

# Templating Aggregation

P. L. Krapivsky<sup>1,2</sup> and S. Redner<sup>2</sup>

<sup>1</sup>*Department of Physics, Boston University, Boston, MA 02215, USA*

<sup>2</sup>*Santa Fe Institute, 1399 Hyde Park Road, Santa Fe, NM 87501, USA*

We introduce an aggregation process based on *templating*, where a specified number of constituent clusters must assemble on a larger aggregate, which serves as a scaffold, for a reaction to occur. A simple example is a dimer scaffold, upon which two monomers meet and create another dimer, while dimers and larger aggregates undergo irreversible aggregation with mass-independent rates. In the mean-field approximation, templating aggregation has unusual kinetics in which the cluster and monomer densities,  $c(t)$  and  $m(t)$  respectively, decay with time as  $c \sim m^2 \sim t^{-2/3}$ . These starkly contrast to the corresponding behaviors in conventional aggregation,  $c \sim \sqrt{m} \sim t^{-1}$ . We then treat three natural extensions of templating: (a) the reaction in which  $L$  monomers meet and react on an  $L$ -mer scaffold to create two  $L$ -mers, (b) multistage scaffold reactions, and (c) templated ligation, in which clusters of all masses serve as scaffolds and binary aggregation is absent.

## I. INTRODUCTION

Irreversible aggregation is a fundamental kinetic process in which two clusters from a heterogeneous population irreversibly merge to form a larger cluster. We may represent the reaction as

$$C_i \oplus C_j \xrightarrow{K_{i,j}} C_{i+j}, \quad (1)$$

where  $C_i$  denotes a cluster of mass  $i$  and  $K_{i,j}$  specifies the rate at which a cluster of mass  $i$  (an  $i$ -mer) joins to a  $j$ -mer to form an  $(i+j)$ -mer. The basic observable in aggregation is the cluster-mass distribution, whose properties depend on the functional form of the reaction kernel  $K_{i,j}$ . In the mean-field approximation in which all reactants are perfectly mixed, the time dependence of the cluster-mass distribution is described by an infinite set of rate equations that accounts for the change in the cluster concentrations due to reactions with other clusters.

The emergence of complex molecules from prebiotic building blocks is a key aspect in theories of the origin of life [1–8]. Aggregation processes that generate growing (and hence more complex) clusters provide a convenient starting point for theoretical analyses. Pure aggregation is too minimal a process, and one would like to enrich the reaction scheme (1) by additional processes that contribute to the emergence of complex entities. In this work, we investigate an aggregation process that is augmented by the mechanism of *templating*. Here a cluster of a specified mass  $s$  serves as a scaffold that facilitates the reaction (Fig. 1). On this scaffold, two clusters of masses  $t < s$  and  $s - t$  meet and merge to form another cluster of mass  $s$ . Clusters of mass  $s$  can continue to serve as scaffolds for subsequent reactions or they can participate in binary aggregation. The templating reaction can be viewed as the autocatalytic replication of scaffolds, a reaction step that seems to be an essential feature in various origin of life models [9–14]; this is the underlying motivation for our model.

Our goal is to determine the kinetics of this template-controlled aggregation. We first treat a simple version of templating aggregation in which the scaffolds are dimers

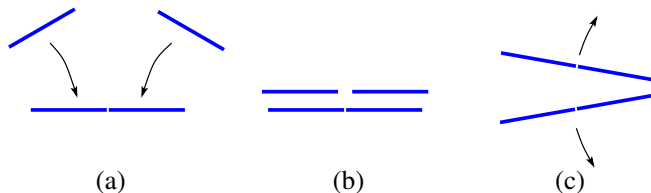
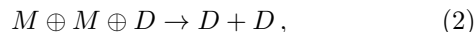


FIG. 1. The steps in templating aggregation on a dimer scaffold: (a) two monomers simultaneously meet on the scaffold and (b) form a second dimer, so that (c) two dimers result.

and all reaction rates are mass independent. When two monomers meet on a dimer, the latter serves as a scaffold, and the monomers merge to create another dimer. Symbolically, this template-controlled merging of dimers is represented by the reaction scheme



where  $M$  denotes a monomer and  $D$  denotes a dimer. Clusters of masses greater than or equal to 2 (the dimer mass), undergo conventional binary aggregation. Thus, the overall reaction is comprised of 2-body and 3-body processes. This mixture of different reaction orders underlies the unusual kinetics of our model.

