Molecular ping-pong Game of Life on a two-dimensional DNA origami array

N. Jonoska¹ and N. C. Seeman²

¹Department of Mathematics and Statistics, University of South Florida, Tampa, FL, USA
²Department of Chemistry, New York University, New York, NY, USA

We propose a design for programmed molecular interactions that continuously change molecular arrangements in a predesigned manner. We introduce a model where environmental control through laser illumination allows platform attachment/detachment oscillations between two floating molecular species. The platform is a two-dimensional DNA origami array of tiles decorated with strands that provide both, the floating molecular tiles to attach and to pass communicating signals to neighbouring array tiles. In particular, we show how algorithmic molecular interactions can control cyclic molecular arrangements by exhibiting a system that can simulate the dynamics similar to two-dimensional cellular automata on a DNA origami array platform.

1. Introduction

As a discipline, computer science, or informatics, aims to advance our lives through new information and computation methodologies, as well as to explain natural processes through our understanding of how information propagates and is being computed in nature. In the past two decades, new computing paradigms inspired by natural processes such as biomolecular computing have been developed. These models are inspired by biological molecular processes and chemical self-assembly and have been shown to advance the nanotechnology needed for new material designs and our understanding of biomolecular processes. DNA-based bottom-up assembly, introduced roughly 35 years ago [1], has been explored by at least 100 laboratories in recent years. Complex DNA motifs that entail the lateral fusion of DNA double helices [2], such as DNA double
(DX), triple (TX), paranemic cross-over molecules [3,4] have been used as tiles and building blocks for large nanoscale arrays [5,6]. In addition to the two-dimensional arrays, three-dimensional structures such as a cube [7], a truncated octahedron [8], tetrahedron [9] and arbitrary graphs [10–12] have been constructed from DNA duplex and junction molecules. Techniques have been further developed for a variety of polyhedra [13–15], and the first macroscopic self-assembled three-dimensional DNA crystals have been reported [16]. The construction of approximately 100 × 100 nm two-dimensional DNA nanostructures was significantly facilitated by Rothemund’s DNA origami [17], where a standard single-stranded vector plasmid is used to outline a shape while short DNA strands connect portions of the plasmid fixing its shape in a rigid form. Since its appearance, DNA origami has been used as a seed for arranging DX tiles in an array [18], nanotube constructions [19], three-dimensional boxes (with cargos) [20,21]. Further, DNA origami, as templates for large DNA-based tiles, were arranged in a two-dimensional crystalline array [22].

The informational character of DNA makes it a perfect molecule for information processing at the nano level. Winfree [5] introduced the Tile Assembly Model and showed that two-dimensional self-assembled arrays made of DX or TX DNA tiles can simulate the dynamics of a bounded one-dimensional cellular automaton and so are capable of potentially performing computations as a Universal Turing machine. Several successful experiments have confirmed computation by array-like DNA self-assembly such as binary addition (simulation of XOR) using TX molecules (tiles) [23], Sierpinski triangle assembly [24,25], and a binary counter [18] by DX molecules. Further, transducer simulations with programmed inputs by TX DNA molecules have also been reported [26–28]. On the other side, ‘DNA fuel’ strands introduced by Yurke et al. [29] became a base for development of DNA strand displacement networks that have been shown to be able to perform digital [30,31] and analogue computation [32]. Several new designs for strand displacement computational networks attached on a two-dimensional origami platform have been theoretically proposed [33,34].

Further, ‘DNA fuel’ strands were used to produce devices that were sequence-dependent [29,35]. Such devices were incorporated in two-dimensional DNA arrays [36] as well as in the programmable DNA transducer where simultaneous programmed molecular movements were achieved [37,38]. The same mechanisms were used for structures that can perform simple ‘walking’ on an arranged platform [39–41]. Three later walking devices [42–44] showed a significant robustness such that the directions and the actions of the walker were guided by a sequence of strand displacements incorporated within the walking platform.

