Design of a Minimal System for Self-replication of Rectangular Patterns of DNA Tiles

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Abstract. Complex nanostructures assembled from DNA tiles cannot be manufactured in large volumes without extensive wet-lab efforts. Self-replication of tile structures would offer a low-cost and efficient nanomanufacturing if it would be based on an automated dynamically controlled assembly and disassembly of tiles — an attribute that is lacking in existing tile self-assembly framework. Here we propose self-replication of rectangular two-dimensional patterns based on the abstract Tile Assembly Model, by designing a system of tiles which replicate a target pattern by replicating its "L"-shaped seed. Self-replication starts by the formation of a mold structure from a "L"-shaped seed of a target pattern. The mold consists of switch-enabled tiles that can be dynamically triggered to dissociate the seed and the mold templates. The dissociated mold and seed structures each further catalyse assembly of new templates of seed and mold structures, respectively, forming the basis of a cross-catalytic exponential replication cycle.

Keywords: Nature-inspired materials, Minimal self-replication, DNA tile, Self-assembly, Switch-enabled tiles.

1 Introduction and Motivation

DNA tile self-assembly [19] is an emerging paradigm for molecular computation and nanomanufacturing. DNA tiles [21], the building blocks of tile self-assembly, can be designed to interact with strength and specificity for the assembly of logically and/or algorithmically directed periodic and aperiodic two-dimensional (2-D) intricate patterns. Erik Winfree has introduced the abstract Tile Assembly Model (aTAM) [14] for theoretical assessment of the tile assembly process. In the aTAM framework, the assembly starts from a single seed tile and grows

A.-H. Dediu et al. (Eds.): TPNC 2014, LNCS 8890, pp. 119–133, 2014.

in 2-D as more tiles adjoin one-by-one to the growing structure. Given any desired rectangular tile pattern, where the tiles can be seen as coloured (or functionalised) over a finite set of colours (or secondary structures), one can always design a finite, though exhaustive, approximate-minimal set of tiles so as to reliably and uniquely assemble the target pattern [2].

A minimal self-replicating chemical system [8] includes two elements: a template molecule and a few substrate molecules capable of self-assembling an exact replica of the template molecule. The assembled replica must be able to dissociate from the template so as to result in two templates: the former template and the newly created template. These templates need to then be able to catalyse a reiteration of the process by self-assembly of two new replicates on the two templates. Such a process theoretically results in an exponential amplification of the number of templates, and could be adopted to design a minimal self-replication system of patterns in the tile self-assembly framework. However, tile assembly was proposed as a purely passive process where tiles are incapable of self-triggering any post-assembly rearrangements. This prohibits the dynamic assembly and disassembly of tile structures, which is essential for the self-replication in the tile assembly framework.

In previous work on self-replication, Schulman and Winfree [15,16] demonstrated the self-replication in the tile self-assembly framework. The underlying principle is that an externally forced random fragmentation of a self-assembling lattice of tiles would create two new nucleation sites for regrowth of lattices. Such a lattice growth followed by fragmentation would eventually result into an amplified number of copies of the sequences. One approach for a post-assembly dissociation of a tile is the use of an enzyme that can selectively break apart fragments from an assembled tile structure. The self-replication of 2-D shapes using such an enzyme- and staged self-assembly model was first demonstrated by Abel et al. [1]. Although this is a shape-independent replication mechanism applicable to both a precise and an infinite yield, usage of enzymes could pose practical limitations.

Another paradigm of active tile self-assembly, without the use of enzymes, is emerging by the joining of tile assembly methodology with associated control of dynamic strand displacement circuitry [13,22,4]. In this framework, tiles can not only assemble in complex patterns through cooperative binding, but tile substructures can also be triggered to disassemble and reassemble. Exponential self-replication of 2-D rectangular patterns of origami tiles [9] using such a framework, namely the Signal Tile Assembly Model (STAM) [13,12], was demonstrated by Keenan et al. [7]. The STAM is derived from the aTAM [14] where tiles are modified to enable signalling and glue activation. A signal propagates through the tile lattice by sending controlled signals to activate and deactivate binding between two connected or remotely placed tiles. A signal-controlled dissociation of tile assemblies provides the basis for separating template from the replicated molecule. Although the technique provides an innovative approach for enzyme-free self-replication of both 2-D and 3-D structures, design and

implementation of such tiles and their self-assembly would pose significant practical challenges [9,13].

