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Molecular design of DNA polyhedra based on genus

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Abstract Topology plays an important role as a guiding principle for the design of novel molecules. It is well known that polyhedral links could be served as mathematical models for DNA polyhedra. In this study, we have proposed a serial of novel design strategies to extend DNA polyhedral links to be embedded in high-genus surfaces. Three families of polyhedral links are theoretically constructed by integrating odd edges, introducing crossed vertices, as well as templating on high-genus substrates. Formulas for calculating the genus of these polyhedral links are given, by using the operation of Seifert construction. Research on genus reveals that these aesthetics and extremely complex architectures provide novel candidates for chemical synthesis, especially for DNA cages.

Keywords DNA polyhedra · Genus · Odd edges · Crossed vertices · Surfaces

1 Introduction

One great challenge in nano-molecular chemistry is the designing of building blocks to attain total control of the arrangement of molecules with polyhedral skeletons [1]. Owing to its double helical structure and self-reorganization ability, DNA is an ideal

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programmable building block for the assembly of a wide range of nanostructures [2]. Since the first synthesis of DNA cube by Chen and Seeman [3], a lot of works used branched DNA junctions to assembly a set of exotic polyhedra, including tetrahedra [4], octahedra [5] and truncated octahedra [6]. More recently, a new synthetic strategy has been proposed to build a dodecahedron and a buckyball by a number of identical n-point stars as building blocks [7–11]. These exciting architectures not only have greatly enriched the knowledge of nano-materials, but also have attracted scientists' extensive attention in their constructional formalism.

Polyhedral links, as mathematical models for DNA polyhedra, have brought some topological viewpoints to phrase and answer structural characteristics of DNA polyhedra [12,13]. As a test to this mathematical model, we have assembled a serial of polyhedral links, with their theoretical characterization in terms of topological invariants [14–17]. It opens broad avenues for charactering DNA polyhedra by the mathematical technique of knot theory [18]. Recently, the Seifert construction of polyhedral links [19] gave a good understanding of DNA nanopolyhedra. It generates the new Euler formula that relates the numbers of components μ, of crossings c, and of Seifert circles s, which states as: $s + \mu = c + 2$. This formula shows that most of DNA polyhedral catenanes synthesized so far are restricted to a sphere, and it also gives a clue for the molecular design based on genus [20–22].

In this paper, we are interested in the molecular design of DNA polyhedra embedded in high-genus surface. The new methods for constructing polyhedral links are based on three simple operations by integrating edges with odd number of twists, introducing crossed vertex configurations, and using high-genus surfaces as templates. By applying the Seifert construction, the structural properties and formulas for calculating genus of the three types of molecules are discussed. The study of genus reveals the intrinsic properties and paves the way for the topology-aided molecular design of DNA polyhedra. As we will, now hope, such novel methodologies can aid synthetic chemists and biologists in testing and developing their synthetic strategies.

2 Topological aspect of polyhedral links: genus

Polyhedral links, the interlinked and interlocked architectures on the basis of the 1-skeleton of a polyhedron, are constructed by using tangle structures to replace its vertices and edges. It has been demonstrated that DNA polyhedral links are all alternating links, which contain crossings alternate between over and under crossings along one component circuit. Furthermore, one strand of each edge is oriented (5′–3′) and the other is in the opposite direction (3′–5′). The understanding of DNA polyhedral links is a first-step to clarify the stereo-chemical controlling mechanisms and the biological self-assembly principle of DNA polyhedra. Another basic object of topology is the surface. As illustrated in Fig. 1c, by fattening up the vertices into disks and the edges into bands connecting these disks, it results a Seifert surface with this link as its boundary. Alternatively, the Seifert surface is connected by a set of Seifert circles distributed at vertices and edges [23]. The topological feature that distinguish these surfaces is the number of Seifert circles, defined as $s(L)$.
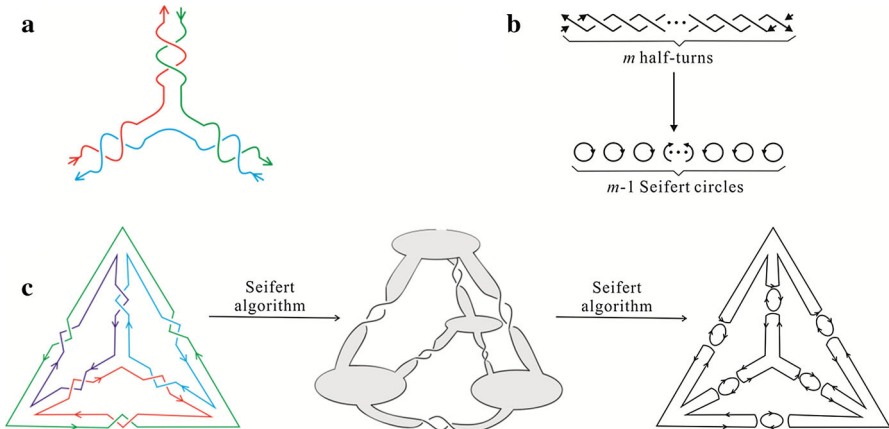
Fig. 1 The construction of branched polyhedral links. **a** A vertex building block of 3-branched curve, **b** an inverted twisted double-line edge as building blocks, and **c** the Seifert construction of a tetrahedral link based on its minimal projection

