Microscopic self-organization in networks

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We report our numerical studies on microscopic self-organization of a reaction system in three types of differently connected networks: a regular network, a small-world network, and a random network. Our simulation results show that the topology of the network has an important effect on the communication among reaction molecules, and plays an important role in microscopic self-organization. The correlation length among reacting molecules in a random or a small-world network is much shorter compared with that in a regular one. As a result, it is much easier to obtain microscopic self-organization in a small-world or a random network. We also observed a phase transition from a stochastic state to a synchronized state when we increased the randomness of a small-world network.

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I. INTRODUCTION

Since the concepts of dissipative structure and self-organization were developed more than 20 years ago [1,2], studies on self-organization in reaction and reaction-diffusion systems have generated fruitful results [3–5]. Hundreds of chemical oscillators have been discovered and studied [3,6]. The mechanism of these chemical oscillators can all be explained by macroscopic self-organization, where time translational symmetry breaking takes place as a result of the nonlinear chemical kinetics of the system. In recent years, Mikhailov and co-workers [7,8] developed a concept of self-organization and proposed a different model to explain self-organization phenomena in a reactor of microscopic length scale. They named the phenomena ''microscopic self-organization.''

In a large reactor, the time for a chemical substance to diffuse across a reactor is long compared with the time for a reaction process. Therefore, reactions can be considered as an instantaneous event. As a result, reactions of different molecules can be considered as independent, and the concept of a Markov process can be applied to develop classical reaction kinetics, known as the mass action law. At the same time, a local equilibrium principle [1] is applicable. These ingredients are necessary for macroscopic self-organization. However, the situation is fundamentally different in a tiny reactor of micrometer size. In this case, the time needed for molecules to diffuse all over the reactor is comparable or even shorter than the time of one cycle of the reaction process. Consequently, the reaction can no longer be considered as instantaneous, and the reactions of different molecules may have strong correlations through diffusive or other kinds of communication. Therefore, the mass action law and local equilibrium principle discussed by Nicolis and Prigogine [1] can no longer be applied here. The mechanism of self-organization changes from nonlinear chemical kinetics to the strong correlations between reaction molecules.

The model of Mikhailov and co-workers [7,8] is based on a hypothetical enzymatic reaction. They assume that the reaction takes place in a tiny reactor which is too small to use a reaction-diffusion model, and studied the reactions with computer simulations. The situation considered is an extreme situation where the diffusion of molecules is treated as an instantaneous event. The diffusive transport of regulatory particles is discarded, and the whole allosteric activation reaction is simplified as a stochastic substrate binding of regulatory molecules to enzymes and subsequent stepping ahead of internal states of activated enzymes. Their simulation results show that when certain conditions are satisfied, this mechanism can lead to the development of strong deviations from equilibrium. As a result, coherent oscillations will be observed. A mean field model was also given [8].

In this paper, we report our model study of microscopic self-organization phenomena in networks rather than in a diffusive medium. In our model, reactions take place at the vertices of a network and the reacting substance moves along edges. Our study concentrates on the role different connection topologies of networks play on the dynamics of the microscopic self-organization. Three types of networks are examined: a regular network, a small-world network, and a random network. A small-world network is situated between completely regular and completely random networks. Watts and Strogatz [9–11] reported that when the randomness of a network increases from a regular one, the average distance between vertices drops very rapidly. (In the model, the distance between two vertices is defined as the least number of edges that constitute a path between the two vertices.) This means that the ability of the network to transfer information increases dramatically as soon as a little randomness is added to a regular network. We found that in certain range of transportation rate, microscopic self-organization can be observed in a random or a small-world network, and the phenomena are very similar to that discussed by Mikhailov and co-workers [7,8], but in a regular network the dynamic behavior of the system is different. It behaves like in a large reactor, where chemical oscillations are much weaker or totally disappear. Transitions from the stochastic state to a synchronized state as a function of the increase of the randomness of a small-world network is observed.

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II. MODEL

Our reaction model is largely based on the model of Mikhailov and Hess [7]. The reaction can be described as

$$S+E\rightarrow ES\rightarrow P, \quad [P]\rightarrow 0,$$

where the binding of substrate S by enzyme E is allosterically activated by product P, and P will die as time passes by with a certain probability. Since in most cases E is much heavier than P, we assume that E is sitting steadily in the vertices of a network, while P is moving along the edges. We also assumed that there are more than enough S, so we need not consider S in our simulations.

