Topics in Current Chemistry (2020) 378:36
https://doi.org/10.1007/s41061-020-0301-0

REVIEW

Directional Assembly of Nanoparticles by DNA Shapes: Towards Designed Architectures and Functionality

Ningning Ma[1,2] · Brian Minevich[3] · Jiliang Liu[4] · Min Ji[1,2] · Ye Tian[1,2,5] · Oleg Gang[3,6,7]

Received: 18 November 2019 / Accepted: 11 March 2020 / Published online: 27 March 2020

Abstract

In bottom–up self-assembly, DNA nanotechnology plays a vital role in the development of novel materials and promises to revolutionize nanoscale manufacturing technologies. DNA shapes exhibit many versatile characteristics, such as their addressability and programmability, which can be used for determining the organization of nanoparticles. Furthermore, the precise design of DNA tiles and origami provides a promising technique to synthesize various complex desired architectures. These nanoparticle-based structures with targeted organizations open the possibility to specific applications in sensing, optics, catalysis, among others. Here we review progress in the development and design of DNA shapes for the self-assembly of nanoparticles and discuss the broad range of applications for these architectures.

Keywords DNA shapes · DNA tiles · DNA origami · Nanoparticles · Self-assembly · Nanomaterials

1 Introduction

In the early 1980s, Seeman first proposed the use of DNA as a molecular building material for constructing well-defined architectures on the nanoscale [1]. Approximately two decades earlier, Holliday had suggested that a branched DNA structure can naturally occur as a key intermediate of the chromosome synapses and recombination [2]. As opposed to the traditional linear conformation of DNA, Seeman realized an opportunity for using these branched DNA architectures, or

Chapter 6 was originally published as Ma, N., Minevich, B., Liu, J., Ji, M., Tian, Y. & Gang, O. Topics in Current Chemistry (2020) 378: 36. https://doi.org/10.1007/s41061-020-0301-0.

✉ Ye Tian
ytian@nju.edu.cn

✉ Oleg Gang
og2226@columbia.edu

Extended author information available on the last page of the article

Holliday junctions, as the basis for crystallizing proteins using the designed periodic DNA structures [1]. These structures are formed through the assembly of two-dimensional (2D) and three-dimensional (3D) networks of oligomeric nucleic acids. He hypothesized that there is a significant potential for creating non-traditional nucleic acid architectures that possess a high degree of spatial orientation and addressability. The initial vision of self-assembled DNA shapes came with three over-arching goals: (1) development of individual DNA constructs with designed architecture, (2) establishing methods for creating large-scale organized assemblies from DNA, and (3) using DNA-based assembly approaches for guiding the organization of nano-objects into finite and periodic structures.

As a direct result of this vision, the field of DNA nanotechnology has emerged as an active field of research. While the challenges outlined in the original vision are not yet fully resolved, the current state of the field and its fast progress show the feasibility of using DNA nanotechnology methods for solving them, as well as for addressing many other scientifically and technologically important problems across a wide range of disciplines, from material science to sensing, and from nanomedicine to information storage. Efforts over the last few decades have been accompanied by the development of various methods for the design and synthesis of complex DNA shapes ranging from DNA tiles, designed using branched junctions [3], double-crossover molecules [4], and triple crossover molecules [5], to three-dimensional DNA shapes, including cubes [6], an octahedron [7], and many others, using a technique known as DNA origami [8]. The ability to generate complex DNA shapes has been used as the basis of various DNA architectures and nano-structuring platforms. Concurrently, efforts were made to integrate inorganic nanoparticles with DNA through the use of chemically modified DNA sequences that are grafted to nanoparticle (NP) surfaces, as was first demonstrated in 1996 by Mirkin and Alivisatos [9, 10]. The ability to form DNA shells of spherical or other morphologies through grafting to NPs directly led to strategies for the self-assembly of NP superlattices, as was demonstrated by the research groups of Gang and Mirkin, respectively, and coworkers in their pioneering 2008 studies [11–13] and expanded upon in later NP-based systems [14–17]. On the other hand, there has been tremendous progress on combining various strategies for guiding DNA-functionalized NPs into one-dimensional (1D), 2D, and 3D assemblies using DNA-based objects. Recent demonstrations of the integration of complex designed 3D DNA constructs with NPs with the aim to produce designed 3D NP organizations [18–20] merged NPs with DNA shaped direction and opens up enormous possibilities for creating designed 3D NP-based materials.

In this review we begin with a detailed discussion of the design of DNA shapes, and the origin and development of DNA tiles for guiding NP organization through scaffolding. We then summarize the development of DNA origami and its application for the programmable organization of NPs, followed by a detailed discussion of 3D polyhedral DNA frames for the assembly of periodic 3D NP organizations [19]. The latter strategy utilizes 3D polyhedral origami, rather than 2D DNA origami motifs, commonly either rectangular [8] or triangular [21], and allows for the guiding of NPs into 3D periodic structures. We conclude the review with a discussion

of applications of these assemblies of NPs based on DNA shapes and the overall impact of these shapes on structural DNA nanotechnology.

2 DNA Tiles

2.1 DNA Tiles: Fundamental Design and Development

The Holliday junction, a branched conformation of DNA, was used as the basis for synthesizing the first generation of DNA structures, known as DNA tiles. This led to the leveraging of more sophisticated designs of DNA tiles, with the realization of larger and more complex DNA architectures [22–25]. Advancements in the design of DNA tiles stemmed from the introduction of so-called "sticky ends," which are unbound regions of single-stranded DNA (ssDNA) used at the site of linking to induce the binding of DNA shapes and structures, as shown in Fig. 1. Due to the accuracy of connection and the programmability of the location of the sticky ends, this became a crucial strategy for the construction of complex architectures from various DNA constructs. The initial immobile junction used was a tetrameric junction formed with oligonucleotides by combining sequence symmetry constraints with equilibrium calculations (Fig. 2a) [3], and the three-arm junction was designed in the same manner (Fig. 2b) [26]. With the development of branched DNA junctions, a set of 3D assemblies were designed, such as a cube [6] (Fig. 2e) and a truncated octahedron (Fig. 2f) [7]. Building upon these design principles, junctions with a higher degree of branching were developed [22], as shown in Fig. 2c. Researchers noted that increasing the degree of branching would reduce the structural stability of the structure and proposed increasing the number of nucleotide base pairings in each arm to mitigate this resultant structural instability. Leveraging this strategy of DNA branched junctions with a greater number of arms, it was possible to design

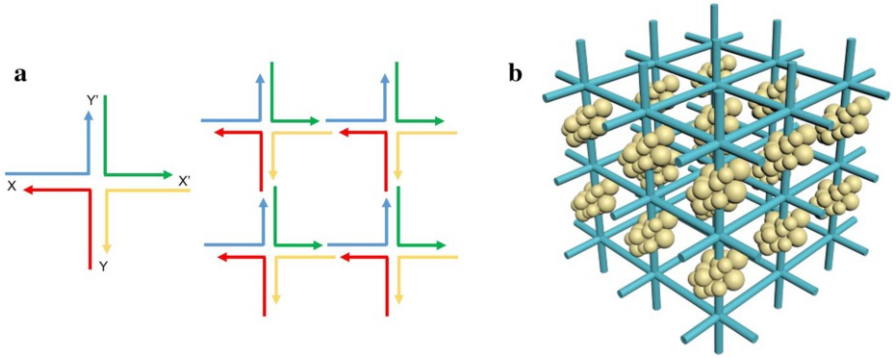

Fig. 1 The core concept of DNA nanotechnology. **a** An immobile Holliday junction and its combination. The junction structure (left) consists of four different single-stranded DNA sequences distinguished by the four colors, and it was designed with four sticky ends: X, Y, and their complements X′ and Y′. Through hybridization, the junction structure can be extended into a two-dimensional (2D) array. **b** Schematic diagram of a three-dimensional (3D) DNA crystal for protein crystallization

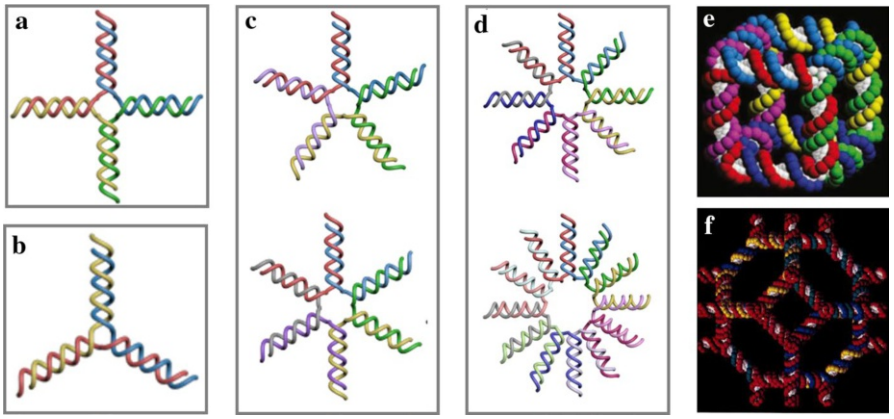

Fig. 2 Library of branched DNA junction structures and their typical assemblies. **a–d** Branched junction structures: **a** Four-arm branched junction, **b** three-arm branched junction, **c** five- and six-arm branched junction, **d** 8- and 12-arm branched junction. **e**, **f** Typical assemblies. **e** Molecule with the connectivity of a cube. Reproduced with permission from Seeman et al. [134], copyright 2017, Materials Research Society. **f** Molecule with the connectivity of a truncated octahedron. Reproduced with permission from Seeman et al. [134], copyright 2017, Materials Research Society

a wide range of 3D polygons, including those from more than ten space-filling networks with 432 symmetries, through the selection and control of the of sticky end design [22]. Continued efforts related to these highly branched junctions resulted in the development of 8- and 12-arm junctions without any branch migration [27] (Fig. 2d). However, it remained vital to stabilize the structure by tuning the number of nucleotide pairs per arm. The 8- and 12-arm connected networks could be used to achieve an N-connected network, which represents highly complex 3D organizations, such as a series of connected cuboctahedra [27]. The development of branched DNA structures enriched the library of elements that could be used for the assembly of DNA architectures and for guiding nano-objects.

Seeman later proposed the use of an alternative DNA shape or motif, named a DNA double-crossover (DX) molecule [4], which could be used as the basis of structural design using DNA (Fig. 3a). In order to assemble crystalline structures or guide the organization of NPs, the fundamental units of the DNA structure require definable intermolecular interactions and sufficient rigidity to ensure the formation of the desired architecture. In the DX motif, two DNA strands follow an approximately continuous helical trajectory, while two additional strands form a crossover to bind the two original sequences together. This strategy results in increased mechanical stability, where the stiffness is twofold higher than that of a conventional linear duplex [double-stranded DNA (dsDNA)]. The DX motif was used to design five structurally unique arrangements, all of which were used as building blocks to assemble 2D structures; this method was then used to produce 2D crystals with specified patterning. A DNA hairpin was incorporated into the design of a DX molecule as a topographic label (Fig. 3a), the periodic spacing of which could be controlled and used to tether nanomaterials of interest [23]. A different motif, a 4×4 branched tile, was later used to generate 2D crystals with a programmable

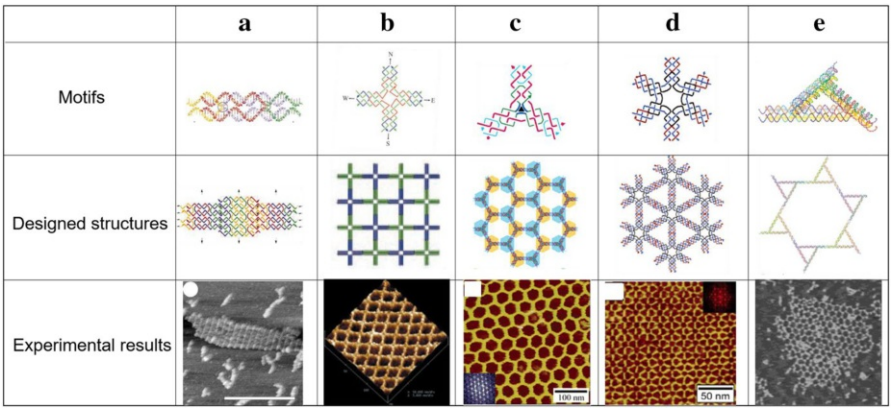

Fig. 3 Library of motifs basing on the double-crossover (DX) structure and their assemblies. **a** DX structure. Reproduced from Winfree at al. [23], with permission, copyright 1998, Nature Publishing Group. **b** 4×4 branched tile. Reproduced from Yan et al. [28], with permission, copyright 2003, *Science*. **c** Three-point-star. Reproduced from He et al. [29], with permission, copyright 2005, American Chemical Society. **d** Six-point-star. Reproduced from He et al. [24], with permission, copyright 2006, American Chemical Society. **e** DX triangle. Reproduced from Ding et al. [31], with permission, copyright 2004, American Chemical Society

designation for proteins and was metallized to demonstrate the assembled structure's functionality as a nanowire [28]. A high-order 2D array that was assembled with the proper designation of sticky ends is shown in Fig. 3b [28]. Additional structures were generated on the basis of these branched units, such as the three-arm branched junction analogue named the three-point-star [29] that can assemble 2D hexagonal arrays (Fig. 3c). The balance of flexibility and stress in the design of DNA motifs, particularly for the three-point-star, was investigated, and it was shown that this balance is critical to the assembly of well-ordered 2D arrays [29, 30]. Based on the same strategy, other DNA shapes were designed for the assembly of 2D crystalline organizations. These included a DNA six-point-star that assembled highly connective 2D arrays, as shown in Fig. 3d [24] and, as shown in Fig. 3e, a new motif that can generate trigonal arrays using the DX triangle whose stiffness had been significantly improved by the geometry of the design [31]. However, there was still a need to develop a platform or design that would allow for assembly in 3D space. It was with this in mind that Zheng et al. introduced key concepts for the synthesis of 3D architectures using DNA shapes [25]. The three simple principles that these researchers introduced to produce precisely designed 3D macroscopic objects were: (1) a robust motif with 3D structure, (2) introduction of affinity interactions to the interior of the motif, and (3) the use of predictable structures that can be assembled based on these interactions. The proposed design was a tensegrity triangle consisting of three helices not in the same plane with six exposed sticky ends. The interactions of these prescribed sticky ends was the basis for the assembly of a 3D periodic lattice [25]. There was an introduction of additional motifs, including the triple-crossover (TX) [5], the DNA parallelogram [32], and layered crossovers (LX) [33], all of which became vital elements for self-assembly in future studies. Meanwhile, efforts

continued on the development of strategies to access additional architectures. One of these efforts consisted of the assembly of DNA nanotubes with half-tube components. Two half-tube species were designed using two different bent TX (BTX) molecules and a single arched four-helix [4-helix bundle (4HB)] component to assemble a 6HB nanotube and an 8HB nanotube array, respectively. This work included an investigation of the influence of the external environment on the self-assembly of these objects into 1D arrays and reported the assemblies of DNA nanotubes with lengths of up to 500 nm [34].