We have drawn motivation from these pattern self-replicators to propose a design of a minimal system of self-replication for 2-D rectangular patterns within the framework of the aTAM [14]. The design adheres to simplicity and implementation feasibility in four aspects: 1) double crossover (DX) tiles are used; 2) all glues are of strength 1; 3) tiles do not carry signals; 4) the replication process is enzyme free. Pattern replication starts with formation of a mold structure around the "L"-shaped seed with the help of a set of SWitch-Enabled Tiles (SWET) that can be activated to switch their binding state from bound (ON) to free (OFF). Further, the assembled mold gets dissociated from the seed structure by a toehold-mediated switching control, which is cyclically triggered at precise time intervals. The dissociated mold structure grows a new copy of the "L"-shaped seed while the dissociated seed structure reiterates the process. The remaining pattern is grown on these self-replicating seed structures by supplying the system with an appropriate set of pattern forming tiles. The terms seed ("L"-shaped seed) and pattern have been interchangeably used in the rest of the article.

2 A Model of Switch-Enabled Tile Assembly

The abstract Tile Assembly Model (*aTAM*) [14], introduced by Winfree, provides a framework where a 2-D target pattern can be self-assembled with the help of a finite set of tiles. In the aTAM, a tile is represented as a unit square with its four edges, North (N), East (E), South (S) and West (W), labelled from Σ, where Σ is a finite set of 'glues', including the special empty glue "0". Therefore, a Tile t can be represented by the quadruple $\{\sigma_N(t), \sigma_E(t), \sigma_S(t), \sigma_W(t)\}$. A zero value of the glue denotes the absence of a sticky-end i.e., zero binding strength. We assume that our tile system is deterministic, and works under the $temperature-2$ assumption. Moreover, all the glues/sticky-ends used herein are assumed to be of *strength 1.*

Physical Basis of Switch-Enabled Tile Assembly. The concept of glue activation/deactivation has earlier been demonstrated by [10,4], by introducing innovative mechanisms of protection and deprotection of tile sticky-ends. Signal passing and glue activation/deactivation was explored in STAM [13]. In the STAM framework, control signals pass through the tiles in order to activate or deactivate the glues of remotely lying tiles. Such a signal traversal involves several concomitant strand displacement steps. Further, in the STAM framework, tiles carry the control signals, and the activation/deactivation of a remotely lying tile would therefore depend on the success of a set of consecutive activation/deactivation events between tiles lying in the signal propagation path.

In order to design a tile assembly system with attributes of active assembly where tiles can activate/deactivate their glues through a localised strand displacement reaction, we introduce the concept of SWitch-Enabled Tile(SWET)

shown in Figure 1(a). A (DX-)tile can be converted to a SWET by extending its sticky-end (S) with a short length switching toehold (SW) that serves as a local switch between two tiles, where switching is controlled by a global signal cyclically generated by an especially designed chemical oscillator system described in Section 4. The switching toehold is used to mediate the binding-breaking (ON-OFF) process in-between a SWET and a DX-tile, see Figure 1(b). In the 'ON' state, a SWET is able to bind a tile using as sticky end the domain (ij), where sections *i, j,* t_s are arbitrarily chosen to be 3, 7 and 3 nucleotides long, respectively, and complementary sections are marked by (*). A periodically available DNA strand (j^*, t_s^*, sgc_1) changes the binding state from 'ON' to 'OFF', where the two tiles would eventually break apart.

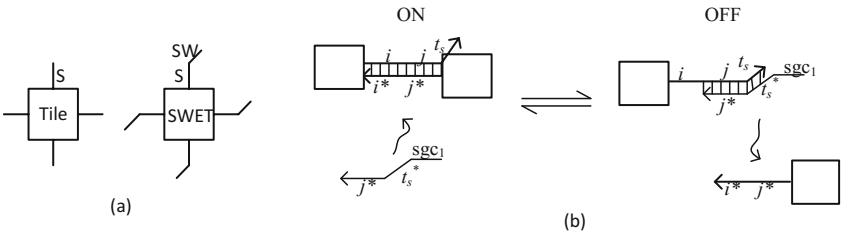

Fig. 1. (a) A normal tile and a SWET tile, (b) Toehold-mediated ON-OFF switching between a simple tile and a SWET tile

