Templating aggregation

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We introduce an aggregation process that is based on *templating*, where a specified number of constituent clusters must assemble on a larger *scaffold* aggregate 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 clusters irreversibly join at mass-independent rates. In the mean-field approximation, templating aggregation has unusual kinetics in which the monomer density $m(t)$ and the density $c(t)$ of all clusters heavier than monomers decay with time as $c \sim m^2 \sim t^{-2/3}$. These strongly contrast with the corresponding behaviors in conventional aggregation, where $c \sim m^{1/2} \sim t^{-1}$. We also 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 does not occur.

I. INTRODUCTION

Irreversible aggregation is a fundamental kinetic process in which two clusters from a heterogeneous population irreversibly merge to form a larger cluster. Symbolically, irreversible aggregation is represented by the reaction scheme

$$C_i \oplus C_j \xrightarrow{K_{i,j}} C_{i+j}, \quad (1)$$
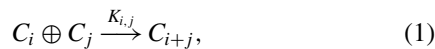
where C_i denotes a cluster of mass i and $K_{i,j}$ specifies the rate at which a cluster of mass i (an i-mer) joins to a j-mer to form an $(i + j)$-mer. The basic observable in aggregation is the cluster-mass distribution, whose properties depend on the functional form of the reaction kernel $K_{i,j}$. 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, however, 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*. In the simplest realization of templating aggregation, clusters of a specified mass s serve as scaffolds that facilitate the reaction (Fig. 1). On this scaffold, two clusters of masses $k < s$ and $s − k$ meet and merge to form another cluster of mass s. Newly created clusters of mass s can then 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. Autocatalysis is a reaction step that seems to be an essential feature in various models of the origin of

life [9–14], and our model may provide some insights about the kinetics of autocatalysis. We also treat simple extensions of our model to multistage scaffold reactions and templated ligation (a self-templating reaction in which clusters of any mass can serve as scaffolds). Similar models might be relevant to the autocatalytic formation, or self-assembly, of larger structures in physical chemistry [15–17].

Our goal is to determine the kinetics of this template-controlled aggregation. We first treat a particularly simple version of templating aggregation in which the scaffolds have mass $s = 2$, namely, they are dimers, and all reaction rates are mass independent. When two monomers meet on a dimer, the latter serves as a scaffold to facilitate the merging of the monomers to create another dimer scaffold (Fig. 1). Symbolically, this template-controlled merging of monomers on a dimer scaffold is represented by the reaction scheme

$$M \oplus M \oplus D \to D + D, \quad (2)$$
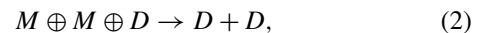
where M denotes a monomer and D denotes a dimer (Fig. 1).

In our modeling, clusters with masses $\geqslant 2$, i.e., dimers and heavier clusters, undergo conventional binary aggregation. The governing equations for this templating aggregation reaction contain contributions from the three-body templating
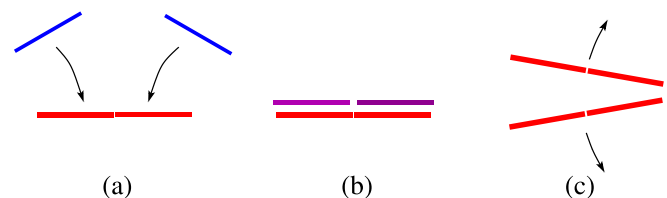

FIG. 1. The steps in templating aggregation on a scaffold of mass $s = 2$ (a dimer): (a) two monomers simultaneously meet on the scaffold and (b) the adsorbed monomers undergo a reaction in the presence of the template to form a second dimer, so that (c) two free dimers result.

reaction and the two-body reactions of conventional aggregation. This mixture of different reaction orders underlies the unusual kinetics of our model. In the templating aggregation with dimer scaffolds, all cluster masses must be even except for monomers, under the assumption that only monomers and dimers are initially present.

