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Engineering DNA Self-Assemblies as Templates for Functional Nanostructures

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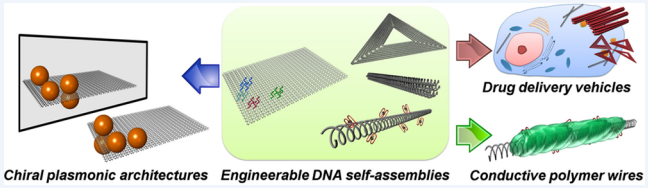
CONSPECTUS: DNA is a well-known natural molecule that carries genetic information. In recent decades, DNA has been used beyond its genetic role as a building block for the construction of engineering materials. Many strategies, such as tile assembly, scaffolded origami and DNA bricks, have been developed to design and produce 1D, 2D, and 3D architectures with sophisticated morphologies. Moreover, the spatial addressability of DNA nanostructures and sequence-dependent recognition enable functional elements to be precisely positioned and allow for the control of chemical and biochemical processes.



The spatial arrangement of heterogeneous components using DNA nanostructures as the templates will aid in the fabrication of functional materials that are difficult to produce using other methods and can address scientific and technical challenges in interdisciplinary research. For example, plasmonic nanoparticles can be assembled into well-defined configurations with high resolution limit while exhibiting desirable collective behaviors, such as near-field enhancement. Conducting metallic or polymer patterns can be synthesized site-specifically on DNA nanostructures to form various controllable geometries, which could be used for electronic nanodevices. Biomolecules can be arranged into organized networks to perform programmable biological functionalities, such as distance-dependent enzyme-cascade activities. DNA nanostructures can carry multiple cytoactive molecules and cell-targeting groups simultaneously to address medical issues such as targeted therapy and combined administration. In this Account, we describe recent advances in the functionalization of DNA nanostructures in different fashions based on our research efforts in nanophotonics, nanoelectronics, and nanomedicine. We show that DNA origami nanostructures can guide the assembly of achiral, spherical, metallic nanoparticles into nature-mimicking chiral geometries through hybridization between complementary DNA strands on the surface of nanoparticles and DNA scaffolds, to generate circular dichroism (CD) response in the visible light region. We also show that DNA nanostructures, on which a HRP-mimicking DNAzyme acts as the catalyst, can direct the site-selective growth of conductive polymer nanomaterials with template configuration-dependent doping behaviors. We demonstrate that DNA origami nanostructures can act as an anticancer-drug carrier, loading drug through intercalation, and can effectively circumvent the drug resistance of cultured cancer cells. Finally, we show a label-free strategy for probing the location and stability of DNA origami nanocarriers in cellular environments by docking turn-off fluorescence dyes in DNA double helices. These functionalizations require further improvement and expansion for realistic applications. We discuss the future opportunities and challenges of DNA based assemblies. We expect that DNA nanostructures as engineering materials will stimulate the development of multidisciplinary and interdisciplinary research.

The development of DNA nanotechnology, started by Seeman,[1] enables DNA to work as a significant engineering material in a wide variety of fields.[2−6] It is noteworthy that progress in the design strategies and synthesis methods of large-sized DNA superstructures has advanced the functional evolution of DNA significantly. Rigid DNA crossovers were used for the tile-assembly construction of 1D nanoconstructs,[7] well-defined 2D periodic lattices,[8−11] 3D nanostructures,[12−14] and macroscopic 3D crystals.[15] Figure 1A exemplifies images of crossover tiles and tile-assembled nanostructures. DNA origami, a milestone in DNA nanotechnology, highlights the programmable folding of a long scaffold by short staple strands following predesigned assembly paths to create arbitrary shapes.[16] Many DNA nanostructures of various complexities have been produced using the origami method,[17,16,18−22] including 2D, quasi-2D, and 3D shapes, as shown in Figure 1B. Compared with the tile-assembly approach, DNA origami offers advantages in the structural diversity, spatial addressability, stoichiometry, and purity requirements of the staple strands. Many computational tools have also been developed for designing 3D origami structures time-savingly and cost-effectively.[23,24] As a recently developed strategy, "DNA bricks" were used to shape hundreds of short distinct-sequence strands into a wide range of predesigned nanostructures exhibiting interior cavities and tunnels,[25,26] Figure 1C.