It was proved that the numbers of components μ, of crossings c, and of Seifert circles s always satisfy a simple and elegant arithmetic relationship [19]:

$$s + \mu = c + 2. \tag{1}$$

We called this equation as the new Euler formula for DNA polyhedra, which detects the topological characteristics including connectedness, holes, and twistedness of polyhedral links. It is easy to see that the relation comes from the spherical character of parent DNA polyhedra. As such, the new Euler formula can be extended to other forms of DNA cages with different topologies by:

$$s + \mu = c + 2 - 2g_s \tag{2}$$

where g_s denotes the genus of a Seifert surface. The genus of an oriented link is the minimum genus of all Seifert surfaces of the oriented link [24]. If applying Seifert's algorithm to an alternating oriented link, a Seifert surface of minimal genus is obtained. So the genus of a polyhedral link g_l equals to the genus of its corresponding Seifert surface g_s, and then

$$s + \mu = c + 2 - 2g_l. \tag{3}$$

The genus is a topological invariant, which relates to the Euler characteristics of the diagram. Its geometrical interpretation is quite simple, which is just the number of holes going through the surface. For example, a DNA polyhedral link with genus zero is just embedded in a surface homeomorphic to a sphere. As a topological invariant, genus recurs the geometry of polyhedra to characterize the topology of polyhedral links. An excepting application is the topological classification of RNA secondary structures with pseudoknots based on the concept of topological genus [25], thus

bridge geometrical structures to the life world. Apart from its mathematical relevance, however, genus is also of substantial interest to nano-molecular chemistry [26]. Here, it provides a systematical tool to design and analysis novel DNA polyhedra.

3 Polyhedral links with odd edges

Two main types of DNA polyhedra have been realized, whose topologies can be described by branched polyhedral links and star polyhedral links, respectively. The genus of these two types of polyhedral links equal zero, i.e. they are embedding in spheres. By intergrading odd twists into edge blocks, the molecular design of DNA polyhedra can be extended to surfaces with higher genus.

3.1 Branched polyhedral links

Two building blocks are needed for the design of branched polyhedral links. One is n-branched curve designed as a vertex building block, where n is equal to the vertices degree. The other is an m-inverted twisted double-line designed as an edge building block. We define edges as even edges if m is an even number, odd edges if m is an odd number. Two examples of building blocks, three-branched junction and m-inverted twisted double-line, are shown in Fig. 1a, b. So far, the most experimental studies focus on DNA polyhedra assembled by all even edges. Now, we are turning to the new molecular design based on both even and odd edges. Figure 2 shows the process of assembling a new polyhedral link by intergrading odd edges into an even polyhedral link.

In the following, we will be concerned with the calculation of genus of branched polyhedral links both consist of even and odd edges. For a DNA polyhedral link, its underlying polyhedral graph has F faces, E edges and V vertices. Applying the Seifert construction to each link will generate a surface that contain two sets of Seifert circles, based on vertex and edge building blocks, respectively. If apply the Seifert operation to the vertices, each vertex generates a Seifert circle independent of the degree of vertex, namely,

$$s_v = V, \tag{4}$$

where s_v denotes the number of Seifert circles derived from vertices. In addition of these circles, other Seifert circles are distributed at edges and the number is s_e.