The toehold-mediated switching of the SWET, from ON to OFF and vice versa is essential for accomplishing dynamic assembly-disassembly of the tile structures. Such a control can be achieved by a cyclic and abrupt increase in the supply of the inhibitor signal i.e., the DNA strand (j^*, t_s^*, sgc_1) in Figure 1(b). This dynamic process can be implemented using an Oregonator autocatalytic reaction-system [3], which in turn can be implemented using DNA molecules as reported in [18]. Moreover, the methodology from [18], based itself on the strand displacement technique, allows for various adjustments of the autocatalytic system parameters, including the length and the amplitude of the cyclic signal, as well as the steepness of its descent. In Section 4 we introduce an ODE-based numeric simulation for the dynamics of one such paired SWET and inhibitor signal showing that indeed the de-activation of the SWET is both cyclic and abrupt as shown in Figure 4.

3 Proposed Self-replication System

In this section we define a minimal self-replicating system for rectangular patterns of tiles as shown in Figure 2. Let P be the pattern to be replicated, and

structure S as its "L"-shaped South-West border, named in the following as *seed*. Although the seed is usually assumed to be a single tile in various other tile assembly frameworks, herein we consider an "L"-shaped structure as seed. This is due to the fact that the glues placed on the interior border of such an "L"-shaped structure uniquely identify the entire rectangular tile-pattern within, assuming the system is deterministic.

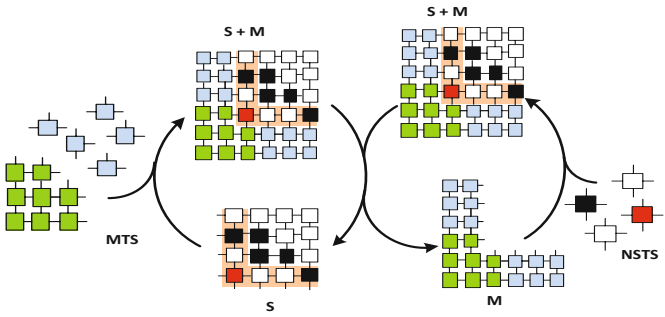

Fig. 2. Minimal self-replicating system of rectangular patterns

The replication process starts by supplying a pre-assembled rectangular pattern (P), which includes its seed structure (S), and a set of mold forming tiles (MTS). We require that the pattern contains a unique, red-coloured tile on its lower-left corner position, which is not used on any other position inside the pattern. Observe that the MTS consists of a pre-assembled corner supertile (CST) that is stable at temperature-2, and is designed to bind (using two strength-1 glues) on the special red-coloured tile. Thus, the CST initiates the mold formation, using as template the seed structure S. The mold assembly further proceeds as more tiles cooperatively join one by one until the entire South-West boundary of the seed structure is covered by a double layer of tiles, creating a seed-mold complex (S+M). Tiles forming the inner layer of the mold are designed as SWET type with switch enabled glue on the side that binds with the seed (pattern). The assembled seed-mold complex undergoes a controlled dissociation, splitting into the seed S and the mold M structures. Observe that the dissociated mold structure have two layers of tiles ensuring its stability under temperature-2 assembly framework.

In the next replication cycle, the dissociated seed structure (S) repeats the left hand side pathway, and thereby, creates two (S+M) complexes, whereas the dissociated mold structure (M) drives the right hand side pathway supplied by a pattern forming tile set (NSTS). Indeed, assuming we have at our disposal a tile set capable of assembling the pattern (we call this set the Nano-Structure Tile Set (NSTS)), we use the mold to first reassemble the seed S (using tiles from

NSTS) and then we reassemble the complete pattern P (using the same NSTS). Thus, by supplying the system with sufficient many copies of the tiles within the MTS and NSTS tile sets, and by continuing the process for n complete cycles, the replicator could theoretically produce 2^{n-1} copies of both the mold and the pattern structures (which is first the seed structure and then the complete pattern). In a potential experimental implementation, one has to provide for an expected time for both the mold formation process (from a template pattern) and the seed formation process (using the mold as a seed). Then, one adjusts the signal inhibitor cycle, which triggers the seed-mold dissociation such as to be at least as long as the maximum of the two expected time values.

Although the above system deals with the replication of only one pattern (P), the method can be easily generalised to other rectangular patterns. Indeed, in Section 5 we are going to assume that we are provided with an arbitrary finite set of patterns, any of them being a potential template for replication. Then, we are going to design appropriate-minimal Mold- and Nano-Structure- Tile Sets, i.e., MTS and NSTS, respectively, such that by inserting any of the above patterns within the system, or even a subset of them, it/they will act as a template for replication. Thus, the result of the process will be an amplification of only the inserted pattern(s).