Nucleic strands can be designed to extend out of the DNA superstructures to capture nanoscale targets through specific recognition. Thus, the shape-programmable DNA superstructures can serve as the templates for fabricating versatile nanoscale self-assemblies. As an example, metal and semiconductor nanoparticles were positioned on the surface of

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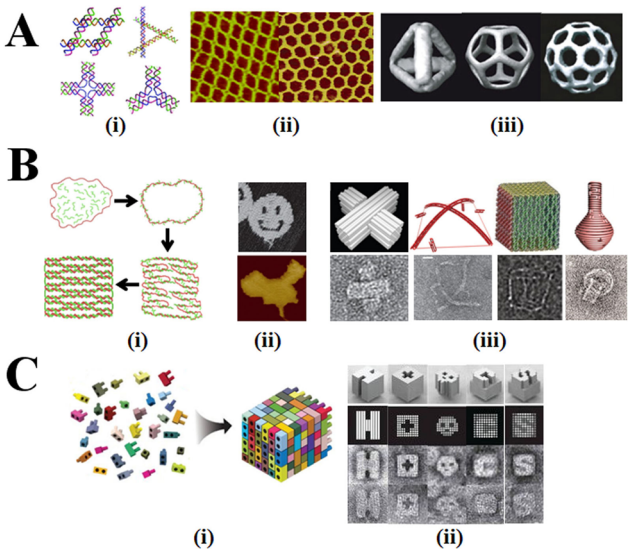

Figure 1. Two- and three-dimensional DNA nanostructures fabricated by various strategies. (A) Tile assembly. (i) Examples of DNA tiles for the assembly.[2] (ii) 2D lattices assembled from symmetric cross motif (left)[10] and three-point-star motifs (right).[11] (iii) 3D hollow polyhedra assembled by three-point-star motifs.[13] (B) Scaffolded DNA origami. (i) DNA origami formation by folding M13 scaffold with staple strands.[24] (ii) 2D smiley face shapes (top)[16] and analogic China map (bottom).[17] (iii) 3D DNA shapes (left to right): slotted cross,[19] buckling kite,[21] box,[18] semisphere, and flask.[22] (C) DNA-brick self-assembly: (i) assembly of distinct DNA bricks into the 6H by 6H by 48B cuboid and (ii) shapes made from a 3D molecular canvas (right).[25] Panel A, parts i and ii (left), reproduced with permission from refs 2 and 10, copyright 2006 and 2005, John Wiley & Sons, Inc. Panel A, part ii (right), reproduced with permission from ref 11. Copyright 2005 American Chemical Society. Panel A, part iii, and panel B, part ii (top) and part of part iii, reproduced with permission from refs 13, 16, 18, 19, and 21, copyright 2008, 2006, 2009, 2009, and 2010 Macmillan Publishers Ltd. Panel B, part of part iii, and panel C, reproduced with permission from refs 22 and 25, copyright 2011 and 2012, AAAS. Panel B, part i, reprinted from ref 24, copyright 2010, with permission from Elsevier. Panel B, part ii (bottom), reprinted from ref 17, copyright 2006, with permission from Springer.

DNA nanostructures with nanometer precision for nanophotonic applications,[27−29] such as optical nanoantenna,[30] chiral response,[31,32] surface-enhanced Raman scattering,[33] or waveguides.[34] Fusion of the metal nanoparticles led to nanopatterns that either copied the morphology of the scaffolds[35,36] or formed the desired geometries on the template[37,38] for use in nanoelectronics. The arbitrary arrangements of the metallic structures give rise to various collective behaviors (e.g., chiral response or antenna effects), depending on the particle shapes, assembly geometries, and interparticle spacing. DNA nanostructures also show the ability to organize carbon nanotubes into cross junctions for field-effect transistors[39] or to bond distinctive fluorophores to control energy-transfer paths at the single-molecule level.[40]

The biological nature of DNA offers DNA assemblies potential for biological applications. The surface of DNA nanostructures can be formulated into patterns of various bionanomaterials. Until now, biologically active species, such as peptides,[41] proteins,[42,43] and RNA,[44] have been associated with DNA nanostructures in a site-specific manner, which leads to the formation of biomolecular networks that can mediate a range of cellular functions.[45] One example is an enzymatic cascade that is inspired by metabolic pathways and photosynthetic reactions. DNA nanotemplates can regulate the cascade activity by controlling the arrangement of the cascaded constituents or the placement of external objects to facilitate interenzyme intermediate diffusion.[46,47] Bioactive elements can also be loaded into DNA nanostructures, based on hollow-geometry inclusion[48] or double-helix intercalation.[49] Selective association with biofunctional components provides the possibility for the DNA nanostructures to target and interfere with specific cellular processes, which is promising to address a few challenging medical issues.

