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Approaching the Limit: Molecular Design of DNA Prisms and Pyramids with One Strand Based on Polyhedral Links

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Abstract

DNA polyhedra have been regarded as an ideal kind of drug delivery in vivo. DNA polyhedral links have been proposed to make fully understanding the mechanisms of these novel structures. In this paper, a series of *n*-order DNA prisms and pyramids are designed and optimized based on polyhedral link models. The strategies are put forward to design and reduce the number of strands of *n*-order DNA prisms and pyramids to the limit, which will provide some theoretical blueprints for laboratory synthesis.

1 Introduction

In 1991, Professor Seeman reported the first man-made DNA nanostructure, a DNA cube[1], which unravels that DNA can be considered as ideal raw material strands to assemble nanostructures with regular patterns[2]. Then, how to design appropriate building blocks and to control their arrangements in space as polyhedral skeletons becoming a great challenge in nano-molecular chemistry[3-4]. A lot of DNA polyhedra have been designed and synthesized in labs[5], which are considered as ideal drug delivers to control the drug release[6-7], such as DNA tetrahedra [8-11], cubes [12-13], octahedra[14-15], dodecahedra[16-17] and icosahedra[18-20]. All these novel structures not only rich the library of DNA polyhedra but also bring new vigor and vitality into theory research about secrets behind these structures.

To make a full understanding of the mechanisms that how did DNA strands fold into desired polyhedral skeletons becoming a fresh area. A lot of scientists turn to mathematics for help, and then topological methods are introduced in. Topology is a mathematical notion that has been used to describe properties of objects that remain unchanged under a certain kind of continuous, invertible, and one-to-one transformation. DNA polyhedral links are reasonable and powerful topological models to simulate DNA nanostructures if regardless of DNA strands as lines without thickness [21-23]. A series of DNA polyhedra links have been designed based on experimental results[24-28] and their characters have been described with mathematical variables[29-32], some of these links have been used as synthesis templates[33-37], for example, in 2019, Mokoto Fujita reported that they have constructed some 3D molecular objects based on polyhedral links[38] . Some scientists have tried to assemble DNA one[39-40] or two DNA strands[41] into defined nanostructures, which want to approach to the limitation of the number of the strands. It is very important to reduce the required components' number of DNA polyhedra to its limitation, which will make the DNA polyhedra designing more effectively.

In common, each edge of a polyhedron is covered by even half-turns and an uncrossed junction located at each vertex. Jonoska and Twarock have put forward a strategy by replacing even half-turn edges with odd ones and they demonstrated that DNA platonic polyhedra can be assembled with two strands successfully [42-44]. And their work made a good beginning for others. Duan has designed a series of Sierpinski links and knots by the method [27, 28]. Can the limitation of strands number can be reduced further to only one? To solve the problem, the general uncrossed vertexes are replaced by crossed ones, this work is also reported by Jonoska and Twarock [42]. All these works pave an avenue to design DNA polyhedra with one DNA strand. However, all these works focus on the simple polyhedra and the regularly repeated structures in spaces are still not be considered. It is noteworthy that the regularly repeated structures in spaces have more cages, which may play a more important role in drug delivery.

In this paper, *n*-order prisms and pyramids are selected as our research subjects for they are regularly repeated structures in space. *n*-order DNA prisms and pyramids based on polyhedral link models will be designed and then the number of strands of them will be reduced to the least. Our research reveals that although most of these aesthetics and extremely complex architectures have not been synthesized in labs, they will be novel candidates for chemical synthesis, especially for complex DNA cages.

2 Method

To make the discussion smoothly, some terms must be defined as follows:

***n*-order prism or pyramid**: planes that parallel to the bottom surface are used to cut a prism or a pyramid and make sure that all parts with equal height, then we call the polyhedron *n*-order prism or pyramid, *n* is the number of parts. For examples, use a plane to cut a pentagonal prism into two equal parts, we will get a *2*-order pentagonal prism, and use two planes, a *3*-order pentagonal prism is obtained (see Figure 1a). As well as pentagonal prisms, *1*-order, *2*-order, and *3*-order hexagonal pyramids also can be got, which is shown in Figure 1b from the left to right.