4 Cyclic ON-OFF Activation of SWET

The centrepiece of the self-replicator is an especially designed autonomous chemical oscillator that cyclically releases an inhibitor signal (DNA strand (j^*, t_s^*, sgc_1) in Figure 1(b)) so as to switch a SWET from ON to OFF and back. Oscillator-controlled ON to OFF switching of the SWET(s) dissociates templates at the end of each cycle. However, as long as the mold remains bound to the pattern with only a few residual glues from SWETs that escape OFF switching it would reassemble instantly with the pattern upon subsequent ON switching. This would result in an overall lower efficient replication cycle, as it removes free templates from the replication process. It is therefore essential that the switching from ON to OFF occurs abruptly and completely, resulting in a comprehensive splitting of all mold-pattern complexes. Herein, an Oregonator autocatalytic reaction-system [3] is used to introduce the dynamics of a chemical oscillator.

Oregonator reactions, adopted from Soloveichik et al. [18], are shown by reactions (1-6) in Table 1. The mass-action based oscillatory dynamics can be implemented by a set of DNA-strand displacement reactions using the mapping proposed in Soloveichik et al. [18]. One of the key features of DNA-strand displacement reactions is their modularity i.e., by attaching multiple moieties to a single DNA strand, a hierarchical system of DNA strand-displacement reactions can be realised. In order to drive the ON-OFF switching of SWET(s), the inhibitor signal moiety (j^*, t_s^*, sgc_1, shown in Figure 1) would be attached with the DNA strand representing the $X2$ species in the Oregonator reaction system. The resulting reversible kinetics of the switching process is given by reaction (7) in Table 1. A bimolecular toehold exchange [23] and a unimolecular thermodynamic dissociation process represent the kinetics of the forward reaction (k_{fw})

and the backward reaction (k_{bw}), respectively. We chose k_{fw} to be $4000M^{-1}s^{-1}$ for a toehold exchange involving both the invader and the incumbent toeholds with lengths 3 nt, based on the toehold exchange model reported by Zhang and Winfree [23]. The value of $k_{bw} = 0.1s^{-1}$ for a 3 nt long duplex is derived by interpolating dsDNA dissociation kinetics data reported by Morrison and Stols [11].

Table 1. Reactions (1)-(6) form the Oregonator model; the reversible reaction (7) models the OFF/ON switching of the SWET(s)

#	Reaction	Rate constant	Species	Initial Concentration
(1)	$X2 \rightarrow X1$	$k_1 = 0.0871s^{-1}$	$X1$	$[X1]_0 = 8.8 \times 10^{-10}M$
(2)	$X2 + X1 \rightarrow \phi$	$k_2 = 1.6 \times 10^9 M^{-1}s^{-1}$	$X2$	$[X2]_0 = 3.4 \times 10^{-7}M$
(3)	$X1 \rightarrow 2X1 + X3$	$k_3 = 520s^{-1}$	$X3$	$[X3]_0 = 10^{-9}M$
(4)	$2X1 \rightarrow \phi$	$k_4 = 3000M^{-1}s^{-1}$		
(5)	$X3 \rightarrow X2$	$k_5 = 443s^{-1}$		
(6)	$X3 \rightarrow \phi$	$k_6 = 2.676s^{-1}$		
(7)	$X2 + SWon \rightarrow SWoff$	$k_{fw} = 4000M^{-1}s^{-1}$; $k_{bw} = 0.1s^{-1}$	$SWon$ $SWoff$	$[SWon]_0 = 9.8 \times 10^{-5}M$ $[SWoff]_0 = 1.8 \times 10^{-6}M$

A deterministic and ODE-based numerical simulation of the dynamics of the $X1$, $X2$, and $X3$ species, shown in Figure 3, has been performed with the COPASI software suite [6]. From the deterministic time course simulations performed by the COPASI simulator, as depicted by the oscillations of the molecule species shown in Figure 4, it is clear that the ON-state SWET and inhibitor transitions from low to high and vice versa, are abrupt. A more realistic simulation capturing the stochasticity of chemical kinetics would give even steeper transitions. The time span in which a spike of the inhibitor signal has significant levels should be larger than the time required to complete a strand displacement process (ON to OFF switching of a SWET). As the oscillator module drives the switching module of the SWET, and both modules are implemented by strand-displacement reactions, a rational design of these reactions must satisfy different timing constraints. In order to realise such a self-replicator system with maximum yield and reliability in a wet-lab implementation, two criteria must be met. First, the dynamics of SWET switching from ON to OFF should be faster than the inhibitor signal dynamics. Second, the SWET switching from ON to OFF should be driven strongly and efficiently in the presence of the inhibitor signal, ideally approaching completion.