The two important concepts in structural DNA nanotechnology, namely, branched DNA structures and the DNA crossover design, were then combined to self-assemble a 1.7-kb nucleotide sequence into a 3D octahedron, as shown in Fig. 4a. In the presence of five 40-mer synthetic oligodeoxynucleotides, the long ssDNA molecule can be folded into the octahedron structure using a denaturation–renaturation procedure. The programmability of this 3D object, which is related to the design of the oligodeoxynucleotides, can also be utilized to position the NPs with precision [35]. It was later proposed that the assembly of many distinct DNA strands could become quite difficult to achieve due to the increased number of DNA strands needed for the assembly of large, complex structures. It can also become quite difficult to design large numbers of unique DNA sequences, which is done in an effort to minimize any parasitic crosstalk and unintentional interactions between the DNA sequences used in a particular design. These difficulties result in a reduction in the overall addressability of the design and can affect the assembly and fidelity of the structure. To simplify the overall design, He et al. used symmetric three-point-star motif as the building block [29]. In subsequent studies, researchers investigated several factors to promote polyhedron formation, and through adjusting the length of

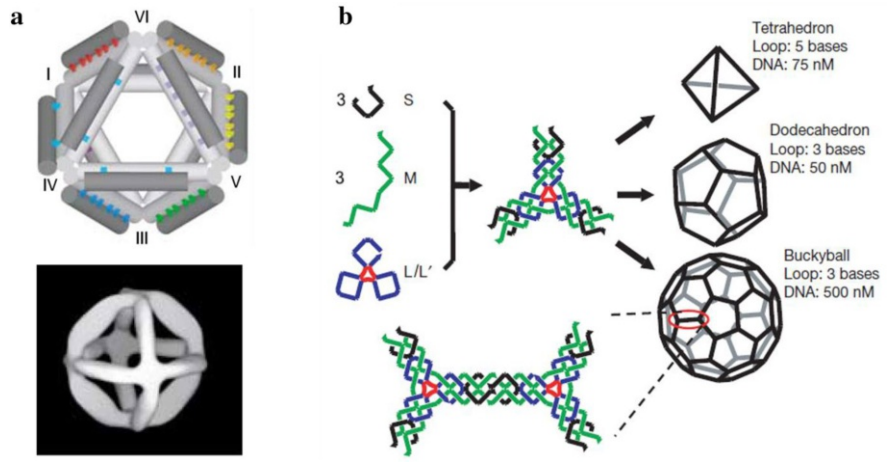

Fig. 4 **a** An octahedron structure folded by a 1669-nucleotide single-stranded DNA and its cryo-electron micrograph. Reproduced from Shih et al. [35], with permission, copyright 2004, Nature Publishing Group. **b** Diagram showing the formation of the symmetric three-point-star motif (left) and the DNA polyhedron (right). Top to bottom: tetrahedron, dodecahedron, and buckyball, respectively. Reproduced from He et al. [36], with permission, copyright 2008, Nature Publishing Group

loops and DNA concentration they were able to synthesize three distinct polyhedral objects (Fig. 4b), a tetrahedron, a dodecahedron, and a buckyball [36]. It was then shown that a modification of this star motif in which there is an increase in the number of points can serve as a building block to assemble an icosahedra [37]. Subsequent comprehensive exploration has resulted in the construction of a wide variety of architectures through the assembly of branched DNA building units becoming a robust strategy for the formation of complex structures. In 2012, Ke et al. proposed a different method to construct 3D architectures. These researchers designed and fabricated a series of short synthetic DNA strands, which were termed "DNA bricks." In a procedure that is analogous to building a structure out of Lego bricks, they fabricated diverse discretionary architectures by using DNA bricks as the building block. With precise design of the functional DNA sticky ends, Ke et al. realized the guidance of NP assembly, which further expanded on structural fabrication and the guiding of nano-objects [38–40].

2.2 Organization of NPs with DNA Tiles

Since the emergence of the research field referred to as DNA nanotechnology, the development of DNA-based approaches for creating ordered materials has been very rapid. These complex structures, composed entirely of DNA, can be leveraged for the organization of nanomaterials into either clusters or crystalline architectures. By appling the methodology proposed for the hierarchical self-assembly of polyhedra from the three-point-star DNA tile motif [36], it was therefore possible to successfully synthesize a wide-range of DNA polyhedrons and utilize these as nanoscale cages for the programmable encapsulation of NPs. The inherit addressability of the design allowed for controlled variation in the number of DNA-functionalized gold NPs (AuNPs) and encapsulation of these AuNPs into correlated DNA cages via hybridization, as shown in Fig. 5a. The reversibility of this system was also demonstrated, whereby the AuNPs could be released from the DNA cages [41]. In another study, DNA polyhedrons were utilized to interrupt the symmetry of spherical NPs and coordinate these with defined valences [42]. The resultant valency of the object would dictate directional bonds for further architectural assembly. These programmable clusters of AuNPs were viewed as atomic and molecular analogs, with a defined valence and bonding direction. Researchers were able to demonstrate various geometries using distinct DNA cages, including a tetrahedron, an octahedron, a trigonal prism, and a D_3 symmetry structure. In the case of the tetrahedral cage, a NP was encapsulated and fixed at the center of the cage and it could only interact with complementary NPs, based on the complementarity of the DNA shells that were grafted onto the surfaces of the respective particles through the faces of the polyhedral cage. These interparticle interactions would organize the NPs into their desired positions. Thus, the five-NP structure can be seen as a molecular analog of methane (CH_4). Additional work with this strategy showed the viability of this structure to generate a sulfur hexafluoride (SF_6)-like structure, hexamethyltungsten $[W(CH_3)]_6$-like structure, and even ethane (C_2H_6)-like structures with two cores (Fig. 5b) [42].

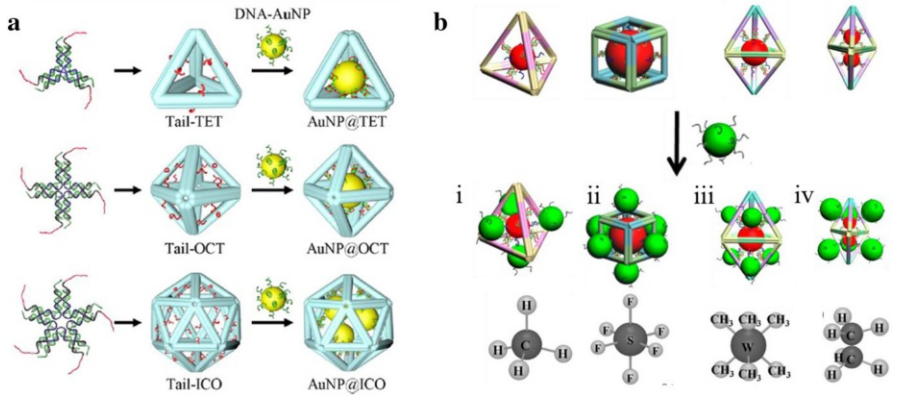

Fig. 5 **a** Schematic diagram of gold nanoparticle–DNA conjugate (*AuNP@DNA*) cage structures fabricated through DNA polyhedrons used to encapsulate AuNPs. Three different DNA polyhedrons are shown: a tetrahedron (*TET*) (top), an octahedron (*OCT*) (middle), and an icosahedron (*ICO*) (bottom). The size of the icosahedron is sufficiently large for encapsulating three AuNPs (bottom), while the other two can only accommodate one AuNP (top and middle). Reproduced from Zhang et al. [41], with permission, copyright 2014, American Chemical Society. **b** Diagram showing the self-assembly of molecule-like NPs directed by DNA polyhedron nanocages. With different polyhedrons, a set of molecule-like nanoparticles are assembled, including methane (CH_4)-like (i), sulfur hexafluoride (SF_6)-like (ii), hexamethyltungsten [$W(CH_3)_6$]-like (iii), and ethane (C_2H_6)-like (iv) structures. Reproduced from Li et al. [42], with permission, copyright 2015, American Chemical Society

The successful fabrication of DNA tiles and subsequent assembly into periodic structures opened up the possibility to organize NPs beyond finite size structures and clusters and enable the organization of low-dimensional arrays. For example, the TX structure was used as a template for guiding NPs into linear arrays, whereby the tiles were modified with two DNA stem loops located at the upper and lower sections of the helices, respectively. The modification of one or both of the two stem loops for the association of the streptavidin molecule resulted in linear arrays of streptavidin, including single- and double-layer designs, as shown in Fig. 6a [43]. Additional efforts made to guide the organization of other nanomaterials via DNA tile assemblies. A 2D array was assembled using the DX molecule design and was used to align AuNPs. Four different DX molecules were integrated and investigated as the scaffold for the 2D crystal. Small AuNPs (diameter 1.4 nm) were arranged into 2D arrays through covalent attachment with controllable interparticle spacings of 4 and 64 nm (Fig. 6b) [44]. As an extension of this work, AuNPs were organized onto arrays of DNA tiles via hybridization rather than covalent bonding. Using DNA hybridization as the method of attachment to the 2D array, the crystal growth conditions and the component synthesis could be independently optimized. Efforts were also made to guide more than one kind of nanomaterial onto a single surface and then to subsequently assemble that unit into periodic 2D arrays. By designing distinct binding sequences, the research group of Kiehl and coworkers successfully guided the positioning of two sizes of AuNPs (diameters 5 and 10 nm) onto a 2D multi-nanocomponent array (Fig. 6c) [45, 46]. In another study, the previously

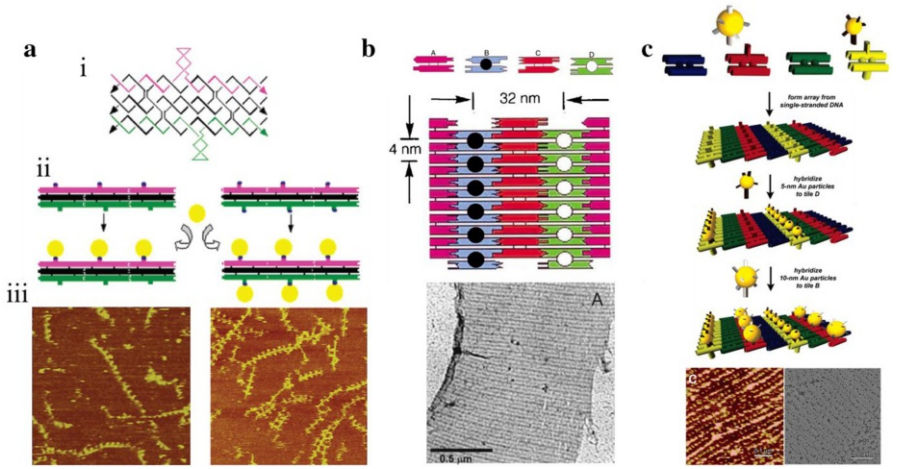

Fig. 6 One-dimensional (1D) and 2D NP arrays assembled by DNA structures. **a** Streptavidin linear arrays fabricated with TX DNA template. i–iii Structure diagram of the TX molecule (i), design and formation of the linear array (ii), and atomic force microscopy (AFM) images of the single-layer and double-layer arrays (iii). Reproduced from Li et al. [43], with permission, copyright 2004, American Chemical Society. **b** Schematic diagram and transmission electron microscopy (TEM) image of 1.4 nm-AuNP 2D array assembled with DX DNA template. Reproduced from Xiao et al. [44], with permission, copyright 2002, Nature Publishing Group. **c** Process of two different size AuNPs arranging into a common 2D array, with the AFM and TEM images shown at the bottom left and bottom right, respectively. Reproduced from Le et al. [45], with permission, copyright 2004, American Chemical Society

mentioned four-arm tiles were used to assemble 2D arrays with precise AuNP positioning whereby the distance between neighboring particles was designed to be ~38 nm [47]. The factors influencing the formation of these 2D arrays were also being studied, including the number of sticky ends, the symmetry and size of the DNA tile, and the programmable distances between the AuNPs relative to the size of the DNA tiles and 2D arrays. Various tiles were mixed together to diversify the types of 2D assemblies that could be obtained, and this mixing resulted in the generation of three different 2D arrays (Fig. 7a) [48]. At approximately the same time, a research group also demonstrated that multiple 2D arrays of NPs could be obtained by using more than one triangular DNA motif in the same design. In particular, the two triangular motifs, based on stiff DX molecules, used could each capture a particle independent of the other tile and then assemble into 2D arrays of ordered NPs (Fig. 7b) [49].

Efforts continued on constructing 3D assemblies based on methods developed for ordering NPs via DNA tiles organized in well-ordered 2D arrays. As such, the 2D assembly method was modified to develop a strategy for the generation of 3D architectures. This strategy consisted of the programmable rolling of a 2D sheet into a variety of 3D tube conformations. Four variants of DX tiles were designed to assemble 2D arrays, including one that had a site ready to associate AuNPs (denoted as "A") and another that had a DNA stem loop located on the opposite side (denoted as "B"). When the arrays were assembled, 5-nm AuNPs were aligned in parallel lines. However, the chosen tiles were packed side by side

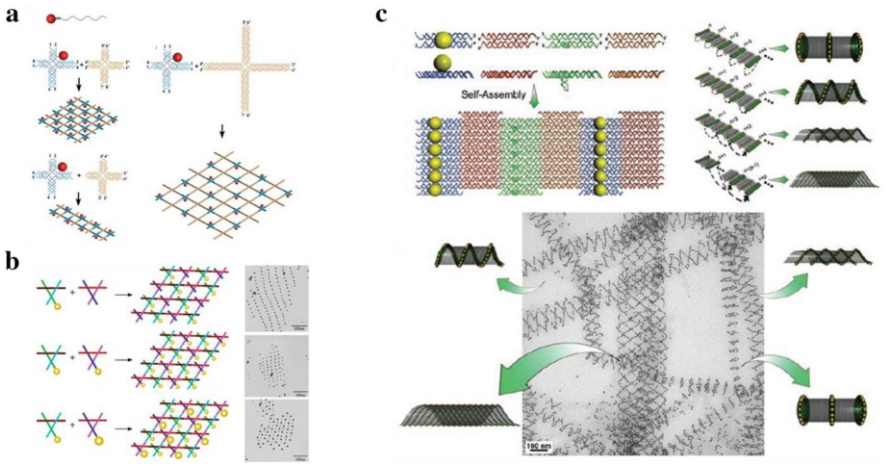

Fig. 7 Schematic representations of 2D AuNP arrays assembled with 4×4 tiles and tensegrity triangles. **a** Diagram showing three different assembly of periodical AuNP nanoarrays. The different forms of the three lattices depends on the design of the tile structure, including size and sticky ends. Reproduced from Sharma et al. [48], with permission, copyright 2006, Wiley-VCH Verlag GmbH and Co. KGaA. **b** Diagram showing the schematic and TEM images of three different AuNP arrays with varying number and size of AuNPs. Reproduced from Zheng et al. [49], with permission, copyright 2006, American Chemical Society. **c** Diagram of 3D DNA nanostructures fabricated with DX tiles showing the design of the DX tiles for AuNPs arranging (top left), two of which are specifically designed, including one that carries a 5-nm AuNP pointing upwards (shown in blue) and one that carries a DNA stem loop pointing downwards (shown in green). Four different 3D tubular structures were assembled through adjustment of the interval of the corresponding edge tiles that associate (top right). The bottom image is the TEM image of the tubular nanoscale architectures. Reproduced from Sharma et al. [50], with permission, copyright 2009, *Science*

at distances of < 5 nm and, consequently, the 2D arrays began to curl due to the strong electrostatic and steric repulsions between the neighboring AuNPs. This design was deemed useful for tuning the 2D NP organization with either neighboring or alternating NP positions. It was noted that when the 2D sheet is rolled into a tube, a variety of 3D NPs can be designed, including stacked rings, single spirals, double spirals, and nested spiral tubes, as shown in Fig. 7c. A follow-up study revealed that the ultimate dominant tube conformation is related to the size of the AuNPs and the design of the DX tiles. In that study, three different sizes of AuNPs were used, and it was discovered that with increasing AuNP size, from 5 to 15 nm, the stacked-ring conformation dominated. For example, in the system with 10-nm AuNPs, 92% of the formed tubes were stacked rings [50]. Significant efforts have since have been made to use DNA tiles for the organization of NPs into complex 2D architectures. However, reliable methods to assemble 3D assemblies of NPs using DNA tiles remain very limited.