No odd edges   3 odd edges
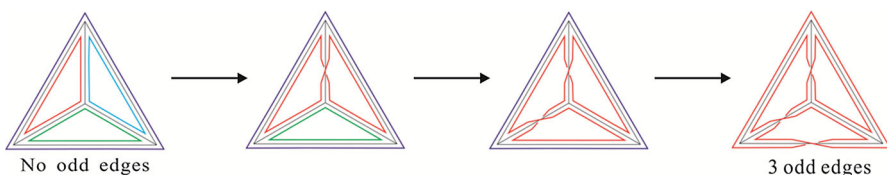
Fig. 2 An even tetrahedral link is transformed into a new type of high-genus link by integrating edges with odd number of twists

Therefore, the number of Seifert circles s of DNA polyhedral links equals:

$$s = s_v + s_e. \tag{5}$$

Consider a polyhedral link has p edges with even half-twists and the number of half-twists are m_1, m_2, ..., m_p, as well as it has q edges with odd half-twists and the number of half-twists are n_1, n_2, ..., n_q, respectively. According to these assumptions, it is easy to determine that twists distributed at edges only have even or odd times, thus of course

$$E = p + q. \tag{6}$$

As stated before, $s = s_v + s_e$, where $s_v = V$.

For an edge with m twists, as shown in Fig. 1b, it generates a set of Seifert circles with number of $m - 1$. Therefore,

$$
\begin{aligned}
s_e &= \sum_{i=1}^{p} (m_i - 1) + \sum_{j=1}^{q} (n_j - 1) \\
&= \sum_{i=1}^{p} m_i - p + \sum_{j=1}^{q} n_j - q \\
&= \sum_{i=1}^{p} m_i + \sum_{j=1}^{q} n_j - (p + q)
\end{aligned}
\tag{7}
$$

Substituting Eq. (6) into Eq. (7) gives

$$s_e = \sum_{i=1}^{p} m_i + \sum_{j=1}^{q} n_j - E \tag{8}$$

So

$$s = s_v + s_e = V + \sum_{i=1}^{p} m_i + \sum_{j=1}^{q} n_j - E \tag{9}$$

The numbers of half-twists on each edge are $m_1, \ldots, m_p$, $n_1, \ldots, n_q$, and each half-twist corresponds to a crossing, thus we have

$$c = \sum_{i=1}^{p} m_i + \sum_{j=1}^{q} n_j \tag{10}$$

Although a DNA polyhedral link with both even and odd number of half-twists is a warp and weft-interwoven network rather than a simple polyhedron, here we still use μ to denote the component number of the link.
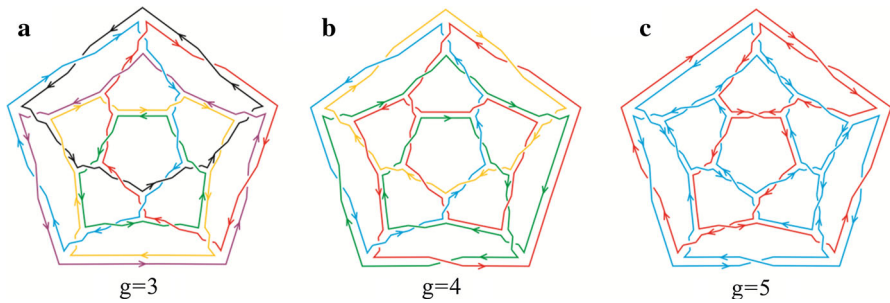
Fig. 3 Some examples of odd dodecahedral links with genus 3 (**a**), 4 (**b**), and 5 (**c**)

Accordingly, substituting Eqs. (9) and (10) into Eq. (3), we obtain the result shown as the following equation:

$$g_l = \frac{F - \mu}{2} \tag{11}$$

Therefore, for the regular polyhedron with face number F, the genus of the corresponding link is only decided by its component number μ, which embeds in a surface with increasing genus as the decrease of the component number.

