

# Designer three-dimensional DNA architectures

## Yonggang Ke



The capability to *de novo* design molecular structures with precise weights, geometries, and functions provides an important avenue not only for scientific explorations, but also for technological applications. Owing largely to its rationalizable design strategies, super-molecular self-assembly with DNA has emerged as a powerful approach to assemble custom-shaped intricate three-dimensional nanostructures with molecular weights up to several megadaltons. Here, we summarize and discuss landmark achievements and important methodologies in three-dimensional DNA nanostructures.

### Addresses

Wallace H. Coulter Department of Biomedical Engineering, Georgia Institute of Technology and Emory University, Atlanta, GA 30322, USA

Corresponding author: Ke, Yonggang ([yonggang.ke@emory.edu](mailto:yonggang.ke@emory.edu), [yonggang.ke@bme.gatech.edu](mailto:yonggang.ke@bme.gatech.edu))

**Current Opinion in Structural Biology** 2014, **27**:122–128

This review comes from a themed issue on **Engineering and design**

Edited by **Shohei Koide** and **Tanja Kortemme**

<http://dx.doi.org/10.1016/j.sbi.2014.07.010>

0959-440X/© 2014 Elsevier Ltd. All rights reserved.

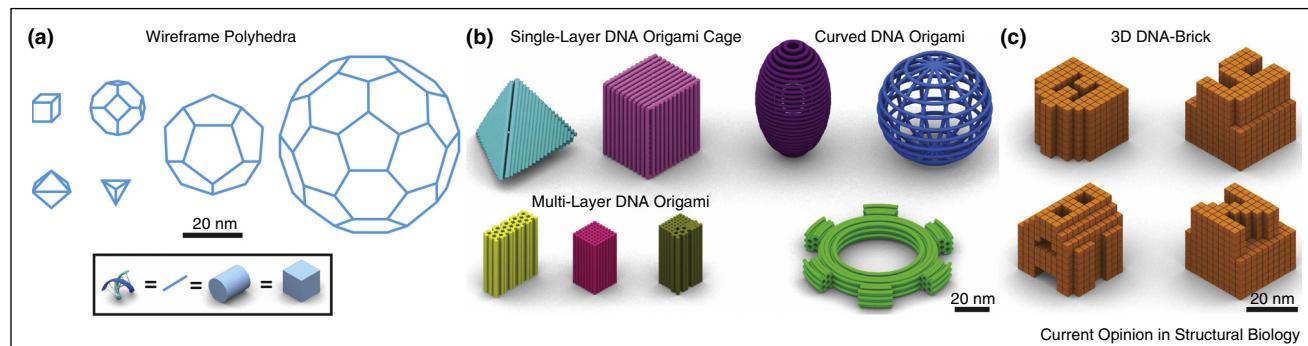
## Introduction

Through billions of years of evolution, biology has revealed an extremely diverse world with amazing structural complexity. Sophisticated, efficient molecular machines, from a small enzyme to a blue whale, remind us what a self-assembled system can achieve in terms of structural complexity and functionality. Biomolecules, especially nucleic acids and proteins, play the most crucial roles behind biological self-assembly, by acting as the information carriers and the basic building materials. Using the same material (DNA) and following the same rules of Watson–Crick base-pairing, structural DNA nanotechnology aims to rationally design and construct artifacts with nanoscale precision. The field was founded by Nadrian Seeman in 1982 [1\*] and has witnessed rapid growth ever since. The fast progress on achieving greater structural complexity using DNA is largely due to the simplicity of DNA's secondary structure — a double helix. Unlike diverse protein structures, a DNA duplex is significantly simpler — complementary DNA duplexes that consist of different sequences typically exhibit the

same double-helical structure with small variation. In addition, there are only four types of residues that form and just two types of connections (G–C, A–T base-pairing). The simplicity of DNA double-helix and Watson–Crick base-pairing make DNA a preferred programmable material for *de novo* bimolecular engineering. The general design process starts with defining the desired shape of a target nanostructure, followed by specification of the arrangement of individual DNA strands. At last, sequences are designated based on strand complementarity. In many cases, special sequence design algorithms (e.g. sequence symmetry minimization) are applied to make the target structure thermodynamically further more favorable than competing structures. Naturally, the trajectory of structural DNA nanotechnology is from small towards large, from simple to complex, and from two-dimensional (2D) to three-dimensional (3D) artifacts. A wide range of DNA structures are now at researchers' disposal, including lattices [2–6], ribbons [7,8], tubes [3,8], finite 2D and 3D objects with defined shapes [9,10\*,11–13,14\*,15–17], and macroscopic crystals [18]. In this review, we will focus on methodologies for constructing self-assembled 3D objects with defined discrete shapes, and discuss some challenges and future directions. However, it is worth noting that there are other exciting subfields, such as dynamic nucleic acid devices [19], which will not be discussed here.