3 Shaping DNA strands with NPs

DNA can be shaped not only through the formation of constructs as discussed above, but also by organizing DNA strands on NP surfaces, a construct referred to as a DNA shell. Concurrent with the efforts expended to design DNA tiles, significant work was directed towards diversifying the assemblies of NPs through the tailoring of DNA shells grafted onto a NP's surface. After the first reports of successfully grafting synthetic DNA to a AuNP [9, 10], it took over a decade to discover the design principles needed to dictate the crystallization of DNA-functionalized NPs [11–13]. It has been shown that NPs whose respective surfaces are functionalized with DNA can assemble into NP lattices when the designs of the DNA shells are favorable for an interaction potential that can stabilize a 3D ordered phase. Moreover, a specific pathway to crystallization is required for proper hybridization of the grafted DNA and for particles repositioning into ordered phases. Two common strategies for directing these interparticle interactions have been direct hybridization [11] and linker-mediated hybridization [12, 14]. Many parameters associated with the DNA shell and its morphology, including composition of the shell [51–53] and length [17] and design of the DNA motifs, with sequence design referring to both a Watson–Crick interacting portion or an entropic spacer [11], optimize interactions favorable for the formation of ordered phases [54, 55]. It is also possible to diversify the structure of the assembled phase of isotropic NPs by varying the number of hybridizing DNA sequences and the hydrodynamic radius [56, 57]. The tuning of two key parameters, namely, DNA linker length and the number of linkers per particle, can dictate the transformations between different ordered and disordered phases [14], as shown in Fig. 8a, b.

The conformation of the DNA shell can also be tuned by grafting DNA to anisotropic NPs. It has been shown computationally that solid polyhedral objects can assemble into a variety of structures [58]. Researchers have demonstrated the 3D assembly of anisotropic NPs grafted with DNA [16] typically favor phases that maximize interparticle hybridizations. However, a range of interesting and unexpected effects can occur in the multi-strand shell. For example, the spontaneous breaking of DNA shell symmetry was observed for nanorods due to the collective hybridization and flexibility of the DNA chains [15], which results in the formation of a ladder-like linear organization rather than smectic or nematic types of organization. These DNA shells have complex morphologies, and Lu et al. discovered for nanocubes that the polymeric effects of DNAs on shaped NPs can result in the anisotropic distribution of sequences on particle surfaces and effective complex shapes [59]. This phenomenon can drastically affect the resultant assembly. These researchers noticed that for a specific range of linker lengths, DNA functionalized nanocubes packed in a peculiar zigzag arrangement [59], which is a breakdown of the orientational symmetry of the underlying nanoscale object (Fig. 8c, d). The shape of DNA shells of anisotropic particles plays a key role in the self-assembly process, particularly for interactions between dissimilarly shaped particles. In one case, functionalized anisotropic particles were used

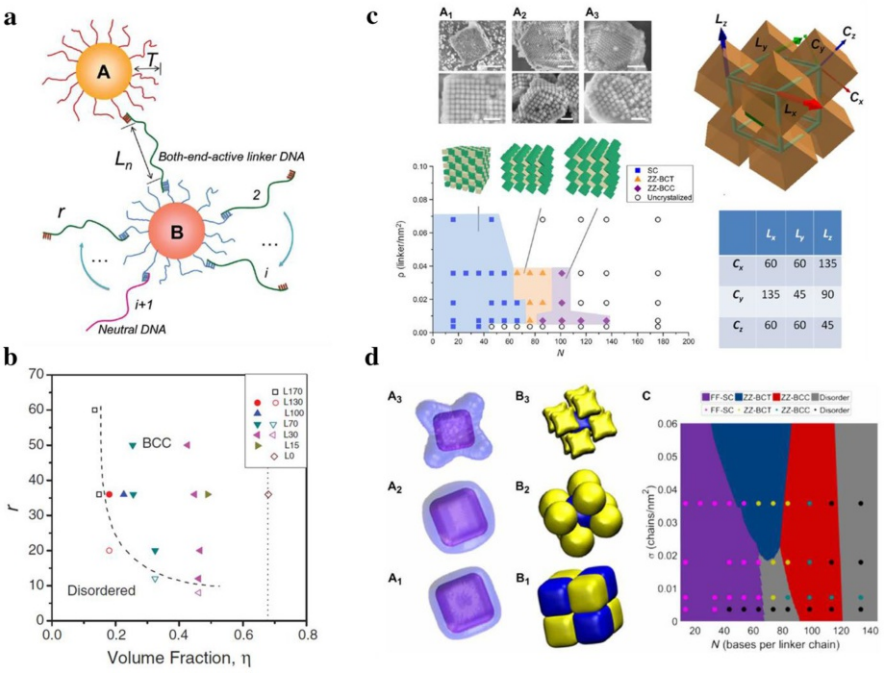

Fig. 8 Design and assembly of spherical and cubic NPs with DNA shells. **a**, **b** Schematic representation of DNA-grafted particles connected by r DNA linkers with length L_n (**a**) and experimental phase diagram showing the transition from the ordered to disordered state as a function of the nominal linker/NP ratio and NP volume fraction (**b**). Dashed line in **b** represents the boundary between dis-ordered and ordered phases. **a**, **b** Reproduced from Xiong et al. [14], with permission, copyright 2009, American Physical Society. **c** Scanning electronic microscopy (SEM) images of nanocube lattices with varying distributions of DNA grafted to the particle surface, and phase diagram of assemblies through variations in grafting density and DNA sequence length. **d** Simulations of DNA corona morphologies as a function of grafting chain length. A combined computational and experimental phase diagram reveals simple cubic, body-centred cubic (*BCC*) or body-centred tetragonal (*BCT*) phases and a novel, so-called ZZ packing arrangement. **c**, **d** Reproduced from Lu et al. [59], with permission, copyright 2019, American Association for the Advancement of Science

to coordinate isotropic particles. The inherit symmetry of the anisotropic particles and its respective shell will dictate the organization of the spherical nanoparticles [60]. In this study, Lu et al. showed that cubic NPs can coordinate spherical particles through local arrangements in the designed DNA shell that cannot be realized for spheres, giving rise to the formation of the unique 3D lattice of alternating cubes and spheres. The particle shape complementarity can be also used to promote a formation of 3D lattices [61]. In this respect, the nature of the DNA shell can be seen as a tunable DNA shape that can leverage a large diversity of existing NP shapes for the prescribed organization of functional nanomaterials.

At the same time, there is a plethora of new nanoscale effects in this regime that remain to be discovered and well understood.

4 DNA Origami

4.1 DNA Origami: Folding by Design

The DNA tile has been demonstrated to be a highly programmable scaffold for guiding NPs into complex architectures. However, The DNA tile has a certain lack of design flexibility that limits the number and complexity of possible NP architectures. In 2006, Rothemund proposed a new method to build DNA structures, which is known as "DNA origami" [8]. Similar to traditional paper origami, DNA origami involves the folding of a long ssDNA sequence, known as the scaffold sequence, through prescribed hybridizations with many shorter sequences, known as staple sequences. The DNA origami technique uses a scaffold sequence, M13mp18, derived from the M13 bacteriophage. The specific interactions between the staple sequences and the scaffold result in the self-assembly of the designed shape, as shown in Fig. 9a. As a direct result of this development, many researchers in various fields were able to utilize this technique for the development of a number of symmetric shapes, such as a square, rectangle, smile face, star, or triangle (Fig. 9b), and even highly asymmetric shapes, such as a dolphin [62] or a Chinese map [63]. Douglas et al. demonstrated the use of DNA origami for the design of a 6HB [64, 65] that was developed to facilitate nuclear magnetic resonance studies of membrane proteins in solution, and this strategy was later extended to realize a 24-helix bundle (24HB) for guiding NPs [66]. This type of tubular structure was also utilized to assemble NPs in a 3D chiral architecture [67].

The cornerstone of DNA nanotechnology is the ability to reliably design and generate target 2D and 3D structures with the prescribed nanoscale features. The

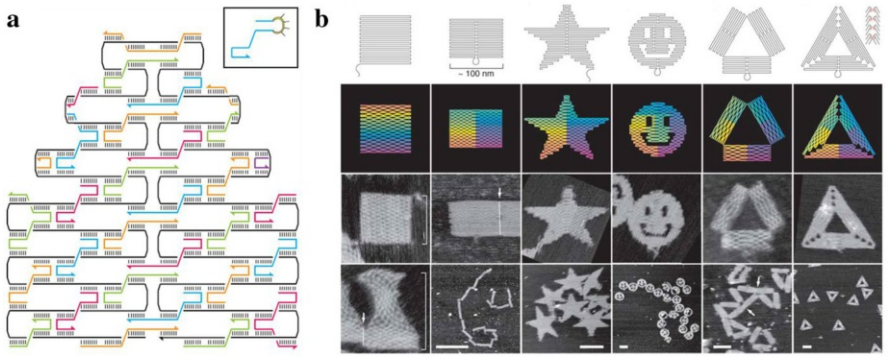

Fig. 9 **a** Schematic representation of the design of DNA origami, **b** 2D patterns designed by the DNA origami technique. **a**, **b** Reproduced from Rothemund [8], with permission, copyright 2006, Nature Publishing Group

introduction of the DNA origami technique enabled research related to a variety of fields and applications as it was a simpler platform to utilize. One example is the work carried out to design a 2D DNA origami sheet subsequently folded into a DNA tetrahedron that could be used as a molecular container [68]. A similar strategy was reported with the development of a nanoscale DNA box with a programmable lid that can open based on a specific DNA input signal [69]. The research group of Shih and coworkers conducted comprehensive studies on the formation of 3D DNA origami that resulted in the successful design and assembly of complex shapes using a honeycomb lattice as the basis of the designs [70–72], as shown in Fig. 10a. These origami shapes included the monolith, square nut, railed bridge, genie bottle, stacked cross, and slotted cross, with precisely controlled dimensions ranging from 10 to 100 nm. To make the design of DNA origami more accessible, a software package, named caDNAno, was developed to aid with scaffold sequence routing and staple sequence design [71, 72]. Ke et al. subsequently reported assembled 3D objects whereby the origami design consisted of double helices with the four nearest neighbors separated by 8 bp and the staple strand positioned to cross over one of its four neighbors, as shown in Fig. 10b. Using this design, the helices were arranged as a square lattice, forming overall a cuboid structure from the successful stacking of two to eight repeating layers [73]. Efforts were also made to design origami and multilayered structures based on hexagonal and hybrid arrangements of helices (Fig. 10c), resulting in four different origami structures. This strategy took full advantage of the three different arrangements of DNA helices within the designed objects, including the honeycomb, square, and the hexagonal lattice of helices, to build a hybrid-lattice origami [74].

The development of additional design strategies and thorough investigation of the origami technique contributed to the increasing number of possible DNA structures, such as a nanotube, a helix bundle, and even more complex 3D structures, each of which could serve as the basis of guiding complex organizations of NPs. An

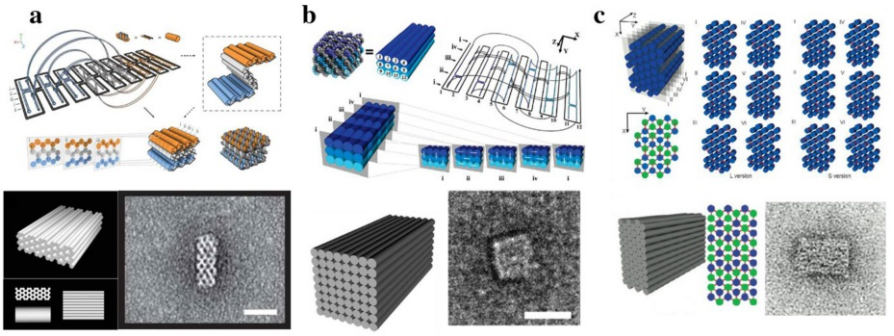

Fig. 10 Three different designs of 3D helices in lattice arrangements within DNA origami and the typical products. **a** Honeycomb lattice. Reproduced from Douglas et al. [72], under the terms of the Creative Commons Attribution Non-Commercial License, copyright 2009, the Authors, published by *Nucleic Acids Research*. **b** Square lattice. Reproduced from Ke et al. [73], with permission, copyright 2009, American Chemical Society. **c** Hexagonal lattice. Reproduced from Ke et al. [74], with permission, copyright 2012, American Chemical Society

example of such a complex DNA origami design is the DNA-origami ball, reported by Han et al. [75], which can be used as a vessel for drug delivery. Building upon this work, the same research group went on to design square, triangle, and 24HB structures of larger sizes but only after incorporating more than one scaffold into the design [76]. Additional efforts have been made to improve the folding efficiency or experimental yield of DNA origami, as this is necessary for DNA origami to become a viable platform for application purposes or use in large-scale manufacturing. Recent studies have shown that DNA can be efficiently folded at constant temperature, which is preferable to the long and complex annealing protocols traditionally performed to achieve DNA origami folding [77, 78].

