

# Dimension Augmentation and Combinatorial Criteria for Efficient Error-resistant DNA Self-assembly

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## Abstract

DNA self-assembly has emerged as a rich and promising primitive for nano-technology. Experimental and analytical evidence indicates that such systems are prone to errors, and accordingly, several error-correction mechanisms have been proposed for the tile model of self-assembly. These error-correction mechanisms suffer either from high resolution loss or a large increase in the number of tile-types. In this paper, we propose dimension augmented proof-reading, a technique that uses the third dimension to do error-correction in two dimensional self-assembling systems. This involves no resolution loss in the two dimensions of interest, results in a smaller increase in the number of tile-types than previous techniques, and appears to have the same error-correction properties.

Error-correcting systems need to be analyzed in the kinetic Tile Assembly Model; such analysis involves complicated Markov Chains and is cumbersome. In this paper, we also present a set of completely combinatorial criteria that can be used to prove properties of error-correcting self-assembling systems. We illustrate these criteria by applying them to two known proof-reading systems, one of which was not previously known to work. We then use these criteria to prove the correctness of dimension augmented proof-reading applied to a self-assembling system that computes the parity of a string.

## 1 Introduction

Since objects at the nano-scale are not easy to manipulate explicitly, bottom-up self-assembly has emerged as a promising primitive for nano-technology. DNA is a particularly useful substrate for molecular self-assembly since its combinatorial nature allows it to store infor-

mation, efficiently and the existence of complementary strands makes it easy for two different fragments to combine with great specificity. In addition, lab techniques for manipulation of DNA are already well developed. As a result DNA self-assembly has been used in a variety of ways including as a means to perform computation [3, 26], to produce patterns [21] and to produce nano-scale machines [19, 29, 18]. While the results we develop here are aimed at DNA self-assembly specifically, other self-assembly models have much in common, and we believe our techniques to be more generally applicable.

DNA tiles which self-assemble according to simple rules have been developed in the lab [25] and also analyzed formally, using the asynchronous Tile Assembly Model (aTAM), introduced by Rothemund and Winfree [15]. Under this model we imagine a set of square tiles with a “glue” on each side. Each glue has a certain affinity for itself called its strength. The process starts from a distinguished seed tile. Assembly proceeds as tiles attach to the structure one by one when the combined strength of nearby matching glues is at least as large as the “temperature” of the system. Many interesting systems have been designed under aTAM including systems that produce counters [1, 15, 9, 2], do Turing-universal computation and produce arbitrary computable shapes [12, 21, 4].

Unfortunately, in the laboratory setting, several events that aTAM does not model have been observed. One problem, the focus of this paper, is that not all attachments happen with what would be considered sufficient strength in the aTAM model. Tiles may attach to the system with strength 1 even if the temperature of the system is 2. Normally, such attachments will not be stable and fall off quickly. Occasionally though, another attachment may occur nearby before the first attachment falls off. When this happens a tile may become stable in a location aTAM would not predict. Such “errors” (or as we call them, “insufficient attachments”) can cause systems that produce good structures in aTAM to get derailed quickly in a laboratory setting. The experimental rate of such attachments is somewhere between 1 and 10 percent, which presents a

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significant obstacle to practical self-assembly. Various schemes to reduce the impact of such events have been studied previously [6, 13, 16, 19, 24, 5]

A more sophisticated stochastic model was introduced by Winfree [21]. This kinetic Tile Assembly Model (kTAM) calculates rates for various types of attachments and removals based on thermodynamic constants. Analysis of systems in this model becomes much more complicated, especially since a bad string of low-strength attachments always has some chance of occurring. Thus, the goal under this model is to prove that the desired structure will form with high probability. Analysis under kTAM involves complex Markov chains and is cumbersome. Even when there is reason to believe a tile system has good error-correction, verifying any properties under the kinetic model from scratch has proved to be very difficult. Further, analysis of one error-correction system does not offer much insight towards analyses of other such systems. What is needed is a general set of criteria that, once verified, guarantee fast, correct assembly in spite of insufficient attachments.

The first error-correction mechanism that was proposed for the tile assembly model was proof-reading [24]. This involved replacing each tile in the original system by a block of  $k \times k$  tiles. Every attachment is “proof-read” by other tiles in the block, and an insufficient attachment results in growth getting stalled and the error ultimately getting corrected with high probability. This technique works well as long as the errors occur at the expected growth locations. However, this scheme does not protect against errors that occur on facets of the growing assembly that are far from the correct growth location. Snaked proof-reading, introduced by Chen and Goel [6], rectifies this problem and under mild assumptions is provably robust. Some preliminary experimental evidence points to the efficacy of this approach [8]. However, this scheme also involves replacing each tile by a  $k \times k$  block of tiles. In order to achieve both near-optimum speeds and low error rates,  $k$  needs to be as large as  $\Omega(\log n)$ , where  $n$  is the size of the shape being self-assembled. We call  $k$  the resolution loss. Since the goal of DNA self-assembly is to produce nano-scale shapes, the large resolution loss required by both schemes is quite problematic. This problem has been an open question over the last few years and has proven to be notoriously hard. Reif et al. [13] proposed the notion of compact proof-reading, which in some cases achieves robustness without a loss of resolution. However, it was later proven that such a scheme cannot possibly work in general, and often requires an exponential (in  $k$ ) increase in the number of distinct tiles used in the self-assembly process in order to match  $k \times k$

proof-reading [19]. Since each such distinct tile is a separate component that needs to be designed, built, and tested, this is also not a desirable solution. Obtaining a system that has both low resolution loss and a small increase in the number of tiles has been an important open problem.