For conventional binary aggregation with mass-independent reaction rates and the monomer-only initial condition, the density $c_k(t)$ of clusters of mass k at time t and the total cluster density $c(t)$ are given by [18–22]

$$c_k(t) = \frac{t^{k-1}}{(1+t)^{k+1}}, \quad c(t) = \sum_{k \geqslant 1} c_k(t) = \frac{1}{1+t}. \quad (3)$$

In the long-time limit, the density $c_k(t)$ of clusters of any fixed mass k and the total cluster density $c(t)$ decay algebraically with time:

$$c_k \simeq t^{-2}, \quad c \simeq t^{-1}. \quad (4)$$

These decay laws are independent of the initial condition and hence universal.

For the specific templating aggregation process where only dimers can act as scaffolds, all clusters heavier than monomers necessarily have even masses. The decay laws for the various cluster densities are algebraic in time, as in ordinary aggregation, cf. (4), but the decay exponents differ:

$$c_1 \simeq \frac{2}{(3t)^{1/3}}, \quad c_2 \simeq \frac{1}{2(3t)^{2/3}}, \quad c \simeq \frac{1}{(3t)^{2/3}}, \quad (5)$$

where here $c = \sum_{k \geqslant 2}$ is the density of clusters of mass 2 or greater. An unusual feature of templating aggregation is that the decay exponents for dimers $c_2(t)$ and the cluster density $c(t)$ are the same. In fact, the asymptotic decay of the density of clusters of any fixed mass k has the same time dependence, $c_k \sim t^{-2/3}$. Another surprising feature is that the monomer density $c_1(t)$ exhibits a slower decay in time than the cluster density $c(t)$. There is no contradiction here because the cluster density in templating aggregation does not include monomers.

In Sec. II, we analyze the template-controlled aggregation with dimer scaffolds and derive the decay laws (5), as well as the decay law for $c_k(t)$ for $k > 2$. In Sec. III, we introduce and study more general models of template-controlled aggregation. First, we consider the model with scaffolds of fixed mass L for arbitrary $L \geqslant 2$. 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

$$D \oplus D \oplus F \rightarrow F + F, \quad (6)$$
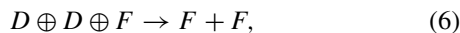
where F represents 4-mers. Under the assumption that clusters of mass 4 and greater undergo ordinary aggregation, we find kinetic behaviors similar to that quoted in Eq. (5). Finally, in Sec. IV, we study templated ligation, in which clusters of all masses serve as scaffolds and in which no binary aggregation 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, $c(t) \sim t^{-1/3}$, while the monomer density exhibits the $t^{-2/3}$ decay.

II. TEMPLATING WITH DIMER SCAFFOLDS

Templating aggregation with dimer scaffolds has nontrivial kinetics only if the densities of monomers and dimers are nonzero at the beginning of the evolution. In the absence of monomers, the process reduces to ordinary aggregation; in the absence of dimers, monomers cannot merge and there is no evolution. The kinetic behavior is particularly clear cut when *only* monomers and dimers are initially present. In this case, the only possible cluster types are monomers and heavier clusters, whose masses must be even.

With 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

$$\frac{dc_1}{dt} = -c_1^2 c_2, \quad (7a)$$

$$\frac{dc_2}{dt} = \frac{1}{2} c_1^2 c_2 - 2c c_2. \quad (7b)$$

Equation (7a) accounts for the decay of monomers when two monomers meet on a scaffold to create a dimer. The first term on the right-hand side of (7b) can be viewed as a time-dependent source of dimers that is driven by the reaction of monomers. Previous work has investigated the influence of a monomer source with an arbitrary time dependence on the aggregation kinetics [23]. Since heavier clusters with masses $k > 2$ undergo conventional aggregation, their densities satisfy

$$\frac{dc_k}{dt} = \sum_{i+j=k} c_i c_j - 2c c_k, \quad (8)$$

with all cluster masses even. A useful check of the consistency of Eqs. (7) and (8) is to verify that the mass density

$$c_1 + \sum_{k \geqslant 2, \, k \, \text{even}} k c_k$$

is conserved.