## 3D DNA architectures

Structural DNA nanotechnology has demonstrated a variety of 3D architectures (Figure 1). For explanation purposes, we divide them into three categories. The first group of structures includes wireframe DNA polyhedra that are each typically assembled from a few to dozens of distinct DNA strands (Figure 1a). These polyhedra include cubes [9], truncated octahedrons [20], octahedrons [21], tetrahedrons [22], dodecahedrons [11], and buckyballs [11]. The second group of structures is DNA origami 3D structures that each contains a long m13 bacteriophage DNA and hundreds of short synthetic strands. These include single-layer hollow container structures [12,13], closely packed parallel-helix structures [14\*,23,24], and structures consisting of bent or twisted DNA helices [15,17,25\*] (Figure 1b). The last group of structures are 3D artifacts, each of which is assembled from hundreds of modular components called 'DNA bricks', which can be removed or added independently to create intricate nanoscale features [26\*\*] (Figure 1c). However, the boundaries between these three categories are somewhat obscure. For instance, DNA origami (as an assembly strategy) can be used to generate wireframe DNA polyhedra (a category of 3D DNA structures)

**Figure 1**

Three-dimensional DNA architectures. Three different models (a, bottom) were used to represent DNA double helices: lines, cylinders, and cubes. (a) Wireframe DNA polyhedra, including a cube [9], a truncated octahedron [20], an octahedron [21], a tetrahedron [22], a dodecahedron, and a buckyball [11]. (b) DNA-origami 3D structures, including single-layer hollow containers [12,13], multi-layer 3D DNA-origami structures in which parallel DNA duplexes are closely packed onto different lattice geometries [14\*,23,24], and 3D DNA-origami with curved DNA duplexes [15,17,25\*]. (c) DNA-brick 3D structures. As a modular approach, DNA-brick method enables self-assembly of sophisticated 3D structures from a common ‘3D canvas’ structure [26\*\*].

[14\*,27], and certain design strategies [21] used for the assembly of 3D DNA polyhedra, prior to the invention of DNA origami, already bore resemblance to the DNA-origami method. In the following three sections, we will discuss these three categories separately, with special emphasis on the most recent methods.

### Wireframe DNA polyhedra

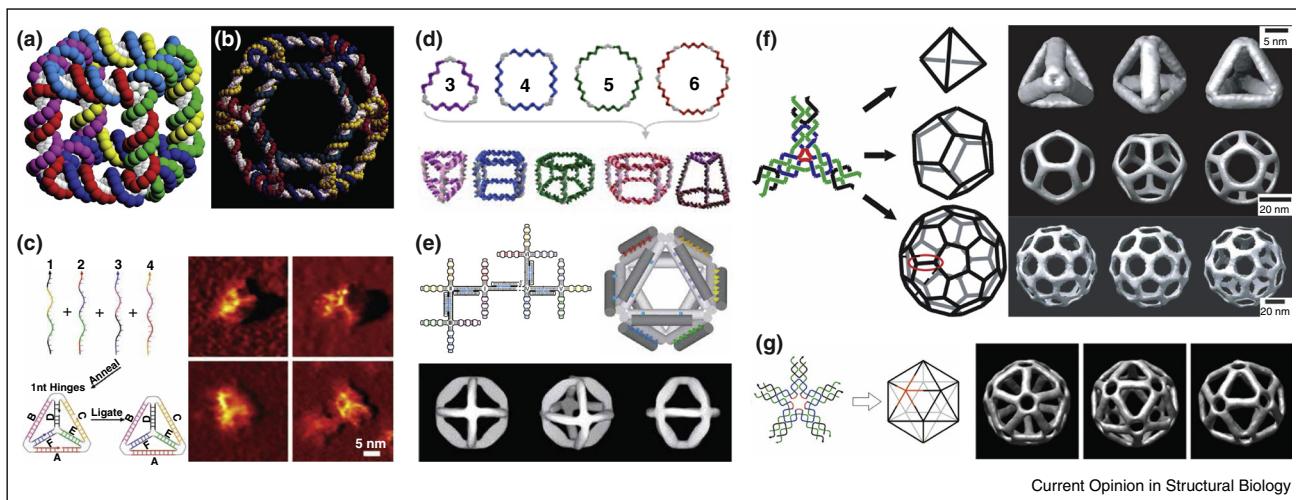
The first wireframe DNA polyhedron is a cube assembled from six single-stranded DNA molecules [9] (Figure 2a). Each strand formed a square and occupied one face of the cube structure. Seeman and coworkers used a multi-step assembly strategy and ligated all DNA strands during the process. As a result, the end product contains six topologically locked circular DNA strands. This design concept for assembling wireframe 3D polyhedra — placing flexible branched junctions at the vertices and engineering DNA duplexes to form edges and to connect the junctions — was then used to construct a variety of polyhedra with different sizes and geometries, including truncated octahedrons [20] (Figure 2b), and tetrahedrons [22] (Figure 2c). Sleiman *et al.* developed a method for synthesizing cyclic DNA concatemers using organic molecules as intermediates for connecting the repeating DNA sequences, and subsequently assembling different DNA concatemers and other short DNA strands into a group of DNA polyhedra, including prisms and a cube [28] (Figure 2d). Folding a ~1.7k-nt single-stranded DNA into an octahedron (~22 nm in diameter) by mixing it with five short synthetic strands (Figure 2e), Joyce *et al.*’s method is a landmark work for DNA polyhedra structures [21]. The usage of a long single-stranded DNA as a central component in fact bore some resemblance to the later DNA-origami method. Another important innovation for constructing DNA polyhedra is Mao’s hierarchical assembly of multi-junction DNA

