A Self-Assembly Model of Time-Dependent Glue Strength *

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Abstract. We propose a self-assembly model in which the glue strength between two juxtaposed tiles is a function of the time they have been in neighboring positions. We then present an implementation of our model using strand displacement reactions on DNA tiles. Under our model, we can demonstrate and study catalysis and self-replication in the tile assembly. We then study the tile complexity for assembling shapes in our model and show that a thin rectangle of size $k \times N$ can be assembled using $O(\frac{\log N}{\log \log N})$ types of tiles.

1 Introduction

Self-assembly is a ubiquitous process in which small objects self-organize into larger and complex structures. Examples in nature are numerous: atoms self-assemble into molecules, molecules into cells, cells into tissues, and so on. Recently, self-assembly has also been demonstrated as a powerful technique for constructing nano-scale objects. For example, a wide variety of DNA lattices made from self-assembled branched DNA molecules (DNA tiles) [9, 19, 21, 22, 40, 42, 43] have been successfully constructed. Peptide self-assembly provides another nanoscale example [8]. Self-assembly is also used for mesoscale constructions using capillary forces [7, 26] or magnetic forces [1].

Mathematical studies of tiling dates back to 1960s, when Wang introduced his tiling model [36]. The initial focus of research in this area was towards the decidability/undecidability of the tiling problem [25]. A revival in the study of tiling was instigated in 1996 when Winfree proposed the simulation of computation [41] using self-assembly of DNA tiles.

In 2000, Rothemund and Winfree [28] proposed the *abstract Tile Assembly Model*, a mathematical model for theoretical studies of self-assembly. This model was later extended by Adleman *et al.* to include the time complexity of generating specified assemblies [3]. Later work includes combinatorial optimization, complexity problems, fault tolerance, and topology changes, in the abstract Tile Assembly Model as well as in some of its variants [4–6, 10–14, 17, 18, 20, 23, 24, 27, 29, 31, 32, 34, 35, 38, 39].

In this paper, we use the term *standard model* to refer to the above *abstract Tile Assembly Model* proposed by Winfree. For detailed description of the *standard model*, see [28].

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Roughly speaking, a tile in the standard model is a unit square where each side of the square has a glue from a set Σ associated with it. In this paper we use the terms *pad* and side of the tile interchangeably. Formally, a tile is an ordered quadruple $(\sigma_n, \sigma_e, \sigma_s, \sigma_w) \in \Sigma^4$, where σ_n, σ_e, σ_s, and σ_w represent the *northern*, *eastern*, *southern*, and *western* side glues of the tile, respectively. Σ also contains a special symbol $null$, which is a zero-strength glue. T denotes the set of all tiles in the system. A tile cannot be rotated. So, $(\sigma_1, \sigma_2, \sigma_3, \sigma_4) \neq (\sigma_2, \sigma_3, \sigma_4, \sigma_1)$. Also defined are various projection functions $n : T \rightarrow \Sigma$, $e : T \rightarrow \Sigma$, $s : T \rightarrow \Sigma$, and $w : T \rightarrow \Sigma$, where $n(\sigma_1, \sigma_2, \sigma_3, \sigma_4) = \sigma_1$, $e(\sigma_1, \sigma_2, \sigma_3, \sigma_4) = \sigma_2$, $s(\sigma_1, \sigma_2, \sigma_3, \sigma_4) = \sigma_3$, and $w(\sigma_1, \sigma_2, \sigma_3, \sigma_4) = \sigma_4$.

A glue strength function $g : \Sigma \times \Sigma \rightarrow \mathbb{R}$ determines the glue strength between two abutting tiles. $g(\sigma, \sigma') = g(\sigma', \sigma)$ is the strength between two tiles that abut on sides with glues σ and σ'. If $\sigma \neq \sigma'$, $g(\sigma, \sigma') = 0$; otherwise it is a positive value. It is also assumed that $g(\sigma, null) = 0, \forall \sigma \in \Sigma$. In the tile set T, there is a special *seed* tile s. There is a system parameter to control the assembly known as *temperature* and denoted as τ. All the ingredients described above constitute a *tile system*, a quadruple $\langle T, s, g, \tau \rangle$. A *configuration* is a snapshot of the assembly. More formally, it is the mapping from $\mathbb{Z}^2$ to $T \bigcup \{EMPTY\}$ where $EMPTY$ is a special tile $(null, null, null, null)$, indicating a tile is not present. For a configuration C, a tile $A = (\sigma_n, \sigma_e, \sigma_s, \sigma_w)$ is attachable at position (i, j) iff $C(i, j) = EMPTY$ and $g(\sigma_e, w(C(i, j+1))) + g(\sigma_n, s(C(i+1, j))) + g(\sigma_w, e(C(i, j-1))) + g(\sigma_s, n(C(i-1, j))) \geq \tau$.

Assembly takes place sequentially starting from a seed tile s at a known position. For a given tile system, any assembly that can be obtained by starting from the *seed* and adding tiles one by one, is said to be *produced*. An assembly is called to be *terminally produced* if no further tiles can be added to it. The *tile complexity* of a shape S is the size of the smallest tile set required to uniquely and terminally assemble S under a given assembly model. One of the well-known results is that the tile complexity of self-assembly of a square of size $N \times N$ in standard model is $\Theta(\frac{\log N}{\log \log N})$ [3, 28].

Adleman introduced a reversible model [2], and studied the kinetics of the reversible linear self-assemblies of tiles. Winfree also proposed a kinetic assembly model to study the kinetics of the self-assembly [37]. Apart from these basic models, various generalized models of self-assembly are also studied [6, 16]: namely, multiple temperature model, flexible glue model, and q-tile model.

Though all these models contribute greatly towards a good understanding of the process of self-assembly, there are still a few things that could not be easily explained or modeled (for example, the process of catalysis and self-replication in tile assembly). Recently, Schulman and Winfree show self-replication using the growth of DNA crystals [33], but their system requires shear forces to separate the replicated units. In this paper we propose a new model, in which catalysis and self-replication is possible without external intervention. In this new model, which is built on the basic framework of *abstract Tile Assembly Model*, the glue strength between different glues is dependent on the time for which they have remained together.

