Universal intermittent dynamics in a random catalytic reaction network, induced by smallness in the molecule number is reported. Stochastic simulations for a random catalytic reaction network subject to a flow of chemicals show that the system undergoes 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 laws with the exponents $4/3$ and $3/2$, respectively. 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 intra-cellular reaction dynamics is also discussed.

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Most intra-cellular reactions progress with the aid of catalysts. These reactions are essential for a cell to survive and grow. All catalysts that are proteins are synthesized within a cell as a result of catalytic reactions. Thus, researchers have started investigating catalytic reaction networks in order to develop a theoretical model of intra-cellular dynamics and protocols for their role in the origin of life\cite{1,2,3,4,5,6,7,8,9}. Research in this field was pioneered by Kauffman\cite{3}. Recent studies on a growing cell model comprising random catalytic reaction networks have also revealed universal statistical laws on chemical abundances. These results are confirmed by the gene expression data of the present cells\cite{6,7}.

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\cite{10,11,12,13}. In such cases, the fluctuation and discreteness in the molecule number are very important as far as temporal variations and steady distribution of chemical concentrations are considered. Indeed, recent studies on catalytic reaction dynamics have demonstrated that discreteness in molecule number can induce drastic changes in the temporal variations and the steady distribution of chemical concentrations obtained from the rate equation model\cite{14,15,16,17}. However, in most thermodynamics studies, the molecule number is assumed to be large while the number of species is assumed to be rather small. In order to study the catalytic reaction network of a cell, it is important to consider the case a large number of chemical species and a small molecule number.

In this study, 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 large, it was observed that the reaction events occurred intermittently, separated by a quiescent state. It was also observed that the number distribution of reaction events during each reaction state obeyed a universal power law, displaying a feature of criticality induced by the discreteness in the molecule number. By referring to the study of \textit{self-organized criticality}, as investigated in models for sand-piles, earthquakes, interface depinning in random media, and so on\cite{18,19,20,21,22,23}, we will explain the origin of this universal power law behavior. Finally, we discuss in brief the possible relevance of our result to the power laws of the distribution of residence time in the quasi-stationary state observed in behaviors of cells.

We introduce a network of elementary, two-body catalytic reactions among a large number of chemical species\cite{8}. 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 $\{n_1,n_2,...,n_M\}$, where $n_i(0, 1, ...) \geq 0$ indicates the number of molecules of each chemical species $i (1 \leq i \leq M)$, with $M$ being the total number of chemical species. Each chemical is transformed to another by (several) reactions. These reactions are catalyzed by another chemical, i.e., the reaction from chemical $B$ to chemical $C$.
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 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 study, we only consider the case where \( K_c < K << M \); \( K_c \) indicates the critical connection number at the percolation threshold in random networks \( (K_c \sim \log(M)) \) [24]. We have not considered an auto-catalytic reaction of the form \( B + C \rightarrow 2C \) because usually such a reaction is not elementary and is realized as a result of a series of (non-auto-catalytic) elementary reactions.

Next, we consider the flow of chemicals into a system from a molecular bath. We assume that \( M_{in} \) chemical species can flow into the system. At each instance, a single molecule from one of the \( M_{in} \) chemical species is added to the system in the rate \( Q/M_{in} \), 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 of chemical species, the total number of molecules \( N = \sum n_j \) varies with time, which is in contrast to our previous study [17].

In this study, 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, \( M_{in} \gg 2\sqrt{M/K} \)), 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 of the system behavior 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 chemical 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 \( M \). In this study, 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 discrete-ness 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 the 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 of \( Q/M_{in} \) per unit time. When the output chemical species \( j \) \((M_{out} < j \leq M)\) is generated by the reaction or the inflow of molecules, it is removed immediately. We have adopted Gillespie’s direct method in order to carry out numerical simulations for this process [24].

Here, we present the results of numerical simulations obtained from a variety of random networks and several sets of parameters. Without losing generality (by redefining the time unit), we can 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 \( t = 0, 1, 2, \ldots \) for \( M = 300 \), 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 between \( t \) and \( t + 1 \). When \( Q \) is large, \( N \) and \( RN \) show stationary, relatively 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.

The reason for change in behaviors of \( N(t) \) and \( RN(t) \) because of the decrease in \( Q \) is as follows. 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

![FIG. 2: (Color online) Typical temporal evolutions of \( N(t) \) (blue) and \( RN(t) \) (red) for \( M = 300 \) and \( K = 12 \) with (a) \( Q = 0.3 \) and (b) \( Q = 0.001 \).](image-url)
and \( \sim \) large deviations are not substantial. Thus, a steady state with stochastic inflows and the reaction process to produce the expected from the fixed point solution of the continuous rate equation. There exists a deviation in \( N \) and \( \rho N \) by stochastic inflows and the reaction process to produce the chemicals that escape from the system. However, these deviations are not substantial. 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. Figs. 3 (a) and (b) are the log-log plots of \( \rho = \bar{N}^2 K M_{\text{out}} / M^2 \) versus \( Q \), whereas Figs. 3 (c) and (d) are the plots of \( \kappa' = \kappa \) as functions of \( Q \) for several \( M, K, M_{\text{in}} = M \) and \( \sim M / K \), and \( M_{\text{out}} = 1, 3, \) and 6. Here, Figs. 3(a) and (c) show the results for \( M_{\text{in}} = M \) and \( M_{\text{out}} = 1 \) and Figs. 3(b) and (d) show the results under \( M = 1000 \).