tiles that consist of stiff double-helix arms connected at a relatively flexible structural center. Using this strategy, a tetrahedron, a dodecahedron, and a buckyball (~5 MDa) were assembled from three-arm-junction tiles [11] (Figure 2f), and an icosahedron was assembled from five-arm-junction tiles [29] (Figure 2g). More recently, Mao’s group demonstrated other DNA polyhedra by connecting two types of multi-junction DNA tiles via engineering the ‘sticky end’ cohesion [30\*].

### DNA origami

The invention of DNA origami [10\*] is considered as one of the most important breakthroughs in structural DNA nanotechnology. For the first time, the method offers a general strategy for constructing arbitrarily shaped megadalton DNA structures with global addressability, by folding a single-stranded m13 bacteriophage ‘scaffold’ DNA (~7k-nt) — via hybridization with hundreds of short synthetic strands — into two-dimensional structures with arbitrary shapes (Figure 3a). These short synthetic DNA oligos — typically shorter than 60 bases — are often called ‘staple strands’. The design process for making a structure can be simply considered as raster-filling a prescribed shape with the m13 scaffold. Helices in DNA origami are connected by both scaffold and staple crossover junctions — a crossover is formed at the position where two DNA duplexes exchange strands.

One way to extend 2D origami into the third dimension is to add unpaired flexible single-stranded segments into single-layer 2D origami and fold it into single-layer containers (Figure 3b and c). A box [13] and a tetrahedron [12] were the first two examples generated using this strategy. Another 3D-origami strategy is to stack single-layer DNA origami to form closely packed multi-layer

**Figure 2**

Current Opinion in Structural Biology

Wireframe DNA polyhedra. **(a)** A DNA cube was assembled from six DNA strands, which were ligated to cyclic strands during multi-step assembly. Adapted with permission from Ref. [9]; Copyright (1991) Nature Publishing Group. **(b)** A DNA truncated octahedron was assembled using similar strategy. Adapted with permission from Ref. [20]; Copyright (1994) American Chemical Society. **(c)** A DNA tetrahedron was assembled from four DNA strands and visualized by atomic force microscope Adapted with permission from Ref. [22]; Copyright (2005) The American Association for the Advancement of Science. **(d)** DNA prisms and a cube were assembled from DNA concatemers that consists of three, four, five, and six reporting units. Adapted with permission from Ref. [28]; Copyright (2009) American Chemical Society. **(e)** A DNA octahedron was assembled by a ~1.7-nt long DNA strand and five short DNA strands. Adapted with permission from Ref. [21]; Copyright (2004) Nature Publishing Group. **(f)** A tetrahedron, a dodecahedron and a buckyball were hierarchically assembled from three-arm-junction DNA tiles. Lengths of single-stranded linkages (red) at the center of tiles determine the flexibility of the tiles and thus the assembly outcome. Adapted with permission from Ref. [11]; Copyright (2008) Nature Publishing Group. **(g)** An icosahedron was assembled from five-arm-junction DNA tiles using similar strategy. Adapted with permission from Ref. [29]; Copyright (2008) National Academy of Sciences, USA.

structures. This approach is a more general design strategy because of its standardized rules, and enables construction of more rigid DNA structures. DNA duplexes in a multi-layer 3D origami can be packed using honeycomb lattices [14•] (Figure 3d), square lattices [23] (Figure 3e), or hexagonal lattices [24] (Figure 3f). Later Shih *et al.* also demonstrated tensegrity 3D origami structures that used multiple segments of unpaired scaffold for connecting rigid DNA helix-bundle units into 3D shapes [16] (Figure 3g).

