased. In the intermittent reaction phase, two temporal regimes with active and halted reactions alternate. The number frequency of reaction events at each active regime and its duration time are shown to obey a universal power law with the exponents $4/3$ and $3/2$, respectively, independently of the parameters and network structure. These power laws are explained by a one-dimensional random-walk representation of the number of catalytically active chemicals. Possible relevance of the result to reaction dynamics in artificial and biological cells is briefly discussed.

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Most intracellular reactions progress with the aid of catalysts. These reactions are essential for a cell to survive and grow, whereas all catalysts that are proteins have to be synthesized as a result of such catalytic reactions. Thus, studies in catalytic reaction networks have gathered much attention in order to develop a theoretical model of protocells for their role in the origin of life [1–6], as well as to unveil universal statistical characteristics in the present cells [7]. Generally, cells consist of a large number of chemical species, some of which flow in and out through the membrane. There are also other chemical species that are not present in a large quantity. However, some chemical species play an important role even at extremely low concentrations amounting to only a few molecules per cell [8]. Then, the fluctuation and discreteness in the molecule number are not negligible. Indeed, recent studies on catalytic reaction dynamics have demonstrated that discreteness in molecule number can induce drastic changes to the chemical concentrations obtained from the rate equation model [9–11]. However, in most thermodynamics studies, the molecule number is assumed to be large while the number of species is rather small. In order to study the catalytic reaction network of a cell, it is important to consider the case with a large number of chemical species and a small molecule number.

In this Rapid Communication, we investigate a simple model of a random catalytic reaction network subjected to a flow of chemicals. In a region with a weak flow, where the discreteness in molecule number is important, it was observed that the reaction events occurred intermittently, separated by a quiescent state. The number distribution of reaction events during each reaction state obeyed a universal power law, displaying criticality induced by the discreteness in the molecule number. By referring to the study of self-organized criticality, as investigated in models for sandpiles, earthquakes, interface depinning in random media, and so forth [12–14], we will explain the origin of this universal power-law behavior.

We introduce a network of elementary two-body catalytic reactions among a large number of chemical species [7]. Assuming that chemicals in the system are well stirred, we discard the spatial dependence of concentration so that the

state of the system can be represented by a set of numbers (n_1, n_2, \dots, n_M) , where $n_i (0, 1, \dots)$ indicates the number of molecules of each chemical species $i (1 \leq i \leq M)$, with M being the total number of chemical species. Every chemical is a reactant and at the same time is a catalysts for (several) reactions. By the reactions, each chemical is transformed to some other species, catalyzed by another chemical, i.e., the reaction from chemical B to chemical A is catalyzed by a third chemical C (see Fig. 1). For simplicity, the reaction rates r of each reaction are set to be identical (the inhomogeneous reaction rate case is discarded as it does not affect the result to be discussed). The growth rate of molecule number n_A (or the decay rate of molecule number n_B) is given by $rn_B n_C / V$, on the average, where V represents the volume of the system.

The entire catalytic reaction network consists of reactions whose reaction paths are chosen randomly (and then fixed). The average number of reaction paths from a chemical i catalyzed by a chemical j is set to a given connection number K . In this Rapid Communication, we only consider the case where $K_c < K \ll M$; K_c indicates the critical connection number at the percolation threshold in random networks [$K_c \sim \log(M)$] [15]. We have not considered an autocatalytic reaction of the form $B + C \rightarrow 2C$ because usually such a reaction is realized as a result of a series of (nonautocatalytic) elementary reactions.

Next, we consider the flow of chemicals into a system

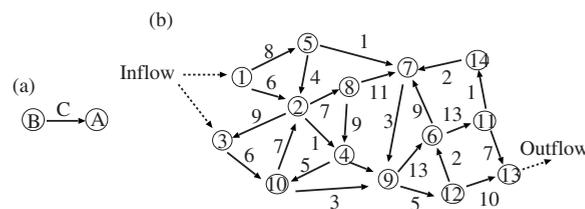


FIG. 1. (a) An illustration of a catalytic reaction $B + C \rightarrow A + C$. Arrows indicate the reaction, their origin and end-point (“B” and “A”) indicate the substrate and product, and the species on the arrow (“C”) indicates the catalyst. (b) An example of a catalytic reaction network.