The rest of the paper is organized as follows. First we define our model formally in Section 2. We then put forth a method to physically implement such a system in Section 3. Then we present the processes of catalysis and self-replication in tile assembly

in our model in Sections 4 and 5, respectively. In Section 6, we discuss the tile complexity of assembly of various shapes. We conclude with the discussion of our results and future research directions in Section 7.

2 Time-Dependent Glue Model

We propose a Time-dependent Glue Model, which is built on the framework described above. In this model, the glue-strength between two tiles is dependent upon the time for which the two tiles have remained together.

Let τ be the temperature of the system. Tiles are defined as in *standard model*. However, in our model, glue strength function g is defined as $g : \Sigma \times \Sigma \times \mathbb{R} \rightarrow \mathbb{R}$.

In $g(\sigma, \sigma', t)$ the argument t is the time for which two sides of the tiles with glue-labels σ and σ' have been juxtaposed. For every pair (σ, σ'), the value $g(\sigma, \sigma', t)$ increases with t up to a maximum limit and then takes a constant value determined by σ and σ'. We define the time when g reaches this maximum as *time for maximum strength*, $tms : \Sigma \times \Sigma \rightarrow \mathbb{R}$. Note $g(\sigma, \sigma', t) = g(\sigma, \sigma', tms(\sigma, \sigma'))$ for $t > tms(\sigma, \sigma')$.

We also have a function *minimum interaction time* defined as $mit : \Sigma \times \Sigma \rightarrow \mathbb{R}$.

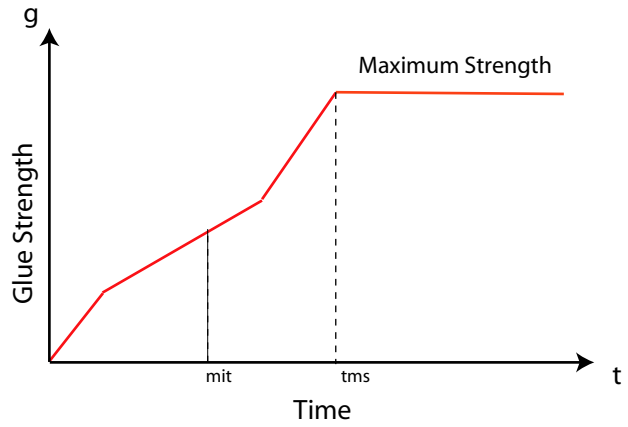

Fig. 1. Figure illustrates the concept of time-dependent glue strength, minimum interaction time, and time for maximum strength

For every pair (σ, σ'), a function $mit(\sigma, \sigma')$ is defined as the minimum time for which the two tiles with abutting glue symbols σ and σ' stay together. If $g(\sigma, \sigma', mit(\sigma, \sigma')) \geq \tau$, the two tiles will stay together; otherwise they will separate if there is no other force holding them in their abutting positions. An example of glue-strength function is shown in Figure 1. Intuitively speaking, *mit* serves as the minimum time required by the pads to decide whether they want to separate or remain joined. We further define $mit(\sigma, null) = 0$, $tms(\sigma, null) = 0$, and $g(\sigma, null, t) = 0$.

Next we give the justification and estimation of *mit* for a pair (σ, σ') of glues. Let $g(\sigma, \sigma', t)$ be the glue strength function. For more realistic estimation of *mit*, consider a physical system in which, in addition to association, dissociation reactions also occur. Let $p(b)$ be the probability of dissociation when the bond strength is b, and $f(t)$ be the probability that no dissociation takes place in the time interval $[0 \ldots t]$. Then,

$$f(t + \delta t) = f(t) \cdot (1 - p(g(t + \delta t))) \cdot \delta t,$$
$$\frac{f(t + \delta t)}{f(t)} = (1 - p(g(t + \delta t))) \cdot \delta t.$$

The probability that the dissociation takes place between time t and $t + \delta t$ is given by $f(t) \cdot p(g(t + \delta t)) \cdot \delta t$. Since *mit* is defined as the time for which two glues are expected to remain together once they come in contact, its expected value is:

$$E[mit] = \lim_{\delta t \to 0} \sum_{t=0}^{\infty} t \cdot f(t) \cdot p(g(t + \delta t)) \cdot \delta t,$$

where $p(b)$ can be determined using Winfree's kinetic model [37]. Hence, based on the knowledge of glue strength function it is possible to determine the expected minimum interaction time for a pair (σ, σ'). For simplicity, we will use the expected value of *mit* as the actual value of *mit* for a pair of glues (σ, σ').

Next we illustrate the time-dependent model with an example of the addition of a single tile to an aggregate. When a position (i, j) becomes available for the addition of a tile A, it will stay at (i, j) for a time interval t_0, where $t_0 = \max\{mit(e(A), w(C(i, j+1))), mit(n(A), s(C(i+1, j))), mit(w(A), e(C(i, j-1))), mit(s(A), n(C(i-1, j)))\}$. Recall that our model requires that if two tiles ever come in contact, they will stay together till the minimum interaction time of the corresponding glues.

After this time interval t_0, if $g(e(A), w(C(i, j+1)), t_0) + g(n(A), s(C(i+1, j)), t_0) + g(w(A), e(C(i, j-1)), t_0) + g(s(A), n(C(i-1, j)), t_0) < \tau$, A will detach; otherwise, A will continue to stay at position (i, j).

We describe in the next section a method to implement our model of time-dependent glue strength with DNA tiles.

3 Implementation of Time-Dependent Glue Model

If the hydrogen bonds between the bases in two hybridizing DNA strands build up sequentially, the total binding force between the two strands will increase with time up to the complete hybridization, which will provide a simple way of obtaining time-dependent glue strength between DNA tiles. However, even if we assume that the hybridization of two complementary DNA strands is instantaneous, we can design a multi-step binding mechanism to implement the idea of time-dependent glue strength, which exploits the phenomenon of strand displacement.