In the simulation shown in Figure 4, ON to OFF switching is 95% complete with arbitrarily chosen parameters of reversible kinetics ($k_{fw} = 4000M^{-1}s^{-1}$ and $k_{bw} = 0.1s^{-1}$ for a three nucleotide long switching toehold) given by reaction(7) in Table 1. In this case, a mold with up to 20 SWET tiles would likely retain one tile that remains in the ON state (meaning a point of binding between mold and pattern) during the switching cycle, constituting a possible re-engagement point for mold and pattern. Although this would cause a reduction of the overall replication efficiency, the ON to OFF switching proportions

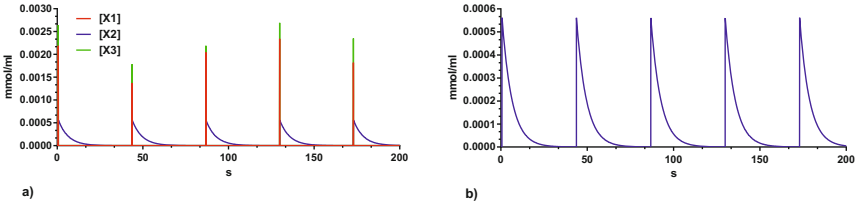

Fig. 3. The dynamics of the Oregonator model; the system parameters are those from Table 1 a) all three species X1, X2, and X3; the concentration of the $X1$ and $X3$ species is overlapping in most of the cases, though at different amplitudes; b) the oscillatory dynamics of the $X2$ species

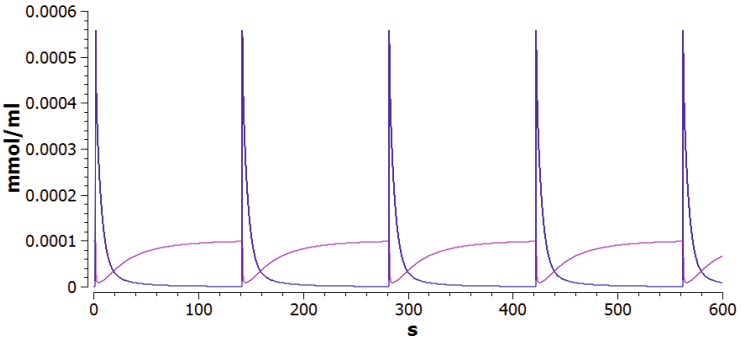

Fig. 4. Cyclic, abrupt, and virtually complete deactivation of a SWET tile using an inhibitor signal modulated by an Oregonator autocatalytic system. The blue line represents the dynamics of the inhibitor signal, while the purple one represents the concentration of the ON-state SWET. The total concentration (ON and OFF) of SWET is $10^{-4}M$.

can further be very significantly improved by increasing the switching toehold length [23] in the SWET. It therefore is reasonable to assume that a rationally designed DNA-strand displacement reaction network would be able to meet both the timing and efficiency demands of SWET-switching enabled template dissociation.

5 Tile Set Design and Implementation

In this section we present the design of tile sets and implementation details of the self-replication system for 2-D nanostructures. Let $\mathcal{P}$ be a finite set of rectangular patterns, each of them being a potential subject for replication. We can suppose without loss of generality that all the patterns have equal height, but variable lengths; otherwise we just complete the pattern using a special tile up to the desired height. We want to construct a finite collection of tiles, such

that by inserting within this system one (or several) of the pattern-types in $\mathcal{P}$, these structures would act as a template and derive only the replication of the chosen pattern (or patterns).

In the following we suggest designs of two sets of tiles — the Nano-Structure Tile Set (*NSTS*) for the self-assembly of the pattern(s) to be replicated, see e.g. Figure 5, and the Mold Tile Set (*MTS*) consisting of SWET tiles for the template assembly of the mold along the boundary of the target nanostructure. All these tiles contain only temperature 1 glues, while the temperature of the entire system is 2. In other words, all tiles require a cooperative binding process from two input sides, in order to stably attach to an existing assembly (or seed/mold).