In many programmed structural self-assembly experiments thus far, as well as in the theoretical Tile Assembly Model, it is assumed that the DNA motifs are predesigned and they follow the programmed design to assemble structures, rarely reacting to environmental input. The cooperation between the motifs is guided by sticky ends, and once a molecule appears within a larger structure, it has no further computational interaction with its immediate environment. Such passive roles of the motifs, and the assembled structures, seem counterintuitive to the dynamic process of computation where programmed molecular interactions could produce continuous structural changes and re-use of the building motifs. Here we propose an experimentally feasible model for programmed cycles of molecular interactions that is able to continuously change molecular arrangements. This proposed system consists of a two-dimensional DNA origami array whose tiles serve as a transmission storage (equipped with ‘communication’ and ‘identity’ strands) and free floating tiles able to attach to their respective ‘identity’ counterparts on the array and transmit signals to their neighbouring locations. The array tiles are divided in a checker-board (red/green) fashion such that in an alternate manner, at each cycle, one of the colours receives the floating tiles and computes the identity of the next cycle tiles to be attached on the other colour tiles in the array. We suggest that environmental control of the cycles can be achieved by equipping red (green) identity tiles with red (respectively, green) dyes whose exposure to appropriate illumination of the appropriate wave length increases temperature and thereby can prevent attachment or disassociate the appropriate floating tiles from the array.
We also initiate a theoretical model for cooperative molecular interactions on a given platform that allows cycles of programmed molecular arrangements and dynamical information processing to be experimentally feasible; moreover, through the proposed signal transmission and molecular interactions on the predesigned array, we show how to implement two-dimensional cellular automata-like iterative arrangements, thereby providing a "modus operandi" for cyclic molecular cooperation. We have chosen a Game of Life-like (GoL-like) cellular automaton rule [45], where a cell assumes a value 1 if and only if two or three of its neighbours also have a value 1, otherwise, the cell assumes a value 0.

2. Cycles of interactive molecular arrangements

We assume a two-dimensional array (platform) where the molecules are arranged. This platform also allows molecular communication from one arrangement step to another. The model is closely related to a cellular automaton, while it differs from it in two aspects: the underlying array is partitioned into two parts and the point values alternate in their updates between these two parts. Another difference is that at a given point, the next state value depends only on the state value of its neighbours that belong to the other partition set, and not on its own value. Cellular automata assume configurations on infinite arrays, which of course cannot be implemented experimentally. We define our general model on an infinite array as well, but assume implementation on a finite rectangular array. Let $\Sigma$ be a finite set of states, which are represented by distinct molecular shapes or markers, $X = \mathbb{Z} \times \mathbb{Z}$ be the integer lattice of the plane, and for a point $v \in X$ let $N_v = \{v + (1,0), v + (0,1), v - (1,0), v - (0,-1)\}$ be the set of all four neighbouring points of $v$ in directions east, north, west, and south. The neighbourhood of each array tile in this case consists of tiles immediately up, down, left and right, also known as the von Neumann neighbourhood.

Let $X = R \cup G$ be a partition of the integer lattice into $R$ = ‘red’ and $G$ = ‘green’ points such that each lattice point has a neighbour of different colour, $v \in R$ has at least one neighbour in $G$, and each $v \in G$ has at least one neighbour in $R$. Lattice points in one of the partition sets are said to be ‘oppositely’ coloured to those of the other set. We denote with $N^C_v$ the neighbours of $v$ that are oppositely coloured from $v$. Figure 1 depicts an example of partitioning $X$ into a red set $R$ and a green set $G$ in a checkerboard fashion. In this case $N_v = N^C_v$. An arrangement is a partial map $\sigma_R : R \to \Sigma$ (red arrangement) or a partial map $\sigma_G : G \to \Sigma$ (green arrangement) indicating molecular arrangements over the red or the green points in the lattice.