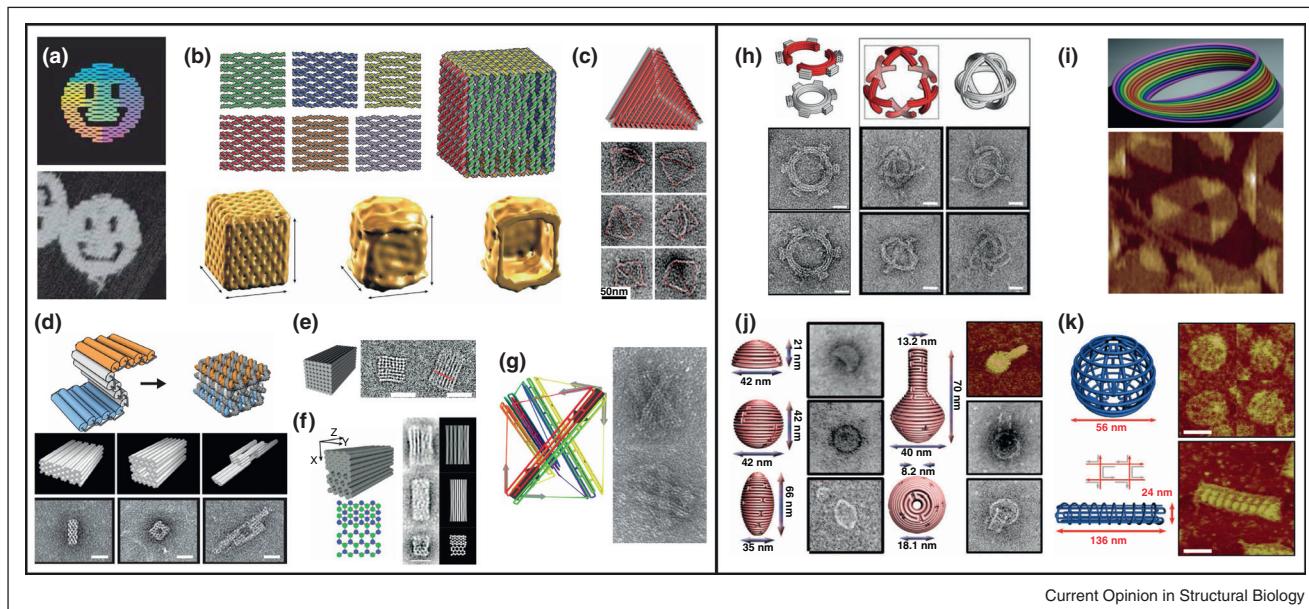
The versatility of 3D DNA origami was further extended by implementing curvatures using bent DNA helices (Figure 3h–k). This can be achieved by adding basepairs to the convex faces and deleting basepairs from the concave faces in a regular multi-layer DNA origami structure, without changing its crossover patterns. Shih *et al.* used this method to create a group of multi-layer 3D origami structures with precisely controlled curvatures [15] (Figure 3h). Yan and coworkers employed different strategies for generating fine curvatures in 3D DNA structures. First, the group made a Möbius strip by engineering special helix-end-to-helix-end connections based on 2D DNA origami [31] (Figure 3i). Later they invented a more interesting strategy in which crossover patterns were adjusted in accordance with the geometry

of single-layer 3D DNA containers [17]. In order to design a target structure, such as 3D spherical shells, ellipsoidal shells, and a nanoflask (Figure 3j), the method first defined the shape, identified the lengths of DNA helices, and then added crossovers to specific locations. Yan's group was also the first to use four-arm junctions to program 3D origami structures with curvatures [25•]. This approach enabled construction of gridiron-like wireframe 3D architectures. One of the most striking structures is a spherical hollow container (Figure 3k), in which a series of four-arm junctions and bent duplexes were used as vertices and connecting struts, respectively.

## DNA bricks

Yin *et al.* recently invented a modular assembly strategy that employed only short synthetic strand called DNA bricks. DNA-brick 3D self-assembly is invented on the basis of previous Single-Stranded-Tile (SST) assembly, which was initially employed to construct tubes with prescribed circumferences [8] and later was further developed to construct arbitrary 2D shapes [32••]. The DNA-brick method not only demonstrated many sophisticated 3D DNA structures that had never been constructed before, but also represents a conceptual breakthrough — large, intricate 3D structures can be assembled from modular components mediated by only local binding interactions.