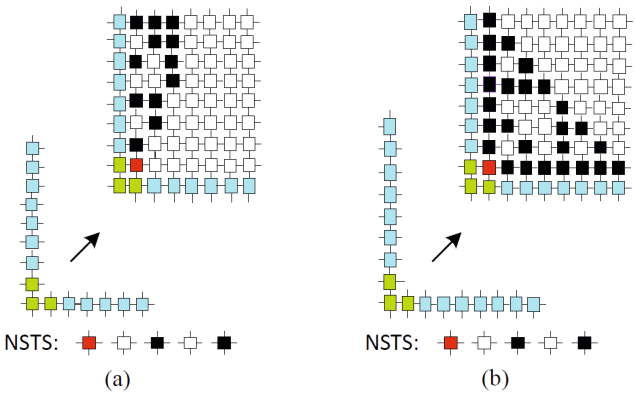

Fig. 5. Pattern assemblies starting from different "L"-shaped mold structures: (a) A three-bit binary counter pattern and a subset of the NSTS assembling it (b) the Sierpinski pattern, and a (possibly different) subset of NSTS assembling it. The two assemblies are initiated from (tile-content wise) different L-shaped mold structures.

5.1 Tile Set Design

NSTS: In order to derive an approximate-minimal tile set that can uniquely self-assemble the nanostructure pattern(s) to be replicated, we are going to employ known PATS search algorithms [5]. Recall that the Pattern self-Assembly Tile set Synthesis (PATS) problem asks to determine a set of coloured tiles such that starting from an "L"-shaped bordering seed structure, the tiles would self-assemble into a given rectangular coloured pattern. The task of finding such minimum-size tile sets is known to be NP-hard [2], even for the case when the coloured pattern is bounded to a predefined finite set of colours [17]. However, there exists an efficient search algorithm for finding approximate-minimal solutions for this problem [5].

Let $\mathcal{P} = \{P_1, P_2, ..., P_m\}$ be the finite set of patterns which might be subject to the replication process. We require (by possibly inserting a new line or column)

that all of these patterns have on their lower left corner position a unique red-coloured tile which does not appear on any other positions inside the patterns. We now create a join pattern as shown in Figure 6, containing a bordered version of the above m patterns. Namely, we introduce a new "grey" border-colour, and create lower- and left-bordered versions for each of the patterns, after which we horizontally concatenate all of them into a unique *Master Pattern*, $pattP$. By applying the PATS search algorithm on $pattP$ and then removing all the "grey"-coloured tiles, we obtain the tiles of our NSTS tile set. Note that in the worst case scenario, this set of tiles consists at most as many elements as the disjoint union of all corresponding PATS solutions for each of the individual P_i patterns.

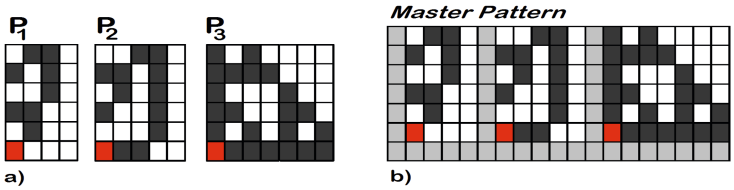

Fig. 6. (a) A set of three patterns subjected to the replication process; (b) The *master pattern* created by the concatenation of the bordered patterns

MTS: Once the NSTS tile set is established, we can construct the Mold Tile Set. This set can be split into the Bottom-Border (BottomB) tile set, forming the lower part of the mold, the Left-Border (LeftB) set, forming the left side, and the corner supertile (CST) serving as a seed for the mold assembly.

The CST seed can be seen as a merger of 8 tiles forming two layers of tiles around the corner — an inner layer of the mold seed (ILMS) having tiles that assemble with the seed of the pattern and an outer layer of the mold seed (OLMS) supporting the inner layer. The inner layer consists of ILMS-North (a SWET enabled with switching on its East glue), ILMS-middle, and ILMS-East (a SWET enabled with switching on its North glue), forming a corner-type structure; represented in green inside all of the above Figures. The outer layer consists of five tiles that are designed as to assemble with the tiles of the inner layer and form a stable structure at temperature-2. In both cases, we require that the East glue of the MS-North tile and the North glue of the MS-East tile agree with the corresponding West and South glues, respectively, of the special red-coloured tile from the NSTS tile set. Also, we define two new glues, mb and mt, and require that the North glue of the ILMS-North tile is mt, while the East glue of the ILMS-East tile is mb.

