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Employing a Self-Developed MATLAB Methodology Based on Binary XOR Operations to Identify the DNA Configurations with Minimal Components

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Abstract

DNA has been utilized as a versatile nanomaterial for synthesizing various functional nanostructures. Various DNA nanostructures synthesized based on the principle of symmetry have demonstrated significant potential for applications. However, designing and synthesizing of these structures in a simple and efficient manner still pose challenges. To address these issues, we have developed a MATLAB algorithm based on binary operations to screen configurations with minimal DNA components. Furthermore, we have analyzed the conversion mechanisms between different configurations, providing theoretical guidance for targeted regulatory in chemistry. The results indicate that this concise algorithm allows us to identify all possible target configurations without laborious calculations, saving time and expanding the pool of potential candidates for DNA tetrahedra, cubes synthesis.

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1 Introduction

Over the past four decades, DNA has consistently demonstrated its exceptional suitability as a fundamental building block for synthesizing diverse nanostructures due to its remarkable addressability, recognition capabilities, and programmability [1–4]. The applied potential of these nanostructures has been demonstrated in the fields of drug delivery [5–8], biological detection [9–12], and disease diagnosis and treatment [13–15]. The utilization of DNA polyhedra, particularly tetrahedra [16–20] and cubes [21, 22], with simplistic architectures has gained significant attention across diverse domains due to their uncomplicated design, rapid synthesis rate, and cost-effectiveness. The majority of tetrahedra and cubes consist of distinct components because the sequence symmetry minimization is implemented in their design. However, this aspect may not pose a significant concern in many scenarios; nevertheless, when employed as a drug delivery vehicle in vivo, it becomes imperative to consider the biocompatibility, toxicity, immunogenicity, degradation characteristics [23] and DNA-catalyzed production [24] associated with each individual component. Obviously, reducing the number of components in polyhedral structures inevitably leads to fewer limitations in their applications. Hence, it is crucial to explore approaches that enable facilitate the fabrication of DNA nanostructures with a reduced number of components while achieving the minimal component number.

Several strategies have been proposed to minimize the number of components required for folding into target polyhedral shapes [25–27]. Yan et al. reported that a nanometer-sized tetrahedron from a single strand of DNA with 286 nucleotides long [28]. By manipulating the number of twists on each edge, N. Jonoska and R. Twarock devised blueprints for a DNA dodecahedron with minimal DNA strands, aided by computer assistance [29, 30]. The results of their study suggested that the construction of a DNA dodecahedron can be achieved using at least two individual DNA strands. Deng and his colleagues also proposed an approach to construct DNA cages by using fewer strands [31], while Liu's group investigated DNA tetrahedral and octahedral configurations from the view

of topological [32, 33]. However, these approaches share a common limitation in effectively controlling the synthesis process and achieving high yield. Moreover, the mechanisms underlying these strategies have not been thoroughly analyzed.

The principle of structural symmetry was employed to facilitate the design and synthesis of a DNA tetrahedron by Yan and his colleagues [34]. In their approach, three types of short components are folded into four three-star motifs, which are subsequently assembled to form the DNA tetrahedron. The strategy provides great inspiration for reducing the number of components based on principle of structural symmetry. Furthermore, Duan and his colleagues have proposed a manual approach to accurately design DNA Platonic polyhedra [35, 36], prisms, pyramids [37] and Archimedean polyhedra [38] with minimal components by utilizing two subunits A and B repetitively. These results demonstrate that we can manually obtain some specific configurations of DNA Platonic polyhedra with the minimal number of components, for example, a tetrahedron is constructed by two kinds of components and a cubes is constructed using a single type of component. It is intriguing that the configurations obtained through our strategy exhibit excellent selectivity, which can be precisely controlled during synthesis. Additionally, these DNA polyhedra composed of repeating building blocks may have potential applications. For example, when used in vivo, each DNA strand's metabolism can be separately explored. However, in these studies, we did not comprehensively enumerate all potential configurations but validated the feasibility of our method by displaying some possible DNA polyhedral configurations with the minimal number of components.