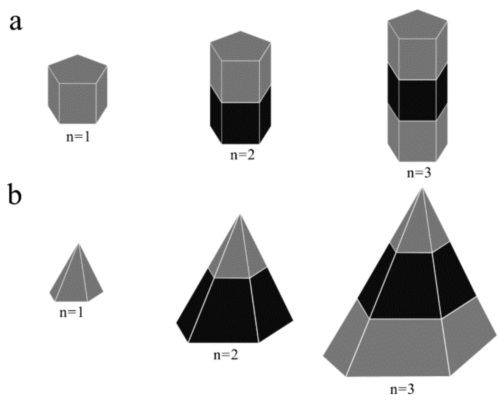

Figure 1. *n*-order prisms and pyramids. a: there are *1*-, *2*- and *3*-order pentagonal prisms from the left to right; b: there are *1*-order, *2*-order and *3*-order hexagonal pyramids from the left to right.

Strands number (*s*): the number of strands that required to assemble a DNA polyhedra, denoted by *s*. In other words, it is equal to the number of circles of a polyhedral link.

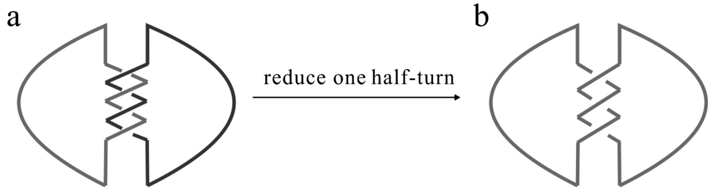

Figure 2. Reduce strands number of polyhedral links by replacing even half-turn with odd ones. a: a polyhedral link with 4 half-turns, s=2; b: a polyhedral knot with 3 half-turns, s=1.

For example, the half-turn number is 4 and the number of strands of the polyhedral link shown in Figure 2a is 2 if we reduce the half-turn number of the link in Figure 2a to 3 and then the strand number *s* of the knot in Figure 2b is 1. This means that we can reduce the strand number of polyhedra links by adding or removing one half-turn, in other words, we can use the odd half-turns to replace the even half-turns.

For most known DNA polyhedra, all edges are covered by even half-turns, so their strand numbers are equal to their face number. As everyone knows, the direction of a strand cannot be changed if an edge is covered by even half-turns, the direction will be changed while the edge is covered by odd half-turns. Therefore, the key to reducing strand number to its limitation is to introduce more and more odd half-turn edges.

3 Results and discussion

In our study, our aim is to assemble *n*-order prisms or pyramids with the least strands based on polyhedral link models. However, some known reports and the example shown in Figure 2 suggest that odd half-turn edge is more conductive than even ones in reducing strands number. Thus, we will start our discussion from *n*-order prisms or pyramids with all odd half-turn edges. This is different from the strategy already reported, which beginning with all even half-turn polyhedral links. Four series of *n*-order prism all odd half-turn polyhedral links have been constructed and diagrammed in Figure 3 from left to right. It is easy to find that the least strand number of some prism links is only one, such as 3-order triangular prisms and 1-order, 2-order and 3-order pentagonal prisms.

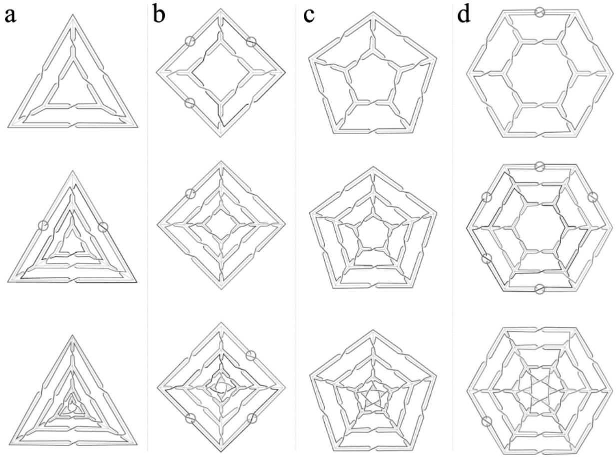

Figure 3. n-order prisms with all odd half-turn edges. a: there are 1-order, 2-order and 3-order triangular prisms from top to bottom; b: there are 1-order, 2-order and 3-order quadrangular prisms from top to bottom; c: there are 1-order, 2-order and 3-order pentagonal prisms from top to bottom; d: there are 1-order, 2-order and 3-order hexagonal prisms from top to bottom.