Figure 3



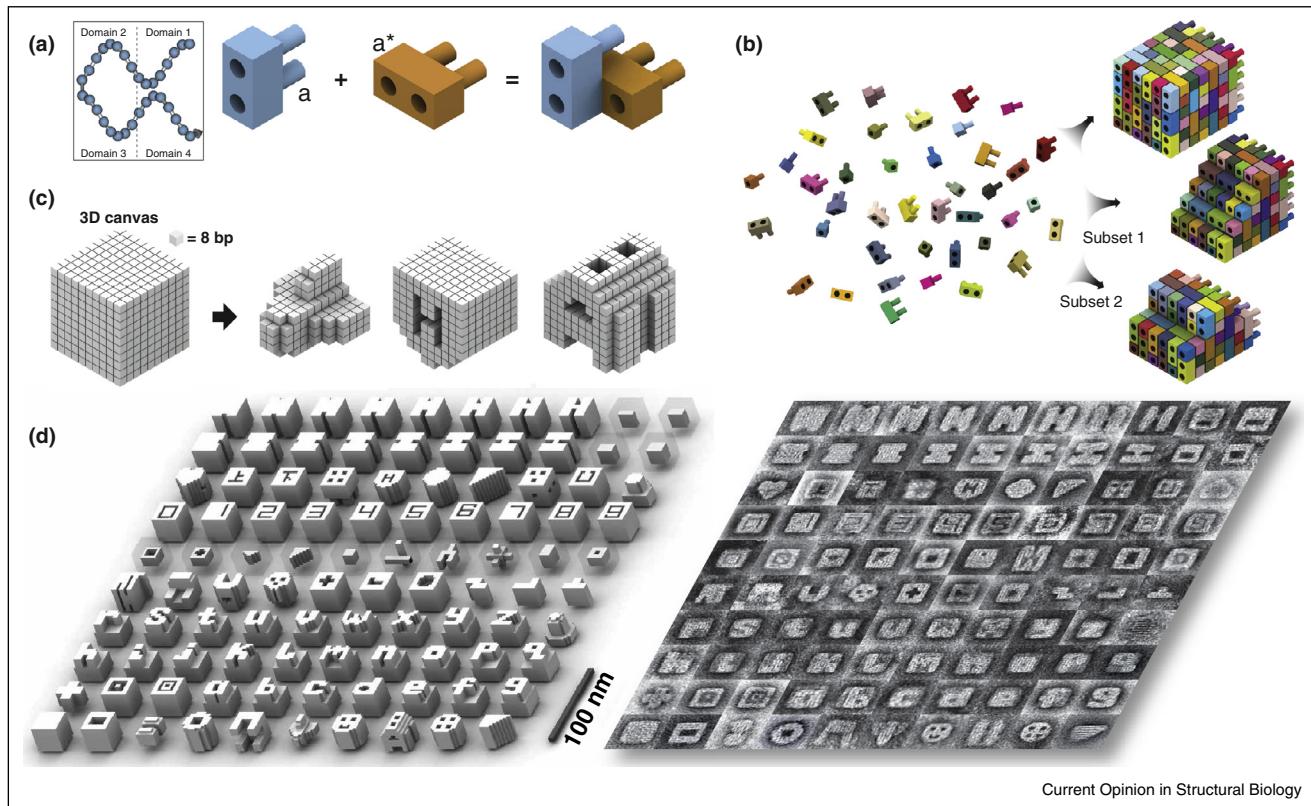
Current Opinion in Structural Biology

DNA origami. (a) DNA origami employed a ~7k-nt m13 scaffold strand that was folded into a prescribe shape by hybridizing with hundreds of synthetic staple strands. Adapted with permission from Ref. [10\*]; Copyright (2006) Nature Publishing Group (b) A single-layer DNA origami box was formed by dividing a origami to six connected rectangular subunits using flexible single-stranded joints. Adapted with permission from Ref. [13]; Copyright (2009) Nature Publishing Group. (c) A single-layer DNA origami tetrahedron was assembled using similar concept [12]. (d)–(f) Multilayer 3D DNA origami. Parallel DNA helices were packed onto honeycomb lattice (d) [14\*], square lattice (e) [23], and hexagonal lattice (f) [24]. Honeycomb lattice was Adapted with permission from Ref. [14\*]; Copyright (2009) Nature Publishing Group. (g) A tensegrity 3D DNA structures. Stiff multi-helix-bundles were connected by unpaired segments of single-stranded m13 scaffold. Adapted with permission from Ref. [16]; Copyright (2009) Nature Publishing Group. (h)–(k) 3D DNA structures with engineered curvatures. (h) Curvatures were generated by adding DNA basepairs from the convex faces and deleting basepairs from the concave faces of multi-helix bundle struts. Adapted with permission from Ref. [15]; Copyright (2009) The American Association for the Advancement of Science. (i) A Möbius strip was assembled by connecting the two ends of a rectangular single-layer DNA origami. Adapted with permission from Ref. [31]; Copyright (2010) Nature Publishing Group. (j) 3D Single-layer DNA origami with fine curvatures. Adapted with permission from Ref. [17]; Copyright (2011) The American Association for the Advancement of Science. Unlike previous DNA origami, the crossover patterns were engineered after the lengths and positions of individual helices were determined, and were different for each shape. (k) 3D spherical structure and tube. Adapted with permission from Ref. [25\*]; Copyright (2013) The American Association for the Advancement of Science. This is the first time four-way junctions were employed for assembling 3D DNA origami structures.