Using the caDNAno software, Tian et al. successfully synthesized an octahedron frame [79] (Fig. 11a), similar to the nanoscale octahedron assembled from the 1.7-kb scaffold [35], except that each strut of the octahedron of this design was a 6HB. Compared to the previous strategy used to form an octahedron, the DNA origami technique enabled a much more straightforward design of a nanoscale octahedron with high yield. This octahedron frame comprised twelve 6HBs and was assembled from a single scaffold sequence and 144 staple sequences. The overall design is highly programmable, whereby sticky ends can be positioned virtually anywhere along the struts of the octahedron. In this case, researchers constructed the octahedron with sticky ends at the vertices of the frame, as well as sticky ends that could be placed facing towards the interior of the frame for the programmable capture of a nanomaterial. This modification in the design of the origami facilitated the assembly of this object and AuNPs into a 3D superlattice. Meanwhile, several other kinds of 3D frames were designed with different symmetries, as shown in Fig. 11b, including a cube, a prism, a triangular bipyramid, and an extended octahedron [19]. The programmability of the DNA origami technique allowed these frames to be incorporated into a library of building blocks for crystal assembly and NP guiding, which

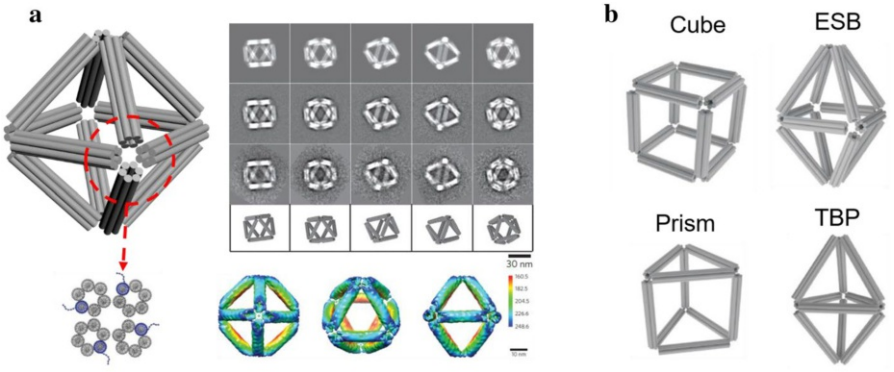

Fig. 11 DNA origami frame structures. **a** Diagram of the octahedron frame (left top) and a detailed view of the design of the vertexes (left bottom). To the right are cryo-electron microscopy images and the reconstructed structures. Reproduced from Tian et al. [79], with permission, copyright 2015, Nature Publishing Group. Additional designs of DNA frames, including the cube, elongated square bipyramid (*ESB*), prism, and triangular bipyramid (*TBP*). Reproduced from Tian et al. [19], with permission, copyright 2016, Nature Publishing Group

was a significant development in the field of structural DNA nanotechnology [19, 79]. The research groups of Bathe and coworkers and Yan and coworkers together developed sophisticated software packages for the design of complex DNA structures [80]. The accuracy of this method will enable the expansion of the overall library of DNA shapes and make many desired shapes easily accessible. Simultaneously, there has been rapid progress in mineralizing DNA structures [81, 82] and expanding the structure size [38, 76], which will enable DNA-based material to be transferred into a broad range of environments and applications.

4.2 Organization of NPs with DNA Origami

As a straightforward strategy for the fabrication of complex architectures, the DNA origami technique has been used to develop a variety of building blocks for assemblies, templating, and bio-applications. Researchers worked on combining two maturing subsets of DNA nanotechnology, namely, the tailoring of the DNA shell grafted to NPs and the use of DNA origami to assemble structures in one, two, and three dimensions to achieve well-ordered NP architectures. The high degree of programmability and addressability of DNA origami allowed access to many desired structures. One example of a programmable DNA origami motif was the "nanoflower" [83], a DNA origami that could host a NP at its center and had tunable interactions at its exterior surface to direct the assembly of either 1D or 2D structures depending on the angles of the prescribed sites of the inter-frame interactions or sticky ends (Fig. 13b). It is also possible to achieve the same complex structures assembled with DNA tiles using DNA origami. The DNA origami

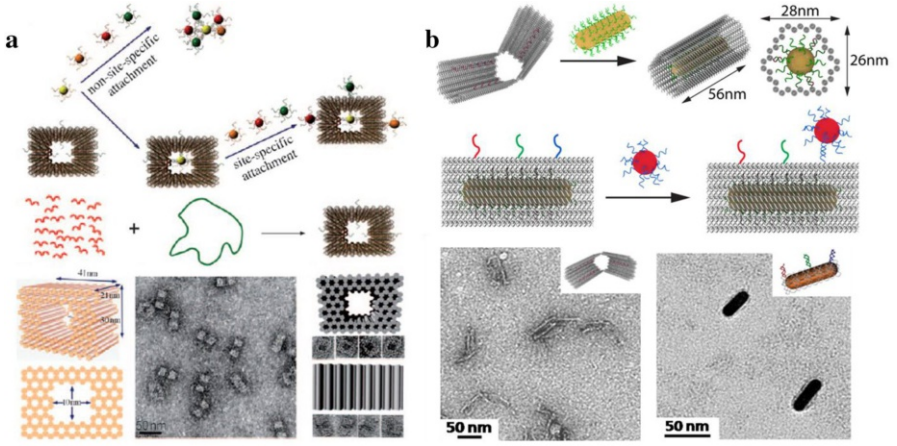

Fig. 12 **a** Design of the DNA nanocage for interrupting the symmetry of AuNPs, and schematic diagram of the site-specific AuNP attachment. TEM images of the DNA nanocages are shown at bottom. Reproduced from Zhao et al. [84], with permission, copyright 2011, Wiley-VCH Verlag GmbH and Co. KGaA. **b** Diagram showing the function of a gold nanorod (AuNR) and the arrangement of AuNPs. TEM images at bottom show the actual state of the nanocage and the functioned AuNR. Reproduced from Shen et al. [85], with permission, copyright 2016, American Chemical Society

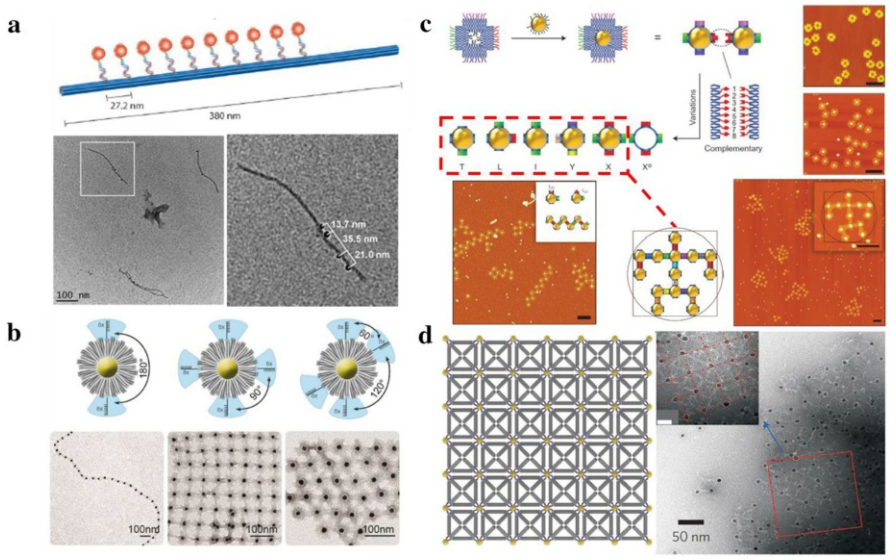

Fig. 13 One-dimensional (1D) and 2D NP arrays fabricated with DNA origami. **a** Schematic diagram and TEM image of linear array of AuNPs arranged with a 380-nm six-helix bundle (6HB). Reproduced from Stearns et al. [86], with permission, copyright 2009, Wiley-VCH Verlag GmbH and Co. KGaA. **b** Diagram showing the design of the "nanoflower" origami motif. With different ssDNA exposed, various AuNP arrays could be fabricated. Reproduced from Schreiber et al. [83], with permission, copyright 2016, American Chemical Society. **c** Fabrication of the DNA-framed NPs and corresponding AFM images. A nanoscale analog of Leonardo da Vinci's Vitruvian Man was assembled with various types of DNA-framed NPs. Reproduced from Liu et al. [92], with permission, copyright 2016, Nature Publishing Group. **d** 2D AuNP arrays fabricated with octahedron frames. Reproduced from Tian et al. [79], with permission, copyright 2015, Nature Publishing Group

technique can be used to design structures for the purpose of breaking the symmetry of spherical NPs and to guide the arrangement of NPs with defined orientation and interparticle distances, one of which was a hollow rectangular prism based on the honeycomb lattice [84], as shown in Fig. 12a. The targeted attachment of distinct particles showed the ability to position particles both inside and outside of the origami cage with designed symmetry. Similar work was done utilizing a hollow, rod-like DNA origami (Fig. 12b) [85]. The realization of DNA nanotubes and N-helix bundles served as additional templates for the high-ordered organization of NPs. Before the introduction of DNA origami in 2006, DNA AuNPs were extensively organized into complex structures with DNA tiles. DNA origami was used by Stearns et al. [86] to direct the in situ nucleation and growth of AuNPs. These researchers designed and synthesized a 380-nm 6HB and chose an A3 peptide as the means to guide the positioning of the generated NPs; following the addition of soluble gold ions, the AuNPs grew 5–10 nm at the designated growth sites (Fig. 13a) [86]. In an effort to expand the number of available materials that can be organized via DNA origami, semiconductor nanocrystals or quantum dots (QDs) were organized into 1D arrays utilizing DNA origami [87]. More complex

assemblies were achieved, as evidenced by the helical assembly of AuNPs onto a DNA origami template [66]. Similarly, helical assemblies of AuNPs were made by first organizing 15-nm AuNPs onto the surface of a rectangular sheet and then rolling the sheet, which resulted in a helical assembly of particles [67].

Based on nanoarrays assembled using DNA tiles, which were used as a means to organize 2D arrays of proteins, a rectangular-shaped DNA origami was shown to exhibit a high degree of flexibility and programmability. This design was no longer bound by the conventional sticky end designation specific to DNA tiles, and the origami could be modified to designate the location of an aptamer at any location on the origami surface. The programmable nature of the origami was used to position proteins in an "S" shape, and these protein arrays could be assembled with high efficiency. Aptamers were used to retain their specific functionality, even after the assembly of complex structures [88]. Supplementary to these efforts, work was done to investigate alternative methods to bind AuNPs to these assembled structures. The use of AuNPs monofunctionalized with lipoic acid-modified DNA sequences was shown to increase functionality and binding efficiency, which rose from 45 to 91% with reduced errors in NP positioning [89]. Work continued on the organization of nanomaterials other than gold. A triangular DNA origami motif was designed to organize silver nanoparticles (AgNPs) at specified positions. Three variations of dimeric AgNP structures were designed, each with specified interparticle spacings, as well as an asymmetric trimetric AgNP structure and a heterodimer of a AuNP and AgNP [21]. Complex clusters from metallic NPs were assembled using rigid linear DNA origami linkers that were used to define large interparticle distances [90]. Recently, Lin et al. demonstrated the use of a site-specific covalent binding, instead of base-pairing, enables the fabrication of supra-architectures from shaped origami and NPs [91].

The research group of Gang and coworkers explored the possibility of using different types of building blocks that could be co-assembled into a complex yet designed cluster and with periodic planar architectures. These researchers realized this aim by using the so-called polychromatic 2D origami frames [92], which possess multiple types of distinguishable bonds arranged in defined anisotropic configuration, resulting in "colored" valence of these building blocks. Different types of these polychromatic frames exhibit differently colored valence, which allows for the building of complex architectures through the selection of a specific set of the polychromatic building blocks. These researchers developed a planar DNA origami structure that had a fourfold valency with respect to its programmable binding interactions, and an empty square window in the interior of the origami was used to hold a DNA-functionalized AuNP, as shown in Fig. 13c [92]. Each of the four exterior faces were decorated with distinct binding interactions, labeled with different colors, resulting in the various species of polychromatic 2D frames. Through the selection of polychromatic building blocks and their valence, it was possible to achieve programmable connectivity of the blocks. By controlling the types of different blocks and their ratio in the multi-component assembly, different periodic and non-periodic structures can be rationally formed, including clusters of different shapes, 1D linear structures, the zig-zag chain, and 2D arrays. This strategy was used to assemble a nanoscale analogue of Leonardo da Vinci's Vitruvian Man [92].

In an effort to achieve designed 3D NP clusters with controlled placement of particles, Tian et al. used polyhedral DNA origami, as discussed in detail in an earlier publication [79]. In this design, the six distinct vertices of the octahedron were used to encode the binding locations for particles of varying size. Using this method, these researchers assembled an octahedral cluster, a square-shape cluster, and non-chiral and chiral hetero-clusters, all based on three types of NPs. Furthermore, 1D and 2D arrays of AuNPs (Fig. 13d) were assembled with the octahedral frames and NPs serving as connectors between the frames [79].

In order to gain further control over NP organization in three dimensions, the research group of Gang and coworkers proposed a strategy in which designed DNA constructs of different shapes could serve as programable topological linkers between NPs [18, 19, 93, 94]. The overall strategy is powerful since it permits the building of different lattice types for the same type of particles; thus, it addresses a major problem in nanotechnology—that of creating different materials from the same type of functional nanoblocks. For example, the octahedron frame was used to assemble 3D superlattices of AuNPs, and this technique was expanded to include a variety of lattice symmetries using multiple polyhedral frames [19], inspiring the development of a set of 3D nanoscale molecular frames and their use in this

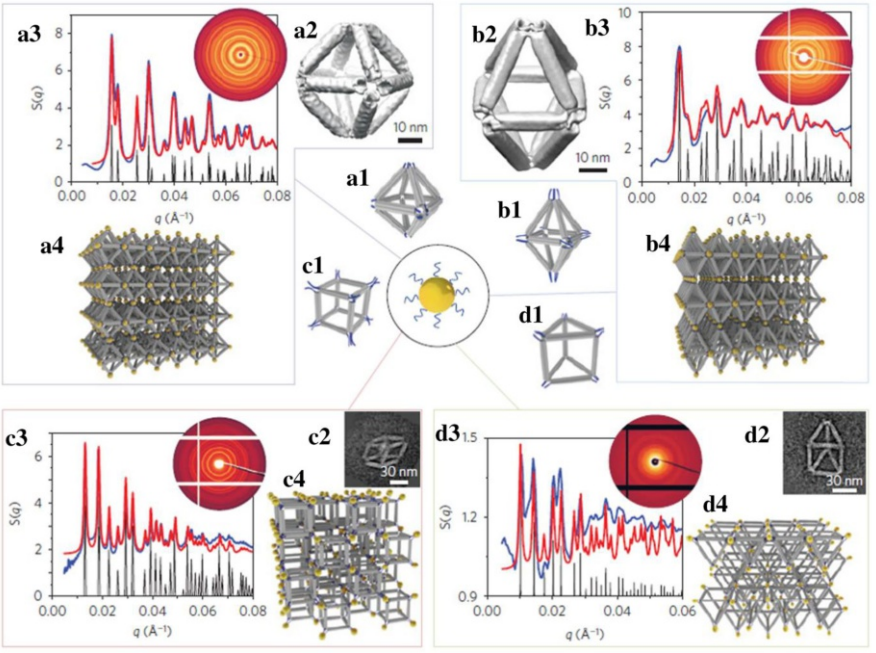

Fig. 14 Schematic diagram of four different DNA origami frames guiding NPs into the ordered 3D lattice. Models of DNA origami shape are shown. **a1**–**d1** Octahedron (**a1**), elongated square bipyramid (**b1**), cube (**c1**), and prism (**d1**). **a2**–**d2** Reconstruction of DNA origami frames from cyro-electron microscopy. **a3**–**d3** X-ray scattering (SAXS) results of different architectures. **a4**–**d4** Models of ordered 3D lattices. Reproduced from Tian et al. [19] with permission, copyright 2016, Nature Publishing Group

self-assembly approach. The structure of these assemblies was investigated using small angle X-ray scattering (SAXS) and shown to have a long-range order with structural characteristics matching their respective designs, as shown in Fig. 14 [19]. This strategy was combined with encapsulation of the NP inside frames to assemble a series of NP superlattices from the cubic diamond family [18], which had up to that point been a considerable challenge in the field of colloidal self-assembly. In this case, tetrahedral DNA origami frames were used to coordinate DNA-functionalized AuNPs (Fig. 15a). Moreover, several design requirements with respect to the particles and origami frames were revealed [95]. The resultant structure could also be tuned by adjusting the size of the NPs, resulting in a zinc blende structure or a "wandering" zinc blende structure [18]. In addition to 3D nanoscale frames, there are a few other viable strategies for the assembly of complex 3D structures. For crystalline assemblies and NP organization, the prerequisites of high rigidity and sufficient