As a matter of fact, Jonoska and Twarock [27] have proposed the blueprint for dodecahedral DNA cages by integrating odd edges. Using Eq. (11), it is easy to calculate that they are embedded on surfaces with genus 3, 4, and 5, as shown in Fig. 3.

3.2 Star polyhedral links

In star polyhedral links, the building block of vertex structure is an n-point star curve, and of edge structure is two-anti parallel DNA duplexes. The key step of this type of DNA polyhedra is to design and control the assembly of n-point star curve, where n is equal to the vertex degree. A three point star, a four point star and a five point star are shown in Fig. 4a. Most recently, Zhang et al. [28] designed a series of more tractable point stars, which could be assembled into some more complex DNA nanostructures. For examples, in Fig. 4b, three-point stars with 2.5 turns, 2.0 turns, and 2.25 turns were designed. It is noteworthy that the three-point star with 2.25 turns can be obtained by deleting and adding a twist from three-point stars with 2.5 turns and 2.0 turns. As a result, a star-polyhedral link with odd twisted edges will be obtained. By applying the Seifert algorithm to their minimal graphs, the genus of such links will be investigated. In this part, we restrict ourselves to the special polyhedral link assembled by 2.25 turns point stars. Two examples, a tetrahedral, and a hexahedral link are shown in Fig. 5a, b.

As proofed in [19], the total number of Seifert circles s can be calculated by:

$$s = 3nV + \sum_{i=1}^{e} k_i \tag{12}$$
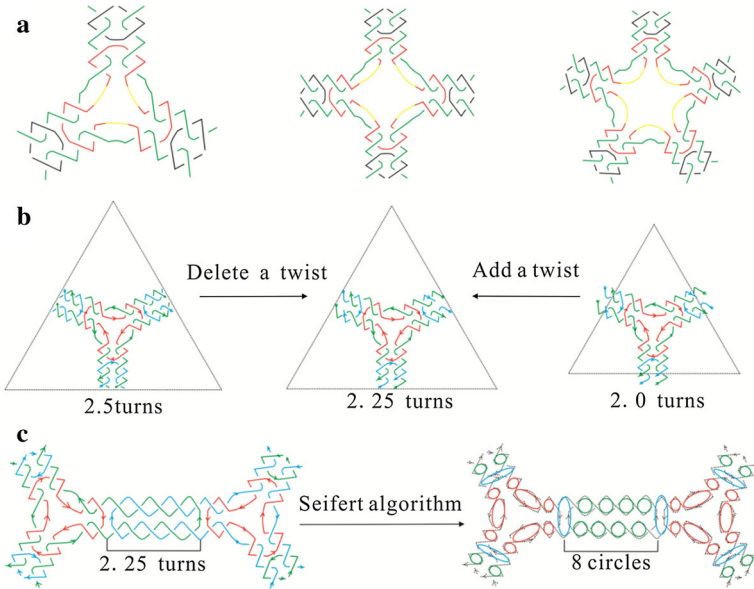
Fig. 4 Star polyhedral links. **a** The vertex building blocks of 3-, 4-, and 5-point stars, **b** integrating odd edges into star polyhedral links by adding and deleting twists in the edge building blocks, **c** the Seifert construction to star polyhedral links with odd edges
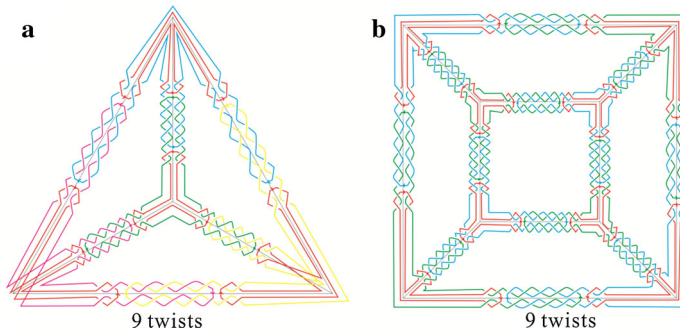
Fig. 5 A DNA tetrahedron (**a**) and a DNA cube (**b**) assembled by star points and odd twisted edges

And the crossing number c meets:

$$c = 4nV + \sum_{i=1}^{e} k_i \tag{13}$$

where k_1, k_2, …, and k_e denote numbers of twists on each edge.