The dynamics of the system are such that it alternates between red and green arrangements. For a given arrangement $\sigma_R$ (respectively, $\sigma_G$), let $\sigma_R(v)$ (respectively, $\sigma_G(v)$) be the state (type of the molecule) of lattice point $v$ in $R$ (respectively, $G$), while $\sigma_G(N^C_v)$ (respectively, $\sigma_R(N^C_v)$) is the state of the oppositely coloured neighbours of $v$. Two types of local rules $\phi_R, \phi_G : \Sigma^i \to \Sigma$ ($i = 1, 2, 3, 4$) associate a state (molecule) in $\Sigma$ to a tuple of states, representing the communication between cells in the red and cells in the green lattice points. These rules change the state of each lattice point according to the set of states of the oppositely coloured neighbouring points; if $v \in R$ then $\sigma_R(v) = \phi_R(\sigma_G(N^C_v))$ (respectively, $\sigma_G(v) = \phi_G(\sigma_R(N^C_v))$).

A system of interactive molecular arrangement is a tuple $S = (R \cup G, \Sigma, \phi_R, \phi_G, \sigma^0_R)$, where $\sigma^0_R$ is the seed arrangement. A computation of $S$ is a sequence of alternating coloured arrangements $\sigma^0_R, \sigma^1_R, \sigma^2_R, \sigma^3_R, \ldots$ such that the state at each lattice point of an arrangement in this sequence is obtained according to the corresponding local rule applied to its oppositely coloured neighbouring states of the predecessor arrangement.

Consider the interactive molecular arrangement system whose lattice partition is the checker board partition of the plane, where $R = \{(i,j) \mid i + j \text{ is odd}\}$ and $G = \{(i,j) \mid i + j \text{ is even}\}$ (figure 1). The system has two states, 0 and 1, and the two types of rules $\phi_R$ and $\phi_G$ are the same providing state value 1 to a given lattice point if and only if there are two or three oppositely coloured neighbours of value 1. These rules are similar to the Conway’s GoL cellular automaton rule where each cell in the plane lattice assumes value 1 if and only if it has two or three neighbours of value 1. Except, in GoL all cells are updated simultaneously and each cell has eight neighbours instead of four defined with $N_p$. We call this system GoL-like. An example of a $5 \times 5$ segment of the board
Figure 1. An example of a checkerboard type of a red–green partition of the plane lattice points. In this case, tile neighbourhoods coincide with the oppositely coloured tile neighbourhoods. (Online version in colour.)

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Figure 2. Iterations of the GoL-like interactive molecular arrangement system on a 5 × 5 grid. (Online version in colour.)

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with arrangements of 0’s and 1’s is depicted in figure 2, top row. The far left (red) arrangement is the seed arrangement $\sigma^0_R$. The local rule $\phi_G$ associates 1 with all green points that are surrounded by two, or three 1’s in the red seed arrangement. The next arrangement $\sigma^0_G$ consists of a green pattern of 0’s and 1’s after application of $\phi_G$, while $\sigma^1_R$ is the red arrangement obtained from $\sigma^0_G$ after applying $\phi_R$ which in this case equals $\phi_C$. In the second row, the arrangements $\sigma^1_R$ and $\sigma^1_G$ are shown under a single arrangement of $\sigma^i$ for $i = 0, 1$.

Given a finite $n \times n$ array size, and the initial $\sigma^0_R$ seed arrangement, for any rules $\phi_R, \phi_G$, the arrangement sequence $\sigma^0, \sigma^1, \ldots$ is eventually periodic. This follows from the fact that there are only a finite number of configurations and the transitions between the iterations are deterministic. For the seed $\sigma^0$ of figure 2, and the GoL-like system the sequence becomes periodic after the first three iterations (figure 3). However, the GoL-like system seems to exhibit quite complicated dynamics. Our initial experimentation on a 15 × 15 grid, as well as a 25 × 25 grid shows periodic behaviour after hundreds (respectively, thousands) of iterations for some seeds.
Figure 3. The arrangement sequence of GoL-like system on a $5 \times 5$ grid. (Online version in colour.)

Figure 4. Shapes obtained from cross-linking tiles with value 1 following GoL-like rules with initial configuration $\sigma^0$. (Online version in colour.)