Prior to the DNA brick work, it was suggested, and generally accepted by the community, that the success of DNA origami is largely attributed to the use of a long scaffold strand as a central organizing component, which avoids the need to control the relative stoichiometry of hundreds of staple strands: ‘because staples are not designed to bind one another, their relative concentrations do not matter’ [10\*]. In contrast, DNA-tile-based assembly often required careful adjustment of strand stoichiometry. A DNA brick can be considered as a special DNA tile, which contains only a single-stranded DNA. However, unlike conventional multi-stranded tiles, DNA-brick 3D structures were assembled from unpurified DNA strands without careful adjustment of the stoichiometry, providing a general design strategy to assemble hundreds of modular components into prescribed 3D shapes, without using a scaffold.

A DNA brick consists of only one floppy single strand. It is void of a canonical rigid structural core and contains only flexible 8-nt sticky ends (Figure 4a, left). By pairing up the sticky ends in different DNA bricks, these structurally flexible bricks collectively form the rigid target structures (Figure 4a, right). DNA-brick is a modular and scalable strategy. Hundreds of DNA bricks can assemble into fully addressable 3D structures with comparable size to DNA origami. Importantly, due to its modular architecture, DNA bricks can be removed independently during the design process. As a result, a master set of DNA bricks can be used for the construction of smaller custom shapes assembled from selected subsets of DNA bricks (Figure 4b). Using a large 8k-basepair DNA-brick-based cuboid as a 1000-voxel ‘3D canvas’ (Figure 4c), Yin and coworkers demonstrated more than 100 3D DNA structures that exhibited many sophisticated features, including intricate interior cavities and

Figure 4



Current Opinion in Structural Biology

Three-dimensional structures assembled from DNA bricks. (a) A DNA brick initially is a floppy 32-nt single strand DNA. It has four 8-nt domains that allow it to connect to four neighbors. Two neighboring DNA bricks form an 8-bp duplex between domain 'a' and its complementary domain 'a\*'. Bricks are fully paired and can be represented by Lego-like blocks that form 90° dihedral angles, which derive from the approximate 3/4 right-handed helical twist of 8-bp of DNA. (b) All bricks are unique in a 3D structure. Smaller shapes can be designed using subsets of the bricks. (c) Intricate 3D shapes designed from a 10 × 10 × 10 voxel '3D canvas', where each voxel is 8-bp (2.5 nm × 2.5 nm × 2.7 nm). (d) TEM images of 100 sophisticated 3D shapes constructed from a 1000-voxel canvas.

tunnels, that have not been achieved before (Figure 4d). Each voxel in the 3D canvas equals to 8 base-pairs, or about 2.5 nm × 2.5 nm × 2.7 nm, and can be added or removed independently. In contrast to the half-synthetic (staples), half-biological (scaffold) DNA origami structures, DNA-brick structures are fully synthetic. The original DNA-brick method used a random-sequence design strategy: the basic rule of strand complementarity is strictly followed, but base sequences are arbitrarily assigned. The fact that such a simple design strategy still produced sequences that successfully assemble into targets structures demonstrates the robustness of DNA-brick assembly. However, to realize its full potential, it is logical to hypothesize that we need take full advantage of *de novo* sequence design for the fully synthetic DNA-brick structures.

### Towards greater structural complexity

Until the DNA-brick method was invented, DNA origami was considered the gold standard for synthesizing

arbitrarily shaped, fully addressable 3D DNA nanostructures—the term ‘DNA origami’ itself has become a synonym for large, complex DNA nanostructures. The surprising success of ‘scaffold-free’ DNA-brick method revealed that there was still a large design space to be explored. As of right now, the DNA-brick method offers a few key advantages to DNA origami: it is modular, fully synthetic, and more scalable. However, the DNA-origami method may offer unique capabilities for constructing certain architectures. One example of this architecture is wireframe polyhedra assembled from multi-arm DNA motifs [14•,33•]. In addition, large structures that contain ‘bent’ DNA helices have been constructed using DNA-origami [15,17,25•], but not through the DNA-brick method yet. A common feature of these two groups of structures is that they all contain ‘off-lattice’ portions in which DNA structures are distorted and less stable than normal B-form DNA. In these special cases, the m13 scaffold strand may provide additional stability to DNA structures.