All these results suggest that the strand number may be reduced to 1 by using our strategy. It is worth noting that there are still some unexpected cases, such as 2-order triangular prism link (the middle of Figure 3a, *s*=3), 1-order, 2-order and 3-order pentagonal prism links (Figure 3b, *s*=4, 2, 4) and hexagonal prism links (Figure 3d, *s*=2, 6, 2).

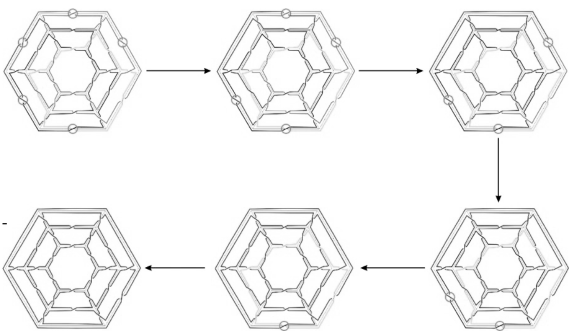

Figure 4. To get a 2-order hexagonal prism link with only one strand by replacing odd half-turn edge with even half-turn edge step by step.

To solve this problem, a reverse strategy is proposed here to reduce their strands number of these special cases to one strand. Unlike the known strategy, we replace some odd half-turn edges with even ones. The detail operation is diagrammed in Figure 4, we set a 2-order hexagonal prism link as an example. The 2-order all odd half-turn hexagonal prism link is composed of six strands, which are marked with six different colors. As Figure 4 shown, we replace an odd half-turn edge where two different strands intertwine with an even half-turn edge, and then the strand number will be reduced one. Therefore, there are five odd half-turn edges that should be replaced, which have been marked with circles. To replace these odd half-turn edges step by step as shown in Figure 4, we will get a 2-order hexagonal prism link that folded by only one strand. The result will give provide a new template for synthesizing DNA polyhedra in laboratories. The result suggests that any *n*-order prism links can be assembled with only one strand. A DNA strand can be designed and annealed to produce an *n*-order DNA prism. However, it is worth noting that these structures are mathematical links without direction. Everyone knows that the two strands of DNA run in opposite directions to each other and are therefore anti-parallel, however, this does not mean that each edge of a DNA polyhedral link is anti-parallel. Our aim is to design the mathematical polyhedral links to show the edges with even or odd half-turns, which will help the synthetic chemists to design the sequence to control the direction.

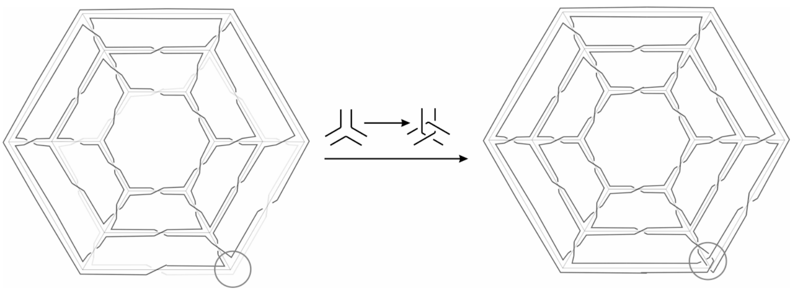

Figure 5. Scheme of reducing strands number by replacing vertex junctions.

The strand number can not only be reduced by adding even-odd half-turn but also by replacing the vertex junction. To our best knowledge, the vertexes of the majority of DNA polyhedra are uncrossed. Therefore, to replace vertex junctions, give reasonable access to solve the problem[42-43]. As shown in Figure 5, a selected uncrossed vertex junction of 2-order hexagonal prism that marked with a circle is substituted with crossed vertex, then the strand number is reduced to 1. Of course, the other *n*-order prism links that composed of one strand can also be produced by this strategy. It is noted that in Figure5, we just showed a 2-order hexagonal prism with 2 strands, however, this strategy also works for *n*-order polyhedral links with other strand numbers.