One can think of the system as a ‘factory’ of shapes. The arrangement of a given set of symbols in each $\sigma^i$ can be used to cross-link parts of the arrangement such that when the floating tiles are disassociated from the the platform, they assume a shape defined by those symbols. For the example above, by cross-linking tiles with label 1, there are three shapes (figure 4) that can be obtained from a $5 \times 5$ grid initialized with $\sigma^0$ and the above GoL-like rules.

3. Experimental implementation

In this section, we describe the experimental process for implementing interactive molecular arrangements systems. There are several recent experimental advances that make implementing cyclic programmable molecular choreography feasible. DNA origami tiles assemble in two-dimensional arrays [22], while incorporated signalling strands within DNA origami have programmed a walking robot to pick-up cargo [42]. Recently, we have achieved controlled step-by-step tile assembly through signal activated sticky ends [46]. This is in contrast to the passive form of self-assembly where molecules can assemble as soon as their sticky ends find their complements, and in order to accomplish cooperative interaction (necessary for computation) one has to calibrate the temperature of the reaction very carefully. In [46], a series of five DX DNA tiles were assembled in an active cascade process. Each DX tile contains an activation site on one end, whose binding releases a signal consisting of a long intramolecular strand that releases a protecting strand on the other end, about 18 nm away. Another experimental advance that supports the feasibility of of the interactive molecular arrangements is the cyclic replication, through selection, of DNA origami dimers controlled by laser illumination and temperature. In [47], a process and a system was designed made of DNA origami tiles that exponentially replicate a seed pattern, doubling the copies in a series of diurnal-like cycles of temperature and UV illumination (for cross-linking), producing more than 7 million copies in 24 cycles. This system was used to demonstrate exponential growth and selection: two similarly growing sub-populations, one with a ‘red’ dye incorporated, the other with a ‘green’ dye, can be controlled by coloured light. The light heats one species reducing its replication rate. The progeny of
the non-absorbing species replicate preferentially and take over the system. All these advances provide a basis for the design described below.

(a) Tiles and signalling

(i) Platform and floating tiles

The proposed system consists of two parts: a platform \((n \times n\) array) assembled from tiles in a checkerboard arrangement and floating tiles that perform the cyclic arrangements by assembling on the platform. We propose to use DNA origami tiles [17] shown in figure 5 that have room to incorporate the necessary signalling and binding elements. It has been shown that these are capable of producing two-dimensional arrays [22]. The tile is constructed by a standard M13 single-stranded vector plasmid used to outline a shape while short DNA strands connect pieces of the plasmid, fixing its shape in a rigid form. The basic tile unit is a square cross structure approximately 100 nm in width and height. The helices on the horizontal part of the cross lie on top of the vertical portion of the cross.

The edges of the tile consist of the ends of six pairs of DNA double helices. The platform tiles have binding sites that are single-stranded portions contained in these helices, so that two tiles that bind would have their edge helices aligned, bound at specific helices through single-stranded overlaps. The remaining edge interactions can be mediated by favourable helix stacking between aligned helices [48]. As DNA origami can assume a variety of shapes [17], imposing geometrically complementary edges by altering the lengths of the edge helices is another method to promote correct edge matching and discourage incorrect binding.

Platform. The platform consists of two species of origami tiles, ‘red’ and ‘green’ tiles arranged in a checkerboard fashion. The checkerboard assembly of the array can be imposed by the sequence design of the edge sticky ends. Each tile is connected with oppositely coloured tiles (figure 6). The two types of tiles distinguish by the sticky ends on the two types of strands, ‘communication’ and ‘identity’ strands, attached on top of each tile (§3b), perpendicular to its plane.