Consider now the Bottom-NSTS (B-NSTS) and the Left-NSTS (L-NSTS) sets consisting of those tiles in NSTS that appear in the bottom line, respectively the left column, of any of the P_i patterns; alternatively, we can choose these sets as the entire NSTS tile set. We define the Bottom-Glue (BG) and the Left-Glue (LG) sets as containing all South glues of tiles within B-NSTS, and all West glues of tiles within L-NSTS, respectively.

The BottomB tile set (within MTS) contains $|BG|$ tiles that form inner layer of the bottom border. For each glue $a \in BG$ we create a SWET with glue a on the North side that is enabled with switching control, and glue mbi on both its East and West sides. Similarly, the LeftB tile set (within MTS) contains $|LG|$ tiles that form the inner layer on the left border. For each glue $b \in LG$ we create a corresponding SWET with glue b on the East side that is enabled with switching control, and glue mti on its North and South sides. A fixed glue mbf is designed for South sides of the tiles of the BottomB and LeftB tile sets, which provides a binding for the tiles forming outer layer of the mold.

5.2 Implementation of the Self-replication Process

We describe here the implementation of the self-replicator for an example case of a rectangular pattern of a 2-bit counter and its seed structure shown in Figure 7(a) and (b), respectively. It is assumed that a pre-assembled pattern or seed is available at the start of the self-replication process. Tile sets required for this replicator consist of NSTS and MTS as shown in Figure 7(c). The NSTS consists of pattern forming tiles (marked by a, b, c and d) and the MTS consists of MS seed, BottomB and LeftB tiles of type SWET. A cross-catalytic cycle of self-replication involving intermediate states *I to VII* is illustrated in Figure 7(d).

The self-replication process starts with mold formation where the CST (seed of mold structure) binds at the corner of the L-shaped seed of the pattern, as shown in state *I*. The mold structure grows further as more tiles from LebtB and BottomB tile sets join as shown in states *II*, such that in stage *III* the nanostructure-mold complex is completely assembled. Recall that the tiles within MTS are all equipped with switching toeholds on their North edges. At the end of stage *III*, these switches are turned off by sending the inhibitor signal (j^*, t_s^*, sgc_1), as described in Figure 1. As a result the nanostructure-mold complex dissociates into the L-shaped seed and the mold, as shown in states *IV* and *V* respectively. The dissociated seed structure resumes the cycle involving the states (*I, II, III, IV*), whereas the newly created mold serves as a seed for the assembly of a new copy of the L-shaped seed that could also grow the rest of the pattern in parallel, see states *V, VI, VII, III*. This process leads to the creation of a new copy of the seed-mold complex, and therefore another cycle starts. The above two parallel cycles, i.e., (*I, II, III, IV*) and (*V, VI, VII, III*), can produce a monotonically increasing number of copies of both the nanostructure and the mold (i.e., 2^{n-1} such copies after n cycles), if supplied with an unlimited amount of tiles from the sets NSTS and MTS. The replication system can also be tweaked to attain a precise replication gain just by stopping the Oregonator oscillator activity. This would result into halting both of the replication cycles. Thus, by stopping the Oregonator cycle at an appropriate time-point, one could provide an exact replication gain (of the form 2^N, for some integer value N).

Taking the assumption that the tile assembly is deterministic, it can be further assumed that both the mold (cycle involving states *I, II, III, IV*) and the seed (cycle *V, VI, VII, III*) assemble in some finite time, say T_m and T_s respectively. For a reliable self-replication, the ON-OFF cycles of the Oregonator oscillator