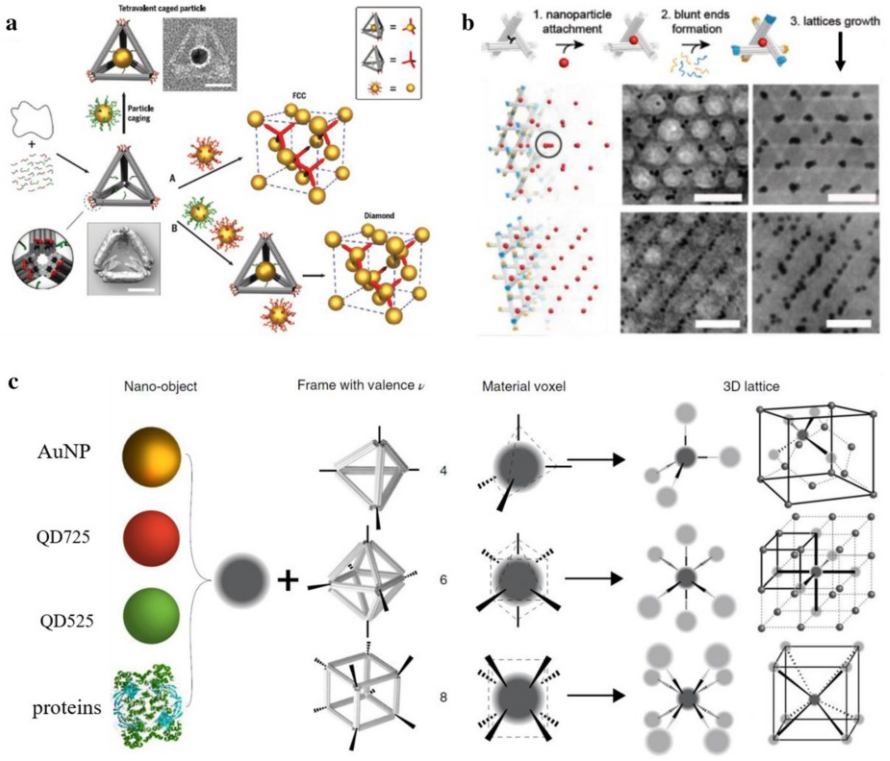

Fig. 15 Three-dimensional (3D) AuNP lattice assembled with 3D DNA origami frames. **a** Schematic diagram of FCC lattice and diamond lattice of AuNP fabricated with tetrahedron DNA origami. Reproduced from Liu et al. [18], with permission, copyright 2016, American Association for the Advancement of Science. **b** Rhombohedral lattices fabricated with the DNA origami tensegrity triangle structure. Reproduced from Zhang et al. [20], with permission, copyright 2018 Wiley-VCH Verlag GmbH and Co. KGaA. **c** Schematic of the broadly applicable platform for 3D lattice assembly from material voxels, showing 3D origami frames of different shapes (tetrahedron, octahedron, cube) that can be integrated with NPs and proteins as desired. Reproduced from Tian et al. [94], with permission, copyright 2020, Nature Publishing Group

open guest space are essential for the design of the building blocks. However, with increasing size, DNA structures become more flexible and lose their ability to precisely control distances at the nanoscale. Recently, a DNA–origami-based tensegrity with a triangle structure was synthesized by the research group of Liedl and coworkers for the purpose of assembling a 3D architecture entirely from DNA [20]. This design yielded a rhombohedral lattice that was constructed using this tensegrity triangle motif that had both sufficient rigidity and available space (Fig. 15b). In this work, these researchers show that this motif can host NPs with a diameter of 20 nm, thereby greatly expanding the application of DNA nanotechnology.

A broadly applicable platform for the assembly of 3D nanomaterials from so-called material voxels, which are 3D origami frames of different shapes that can be integrated with NPs, proteins and enzymes, was recently demonstrated by Tian et al. [94]. This strategy decouples the assembly process, governed by DNA programmable bonds between origami, from nano-object details, as shown in Fig. 15c. This decoupling allows for the assembly of 3D designed, functional arrays from NPs, proteins and enzymes using the same assembly approach. Novel optical and chemical properties were shown in this study for QDs and enzymatic arrays, respectively.

5 Applications of DNA Architectures for Nanomaterials

Despite the field of DNA nanotechnology emerging from the concept of specifically crystallizing proteins into ordered 3D structures, there have been tremendous efforts to utilize numerous functional nanomaterials in a variety of real-life applications. A significant portion of this review has been dedicated to the organization of metallic NPs through the use of DNA tiles and origami, and these studies are of particular interest because the optical properties of plasmonic NPs can be controlled based on their structure. Researchers used dsDNA to fabricate chiral nanostructures in which the DNA was folded into a pyramid so that the vertices of the pyramid designated a particle binding site [96]. Additional study was directed towards investigating this design while incorporating various materials into the structure [97]. This strategy proved to be highly effective for the generation of single- or multicomponent chiral isomers with strong R/S optical activity. The incorporation of gold nanorods (AuNRs) with DNA origami assembly strategies has also been a popular strategy in the research field of plasmonic properties. Pal et al. used a triangular DNA origami motif to immobilize anisotropic AuNRs onto the origami surface and demonstrate the control of NR orientation in dimer structures (Fig. 16a) and in AuNP–AuNR heterodimers [98]. A 2D DNA origami can have two programmable surfaces, and both can be utilized to immobilize AuNRs to fabricate chiral structures (Fig. 16b) [99, 100]. This dual-faced functionalization of the 2D origami was also used to assemble the AuNR helix structure shown in Fig. 16c [101]. The strategy of using planar origami plates tor assemble complex supra-NP linear architectures from AuNPs and QDs was recently demonstrated by Tian et al. [102]. This approach allowed these researchers to investigate plasmonic effects in linear meso-structures [102]. Recently, the research group of Gang and coworkers demonstrated single QD polarized emitters that were assembled by 3D origami from plasmonic and

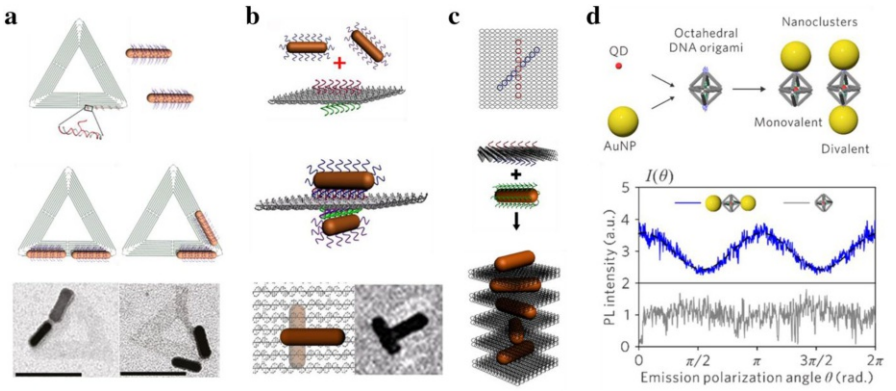

Fig. 16 Plasmonic structures assembled with 2D DNA origami. **a** AuNR dimer structures with different angles (180° and 60°) between AuNPs based on a triangular origami. Reproduced from Pal et al. [98], with permission, copyright 2011, American Chemical Society. **b** AuNR dimer structures with various relative positions were fabricated with a bifacial DNA origami. Reproduced from Lan et al. [99], with permission, copyright 2013, American Chemical Society. **c** The AuNR helix was assembled with bifacial DNA origami as template. Reproduced from Lan et al. [101], with permission, copyright 2015, American Chemical Society. **d** Light-emitting (*PL* photoluminescence) clusters with polarized emission were assembled from 3D octahedral origami, AuNPs and quantum dots (*QDs*). Reproduced from Zhang et al. [103], with permission, copyright 2019, American Chemical Society

light-emitting NPs (Fig. 16d) [103]. This integration permitted the control of active optical elements at the nanoscale, thereby providing opportunities for the manipulation of emitted light.

Assemblies of AuNRs organized by DNA origami motifs have been developed to have dynamic properties. Based on the same AuNR–DNA origami design, one of the AuNRs was stationary ("stator") while the AuNR bound to the opposite side of the DNA origami could move across the origami in one direction in programmable intervals ("walker") based on DNA strand displacement reactions. This type of AuNR walking was also achieved using a DNA origami design with a more complex topology (Fig. 17a) [104]. This research was built upon to include multiple walkers relative to a single stator, where the walkers could walk either independently or together (Fig. 17b) [105]. The orientations of the AuNRs could also be programmed through the use of a pair of 14HB origami. The relative angle of the rods was controlled by two DNA locks, and these locks could be reconfigured to tune this angle based on strand displacement reactions (Fig. 17c) [106]. This lock design was modified to be tuned by UV-light when azobenzene-modified DNA oligonucleotides [107] were used or by changes in pH based on Hoogsteen interactions whereby a duplex and ssDNA could hybridize into triplets [108]. This design has recently been utilized as a platform to detect viral RNA at picomolar concentrations [109].

DNA origami has also been leveraged in multiple ways for the chiral assembly of spherical gold NPs (Fig. 18). To achieve this goal, various DNA origami templates have been used, such as 14HB [66], DNA origami sheet subsequently rolled up into a tube [67], tubular DNA origami for prescribed AuNR and AuNP helixes [110], a DNA origami toroid [111], or a bifacial DNA origami [112].

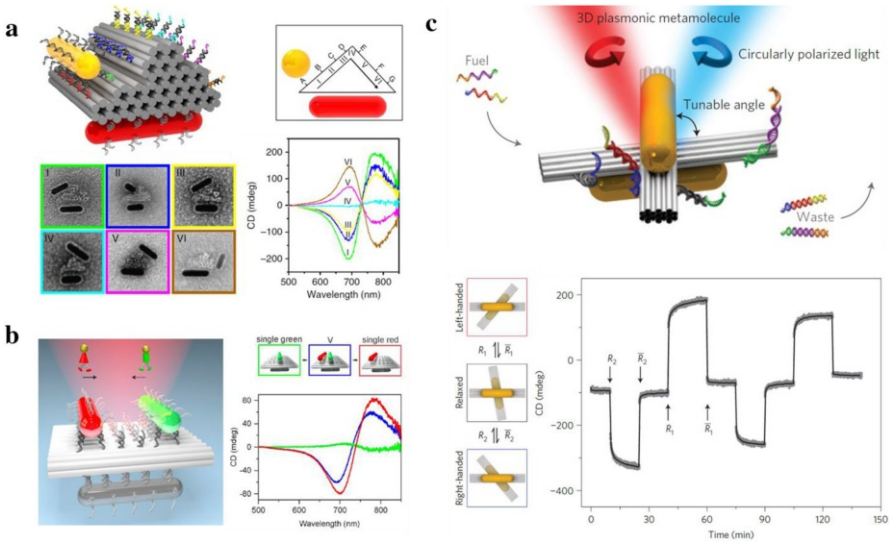

Fig. 17 Dynamic chiral plasmonic devices assembled by DNA origami. **a** A plasmonic AuNR can walk on a triangular prism origami using DNA strand displacement reactions. The TEM images and the circular dichroism (*CD*) spectra show the movement of the AuNR (Movement of AuNRs shown from I–VI positions). Reproduced from Zhou et al. [104] under a Creative Commons Attribution 4.0 International License, copyright 2015, Nature Publishing Group. **b** Diagram showing that two AuNRs could walk stepwise on DNA origami separately or together. Movements are shown by the CD spectra. Reproduced from Urban et al. [105], with permission, copyright 2015, American Chemical Society. **c** 3D plasmonic metamolecule could tune the angle of two bundles and switch between the left-handed and right-handed states through the strand displacement reaction. The change in angle is shownby CD spectra. Reproduced from Kuzyk et al. [106], with permission, copyright 2014, Nature Publishing Group

Subsequent work with the 14HB template design resulted in a dynamic two-state plasmonic material in which the optical response of the system is switchable [113]. DNA origami was also used to construct plasmonic nano-antennas to enhance the fluorescence intensity in a plasmonic hotspot [114]. Similar efforts were made to probe surface-enhanced Raman spectroscopy and future sensing applications [115–117]. The nanometer precision of DNA origami was utilized to prescribe the relative positions of QDs and AuNPs in various geometries to control the average photon count rate and lifetime of the QD [118]. A triangular DNA origami was used to study long-range quenching of QDs based on its distance to a AuNP [119].

The stability and rigidity of DNA origami allowed these structures to be used as molds with desired cavity morphologies. A branched DNA origami structure was metallized in a two-step process that was a significant development towards DNA-templated nanocircuits [120]. Origami templates were also used to synthesize gold structures with arbitrary shapes, including rings, pairs of parallel bars, H shapes, gold nanocuboids and nanodonuts (Fig. 19a) [121, 122]. The same strategy was employed to adjust the size of AuNPs for further application, such as optoelectronics [66, 90]. A new concept was introduced to seed AuNPs inside of 3D DNA origami nanostructures to nucleate the growth of gold structures into

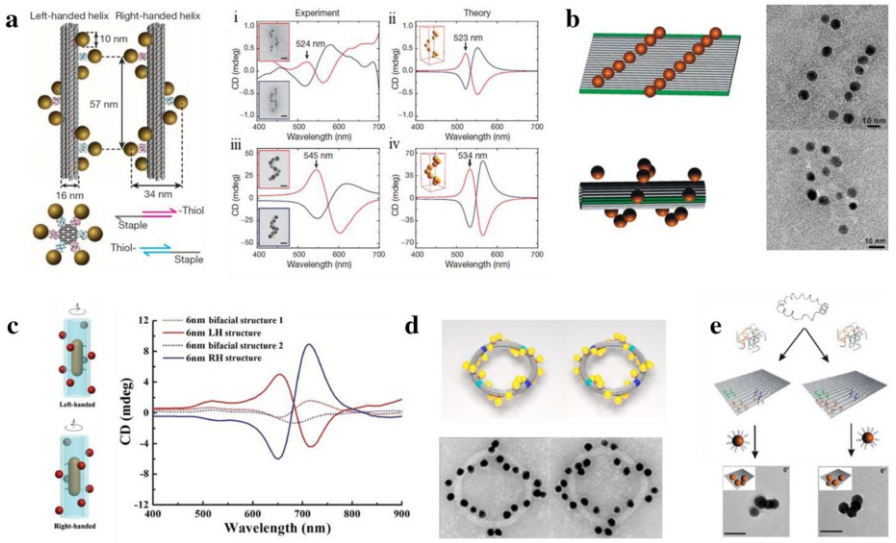

Fig. 18 Anisotropic chiral plasmonic structures assembled by DNA origami. **a** Diagram showing a chiral AuNP helix assembled with a 24HB. In designing different sites, right-handed and left-handed structures are obtained. Various sizes of AuNPs are assembled, and a peak shift is captured by CD spectra (i–iv). Reproduced from Kuzyk et al. [66], with permission, copyright 2012, Nature Publishing Group. **b** An AuNP helix structure assembled through rolling up a rectangular origami. Reproduced from Shen et al. [67], with permission, copyright 2012, American Chemical Society. **c** Schematic diagram of the AuNP@AuNR structure and its CD spectra (*RH* right-handed, *LH* left-handed). Reproduced from Shen et al. [110], with permission, copyright 2017, Wiley-VCH Verlag GmbH and Co. KGaA. **d** Diagram of toroidal super-chiral plasmonic structure assembled with DNA origami and its TEM images. Reproduced from Urban et al. [111], with permission, copyright 2016, American Chemical Society. **e** Four AuNPs arranged into RH and LH structures with bifacial DNA origami. Reproduced from Shen et al. [112], with permission, copyright 2013, American Chemical Society

shapes whose resultant structure would be determined by the DNA origami mold (for example, see Fig. 19b) [123]. In another study, a series of shape-controlled inorganic nanostructures were reported, including gold and silver nanostructures, using DNA origami structures with different cavities; examples of the shape of these cavities are cuboid, triangle, sphere and Y-shape. Silver and QDs were also combined to fabricate a novel structure (Fig. 19c). To meet the demand of the casting highly stiff DNA origami molds were created [124]. Recently, there have been reports of the mineralization of DNA origami shapes and structures through a sol–gel chemistry that results in biomimetic silica nanostructures that are more robust. Compared to their precursor DNA nanostructure, these DNA–silica hybrid materials possess greater stability against a variety of factors, including temperature, pressure, salt concentration, and other buffer conditions [81, 82].