Figure 2 (a) illustrates the process of strand displacement in which strand B displaces strand C from strand A. Figure 2 (b) illustrates one step during this process. At any time either the hybridization of B with A (and hence dehybridization of C from

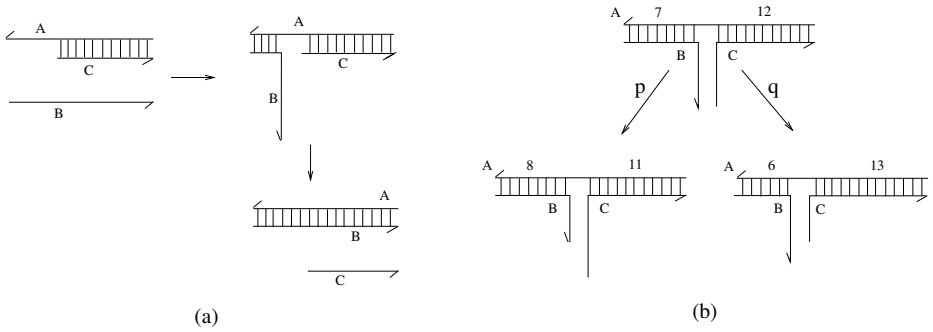

Fig. 2. Figure (a) illustrates the process of strand displacement. Figure (b) shows a single step of strand-displacement as single step of random walk. In (b), the numbers represent the number of DNA base pairs

A) or hybridization of C with A (and hence dehybridization of B from A) can proceed with 1/2 probability. Hence, we can model the strand displacement process as a random walk, with forward direction corresponding to hybridization between B and A, and backward direction corresponding to hybridization between C and A. To simplify the model, we can assume that the step length in this random walk is 1 base pair long. Hence, if the length of C is n bases, the expected number of steps required for B to replace C is n^2 [15].

Next we describe the design of the pads of DNA tiles with time dependent glue using the above mechanism of strand displacement.

To make the glue between pad A and pad B time-dependent, we need a construction similar to the one in Figure 3 (a). Strand representing pad A has various smaller strands (C_i's, called *protector strands*) hybridized to it as shown in Figure 3 (a). Strand B will displace these protector strands C_i sequentially.

The variable *tms* here will be the time required for B to displace all the C_i's. In the case when there are k different small strands C_i of length n_i attached to A, *tms* is $\sum_{i=1}^{k} n_i^2$.

Figure 3 gives the step by step illustration of the above process. The variation of glue strength between A and B is shown in Figure 3 (i). By controlling the length of various C_i's (*i.e.* $n_1, n_2, \ldots, n_k$), we can control the glue-strength function g for a pair of tile-pads (or glues). Thus, we have shown a method to render the DNA tiles the characteristic of time-dependent glue strength.

An interesting property is that the individual strand displacement of B against C_i is modeled as a random walk, but the complete process described above can be viewed as *roughly* monotonic. As shown in Figure 3 (i), the strength of the hybridization between strand A and strand B increases in a roughly monotonic fashion with the removal of every C_i. However during the individual competition between B and C_i, the increase is not monotonic.

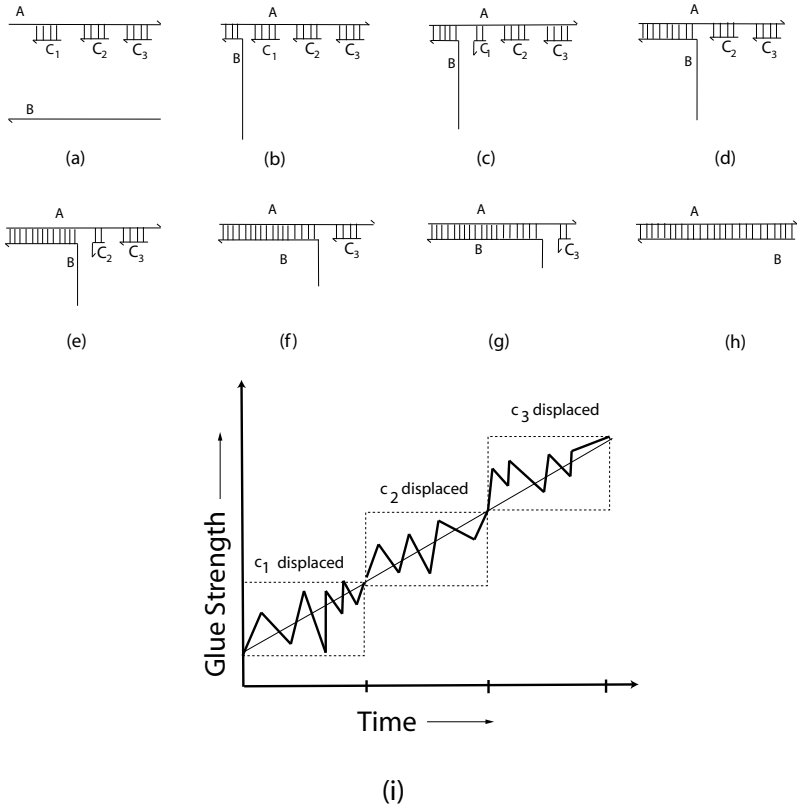

Fig. 3. Figures (a) to (h) illustrate a mechanism by which strand displacement reaction is used to implement time-dependent glue between two pads. They show step by step removal of C_i's by B from A. In Figure 3 (i) an imaginary graph illustrates the variation of glue-strength between A and B w.r.t. time

4 Catalysis

Catalysis is the phenomenon in which an external substance facilitates the reaction of other substances, without itself being used up in the process. The following question was posed by Adleman [2]: can we model the process of catalysis in self-assembly of tiles? In this section, we present a model for catalysis in self-assembly of tiles using time-dependent glue model. Now consider a supertile $\mathcal{X}$ (composed of two attached tiles C and D) and two single tiles A and B as shown in Figure 4 (a). We describe below how $\mathcal{X}$ can serve as a catalyst for the assembly of A and B. Assume $t_0 = mit(e(A), w(B))$ such that $g(e(A), w(B), t_0)$ is less than the temperature τ. Let $mit(s(A), n(C)) = mit(s(B), n(D)) = t_1 > t_0$. Also assume $g(s(A), n(C), t_1) + g(s(B), n(D), t_1) < \tau$ and $g(e(A), w(B), t_1) \geq \tau$.

The graph in Figure 4 (b) illustrates an example set of required conditions for the glue strength functions in the system.