However, different configurations of DNA polyhedra may serve distinct roles and functions. Consequently, it is undeniable that numerous structures with diverse functionalities may have been overlooked if we rely solely on manual strategies to explore the transformation mechanism between different configurations. Therefore, it is crucial to list all conceivable DNA polyhedral configurations for a given polyhedron to fill the gap. To address these issues, we developed a concise and innovative MATLAB algorithm based on binary XOR operations. Using tetrahedron and hexahe-

dron as exemplars, we successfully executed our manual approach within minutes and generated a comprehensive set of feasible configurations. Subsequently, we identified target configurations with the minimum number of components from this dataset, further validating prior conclusions resulting from our manual method while also providing more precise targets for subsequent experimental synthesis.

2 Methods

In the manual approach, we decomposed a regular polyhedron into its constituent faces. Each face is covered by a single strand of DNA due to an even number of windings on each edge. Treating each individual strand as a component, which is composed of several subunits. If the length of each subunit corresponds to the length of sides of the given polygon, then every component can be made up of a specific number of subunits. The fewer subunits present, the fewer components are likely to be formed; in other words, reducing the number of subunits help minimize the required number of components for constructing the given polyhedra. Therefore, forming distinct components require repeated utilization of only two complementary paired subunits A and B. These components were then utilized to construct diverse DNA polyhedral configurations, offering numerous possibilities for a given polyhedron.

Even for simple tetrahedrons, the vast number of DNA polyhedral configurations generated by our method pose a challenge in manually enumerating all possible structures and increases the probability of overlooking significant configurations. Therefore, leveraging computational assistance has emerged as the optimal approach to accomplish this objective swiftly and accurately. Initially, we attempted to determine precise target structures with the fewest number of components directly. However, we discovered that this was unattainable within our available resources after many attempts. Consequently, we have to consider employing an exhaustive algorithm which, despites potentially being time-consuming, offers easier implementation and reduces susceptibility to errors.

The problem is addressed by implementing a self-developed MATLAB

algorithm, which provides a systematic guide for screening the target architectures. The algorithm draws inspiration from the binary XOR operation commonly used in computer science. The details of the algorithm are given as pseudocode as follows:

Algorithm 1: Computing DNA polyhedral using XOR

Input: edge set C, face type set T, $edgeNum$

Output: result set R

$allType = 2^{edgeNum*2+1} - 1$;
$startType = 2^{edgeNum} - 1$;
$tureResult = 2^{edgeNum} - 1$;
$tempType = startType$;
while *tempType not equal allType* **do**
  $biTemp$ = get bit version of $tempType$;
  $highValue$ = get the high digits of $biTemp$ from middle;
  $lowValue$ = get the low digits of $biTemp$ from middle;
  orResult = bitXOR($highValue$, $lowValue$);
  if *orResult equals tureRerult* **then**
    transfer $tempType$ into its edge form $tempEdges$ according to C and T;
    add $tempEdges$ into result set R;
    $tempType$ =$tempType$ + $startType$;
  else
    continue;
  end
end

The details of the algorithm are outlined as follows:

Step I: Sequence the faces of the given polyhedron, assign a unique edge number to each edge, and then encode each side of edges.

It is necessary to arrange the faces of the given polyhedron sequentially, assign a unique numerical identifier to each edge, and encode each side of edges. For example, the four faces of a tetrahedron, as depicted in Figure 1, are labeled sequentially as front, left, right, and bottom. Additionally, each edge of the tetrahedron is assigned a specific number. In this way, if

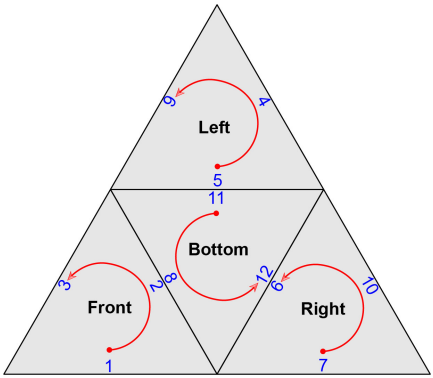

Figure 1. Sequence the faces of a regular tetrahedron

the numbers are arranged in the counterclockwise direction indicated by the arrows, each face can be represented by a unique set of numbers. For example, the bottom face can be represented as (11,8,12). The purpose of this not only determines the algorithm's execution order but also facilitates accurate translation of the output into DNA polyhedral configurations during step IV. Since each edge has two sides, our strategy defines that each side of an edge contains two slots capable of accommodating either subunit A or B. As depicted in Figure 2a, there are four possible permutations and combinations resembling binary XOR operation principles which inspired us.