We have not been able to find a 2-dimensional system that has the above properties. The lack of good analysis techniques has been another problem. We make progress in both directions by introducing combinatorial criteria (under mild assumptions) for correctness of error-correction schemes in the kinetic Tile Assembly Model, and by using the third dimension for proof-reading a two-dimensional self-assembly.

## Our results

**Combinatorial criteria:** Generally we have some intuition about how a tile system should grow “normally” given an error-correcting scheme. Turning such intuitions into proofs has proven extremely daunting. The large number of cases that must be considered makes direct analysis intractable, and we believe the lack of proof techniques has been a fundamental barrier to progress in this field. We provide a simple framework that can be used as a black box to analyze error-correcting systems for self-assembly. Towards this end, we first introduce the notion of “milestone graphs” that reflect our idea of how progress should occur and so that given one milestone we will reach the next milestone before any unrecoverable errors happen. If we can show that we make it from milestone to milestone with high probability, eventually we’ll get to the structure we want. We present combinatorial criteria that make this intuition rigorous and allow us to present a proof of reliable assembly for new error correction systems quickly. These criteria assume that tiles held by strictly larger strength than the temperature never fall off. Removing this assumption remains an interesting open problem. These criteria are presented in section 3. We then illustrate these criteria by applying them to an error-correction system that was previously believed to have good properties but lacked a proof in section 3.3. We also use these criteria to obtain a more concise proof of the correctness of the snaked proof reading system in section 3.4. We finish by proving the correctness of these criteria in section 5.

**Dimension augmented proof-reading:** As mentioned previously, low resolution loss error-correction has been a challenging problem. We propose a method of producing a system that has no resolution loss in the original dimensions of growth and only a small increase in the number of tiles. To achieve this result, we use a previously unstudied method: growing

our tile system into the third dimension. While 3-d tile sets do not yet exist in the lab, some preliminary work has been done toward constructing three-dimensional systems experimentally [10, 27]. If we had such a tile set we could harness the extra dimension by laying multiple copies of the same system on top of each other, so that an error must occur in each copy before it is likely to persist. We believe such a system can guarantee correctness for arbitrary rectilinear systems, but we have no complete proof so far. Still, as proof of concept though, we can show that dimension augmentation provides correctness for the parity system, which calculates the parity of a string given as input. To achieve this result, we use our combinatorial criteria in section 4.

There are other aspects to error-correction, including self-healing [23, 7] and controlled seed nucleation [16]. Also, other paradigms for DNA self-assembly have been proposed, most notably DNA origami [14]. Finally, great progress has been made recently in designing DNA machines that have a self-assembly flavor [17, 28, 18, 20]. A detailed treatment of these issues is beyond the scope of this paper; however, we encourage the reader to pursue some of these threads. Before proceeding with the rest of this paper, we provide formal definitions for many of the terms we have been using informally.

## 2 Definitions

The tile assembly model we use here was originally presented by Rothemund and Winfree [15]. Informally, we can think of a tile as a square with glues on each side. Two tiles will want to attach to each other if they have compatible glues.

Formally, tile assembly takes place on a  $d$ -dimensional rectangular lattice ( $d$  is 2 or 3 in our examples).  $\Sigma$  is an abstract set of glues including a special glue *null*. A *tile*  $t$  is an element of  $\Sigma^{2d}$ . There is a strength function  $\sigma$  from  $\Sigma$  to  $\mathbb{Z}_{\geq 0}$  with  $\sigma(\text{null}) = 0$ . We associate each coordinate of  $t$  with one of the outgoing directions on the rectangular lattice. A *tile system* is a tuple  $\langle T, s, \Sigma, \sigma, \tau \rangle$ . Here,  $T$  is a set of tiles,  $s$  is a distinguished *seed tile* drawn from  $T$ , and  $\Sigma$  and  $\sigma$  are defined as above.  $\tau$  is the *temperature* of the system. A *tile configuration* is a mapping from  $\mathbb{Z}^d$  to  $T \cup \{\text{empty}\}$ . Initially, our configuration consists of  $s$  at the origin and *empty* at all other coordinates. In the *asynchronous Tile Assembly Model* a tile  $t$  may attach at an *empty* position  $p$  if the sum of the strength of its glues that match the corresponding glues in adjacent positions is at least  $\tau$ . Formally, if  $B$  is the set of vectors that are plus or minus one on one coordinate and 0 elsewhere,  $t_b$  is the glue corresponding to the direction indicated by

$b \in B$ , and  $\text{tile}(p)$  is the tile occupying coordinate  $p$  then  $t$  may attach at  $p$  if  $\sum_{b \in B | \text{tile}(p+b)_{-b} = t_b} \sigma(t_b) \geq \tau$ . Assembly proceeds by selecting non-deterministically from all possible attachments.

In practice, attachments happen that don't conform to aTAM. In general, any tile may attach to any other with even one matching glue, leading to assemblies that may not be possible in the aTAM model. The *kinetic Tile Assembly Model* (kTAM) originally presented by Winfree [21] more accurately reflects this possibility. Under this model we again assume that assembly only proceeds by single tiles attaching to an existing assembly. The model uses two thermodynamic parameters  $G_{mc}$  and  $G_{se}$ . In *kTAM* tiles attach to any matching glue at the *forward rate*  $f = \alpha e^{-G_{mc}}$ . A tile held by strength  $b$  will fall off at rate  $\alpha e^{-bG_{se}}$  (for  $b = \tau$  we call this quantity the *reverse rate*  $r$ ) for some constant  $\alpha$ . By tuning  $G_{se}$  and  $G_{mc}$  (in practice, by altering the temperature of the solution and the lengths of the strands) we can alter the stochastics of the assembly process.