As stated above, we postulate that initially

$$c_1(0) > 0, \quad c_2(0) > 0, \quad c_k(0) = 0 \quad (k > 2). \quad (9)$$

By construction of the model, dimer scaffolds are always present and they catalyze the continuous creation of new scaffolds, leading to unusual kinetics, as we demonstrate below. The precise values of $c_1(0)$ and $c_2(0)$ affect only early-time behavior. We often set $c_1(0) = 1$ for simplicity and vary only $c_2(0) = c(0) = \rho$.

To determine the asymptotic behavior of templating aggregation, we begin by adding the Eqs. (7b) and (8) to give

$$\frac{dc}{dt} = \frac{1}{2} c_1^2 c_2 - c^2. \quad (10)$$

Equations (7) and (10) constitute a closed system of three coupled nonlinear ordinary differential equations (ODEs) whose solution determines the resulting kinetics.

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

$$\tau = \int_0^t dt' \, c_2(t'), \quad (11)$$

to recast the rate equation (7a) for monomer density into

$$\frac{dc_1}{d\tau} = -c_1^2,$$

with solution

$$c_1(\tau) = \frac{c_1(0)}{1 + c_1(0)\tau}. \tag{12}$$

The leading asymptotic behavior is $c_1 \simeq \tau^{-1}$, independent of $c_1(0)$. Below we show that the dependence of $c_1(t)$ on the original time variable is also asymptotically independent of $c_1(0)$. Therefore we adopt the initial condition $c_1(0) = 1$ so that $c_1(\tau) = 1/(1 + \tau)$.

Using the modified time variable (11), as well as the solution (12), we rewrite the equation for the dimer and cluster concentrations as

$$\frac{dc_2}{d\tau} = \frac{1}{2(1 + \tau)^2} - 2c, \tag{13a}$$

$$\frac{dc}{d\tau} = \frac{1}{2(1 + \tau)^2} - \frac{c^2}{c_2}, \tag{13b}$$

subject to the initial condition $c_2(0) = c(0) = \rho$. The initial-value problem (13) with this initial condition appears to be intractable. Since we are mainly interested in the long-time behavior which is independent of the initial density ρ, we resort to the method of dominant balance [24]. This method relies on neglecting one of the three terms in (13a) and (13b) and selecting the alternative that leads to a consistent solution.

Using this trial and error approach, we deduce that in both equations in (13), the right-hand side (RHS) dominates the left-hand side (LHS). Neglecting the LHS in Eqs. (13), we find

$$c \simeq \frac{1}{4(1 + \tau)^2}, \quad c_2 \simeq \frac{1}{8(1 + \tau)^2}, \tag{14}$$

as $\tau \to \infty$. A more detailed but straightforward asymptotic analysis of Eqs. (13a) and (13b) gives the more complete long-time behavior

$$c = \frac{1}{4(1 + \tau)^2} + \frac{1}{8(1 + \tau)^3} - \frac{1}{8(1 + \tau)^5}, \tag{15a}$$

$$c_2 = \frac{1}{8(1 + \tau)^2} - \frac{1}{16(1 + \tau)^4} - \frac{1}{16(1 + \tau)^5}, \tag{15b}$$

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

To find the dependence of the cluster densities on the physical time, we substitute c_2 from (14) into the definition of the modified time (11) and invert this relation to give

$$t = \int_0^\tau \frac{d\tau'}{c_2(\tau')} \simeq 8 \int_0^\tau d\tau' (1 + \tau')^2 \simeq \frac{8}{3} \tau^3. \tag{16}$$

If we employ the more accurate asymptotic formula in (15) for $c_2(\tau)$, we instead obtain the expansion

$$t = \frac{8}{3} \tau^3 + 8\tau^2 + \frac{11}{6} \tau + O(1), \tag{17}$$

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,
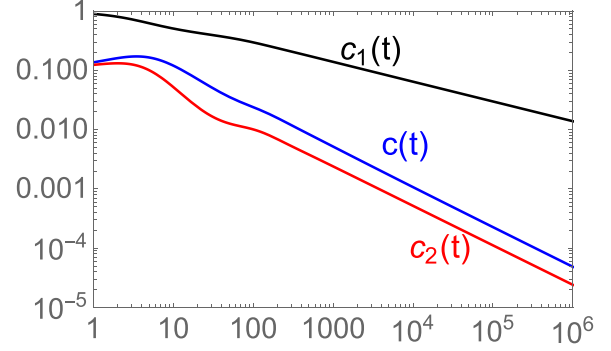