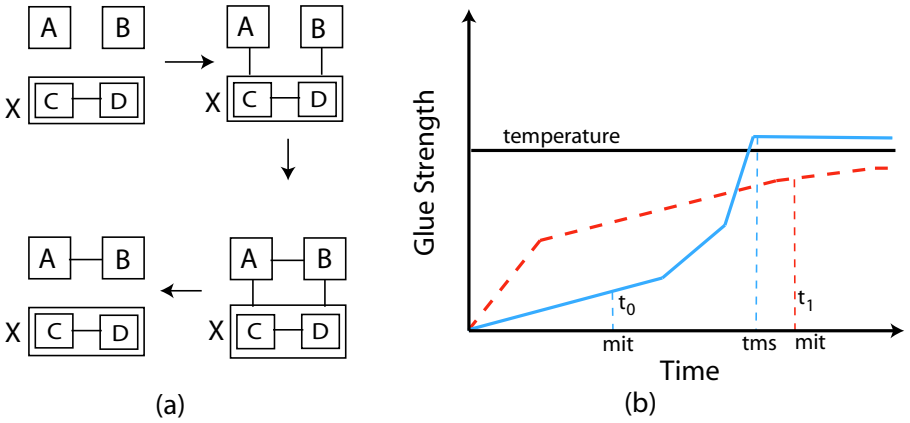

Fig. 4. Figure (a) shows catalyst $\mathcal{X}$ with the tiles C and D catalyzes the formation of $A \cdot B$. (b) shows the conditions required for catalysis in terms of the glue strength function. Solid line shows the plot of $g(e(A), w(B), t)$ and dashed line shows the plot of $g(s(A), n(C), t) + g(s(B), n(D), t)$

To show that $\mathcal{X}$ acts as a catalyst, we first show that without $\mathcal{X}$ stable $A \cdot B$ can not form. Next we show that $A \cdot B$ will form when $\mathcal{X}$ is present and $\mathcal{X}$ will be recovered unchanged after the formation of $A \cdot B$.

Without $\mathcal{X}$ in the system, A and B can only be held in neighboring positions for time $t_0 = mit(e(A), w(B))$, since $g(e(A), w(B), t_0) < \tau$. Hence, at t_0, A and B will fall apart.

However, in the presence of $\mathcal{X}$, the situation changes. Supertile $\mathcal{X}$ has two neighboring tiles C and D. Tiles A and B attach themselves to C and D as shown in Figure 4 (a). Since we let $mit(s(A), n(C)) = mit(s(B), n(D)) = t_1 > t_0$, tiles A and B are

held in the same position for time t_1. By our construction, as shown in Figure 4 (b), the following two events will occur at time t_1:

- At t_1, the glue strength between A and B is $g(e(A), w(B), t_1) \geq \tau$ and hence A and B will be glued together. That is, in the presence of $\mathcal{X}$, A and B remain together for a longer time, producing stably glued $A \cdot B$.
- At t_1, the total glue strength between $A \cdot B$ and $\mathcal{X}$ is $g(s(A), n(C), t_1) + g(s(B), n(D), t_1) < \tau$, and the glued $A \cdot B$ will fall off $\mathcal{X}$. $\mathcal{X}$ is recovered unchanged from the reaction and the catalysis is complete. Now $\mathcal{X}$ is ready to catalyze other copies of A and B.

Note that if only A (resp. B) comes in to attach with C (resp. D), it will fall off at the end of time $mit(s(A), n(C))$ (resp. $mit(s(B), n(D))$). If assembled $A \cdot B$ comes in, it will also fall off, at time t_1. These two reactions are futile reactions, and do not block the desired catalysis reaction. However, as the concentration of $A \cdot B$ increases and the concentration of unattached A and B decreases, the catalysis efficiency of $\mathcal{X}$ will decrease due to the increased probability of the occurrence of futile reaction between $A \cdot B$ and $C \cdot D$.

5 Self-replication

Self-replication process is one of the fundamental process of nature, in which a system creates copies of itself. We discuss below an approach to model self-replication using the time-dependent glue model.

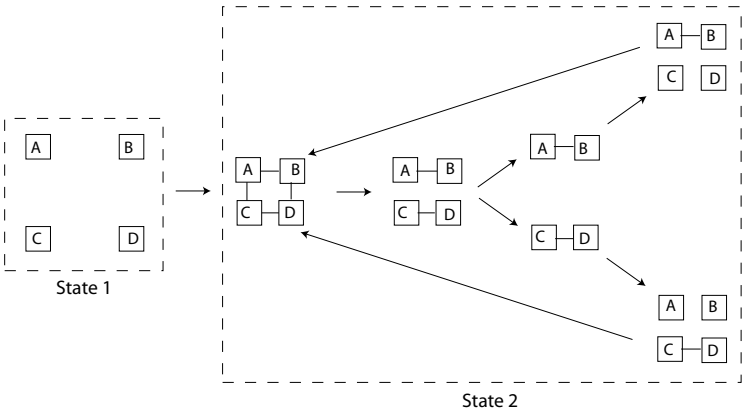

Fig. 5. A schematic of self-replication

Our approach is built on the above described process of catalysis: a product $A \cdot B$ catalyzes the formation of $C \cdot D$, which in turn catalyzes the formation of $A \cdot B$. And hence an exponential growth of self-replicated $A \cdot B$ and $C \cdot D$ takes place.

More precisely, let $t_0 < t_1$, consider tiles A, B, C, and D, such that :

$$\begin{aligned} mit(e(A), w(B)) = mit(e(C), w(D)) &= t_0, \\ mit(s(A), n(C)) = mit(s(B), n(D)) &= t_1, \\ g(e(A), w(B), t_0) = g(e(C), w(D), t_0) &< \tau, \\ g(e(A), w(B), t_1) = g(e(C), w(D), t_1) &> \tau, \\ g(s(A), n(C), t_1) + g(s(B), n(D), t_1) &< \tau. \end{aligned}$$

A system containing these four types of tiles has two states:

State 1. If there is no template $A \cdot B$ or $C \cdot D$ in the system, no assembled supertile exists since no two tiles can be held together long enough to form strong enough glue between them such that they become stably glued. Since $mit(e(A), w(B)) = mit(e(C), w(D)) = t_0$ and $g(e(A), w(B), t_0) = g(e(C), w(D), t_0) < \tau$, neither stable $A \cdot B$ nor stable $C \cdot D$ can form. Similarly, $mit(s(A), n(C)) = mit(s(B), n(D)) = t_1$, $g(s(A), n(C), t_1) < \tau$, and $g(s(B), n(D), t_1) < \tau$ implies that neither stable $A \cdot C$ nor stable $B \cdot D$ can form.