For the purposes of this paper we will further assume that tiles held by strength greater than  $\tau$  do not fall off. We define two adjacent positions containing tiles to be *connected* in a configuration if there is a strength one or greater glue between them. A set of positions in a configuration is a *connected structure* if there is a connected path from any position to any other in the structure. We define an insufficient attachment to be the addition of a tile at strength less than  $\tau$ , counting an attachment at strength  $\tau - i$  as  $i$  insufficient attachments. A set of positions is *semi-connected* in a configuration if it can be made connected without further insufficient attachments (i.e. under aTAM). A *k-bottleneck* is a structure that can only appear in configurations that cannot be assembled with fewer than  $k$  insufficient attachments. For two configurations  $C$  and  $D$  we say  $C \rightarrow D$  if  $D$  can be produced from  $C$  with a single attachment of strength  $\tau$  or greater and  $C \rightsquigarrow D$  if there is a sequence of such attachments from  $C$  to  $D$ .

## 3 Combinatorial Criteria for error-resistant assembly

In this section we present our combinatorial criteria. Any system that obeys our criteria can be made to assemble quickly and reliably under kTAM. At first look our criteria are complicated, and we need to make several auxiliary definitions to describe them. However, when looked at in the context of an actual tile system the definitions make much more sense and are generally easy to verify. First, we present the definitions of the augmentations to our system. Then we lay out the actual criteria. Finally, we illustrate the criteria by

applying it to two systems.

**3.1 Tile System Augmentation** To prove our desired theorems we will need to define auxiliary structures on top of our tile assembly model. These should be thought of as guidelines to a proof, and we are free to choose them however we want. Provided they obey the criteria in the next subsection, our theorems will hold.

For non-empty coordinate  $p$  and tile configuration  $C$  define  $E(p, C)$  a boolean *malignancy function*. If  $E$  is true for a given position and configuration we say the position is *malignant* in the configuration. Otherwise, it is *benign*. Any position with a tile we would consider incorrect (i.e. not the tile that is supposed to be there in the final assembly) should be malignant, but other tiles may be malignant if, for example, they are correct but attached using an incorrect tile. A set of positions is malignant in a configuration if every tile in it is malignant in that configuration. The malignancy range of a malignant tile  $t$  at  $p$  is the union of all positions in connected malignant structures that are not  $k$ -bottlenecks and have  $t$  at  $p$ . We say a malignant tile  $t$  gets corrected at time  $S$  in an assembly process if every tile in  $t$ 's malignancy range is benign at time  $S$ . In addition, we have a directed acyclic graph  $G = (V, E)$  called the *milestone graph*. We have two functions from the milestone graph to the configuration space,  $\Phi_1$  and  $\Phi_2$ . The graph and its associated configurations represent checkpoints we expect to reach during assembly, with  $\Phi_1$  representing a configuration that should be around long enough once we reach  $\Phi_2$ . The graph has a unique source  $v_s$  and a unique sink  $v_t$  with  $v_s$  representing the seed structure we want to build from and  $v_t$  representing the structure we want at the end. In addition we need to bound the size of various quantities in our system, so we add five polynomially bounded functions,  $p_1$  through  $p_5$ .  $p_1(k)$  bounds the size of a malignant structure that is not a  $k$ -bottleneck. Functions  $p_2$  and  $p_3$  are used to bound the number of tiles needed to attach to go from a configuration of one node on the milestone graph to an adjacent node. Functions  $p_4$  and  $p_5$  are used to bound the number of distinct types of tiles.

**3.2 The Combinatorial Criteria** Once we have defined the augmentations we need to verify that they obey a set of criteria. We are given a sequence of increasingly large assembly systems parameterized by  $n$ . For each of these systems, we produce a set of error-correction schemes parameterized by  $k$ . While the criteria seem esoteric at first, they are natural constraints given that the functions represent what we think they should. In practice, most of these criteria

should be easy to prove given good definitions as we show in the next subsection.

**DEFINITION 3.1.** *An augmented tile assembly system obeys the error-free assembly criteria if the following are true:*

1. *If  $E(p, C)$  is benign for all  $p$  then no malignant tile may attach to  $C$  with strength  $\tau$ .*
2. *If the tile at  $p$  is benign in  $C$  then it is benign in all configurations reachable from  $C$  by removal of tiles attached with strength less than or equal to  $\tau$  or by arbitrary tile additions.*
3. *For any configuration  $C$  if  $C(p) \neq \Phi_1(t)(p)$  then  $p$  is malignant in  $C$ .*
4. *For any configuration  $C$  that is not a  $k$ -bottleneck all semi-connected malignant structures have size bounded by  $p_1(k)$ .*
5. *For any configuration  $C$  that is not a  $k$ -bottleneck all malignant structures have at least one tile held by strength less than or equal to  $\tau$ .*
6. *The longest path in  $G$  has length at most  $n$  and  $|V| \leq n^2$ .*
7. *For any node  $v \in V$  either  $\Phi_1(v) = \Phi_2(v)$  with each tile held by strength at least  $\tau + 1$  or  $\Phi_1(v)$  can be constructed from  $\Phi_2(v)$  using  $\Omega(\log n)$  attachments such that each attachment is adjacent to the previous and every tile but the newest one is held by strength  $\tau + 1$  in all intermediate structures.*
8. *For any edge  $(u, v)$  in  $G$ ,  $\Phi_i(u) \rightsquigarrow \Phi_i(v)$ .*
9. *For any node  $v$  with incoming nodes  $v_1, \dots, v_i$   $\Phi_1(v)$  can be formed from the union of all  $\Phi_2(v_i)$  using either  $p_2(k) + p_3(\log \log n)$  tile additions in arbitrary positions or  $2^{p_2(k) + p_3(\log \log n)}$  sequential tile additions such that each added tile is connected to the previous. Note that the previous two criteria imply that this union is well-defined.*
10. *The number of distinct tiles is at most  $2^{p_4(k)} p_5(\log(n))$*

The criteria guarantee quick error-free assembly of the final structure as is expressed by the following theorem.