For binary aggregation with mass independent reaction rates and the monomer-only initial condition, the density of clusters of mass  $k$  at time  $t$ ,  $c_k(t)$ , is given by [15–19]

$$c_k(t) = \frac{1}{(1+t)^2} \left( \frac{t}{1+t} \right)^{k-1} \xrightarrow{t \rightarrow \infty} \frac{1}{t^2} e^{-k/t}.$$

From this solution, the monomer density  $c_1(t)$  and the total cluster density,  $c(t) \equiv \sum_{k \geq 1} c_k(t)$  both decay algebraically with time:

$$c_1 \simeq \frac{1}{t^2}, \quad c \simeq \frac{1}{t}. \quad (3)$$

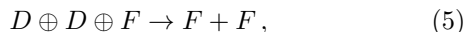
These decay laws are independent of the initial condition and hence universal. For templating aggregation with scaffold mass  $s = 2$ , it is convenient to denote the

monomer density as  $m(t)$  and the density of clusters of mass  $2k$  as  $c_k(t)$ . In contrast to (3), here we find

$$m \simeq \frac{2}{(3t)^{1/3}}, \quad c_1 \simeq \frac{1}{2(3t)^{2/3}}, \quad c \simeq \frac{1}{(3t)^{2/3}}. \quad (4)$$

Surprisingly, the monomer density decays slower than the cluster density, while the opposite occurs in conventional aggregation. Another unusual feature of templating aggregation is that the decay exponents for dimers and the total cluster density are the same.

In Sec. II, we analyze the template-controlled aggregation with dimer scaffolds and derive the decay laws (4), as well as the decay law for  $c_k(t)$ , the density of clusters of mass  $2k$ . In Sec. III, we study more general models of template-controlled aggregation. First, we consider the model with scaffolds of fixed mass  $L$  for arbitrary  $L \geq 2$ . Then we analyze the effect of multiple levels of templating. Specifically, we treat a model with two types of templates, dimers and 4-mers, and the template-controlled reaction in (2) is supplemented by the reaction



where  $F$  represents 4-mers. Under the assumption that clusters of mass 4 and greater undergo ordinary aggregation, we find kinetic behaviors similar to that quoted in Eq. (4). Finally, in Sec. IV, we study templated ligation, in which clusters of all masses serve as scaffolds and in which no binary aggregation reactions occur. In distinction to the reactions where the scaffolds have a specified mass, we now find that the cluster density is the most slowly decaying quantity at long times, with  $c \sim t^{-1/3}$ , while the monomer density asymptotically decays  $c_1 \sim t^{-2/3}$ .

## II. TEMPLATING WITH DIMER SCAFFOLDS

Under the assumption that clusters are perfectly mixed and that the reaction rates are mass-independent, the rate equations for the monomer and dimer densities are

$$\begin{aligned} \frac{dm}{dt} &= -m^2 c_1, \\ \frac{dc_1}{dt} &= \frac{1}{2} m^2 c_1 - 2c c_1, \end{aligned} \quad (6)$$

while the densities of heavier clusters satisfy

$$\frac{dc_k}{dt} = \sum_{i+j=k} c_i c_j - 2c c_k \quad (k \geq 2). \quad (7)$$

The first of Eqs. (6) accounts for the decay of monomers when two monomers meet on a scaffold to create a dimer. Dimer creation is encapsulated by the first term on the right of the second of Eqs. (6). Equations (7) account for the conventional aggregation reactions of

heavier-mass clusters. A useful check of the consistency of Eqs. (6)–(7) is to verify that the mass density

$$m + 2 \sum_{k \geq 1} k c_k$$

is conserved. For templating aggregation, we must additionally postulate that both  $m(0) > 0$  and  $c_1(0) > 0$ . This condition ensures that scaffolds are always present to catalyze continuous evolution of the cluster mass distribution.