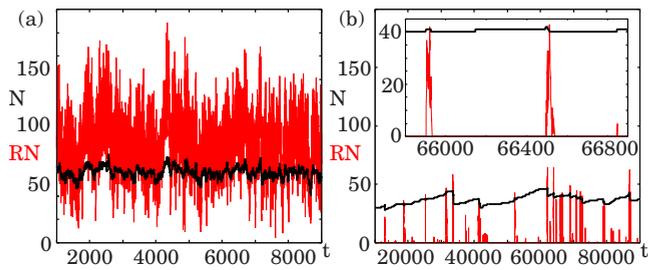


FIG. 2. (Color online) Typical temporal evolutions of $N(t)$ (black) and $RN(t)$ [gray (red online)] for $M=300$ and $K=12$ with (a) $Q=0.3$ and (b) $Q=0.001$.

from a molecular bath. We assume that M_{in} chemical species can flow into the system. A single molecule from one of the M_{in} chemical species is added to the system in the rate Q/M_{in} per unit time, where Q indicates the inflow rate of molecules. For simplicity, the flow rates of all chemical species are assumed to be the same; however, this assumption can be relaxed. We also assume that M_{out} chemical species flow out (or are decomposed) from the system. Because of this inflow and outflow, the total number of molecules $N=\sum_j n_j$ varies with time, in contrast to our previous paper [11].

In this Rapid Communication, we assume that M_{in} is sufficiently larger than $\sqrt{M/K}$. It should be noted that the average number of reaction paths through which the M_{in} “input” chemicals are catalyzed by one of themselves is given as $M_{in}K \times M_{in}/M$. This number is much greater than unity when $M_{in} \gg \sqrt{M/K}$. As long as this condition is satisfied (empirically, $M_{in} \gtrsim 2\sqrt{M/K}$), a chemical reaction takes place even if the total molecule number is null initially. With this constraint on M_{in} , the behavior of the system is observed independent of M_{in} . Here, we mainly show the results for $M_{in}=M$. Our second assumption is that M_{out} is much smaller than M . If the value of M_{out} is comparable to that of M , the number of extinct chemical species increases. As a result, the number of surviving species is much smaller than M , thereby reducing the effective system size considerably. On the other hand, if this assumption is true, the qualitative behavior of the system is determined by M . Here, we mainly present the results of the system behavior for $M_{out}=1$.

We perform stochastic particle simulation in order to study the possible effects of stochasticity and discreteness in molecule numbers. The simulation procedure is as follows: at each simulation step, we randomly select a pair of molecules. If the pair consists of a substrate and one of its catalysts, then, according to the rule of catalytic reaction network, the substrate molecule is replaced by the product molecule with the probability r . The molecule number n_i of input chemical ($1 \leq i \leq M_{in}$) is incremented by one with a probability Q/M_{in} per unit time. When the output chemical species j is generated by the reaction or the inflow, it is removed immediately. We have adopted Gillespie’s direct method [16].

Here, we present the results obtained from a variety of random networks and several sets of parameters. Without losing generality (by redefining the time unit), we assume $r=1$ and $V=1$. Figure 2 shows the plots of typical temporal

evolutions of the total number of molecules in the system, $N(t)$, and the reaction number, $RN(t)$, for $t=0,1,2,\dots$, $M=300$, and $K=12$ with (a) $Q=0.3$ and (b) $Q=0.001$. Here, $RN(t)$ is defined as the number of reaction events that have occurred during a unit time between t and $t+1$. When Q is large, N and RN show stationary small fluctuation around their mean values. On the other hand, when Q is small, there are intermittent bursts in RN , while N increases gradually until the increase is replaced by the drastic drop in N as a result of such bursting reactions. These two regimes alternate.