DNA shapes have also shown potential for utilization in biomedical applications as chemical nanoreactors and for drug delivery. One study reported a hexagonal barrel made using DNA origami capable of carrying nanoscale cargo, with a lock and key mechanism whereby the lock consisted of a DNA aptamer and

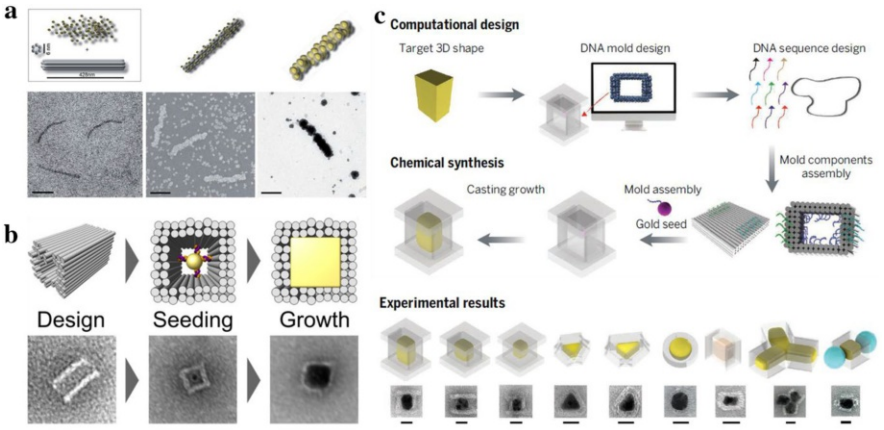

Fig. 19 Shaped-controlled growth of inorganic nanostructures. **a** Schematic diagram of a AuNP cluster assembled by DNA origami and growth of NPs. The TEM images (bottom) show the structures in different states. Reproduced from Schreiber et al. [121], with permission, copyright 2011, Wiley-VCH Verlag GmbH and Co. KGaA. **b** Cuboid gold nanostructure is synthesized using DNA origami with a rectangular cavity. The diagram shows the process and the TEM images of each step (bottom). Reproduced from Helmi et al. [123], with permission, copyright 2014, American Chemical Society. **c** Schematic diagram showing the design of the DNA origami and various shape-controlled growth of inorganic nanostructures. Reproduced from Sun et al. [124], with permission, copyright 2014, American Association for the Advancement of Science

complementary strand and the key was the corresponding antigen [125]. DNA tiles were used to design a tweezer-like structure that is used to actuate the activity of an enzyme–cofactor pair [126]. 3D DNA origami structures were developed as nanoscale reactor vessels; in one case a hexagonal cylinder origami was used as a nanoreactor to confine a cascading enzymatic reaction between glucose oxidase and horseradish peroxidase [127]. DNA origami was also used in efforts to compartmentalize enzyme to enhance their catalytic activity and stability [128] and was also studied as a molecular delivery system for targeted therapeutics [129].

DNA nanotechnology is considered to be a powerful method for the development nanoelectronics. However, during the past decade, the guiding and fabricating reactions of NPs have always occurred in the liquid phase, and the organization or aggregation is formless and difficult to predict. Kershner et al. proposed a strategy to construct controllable and predictable DNA architectures [130]. These researchers designed a template involving the self-assembly of DNA origami and a top–down microfabrication technique known as lithography to pattern a substrate. After the triangular origami was arranged on the templated-substrate, the desired architecture was obtained, as shown in Fig. 20. The final positions of the AuNPs could be determined and were found to be quite accurate according to the design. This methodology can be applied to a wide range of application in the fabrication of functional devices [131].

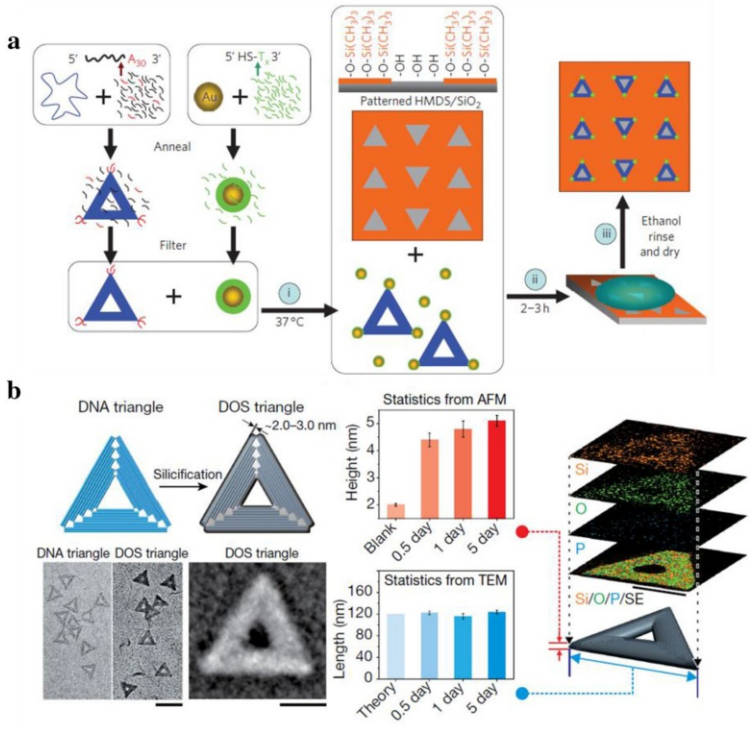

Fig. 20 **a** Diagram shows that results from combining the lithography technique and DNA origami with NPs attached could be predictable arranged. Reproduced from Hung et al. [131], with permission, copyright 2010, Nature Publishing Group. **b** Method for creating silica nanostructures from DNA templates by a sol–gel chemistry shown for triangular origami with height mapping and corresponding energy-dispersive X-ray spectroscopy (EDS) spectra [81]. Reproduced with permission. Copyright 2018, Nature Publishing Group

6 Summary and Outlook

DNA nanotechnology was originally proposed to address a problem in protein crystallography, but in only a few decades it has become a powerful methodology for building at nanoscale. DNA nanotechnology has become a rapidly maturing field that extends to many new conventional and nonconventional applications in material science, chemistry, biotechnology, and nanomedicine. The development of DNA tiles [4, 6, 32, 65] and DNA origami [33, 62, 71–73, 130] enabled the realization of complex architectures, from low-dimension arrays [18, 46, 48, 79, 98] to complex structures [18–20, 50, 92, 132, 133], and from static structures [98–101] to dynamic architectures [104–108]. The programmability of DNA shapes provided a new nanotechnology toolbox for establishing platform approaches for the designed NP organizations [18, 19, 134, 135], particularly in three dimensions, where conventional nanofabrication methods are limited. These advances in DNA nanotechnology have been applied to the development of materials with specific function. Even with

complex programmable characteristics, DNA structures might retain their stability in the bio-environment, which is an attractive feature for emerging biomedical applications [125–128].

The discovery and design of functional nanomaterials for a diverse application require the design and synthesis of specifically designed DNA structures, the ability to integrate them with nanoscale building blocks, and the ability to assemble them into the desired structures.

Acknowledgements The work was supported by National Natural Science Foundation of China (Grant nos. 21971109 and 21834004), Jiangsu Youth Fund (Grant no. BK20180337), the Fundamental Research Funds for the Central Universities (Grant no. 14380151), and the US Department of Energy, Office of Basic Energy Sciences (Grant DE-SC0008772). The research carried out at the Center for Functional Nanomaterials, Brookhaven National Laboratory was supported by US Department of Energy, Office of Science Facility, under Contract No. DE-SC0012704. This work was also supported by the Program for Innovative Talents and Entrepreneur in Jiangsu (No. 133181), Shenzhen International Cooperation Research Project (No. GJHZ20180930090602235) and Nanjing Science and Technology Innovation Project for Oversea Scholars' Merit Funding (No. 133170).

References

1. Seeman NC (1982) Nucleic acid junctions and lattices. J Theor Biol 99(2):237–247. https://doi.org/10.1016/0022-5193(82)90002-9
2. Holliday R (1964) A mechanism for gene conversion in fungi. Genet Res. https://doi.org/10.1017/s0016672300001233
3. Kallenbach NR, Ma RI, Seeman NC (1983) An immobile nucleic-acid junction constructed from oligonucleotides. Nature 305(5937):829–831. https://doi.org/10.1038/305829a0
4. Fu TJ, Seeman NC (1993) DNA double-crossover molecules. Biochemistry 32(13):3211–3220. https://doi.org/10.1021/bi00064a003
5. LaBean TH, Yan H, Kopatsch J, Liu FR, Winfree E, Reif JH, Seeman NC (2000) Construction, analysis, ligation, and self-assembly of DNA triple crossover complexes. J Am Chem Soc 122(9):1848–1860. https://doi.org/10.1021/ja993393e
6. Chen JH, Seeman NC (1991) Synthesis from DNA of a molecule with the connectivity of a cube. Nature 350(6319):631–633. https://doi.org/10.1038/350631a0
7. Zhang YW, Seeman NC (1994) Construction of a DNA-truncated octahedron. J Am Chem Soc 116(5):1661–1669. https://doi.org/10.1021/ja00084a006
8. Rothemund PWK (2006) Folding DNA to create nanoscale shapes and patterns. Nature 440(7082):297–302. https://doi.org/10.1038/nature04586
9. Alivisatos AP, Johnsson KP, Peng X, Wilson TE, Loweth CJ, Bruchez MP, Schultz PG (1996) Organization of 'nanocrystal molecules' using DNA. Nature 382(6592):609–611. https://doi.org/10.1038/382609a0
10. Mirkin CA, Letsinger RL, Mucic RC, Storhoff JJ (1996) A DNA-based method for rationally assembling nanoparticles into macroscopic materials. Nature 382(6592):607–609. https://doi.org/10.1038/382607a0
11. Nykypanchuk D, Maye MM, van der Lelie D, Gang O (2008) DNA-guided crystallization of colloidal nanoparticles. Nature 451(7178):549–552. https://doi.org/10.1038/nature06560
12. Park SY, Lytton-Jean AKR, Lee B, Weigand S, Schatz GC, Mirkin CA (2008) DNA-programmable nanoparticle crystallization. Nature 451(7178):553–556. https://doi.org/10.1038/nature06508
13. Xiong HM, van der Lelie D, Gang O (2008) DNA linker-mediated crystallization of nanocolloids. J Am Chem Soc 130(8):2442–2443. https://doi.org/10.1021/ja710710j
14. Xiong H, van der Lelie D, Gang O (2009) Phase behavior of nanoparticles assembled by DNA linkers. Phys Rev Lett 102(1):015504. https://doi.org/10.1103/PhysRevLett.102.015504

15. Vial S, Nykypanchuk D, Yager KG, Tkachenko AV, Gang O (2013) Linear mesostructures in DNA–nanorod self-assembly. ACS Nano 7(6):5437–5445. https://doi.org/10.1021/nn401413b
16. Jones MR, Macfarlane RJ, Lee B, Zhang J, Young KL, Senesi AJ, Mirkin CA (2010) DNA–nanoparticle superlattices formed from anisotropic building blocks. Nat Mater 9(11):913–917. https://doi.org/10.1038/nmat2870
17. Macfarlane RJ, Lee B, Jones MR, Harris N, Schatz GC, Mirkin CA (2011) Nanoparticle superlattice engineering with DNA. Science 334(6053):204–208. https://doi.org/10.1126/science.1210493
18. Liu W, Tagawa M, Xin HL, Wang T, Emamy H, Li H, Yager KG, Starr FW, Tkachenko AV, Gang O (2016) Diamond family of nanoparticle superlattices. Science 351(6273):582–586. https://doi.org/10.1126/science.aad2080
19. Tian Y, Zhang Y, Wang T, Xin HL, Li H, Gang O (2016) Lattice engineering through nanoparticle-DNA frameworks. Nat Mater 15(6):654–661. https://doi.org/10.1038/nmat4571
20. Zhang T, Hartl C, Frank K, Heuer-Jungemann A, Fischer S, Nickels PC, Nickel B, Liedl T (2018) 3D DNA origami crystals. Adv Mater 30(28):e1800273. https://doi.org/10.1002/adma.201800273
21. Pal S, Deng Z, Ding B, Yan H, Liu Y (2010) DNA-origami-directed self-assembly of discrete silver-nanoparticle architectures. Angew Chem Int Ed Engl 49(15):2700–2704. https://doi.org/10.1002/anie.201000330
22. Wang YL, Mueller JE, Kemper B, Seeman NC (1991) Assembly and characterization of 5-arm and 6-arm DNA branched junctions. Biochemistry 30(23):5667–5674. https://doi.org/10.1021/bi00237a005
23. Winfree E, Liu FR, Wenzler LA, Seeman NC (1998) Design and self-assembly of two-dimensional DNA crystals. Nature 394(6693):539–544. https://doi.org/10.1038/28998
24. He Y, Tian Y, Ribbe AE, Mao C (2006) Highly connected two-dimensional crystals of DNA six-point-stars. J Am Chem Soc 128(50):15978–15979. https://doi.org/10.1021/ja0665141
25. Zheng J, Birktoft JJ, Chen Y, Wang T, Sha R, Constantinou PE, Ginell SL, Mao C, Seeman NC (2009) From molecular to macroscopic via the rational design of a self-assembled 3D DNA crystal. Nature 461(7260):74–77. https://doi.org/10.1038/nature08274
26. Ma RI, Kallenbach NR, Sheardy RD, Petrillo ML, Seeman NC (1986) 3-Arm nucleic-acid junctions are flexible. Nucleic Acids Res 14(24):9745–9753. https://doi.org/10.1093/nar/14.24.9745
27. Wang X, Seeman NC (2007) Assembly and characterization of 8-arm and 12-arm DNA branched junctions. J Am Chem Soc 129(26):8169–8176. https://doi.org/10.1021/ja0693441
28. Yan H, Park SH, Finkelstein G, Reif JH, LaBean TH (2003) DNA-templated self-assembly of protein arrays and highly conductive nanowires. Science 301(5641):1882–1884. https://doi.org/10.1126/science.1089389
29. He Y, Chen Y, Liu HP, Ribbe AE, Mao CD (2005) Self-assembly of hexagonal DNA two-dimensional (2D) arrays. J Am Chem Soc 127(35):12202–12203. https://doi.org/10.1021/ja0541938
30. He Y, Mao C (2006) Balancing flexibility and stress in DNA nanostructures. Chem Commun (Camb) 9:968–969. https://doi.org/10.1039/b513962g
31. Ding BQ, Sha RJ, Seeman NC (2004) Pseudohexagonal 2D DNA crystals from double crossover cohesion. J Am Chem Soc 126(33):10230–10231. https://doi.org/10.1021/ja047486u
32. Mao CD, Sun WQ, Seeman NC (1999) Designed two-dimensional DNA Holliday junction arrays visualized by atomic force microscopy. J Am Chem Soc 121(23):5437–5443. https://doi.org/10.1021/ja9900398
33. Hong F, Jiang S, Wang T, Liu Y, Yan H (2016) 3D framework DNA origami with layered crossovers. Angew Chem Int Ed 55(41):12832–12835. https://doi.org/10.1002/anie.201607050
34. Kuzuya A, Wang R, Sha R, Seeman NC (2007) Six-helix and eight-helix DNA nanotubes assembled from half-tubes. Nano Lett 7(6):1757–1763. https://doi.org/10.1021/nl070828k
35. Shih WM, Quispe JD, Joyce GF (2004) A 1.7-kilobase single-stranded DNA that folds into a nanoscale octahedron. Nature 427(6975):618–621. https://doi.org/10.1038/nature02307
36. He Y, Ye T, Su M, Zhang C, Ribbe AE, Jiang W, Mao C (2008) Hierarchical self-assembly of DNA into symmetric supramolecular polyhedra. Nature 452(7184):198-U141. https://doi.org/10.1038/nature06597
37. Zhang C, Su M, He Y, Zhao X, Fang P-A, Ribbe AE, Jiang W, Mao C (2008) Conformational flexibility facilitates self-assembly of complex DNA nanostructures. Proc Natl Acad Sci USA 105(31):10665–10669. https://doi.org/10.1073/pnas.0803841105
38. Ong LL, Hanikel N, Yaghi OK, Grun C, Strauss MT, Bron P, Lai-Kee-Him J, Schueder F, Wang B, Wang P, Kishi JY, Myhrvold C, Zhu A, Jungmann R, Bellot G, Ke Y, Yin P (2017)