**THEOREM 3.1.**  *$\Phi_1(v_t)$  will be assembled in time  $O(n^{1+\epsilon})$  with high probability for any  $\epsilon > 0$ .*

The proof of this theorem is quite complicated and we defer it until later. Instead, we now illustrate the application of the criteria to a system.

**3.3 Using the combinatorial criteria** In this section, we illustrate the utility of the combinatorial criteria, by proving the correctness of proofreading scheme. The scheme was proposed by Winfree [22] but its correctness was previously unknown. The scheme improves systems of the following type:

The system works at temperature two and has an L-shaped seed with  $n$  tiles on each arm. It has a number of tiles bound by a polynomial function of  $\log \log n$  with only strength 1 glues and the growth occurs in a rectilinear fashion - from south to north and from west to east. With correct growth, it forms an  $n \times n$  square with a unique pattern.

To improve this kind of system, each tile  $T$  in the original system is replaced by a  $(k+1) \times (k+1)$  block  $T_{1,1}, T_{1,2}, \dots, T_{k+1,k+1}$ . The glues between  $T_{k,k}$  and  $T_{k,k+1}$ , between  $T_{k,k}$  and  $T_{k+1,k}$  and between  $T_{k,k+1}$  and  $T_{k+1,k+1}$  have strength two; the glues between  $T_{k,1}$  and  $T_{k+1,1}$  and between  $T_{1,k}$  and  $T_{k,1}$  are inert; all the other internal glues have strength one. An illustrative example with  $k=3$  is shown in figure 1(a) with the growth order described by figure 1(b). When all striped tiles on a block are attached they are all held by strength at least three and will not fall off.

The glues internal to the block are unique within the block and don't repeat in any other blocks. Informally, the blocks attach to each other using the same logic as the original system. The new system has an L-shaped seed with  $(k+1)n$  tiles on each arm. With correct growth, it will make a  $(k+1)n \times (k+1)n$  square with the same pattern as the original system. We denote the block in the  $i$ -th column counting from the west and the  $j$ -th row counting from the south by  $B_{i,j}$ . Now we can define the certificate for the combinatorial criteria.

**Certificate:**

**The milestone graph:** The milestone graph has  $(n+1)^2$  vertices  $V_{i,j}$ ,  $0 \leq i, j \leq n$ .  $\Phi_1(V_{i,j}) = \Phi_2(V_{i,j})$  is the configuration where the blocks  $B_{u,v}$  are in place for  $1 \leq i < u$  and  $1 \leq j < v$ , all striped tiles in blocks  $B_{i,x}$  and  $B_{y,j}$  are attached for  $1 \leq x \leq j$  and  $1 \leq y \leq i$  and all the other locations are empty. There is a directed edge between  $V_{i-1,j}$  and  $V_{i,j}$  and between  $V_{i,j-1}$  and  $V_{i,j}$  for every  $i, j$ . The source  $s = V_{0,0}$  and the sink  $t = V_{n,n}$ .

**Malignancy function:** We call position  $X_i$  be another position  $X_j$ 's ancestor if a tile must attach at location  $X_i$  before any tile can attach at location  $X_j$  in aTAM. Given a configuration  $C$  and location  $X$  in  $B_{i,j}$ , the malignancy function  $E(X, C)$  is benign if and only if either all for all locations  $Y$  which is an ancestor of  $X$ , we have  $C(Y) = C_1(t)(Y)$  and  $C(X) = C_1(t)(X)$  or  $C(X)$  is empty.

**Polynomially bounded functions:** We also set  $p_1(x) = x^3$ ,  $p_2(x) = x^2$ ,  $p_3(x) = 0$ ,  $p_4(x) = x^2$ ,  $p_5(x) = x$ .

In the rest of this section, we prove that the ten criteria mentioned in the previous section are all satisfied.

**Criterion 1:** Criterion 1 says that when all tiles are correct, bad tiles cannot attach without an insufficient attachment. Notice that all tiles are benign if and only if the current configuration can be reached using aTAM. In such a configuration, adding tiles with strength  $\tau$  will result in another configuration reachable using aTAM, and thus all tiles are still benign.

**Criterion 2:** Criterion 2 says that a tile that is benign in the current configuration should remain benign in all configurations reachable from that configuration under aTAM. If a tile is benign, then all its ancestor locations are filled with benign tiles held by strength at least three. Hence, the tile is still benign if some tiles held by strength at most 2 are removed. Adding tiles also doesn't change any benign tile to be malignant.

**Criterion 3** Criterion 3 says that any position that has a tile it shouldn't have in the final configuration should be considered malignant and follows directly from the definition of the malignancy function.

**Criterion 4:** Criterion 4 says that a malignant structure cannot get too big unless there are a lot of errors. We prove Criterion 4 using the lemmas below. Since all glues interior to a block are unique to that block, it suffices to consider malignant structures on the boundary of blocks. Consider a malignant that happens on the east edge of the assembly. Define a *nucleation site* on the east boundary to be a block shifted by one row to the south.

LEMMA 3.1. *For  $m$  insufficient attachments ( $1 \leq m < k$ ), the width of the resultant tile attachments (number of columns attached) is at most  $2m$  and the height is at most  $m$ .*

*Proof.* Since there are no strength two glues between any two columns in the first  $k-1$  columns, one insufficient attachment is required for the width to increase by one. The lemma follows.