When N is not large enough due to low inflow rate Q , the molecules therein do not react with each other because catalyst molecules for each of existing chemical species are absent. The reaction then stops and RN is constant at 0 until a flow of necessary catalysts restarts the reaction process. When the reactions start, the process of production and elimination of catalysts is repeated until the catalysts for all molecules in the system disappear.

If Q is sufficiently large, the system is in a steady state expected from the fixed-point solution of the continuous rate equation. Deviations in N and RN due to stochastic inflows and outflows are not significant. Thus, a steady state with large N is sustained so that the reaction does not stop.

We have plotted \bar{N} , the long time average of N versus the change in Q for statistical characterization of the transition mentioned above. Figures 3(a) and 3(b) are the log-log plots of $\rho=\bar{N}^2KM_{out}/M^2$ versus Q , whereas Figs. 3(c) and 3(d) are the plots of $\kappa=\frac{\bar{N}K}{M}$ and $\kappa'=\kappa-1$ as functions of Q for several M , K , M_{in} ($=M$, and $\sim M/K$), and M_{out} ($=1, 3$, and 6). Here, Figs. 3(a) and 3(c) show the results for $M_{in}=M$ and $M_{out}=1$ and Figs. 3(b) and 3(d) show the results under $M=1000$. ρ and κ indicate the outflow rate and the effective reaction paths number, respectively, as shown below.

In Figs. 3(a) and 3(b), $\rho \approx Q$ holds for large $Q \gtrsim M_{out}/K$. This can be explained as follows. In the steady state, the average molecule number for each chemical is \bar{N}/M , which also gives the number of catalysts per reaction path. Then, the average number of the reaction paths for each chemical species is $\frac{\bar{N}K}{M}$ ($=\kappa$) that indicates the rate of production of each chemical is $\sim K(\bar{N}/M)^2$. Thus the outflow rate is estimated as $M_{out}K(\bar{N}/M)^2=\rho$ which should balance with the inflow rate Q at the steady state.

On the other hand, for a small Q , \bar{N} is constant independent of Q . This is explained by the estimate of the number of molecules for the discreteness-induced transition [11]. Here, the reactions tend to stop if the average number of reaction paths that have corresponding nonzero catalyst for each chemical is smaller than unity, i.e., if $\frac{\bar{N}K}{M} \lesssim 1$. In this case, most chemical species cannot react because the required catalysts do not exist. Then, the outflow of molecules is suppressed, while N increases because of the inflow of molecules until it satisfy the condition $\frac{\bar{N}K}{M} \gtrsim 1$. Hence, \bar{N} remains at a constant value that is slightly larger than M/K for small Q . Indeed, Figs. 3(c) and 3(d) for small Q indicate that the Q versus κ and Q versus κ' relations for a large K are fitted by a single curve for each M and M_{out} , independent of K and M_{in} , while κ' approaches 0 with an increase in M and M_{out} .