A variety of controlled chemical and biochemical processes can be directed on DNA-based templates, resulting in various functional materials that are difficult to produce using other methods.

CHIRAL SELF-ASSEMBLY OF SPHERICAL METAL NANOPARTICLES

Chiral molecules preferentially interact with left- or right-polarized light and produce an optical response known as circular dichroism (CD). Natural chiral molecules, such as amino acids and DNA, play an important role in biochemical processes but only exhibit a CD signal in the UV range. Optical chirality can now reach visible and infrared ranges due to the development of artificial plasmonic structures.[50] Rationally designed DNA nanotemplates enable the precise arrangement of plasmonic components; thus, the chiral optical response can be engineered. Noble metal nanoparticles exhibit localized surface plasmon resonance (LSPR), which is the collective oscillation of surface electrons stimulated by incident light. The hybridization of localized plasmons occurs when the particles are neighboring, termed as near-field plasmonic coupling. DNA-directed self-assembly can achieve geometric regulation of the nanoparticle construction, resulting in a few modes of plasmonic resonance with tunable field-enhancement effects.[51] An example can be seen in the fabrication of centrally symmetric chains with progressively decreasing sizes and separations of six gold nanoparticles (AuNPs).[52] This self-similar structure can theoretically enhance the local field by orders of magnitude.[53] The assembly procedure is as follows: First, 18 DNA capture strands were designed as the extension of the selected staple strands of the origami template and were displayed at the desired locations on the template surface. Three capture strands with identical sequence were grouped into one binding site to immobilize each AuNP. Thus, the origami surface localized six different DNA-modified AuNPs through hybridization, as shown in Figure 2A. The interparticle spacing was strictly controlled by the location of these capture strands. If AuNPs are arranged into the structures with asymmetrical geometries and small interparticle distances, the plasmonic coupling could induce the CD effect. This phenomenon is ascribed to the integration of the dynamic Coulombic dipole−dipole and electromagnetic interactions, which can be observed from tetramers, pyramids, and helices.[54] From a biomimetic standpoint, the chiral assemblies of plasmonic nanoparticles resemble biological chiral structures, such as nucleic helices or amino acids. Moreover, the geometrical parameters largely affect the CD shape and intensity. In the case of helically arranged spherical nanoparticles, the parameters include the helical pitch, radius, interparticle spacing, and particle number.[55] The chiral response of plasmonic assemblies can be regulated using

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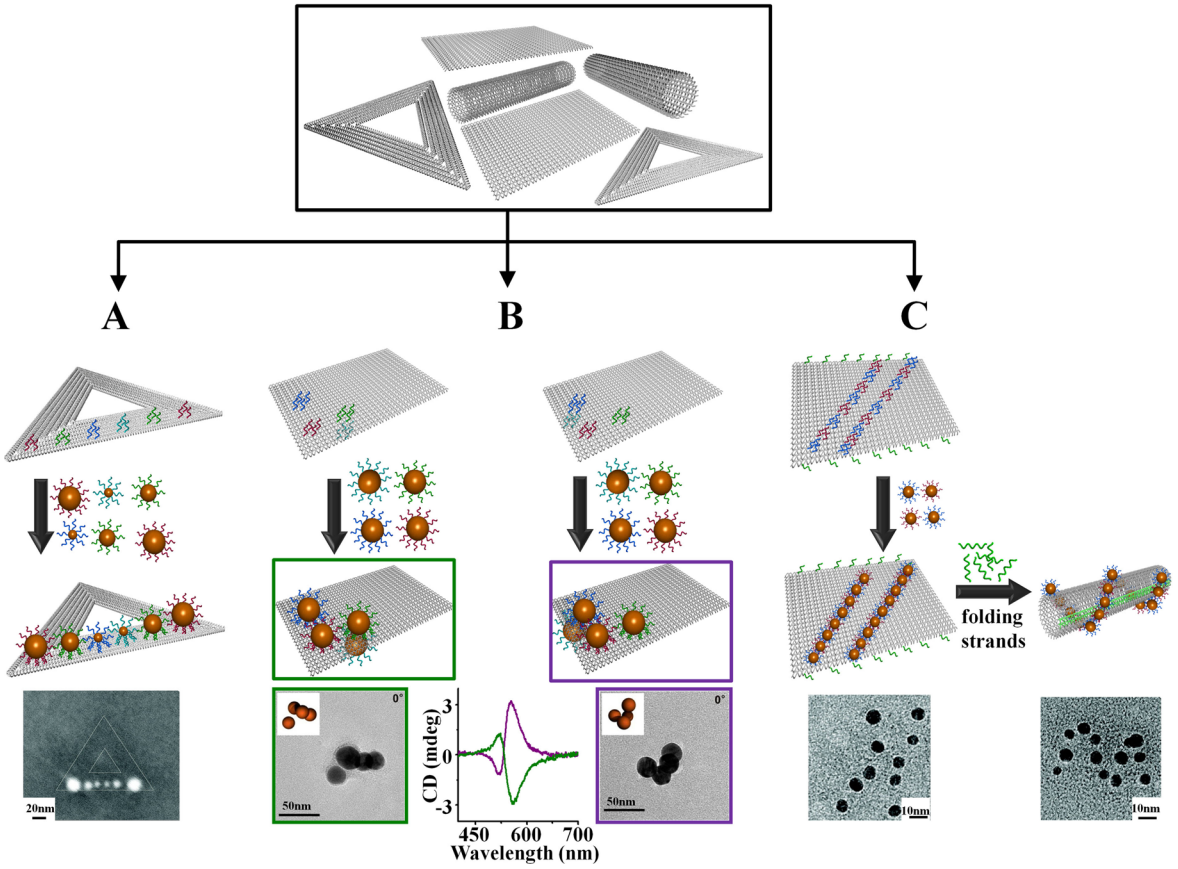