In Figs. 3(a) and (b), \( \rho \approx Q \) holds for large \( Q \gtrsim M_{\text{out}} / K \). 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 rate of production of each chemical is \( \sim K (\bar{N} / M)^2 \). Thus the outflow rate is estimated as \( M_{\text{out}} \times K (\bar{N} / M)^2 = \rho \) 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. Here, the reactions tend to stop if the average number of reaction paths that have corresponding non-zero catalyst for each chemical is smaller than unity, i.e., if \( \frac{N K}{M} \lesssim 1 \). In this case, the outflow of molecules is suppressed; however, \( N \) increases because of the inflow of molecules, until it satisfies the condition \( \frac{N K}{M} \gtrsim 1 \). Hence, \( \bar{N} \) remains at a constant value that is slightly larger than \( M / K \) for small \( Q \). Indeed, Figs. 3(c) and (d) for small \( Q \) indicate that the \( Q \) versus \( \kappa \) and \( Q \) versus \( \kappa' \) relations for a large \( K \) are fitted by a single curve for each \( M \) and \( M_{\text{out}} \), independent of \( K \) and \( M_{\text{in}} \), while \( \kappa' \) approaches 0 with an increase in \( M \) and \( M_{\text{out}} \). Moreover, the crossover point between the above two states is estimated as \( Q_c \sim M_{\text{out}} / K \).

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 \( \rho N(t) \) between the interval of quiescent states where the molecules therein can not act with each other. Figure 4 shows the frequency of the reaction size \( S \), for a system with \( M = 1000, K = 18 \) and 36, \( Q = 0.0003 \), with \( M_{\text{in}} = M \) and \( M_{\text{out}} = 1 \) for (a) and \( M_{\text{in}} \sim M / K \) and \( M_{\text{out}} = 3 \) 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

![Figure 3](image-url)

**FIG. 3:** (Color online) \( \rho, \kappa, \) and \( \kappa' \) as a function of \( Q \) for several \( M, K, M_{\text{in}}, \) and \( M_{\text{out}}, \rho, \kappa, \) and \( \kappa' \) are computed by sampling with a step size of \( 10^9 \).

![Figure 4](image-url)

**FIG. 4:** (Color online) Frequencies of \( S \) for \( M = 1000, K = 18 \) and 36, \( Q = 0.0003 \) with (a) \( M_{\text{in}} = M \) and \( M_{\text{out}} = 1 \) and (b) \( M_{\text{in}} \sim M / K \) and \( M_{\text{out}} = 3 \) (\( M_{\text{in}} = 55 \) for \( K = 18 \) and \( M_{\text{in}} = 27 \) for \( K = 36 \)). These histograms are computed by sampling with a step size of \( 10^6 \).
satisfied even for other values of $M$, $M_{in}$, $M_{out}$, and $K$.

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 that species which is present in the system along with its catalysts. 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, $M_A(t)$ increase 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 of $M_A$ is approximated by a one-dimensional random walk with $0 \leq M_A \leq M$. Then, the frequency of $D$ is given by $P(D) \sim D^{−α} = D^{−3/2}$, 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 $S \sim D^β = D^{3/2}$. Then, the exponent $γ$ for $P(S) \sim S^{−γ}$, is given by the standard relation between the exponents $α$, $β$, and $γ$: $γ = 1 + (α − 1)/β = 4/3$.

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). The Figs. 5 (a) and (b) support the relation $P(D) \sim D^{−3/2}$ and $S \sim D^{3/2}$. 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.

In this study, the dynamic aspects of a random catalytic reaction network subjected to a flow of chemicals was studied. With a decrease in the inflow rate, the system undergoes a transition from a stationary to an 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, respectively. 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,..) in the molecule number. In other words, discreteness induced self-organized criticality (SOC).

Power law of the residence time distributions in a certain state are often reported in the behavior of cells, such as the residence time at a counter-clockwise rotations of flagella motor in E-coli, the frequency of the inter-event intervals for spontaneous vesicular release at a Xenopus neuromuscular junction, and the frequency of the inter-beat time interval in cardiac muscle cell, where non-stationary behaviors are a result of intra-cellular reaction dynamics. Since our random reaction network model is rather simple, we cannot make a detailed comparison with these experiments; however, the discovery of a universal power law may help us to understand the ubiquity of non-stationary intra-cellular dynamics and power law behaviors.

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