As in the report of Mikhailov and Hess [7], we use the integer phase variable Φ and discrete time to describe the process of the reaction. Φ stands for the states of an enzyme in a reaction cycle. It takes values between 0 and S_0. Here $\Phi=0$ is the rest state. The reaction starts at $\Phi=1$ and proceeds as Φ increases. At $\Phi=S_1$ a P is produced, so that $1\leqslant\Phi\leqslant S_1$ is the reacting state. After the production of P, the enzyme enters into recovery states, $S_1<\Phi\leqslant S_0$. When Φ attains the value of S_0, the enzyme goes back to the rest state $\Phi=0$, and a reaction cycle is completed.

We divide time into units, each unit of time being Δt. We assume that the transition from $\Phi=0$ to $\Phi=1$ can occur only at discrete time moments $t_n=n\Delta t$, $n=1,2,3,\ldots$. In each unit of time, each P, which is moving randomly along the edges of the network, will visit n_d vertices. If it meets an E that is staying on state $\Phi=0$, the E will convert from state $\Phi=0$ to $\Phi=1$ with probability P_r. If it meets an E that is staying on a state other than $\Phi=0$, the P will go on to the next vertex, which is chosen randomly from the vertices that are linked directly to this vertex. This process will go on until the P has meet n_d vertices. In the meantime, other enzymes which are at rest and not meet a P will remain at the rest state, and those enzymes which are not staying at rest state will convert from state Φ to state $\Phi+1$. When an E reaches the state $\Phi=S_1$, a P will be released. If Φ reaches S_0, the E will return to state $\Phi=0$. The corresponding mathematical formula is the following:

$$\Phi(n+1)=\begin{cases}\Phi(n)+1 & \text{if } 0<\Phi(n)<S_0-1,\\ 0 & \text{if } \Phi(n)=S_0-1,\\ 1 & \text{with probability } P_r, \text{ if } \Phi(n)=0 \text{ and there is a } P,\\ 0 & \text{with probability } 1-P_r, \text{ if } \Phi(n)=0 \text{ and there is a } P,\\ 0 & \text{if } \Phi(n)=0 \text{ and there is no } P.\end{cases} \tag{1}$$

In every unit time, a P will die with a certain probability P_d. Here P_d is chosen to be big enough to assure that the average life span of P is much shorter than the period of a reaction cycle. Thus the total number of P at time $n+1$ can be calculated as

$$N_P(n+1)=N_P(n)+\sum_{i=1}^{N}\Delta(\Phi_i(n)-S_1)-k_d, \tag{2}$$

in which

$$\Delta(x)=\begin{cases}0 & \text{if } x\neq 0,\\ 1 & \text{if } x=0,\end{cases}$$

where N_P is the number of P, and k_d is the number of P which die in this unit time.

Our networks are based on the model developed by Watts and Strogatz [9]. To make it clear, we give a brief summary here. We start from a ring lattice with N vertices and K edges per vertex which are linked to the nearest K vertices. The topology of this network is obviously regular. We randomly chose $X\times N\times K/2$ $(0\leqslant X\leqslant 1)$ edges from the network and rewired them randomly. When X is 0, there will never be any edge which is rewired, so that the network is totally regular. When X is 1, all the edges will be randomly rewired, so the network is totally random. If X stands between 0 and 1, it is a small-world network. By tuning X, we can set up different networks with different connection topologies which can change from completely regular to completely random. As Watts and Strogatz reported [9], the average distance between vertices (L) drops very rapidly as X increases, as shown in Fig. 1.

In our simulation, the total number of vertex is 4096 ($N=4096$), and each vertex has 16 edges on average ($K=16$). On every vertex there is an enzyme E. A reaction

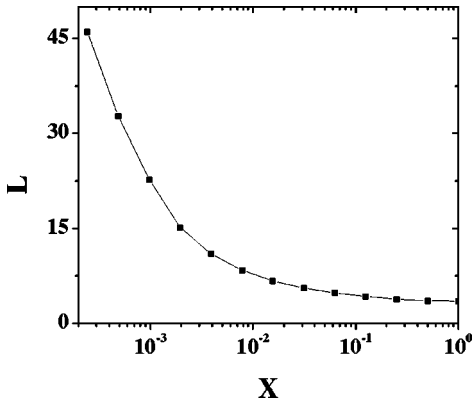

FIG. 1. The average distance L of networks as a function of randomness X in the small-world network model.