Figure 2. Construction of AuNP self-assemblies on DNA origami scaffolds for collective plasmonic behaviors. (A) Self-assembly of six different AuNPs onto the origami triangle to generate self-similar chains.[52] (B) Self-assembly of AuNPs to the asymmetrically arranged four binding sites to generate AuNP tetramers with left-handed or right-handed configuration. At the bottom are the measured CD spectra of these structures.[31] (C) Assembly of AuNPs to the rectangular origami scaffold, which is rolled up with folding strands to generate a left-handed AuNP helix.[59] Reproduced with permission from refs 31, 52, and 59. Copyright 2013, 2010, and 2012 American Chemical Society.

DNA nanostructures as the templates, by tailoring the geometries or components.

A minimum of four identical spherical nanoparticles are needed to compose a 3D chiral geometry. The plasmonic nanoparticles can self-assemble into a tetrahedral geometry through DNA hybridization between each DNA-modified nanoparticle.[56,57] The size difference and heterogeneity of the particles can break the symmetry of the frame, resulting in enantiomers that exhibit mirrored CD signals.[57] However, the metal NP tetrahedrons built using this strategy usually lack rigidity and may result in inefficient plasmonic coupling and a weak chiral response. As an alternative, DNA origami provides a rigid template for accurately positioning four identical spherical AuNPs into an asymmetric tetrahedron,[31] Figure 2B. The four binding sites were arranged in left- and right-handed configurations, with three on the top surface of the rectangular template and one on the opposite side. DNA-modified AuNPs were organized and produced left- and right-handed 3D plasmonic structures, exhibiting characteristic mirrored bisignate peak−dip and dip−peak CD profiles. The CD shapes of the 3D plasmonic geometries agreed well with classical electrodynamics calculations.

Increasing the number of the arranged AuNPs can lead to helices that theoretically generate a strong CD response.[55] DNA origami nanotubes with well-defined sizes and addressable binding sites can serve as an ideal template to create helical nanoparticle assemblies.[58] Using the strategy of rolling up a 2D structure, Ding, Liu, and co-workers assembled AuNPs into the helices on DNA origami nanotubes.[59] The assembly process is shown in Figure 2C. Fifteen binding sites were displayed on one side of the origami along two parallel lines. Each binding site included three capture strands with identical sequence to immobilize individual DNA-modified AuNPs. Therefore, mixing AuNPs with the origami template resulted in the assembly of AuNPs at the predesigned positions and the formation of two chains. The interparticle spacing was controlled by the locations of the capture strand groups. Upon the addition of folding strands complementary to the protruding sequence of the long sides of the origami template, the sheet rolled up to minimize steric and electrostatic interparticle repulsion, leading to AuNP helices with defined helical parameters. The nanoparticle helices exhibited a bisignate peak−dip CD line shape in the vicinity of the plasmonic resonance of AuNPs. Furthermore, the increase in the nanoparticle size resulted in smaller interparticle distances and stronger plasmon coupling effects, producing an enhanced chiral response. As a step forward, Liedl and co-workers[38] used rigid DNA cylindrical nanostructures with nine helically arranged binding sites on the outer surface to assemble DNA-coated AuNPs into a left- or right-handed helical geometry. CD signals with characteristic bisignate mirrored shapes and higher intensities were achieved. The CD response could be enhanced by increasing the particle size or by plating