It is easy to check that no matter how many twists on each edge of a polyhedron assembled by n-point stars; the Seifert circle number s and crossing number c are given by:

$$s - c = -nV \qquad (14)$$

Furthermore, applying Seifert algorithm to odd twisted edge of star polyhedral links is easy to conclude that the component number is twice of vertex number, namely:

$$\mu = 2V \qquad (15)$$

Substituting Eqs. (14) and (15) into (3), we can obtain the genus of this kind of DNA polyhedra, yields:

$$g_l = F - 1. \qquad (16)$$

4 Crossed polyhedral links

Another way of generalizing construction method of DNA polyhedra is borrowed from protein chains. Inspired by the bacteriophage HK97 capsid, we have constructed a series of polyhedral links through "three-cross-double-line covering" and "*m*-crossover-double line covering" methods [29]. In view of their vertex configurations, we call this type of links as *three-crossed polyhedral links*. By assessing the opposite directions in the double line of each edge, we try to extend this method to design potential models for DNA polyhedra. It is easy to found that three-crossed polyhedral links could fall into three general families: the first type contains no twists (Fig. 6a), the second one is constructed with all even edges (Fig. 6b), and the third one is integrated by odd edges (Fig. 6c). To simplify, all structures in figures use two crossings to denote $2k$ crossings on each edge. However, we limit ourselves here to
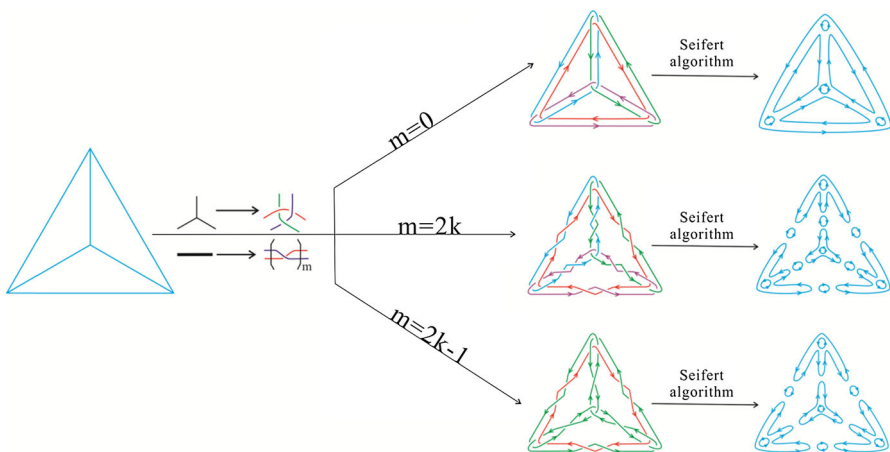
Fig. 6 The molecular design of crossed polyhedral links and their Seifert construction. **a** A tetrahedral link with no twists on edges, **b** with all even edges, **c** by integrating odd edges

consider the first two types of three-crossed polyhedral links as two simplest examples
to investigate their embedding surface and related genus.

As shown in Fig. 6a, each Seifert circle is distributed at each vertex and each face,
so the Seifert circle number is the sum of vertex number V and face number F, thus

$$s_v + s_f = V + F \tag{17}$$

In addition, the crossing number c and component number μ satisfies the following
two equations:

$$c = nV \tag{18}$$
$$\mu = F \tag{19}$$

where $n = 3$ is degree of vertex.

To substitute these equations into Eq. (3), the genus of such polyhedral link can be
figured out by the following result:

$$g_l = \frac{V}{2} - 1 \tag{20}$$

For example, the genus of the polyhedral link shown in Fig. 6a is one, thus, it embedded
in the surface that correspond to a torus, which is the simplest two-manifold such as
a doughnut, bagel or anchor ring.