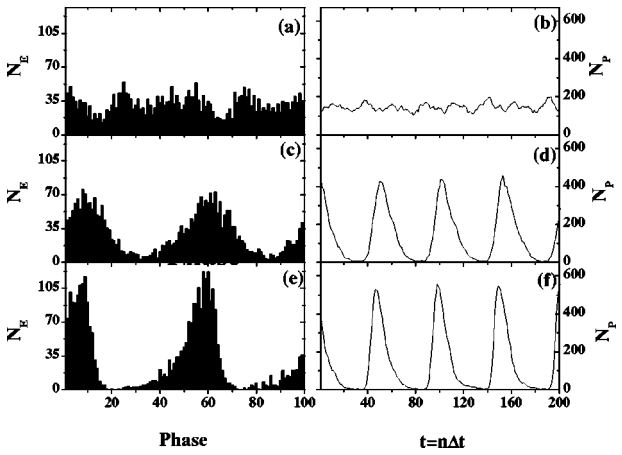

FIG. 2. The histogram of phase distribution of enzyme E at a fixed time [(a),(c),(e)] and the concentration of product P as a function of time [(b),(d),(f)]. (a) and (b) a regular network, $X=0$; (c) and (d) a small-world network, $X=0.0122$; (e) and (f) a random network, $X=1$. The other parameters were fixed: $n_d=5$, $P_r=0.4248$, and $P_d=0.2441$.

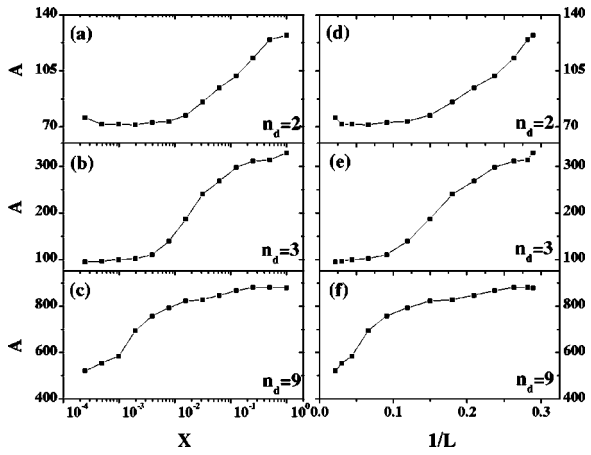

FIG. 3. The changes of amplitude A as a function of randomness of network X [(a)–(c)] and as a function of the inverse of the network distance $1/L$ [(d)–(e)] for different transportation rates n_d of product P. Other parameters were fixed: $P_r=0.4248$ and $P_d=0.2441$.

cycle takes 100 unit of time ($S_0=100$) and a P is released in half of a cycle ($S_1=50$). At the beginning, there are 300 P randomly distributed in the network, and all the E stay at the rest ($\Phi=0$) state.

III. RESULTS

Define $N_E(S)$ as the number of E which are staying at state $\Phi=S$; define N_P as the number of P at a unit time. Figure 2 gives examples of the stochastic and synchronized behavior of the system. The left column of the figure shows the phase distribution of the enzymatic reaction; the right column gives the product population N_P as a function of time. One observes that, with a given diffusion rate ($n_d=5$), there is almost no oscillation in a regular network, as shown in Figs. 2(a) and 2(b), so that the reaction events are uncorrelated or stochastic. As soon as only about 1% of edges ($X=0.01$) are randomly rewired, strong oscillations appear, as shown in Figs. 2(c) and 2(d), so that the reaction events are correlated and synchronized. The amplitude of oscillations increases as the randomness of the network increases. When $X=1$, corresponding to a random network, the amplitude increases to the maximum, as shown in Figs. 2(e) and 2(f). If we change the value of S_1, we can have a different number of peaks in the phase distribution (not shown), as reported by Mikhailov and Hess [7].

In order to study the transition behavior of the system, we define the amplitude of the oscillations A as

$$A=\max\{N_P(\tau)|t\leqslant\tau\leqslant t+S_0\Delta t\}-\min\{N_P(\tau)|t\leqslant\tau\leqslant t+S_0\Delta t\} \quad (3)$$

and plot A as a function of control parameters. Figure 3 shows some transition diagrams of the system. The left column of Fig. 3 gives the amplitude A as a function of randomness of the network X. In these plots, one observes that with a given transport rate n_d, there exists a critical value of $X=X_c$, below which the amplitude of oscillation stays almost constant or increases little as the increase of X, beyond which it increases rapidly. In other words, when X increase, the system undergoes a transition from a stochastic phase where the reaction events are independent to a synchronized phase where reaction events are correlated. The principal cause of the transition is that the distance between two vertices (defined as the least number of edges that constitute a path between the two vertices) decreases dramatically as the randomness of the network X increases, so that communication among molecules becomes much easier. This view can be well verified by the plots of the right column in Fig. 3, which shows the increase of A as a function of $1/L$. One observes that the shapes of the curves between the plots of left and right columns are very similar. In fact, we can define L_c as the critical value of L.