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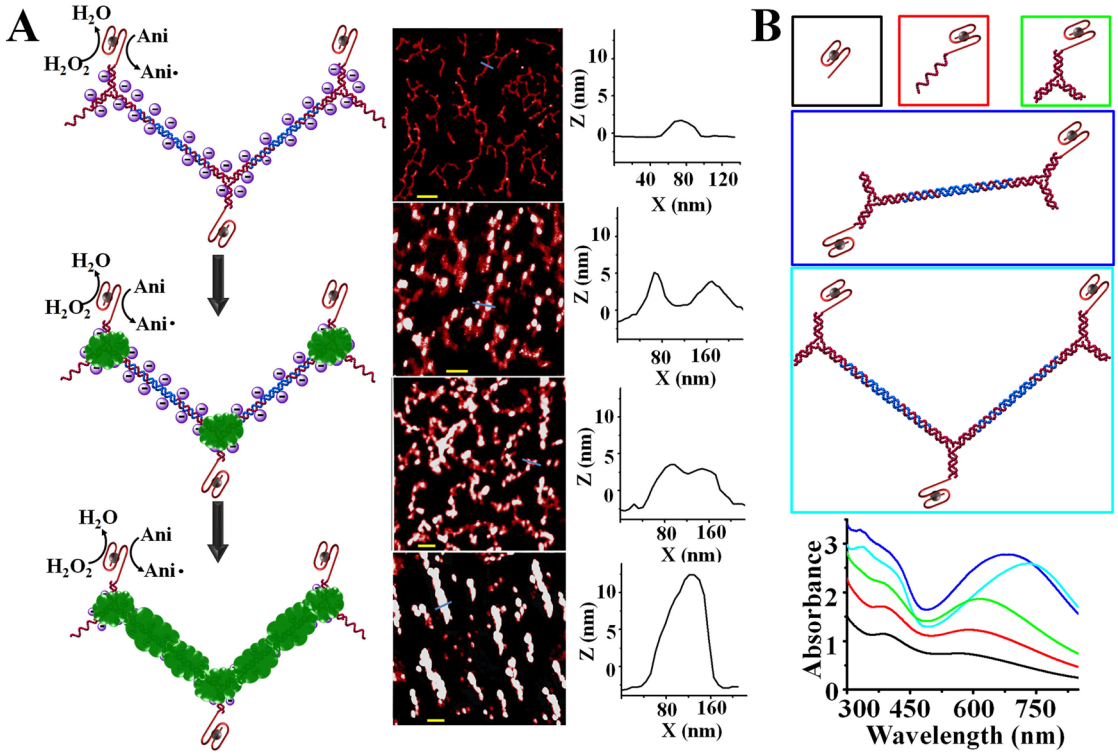

Figure 3. Catalytic growth of conductive polyaniline on the self-assembled DNA templates. (A) Schematic and AFM-monitoring of DNAzyme guided growth of polyaniline on the linear DNA templates. Right is the height of the corresponding cross-section. (B) Dependence of absorption spectra of polyaniline on the configurations of the DNA templates.[65] Reproduced with permission from ref 65. Copyright 2013 American Chemical Society.

silver onto gold, because of the enhanced interparticle near-field coupling.

DNA-based assembly provides a scalable approach to synthesize isotropic dispersions of chiral metamolecules with predefined complexity and optical properties. An important application enabled by this strategy is chiral sensing.[60] When enantiomers of chiral chemicals are in close proximity to the surface of chiral plasmonic assemblies, different CD signals may be obtained, allowing for determination of the enantiomers. Enzymatic digestion may cause key strand cleavage in the DNA nanostructures and perturb the asymmetry of the chiral metallic assemblies, causing immediate CD spectral changes.