State 2. In contrast, if there is an initial copy of stable $A \cdot B$ in the system, self-replication occurs as follows. $A \cdot B$ serves as catalyst for the formation of $C \cdot D$, and $C \cdot D$ and $A \cdot B$ separate from each other at the end of the catalysis period, as described in Section 4; in turn, $C \cdot D$ serves as catalyst for the formation of $A \cdot B$. Thus we have a classical self-replication system: one makes a copy of itself via its complement. The number of the initial template ($A \cdot B$) and its complement ($C \cdot D$) grows exponentially in such system.

Hence, if the system is in state 1, it needs a triggering activity (formation of an stable $A \cdot B$ or $C \cdot D$) to go into state 2. Once the system is in state 2, it starts the self-replication process. Figure 5 illustrates the process of self-replication in the assembly of tiles.

If the system is in state 1, then the triggering activity (formation of an stable $A \cdot B$ or $C \cdot D$) can take place only if A, B, C, D co-position themselves so that the east side of A faces the west side of B and the south side of A faces the north side of C, and at the same time the south side of B faces the north side of D. In such a situation, A and C will remain abutted till time t_1, B and D will remain abutted till time t_1, and A and B (and C and D) might also remain together for time t_1, producing stable $A \cdot B$ and stable $C \cdot D$. And this will bring the system to state 2. But such copositioning of 4 tiles is a very low probability event. Thus a very low probability event can perturb a system in state 1 and triggers tremendous changes by bringing the system to state 2 where self-replication occurs.

6 Tile Complexity Results

In the standard model, the tile complexity of assembling an $N \times N$ square is $\Theta(\frac{\log N}{\log \log N})$ [3, 28]. It is also known that the upper bound on the tile complexity of assembling a $k \times N$ rectangle in the standard model is $O(k + N^{1/k})$ and that the lower bound on tile complexity of assembling a $k \times N$ rectangle is $\Omega(\frac{N^{1/k}}{k})$ [6]. For small values of

k this lower-bound is asymptotically larger than $O(\frac{\log N}{\log \log N})$. Here we claim that, in our model, as in the multi-temperature model defined in [6], a $k \times N$ rectangle can be self-assembled using $O(\frac{\log N}{\log \log N})$ types of tiles, even for small values of k. The proof technique follows the same spirit as in [6].

Theorem 1. *In time-dependent glue model, the tile complexity of self-assembling a $k \times N$ rectangle for an arbitrary integer $k \geq 2$ is $O(\frac{\log N}{\log \log N})$.*

Proof. The tile complexity of self-assembling a $k \times N$ rectangle is $O(N^{\frac{1}{k}} + k)$ for the standard model [6]. In time dependent glue model, we can use the similar idea as in [6] to reduce the tile complexity of assembling thin rectangles. For given k and N, build a $j \times N$ rectangle with $j > k$ such that the glues among the first k rows become strong after their *mit* (*minimum interaction time*), while the glues among the last $j - k$ rows do not become as strong. As such, these $j - k$ rows, referred to as *volatile rows*, will fall apart after certain time and produce the target $k \times N$ rectangle.

The tile set required to accomplish this construction is shown in Figure 6, which is similar to the one used in [6]. For more detailed illustration of this tile set, refer to [6]. First, a j-digit m-base counter is assembled as follows. Starting from the west edge of the seed tile, a chain of length m is formed in the first row using m chain tiles. At the same time tiles in the seed column also start assembling. It should be noted that first k tiles in the seed column have sufficient glue-strength and they are stable. Now starting from their west edges, the 0 normal tiles start filling the $m - 1$ columns in the upper rows. Then the hairpin tiles H_1^P and H_1^R assemble in the second row, which causes the assembly of further m chain tiles in the first row, and the assembly of 1 normal tiles in the second row (and 0 normal tiles in the upper rows) in the next section of m columns. Generally speaking, whenever a C_{m-1} chain tile is assembled in the first row, probe tiles in the upper rows are assembled until reaching a row that does not contain an $m - 1$ normal tile. In such a row, the appropriate hairpin tiles are assembled and this further propagates the assembly of return probe tiles downwards until the first row is reached, where a C_0 chain tile gets assembled. This again starts an assembly of a chain of length m. The whole process is repeated until a $j \times m^j$ rectangle is assembled.

Next we describe our modifications which are required for the $j - k$ upper volatile rows to get disassembled after the complete assembly of the $j \times m^j$ rectangle. First of all we need to have a special $(k + 1)$-th row ($**$ row), which will assemble to the north of the k-th row ($*$ row), as shown in Figure 6.

The operating temperature $\tau = 2$. Assume that for all glue-types, $mit = t_0$ and $tms = t_1$. There are three kinds of glues shown in Figure 6: black, gray, and dashed. Assume that the glue-strength function for a single black glue is $g_{\text{black}}(t)$, a single gray glue is $g_{\text{gray}}(t)$, and a single dashed glue is $g_{\text{dashed}}(t)$. They are defined as

$$g_{\text{black}}(t) = \begin{cases} \frac{4t}{5t_0} & t < t_0 \\ \frac{4}{5} + \frac{t - t_0}{5(t_1 - t_0)} & t_0 \leq t < t_1 \\ 1 & t \geq t_1 \end{cases}$$

$$g_{\text{gray}}(t) = \begin{cases} \frac{2t}{5t_0} & t < t_0 \\ \frac{2}{5} + \frac{t - t_0}{10(t_1 - t_0)} & t_0 \leq t < t_1 \\ \frac{1}{2} & t \geq t_1 \end{cases}$$