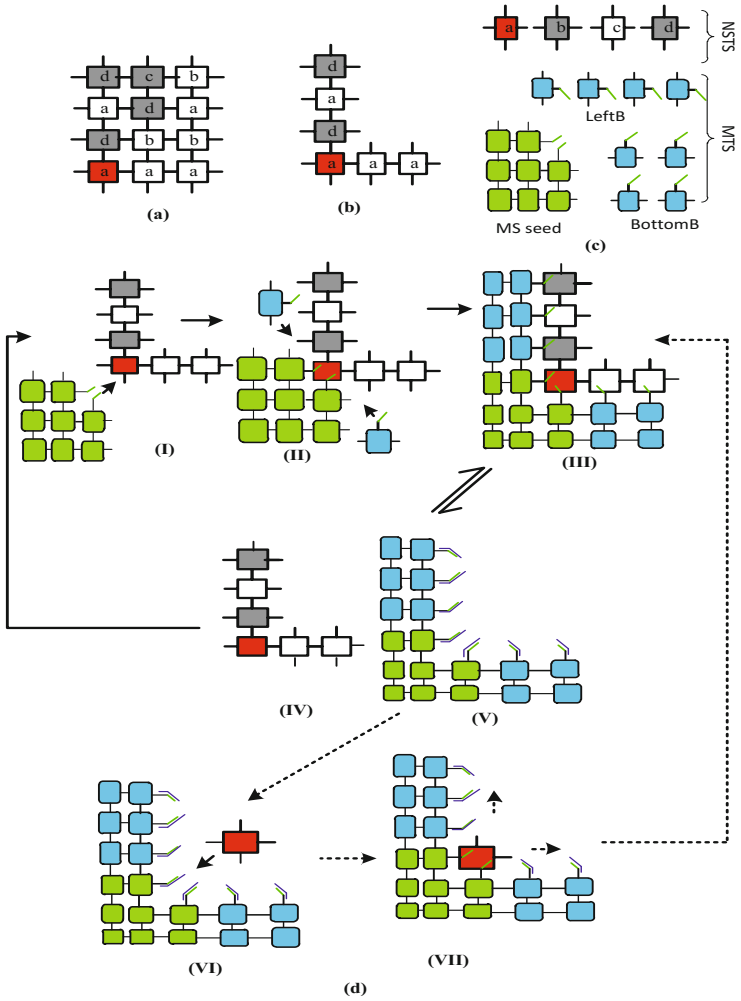

Fig. 7. Implementation of the replication process for a rectangular pattern of a 2-bit counter: (a) 2-bit binary counter pattern of tiles, (b) L-shaped seed structure of the pattern, (c) tile sets for replicator assembly and (d) cross-catalytic cycle of self-replication process

model described in Section 4 have to be synchronised with the times T_m and T_s, for example, the ON period should be larger than the largest of the T_m, T_s. In order to test if the designed oscillator can be implemented for different time periods of oscillations so as to synchronise it with the above timing requirement, we performed a parameter scan only on the activation reaction, i.e., the backward rate constant k_{bw} of reaction (7) in Table 1. We observed that the time of each

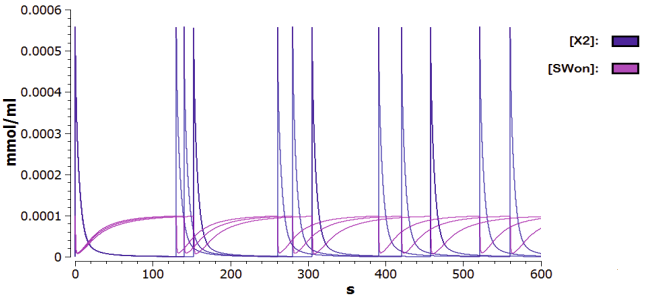

Fig. 8. A parameter scan for the rate constant k_{bw} in Table 1 for the values 0.085, 0.1, and $0.115s^{-1}$, respectively

cycle, in between two spikes of the inhibitor signal $X2$, becomes highly tunable, see e.g. Figure 8.

6 Conclusion and Future Work

To self-replicate 2-D rectangular patterns, we proposed a minimal self-replication system of DNA tiles under the aTAM framework. The replication mechanism is based on a cross-catalytic cycle, where an L-shaped seed of the desired pattern is replicated and the remaining pattern grows in parallel. The self-replicator is implemented with the help of DX-tiles and SWitching-enabled Tiles (SWET), which form the basis of an active tile assembly process where structures are dynamically assembled and disassembled with the help of an autonomous chemical oscillator that can be implemented using DNA strand displacement cascades. We also proposed a strategy for designing an approximate-minimal tile set in order to efficiently assemble a unique pattern (or a subset of patterns) out of a finite collection of possible patterns that might be subject to replication.

This work is a step forward in the direction of nanostructure self-replication, but assembly errors [20], which are common in the tile self-assembly process, pose an important potential problem that should be addressed in further work. A reliable self-replicator with error levels not exceeding a minimum threshold may further open up new directions for investigation of fundamental principles behind reproduction and selection-driven evolution.

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