Programmable self-assembly of three-dimensional nanostructures from 10,000 unique components. Nature 552(7683):72–77. https://doi.org/10.1038/nature24648
39. Ke Y, Ong LL, Sun W, Song J, Dong M, Shih WM, Yin P (2014) DNA brick crystals with prescribed depths. Nat Chem 6(11):994–1002. https://doi.org/10.1038/nchem.2083
40. Ke Y, Ong LL, Shih WM, Yin P (2012) Three-dimensional structures self-assembled from DNA bricks. Science 338(6111):1177–1183. https://doi.org/10.1126/science.1227268
41. Zhang C, Li X, Tian C, Yu G, Li Y, Jiang W, Mao C (2014) DNA nanocages swallow gold nanoparticles (AuNPs) to form AuNP@DNA cage core–shell structures. ACS Nano 8(2):1130–1135. https://doi.org/10.1021/nn406039p
42. Li Y, Liu Z, Yu G, Jiang W, Mao C (2015) Self-assembly of molecule-like nanoparticle clusters directed by DNA nanocages. J Am Chem Soc 137(13):4320–4323. https://doi.org/10.1021/jacs.5b01196
43. Li HY, Park SH, Reif JH, LaBean TH, Yan H (2004) DNA-templated self-assembly of protein and nanoparticle linear arrays. J Am Chem Soc 126(2):418–419. https://doi.org/10.1021/ja0383367
44. Xiao SJ, Liu FR, Rosen AE, Hainfeld JF, Seeman NC, Musier-Forsyth K, Kiehl RA (2002) Self assembly of metallic nanoparticle arrays by DNA scaffolding. J Nanopart Res 4(4):313–317. https://doi.org/10.1023/a:1021145208328
45. Le JD, Pinto Y, Seeman NC, Musier-Forsyth K, Taton TA, Kiehl RA (2004) DNA-templated self-assembly of metallic nanocomponent arrays on a surface. Nano Lett 4(12):2343–2347. https://doi.org/10.1021/nl048635+
46. Pinto YY, Le JD, Seeman NC, Musier-Forsyth K, Taton TA, Kiehl RA (2005) Sequence-encoded self-assembly of multiple-nanocomponent arrays by 2D DNA scaffolding. Nano Lett 5(12):2399–2402. https://doi.org/10.1021/nl0515495
47. Zhang JP, Liu Y, Ke YG, Yan H (2006) Periodic square-like gold nanoparticle arrays templated by self-assembled 2D DNA nanogrids on a surface. Nano Lett 6(2):248–251. https://doi.org/10.1021/nl052210l
48. Sharma J, Chhabra R, Liu Y, Ke YG, Yan H (2006) DNA-templated self-assembly of two-dimensional and periodical gold nanoparticle arrays. Angew Chem Int Ed 45(5):730–735. https://doi.org/10.1002/anie.200503208
49. Zheng J, Constantinou PE, Micheel C, Alivisatos AP, Kiehl RA, Seeman NC (2006) Two-dimensional nanoparticle arrays show the organizational power of robust DNA motifs. Nano Lett 6(7):1502–1504. https://doi.org/10.1021/nl060994c
50. Sharma J, Chhabra R, Cheng A, Brownell J, Liu Y, Yan H (2009) Control of self-assembly of DNA tubules through integration of gold nanoparticles. Science 323(5910):112–116. https://doi.org/10.1126/science.1165831
51. Maye MM, Nykypanchuk D, van der Lelie D, Gang O (2007) DNA-regulated micro- and nanoparticle assembly. Small 3(10):1678–1682. https://doi.org/10.1002/smll.200700357
52. Maye MM, Nykypanchuk D, Cuisinier M, van der Lelie D, Gang O (2009) Stepwise surface encoding for high-throughput assembly of nanoclusters. Nat Mater 8(5):388–391. https://doi.org/10.1038/nmat2421
53. Song M, Ding Y, Zerze H, Snyder MA, Mittal J (2018) Binary superlattice design by controlling DNA-mediated interactions. Langmuir 34(3):991–998. https://doi.org/10.1021/acs.langmuir.7b02835
54. Zhang YG, Lu F, Yager KG, van der Lelie D, Gang O (2013) A general strategy for the DNA-mediated self-assembly of functional nanoparticles into heterogeneous systems. Nat Nanotechnol 8(11):865–872. https://doi.org/10.1038/nnano.2013.209
55. Zhang YG, Pal S, Srinivasan B, Vo T, Kumar S, Gang O (2015) Selective transformations between nanoparticle superlattices via the reprogramming of DNA-mediated interactions. Nat Mater 14(8):840–847. https://doi.org/10.1038/Nmat4296
56. Srinivasan B, Vo T, Zhang Y, Gang O, Kumar S, Venkatasubramanian V (2013) Designing DNA-grafted particles that self-assemble into desired crystalline structures using the genetic algorithm. Proc Natl Acad Sci USA 110(46):18431. https://doi.org/10.1073/pnas.1316533110
57. Vo T, Venkatasubramanian V, Kumar S, Srinivasan B, Pal S, Zhang Y, Gang O (2015) Stoichiometric control of DNA-grafted colloid self-assembly. Proc Natl Acad Sci USA 112(16):4982–4987. https://doi.org/10.1073/pnas.1420907112
58. Damasceno PF, Engel M, Glotzer SC (2012) Predictive self-assembly of polyhedra into complex structures. Science 337(6093):453–457. https://doi.org/10.1126/science.1220869

59. Lu F, Vo T, Zhang Y, Frenkel A, Yager KG, Kumar S, Gang O (2019) Unusual packing of soft-shelled nanocubes. Sci Adv 5(5):eaaw2399. https://doi.org/10.1126/sciadv.aaw2399
60. Lu F, Yager KG, Zhang Y, Xin H, Gang O (2015) Superlattices assembled through shape-induced directional binding. Nat Commun 6(1):6912. https://doi.org/10.1038/ncomms7912
61. O'Brien MN, Jones MR, Lee B, Mirkin CA (2015) Anisotropic nanoparticle complementarity in DNA-mediated co-crystallization. Nat Mater 14:833. https://doi.org/10.1038/nmat4293
62. Andersen ES, Dong M, Nielsen MM, Jahn K, Lind-Thomsen A, Mamdouh W, Gothelf KV, Besenbacher F, Kjems J (2008) DNA origami design of dolphin-shaped structures with flexible tails. ACS Nano 2(6):1213–1218. https://doi.org/10.1021/nn800215j
63. Qian L, Wang Y, Zhang Z, Zhao J, Pan D, Zhang Y, Liu Q, Fan C, Hu J, He L (2006) Analogic China map constructed by DNA. Chin Sci Bull 51(24):2973–2976. https://doi.org/10.1007/s11434-006-2223-9
64. Douglas SM, Chou JJ, Shih WM (2007) DNA-nanotube-induced alignment of membrane proteins for NMR structure determination. Proc Natl Acad Sci USA 104(16):6644–6648. https://doi.org/10.1073/pnas.0700930104
65. Mathieu F, Liao SP, Kopatscht J, Wang T, Mao CD, Seeman NC (2005) Six-helix bundles designed from DNA. Nano Lett 5(4):661–665. https://doi.org/10.1021/nl050084f
66. Kuzyk A, Schreiber R, Fan Z, Pardatscher G, Roller EM, Hogele A, Simmel FC, Govorov AO, Liedl T (2012) DNA-based self-assembly of chiral plasmonic nanostructures with tailored optical response. Nature 483(7389):311–314. https://doi.org/10.1038/nature10889
67. Shen X, Song C, Wang J, Shi D, Wang Z, Liu N, Ding B (2012) Rolling up gold nanoparticle-dressed DNA origami into three-dimensional plasmonic chiral nanostructures. J Am Chem Soc 134(1):146–149. https://doi.org/10.1021/ja209861x
68. Ke Y, Sharma J, Liu M, Jahn K, Liu Y, Yan H (2009) Scaffolded DNA origami of a DNA tetrahedron molecular container. Nano Lett 9(6):2445–2447. https://doi.org/10.1021/nl901165f
69. Andersen ES, Dong M, Nielsen MM, Jahn K, Subramani R, Mamdouh W, Golas MM, Sander B, Stark H, Oliveira CLP, Pedersen JS, Birkedal V, Besenbacher F, Gothelf KV, Kjems J (2009) Self-assembly of a nanoscale DNA box with a controllable lid. Nature 459(7243):73–U75. https://doi.org/10.1038/nature07971
70. Dietz H, Douglas SM, Shih WM (2009) Folding DNA into twisted and curved nanoscale shapes. Science 325:725–730. https://doi.org/10.1126/science.1174251
71. Douglas SM, Dietz H, Liedl T, Hoegberg B, Graf F, Shih WM (2009) Self-assembly of DNA into nanoscale three-dimensional shapes. Nature 459(7245):414–418. https://doi.org/10.1038/nature08016
72. Douglas SM, Marblestone AH, Teerapittayanon S, Vazquez A, Church GM, Shih WM (2009) Rapid prototyping of 3D DNA-origami shapes with caDNAno. Nucleic Acids Res 37(15):5001–5006. https://doi.org/10.1093/nar/gkp436
73. Ke Y, Douglas SM, Liu M, Sharma J, Cheng A, Leung A, Liu Y, Shih WM, Yan H (2009) Multilayer DNA origami packed on a square lattice. J Am Chem Soc 131(43):15903–15908. https://doi.org/10.1021/ja906381y
74. Ke Y, Voigt NV, Gothelf KV, Shih WM (2012) Multilayer DNA origami packed on hexagonal and hybrid lattices. J Am Chem Soc 134(3):1770–1774. https://doi.org/10.1021/ja209719k
75. Han D, Pal S, Nangreave J, Deng Z, Liu Y, Yan H (2011) DNA origami with complex curvatures in three-dimensional space. Science 332(6027):342–346. https://doi.org/10.1126/science.1202998
76. Yang Y, Han D, Nangreave J, Liu Y, Yan H (2012) DNA origami with double-stranded DNA as a unified scaffold. ACS Nano 6(9):8209–8215. https://doi.org/10.1021/nn302896c
77. Sobczak J-PJ, Martin TG, Gerling T, Dietz H (2012) Rapid folding of DNA into nanoscale shapes at constant temperature. Science 338(6113):1458–1461. https://doi.org/10.1126/science.1229919
78. Iinuma R, Ke Y, Jungmann R, Schlichthaerle T, Woehrstein JB, Yin P (2014) Polyhedra self-assembled from DNA tripods and characterized with 3D DNA-PAINT. Science 344(6179):65–69. https://doi.org/10.1126/science.1250944
79. Tian Y, Wang T, Liu W, Xin HL, Li H, Ke Y, Shih WM, Gang O (2015) Prescribed nanoparticle cluster architectures and low-dimensional arrays built using octahedral DNA origami frames. Nat Nanotechnol 10(7):637–644. https://doi.org/10.1038/nnano.2015.105