If we compare the three plots of the left (or right) column in Fig. 3, we see that X_c (or $1/L_c$) decreases as the transport rate n_d increases. Defining the transition point as the point at which A increase most rapidly as a function of X or $1/L$, the transition point is $X_c=0.0077$ or $1/L_c=0.12$ for $n_d=2$; they become $X_c=0.0039$ or $1/L_c=0.091$ with $n_d=3$, and decrease to $X_c=9.8\times10^{-4}$ or $1/L_c=0.044$ when n_d increases to 9. This behavior is also understandable in terms of communication among enzyme molecules, since the increase of the transport rate favors the communication. The phenomenon can be observed more clearly in a phase diagram shown in Fig. 4, where n_d and X are the control parameters. The light part of the figure is in a random state and the dark part is in a synchronized state. The thick black line in the figure defines the boundary of the transition between these two states. Figure 4 shows that in order to keep the system in a synchronized state, it needs more random links with a low transport rate; the requirement of randomness of the network becomes less as the increase of the transport rate; when n_d is more than 10, the transition is more or less independent of the randomness of the network.

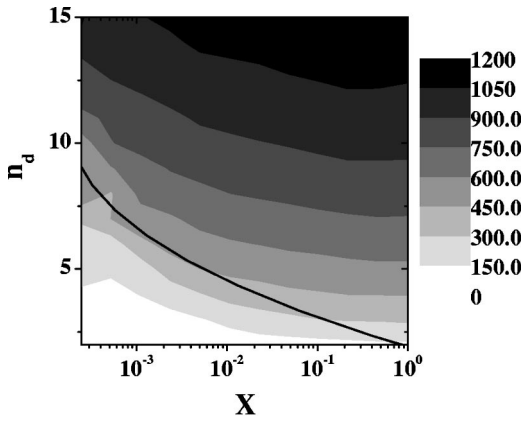

FIG. 4. The phase diagram as a function of n_d and X, with $P_r = 0.4248$ and $P_d = 0.2441$. The grey level of the figure represents the amplitude of oscillations.

IV. DISCUSSION AND CONCLUSION

This self-organization phenomenon can be explained as follows. As described earlier, in the model, each enzyme (E) has its own reaction cycle, so that the reaction of each enzymes is periodic. However, different enzymes will have a random phase in the reaction cycle, so that globally the periodicity will be averaged out. In order to have a self-organization, messengers are needed to spread information of the phases of each E all over the network and to synchronize all these reaction cycles. The product molecule P serves as the role of the messenger. In the model, P has two features. First, it carries the phase information of the E that generates it. Since P has a large decay rate and will die soon after its generation, if we find a P in the network, we can affirm that there must be an E that passed the state S_1 just a little time ago. The second character of P is that it catalyzes the enzymatic reaction. These two features enable P to spread the phase information of E in the network.

However, only these two features do not guarantee synchronizations among enzymes to engender oscillations. Another requirement is needed. The information must be diffused quickly all over the network. Oscillations will not be observed, unless the information-diffusion ability of the network is strong enough. Since the ability to transport information will increase dramatically when we add some randomness to a regular network [9], oscillations will start as soon as one adds a small number of random links to a regular network, as shown in Fig. 2. The amplitude of oscillations will increase rapidly as a function of randomness of network, and attains to a maximum in a random network. In other words, the topology of the network affects the self-organization of the system.

In this model, the diffusion rate must be large enough to ensure P has a large enough possibility to be diffused to any corner of the network before it decays. It is much easier to do so when the transport rate n_d is large. As a result, the oscillation will be less dependent on the topology of the network when n_d is large. This explains the decrease of X_c as n_d increases, as shown in Fig. 4. When n_d is large enough, P can diffuse fast enough even in a regular network, so that the synchronized state is in any of the networks. In this case, there is no phase change, as the increase of X and critical point will stay at $X=0$.

There is also weak oscillations in a regular network, as shown in Figs. 2(a) and 2(b). The amplitude is very small compared with a small-word and a random one. This occurs because the size of the network in the model is not large enough, so that the diffusion of P covers quite a part of the regular network. This makes the information diffusion quasi-global. When the network becomes larger, the oscillation in a regular network will become weaker and finally disappear.

One of the most interesting results of the researches conducted by Mikhailov and Hess [7] may lie in the fact that the size of their tiny reactor is comparable with the size of a biological cell. Since a living biological cell is a natural tiny chemical reactor, this model may be a way to explain self-organization in living cells [12]. But their model has an assumption that all molecules are diffusion randomly in the tiny reactor. This premise cannot be met in living cells. Some researches indicate that the substances in a living body travels along networks. The statement has been proved by various experiments, including the transportation of nutriment among organs and the diffusion of molecules in a single living cell [13]. This makes our model more relevant to a real world. While no further evidence shows that the situation in living cells is similar as our model for simulations, we hope our researches can shed light on the chemical dynamics of living bodies.

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