To determine the asymptotic behavior of templating aggregation, we begin by adding the second of Eqs. (6) and all Eqs. (7) to give

$$\frac{dc}{dt} = \frac{1}{2} m^2 c_1 - c^2, \quad (8)$$

where  $c \equiv \sum_{k \geq 1} c_k$  is the total cluster density. The first two of Eqs. (6) and Eq. (8) constitute a closed system of three differential equations whose solution would determine the resulting kinetics.

The form of the equation for the monomer density suggests introducing the modified time variable

$$\tau = \int_0^t dt' c_1(t'), \quad (9)$$

to recast the rate equation for the monomer density into  $\frac{dm}{d\tau} = -m^2$ , with solution

$$m(\tau) = \frac{m(0)}{1 + m(0)\tau}. \quad (10)$$

Since the long-time asymptotic behavior is  $m \simeq \tau^{-1}$ , independent of  $m(0)$ , we adopt the simple initial condition  $m(0) = 1$  for simplicity henceforth.

Using the time modified time variable (9), as well as the solution (10), we rewrite the equation for the dimer and cluster concentrations as (8) as

$$\begin{aligned} \frac{dc_1}{d\tau} &= \frac{1}{2(1+\tau)^2} - 2c, \\ \frac{dc}{d\tau} &= \frac{1}{2(1+\tau)^2} - \frac{c^2}{c_1}. \end{aligned} \quad (11)$$

Without loss of generality, we choose the initial condition  $c_1(0) = c(0) = \rho$ . While the full initial-value problem (11) subject to this initial condition appears to be intractable, we can deduce the physically relevant long-time behavior by the method of dominant balance [20], in which we neglect one of the three terms in each of Eqs. (11) and check that the assumption is self-consistent.

By this approach, we deduce that in both Eqs. (11), the right-hand side (RHS) dominates the left-hand side (LHS). Neglecting the LHS in Eqs. (11), we find

$$c \simeq \frac{1}{4(1+\tau)^2}, \quad c_1 \simeq \frac{1}{8(1+\tau)^2}. \quad (12)$$

as  $\tau \rightarrow \infty$ . A more detailed but straightforward asymptotic analysis of Eqs. (11) gives the more complete long-time behavior

$$\begin{aligned} c_1 &= \frac{1}{8(1+\tau)^2} - \frac{1}{16(1+\tau)^4} - \frac{1}{16(1+\tau)^5}, \\ c &= \frac{1}{4(1+\tau)^2} + \frac{1}{8(1+\tau)^3} - \frac{1}{8(1+\tau)^5}, \end{aligned} \quad (13)$$

where we drop terms of  $O(\tau^{-6})$  and lower. All algebraic correction terms are universal, i.e., independent of the initial conditions. Only terms that are exponentially small in the  $\tau \rightarrow \infty$  limit depend on the initial condition.

To find the dependence of the cluster densities on the physical time, we substitute  $c_1$  from (12) in the definition of the modified time (9) and invert this relation to give

$$t = \int_0^\tau \frac{d\tau'}{c_1(\tau')} \simeq 8 \int_0^\tau d\tau' (1+\tau')^2 \simeq \frac{8}{3} \tau^3. \quad (14)$$

If we employ the more accurate asymptotic formula in (13) for  $c_1(\tau)$ , we instead obtain the expansion

$$t = \frac{8}{3} \tau^3 + 8\tau^2 + \frac{11}{6} \tau + O(1), \quad (15)$$

with three exact terms. The last term, a constant, cannot be determined analytically since it depends on the initial condition. Limiting ourselves to the leading asymptotic behavior, we substitute  $\tau \simeq (3t/8)^{1/3}$  into (10) and (12) to arrive at the central results given in Eq. (4).