Floating tiles. Although the floating tiles could have different geometry than the platform tiles, we show the same shape as the platform tiles for simplicity. These tiles have no sticky ends on
the edge helices and do not interact with the others except through single-stranded extensions perpendicular to the plane of the tile. These extensions bind to the platform identity strands and send signals to the neighbouring locations on the platform. There are two species of floating tiles, ‘red’ and ‘green’ species that can bind to the ‘red’ (respectively, ‘green’) tiles on the platform. The two species are distinguished by the IR Dyes attached on their ‘identity’ and ‘signal initiation’ strands (figure 8). The red (respectively, green) floating tiles will have IR Dyes 800 (respectively, IR Dyes 700) attached that generate heat when exposed to a 785 nm laser beam (respectively, 685 nm). The heat then both prevents hybridization in its vicinity and disassociates previously hybridized duplex. As mentioned, current experimental findings show that iterative hybridization of appropriately labelled single floating origami tiles to a system of duplex origami tiles equipped with dye labelled single strands can be controlled with laser beams [47]. Each species of floating tiles can be hairpin decorated on the opposite side of the plane from the extension strands to indicate their values (whether 0 or 1).

(b) Signal mechanism from one species to the neighbouring locations

(i) Platform strand extensions

Each platform tile is equipped with single stranded extensions, two pairs on each edge (figure 7). One of the edge extensions is the ‘communication’ signal and the other is the ‘identity’ strands.

The red (respectively, green) communication signals on the red (respectively, green) platform tiles, when triggered, interact with the green (respectively, red) identity strands on the green (respectively, red) platform tiles at the neighbouring locations. The labels on the strands indicate distinct sequences encoding that label. Barred symbols indicate Watson–Crick complements. The primed symbols 0’, 1’, etc., on the green tile indicate distinct sequences encoding the equivalent role values as 0 and 1 on the red tile. The arrows in figure 6 show the communication between the two types of tiles. The red tiles send red signals to the green tiles, and the green tiles send green signals to the red tiles. The default setting of the identity strands on the platform tiles is 0 (as depicted in figure 7). If a tile of value 1 is attached to the platform, then the identity strands of the neighbouring locations assume value 1.
Figure 7. Extension strands on the platform. The default value of the identity strands is 0, as both $\bar{0}$ and $\bar{0}'$ sequences are exposed on the red and green identity tiles (ID). If a red tile of value 1 attaches to the platform, $\bar{0}$ and $\bar{y}$ will initiate strand displacement on the floating tile (figure 8) exposing segment $\bar{B}$ on the red communication duplex (CM). This will allow the free segment $B$ on the green identity duplex to interact with the newly freed $\bar{B}$ and expose $\bar{1}'$ on the green identity tile as that green edge value in the next cycle. (Online version in colour.)

Figure 8. Extension strands on the platform and on the floating tiles. (Online version in colour.)

(ii) Floating tile extensions

Each edge of a floating tile is equipped with an identity strand. Each identity strand hybridizes to an identity strand on the platform (there are four such strands on the platform tile) and ‘recognizes’ the value of the neighbouring tile. The combination of the four identity strands determines the value of the tile (i.e. in our case, if there are 2 or 3 identity strands with value 1, then the floating tile has value 1, otherwise it has a value 0). The value of the tile is indicated with hairpin labelling on the other side of the tile. Only tiles of value 1, when attached to the platform, transmit signals to the neighbouring locations indicating their value 1. Tiles of value 0 do not transmit their value. In figure 8, an edge on a red tile with identity attachment strand 1 is depicted. An identity attachment strand 0 on a tile of value 1 has a similar construction, except in that case the single stranded portion is 0 instead of 1.