LEMMA 3.2. *Any connected malignant structure  $X$  that is not a  $k$ -bottleneck only has tiles in at most  $k-1$  nucleation sites.*

*Proof.* By lemma 3.1, we know that there is no strength two glue anywhere inside the malignant structure. There is an inert edge at the first column (counting from west) between every two adjacent nucleation sites. Therefore, no tile can attach at a nucleation site unless

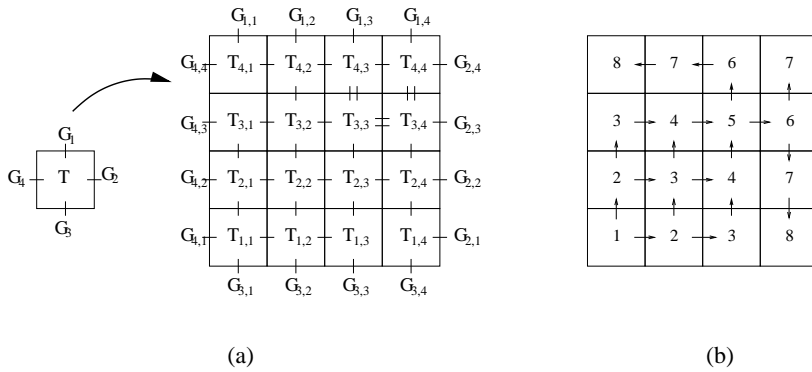


Figure 1: (a) The structure of 4x4 block. (b) The order of the growth.

one insufficient attachment happens and the lemma is proved.

The above two lemma shows that any semi-connected malignant structure on the east side that is not a  $k$ -bottleneck has size at most  $(k+1)(k-1)^2$ . The malignant structures on the north side are similar.

**Criterion 5:** Criterion 5 says that all malignant structures that are not caused by too many errors have a tile that can fall off. Since the height of the malignant structure is at most  $k$ , we know that all interior glues have strength at most one. Therefore, the tile on the northeast corner of the structure are held by strength at most two.

**Criterion 6:** Criterion 6 says that it doesn't take too many steps to get from the beginning to the end of the milestone graph and is true by definition.

**Criterion 7:** Criterion 7 says it takes a long time for enough of  $\Phi_2(v)$  to fall off to get to  $\Phi_1(v)$ . For all nodes  $v$ , we know the  $\Phi_1(v) = \Phi_2(v)$  and all tiles in  $\Phi_1(v)$  are held by strength at least three.

**Criterion 8:** Criterion 8 says that configurations corresponding to nodes in the milestone graph are reachable from the configurations of its predecessor nodes and is true by definition of the milestone graph.

**Criterion 9:** Criterion 9 says that it doesn't take too long to move from one step in the milestone graph to the next. When both  $\Phi_2(v_{i-1,j})$  and  $\Phi_2(v_{i,j-1})$  are given, then  $\Phi_1(v_{i,j})$  can be assembled using  $(k+1)^2 - 2(k-1)$  tile additions.

**Criterion 10:** Criterion 10 says that the number of tiles used in our error correction scheme is small. The total number of tile types is the number of tile types in the original system times the size of the snaked proofreading block, which is  $O(\text{poly log log } n) \times (k+1)^2$ .

Thus, we have shown that the proofreading system described here can produce an  $n \times n$  square of  $(k+1) \times (k+1)$  blocks correctly in  $O(n^{1+\epsilon})$  time with high probability.

**3.4 Applying the combinatorial criteria to the snaked tile system** We can also use the combinatorial criteria to show that the snaked proofreading system [6] can produce fast error-free assembly. This result was previously known, but the original proof was quite intricate. The snaked proof-reading system can be applied to any system of the same type as in the previous section.

The snaked tile system replaces each tile in the original system with a  $2k \times 2k$  block. An example with  $k=2$  is shown in figure 2(a) with figure 2(b) showing the growth order.

The proof is similar to the one given in section 3.3, and is deferred to the full version of the paper due to space constraints.

#### 4 Dimension Augmented Proof-reading

We now investigate the possibility of using the third dimension to do error correction. The idea is to make the duplicates on the third dimension and force an entire column of tiles to complete as an integrity check before the assembly goes on. We call a position *even* if the sum of its coordinates is even, and *odd* otherwise.

For a given two-dimensional rectilinear tile system, one that only grows north and east from an L-shaped seed, we convert to a three-dimensional system as follows. First, if the original system consists of tiles  $T_1, T_2, \dots, T_v$ , we make two duplicates  $T_{1A}, T_{2A}, \dots, T_{vA}$  and  $T_{1B}, T_{2B}, \dots, T_{vB}$ . The glues on  $T_{iA}$  and  $T_{jB}$  match if and only if the corresponding glues on tiles  $T_i$  and  $T_j$  match in the original rectilinear system. Glues between  $T_{iA}$  and  $T_{jA}$  or  $T_{iB}$  and  $T_{jB}$  do not match for any  $i$  and  $j$ . The new tile system assembles into the same pattern as the original rectilinear pattern but the odd positions are tiles of the form  $T_{iA}$  and even positions are tiles of the form  $T_{iB}$ . Then, we make  $k$  duplicates of this new system and add a strength one glue between each pair of corresponding tiles in the  $i$ -th