TEMPLATED POLYMERIZATION FOR ENHANCING SURFACE CONDUCTIVITY

Polyaniline is an attractive conductive polymer, mainly because of its easy synthesis, environmental stability, and simple doping/dedoping chemistry. DNA nanostructures have several features that make them promising templates for the synthesis of nanostructured polyaniline. First, the DNA phosphodiester backbone provides negative charges as requisite counterions for the synthesis of polyaniline with extended conjugate molecular structures. Second, shape-programmable DNA templates can potentially produce a variety of morphology-defined polyaniline. Linear calf-thymus DNA templates were utilized to produce 1D polyaniline nanowires threaded around the double-helical backbones, using horseradish peroxidase (HRP) as the catalyst and H_2O_2 as the oxidant.[61] At pH values lower than the pK_a of aniline, aniline was catalytically oxidized into the emeraldine form of polyaniline, which showed reversible doping−dedoping behavior and switchable electrical conductivity. The enzymatic polymerization offers a high degree of control over the kinetics of the reaction and enables polyaniline/DNA nanostructures to be produced with a high yield.[62]

Compared with the use of the calf-thymus DNA template, the growth of polyaniline on DNA self-assemblies is more intriguing. However, the limited negatively charged area provided by self-assembled DNA can substantially reduce the yield of conductive polyaniline synthesis. Two strategies were reported to address this obstacle. The first strategy incorporates aniline monomers covalently into the contiguous bases of a single DNA strand,[63] which subsequently hybridizes with another strand. This ensures persistent interaction between the aniline and the negatively charged DNA. In the second strategy, the catalytic sites are associated with the nucleic templates. HRP can be chemically conjugated to nucleic strands participating in DNA self-assembly; and in the presence of H_2O_2, conductive polyaniline is produced around the DNA duplex.[64] However, the multistrand-modified HRP can potentially cause cross-linking of the DNA nanostructures. On the other hand, HRP functionality can be mimicked by a hemin-complexing DNA strand, which can assemble with the templates to produce discrete catalytic DNA nanostructures. Based on this concept, Wang, Ding, and co-workers associated a HRP-mimicking DNAzyme with DNA monomers, which then assembled into 1D DNA nanostructures via sticky-ends hybridization.[65] The artificial enzyme was first oxidized by H_2O_2 into an intermediate, which then oxidized the aniline monomers into aniline radicals. The DNAzyme interacted with the template efficiently, so that the aniline radicals could rapidly diffuse to the negatively charged template and undergo coupling to produce dimers. Successive oxidization and coupling reactions eventually resulted in the formation of

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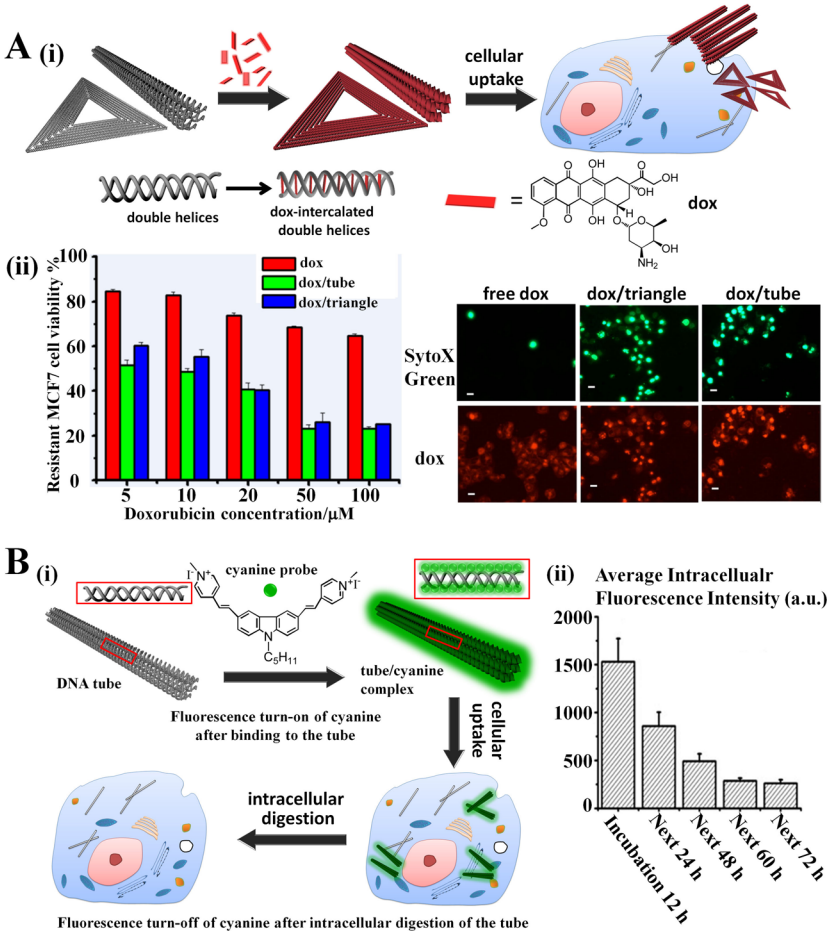