(c) Cyclic communication on the platform

We propose that the signalling across and between tiles be accomplished with a combination similar to the reversible strand exchange mechanism [30,31] (figure 9). This method is based on the toehold-mediated strand exchange introduced by Yurke et al. [29] and was also used by the authors for designing a programmable input for finite-state automata with output. It is closely related to the Omabegho et al. [43] autonomous cascade walker. The essence of the method is in the following: if in a solution containing two strands $ab$ and $\bar{c}\bar{b}$, where $b$ and $\bar{b}$ form a duplex, a third strand $\bar{a}b$ complementary to $ab$ is introduced, the strand $\bar{c}\bar{b}$ is replaced in the duplex by $\bar{a}\bar{b}$. In this case, the sequence $a$ is said to be a ‘toehold’.
Interaction leaves toehold B the corresponding complementary signal initiation strand on the floating tile (figure 9). The middle duplex with complementary $\bar{x} \cdot x$ starts forming. (b) Middle duplex $\bar{x} \cdot y$ on the red floating tile is formed and the red signal strand $\bar{A} \cdot \bar{B} \cdot \bar{1}$ is exposed. (c) Toehold A from the red communication strand interacts with the red signal strand on the floating tile forming the duplex $\bar{A} \cdot \bar{B} \cdot \bar{1}$ and freeing the toehold B on the green identity tile to interact with $\bar{B}$ segment on the newly formed single strand of the communication duplex. This exposes $\bar{1} \cdot \bar{0} \cdot y$ on the green identity tile. (d) Green laser beam stops and green floating tile whose corresponding edge value is 1 is being attached (indicated with a small green square for clarity). (e) Red laser beam is activated and duplexes formed with strands containing the red dye are dissociated. If the attached green floating tile has value 1, signal transmission equivalent to (a–c) on the red floating tile is initiated but is not depicted. (f) The red tile detaches and toeholds A and 0 in the middle duplex start reacting with the single-stranded portions with dyes bringing the strands on the red floating tile edge in the original form. (Online version in colour.)

Figure 9 shows a schematic view of the cascading signal transmission on the platform upon attachment of a red tile of value 1 with edge identity strand of value 1. With each strand displacement, there is a gain of some base pairs (we anticipate 4 base pair gain). Figure 9a shows an edge of a red tile attached to the platform. Due to the 685 nm laser beam emission, the green tiles are not attached. Upon hybridization of the portion $1 \cdot 0 \cdot y$ on the identity strands, the portion $x \cdot y$ in the middle duplex of the floating tile forms, and dissociates the segment A from the side strand containing $A \cdot B \cdot 1'$ with the red dye. This process ensures that there is no communication on the platform before the floating tile is being attached, and the strand migration process leaves a time lapse between the attachment of the red tile and the release of the toehold A (figure 9b). The toehold A on the communication strand of the platform is free to interact with the corresponding complementary signal initiation strand on the floating tile (figure 9c). This interaction leaves toehold B to interact with the identity strands on the green tile leaving $\bar{y} \cdot \bar{0} \cdot \bar{1}'$ free to ‘identify’ a green tile. As soon as the green laser beam is stopped, the green dyes stop emitting heat and the green floating tiles are free to attach to the platform (figure 9d). In figure 9d, the green tile is depicted with a small green square for clarity of the figure. If the attached green tile has value 1, the strand interactions on the green tile appears, similarly to the red floating tile depicted in figure 9a,b but is not pictured.

When the red 785 nm laser beam is activated, both red and green floating tiles are attached on the platform but only the red dyes on the red floating tiles start emitting heat and disassociate the labelled strands from their complements (figure 9e). The amount of heat is proportional with the reciprocal value of the distance $r$, i.e. $T(r) = T_0 + \Delta T(R/r)$, where $T_0$ is the ambient temperature and $\Delta T$ is the change in temperature over distance $r$ with heat source of radius $R$. This means that...
at distance 28–30 nm there is a change of 1°C when a sphere of the DNA duplex size (3.5 nm) is heated by 8°C. The origami tile allows for more than 30 nm distance between the red and green monochromatic duplexes in (figure 9d), hence the effect of the heat emitting red dye on the green duplexes can be kept on less than 1°C. With the application of 785 nm laser beam, the floating red tile is not attached to the platform any more and is free to float in the solution. The energetically favourable base pair gain (i.e. increased favourability of ΔG) eventually brings the identity and signal initiation strands of the floating tile to their original condition and leaves the identity and the communication duplex on the platform red tile in the same condition as when no red tile was attached figure 9f. If the attached green tile has value 1, then its attachment (equivalently to the red tile) would communicate its value to the red identity strand on the red platform tile, such that when the red 785 nm laser beam is stopped, the red floating tiles can attach to the platform and the cycle can continue from situation (a).