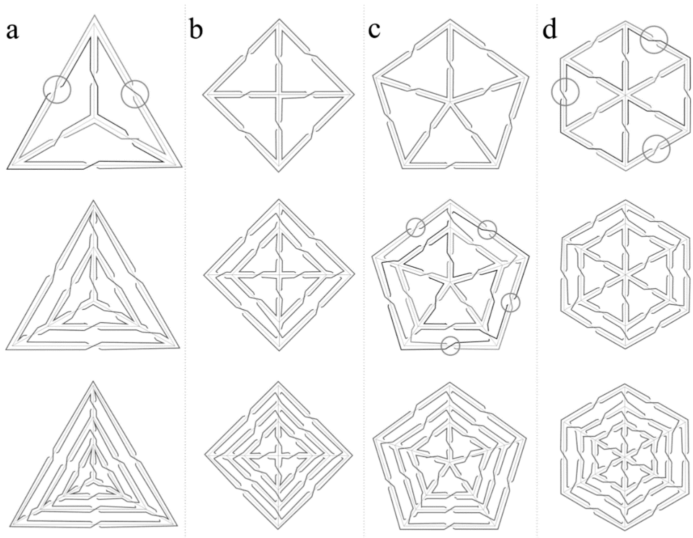

Figure 6. *n*-order pyramids links with all odd half-turn edges. a: there are 1-order (s=3), 2-order (s=1) and 3-order (s=1) triangular pyramid links from top to bottom; b: there are 1-order (s=1), 2-order (s=1) and 3-order (s=1) rectangular pyramid links from top to bottom; c: there are 1-order (s=1), 2-order (s=4) and 3-order (s=1) pentagonal pyramid links from top to bottom; d: there are 1-order (s=3), 2-order (s=1) and 3-order (s=1) hexagonal pyramid links from top to bottom.

To verify the applicability of our strategies, we tested *n*-order pyramids and found that the strategies are also applicative. In Figure 6, some *n*-order pyramids links with all odd half-turn edges are shown. Most of them are folded by only one strand. There are three special cases diagrammed in Figure 6, 1-order triangular pyramid link with three strands, 2-order pentagonal pyramid link with five strands and 1-order hexagonal pyramid link with three strands. As well as *n*-order prism links, their strands number can be reduced to one by replacing odd-half turn edges and uncrossed vertexes. Take the triangular pyramid, for example, two odd half-turn edges need to be replaced by even half-turn edges to get 1-order triangular pyramid links that made of one DNA strand. We can also replace one odd half-turn edge and one uncrossed vertex to reduce the number of strands to one as shown in Figure 5. The odd-half turn edges of the 2-order pentagonal pyramid link and 1-order hexagonal pyramid link that should be replaced by even-half turn have been marked with circles.

4 Conclusion

In this paper, we focus on reducing the strands number of *n*-order prisms and pyramids polyhedral links, we have proposed simple methods to reduce the numbers to their limitations. We started from all odd-half edges and then replaced edges with even-half edges and replaced vertexes with crossed vertexes, and a series of *n*-order prisms and pyramids polyhedral knots have been designed. These mathematical links suggest that all these structures can be composed of one DNA strand if the strand is long enough and we hope that all these results can provide some theoretical instruction for designing other types of DNA polyhedral nanostructures.

We started from *n*-order prisms and pyramids with all odd half-turn edges and replacing odd half-turn edges with even ones, we successfully reduced the number of strands to any number we want. However, the limited number of strands is only one, which demonstrates that all *n*-order prisms and pyramids can be folded by only one DNA strand.

We can also use a combinational strategy to reduce the number of strands, reduce the number of strands to 2 by replacing odd-half turns and then replacing one uncrossed vertex by one crossed vertex, finally the strand number of *n*-order prisms and pyramids are reduced further to only one. This strategy paves a new way to design and synthesize more novel structures that folded with a single strand. However, these exotic molecules would mark a beginning, not an end. The study of these simple strategies implies many opportunities and challenges to design more exotic DNA polyhedra.

In summary, we hope that the theoretical molecular design of DNA polyhedral links with the least strands will stimulate chemists to search for molecular realizations. Their chemical applications in DNA nanotechnology also require further studies in the future.

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