Figure 2 shows the time dependence of  $m(t)$ ,  $c(t)$  and  $c_1(t)$  obtained by numerical integration of the first two of Eqs. (6) and Eq. (8) by Mathematica. As the initial condition we use  $m(0) = 1$  and  $c_1(0) = c(0) = 0.1$ .

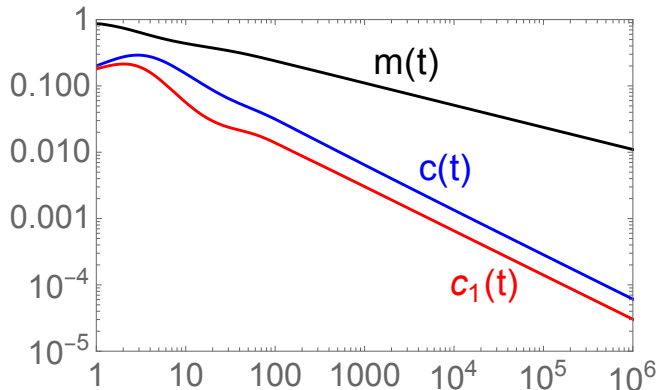


FIG. 2. Time dependence of  $m(t)$ ,  $c(t)$ , and  $c_1(t)$  on a double logarithmic scale, with asymptotic decay of  $t^{-1/3}$  for  $m(t)$  and  $t^{-2/3}$  for both  $c(t)$  and  $c_1(t)$ , as predicted by Eq. (4). The ratio  $c(t)/c_1(t)$  quickly approaches 2 for increasing time, as predicted by (12).

Having found the dimer concentration  $c_1(t)$ , we now outline how to obtain all the cluster densities. Based on the form of the rate equation for  $c_k(t)$  for  $k \geq 2$ , we

anticipate that  $c_k = A_k c$ ; that is, all individual cluster densities are of the same order as the total cluster density. Substituting this ansatz into the last of Eqs. (6) we obtain the following recursion for the amplitudes:

$$\sum_{i+j=k} A_i A_j = 2A_k \quad k \geq 2. \quad (16)$$

The already known value  $A_1 = \frac{1}{2}$  plays the role of the initial condition for this recursion. Solving (16) subject to this initial condition gives

$$\frac{c_k}{c} = \frac{1}{\sqrt{4\pi}} \frac{\Gamma(k - \frac{1}{2})}{\Gamma(k + 1)} \simeq \frac{1}{\sqrt{4\pi}} \frac{1}{k^{3/2}}, \quad (17)$$

where the last asymptotic is valid when  $k \gg 1$  and generally (17) holds in the  $t \rightarrow \infty$  limit.

The large- $k$  asymptotic,  $A_k \sim k^{-3/2}$ , holds only up to a cutoff value  $k^*$ , beyond which the  $A_k$  must decay faster than any power law. To understand the origin of this cutoff, we note that the sum  $\sum_{k \geq 1} k A_k$  diverges if  $A_k \sim k^{-3/2}$  for all  $k$ . This divergence contradicts the mass conservation statement that  $\sum_{k \geq 1} k c_k \rightarrow \text{const}$ . To resolve this apparent divergence, the power-law behavior of  $A_k$  must break down beyond a cutoff value  $k^*$ . To determine  $k^*$ , we compute

$$\sum_{k \geq 1} k c_k \sim c \sum_{1 \leq k \leq k^*} k \times k^{-3/2} \sim c \sqrt{k^*}.$$

Since both sums are constant, we see that the threshold mass is given by  $k^* \sim c^{-2} \sim \tau^4 \sim t^{4/3}$ . Thus the power-law mass distribution is cut off at  $k^*$  to ensure mass conservation. This cutoff is analogous to what happens in constant-kernel aggregation with a steady monomer source [19]. In this latter example, the cutoff is determined by the condition that the total mass in the system equals to the total mass that is injected up to a given time.