FIG. 2. Time dependences of $c_1(t)$, $c(t)$, and $c_2(t)$ on a double logarithmic scale, with asymptotic decay of $t^{-1/3}$ for $c_1(t)$, and $t^{-2/3}$ for both $c(t)$ and $c_2(t)$, as predicted by Eq. (5). The ratio $c(t)/c_2(t)$ quickly approaches 2 for increasing time, as predicted by (14).

we substitute $\tau \simeq (3t/8)^{1/3}$ into (12) and (14) to arrive at the central results given in Eq. (5).

Figure 2 shows the time dependence of $c_1(t)$, $c(t)$, and $c_2(t)$ obtained by numerical integration of Eqs. (7a)-(7b) and (10) by *Mathematica*. As the initial condition we use $c_1(0) = 1$ and $c_2(0) = c(0) = 0.1$. The results of this numerical integration are fully consistent with the results of Eq. (5).

Having found the dimer concentration $c_2(t)$, we now outline how to obtain all the cluster densities. Based on the form of the rate equation for $c_k(t)$ for $k > 2$, we anticipate that $c_k = A_k c$; that is, all individual cluster densities are of the same order as the total density of clusters of mass 2 or greater. Substituting this ansatz into Eq. (8) we obtain the following recursion for the amplitudes:

$$\sum_{i+j=k} A_i A_j = 2A_k \quad k > 2, \tag{18}$$

again with all indices necessarily even. The already known value $A_2 = \frac{1}{2}$ plays the role of the initial condition for this recursion. Solving (18) subject to this initial condition gives

$$\frac{c_k}{c} = \frac{1}{\sqrt{4\pi}} \frac{\Gamma(k/2 - \frac{1}{2})}{\Gamma(k/2 + 1)} \simeq \sqrt{\frac{2}{\pi}} \frac{1}{k^{3/2}}, \tag{19}$$

where the last asymptotic is valid when $k \gg 1$ and generally (19) holds in the $t \to \infty$ limit.

This 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 $\sum_{k \geqslant 1} kA_k$ diverges if $A_k \sim k^{-3/2}$ for all k. This divergence contradicts the mass conservation statement that $\sum_{k \geqslant 1} kc_k \to$ 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

$$\sum_{k \geqslant 1} kc_k \sim c \sum_{1 \leqslant k \leqslant k^*} k \times k^{-3/2} \sim c\sqrt{k^*}.$$

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 [22]. In this latter example, the cutoff is determined by the condition that the total mass in the system is equal to the total mass that is injected up to a given time.

III. GENERAL TEMPLATING REACTIONS

There are two natural generalizations of templating aggregation that we now explore. One such example is scaffolds that are heavier than dimers, and another example is 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 a nonzero density of 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. Within this model, Eqs. (7a)-(7b) and (10) become

$$\frac{dc_1}{dt} = -c_1^L c_L, \tag{20a}$$

$$\frac{dc_L}{dt} = \frac{1}{L} c_1^L c_L - 2c\, c_L, \tag{20b}$$

$$\frac{dc}{dt} = \frac{1}{L} c_1^L c_L - c^2, \tag{20c}$$

which again constitute a closed system of three coupled nonlinear ODEs. In terms of the modified time variable defined in (11), the solution for the monomer density for the initial condition $c_1(0) = 1$ now is

$$c_1(\tau) = \frac{1}{[1 + (L-1)\tau]^{1/(L-1)}}. \tag{21}$$

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

$$c \simeq \frac{1}{2L} \frac{1}{[1 + (L-1)\tau]^{L/(L-1)}}, \tag{22a}$$

$$c_L \simeq \frac{1}{4L} \frac{1}{[1 + (L-1)\tau]^{L/(L-1)}}. \tag{22b}$$

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

$$t = \int \frac{d\tau'}{c_L(\tau')} \simeq \frac{4L}{2L-1} [1 + (L-1)\tau]^{(2L-1)/(L-1)}. \tag{23}$$