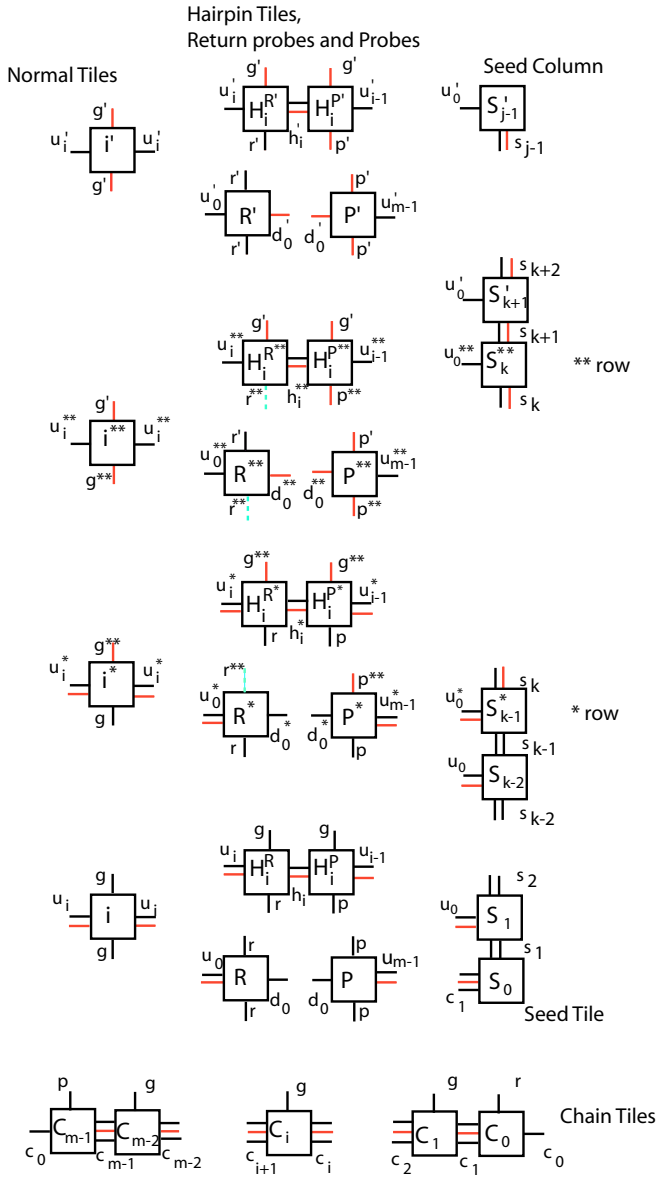

Fig. 6. Tile set to construct a $k \times N$ rectangle using only $O(N^{1/j} + j)$ tiles. The glue strength functions of gray, dashed, and black glues are defined in the proof

$$g_{\text{dashed}}(t) = \begin{cases} \frac{2t}{5t_0} & t < t_0 \\ \frac{2}{5} & t \geq t_0 \end{cases}$$

Multiple glues shown on the same side of a tile in Figure 6 are additive. For example, the glue strength between C_i and C_{i+1} ($0 \leq i \leq m-2$) is $2g_{\text{black}}(t) + g_{\text{gray}}(t)$.

This system will start assembling like a base $N^{1/j}$ counter of j digits, as briefed above and detailed in [3, 6]. It will first construct a rectangle of size $j \times N$ using $N^{1/j}+j$ type of tiles. Once the rectangle is complete, the tile on the north-west corner will start the required disassembly of the upper $(j-k)$ volatile rows, which results in the formation of a $k \times N$ rectangle. We call these two phases *Assembly phase* and *Disassembly phase* respectively, and describe them below.

Assembly Phase:

In the Assembly Phase, we aim at constructing a $j \times N$ rectangle. In the time dependent model, the assembly proceeds as in the standard model until the assembly of P^* tile in the k-th row ($*$ row). At this point, an $H^{R^{**}}$ tile is required to get assembled. However, when the $H^{R^{**}}$ tile is assembled in the $(k+1)$-th row, the total support on $H^{R^{**}}$ from its east neighbor is only $\frac{4}{5} + \frac{2}{5} < 2$ at the end of mit. Thus $H^{R^{**}}$ must obtain additional support; otherwise it will get disassembled, blocking the desired assembly process. The additional support comes both from its south neighbor and its west neighbor. (1) On the south front, tile R^* can arrive and be incorporated in the k-th row ($*$ row) of the assembly. It holds $H^{R^{**}}$ for another time interval of mit and provides a support of $\frac{2}{5}$. Further note that during this second interval, an R tile can be assembled in the $(k-1)$-th row, and the R^* tile in the k-th row will then have support 2 at *mit* and hence stay attached. In addition, tile R has support 2 at *mit*, so it will also stay attached. Regarding $H^{R^{**}}$, the end result is that it receives an additional *stable* support $\frac{2}{5}$ from its south neighbor. However, the maximum support from both the south and the east is at most $1 + \frac{1}{2} + \frac{2}{5}$, which is still less than $\tau = 2$. Fortunately, additional rescue comes from the west. (2) On the west front, an i^{**} tile can get attached to $H^{R^{**}}$, and stabilize it by raising its total support above 2. However, this support is unstable, or *volatile*, in the sense that i^{**} itself needs additional support from its own west and south neighbors to stay attached. If this support can not come in time, that is, before *mit*, i^{**} will get disassembled, in turn causing the disassembly of $H^{R^{**}}$. The key observation here is that this assembly/disassembly is a reversible dynamic process: the disassembly may stop and start going backwards (*i.e.* assembling again) at any point. Thus in a dynamic, reversible fashion, the target structure of the Assembly Phase, namely the $j \times N$ rectangle, can be eventually constructed.

The above added complication is due to the fact that we require the $H^{R^{**}}$ tiles in the $(k+1)$-th row to get a total support of < 2 from the south and the east. This is crucial because during the subsequent Disassembly Phase (as we describe next) the desired disassembly can only carry through if the total support of each volatile tile from the south and the east is < 2.

Disassembly Phase:

In the Disassembly Phase, we will remove the $j-k$ volatile rows, and reach the final target structure, a $k \times N$ rectangle. Once the $j \times N$ rectangle is complete, the tile T at the north-west corner (P' tile in the j-th row) initiates the disassembly. When the *mit* of the glue-pairs between tile T and its neighbors is over, tile T will get detached because

the total glue strength that it has accumulated is $\frac{4}{5} + \frac{2}{5} < \tau = 2$. Note that, unlike the above case for $H^{R^{**}}$, no additional support can come from the west for tile T since T is the west-most tiles. As such, T is doomed to get disassembled. With T gone, T's east neighbor will get removed next, since it now has a total glue strength $\leq 1 + \frac{1}{2} < \tau$. Similarly, all the tiles in this row will get removed one by one, followed by the removal of the tiles in the next row (south row). Such disassembly of the tiles continues until we are left with the target rectangle of size $k \times N$, whose constituent tiles, at this stage, all have a total glue strength no less than $\tau = 2$, and hence stay stably attached.