### III. MORE GENERAL TEMPLATING REACTIONS

There are two natural generalizations of templating aggregation that we now explore. One generalization is to consider scaffolds that are heavier than dimers, and another to analyze what happens when there are multiple stages of scaffold reactions.

#### A. Templating with scaffolds of mass $L$

Suppose the scaffold has mass  $L$  and the simultaneous presence of  $L$  monomers on the scaffold is required to create a second  $L$ -mer. Aggregates of mass  $L$  and heavier also undergo conventional aggregation. We assume that the process begins with monomers and scaffolds. By

construction, the masses of heavier aggregates are integer multiples of  $L$ .

We can determine the kinetics of this model by adapting the analysis of the previous section in a straightforward way. In what follows  $c_k$  now denotes the concentration of clusters of mass  $kL$ . Within this model, the first two of Eqs. (6) and Eq. (8) become

$$\begin{aligned}\frac{dm}{dt} &= -m^L c_1, \\ \frac{dc_1}{dt} &= \frac{1}{L} m^L c_1 - 2cc_1, \\ \frac{dc}{dt} &= \frac{1}{L} m^L c_1 - c^2.\end{aligned}\quad (18)$$

In terms of the modified time variable defined in (9), the solution for the monomer density for the initial condition  $m(0) = 1$  now is

$$m(\tau) = \frac{1}{[1 + (L-1)\tau]^{1/(L-1)}}. \quad (19)$$

Using this solution for the monomer density and also employing the same dominant balance method as in the previous section, we obtain

$$\begin{aligned}c &\simeq \frac{1}{2L} \frac{1}{[1 + (L-1)\tau]^{L/(L-1)}}, \\ c_1 &\simeq \frac{1}{4L} \frac{1}{[1 + (L-1)\tau]^{L/(L-1)}}.\end{aligned}\quad (20)$$

We now express these two densities in terms of the physical time:

$$t = \int \frac{d\tau'}{c_1(\tau')} \simeq \frac{4L}{2L-1} [1 + (L-1)\tau]^{(2L-1)/(L-1)}. \quad (21)$$

Combining (19) and (20) with (21), we thereby find the densities of monomers,  $L$ -mers, and the total cluster density decay as

$$\begin{aligned}m(t) &\simeq \left(\frac{2L-1}{4L} t\right)^{-1/(2L-1)}, \\ c(t) &\simeq \frac{1}{2L} \left(\frac{2L-1}{4L} t\right)^{-L/(2L-1)}, \\ c_1(t) &\simeq \frac{1}{4L} \left(\frac{2L-1}{4L} t\right)^{-L/2L-1}.\end{aligned}\quad (22)$$

As one might expect, the overall reaction kinetics slows down as the scaffold size and consequently the reaction order  $L$  increases. The ratios  $c_k/c$  are again stationary in the long-time limit and are given by the same formula (17) as for  $L = 2$ . Stationarity again holds up to a threshold mass  $k^*$  that grows as  $k^* \sim c^{-2} \sim t^{2L/(2L-1)}$ .

## B. Multiple levels of templating

Another natural scenario is a reaction that relies on multiple levels of templating. Here we treat the simplest case of two levels of templating in which: (a) a new dimer template is created when two monomers react on an existing dimer template, and (b) a new 4-mer template is created when two dimers react on an existing 4-mer template (Fig. 3). In this formulation, dimers are not free to aggregate; only clusters of mass 4 and greater can react via conventional aggregation.

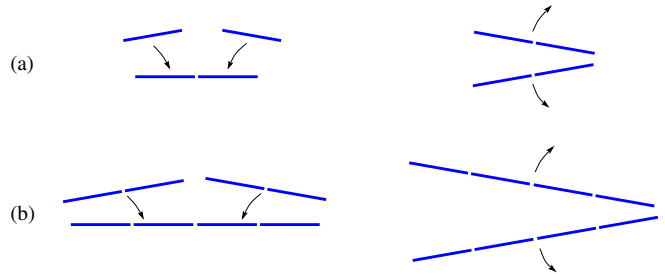


FIG. 3. Templating aggregation with two levels of templating: (a) two monomers react on a dimer scaffold, (b) two dimers react on a 4-mer scaffold.