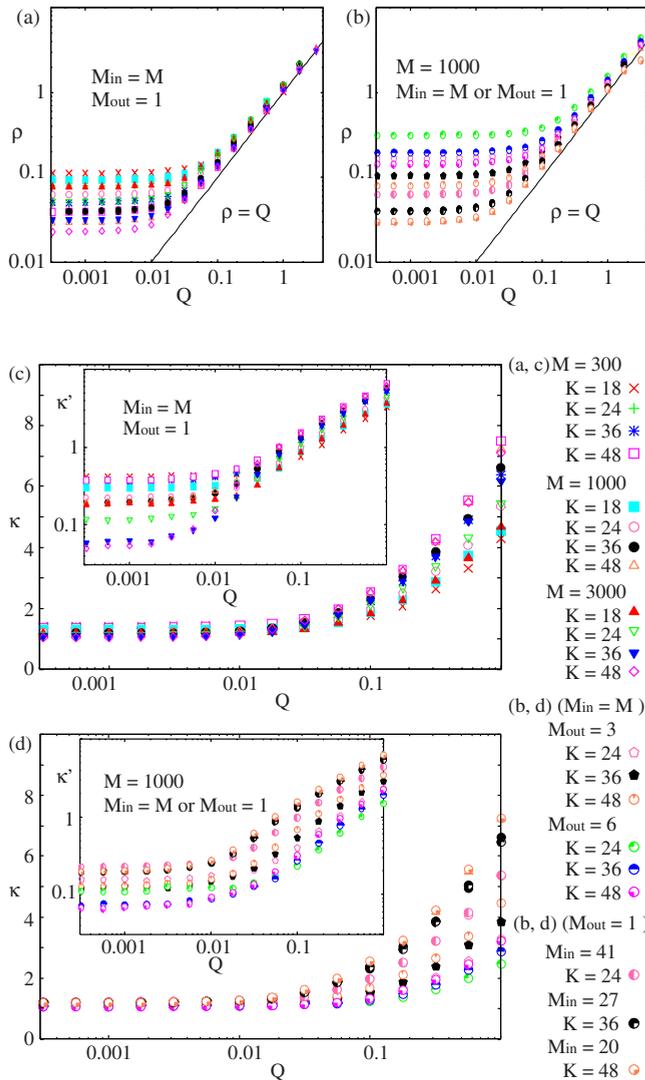


FIG. 3. (Color online) ρ , κ , and κ' as a function of Q for several M , K , M_{in} , and M_{out} . ρ , κ , and κ' are computed by sampling data over $10^4 \leq t \leq 10^7$.

Moreover, the crossover point between the above two states is estimated as $Q_c \sim M_{out}/K$.

We now focus on the statistical properties of the system at the regime of small Q with a constant \bar{N} . In this regime, the inflow of molecules continues even after the successive reactions have been completed. This situation will continue until an inflow triggers the next successive reactions, as shown in Fig. 2(b). Then, we focus on statistical properties of the reaction size S . S is defined as the sum of $RN(t)$ between the intervals of quiescent states where the molecules therein cannot react with each other. Figure 4 shows the frequency of the reaction size S for a system with $M = 1000$ and some values of K and Q , with $M_{in} = M$ and $M_{out} = 1$ for (a) and $M_{in} \sim M/K$ and $M_{out} = 3$ for (b). As shown, the frequency distribution of S , $P(S)$, obeys a universal power law $P(S) \sim S^{-\gamma}$ with the exponent $\gamma \sim 4/3$ for small enough Q . The same universal power law is satisfied even for other values of M , M_{in} , M_{out} , and K .

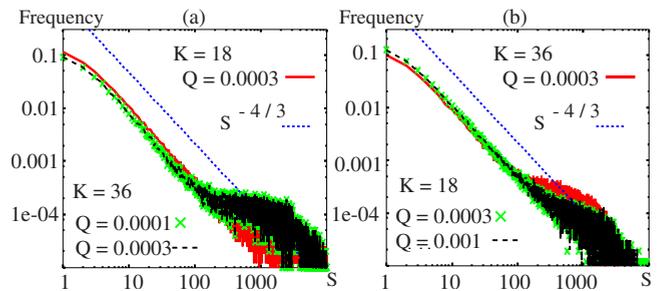


FIG. 4. (Color online) Frequency of S for $M = 1000$ and some values of K and Q , with $M_{in} = M$ and $M_{out} = 1$ for (a) and $M_{in} \sim M/K$ and $M_{out} = 3$ for (b). These histograms are computed by sampling data over $10^4 \leq t \leq 10^9$.

Now we discuss the origin of this universal power law for a small Q . Let us split the chemical species into active and inactive ones. An active chemical species is defined as (i) its number is nonzero and (ii) at least one catalyst molecule to transform it exists. We define $M_A(t)$ as the number of the active chemical species. When $M_A(t) = 0$, the system is said to be in the inactive state, and when $M_A(t) > 0$, the system is said to be in the active state.