(d) Game of Life-like implementation

Tile types. For the implementation of the interactive molecular arrangement system that simulates the GoL-like function, we need six types of floating tiles in each species of red and green tiles. Because the origami tiles are symmetric and the function that we propose depends on only the number of neighbouring tiles being 1 or 0, and not on their locations (north, south, east or west), there are three types of 0-tiles and three types of 1-tiles. The schematic of the tiles is depicted in figure 10. The values of the edges of the tiles indicate the values of the identity strands attached on the floating tiles, and according to their values, the tile takes the identity 0 or 1. The edges of the 1-tiles are also equipped with signal initiation strands such that upon their attachment they communicate through the platform with the neighbouring locations.

Initialization and computation. As the default values of the platform identity strands is 0, one can establish the control between the attachment and detachment cycles with all values 0 first. For a platform initialized σ^0_R as in figure 2, a platform can be constructed by first hybridizing a red floating tile of the appropriate value to the red platform tile at the appropriate location, and then the duplex of red tiles would be used together with the green platform tiles to assemble the initialized platform. Each platform tile can have its location specified by the location designed sticky ends; therefore, the platform tile of the red duplex of platform-floating tile can take its place in the array at the appropriate location guided by its and neighbouring green platform tile sticky ends. As the platform is initialized, the communication signals on the platform will interact with the green platform tiles. The situation at that stage is as in figure 9b. Subsequently, the cyclic molecular arrangement continues as described in §3c. A robust error control used in [49] can be applied to prevent attachments of partially matched floating tiles while allowing complete matching of the floating tiles.

4. Concluding remarks

The proposed laser illumination technique introduces ‘clock’ controlled programmed dynamics in molecular arrangements, and the platform/floating tile signals introduce molecular
communication for cyclic molecular arrangements thereby providing a controlled molecular choreography over a predesigned array. There are many examples of incorporating signal-transmission strands on a DNA origami, and most of these models are based on the Yurke et al. [29] design for a strand-displacement mechanism using toeholds. These signals are used for either static control of tile assemblies [50–52], or for designs of pathways simulating logic gates (e.g. [33,34]). In the first case, the assembled structure is static once assembled; while in the latter case, there are no arrangements except signal propagation throughout the system of logic gates. The use of environmental control (laser beam) to move from one arrangement cycle to another, introduces time steps in an intrinsically asynchronous system of molecular assemblies.

A clocked control is an essential part of information processing, so many new models where molecular interactions follow a step-by-step dynamics could be designed. Here we have shown one such model where the molecular arrangements represent the time-step development of a two-dimensional cellular automaton like function thereby initiating the study of such systems. Our suggestion of using two types of IR Dyes to control the clock is only one way for such clock. It has been observed that other materials attached to DNA can produce heat locally upon laser illumination such as small gold nanoparticles (1.4 nm gold particle melting a 7 base duplex [53]) and different shapes of particles (coated gold ‘nanorods’ and ‘nanobones’ absorbing and melting DNA at two different wavelengths [54]). Further experimentation will examine the limitations and possibilities of these approaches.

The theoretical limits of the proposed new approach to molecular arrangements are not yet known. It is well known that the GoL has universal computational power. It is also known that predicting the value of a cell in $n$ iterations of the GoL is P-complete [55]. The finiteness of the implemented system (finite platform) restricts the power significantly, so its actual computational capability warrants further investigations. The computation in the proposed system also depends on the type of partition that is assigned to the plane lattice. Some possibilities are depicted in figure 11. There are patterns that can be obtained over one partition, but could not be acquired over others, hence investigation of these questions is of interest. Furthermore, an experimental confirmation of the cyclic dynamic algorithmic arrangement would be the first demonstration of programmed cyclic molecular movements that can be seen as an incarnation of nucleic acid robots (nubots) acting on a platform. Although there are theoretical models for nubots (e.g. [56]), there are no experimental suggestions for their development. While the last years’ robotics breakthroughs [57,58] were achieved with electronic components, the proposed system opens doors for advancing such designs at a molecular level.

**Competing interests.** We declare we have no competing interests.

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