Let  $m(t)$  and  $D(t)$  denote the density of monomers and dimers, respectively, and let  $c_k$  with  $k \geq 1$  now denote the density of clusters of mass  $4k$ . In close analogy with Eqs. (6), the rate equations for the various cluster densities now are:

$$\begin{aligned}\frac{dm}{dt} &= -m^2 D, \\ \frac{dD}{dt} &= \frac{1}{2} m^2 D - D^2 c_1, \\ \frac{dc_1}{dt} &= \frac{1}{2} D^2 c_1 - 2cc_1,\end{aligned}\quad (23)$$

while the densities of heavier clusters satisfy Eqs. (7). Summing the last of Eqs. (23) and all of Eqs. (7) we deduce the evolution equation for the total cluster density

$$\frac{dc}{dt} = \frac{1}{2} D^2 c_1 - c^2. \quad (24)$$

Equations (23) and (24) again constitute a closed system from which we can, in principle, determine the kinetic behavior. However, these coupled nonlinear equations do not possess an exact solution. Instead, we again use the method of dominant balance to infer the asymptotic behavior. We first neglect the LHS in the last of Eqs. (23) to give  $c \simeq D^2/4$ . We substitute this result into (24), where we also neglect the LHS to find  $c_1 \simeq D^2/8$ . Thus

$$c \simeq \frac{1}{4} D^2, \quad c_1 \simeq \frac{1}{8} D^2. \quad (25)$$

There are various choices of which terms to neglect in Eqs. (23), and the dominant balance that proves consistent is to keep the LHS in the second of Eqs. (23). Since

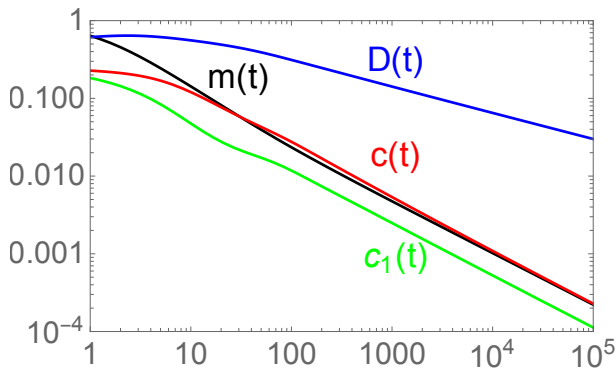


FIG. 4. Time dependence of  $m(t)$ ,  $D(t)$ ,  $c(t)$ , and  $c_1(t)$  on a double logarithmic scale, with asymptotic decay of  $t^{-1/3}$  for  $D(t)$  and  $t^{-2/3}$  for  $m(t)$ ,  $c(t)$ , and  $c_1(t)$ .

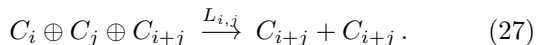
this term is negative, the simplest choice now is to neglect the first term on the RHS of this equation. We thus have  $\frac{dD}{dt} = -D^4/8$ . Solving this equation and substituting this solution into (25) and also into the first of Eqs. (23) and solving these two equations we finally obtain

$$m \simeq c \simeq 2c_1 \simeq (3t)^{-2/3}, \quad D \simeq 2(3t)^{-1/3}. \quad (26)$$

The decay laws for  $c$  and  $c_1$  are the same as in the templating with dimer scaffolds, and even the amplitudes are identical [cf. (4)]. The density of monomers decays similarly to  $c$  and  $c_1$ , and only the dimer density has the slowest decay of  $t^{-1/3}$ . We used Mathematica to numerically integrate Eqs. (23) and (24) and the results are shown in Fig. 4. The asymptotic behaviors are in excellent agreement with the theoretical predictions (26).