Combining (21) and (22) with (23), we thereby find that the densities of monomers and L-mers, and the total cluster density decay as

$$c_1(t) \simeq \left(\frac{2L-1}{4L} t\right)^{-1/(2L-1)}, \tag{24a}$$
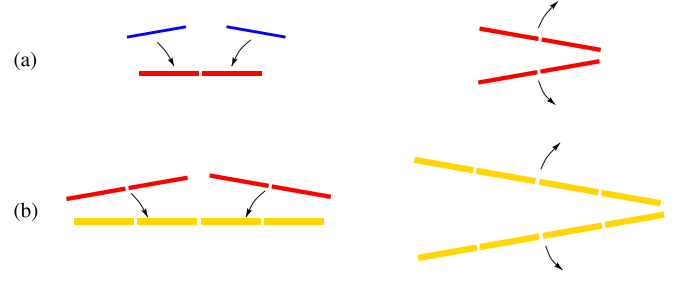

FIG. 3. Templating aggregation with two levels of templating: (a) two monomers react on a dimer scaffold; (b) two dimers react on a 4-mer scaffold.

$$c(t) \simeq \frac{1}{2L} \left(\frac{2L-1}{4L} t\right)^{-L/(2L-1)}, \tag{24b}$$

$$c_L(t) \simeq \frac{1}{4L} \left(\frac{2L-1}{4L} t\right)^{-L/2L-1)}. \tag{24c}$$

As one might expect, the overall reaction kinetics slows down as the scaffold size and consequently the reaction order L increases. The ratios c_{kL}/c are again stationary in the long-time limit and are given by the same formula (19) as for the case $L = 2$. 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. Monomers *and* dimers now play special roles in the reaction.

In close analogy with Eq. (7), the rate equations for the densities of monomers, dimers, and 4-mers are

$$\frac{dc_1}{dt} = -c_1^2 c_2, \tag{25a}$$

$$\frac{dc_2}{dt} = \frac{1}{2} c_1^2 c_2 - c_2^2 c_4, \tag{25b}$$

$$\frac{dc_4}{dt} = \frac{1}{2} c_2^2 c_4 - 2c\, c_4. \tag{25c}$$

The densities of heavier clusters satisfy the same Eq. (8) as in our previous models. Summing Eq. (25c) and Eq. (8) we deduce the evolution equation,

$$\frac{dc}{dt} = \frac{1}{2} c_2^2 c_4 - c^2, \tag{26}$$

for the density of clusters of mass 4 and greater.

Equations (25) and (26) again constitute a closed system of four coupled nonlinear ODEs from which we can, in principle, determine the kinetic behavior. These equations, subject to the initial conditions $c_1(0) > 0$, $c_2(0) > 0$, and $c_4(0) = c(0) > 0$, do not possess an exact solution. Instead, we again use the method of dominant balance to infer the asymptotic behavior.
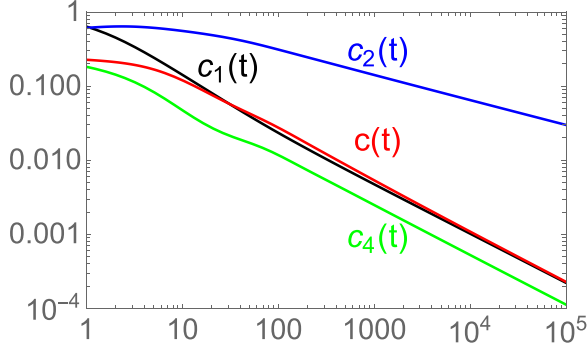
FIG. 4. Time dependence of $c_1(t)$, $c_2(t)$, $c(t)$, and $c_4(t)$ on a double logarithmic scale, with asymptotic decay of $t^{-1/3}$ for $c_2(t)$ and $t^{-2/3}$ for $c_1(t)$, $c(t)$, and $c_4(t)$.