During the inactive state, the probability that $M_A(t)$ becomes $M_A(t) > 0$ increases due to the inflow of some molecules. Reactions start taking place due to this inflow and production and elimination of several chemicals (catalysts) are repeated leading to an increase and then a decrease in $M_A(t)$. This process continues until $M_A(t)$ returns to 0, i.e., when the catalysts for all the molecules in the system have disappeared. Let us define the duration of reactive state D as the time interval with $M_A(t) > 0$. Note that $RN(t)$ is considered to be proportional to $M_A(t)$ on average.

Since the system under consideration is a random catalytic reaction network, we assume that the change in M_A is approximated by a one-dimensional random walk with $0 \leq M_A \leq M$. Then, the frequency of D is given by $P(D) \sim D^{-\alpha} = D^{-3/2}$, on the basis of the first return time distribution for the one-dimensional random walk. The reaction size S , which is proportional to the area below the random walk before its first return, scales as $S \sim D^\beta = D^{3/2}$. Then, the exponent γ for $P(S) \sim S^{-\gamma}$ is given by the standard relation between the exponents α , β , and γ : $\gamma = 1 + (\alpha - 1)/\beta = 4/3$ [14].

In order to confirm the validity of the above argument, we have examined the frequency of D and the relationship between D and S . Figure 5(a) shows the frequency of D and Fig. 5(b) shows the D - S characteristics for $K = 18$ and $K = 36$ with $M = 1000$, $M_{in} = M$, $M_{out} = 1$, and $Q = 0.0003$, which are obtained from the same simulation as the data plotted in Fig. 4(a). Figures 5(a) and 5(b) support the relation $P(D) \sim D^{-3/2}$ and $S \sim D^{3/2}$ [17]. Note that a similar random-walk description was adopted in a model of self-organized criticality in the anisotropic interface depinning in a quenched random medium [14].

In this Rapid Communication, the dynamic aspects of a random catalytic reaction network subjected to a flow of chemicals were studied. With a decrease in the inflow rate, the system undergoes a transition from a stationary to an

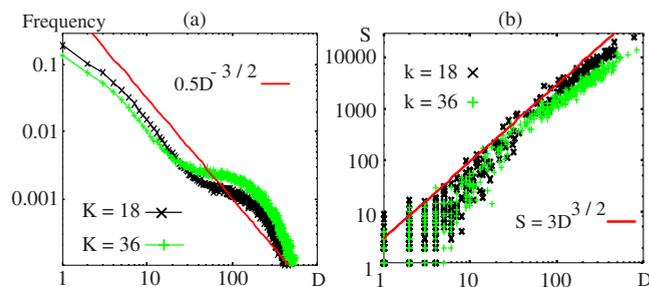


FIG. 5. (Color online) (a) Frequencies of D for $M=1000$, $Q=0.0003$, $M_{in}=M$, and $M_{out}=1$ with $K=18$ and $K=36$, and (b) D - S characteristics for the same conditions. The histograms are computed by sampling data over (a) $10^4 \leq t \leq 10^9$ and (b) $10^4 \leq t \leq 2 \times 10^6$.

intermittent reaction state; however, discreteness in molecule number in the latter state is essential. The frequency of the reaction size and duration of the reactive states obey the universal power laws with exponents $4/3$ and $3/2$, respec-

tively. Note that this critical behavior is obtained without any tuning parameter values and as long as the inflow rate is small enough to maintain the discreteness $(0,1,\dots)$ in the molecule number. In other words, discreteness induced self-organized criticality.

There are growing experimental progress in constructing a catalytic reaction network system toward synthesis of protocells [18]. We expect that intermittent reaction process through bottlenecks as observed in the present Rapid Communication can be confirmed in such *in vitro* experiments. It is also interesting that power law of the residence time distributions in cellular states are often reported [19]. Even though our random reaction network model is rather simple, the discovery of a universal power law may shed light in understanding nonstationary dynamics in the artificial catalytic reaction networks and cells.

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