#### IV. TEMPLATED LIGATION

We now investigate a self-templating reaction in which clusters of all masses can serve as scaffolds. This templated ligation process [9, 10, 14, 21, 22] is represented by the reaction scheme



We assume that this ligation reaction is the only dynamical process in the system. In particular, binary aggregation of clusters does not occur in this model. The absence of aggregation reactions means that an initially compact mass distribution with a maximum mass  $J$  remains compact forever; that is,  $c_j(t) = 0$  for all  $j > J$ . However, for unbounded initial mass distributions that decay sufficiently rapidly with mass, the emergent behaviors are universal, that is, asymptotically independent of the initial condition. One such example is the exponential initial mass distribution  $c_j(0) = 2^{-j-1}$  whose mass density is normalized to 1:

$$\sum_{j \geq 1} c_j(t) = 1 \quad (28)$$

If the ligation rates  $L_{i,j}$  are mass independent, the equations for the evolution of the cluster-mass distribution are

$$\frac{dc_k}{dt} = c_k \sum_{i+j=k} c_i c_j - 2c_k \sum_{j \geq 1} c_j c_{j+k}. \quad (29)$$

These equations are hierarchical and therefore appear to be unsolvable. A mathematically related non-recurrent structure arises in the rate equations for cluster eating [23] and for combined aggregation-annihilation reactions [24], albeit these problems are more tractable since reactions are binary. We also notice that in templated ligation, the total cluster density,  $c = \sum_{k \geq 1} c_k$ , and the monomer density  $c_1$  satisfy

$$\frac{dc}{dt} = - \sum_{i,j \geq 1} c_i c_j c_{i+j}, \quad (30a)$$

$$\frac{dc_1}{dt} = -2c_1 \sum_{j \geq 1} c_j c_{j+1}. \quad (30b)$$

and these cannot be solved recursively. In contrast, in aggregation with mass-independent reaction rates, the analogous equations  $\frac{dc}{dt} = -c^2$ ,  $\frac{dc_1}{dt} = -2cc_1$ , are closed and readily solvable.

Nevertheless, we can extract the essential long-time behavior from Eqs. (29) by invoking scaling. Similarly to aggregation [25, 26] (see also [18, 19] for reviews), one expects that the mass distribution approaches the scaling form

$$c_k(t) = c^2 \Phi(kc) \quad (31)$$

in the scaling limit  $t \rightarrow \infty$ ,  $k \rightarrow \infty$ , with  $kc = \text{finite}$ .

The mass conservation statement (28) and the definition of the cluster density then lead to the integral constraints

$$\int_0^\infty dx x \Phi(x) = 1, \quad \int_0^\infty dx \Phi(x) = 1. \quad (32)$$

Here we have replaced the summations by integrations, which is appropriate in the long-time limit where scaling is valid.

Substituting the scaling ansatz (31) into (30a), the time dependence of the total cluster density is given by

$$\frac{dc}{dt} = -Bc^4, \quad (33a)$$

with

$$B = \int_0^\infty dx \int_0^\infty dy \Phi(x) \Phi(y) \Phi(x+y). \quad (33b)$$

Solving the first of these equations gives the time dependence of the cluster density

$$c \simeq (3Bt)^{-1/3}. \quad (34)$$

Using (34) and the scaling form (31) we conclude that the density of monomers is then

$$c_1 \simeq \Phi(0)(3Bt)^{-2/3}. \quad (35)$$

We can obtain an alternative expression for the amplitude  $B$  from the integral of the scaled mass distribution that is simpler than the the double integral in Eq. (33b). Assuming  $\Phi(0) > 0$  and substituting (35) into (30b) we obtain

$$B = \int_0^\infty dy \Phi^2(y). \quad (36)$$

To obtain the scaling function itself, we substitute the scaling form (31) into the governing equations (29) and find that the scaling function  $\Phi(x)$  obeys the non-linear integro-differential equation

$$B \left[ 2\Phi(x) + x \frac{d\Phi(x)}{dx} \right] = 2\Phi \int_0^\infty dz \Phi(z)\Phi(z+x) - \Phi \int_0^x dy \Phi(y)\Phi(x-y). \quad (37)$$

Notice that integrating (37) over all  $x$ , we recover (33b). In the limit  $x \rightarrow 0$ , Eq. (37) reduces to (36). These relations serve as useful consistency checks.