For an even crossed polyhedral links with $2k$ crossings in each edge, the number of
Seifert circles generated by vertex building blocks s_v and edge building blocks s_e are:

$$s_v = 2V \tag{21}$$
$$s_e = \sum_{i=1}^{e} 2k_i - 1 \tag{22}$$

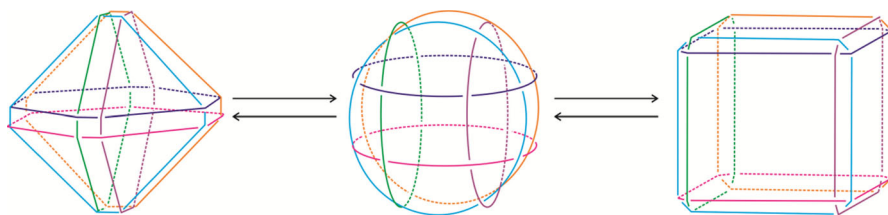Therefore, the total number of Seifert circles is:

$$s = 2V + \sum_{i=1}^{e} 2k_i - 1 \tag{23}$$

And the crossing number c and component number μ also satisfy the following equa-
tions

$$c = nV + \sum_{i=1}^{e} 2k_i \tag{24}$$
$$\mu = F \tag{25}$$

where n is degree of vertex.

Fig. 7 The operation of sphere-surface-movement between a fair of dual polyhedral links (an octahedral link versus a hexahedral link)

Keeping in mind Eq. (3), the genus of this type of DNA polyhedra can be calculated by:

$$g_l = \frac{n-1}{2} V \qquad (26)$$

For example, the tetrahedron shown in Fig. 6b has genus of 4, which embedded in a closed surface that is equivalent to a sphere with four holes or handles.

Of course, there are a lot of limitations in the design of crossed polyhedral links. A more extensive discussion of crossed polyhedral links can be found in our previous work [30]. It is important to mention that our method can only be applied to polyhedra whose vertices are of order three. Fortunately, dual polyhedral links provide tools to the molecular design of crossed polyhedral links based on more general polyhedra [31]. For example in Fig. 7, the operation of sphere-surface-movement implies three new construction methods: "four-cross-curve and double-line covering", "five-cross-curve and double-line covering" and "cross-curve and single-line covering". This dual process also shows that dual polyhedral links are topologically equivalent, and they embedded in two homotopic surfaces with the same genus.

5 Surface polyhedral links

Closed surfaces are basic objects in topology, which can be divided into two parts, orientable and non-orientable. In particular, a polyhedron embedded in the given closed surface S has its own Euler characteristic, the topological invariant that distinguish surfaces and can be obtained from their genus, which can be expressed as:

$$\chi = V + F - E = 2 - 2g_s \quad \text{\{for an orientable surface\}} \qquad (27)$$
$$\chi = V + F - E = 2 - g_s \quad \text{\{for a non-orientable surface\}} \qquad (28)$$

Some common closed surfaces are shown in Fig. 8, including orientable surfaces such as a tours (Fig. 8a), K_5 (Fig. 8b) and K_6 (Fig. 8c) polyhedra; non-orientable surfaces such as a Klein bottle (Fig. 8d), a Mobiüs band (Fig. 8e), and a real projective plane (Fig. 8f). The Euler number, orientability and genus of different surfaces are listed in Table 1. The systematical study of these high-genus surfaces is reminiscent of the tiling of more complex chemical molecules, especially for fullerenes [32,33].
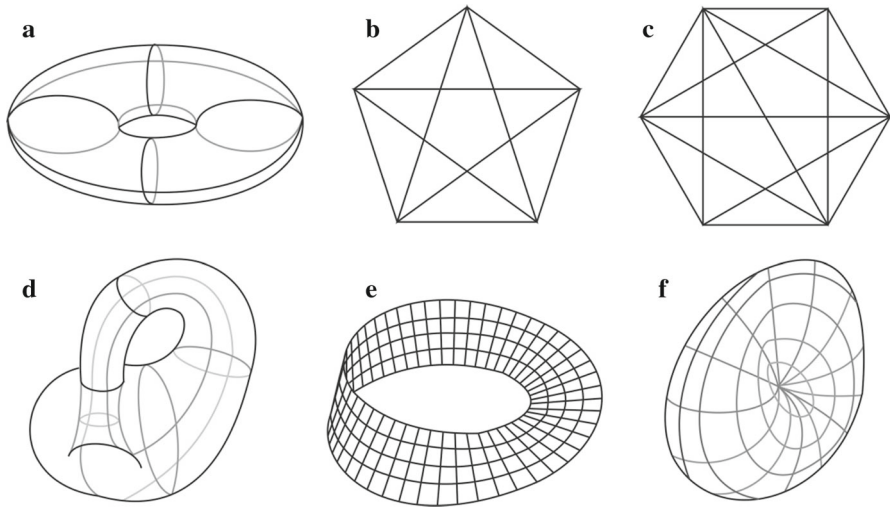
Fig. 8 Some common closed surfaces with high-genus. **a** A torus, **b** a K_5 polyhedron, **c** a K_6 polyhedron, **d** a Klein bottle, **e** a Mobius band and **f** a projective plane