We first neglect the LHS in Eq. (25c) to give $c \simeq c_2^2/4$. We substitute this result into (26), where we also neglect the LHS to find $c_4 \simeq c_2^2/8$. Thus

$$c \simeq \frac{1}{4}c_2^2, \quad c_1 \simeq \frac{1}{8}c_2^2. \qquad (27)$$

There are various choices of which terms to neglect in Eqs. (25a) and (25b). An elementary but lengthy trial and error approach shows that the consistent dominant balance is to keep the LHS in Eq. (25b). Since this term is negative, the simplest choice is to neglect the first term on the RHS of this equation. This gives

$$\frac{dc_2}{dt} = -\frac{1}{8}c_2^4.$$

Solving this equation and substituting this solution into both Eqs. (25a) and (27), and again solving, gives

$$c_1 \simeq c \simeq 2c_4 \simeq (3t)^{-2/3}, \quad c_2 \simeq 2(3t)^{-1/3}. \qquad (28)$$

The decay laws for c and c_4 are the same as in the templating with dimer scaffolds, and even the amplitudes are identical [cf. Eq. (5)]. The density of monomers decays similarly to c and c_4, and only the dimer density has the slowest decay of $t^{-1/3}$. We used *Mathematica* to numerically integrate Eqs. (25) and (26) and the results are shown in Fig. 4. These asymptotic behaviors are in excellent agreement with the theoretical predictions (28).

IV. TEMPLATED LIGATION

We now investigate a self-templating reaction in which clusters of all masses can merge only in the presence of a scaffold with mass equal to the sum of masses of the reaction partners. Furthermore, we postulate that all clusters (apart from monomers) serve as scaffolds. This templated ligation process [9,10,14,25,26] is represented by the reaction scheme

$$C_i \oplus C_j \oplus C_{i+j} \xrightarrow{L_{i,j}} C_{i+j} + C_{i+j}. \qquad (29)$$
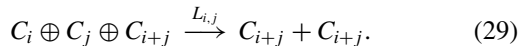
We assume that this ligation reaction is the only dynamical process in the system. In particular, binary aggregation of clusters does not occur. The absence of aggregation reactions means that an initially compact mass distribution with a maximum mass J remains compact forever; that is, $c_j(t) = 0$ for

all $j > J$. However, for unbounded initial mass distributions that decay sufficiently rapidly with mass, we anticipate that 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:

$$\sum_{j \geqslant 1} j\, c_j(t) = 1. \qquad (30)$$

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

$$\frac{dc_k}{dt} = c_k \sum_{i+j=k} c_i c_j - 2c_k \sum_{j \geqslant 1} c_j c_{j+k}. \qquad (31)$$

While purely ternary aggregation reactions, as embodied by the RHS of Eq. (31), are rare, they are relevant in certain situations. For example, the evolution of aligned spin domains in an Ising chain with zero temperature Swendsen-Wang or Wolff dynamics [27,28] is governed by purely ternary aggregation processes. However, for these two examples the governing equations are recursive and solvable. In contrast, Eq. (31) is hierarchical and appears to be unsolvable. A mathematically related nonrecurrent structure arises in the rate equations for cluster eating [29] and for combined aggregation-annihilation [30]; albeit these problems are more tractable since the underlying reactions are binary.

In the models analyzed in Secs. II and III, the evolution equations for the lightest cluster species and the total cluster density constitute a closed system of ODEs. There is no such simplification in templated ligation because of the ternary structure of the equations for the total cluster density and the monomer density:

$$\frac{dc}{dt} = -\sum_{i,j \geqslant 1} c_i c_j c_{i+j}, \qquad (32a)$$

$$\frac{dc_1}{dt} = -2c_1 \sum_{j \geqslant 1} c_j c_{j+1}. \qquad (32b)$$

Nevertheless, we can extract the long-time behavior from Eq. (31) by invoking scaling. Similarly to aggregation [31,32] (see also [21,22] for reviews) and the related catalytic aggregation model [33], we expect that the mass distribution approaches the scaling form

$$c_k(t) = c^2 \Phi(kc) \qquad (33)$$

in the scaling limit $k, t \to \infty$, $c \to 0$, with $kc = $ finite.