Figure 4. DNA nanostructures for biomedical applications. (A) Therapeutic origami–dox complexes.[49] (i) Schematic dox intercalation into double-helices of origami nanostructures followed by administration to the MCF-7 cells. (ii) Cytotoxicity of dox/origami to dox-resistant MCF-7 cells: cell viability (left) and stained cells (right). SYTOX Green can indicate dead-cell nuclei within a population. Reproduced with permission from ref 49. Copyright 2012 American Chemical Society. (B) Origami–cyanine complex system.[80] (i) Docking of cyanine into DNA tube, followed by cellular uptake and intracellular digestion that results in cyanine fluorescence turn-off. (ii) Intracellular stability of DNA tube–cyanine probes, indicated by quantitative confocal fluorescence. Reproduced from ref 80 with permission from the Centre National de la Recherche Scientifique (CNRS) and The Royal Society of Chemistry.

para-directed polyaniline. The growth of polyaniline preferentially started around the catalytic site, expanding over the overall template surface, a means of site-selective polymerization (Figure 3A). The templated polyaniline exhibited right-handedness, revealing the tight DNA–polyaniline interaction that transferred chirality from the duplex to the polyaniline. The molecular spectra of the polyaniline exhibited the dependence on the charge density of the template, affected by the template configuration (Figure 3B). This work suggests that the shape of polyaniline can be controlled on 2D or 3D origami surfaces by arranging the spatial positions of the catalytic sites.

In addition to polyaniline, other conducting-polymer nanomaterials, such as polypyrrole[66] or polythiophene derivatives,[67] have been synthesized using chemical oxidization on DNA templates. As an interesting example,[68] 2,5-bis(2-thienyl)-pyrrole was covalently linked to selected bases of DNA modules, which then self-assembled into closed-cycle or linear arrays of aligned pyrrole derivatives through the hybridization of unmodified bases. Enzymatic oxidization produced cyclic or linear conductive oligomers that exhibited the chemical and optical properties of thiophene-like polymers.

DNA-templated synthesis of conductive polymers endows DNA nanostructures with dopant-dependent conductivity and even enables DNA nanostructures to behave similarly to electronic boards on which conductive patterns are formed site-specifically. In turn, the use of DNA as a template gives rise to novel electrical properties for conductive polymers, such as Schottky emission-dominated conduction and the rectification effect.[69] Novel functions were also exhibited, such as promoted ion diffusion by a DNA-supported polythiophene porous pattern,[67] which has promising applications in supercapacitors.

DRUG LOADING AND DELIVERY FOR THERAPEUTICS

Self-assembled DNA nanostructures have great potential as drug delivery vehicles. First, 3D DNA constructs and origami nanostructures have shown high structural resistance to multiple nucleases and cellular digestion, compared with duplex plasmid DNA.[70−72] This resistance allows the DNA constructs to be durable in extracellular and cytoplasm environments to accomplish a predefined task. Second, DNA nanostructures exhibit low cytotoxicity and can be tolerated by the mammalian immune system.[71,73] Third, DNA nanostructures are capable of carrying multiple functionalities that simultaneously achieve

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synergetic biological effects and cell imaging. For example, DNA nanotubes containing folate groups and fluorescent dyes can be taken up by folate receptor-overexpressing cancer cells for fluorescence imaging.[74] Another example is found in the dual-functionalization of the DNA tetrahedral constructs with cancer targeting molecules and siRNA.[75] The targeting molecules cooperate with siRNA to silence genes in target tumor cells. Fourth, nanostructured DNA carriers can be designed to perform robotic functions, because of their dynamic nucleic properties, which enable the controlled release of loaded drugs. Douglas and co-workers[76] designed a barrel-shaped DNA origami structure, in which two halves were held together by aptamer switch-encoded DNA duplexes. Antibody fab fragments acted as the molecular payload to be anchored inside the barrel. Upon recognition of the surface expression of antigen in leukemia cells by both aptamers, the duplexes were unlocked and the barrels were opened. Then, the antibody payload bound to the cell-surface receptors and inhibited the growth of the target cells. Hollow DNA nanostructures such as origami boxes also have the potential to release payloads when the structures are unsealed.[18]