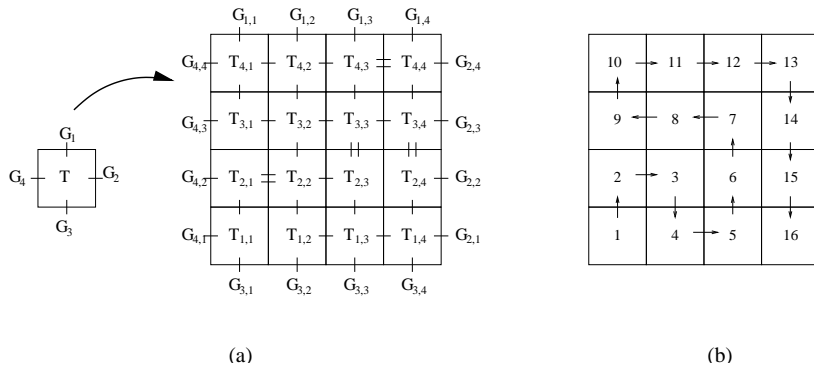


Figure 2: (a) The structure of 4x4 block. (b) The order of growth.

and  $(i + 1)$ -th duplicates on the third dimension. Third, we increase the strength of the north glue of tiles  $T_{iA}$  by 1 for all  $i$  in the first duplicate and increase the strength of the north glue of  $T_{jB}$  by 1 for all  $j$  in the  $k$ -th (last) duplicate. In the end, we increase the temperature of the system by one. As a result, a new tile can only be added to the original system at the top copy for odd squares and the bottom copy for even squares. Thus, the assembly must cross all the copies each time a new tile of the original system is added.

We analyze the 3D error correction scheme for the parity system [6], a special case of the construction above. The parity system is shown on the right hand side of figure 3. It has an L-shaped seed that encodes the input string with the rule tiles attaching on top of the seed tiles to compute the parity of the input string. Under the correct growth order, the tiles will grow in a zig-zag manner as shown in the figure.

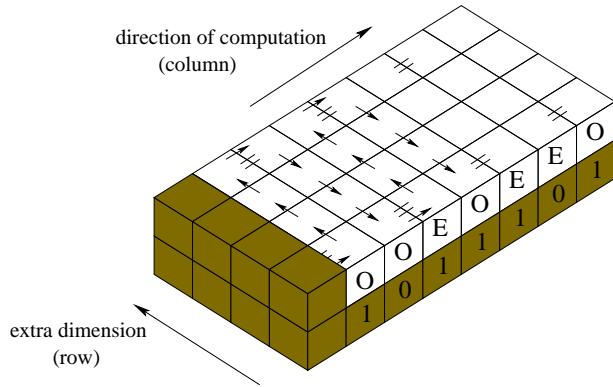


Figure 3: An example of a parity system with our 3D error correction scheme. Here, the original parity system is duplicated four times. The double lines represent glues of strength two. Shaded tiles are the seed tiles. The small arrows on top indicate the direction of tile growth.

For a parity system with input size  $n$ , we set the

$k$ -th error correction system to be the system with  $2k$  duplicates on the third dimension. The following is a certificate of the error correction system:

**Tile System Augmentation:**

The system has a unique terminal assembly in aTAM, which fills the entire  $n \times k$  rectangle and computes the parity of the input string.

The milestone graph is a single path  $v_0, \dots, v_{n/\log n}$ , where  $v_s = v_0$  and  $v_t = v_{n/\log n}$ .  $\Phi_1(v_t)$  is the unique terminal assembly described above.  $\Phi_1(v_i)$  and  $\Phi_2(v_{i+1})$  both denote the configuration where the first  $i \log n$  rows are correctly assembled and all other rows remain empty. The malignancy function  $E(p, C)$  is benign if and only if  $C(p)$  is either empty or equal to  $\Phi_1(t)(p)$ . Finally, we set  $p_1(x) = 2k^2$ ,  $p_2(x) = 1$ ,  $p_3(x) = x^2$ ,  $p_4(x) = 3 \log(x)$ , and  $p_5(x) = 1$ .

We prove criteria 4 and 5 here. The rest of the criteria are trivial.

LEMMA 4.1. *If there is a malignant tile attached in columns  $i$  or  $i + 1$ , then at least one insufficient attachment must have happened in this region.*

*Proof.* The first malignant tile that attaches in those two columns can only get strength 1 from the column it wants to attach to and strength 1 from an adjacent column and, so it must be an insufficient attachment.

LEMMA 4.2. *Any semi-connected malignant structure that is not a  $k$ -bottleneck has size at most  $4k^2$ . (Criterion 4)*

*Proof.* Lemma 4.1 shows that any semi-connected malignant structure that is not a  $k$ -bottleneck cannot have malignant tiles in all columns. Hence, this structure cannot have tiles in both the first and the  $(2k)$ th column. Without loss of generality, we may assume that it has no tiles in the  $(2k)$ th column. This means that all glues between the  $2i$ th and  $(2i + 1)$ th row in this malignant structure have strength 1, for any  $i$ . Hence, if the

malignant structure has tiles in the  $(2j - 1)$ th and  $2j$ th row, then at least one insufficient attachment must have happened in that region. Therefore, the structure has tiles in less than  $2k$  rows and  $2k$  columns, which proves the lemma.

LEMMA 4.3. *Any connected malignant structure that is not a  $k$ -bottleneck has at least one tile held by strength at most 3. (Criterion 5)*

*Proof.* Without loss of generality, we may assume that this structure has tiles in column 1 through column  $i$  but does not have tiles in column  $i + 1$ . We will show that the malignant tile with the lowest row number  $j$  is attached with strength at most 3. First, since this tile is malignant but the tile in column  $i + 1$  adjacent to it doesn't belong to the same malignant structure, the two tiles must have a mismatch. Similarly, there must be another mismatch between this tile and either the seed tile below it or the tile at column  $i$  and row  $j - 1$ . Hence, the malignant tile at column  $i$  and row  $j$  is held by strength at most 3.

Hence, we know this scheme provides error-correction for parity systems without resolution loss in the original dimensions.

This dimension augmentation scheme can similarly be applied to any two dimensional tile system in which every tile has a fixed set of input sides, including the south side similarly. Notice that the binary counter and the Chinese remaindering counter belong to this category. It is open whether the resulting system always provides good error-correction.