Any molecular assembly methods for one-step-assembly of large and fully-addressable structures, including DNA origami and DNA bricks, will inevitably reach a limit in terms of structure size and shape complexity. Therefore, developing hierarchical assembly strategies that are capable of effectively connecting multiple large 3D DNA units will be the key for further advancing the capability of structural DNA nanotechnology. Recent works have shown promising progress towards this direction. Yin *et al.* invented a DNA-origami-based three-arm-junction motif called ‘DNA tripod’ with precisely controlled inter-arm angles [33°]. Hierarchical assembly using DNA tripods successfully demonstrated a group of larger polyhedra, including a tetrahedron (20 MDa), a triangular prism (30 MDa), a cube (40 MDa), a pentagonal prism (50 MDa), and a hexagonal prism (60 MDa).

## Conclusions

Programmable DNA self-assembly is not only one of few ways to precisely control nanoscale features on complex structures, but it can also be used to interface in a versatile fashion with the larger molecular world, for example, to direct materials arrangement, chemical reactions, and biomolecular interactions. Recent examples of applications of 3D DNA structures include DNA-templated nanoparticles for photonic applications [34,35], smart delivery vehicles [36], and synthetic membrane channels [37]. The future of structural DNA nanotechnology will rely on our persistent pursuit of greater structural complexity, its integration with other scientific fields, and its enabling applications. We can envision that one day 3D artificial systems as large, and as complex as their biological counterparts will be rationally programmed and assembled for prescribed functional purposes.

## Conflict of interest

Nothing declared.

## Acknowledgements

The authors sincerely thank Peng Yin for insightful discussions and for involvement in draft preparation; and Elena Chen for proofreading the draft. This work is supported by a Wallace H. Coulter Department of Biomedical Engineering Faculty Startup Grant, and a Winship Cancer Institute Billi and Bernie Marcus Research Award to YK.

## References and recommended reading

Papers of particular interest, published within the period of review, have been highlighted as:

- of special interest
  - of outstanding interest
1. Seeman NC: **Nucleic acid junctions and lattices.** *J Theor Biol* 1982, **99**:237-247.  
This work described the conceptual foundation of engineering artificial DNA nanostructures.
  2. Winfree E, Liu F, Wenzler LA, Seeman NC: **Design and self-assembly of two-dimensional DNA crystals.** *Nature* 1998, **394**:539-544.
  3. Yan H, Park SH, Finkelstein G, Reif JH, LaBean TH: **DNA-templated self-assembly of protein arrays and highly conductive nanowires.** *Science* 2003, **301**:1882-1884.
  4. Yan H, LaBean TH, Feng L, Reif JH: **Directed nucleation assembly of DNA tile complexes for barcode-patterned lattices.** *Proc Natl Acad Sci U S A* 2003, **100**:8103-8108.
  5. Liu D, Wang M, Deng Z, Walulu R, Mao C: **Tensegrity: construction of rigid DNA triangles with flexible four-arm DNA junctions.** *J Am Chem Soc* 2004, **126**:2324-2325.
  6. Rothemund PWK, Papadakis N, Winfree E: **Algorithmic self-assembly of DNA Sierpinski triangles.** *PLoS Biol* 2004, **2**:2041-2053.
  7. Park SH *et al.*: **Programmable DNA self-assemblies for nanoscale organization of ligands and proteins.** *Nano Lett* 2005, **5**:729-733.
  8. Yin P *et al.*: **Programming DNA tube circumferences.** *Science* 2008, **321**:824-826.
  9. Chen J, Seeman NC: **The synthesis from DNA of a molecule with the connectivity of a cube.** *Nature* 1991, **350**:631-633.
  10. Rothemund PWK: **Folding DNA to create nanoscale shapes and patterns.** *Nature* 2006, **440**:297-302.  
This work demonstrated two-dimensional scaffolded DNA origami method.
  11. He Y *et al.*: **Hierarchical self-assembly of DNA into symmetric supramolecular polyhedra.** *Nature* 2008, **452**:198-201.
  12. Ke Y *et al.*: **Scaffolded DNA origami of a DNA tetrahedron molecular container.** *Nano Lett* 2009, **9**:2445-2447.
  13. Andersen ES *et al.*: **Self-assembly of a nanoscale DNA box with a controllable lid.** *Nature* 2009, **459**:73-76.
  14. Douglas SM *et al.*: **Self-assembly of DNA into nanoscale three-dimensional shapes.** *Nature* 2009, **459**:414-418.  
This work showed three-dimensional structure could be constructed using DNA origami method.
  15. Dietz H, Douglas SM, Shih WM: **Folding DNA into twisted and curved nanoscale shapes.** *Science* 2009, **325**:725-730.
  16. Liedl T, Höglberg B, Tytell J, Ingber DE, Shih WM: **Self-assembly of three-dimensional prestressed tensegrity structures from DNA.** *Nat Nanotechnol* 2010, **5**:520-524.
  17. Han D *et al.*: **DNA origami with complex curvatures in three-dimensional space.** *Science* 2011, **332**:342-346.
  18. Zheng JP *et al.*: **From molecular to macroscopic via the rational design of a self-assembled 3D DNA crystal.** *Nature* 2009, **461**:74-77.
  19. Bath J, Turberfield AJ: **DNA nanomachines.** *Nat Nanotechnol* 2007, **2**:275-284.
  20. Zhang Y, Seeman NC: **Construction of a DNA-truncated octahedron.** *J Am Chem Soc* 1994, **116**:1661-1669.
  21. Shih WM, Quispe JD, Joyce GF: **A 1.7-kilobase single-stranded DNA that folds into a nanoscale octahedron.** *Nature* 2004, **427**:618-621.
  22. Goodman RP *et al.*: **Rapid chiral assembly of rigid DNA building blocks for molecular nanofabrication.** *Science* 2005, **310**:1661-1665.
  23. Ke Y *et al.*: **Multilayer DNA origami packed on a square lattice.** *J Am Chem Soc* 2009, **131**:15903-15908.
  24. Ke Y, Voigt NV, Goethel KV, Shih WM: **Multilayer DNA origami packed on hexagonal and hybrid lattices.** *J Am Chem Soc* 2012, **134**:1770-1774.
  25. Han D *et al.*: **DNA gridiron nanostructures based on four-arm junctions.** *Science* 2013, **339**:1412-1415.  
This study showed a design strategy to create gridiron-like DNA structures. This is the first example of using four-arm junctions for programming 3D origami structures with curvatures.
  26. Ke Y, Ong LL, Shih WM, Yin P: **Three-dimensional structures self-assembled from DNA bricks.** *Science* 2012, **338**:1177-1183.

This work demonstrated a modular strategy for assembling complex 3D molecular structures from small components mediated strictly by local binding interactions.

27. Smith DM et al.: **A structurally variable hinged tetrahedron framework from DNA origami.** *J Nucl Acids* 2011, **2011**: 360954-360959.
28. Aldaye F, Sleiman H: **Modular access to structurally switchable 3D discrete DNA assemblies.** *J Am Chem Soc* 2009, **129**:13376-13377.
29. Zhang C et al.: **Conformational flexibility facilitates self-assembly of complex DNA nanostructures.** *Proc Natl Acad Sci U S A* 2008, **105**:10665-10669.
30. Tian C et al.: **Directed self-assembly of DNA tiles into complex nanocages.** *Angew Chem Int Ed Engl* 2014, **126**.  
This study showed a design strategy to create 3D DNA polyhedral from multiple types of branched DNA tiles.
31. Han D, Pal S, Liu Y, Yan H: **Folding and cutting DNA into reconfigurable topological nanostructures.** *Nat Nanotechnol* 2010, **5**:712-717.

32. Wei B, Dai M, Yin P: **Complex shapes self-assembled from single-stranded DNA tiles.** *Nature* 2012, **485**:623-626.  
This paper showed that single-stranded tiles could self-assemble into discrete two-dimensional structures with complex arbitrary shapes.
33. Iinuma R et al.: **Polyhedra self-assembled from DNA tripods and characterized with 3D DNA-PAINT.** *Science* 2014, **344**:65-69.  
This study showed that large DNA polyhedra can be assembled from modular origami monomers. The origami monomer contains features that can be used to adjust the precise conformation of DNA origami.
34. Kuzyk A et al.: **DNA-based self-assembly of chiral plasmonic nanostructures with tailored optical response.** *Nature* 2012, **483**:311-314.
35. Acuna GP et al.: **Fluorescence enhancement at docking sites of DNA-directed self-assembled nanoantennas.** *Science* 2012, **338**:506-510.
36. Douglas SM, Bachelet I, Church GM: **A logic-gated nanorobot for targeted transport of molecular payloads.** *Science* 2012, **335**:831.
37. Langecker M et al.: **Synthetic lipid membrane channels formed by designed DNA nanostructures.** *Science* 2012, **338**:932-936.