The XOR operation involves manipulating two 1-bit numbers as inputs. Herein, we assign the number 1 to represent subunit A and number 0 to denote subunit B. To facilitate application of XOR operation, it is imperative to encode each side of edges accordingly. We employ a binary code with a length equaling twice that number of edges (2n) for encoding polyhedra instances. Taking regular tetrahedron as an illustrative example, its binary code possesses length equivalent to twice that of edges (2×6=12), given it encompasses six edges.

Step II: Run the XOR algorithm on the binary coded structure to determine whether the structure meets the complementary base pairing rule.

The coded result is then divided into two segments at its midpoint, and

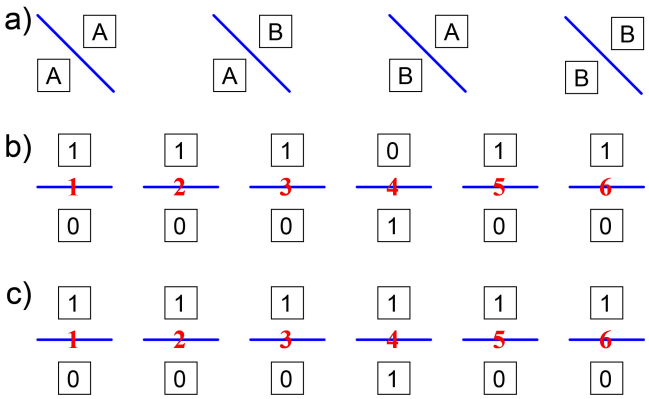

Figure 2. (a) Four possible permutations and combinations for an edge; (b) A possible placement for a regular tetrahedron; (c) An impossible placement of a regular tetrahedron due to that the edge 4 represents two subunits A paired.

each position of the code is mapped onto the corresponding polyhedron. The mapping procedure involves selecting a number from the first segment and assigning it to one side of an edge, followed by choosing another number from the second segment and assigning it to the opposite side of that edge. Figure 1 illustrates the resulting mapping outcome for a regular tetrahedron. Importantly, distinct segments of the code are assigned to each side of an edge.

Based on the permutations and combinations, we can comprehensively enumerate all potential combinations. However, not all of these combinations meet the criteria to be classified as DNA polyhedra. Therefore, it is necessary to individually examine each configuration to verify if it satisfies the requirement of complementary base pairing, which necessitates that the two subunits adjacent to an edge should differ.

Therefore, we initialize the code and increment it by 1 iteratively to assess whether each new configuration adheres to DNA polyhedral requirements. The evaluation criterion involves performing a bitwise XOR operation between two code segments and retaining only those configurations that yield a result equal to 2^n-1. Figure 2b illustrates a feasible arrangement for a regular tetrahedron, sequences "111011" and "000100" will yield "111111" (equivalent to decimal value 2^6-1=63) when the application of

bitwise XOR on them. Conversely, when applying bitwise XOR on the arrangement shown in Figure 2c, the result is 111011 (equivalent to decimal value 59), which is deemed unviable due to an inherent contradiction between segments of the code pertaining to edge 4.

Step III: Convert the codes into the corresponding DNA polyhedral configurations and eliminate duplicate configurations and then output results.

Convert all codes into rational polyhedral configurations and numerous potential configurations; however, not all of them align with our target configurations. In our previous study [35], we defined certain equivalent components by considering the self-recognition capability of DNA strands. For instance, the triangular components AAB, BAA, and ABA were deemed equivalent, as well as BBA, ABB, and BAB; consequently, we substituted them with ABA and BAB respectively. These equivalent components lead to an increase in duplicate configurations and thus necessitates their exclusion through algorithmic means prior to obtaining the results. Similarly, quadrilateral components such as AAAB, AABA, ABAA and BAAA are considered equivalent to AAAB; the components AABB, ABBA, BBAA and BAAB are replaced by AABB; ABAB and BABA are denoted by ABAB; ABBB, BBBA, BBAB and BABB are presented as ABBB. Completing this step can significantly alleviate the difficulty and workload associated with data analysis.

Step IV: Screen the target structures with minimal components number and check.

Screen target structures with the fewest number of components and then output the results in an Excel spreadsheet. Identify the DNA polyhedral configurations that have the lowest number of components from the output table, followed by a comprehensive analysis of these configurations.