Table 1 The Euler number, orientability and genus of different surfaces and their links

Surface S	The Euler number $\chi(S)$	Orientable	g_s	g_l
Sphere	2	Yes	0	0
Torus	0	Yes	1	1
Klein bottle	0	No	2	2
Projective plane	1	No	1	1
Möbius band	0	No	2	2
2-Holed torus	−2	Yes	2	2
g-Holed torus	2−2g	Yes	g	g
Disk	1	Yes	1/2	1/2
Cylinder/annulus	0	Yes	1	1
Sphere with c cross caps	2−c	No	c	c

Here, we proposed that orientable surfaces could serve as new substrates to design DNA polyhedral links with higher genus via templating on them directly. Using polyhedral lattices embedded in an orientable surface as an accurate geometric framework, branched or star DNA junctions can be assembled into the final linked structures. We defined interlinked and interlocked architectures on the basis of the polyhedral lattices on a surface as *surface polyhedral links*. In the present paper, we selected three surfaces as examples to describe our strategy: the torus T^2, the K_5 polyhedron, and the K_6 polyhedron. All these surfaces are orientable with $g_s = 1$. It is a hard challenge for us to construct links on curved surfaces. To make the discussion smoothly, we only construct DNA curved faces with even twists edges. For examples, torus polyhedral links assembled with branched junctions and n-point star are showed in Fig. 9a, d, K_5
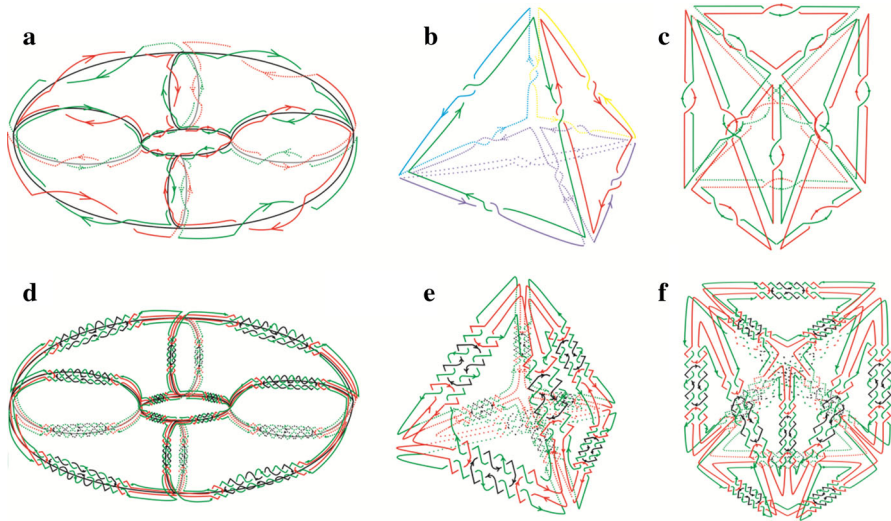
Fig. 9 DNA polyhedral inks with genus of one. Torus polyhedral links with branched junctions (**a**) and $n-$point star (**d**), K_5 polyhedral links with branched junctions (**b**) and $n-$ point star (**e**), K_6 polyhedral links with branched junctions (**c**) and n-point star (**f**)

polyhedral links with branched junctions and $n-$point star are showed in Fig. 9b, e, K_6 polyhedral links with branched junctions and n-point star are showed in Fig. 9c, f.