Note that, similar as in the Assembly Phase, the volatile tiles that just got removed might come back. But again, ultimately they will have to *all* fall off (after the *mit*), and produce the desired $k \times N$ rectangle.

Concluding the Proof:
We can construct a $k \times N$ rectangle using $O(N^{1/j} + j)$ type of tiles (where $j > k$). As in [6], it can be reduced to $O(\frac{\log N}{\log \log N})$ by choosing $j = \frac{\log N}{\log \log N - \log \log \log N}$. □

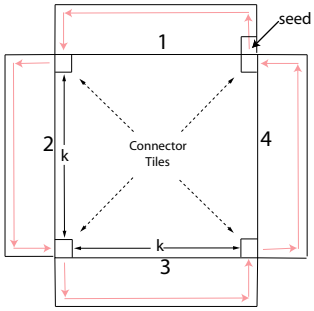

Fig. 7. Direction of the gray arrow shows the direction of construction of a square with a hole, starting from the indicated seed

Thin rectangles can serve as building blocks for the construction of many other interesting shapes. One example is a square of size $N \times N$ with a large square hole of size $k \times k$ ($k \sim N$). Under the standard model, the lower bound can be shown to be $\Omega(\frac{(k)^{\frac{2}{N-k}}}{N-k})$ by a lower bound argument similar to the one in [6]. Note that as $N - k$ decreases, *i.e.* the square hole in the square increases, the lower bound increases. In the case when $N - k$ is smaller than $\frac{\log N}{\log \log N - \log \log \log N}$, the lower bound is more than $\frac{\log N}{\log \log N}$. In the case when $N - k$ is a small constant, the complexity is almost N^c, where c is some constant < 1. However, in time-dependent model, the tile complexity of this shape can be reduced to $O(\frac{\log k}{\log \log k})$ even for small values of $N - k$, using our thin rectangle construction.

The basic idea is quite simple. We sequentially grow four different $(\frac{N-k-2}{2}) \times (k + 2)$ rectangles that will make up the major part of the square's sides. To enable the sequential growth of these rectangles, we introduce four *connector tiles* that concatenate

them. After the completion of one rectangle the connector tile will assemble and provide basis for the assembly of the subsequent rectangle. Finally, some more constant type of tiles will be introduced to fill in the gaps at the four corners this $N \times N$ square, and the gap between two subsequent connector tiles, producing the target $N \times N$ square with a $k \times k$ hole.

The upper bound on the number of tiles is exactly the same as the upper bound for constructing the four thin rectangles, which is $O(\frac{\log k}{\log \log k})$.

7 Discussion and Future Work

In this paper, we define a model in which the glue strength between tiles depends upon the time they have been abutting each other. Under this model, we demonstrate and analyze catalysis and self-replication, and show how to construct a thin $k \times N$ rectangle using $O(\frac{\log N}{\log \log N})$ tiles. The upper bound on assembling a thin rectangle is obtained by applying similar assembly strategy as in the multi-temperature model [6]. Thus, an interesting question is whether the multi-temperature model can be simulated using our time-dependent model. We also want to further investigate if under our model the lower bound of $\Omega(\frac{\log N}{\log \log N})$ for the tile complexity of an $N \times N$ square can be further improved.

Another interesting direction is to study the kinetics of the catalysis and self-replication analytically. Winfree's kinetic model [37] can be used to study them, but the challenge here is that the rate constant for the dissociation for a particular species varies with time because of changing glue strengths of its bonds. This makes the analytical study hard. However, these catalytic and self-replicating systems can be modeled as a continuous time markov chain, and studied using computer simulation to obtain empirical results.

References

1. http://mrsec.wisc.edu/edetc/selfassembly/.
2. L. Adleman. Towards a mathematical theory of self-assembly. Technical Report 00-722, University of Southern California, 2000.
3. L. Adleman, Q. Cheng, A. Goel, and M.D. Huang. Running time and program size for self-assembled squares. In *Proceedings of the thirty-third annual ACM symposium on Theory of computing*, pages 740–748. ACM Press, 2001.
4. L. Adleman, Q. Cheng, A. Goel, M.D. Huang, D. Kempe, P.M. de Espans, and P.W.K. Rothemund. Combinatorial optimization problems in self-assembly. In *Proceedings of the thirty-fourth annual ACM symposium on Theory of computing*, pages 23–32. ACM Press, 2002.
5. L. Adleman, J. Kari, L. Kari, and D. Reishus. On the decidability of self-assembly of infinite ribbons. In *Proceedings of the 43rd Symposium on Foundations of Computer Science*, pages 530–537, 2002.
6. G. Aggarwal, M.H. Goldwasser, M.Y. Kao, and R.T. Schweller. Complexities for generalized models of self-assembly. In *Proceedings of 15th annual ACM-SIAM Symposium on Discrete Algorithms (SODA)*, pages 880–889. ACM Press, 2004.
7. N. Bowden, A. Terfort, J. Carbeck, and G.M. Whitesides. Self-assembly of mesoscale objects into ordered two-dimensional arrays. *Science*, 276(11):233–235, 1997.
8. R.F. Bruinsma, W.M. Gelbart, D. Reguera, J. Rudnick, and R. Zandi. Viral self-assembly as a thermodynamic process. *Phys. Rev. Lett.*, 90(24):248101, 2003 June 20.