The time dependence given in Eq. (34) together with the equation (37) for  $\Phi$  constitutes a formal solution cluster-mass distribution for the ligation reaction. While the explicit solution of (37) is likely not possible, we have found, in a direct way, the time dependence of the cluster densities.

## V. SUMMARY AND DISCUSSION

We introduced an aggregation model that is driven by templating. Here an aggregate of a specified mass acts as a scaffold upon which smaller clusters meet and merge to create a cluster that also can act as a scaffold. Clusters whose mass is either larger than or equal to the scaffold mass also undergo conventional aggregation. Within the mean-field description and also under the assumption that the all reaction rates are mass independent, we solved for the kinetics of the cluster mass distribution.

One basic result for this type of templating-controlled aggregation is that the ensuing kinetics is much slower than in conventional aggregation. For the simple case where the scaffold is a mass-2 dimer and two monomers must meet on this scaffold to create another dimer, we found that the monomer density decays with time as  $t^{-1/3}$ , while the densities of clusters of mass 2 or greater, as well as the total cluster density, all decay as  $t^{-2/3}$ . Therefore the decay of the monomer density is *slower* than that of the cluster density. In conventional aggregation, the density of clusters of any mass decays as  $t^{-2}$ , while the total cluster density decays as  $t^{-1}$ . Thus the monomer density decays *faster* than the cluster density.

To summarize, the relation between the monomer and cluster densities is  $m \sim c^2$  in ordinary aggregation and  $m \sim \sqrt{c}$  in templating aggregation.

The templating reaction is three-body in nature, and this feature is the underlying reason for the much slower kinetics compared to conventional aggregation. Intriguingly, the relative cluster densities  $c_k/c$  in templating aggregation, Eqs. (17), are the same as in ordinary aggregation driven by the source of small mass clusters [18, 19]. This property is the chief qualitative difference with ordinary aggregation where the mass distribution approaches a scaling form in the long time limit.

We extended our model to a scaffold of arbitrary mass  $L$ , upon which  $L$  monomers meet and react to create another  $L$ -scaffold. Another natural extension that we studied is to allow multiple levels of templating. For a two-stage templating reaction in which dimers and 4-mers act as scaffolds to promote the reaction, we observed similar behavior as in single-stage templating in which nearly all cluster densities decay as  $t^{-2/3}$ . In this two-stage reaction, it is only the dimer density that now decays as  $t^{-1/3}$ .

We also introduced and investigated a templated ligation reaction, where clusters of all masses serve as scaffolds, and there is no free aggregation. The ensuing kinetics is much slower than in templating aggregation. Namely, the total cluster density decays as  $t^{-1/3}$ , while individual cluster densities decay as  $t^{-2/3}$ . In contrast to templating aggregation, the mass distribution in templated ligation approaches a scaling form. However, even with mass-independent ligation rates, templated ligation is theoretically more challenging than templating aggregation. We were able to only determine the time dependence of basic observables, but the amplitudes of these decay laws and the precise form of the scaled mass distribution remain unknown.

At a theoretical level, templating-driven aggregation can be viewed as a form of conventional binary aggregation, but with a non-trivial time dependent source of scaffolds (either dimer or dimer and 4-mer) that serve as the input to the aggregation process. It is remarkable that the non-trivial and slow time dependence of these small elemental clusters modifies the densities of all heavier clusters so that the overall aggregation reaction also has a slow time dependence compared to conventional aggregation. From the perspective of applications, there are many situations where the notion of templating plays a major role of many types of reactions. In addition to the applications for models of the origin of life mentioned in the introduction [1–14], other applications include, for example, self assembly of colloids [27], synthesis of exotic materials [28–30], and protein aggregation [31]. Perhaps our simple modeling can provide a starting point for understanding these types of template-controlled reactions.

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