3 Results

The program is used to input parameters and perform calculations based on the geometric characteristics of various polyhedra, automatically generating an Excel table that lists all DNA polyhedral configurations meeting

the specified criteria. Due to their simple structure, low computational cost, and potential for practical applications, this paper focuses solely on regular tetrahedra and hexahedra. These two categories of polyhedra correspond to regular polyhedra composed of odd-sided and even-sided polygons, respectively. The primary objective of this study is to automatically identify potential configurations of DNA polyhedra by minimizing the number of constituent components. Therefore, in subsequent sections, we will discuss DNA tetrahedral and hexahedral configurations separately. The experiments were carried out on an 8-core Intel Core i9-9800H CoffeeLake processor, with 256KB L2 cache per core, 16MB L3 cache per core.

3.1 DNA tetrahedral configurations

A tetrahedron is universally recognized as the most elementary regular polyhedron, consisting of four triangles and adhering to Euler's theorem V + F - E = 2. It has four faces, four vertices, and six edges. As depicted in Figure 1, the four faces of the regular tetrahedron are sequentially designated as front, left, right, and bottom. The six edges of a tetrahedron are also labeled in a way that facilitates easy determination of their position and order during the calculation. The front face is labeled counterclockwise based on the numbering of its edges represented as (1,2,3), while edges of the left, right, and bottom faces are denoted by (5,4,9), (7,10,6) and (11,8,12), respectively. After completing these steps, input the relevant parameters of the regular tetrahedron and execute the MATLAB program.

Here, we apply the basic principles of binary algorithms to screen for DNA polyhedral configurations creatively with the minimum number of components. After implementing the MATLAB program closure, four plausible DNA tetrahedral configurations are exported to an Excel table (refer to Table 1) within a remarkable time of 0.3s, the planar views of these four configurations are shown in Figure 3a-d. Notably, our results reveal that the configurations No. 2, 3 and 4 each require two components. The configuration No. 3 aligns perfectly with the outcomes of our previous research [35], underscoring the precision and applicability of our

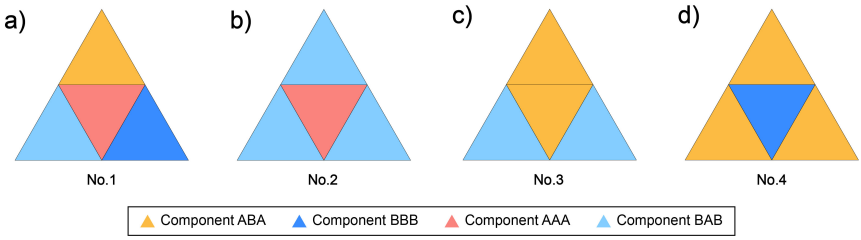

Figure 3. (a) The tetrahedral configuration is composed of four components AAA, BBB, ABA and BAB; (b) The tetrahedral configuration is composed of two components AAA and BAB; (c) The tetrahedral configuration is composed of two components ABA and BAB; (d) The tetrahedral configuration is composed of two components ABA and BBB.

Table 1. All reasonable DNA tetrahedral configurations

No.	Com I	Com II	Com III	Com IV	Com number
1	AAA	BBB	ABA	BAB	4
2	AAA	BAB	BAB	BAB	2
3	ABA	BAB	ABA	BAB	2
4	ABA	ABA	ABA	BBB	2

algorithm. With the aid of computer, it saves a lot of manpower and time costs. This not only demonstrates the practicability and correctness of our algorithm but also effectively avoids the possible omissions (configurations No. 2 and 4) in manual calculation.

The final configuration not only provides a qualitative representation of the components in synthesizing a DNA tetrahedron but also reveals the quantitative relationships between different components. For instance, the synthesis of a DNA tetrahedron in accordance with the configuration No.1 (as shown in Figure 3a) requires four distinct components in a composition ratio of 1:1:1:1, whereas for configuration No.3 (as shown in Figure 3c), only two components (ABA and BAA) are needed with a composition ratio of 1:1.