## 5 Proving the Guarantees of the Combinatorial Criteria

In this section we show that a system obeying the error-free assembly criteria will form its final structure quickly with high probability for suitable thermodynamic parameters. We use kTAM with the assumption that tiles held by strength greater than  $\tau$  do not fall off. In all our assemblies, we set the forward rate to be twice the reverse rate ( $f = 2r$ ). This restriction fixes  $G_{mc}$  as a function of  $G_{se}$ , but we will tune  $G_{se}$  to get our results. Let  $s$  be the number of tiles in our system.

LEMMA 5.1. *Any connected malignant structure  $A$  that is not a  $k$ -bottleneck will be corrected in expected time less than  $\frac{2^{3^d p_1^d(k) \times d \log 3s p_1(k)}}{\tau}$  if we add the restriction that tiles held by strength less than  $\tau$  cannot attach.*

*Proof.* It follows from criterion 4 that the malignancy range of a tile has area less than  $2^d p_1^d(k)$ . Since  $A$  is at most  $p_1(k)$  tiles long the union of the malignancy ranges

for all its tiles is at most  $3^d p_1^d(k)$ . The total number of places tiles can attach to the structure is  $3^d p_1^d(k)$  since such an attachment would be considered malignant, so the total rate of attachment is bounded by  $s 3^d p_1^d(k) f$ . Tiles fall from  $A$  with rate at least  $f/2$  by criterion 5, so the whole malignant structure will be corrected in expected time less than  $\frac{2^{3^d p_1^d(k) \times d \log 3s p_1(k)}}{\tau}$  from naive analysis of the weighted random walk.

Next we show that the extra restriction that tiles held by strength less than  $\tau$  cannot attach can be weakened to no insufficient attachments happening in the vicinity of the malignant structure.

LEMMA 5.2. *For suitable choices of thermodynamic parameters, any semi-connected malignant structure  $A$  that is not a  $k$ -bottleneck will get corrected in expected time  $\frac{2^{4 \times 3^d p_1^d(k) \times d \log 3s p_1(k)}}{\tau}$  given no further insufficient attachments within distance  $p_1(k)$  of  $A$ .*

*Proof.* At first look, this lemma is similar to lemma 5.1, since all tiles that attach with strength less than  $\tau$  fall off before some other tiles attach next to them. However, the lemmas are different in the following two ways. First, tiles may attach with strength less than  $\tau$  and prevent the tiles originally held by strength  $\tau$  from falling off. Second, the fact that no insufficient attachment happens in the two nucleation sites might change the probability of each event. In this proof, we will show that the effect of these two situations are limited.

First, for a tile  $T$  held by strength exactly  $\tau$ , there are at most  $2d - 1$  adjacent positions where tiles can attach with strength less than  $\tau$ . For each of these positions, at most  $s$  tiles can attach with strength less than  $\tau$ , where  $s$  is the number of tiles in the original system. Each of these tiles attaches with rate  $f = 2r$  and falls off with rate  $re^{G_{se}}$  and together they can only hold the tile  $A$  at most  $(4d - 2)se^{-G_{se}}$  fraction of the time. Second, there are at most  $p_1^3(k)$  locations that insufficient attachments can happen. For each of these locations, there are at most  $O(s)$  different kinds of insufficient attachments. Hence, the rate of insufficient attachments is at most  $sp_1^3(k)e^{-G_{se}}f$ . Therefore, if we set  $e^{G_{se}} \gg p_1^3(k)p_4(k)p_5(\log n) > 4sp_1(k)$  for some constant  $c$ , then both of these two effects only change the rate at which tiles attach/detach by a factor of some small  $\epsilon$ . Hence, the expected time for  $X$  to fall off is  $\frac{2^{4 \times 3^d p_1^d(k) \times d \log 3s p_1(k)}}{\tau}$ .

For convenience, define  $\gamma = p_2(k) + p_3(\log \log n)$ .

THEOREM 5.1. *With appropriate thermodynamic parameters, no  $k$ -bottleneck will happen within time  $n \log n \frac{T}{\tau} = n \log n \times 8 \log n \frac{3^d p_1^d(k) \times d \log 3s p_1(k) + \gamma}{\tau}$*



$2p_1^3(k)+p_2^2(k)+p_3^2(\log \log n)n \times 1/f$ , denoted by  $2T_2n/f$  with probability at least  $1 - 1/n^3$ .

*Proof.* By definition,  $k$  insufficient attachments are required before a  $k$ -bottleneck happens. For any semi-connected malignant structure  $A$  formed by  $i < k$  insufficient attachments, one of two things will happen. First, one more insufficient attachment occurs. Consider any structure  $A$  caused by  $i$  insufficient attachments. By the criteria, the size of  $X$  is at most  $p_1(k)$ , hence, the number of insufficient attachment locations that can cause this structure to grow larger is at most  $2dp_1(k)$ . So, the process of the  $(i + 1)$ -th insufficient attachment happening has an exponential distribution with average rate at most  $4sp_1(k)fe^{-G_{se}}$ . Second, all the attached tiles could fall off. By lemma 5.2, the expected time for all the attached tiles to fall off is  $\frac{2^{4 \times 3^d p_1^d(k) \times d \log 3sp_1(k)}}{r}$ .