It is noteworthy that, the component numbers, Seifert circle numbers, and crossing numbers of these surface polyhedral links depend on the corresponding polyhedral lattices embedded in surfaces. For example, the component numbers μ of such polyhedral links are also equal to face numbers F. Additionally, a polyhedral lattice embedded in an orientable surface obeys the Euler theorem. Therefore, the genus g_l of these curved links will satisfy:

$$V + F - E = 2 - 2g_l \tag{29}$$

Substituting Eq. (29) into Eq. (27) will yields:

$$g_l = g_s \tag{30}$$

The Eq. (30) suggests that if the number o twists on each edge of a surface is even, the genus of links just equal to the genus of the corresponding orientable surface, regardless of branched junctions or n-point stars are used as building blocks.

In comparison with orientable surfaces, a non-orientable surface has only one side. In that way, the space structure of any non-orientable closed surface should contain self-intersections. Therefore, how to design a DNA polyhedral link in such knotted or linked surfaces must be very difficult, which fall out the scope of this paper. In fact, numerous DNA curved surfaces have been synthesized in labs, such as DNA bottles [34], and DNA Mobius band [35]. However, most of them are assembled on basis of origami scaffolds. On the other hand, Jablan et al. [36] investigated the possibility of

forming virtual knots and links via templating on graphs K_5 and $K_{3,3}$. As far as we know, there is no one try to simulate and design such structures with link models. Therefore, our attempts may fill in the blank of this area.

6 Discussion and conclusions

Research on the relationship between the construction of polyhedral links and their underlying surfaces have proposed three simple methods to design DNA polyhedra with higher genus. The construction of DNA polyhedral links including the integration of odd edges, the introduction of crossed vertices, and the molecular design based on high-genus surface, is systematically discussed. Application of Seifert construction to these polyhedral links is used to generate simple formulas for calculating their genus. Accordingly, the genus of odd polyhedral links, crossed polyhedral links and surface polyhedral links are based on the number of odd edges, the type of vertex configurations, and the topology of underlying surfaces, respectively.

The study of new Euler formula shows that the genus of most of DNA polyhedra synthesized so far equal to zero, which means that they correspond to the simplest and prefect chemical spaces that are homeomorphic to spheres. Polyhedral links discussed in our work belong to surfaces with higher genus, which correspond to some distorted chemical spaces with more complexity. These structures are still purely hypothetical in nature but can pose some serious challenges for the synthetic chemist. Therefore, the genus of DNA polyhedra thereby brings a concept developed in the context of mathematics into the realm of synthetic chemistry and structural biology.

However, these exotic molecules would mark a beginning, not an end. The study of these simple operations implies many opportunities and challenges to design more exotic DNA polyhedra with higher-genus by two immediately composite operations:

1. The combinations of using crossed vertices and odd edges. As a mathematical model for a DNA tetrahedron, Fig. 6c shows a crossed polyhedral link with three odd edges.
2. The integration of crossed vertices based on the substrate of a high-genus surface. For example, see Fig. 10, it demonstrates a torus polyhedral link assembled form

Fig. 10 A polyhedral link (*arrows* are omitted) constructed by two composite operations of introducing crossed vertex configurations based on torus
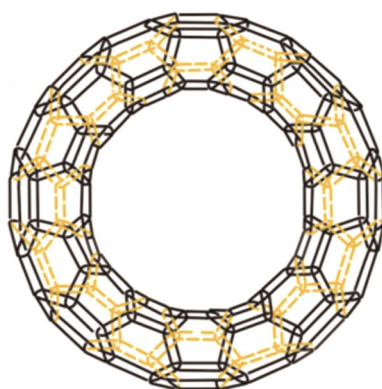
three-crossed vertices, or a crossed polyhedral links via templating on a toroidal substrate.

In summary, we hope that the theoretically molecular design of DNA polyhedral links with high-genus will stimulate chemist to search for their molecular realizations, and their chemical applications in DNA nanotechnology also require further studies in the future.

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