Since subunits A and B are complementary pairs, their numbers must be the same. If a reasonable DNA polyhedron configuration contains AAA or BBB component, it will result in the remaining component number greater than 1. The results in Table 1 are in complete agreement with the

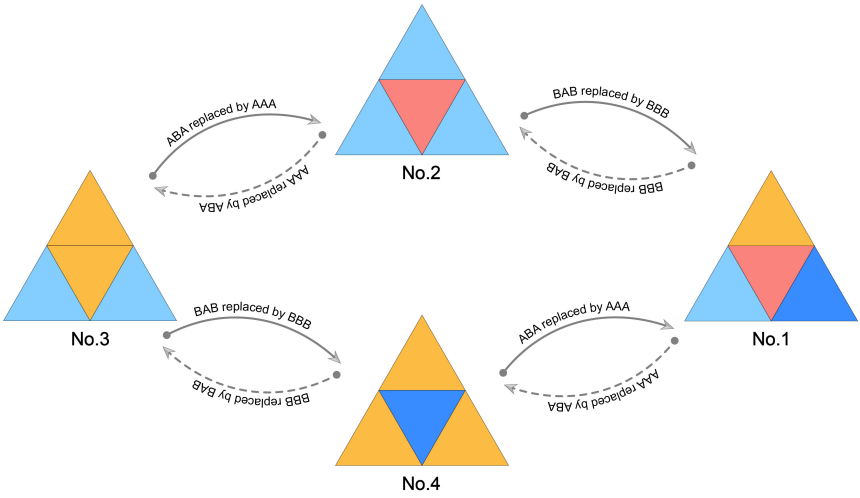

Figure 4. Different transition pathways from the DNA tetrahedral configuration No. 3 to No.1.

conclusion. To investigate the role of different components in reducing the number of components, we made the following modifications: by replacing one component in configuration No.3 with either an AAA or BBB, the final configuration automatically adjusts to become configuration No. 2 or No.4. By adding more BBB or AAA components to configurations No.2 or No.4, the result becomes self-consistent and transitions into configuration No.1. Conversely, starting from configuration No.1 eventually leads to obtaining configuration No.3. The forward and reverse conversion pathways are presented in Figure 4. Thus, we can consider when assembled into tetrahedral configurations, components AAA and BBB show low compatibility and are not conducive to reducing the component number. This point is probably more evident in the octahedron and icosahedron.

3.2 DNA hexahedral configurations

A hexahedron has six faces, eight vertices and twelve edges. Unlike tetrahedra, a hexahedron is made of even-polygons, which may exhibit some phenomena different from a tetrahedron. Therefore, we have made some minor modifications while keeping the core algorithm unchanged. Similar

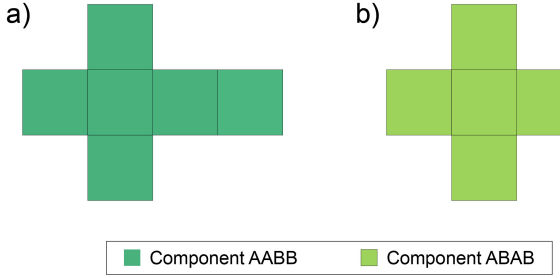

Figure 5. (a) The hexahedral configuration consists six component AABB; (b) The hexahedral configuration consists six component ABAB.

to a tetrahedron, the six faces of the cube are arranged in a specific order, and the sides of each quadrilateral are labeled clockwise as (1,2,3,4), (5,6,7,8), (9,18,10,14), (11,20,12,16), (17,21,13,23) and (19,22,15,24).

After successfully running the algorithm for 4.8 seconds, certain duplicate configurations were excluded. The output revealed that there were 37 configurations satisfy the requirements, as listed in Table 2. These configurations not only offer some potential targets for experimental synthesis but also provide qualitative and quantitative insights into synthesizing various DNA regular hexahedra. Unlike DNA tetrahedral configurations, there are only two hexahedral DNA configurations with a minimal component number, meaning that the final configuration is composed of either six AABB or six ABAB, as shown in Figure 5a and b.

The role of various quadrilateral components in reducing the number of components can be examined by constructing conversion pathways from the configurations No.5 to No.36 or No.37, or reversible paths from the configurations No.36 or No.37 to No.5. The results also indicated that these two components AABB and ABAB have high compatibility in the architecture of DNA hexahedral configurations with minimal component numbers, while the components AAAA, BBBB, AAAB and ABBB show poor compatibility.