The mass conservation statement (30) and the definition of the cluster density then lead to the integral constraints:

$$\int_0^\infty dx\, x\, \Phi(x) = 1, \quad \int_0^\infty dx\, \Phi(x) = 1. \qquad (34)$$

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

Substituting the scaling ansatz (33) into (32a), the time dependence of the total cluster density is given by

$$\frac{dc}{dt} = -Bc^4, \qquad (35a)$$

with

$$B = \int_0^\infty dx \int_0^\infty dy \, \Phi(x)\Phi(y)\Phi(x+y). \quad (35b)$$

Solving (35a) gives the time dependence of the cluster density:

$$c \simeq (3Bt)^{-1/3}. \quad (36)$$

Using (36) and the scaling form (33) we conclude that the density of monomers is then

$$c_1 \simeq \Phi(0)(3Bt)^{-2/3}. \quad (37)$$

We can derive 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. (35b). Assuming $\Phi(0) > 0$ and substituting (37) into (32b) we obtain

$$B = \int_0^\infty dy \, \Phi^2(y). \quad (38)$$

To obtain the scaling function itself, we substitute the scaling form (33) into the governing equations (31) and find that the scaling function $\Phi(x)$ obeys the nonlinear integro-differential equation:

$$B\left[2\Phi(x) + x\frac{d\Phi(x)}{dx}\right] = 2\Phi\int_0^\infty dz \, \Phi(z)\Phi(z+x)$$
$$- \Phi\int_0^x dy \, \Phi(y)\Phi(x-y). \quad (39)$$

Notice that by integrating (39) over all x, we recover (35b). In the limit $x \to 0$, Eq. (39) reduces to (38). These relations serve as useful consistency checks.

The time dependence given in Eq. (36) together with Eq. (39) for Φ constitutes a formal solution cluster-mass distribution for the ligation reaction. While the explicit solution of (39) 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 based on the mechanism of templating. Here an aggregate of a specified mass acts as a scaffold upon which smaller clusters meet and merge to create a cluster that can also act as a scaffold. Clusters whose mass is either larger than or equal to the scaffold mass additionally undergo conventional aggregation. Within a mean-field description and also under the assumption that all the reaction rates are mass independent, we determined the time evolution of the cluster-mass distribution.

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

To summarize, the relation between the monomer and cluster densities is $c_1 \sim c^2$ in ordinary aggregation and $c_1 \sim c^{1/2}$ in templating aggregation.

In templating aggregation with dimer scaffolds, a three-body reaction drives the evolution of monomers and dimers, while heavier clusters undergo conventional aggregation via two-body reactions. This mixture of different reaction orders is the underlying reason for the much slower kinetics compared to conventional aggregation. Intriguingly, the relative cluster densities c_k/c in templating aggregation, Eq. (19), are the same as those in conventional aggregation which is augmented by a steady source of small-mass clusters [21,22].

We extended our model to a scaffold of arbitrary mass L, upon which L monomers must meet and react to create another L scaffold. Another natural extension 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 cluster densities of mass 4 and greater decay as $t^{-2/3}$, while only the dimer density 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 binary aggregation. For this purely ternary reaction, the total cluster density decays as $t^{-1/3}$, while individual cluster densities decay as $t^{-2/3}$. These decays are slower than those in templating aggregation. Also in contrast to templating aggregation, the mass distribution in templated ligation was predicted to approach a scaling form. Even with mass-independent reaction rates, templated ligation is calculationally quite challenging. We were able to 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.

More generally, templating-driven aggregation can be viewed as a modification of conventional binary aggregation, but with a nontrivial time-dependent source of scaffolds (either dimers or dimers and 4-mers) that serve as the input to the aggregation process. It is remarkable that the nontrivial and slow time dependence of these small elemental clusters modifies the densities of all heavier clusters so that the overall aggregation reaction has a slower dynamics compared to conventional aggregation. From the perspective of applications, there are many situations where templating plays a major role in many types of reactions. In addition to applications for models of the origin of life mentioned in the Introduction [1–14], other applications include, for example, self assembly of colloids [34], synthesis of exotic materials [35–37], and protein aggregation [38]. Perhaps our simple modeling can provide a starting point for understanding these types of template-controlled reactions.

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