9. N. Chelyapov, Y. Brun, M. Gopalkrishnan, D. Reishus, B. Shaw, and L. Adleman. DNA triangles and self-assembled hexagonal tilings. *J. Am. Chem. Soc.*, 126:13924–13925, 2004.
10. H.L. Chen, Q. Cheng, A. Goel, M.D. Huang, and P.M. de Espanes. Invadable self-assembly: Combining robustness with efficiency. In *Proceedings of the 15th annual ACM-SIAM Symposium on Discrete Algorithms (SODA)*, pages 890–899, 2004.
11. Q. Cheng and P.M. de Espanes. Resolving two open problems in the self-assembly of squares. Technical Report 03-793, University of Southern California, 2003.
12. Q. Cheng, A. Goel, and P. Moisset. Optimal self-assembly of counters at temperature two. In *Proceedings of the first conference on Foundations of nanoscience: self-assembled architectures and devices*, 2004.
13. M. Cook, P.W.K. Rothemund, and E. Winfree. Self-assembled circuit patterns. In *DNA Based Computers 9*, volume 2943 of *LNCS*, pages 91–107, 2004.
14. K. Fujibayashi and S. Murata. A method for error suppression for self-assembling DNA tiles. In *DNA Based Computing 10*, pages 284–293, 2004.
15. B.D. Hughes. *Random Walks and Random Environments, Vol. 1: Random Walks.* New York: Oxford University Press, 1995.
16. M. Kao and R. Schweller. Reduce complexity for tile self-assembly through temperature programming. In *Proceedings of 17th annual ACM-SIAM Symposium on Discrete Algorithms (SODA) (to appear)*. ACM Press, 2006.
17. E. Klavins. Directed self-assembly using graph grammars. In *Foundations of Nanoscience: Self Assembled Architectures and Devices*, Snowbird, UT, 2004.
18. E. Klavins, R. Ghrist, and D. Lipsky. Graph grammars for self-assembling robotic systems. In *Proceedings of the International Conference on Robotics and Automation*, 2004.
19. T.H. LaBean, H. Yan, J. Kopatsch, F. Liu, E. Winfree, J.H. Reif, and N.C. Seeman. The construction, analysis, ligation and self-assembly of DNA triple crossover complexes. *J. Am. Chem. Soc.*, 122:1848–1860, 2000.
20. M.G. Lagoudakis and T.H. LaBean. 2-D DNA self-assembly for satisfiability. In *DNA Based Computers V*, volume 54 of *DIMACS*, pages 141–154. American Mathematical Society, 2000.
21. D. Liu, M. Wang, Z. Deng, R. Walulu, and C. Mao. Tensegrity: Construction of rigid DNA triangles with flexible four-arm dna junctions. *J. Am. Chem. Soc.*, 126:2324–2325, 2004.
22. C. Mao, W. Sun, and N.C. Seeman. Designed two-dimensional DNA holliday junction arrays visualized by atomic force microscopy. *J. Am. Chem. Soc.*, 121:5437–5443, 1999.
23. J.H. Reif, S. Sahu, and P. Yin. Compact error-resilient computational DNA tiling assemblies. In *Proc. 10th International Meeting on DNA Computing*, pages 248–260, 2004.
24. J.H. Reif, S. Sahu, and P. Yin. Complexity of graph self-assembly in accretive systems and self-destructible systems. In *Proc. 11th International Meeting on DNA Computing*, pages 101–112, 2005.
25. R.M. Robinson. Undecidability and non periodicity of tilings of the plane. *Inventiones Math*, 12:177–209, 1971.
26. P.W.K. Rothemund. Using lateral capillary forces to compute by self-assembly. *Proc. Natl. Acad. Sci. USA*, 97(3):984–989, 2000.
27. P.W.K. Rothemund. *Theory and Experiments in Algorithmic Self-Assembly*. PhD thesis, University of Southern California, 2001.
28. P.W.K. Rothemund and E. Winfree. The program-size complexity of self-assembled squares (extended abstract). In *Proceedings of the thirty-second annual ACM symposium on Theory of computing*, pages 459–468. ACM Press, 2000.
29. P. Sa-Ardyen, N. Jonoska, and N.C. Seeman. Self-assembling DNA graphs. *Lecture Notes in Computer Science*, 2568:1–9, 2003.
30. S. Sahu, P. Yin, and J.H. Reif. A self-assembly model of DNA tiles with time-dependent glue strength. Technical Report CS-2005-04, Duke University, 2005.

31. R. Schulman, S. Lee, N. Papadakis, and E. Winfree. One dimensional boundaries for DNA tile self-assembly. In *DNA Based Computers 9*, volume 2943 of *LNCS*, pages 108–125, 2004.
32. R. Schulman and E. Winfree. Programmable control of nucleation for algorithmic self-assembly. In *DNA Based Computers 10*, LNCS, 2005.
33. R. Schulman and E. Winfree. Self-replication and evolution of DNA crystals. In *The 13th European Conference on Artificial Life (ECAL)*, 2005.
34. D. Soloveichik and E. Winfree. Complexity of compact proofreading for self-assembled patterns. In *Proc. 11th International Meeting on DNA Computing*, pages 125–135, 2005.
35. D. Soloveichik and E. Winfree. Complexity of self-assembled shapes. In *DNA Based Computers 10*, LNCS, 2005.
36. H. Wang. Proving theorems by pattern recognition ii. *Bell Systems Technical Journal*, 40:1–41, 1961.
37. E. Winfree. Simulation of computing by self-assembly. Technical Report 1998.22, Caltech, 1998.
38. E. Winfree. Self-healing tile sets (draft). 2005.
39. E. Winfree and R. Bekbolatov. Proofreading tile sets: Error correction for algorithmic self-assembly. In *DNA Based Computers 9*, volume 2943 of *LNCS*, pages 126–144, 2004.
40. E. Winfree, F. Liu, L.A. Wenzler, and N.C. Seeman. Design and self-assembly of two-dimensional DNA crystals. *Nature*, 394(6693):539–544, 1998.
41. E. Winfree, X. Yang, and N.C. Seeman. Universal computation via self-assembly of DNA: Some theory and experiments. In L.F. Landweber and E.B. Baum, editors, *DNA Based Computers II*, volume 44 of *DIMACS*, pages 191–213. American Mathematical Society, 1999.
42. H. Yan, T.H. LaBean, L. Feng, and J.H. Reif. Directed nucleation assembly of DNA tile complexes for barcode patterned DNA lattices. *Proc. Natl. Acad. Sci. USA*, 100(14):8103–8108, 2003.
43. H. Yan, S.H. Park, G. Finkelstein, J.H. Reif, and T.H. LaBean. DNA-templated self-assembly of protein arrays and highly conductive nanowires. *Science*, 301(5641):1882–1884, 2003.