Table 2. All reasonable DNA hexahedral configurations

No.	Com I	Com II	Com III	Com IV	Com V	Com VI	Com num
1	AAAA	AAAA	ABAB	ABAB	BBBB	BBBB	3
2	AAAA	AAAA	ABAB	ABBB	BBBB	ABBB	4
3	AAAA	AAAA	ABBB	ABBB	ABBB	ABBB	2
4	AAAA	AAAB	ABAB	AAAB	BBBB	BBBB	4
5	AAAA	AAAB	ABAB	AABB	BBBB	ABBB	6
6	AAAA	AAAB	ABAB	ABBB	ABBB	ABBB	4
7	AAAA	AAAB	ABBB	AAAB	BBBB	ABBB	4
8	AAAA	AAAB	ABBB	AABB	ABBB	ABBB	4
9	AAAA	AAAB	BBBB	ABBB	ABAB	ABAB	5
10	AAAA	AABB	ABAB	AABB	BBBB	AABB	4
11	AAAA	AABB	ABAB	AABB	ABBB	ABBB	4
12	AAAA	AABB	ABBB	AAAB	BBBB	AABB	5
13	AAAA	AABB	ABBB	AABB	ABBB	AABB	3
14	AAAA	ABAB	AABB	AABB	BBBB	ABAB	4
15	AAAA	ABAB	AABB	ABBB	ABBB	ABAB	4
16	AAAA	ABAB	ABBB	ABBB	ABAB	ABAB	3
17	AAAA	BBBB	AABB	AABB	AABB	AABB	3
18	AAAB	AAAB	ABAB	AAAB	BBBB	ABBB	4
19	AAAB	AAAB	ABAB	ABAB	ABBB	ABBB	3
20	AAAB	AAAB	ABBB	AAAB	ABBB	ABBB	2
21	AAAB	AAAB	BBBB	ABAB	ABAB	ABAB	3
22	AAAB	AAAB	ABAB	AABB	BBBB	AABB	4
23	AAAB	AAAB	ABAB	AABB	ABBB	ABBB	4
24	AAAB	AAAB	ABBB	AAAB	BBBB	AABB	4
25	AAAB	AAAB	ABBB	AABB	ABBB	AABB	3
26	AAAB	AABB	ABAB	ABAB	ABBB	AABB	4
27	AAAB	AABB	BBBB	ABAB	ABAB	AAAB	4
28	AAAB	AAAB	AAAB	AAAB	BBBB	BBBB	2
29	AAAB	ABAB	AABB	ABAB	ABBB	ABAB	4
30	AAAB	ABAB	ABBB	ABAB	ABAB	ABAB	3
31	AAAB	AABB	AAAB	AABB	BBBB	AABB	3
32	AAAB	AABB	AABB	AABB	ABBB	AABB	3
33	AAAB	AABB	AABB	AABB	ABAB	ABBB	4
34	AABB	ABAB	AABB	ABAB	ABAB	AABB	2
35	AABB	AABB	AABB	AABB	ABAB	ABAB	2
36	AABB	AABB	AABB	AABB	AABB	AABB	1
37	ABAB	ABAB	ABAB	ABAB	ABAB	ABAB	1

4 Discussion

In this paper, two complementary subunits A and B were utilized to construct diverse components. Subsequently, a comprehensive self-developed MATLAB algorithm based on binary XOR operation was implemented to identify DNA polyhedral configurations with minimal component number. The aim was to provide additional potential candidates for DNA nanostructure synthesis. The results demonstrate the successful achievement of our algorithmic goals. Specifically, we have successfully obtained DNA tetrahedral configurations composed of two distinct kinds of component and DNA hexahedral configurations composed of one type of component.

These results not only corroborate previous research findings, but also unveil several overlooked structures, substantiating the reliability and accuracy of the algorithm. Furthermore, the presented results offer both qualitative and quantitative evidence to support the experimental synthesis of these potential configurations.

The algorithm is exhaustive, however, the calculations of tetrahedron and hexahedron can be completed within a few seconds. Therefore, this algorithm not only ensures accurate results but also significantly saves time and mitigates potential omissions. Nevertheless, when applied to complex dodecahedra, the computational load increases along with longer duration due to computer configuration limitations. Nonetheless, these results suggest that our algorithm exhibits advantages in solving simple polyhedra while leaving room for optimization when dealing with complex ones; thus, further development of superior algorithms are still needed.