80. Veneziano R, Ratanalert S, Zhang K, Zhang F, Yan H, Chiu W, Bathe M (2016) Designer nanoscale DNA assemblies programmed from the top down. Science 352(6293):1534. https://doi.org/10.1126/science.aaf4388
81. Liu X, Zhang F, Jing X, Pan M, Liu P, Li W, Zhu B, Li J, Chen H, Wang L, Lin J, Liu Y, Zhao D, Yan H, Fan C (2018) Complex silica composite nanomaterials templated with DNA origami. Nature 559(7715):593–598. https://doi.org/10.1038/s41586-018-0332-7
82. Linh N, Doeblinger M, Liedl T, Heuer-Jungemann A (2019) DNA-origami-templated silica growth by sol–gel chemistry. Angew Chem Int Ed 58(3):912–916. https://doi.org/10.1002/anie.201811323
83. Schreiber R, Santiago I, Ardavan A, Turberfield AJ (2016) Ordering gold nanoparticles with DNA origami nanoflowers. ACS Nano 10(8):7303–7306. https://doi.org/10.1021/acsnano.6b03076
84. Zhao Z, Jacovetty EL, Liu Y, Yan H (2011) Encapsulation of gold nanoparticles in a DNA origami cage. Angew Chem Int Ed Engl 50(9):2041–2044. https://doi.org/10.1002/anie.201006818
85. Shen C, Lan X, Lu X, Meyer TA, Ni W, Ke Y, Wang Q (2016) Site-specific surface functionalization of gold nanorods using DNA origami clamps. J Am Chem Soc 138(6):1764–1767. https://doi.org/10.1021/jacs.5b11566
86. Stearns LA, Chhabra R, Sharma J, Liu Y, Petuskey WT, Yan H, Chaput JC (2009) Template-directed nucleation and growth of inorganic nanoparticles on DNA scaffolds. Angew Chem Int Ed Engl 48(45):8494–8496. https://doi.org/10.1002/anie.200903319
87. Bui H, Onodera C, Kidwell C, Tan Y, Graugnard E, Kuang W, Lee J, Knowlton WB, Yurke B, Hughes WL (2010) Programmable periodicity of quantum dot arrays with DNA origami nanotubes. Nano Lett 10(9):3367–3372. https://doi.org/10.1021/nl101079u
88. Chhabra R, Sharma J, Ke Y, Liu Y, Rinker S, Lindsay S, Yan H (2007) Spatially addressable multiprotein nanoarrays templated by aptamer-tagged DNA nanoarchitectures. J Am Chem Soc 129(34):10304–10305. https://doi.org/10.1021/ja072410u
89. Sharma J, Chhabra R, Andersen CS, Gothelf KV, Yan H, Liu Y (2008) Toward reliable gold nanoparticle patterning on self-assembled DNA nanoscaffold. J Am Chem Soc 130(25):7820–7821. https://doi.org/10.1021/ja802853r
90. Schreiber R, Do J, Roller EM, Zhang T, Schuller VJ, Nickels PC, Feldmann J, Liedl T (2014) Hierarchical assembly of metal nanoparticles, quantum dots and organic dyes using DNA origami scaffolds. Nat Nanotechnol 9(1):74–78. https://doi.org/10.1038/nnano.2013.253
91. Lin ZW, Xiong Y, Xiang ST, Gang O (2019) Controllable covalent-bound nanoarchitectures from DNA frames. J Am Chem Soc 141(17):6797–6801. https://doi.org/10.1021/jacs.9b01510
92. Liu W, Halverson J, Tian Y, Tkachenko AV, Gang O (2016) Self-organized architectures from assorted DNA-framed nanoparticles. Nat Chem 8(9):867–873. https://doi.org/10.1038/nchem.2540
93. Liu WY, Mahynski NA, Gang O, Panagiotopoulos AZ, Kumar SK (2017) Directionally interacting spheres and rods form ordered phases. ACS Nano 11(5):4950–4959. https://doi.org/10.1021/acsnano.7b01592
94. Tian Y, Lhermitte JR, Bai L, Vo T, Xin HL, Li H, Li R, Fukuto M, Yager KG, Kahn JS, Xiong Y, Minevich B, Kumar SK, Gang O (2020) Ordered three-dimensional nanomaterials using DNA-prescribed and valence-controlled material voxels. Nat Mater. https://doi.org/10.1038/s41563-019-0550-x
95. Emamy H, Gang O, Starr FW (2019) The stability of a nanoparticle diamond lattice linked by DNA. Nanomaterials (Basel) 9(5):661. https://doi.org/10.3390/nano9050661
96. Mastroianni AJ, Claridge SA, Alivisatos AP (2009) Pyramidal and chiral groupings of gold nanocrystals assembled using DNA scaffolds. J Am Chem Soc 131(24):8455–8459. https://doi.org/10.1021/ja808570g
97. Yan W, Xu L, Xu C, Ma W, Kuang H, Wang L, Kotov NA (2012) Self-assembly of chiral nanoparticle pyramids with strong R/S optical activity. J Am Chem Soc 134(36):15114–15121. https://doi.org/10.1021/ja3066336
98. Pal S, Deng Z, Wang H, Zou S, Liu Y, Yan H (2011) DNA directed self-assembly of anisotropic plasmonic nanostructures. J Am Chem Soc 133(44):17606–17609. https://doi.org/10.1021/ja207898r
99. Lan X, Chen Z, Dai G, Lu X, Ni W, Wang Q (2013) Bifacial DNA origami-directed discrete, three-dimensional, anisotropic plasmonic nanoarchitectures with tailored optical chirality. J Am Chem Soc 135(31):11441–11444. https://doi.org/10.1021/ja404354c
100. Shen X, Zhan P, Kuzyk A, Liu Q, Asenjo-Garcia A, Zhang H, de Abajo FJ, Govorov A, Ding B, Liu N (2014) 3D plasmonic chiral colloids. Nanoscale 6(4):2077–2081. https://doi.org/10.1039/c3nr06006c

101. Lan X, Lu X, Shen C, Ke Y, Ni W, Wang Q (2015) Au nanorod helical superstructures with designed chirality. J Am Chem Soc 137(1):457–462. https://doi.org/10.1021/ja511333q
102. Tian C, Cordeiro MAL, Lhermitte J, Xin HLL, Shani L, Liu MZ, Ma CL, Yeshurun Y, DiMarzio D, Gang O (2017) Supra-nanoparticle functional assemblies through programmable stacking. ACS Nano 11(7):7036–7048. https://doi.org/10.1021/acsnano.7b02671
103. Zhang H, Li M, Wang K, Tian Y, Chen J-S, Fountaine KT, DiMarzio D, Liu M, Cotlet M, Gang O (2020) Polarized single-particle quantum dot emitters through programmable cluster assembly. ACS Nano 14(2):1369–1378. https://doi.org/10.1021/acsnano.9b06919
104. Zhou C, Duan X, Liu N (2015) A plasmonic nanorod that walks on DNA origami. Nat Commun 6:8102. https://doi.org/10.1038/ncomms9102
105. Urban MJ, Zhou C, Duan X, Liu N (2015) Optically resolving the dynamic walking of a plasmonic walker couple. Nano Lett 15(12):8392–8396. https://doi.org/10.1021/acs.nanolett.5b04270
106. Kuzyk A, Schreiber R, Zhang H, Govorov AO, Liedl T, Liu N (2014) Reconfigurable 3D plasmonic metamolecules. Nat Mater 13(9):862–866. https://doi.org/10.1038/nmat4031
107. Kuzyk A, Yang Y, Duan X, Stoll S, Govorov AO, Sugiyama H, Endo M, Liu N (2016) A light-driven three-dimensional plasmonic nanosystem that translates molecular motion into reversible chiroptical function. Nat Commun 7:10591. https://doi.org/10.1038/ncomms10591
108. Kuzyk A, Urban MJ, Idili A, Ricci F, Liu N (2017) Selective control of reconfigurable chiral plasmonic metamolecules. Sci Adv. https://doi.org/10.1126/sciadv.1602803
109. Funck T, Nicoli F, Kuzyk A, Liedl T (2018) Sensing picomolar concentrations of RNA using switchable plasmonic chirality. Angew Chem Int Ed 57(41):13495–13498. https://doi.org/10.1002/anie.201807029
110. Shen C, Lan X, Zhu C, Zhang W, Wang L, Wang Q (2017) Spiral patterning of Au nanoparticles on Au nanorod surface to form chiral AuNR@AuNP helical superstructures templated by DNA origami. Adv Mater. https://doi.org/10.1002/adma.201606533
111. Urban MJ, Dutta PK, Wang P, Duan X, Shen X, Ding B, Ke Y, Liu N (2016) Plasmonic toroidal metamolecules assembled by DNA origami. J Am Chem Soc 138(17):5495–5498. https://doi.org/10.1021/jacs.6b00958
112. Shen X, Asenjo-Garcia A, Liu Q, Jiang Q, García de Abajo FJ, Liu N, Ding B (2013) Three-dimensional plasmonic chiral tetramers assembled by DNA origami. Nano Lett 13(5):2128–2133. https://doi.org/10.1021/nl400538y
113. Schreiber R, Luong N, Fan Z, Kuzyk A, Nickels PC, Zhang T, Smith DM, Yurke B, Kuang W, Govorov AO, Liedl T (2013) Chiral plasmonic DNA nanostructures with switchable circular dichroism. Nat Commun 4(1):2948. https://doi.org/10.1038/ncomms3948
114. Acuna GP, Möller FM, Holzmeister P, Beater S, Lalkens B, Tinnefeld P (2012) Fluorescence enhancement at docking sites of DNA-directed self-assembled nanoantennas. Science 338(6106):506. https://doi.org/10.1126/science.1228638
115. Thacker VV, Herrmann LO, Sigle DO, Zhang T, Liedl T, Baumberg JJ, Keyser UF (2014) DNA origami based assembly of gold nanoparticle dimers for surface-enhanced Raman scattering. Nat Commun 5:3448. https://doi.org/10.1038/ncomms4448
116. Kuhler P, Roller EM, Schreiber R, Liedl T, Lohmuller T, Feldmann J (2014) Plasmonic DNA-origami nanoantennas for surface-enhanced Raman spectroscopy. Nano Lett 14(5):2914–2919. https://doi.org/10.1021/nl5009635
117. Simoncelli S, Roller EM, Urban P, Schreiber R, Turberfield AJ, Liedl T, Lohmuller T (2016) Quantitative single-molecule surface-enhanced raman scattering by optothermal tuning of DNA origami-assembled plasmonic nanoantennas. ACS Nano 10(11):9809–9815. https://doi.org/10.1021/acsnano.6b05276
118. Ko SH, Du K, Liddle JA (2013) Quantum-dot fluorescence lifetime engineering with DNA origami constructs. Angew Chem Int Ed 52(4):1193–1197. https://doi.org/10.1002/anie.201206253
119. Samanta A, Zhou Y, Zou S, Yan H, Liu Y (2014) Fluorescence quenching of quantum dots by gold nanoparticles: a potential long range spectroscopic ruler. Nano Lett 14(9):5052–5057. https://doi.org/10.1021/nl501709s
120. Liu J, Geng Y, Pound E, Gyawali S, Ashton JR, Hickey J, Woolley AT, Harb JN (2011) Metallization of branched DNA origami for nanoelectronic circuit fabrication. ACS Nano 5(3):2240–2247. https://doi.org/10.1021/nn1035075
121. Schreiber R, Kempter S, Holler S, Schuller V, Schiffels D, Simmel SS, Nickels PC, Liedl T (2011) DNA origami-templated growth of arbitrarily shaped metal nanoparticles. Small 7(13):1795–1799. https://doi.org/10.1002/smll.201100465

122. Pilo-Pais M, Goldberg S, Samano E, Labean TH, Finkelstein G (2011) Connecting the nanodots: programmable nanofabrication of fused metal shapes on DNA templates. Nano Lett 11(8):3489–3492. https://doi.org/10.1021/nl202066c
123. Helmi S, Ziegler C, Kauert DJ, Seidel R (2014) Shape-controlled synthesis of gold nanostructures using DNA origami molds. Nano Lett 14(11):6693–6698. https://doi.org/10.1021/nl503441v
124. Sun W, Boulais E, Hakobyan Y, Wang WL, Guan A, Bathe M, Yin P (2014) Casting inorganic structures with DNA molds. Science 346(6210):1258361. https://doi.org/10.1126/science.1258361
125. Douglas SM, Bachelet I, Church GM (2012) A logic-gated nanorobot for targeted transport of molecular payloads. Science 335(6070):831–834. https://doi.org/10.1126/science.1214081
126. Liu M, Fu J, Hejesen C, Yang Y, Woodbury NW, Gothelf K, Liu Y, Yan H (2013) A DNA tweezer-actuated enzyme nanoreactor. Nat Commun 4:2127. https://doi.org/10.1038/ncomms3127
127. Linko V, Eerikainen M, Kostiainen MA (2015) A modular DNA origami-based enzyme cascade nanoreactor. Chem Commun (Camb) 51(25):5351–5354. https://doi.org/10.1039/c4cc08472a
128. Zhao Z, Fu J, Dhakal S, Johnson-Buck A, Liu M, Zhang T, Woodbury NW, Liu Y, Walter NG, Yan H (2016) Nanocaged enzymes with enhanced catalytic activity and increased stability against protease digestion. Nat Commun 7:10619. https://doi.org/10.1038/ncomms10619
129. Wang P, Rahman MA, Zhao Z, Weiss K, Zhang C, Chen Z, Hurwitz SJ, Chen ZG, Shin DM, Ke Y (2018) Visualization of the cellular uptake and trafficking of DNA origami nanostructures in cancer cells. J Am Chem Soc 140(7):2478–2484. https://doi.org/10.1021/jacs.7b09024
130. Kershner RJ, Bozano LD, Micheel CM, Hung AM, Fornof AR, Cha JN, Rettner CT, Bersani M, Frommer J, Rothemund PW, Wallraff GM (2009) Placement and orientation of individual DNA shapes on lithographically patterned surfaces. Nat Nanotechnol 4(9):557–561. https://doi.org/10.1038/nnano.2009.220
131. Hung AM, Micheel CM, Bozano LD, Osterbur LW, Wallraff GM, Cha JN (2010) Large-area spatially ordered arrays of gold nanoparticles directed by lithographically confined DNA origami. Nat Nanotechnol 5(2):121–126. https://doi.org/10.1038/nnano.2009.450
132. Chao J, Wang JB, Wang F, Ouyang XY, Kopperger E, Liu HJ, Li Q, Shi JY, Wang LH, Hu J, Wang LH, Huang W, Simmel FC, Fan CH (2019) Solving mazes with single-molecule DNA navigators. Nat Mater 18(3):273–279. https://doi.org/10.1038/s41563-018-0205-3
133. Kwon PS, Ren S, Kwon S-J, Kizer ME, Kuo L, Zhou F, Zhang F, Kim D, Fraser K, Kramer LD, Seeman NC, Dordick JS, Linhardt RJ, Chao J, Wang X (2020) Designer DNA architecture offers precise and multivalent spatial pattern-recognition for viral sensing and inhibition. Nat Chem 12(1):26–35. https://doi.org/10.1101/608380
134. Seeman NC, Gang O (2017) Three-dimensional molecular and nanoparticle crystallization by DNA nanotechnology. MRS Bull 42(12):904–912. https://doi.org/10.1557/mrs.2017.280
135. Zhang YN, Chao J, Liu HJ, Wang F, Su S, Liu B, Zhang L, Shi JY, Wang LH, Huang W, Wang LH, Fan CH (2016) Transfer of two-dimensional oligonucleotide patterns onto stereocontrolled plasmonic nanostructures through DNA-origami-based nanoimprinting lithography. Angew Chem Int Ed 55(28):8036–8040. https://doi.org/10.1002/anie.201512022

Affiliations

Ningning Ma[1,2] · Brian Minevich[3] · Jiliang Liu[4] · Min Ji[1,2] · Ye Tian[1,2,5] · Oleg Gang[3,6,7]

[1] College of Engineering and Applied Sciences, National Laboratory of Solid State Microstructures, Collaborative Innovation Center of Advanced Microstructures, Jiangsu Key Laboratory of Artificial Functional Materials, Nanjing University, Nanjing 210093, China

[2] Chemistry and Biomedicine Innovation Center, Nanjing University, Nanjing 210023, China

[3] Department of Chemical Engineering, Columbia University, New York, NY 10027, USA

[4] National Synchrotron Light Source II, Brookhaven National Laboratory, Upton, NY 11973, USA

[5] Shenzhen Research Institute of Nanjing University, Shenzhen 518000, China

[6] Center for Functional Nanomaterials, Brookhaven National Laboratory, Upton, NY 11973, USA

[7] Department of Applied Physics and Applied Mathematics, Columbia University, New York, NY 10027, USA