We can derive the following facts from the above: first, for probability at least  $1 - 1/c$ , all the tiles will fall off in time  $c \frac{2^{4 \times 3^d p_1^d(k) \times d \log 3sp_1(k)}}{r}$ , for any constant  $c$ ; second, there will be no insufficient attachment within the given area and time  $c \frac{2^{4 \times 3^d p_1^d(k) \times d \log 3sp_1(k)}}{r}$  with probability  $1 - e^{-4sp_1(k)fe^{-G_{se}}} \times c \frac{2^{4 \times 3^d p_1^d(k) \times d \log 3sp_1(k)}}{r}$ . Hence, if  $4sp_1(k)fe^{-G_{se}} \times \frac{2^{4 \times 3^d p_1^d(k) \times d \log 3sp_1(k)}}{r} = 1/c^2 \ll 1$ , then we know that the probability that the  $i+1$ -th insufficient attachment happens given that the  $i$ -th insufficient attachment happened is at most  $2/c$ . Therefore, after the first insufficient attachment takes place, the probability of a  $k$ -bottleneck happening before all the attached tiles fall off is less than  $\frac{2}{c}k^{-1}$ . Within time  $n \log n \frac{T}{r}$ , the expected length of the assembly is at most  $n \log n T$ . Therefore, the expected number of insufficient attachments is less than  $n^3 \log^3 n T^3 se^{-G_{se}}$ .

Thus, the probability for a  $k$ -bottleneck to happen within time  $2T_2n \times 1/f$  is less than  $n \log n T se^{-G_{se}} \times \frac{2}{c}k^{-1}$ .

Hence, if we set  $e^{-G_{se}}$  to be smaller than  $\frac{1}{8sp_1(k) \times 2^{4 \times 3^d p_1^d(k) \times d \log 3sp_1(k)}}(nTs \log n)^{-6/k}$ , then the probability for a  $k$ -bottleneck to happen within time  $2T_2n \times 1/f$  is less than  $1/n^3$ .

**THEOREM 5.2.** *For a node  $v$  with incident nodes  $v_1, v_2, \dots, v_i$ , if the union of all  $\Phi_2(v_i)$  never fall off and there is no  $k$ -bottleneck in the assembly,  $\Phi_1(v)$  will be assembled in time  $\frac{T}{r} = 8 \log n \frac{3^d p_1^d(k) d \log 3sp_1(k) + \gamma^\gamma}{r}$ .*

*Proof.* We only need to worry about the malignancy range of the  $2^\gamma$  tiles in  $\Phi_1(v)$  but not in  $\Phi_2(v_i)$ , which is an area of size  $2^\gamma \times 2^d p_1^d(k)$  since all other insufficient attachments will not affect the area of interest without

$k$ -bottlenecks (by criteria 4). If we set  $e^{G_{se}}$  to be  $sn^{-3/k}2^{-\gamma}2^{-d}p_1^{-d}(k)T^{-1}$ , then less than  $k$  insufficient attachments will happen in this area in time  $T/r$  with probability  $1 - \frac{1}{n^3}$ . Hence, with probability at least  $1 - 1/n^3$  there will be a time interval of length

$\frac{T}{r} = 8 \log n \frac{3^d p_1^d(k) \times d \log 3sp_1(k) + \gamma^\gamma}{r}$  when no insufficient attachments happen in this area. Hence, by lemma 5.2, all the erroneous tiles will fall off in time  $\frac{2^{3^d p_1^d(k) \times d \log 3sp_1(k)}}{r} \times 8 \log n$  with probability at least  $1 - \frac{1}{n^4}$ . Also, by criteria 9,  $\Phi_1(v)$  can be assembled within  $\frac{(p_2(k)+p_5(\log \log n))^{p_2(k)+p_5(\log \log n)}}{f} \times 8 \log n$  with probability at least  $1 - \frac{1}{n^4}$ .

*Proof of Theorem 3.1:* From theorem 5.1, we know that with probability  $1 - \frac{1}{n^3}$ , no  $k$ -bottleneck will happen within the given time. From criterion 8, we know that for any node  $v$  in the milestone graph, when  $\Phi_1(v)$  is assembled, all tiles in  $\Phi_2(v)$  will not fall off in  $\Omega(n \frac{T}{r})$  time with probability  $1 - \frac{1}{n^3}$ . From theorem 5.2 and the above facts, we know that the assembly process will follow the milestone graph and each step can be done in  $\frac{T}{r}$  time with probability at least  $1 - O(\frac{1}{n^3})$ . Hence,  $\Phi_1(t)$  will be assembled within  $O(n \frac{T}{r})$  with probability  $1 - O(\frac{1}{n})$  since there are at most  $n^2$  vertices in the milestone graph and the longest chain has length  $n$ .

In a self-assembly system with temperature  $\tau$ , we have  $f = 2r = 2e^{-\tau G_{se}}$ . We choose  $e^{G_{se}}$  to be  $2^{\Omega(p(k)+p(\log \log n))}n^{\Omega(1/k)}$  for some polynomial  $p$  in order to satisfy the constraints in the previous systems. Therefore, if we choose  $k$  to be  $O(\log \log n)$  and  $\Omega(1)$ , the correct assembly can be produced in  $O(n^{1+\epsilon})$  time with high probability.  $\square$

Table 1 summarizes the trade-off between assembly speed, resolution loss and changes required in thermodynamic parameters for several error-correction schemes.

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	# of tiles	resolution loss	assembly time	free energy change
Snaked proofreading [6]	$O(\log^2 n)$	$O(\log n)$	$O(n \text{polylog}(n))$	$O(\log \log n)$
Thermodynamics [21]	1	none	$O(n^3)$	$O(\log n)$
3D error correction	$k(n)$	none <sup>(*)</sup>	$O(n^{1+\frac{1}{k(n)}})$	$O(\frac{\log n}{k(n)})$

Table 1: A comparison of some error correction schemes. The function  $k(n)$  can be unbounded, non-decreasing function. (\*) For the 3D error correction scheme, the resolution loss of  $k(n)$  only occurs in added dimension.

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