In our approach, we not only focused on screening the target structures but also gained a comprehensive understanding of the roles of distinct components in reducing the number of components in the target configurations. For triangular structures, except for the combinations the components BAB and AAA, ABA, and BBB, the presence of components AAA and BBB is counterproductive to minimizing component number; hence, these components can be considered incompatible with our target configurations. Similarly incompatible components such as AAAB and ABBB are also observed in DNA hexahedral configurations. The discovery not only enhances our comprehension of component actions but also provides insights for optimizing algorithms and even inspires subsequent algorithms aimed at solving complex polyhedra.

The conformational change between tetrahedral configurations No. 1 and No. 3, as exemplified in Figure 6a is used for analyzing the transition mechanism between different configurations. It is worth noting that in Figure 6b when substituting BBB component corresponding to face (7,10,6) with BAB, it's intriguing that only face (5,4,9) transforms into BAB while maintaining an equal number of subunits A and B. Furthermore, after replacing AAA component associated with face (11,8,12) by ABA, the corresponding components of (5,4,9) revert back to ABA. Obviously al-

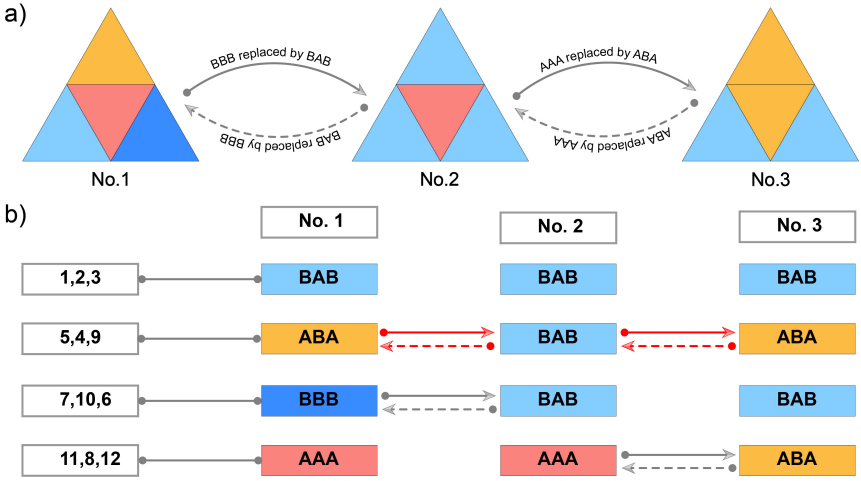

Figure 6. (a) The conversion pathway between the tetrahedral configuration No. 1 and No. 3; (b) The targeted regulatory mechanism between the tetrahedral configuration No. 1 and No. 3.

though participates throughout the transformation process, face (5,4,9) remains unchanged its corresponding components at final outcome. This finding highlights that altering either components related to face (7,10,6) or (11,8,12), can selectively regulate components of face (5,4,9). Such targeted regulatory mechanisms also apply to reverse processes and hexahedra.

5 Conclusion

In this paper, a binary-based MATLAB algorithm is employed to effectively filter DNA tetrahedral and hexahedral configurations with minimal component numbers. Our algorithm successfully constructs DNA tetrahedral configurations comprising two distinct types of component and DNA hexahedral configurations composed of a single kind of component. The algorithm exhibits conciseness, reliability, and ease of implementation, as evidenced by the output results, particularly for simple polyhedra. However, given our current level, there is still room for optimizing the algo-

rithm to effectively address the challenge posed by complex polyhedra. Fortunately, the targeted regulation mechanism in tetrahedral configurations and parallel computation techniques may potentially mitigate the computational burden imposed by complex polyhedra.

Distinct components can play various roles in the formation of DNA polyhedra; by performing calculations and analyzing results, we have successfully identified the beneficial components to reduce their number. This discovery has facilitated algorithm optimization and allowed targeted configuration selection, thus providing insights into implementing optimal algorithms for screening complex polyhedral configurations.

Our results not only present a methodology for screening simple polyhedra with the minimum number of components but also offer numerous potential configurations for laboratory synthesis. Our approach can provide both quantitative and qualitative indications for synthesizing these candidates. The targeted regulatory mechanism also provides novel insights into the design and functionalization of DNA polyhedra.

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