The biomedical studies of DNA nanostructures provide an opportunity to address a medical challenge: chemotherapy with high efficacy and minimal side effects. To achieve this goal, DNA nanostructures can be equipped with multiple anticancer drugs and cancer-targeting groups, so that the cytotoxic drugs can be delivered exclusively to the target cells. This concept of chemotherapy was proven through the delivery of doxorubicin (Dox), a commercial broad-spectrum antibiotic with well-known adverse effects on some organs. Through intercalating with DNA double helices, Dox was loaded into DNA icosahedra that were modified with aptamers against MUC1, a tumor surface marker uniquely and abundantly expressed on epithelial cells. The aptamer-conjugated icosahedra showed a higher efficiency of cellular internalization and greater cytotoxicity against a MUC1-positive human breast cancer cell line.[77] No such selectivity occurred in the MUC1-negative cell line, indicating a potential cancer-targeting chemotherapy.

Compared with DNA polyhedra, DNA origami structures have a greater flexibility in morphological tuning and contain more docking sites for Dox intercalation. The twist degree of the double helix in the origami can even be relaxed to control the release and cytotoxicity of Dox.[78] Ding and co-workers demonstrated that Dox-encapsulated origami structures (tubular and triangular shapes) caused effective cytotoxicity to Dox-resistant human cancer cells, as well as regular cancer cells.[49] Figure 4A shows a schematic of the cellular uptake of Dox-intercalated origami structures and cytotoxicity against Dox-resistant cancer cells. Two factors contribute to the circumvention of Dox resistance: (i) Increased internalization. Decreased drug uptake is a common way that cultured cancer cells become resistant to anticancer drugs, while the origami carriers facilitate Dox internalization markedly. (ii) Drug redistribution. In resistant tumor cells, the anticancer drugs are confined to the most acidic organelles, such as the lysosomes, and are incapable of dispersing throughout the cytoplasm and nucleus. However, the Dox/origami complex inhibited lysosomal acidification, facilitating drug redistribution to the active sites. In addition to Dox, the unmethylated CpG oligodeoxynucleotides were also loaded into DNA nanostructures for chemotherapy. The loading of CpG motifs was achieved through hybridization, and the delivery of CpG motifs induced immunostimulatory effects, which produced high-level secretion of various cytokines including tumor necrosis factors.[79]

The identification of DNA structural integrity in cellular environments is important to understand the drug delivery process, which is assumed to occur through DNA nanostructure dissociation. To directly observe the location and stability of DNA carriers, a fluorescent carbazole-based biscyanine molecule was anchored into DNA origami structures.[80] Selective binding of the cyanine molecule to AT-rich regions restricts the intramolecular rotation of the central C−C bonds of cyanine and causes a large reduction in the nonradiative fluorescence decay.[81] Binding to DNA duplexes significantly enhances the fluorescence emission of cyanine molecules, which serve as a turn-on dye. Digestion of the DNA duplex by DNaseI can turn off the cyanine fluorescence. This label-free probe strategy allows for time-resolved imaging of cyanine-docked origami nanostructures in live human breast cells. The study by Ding and co-workers[80] revealed that most DNA origami tubes were localized in the lysosomes after a 12-h culture time and that the structures dissociated markedly after 48 h of culture time, with most being dissociated after 60 h. This observation coincided with the remarkable cytotoxicity of origami/Dox against cancer cells observed after a 48-h culture time[49] and also predicted that 60 h should be the optimal time for cancer cell death. The schematic drawing and corresponding optical images are shown in Figure 4B.

Currently, drug-loaded DNA nanostructures are mainly used in vitro, providing a wealth of information for in vivo chemotherapeutics. Molecular imaging will enable dynamic and noninvasive monitoring of the anticancer efficacy of drug-loaded DNA carriers. Additionally, DNA origami nanostructures with customized sizes may exhibit remarkable EPR (enhanced permeability and retention) effects, resulting in drug accumulation in the tumor region. This passive tumor targeting will reduce the nonspecific body distribution of cytotoxic drugs. The low pH environment of tumor regions could trigger drug release because of acidification-induced instability of the DNA carrier. However, there are still many challenges, such as combined administration of multiple drugs (e.g., antibiotics, siRNA), multiple barriers that may hinder drugs from approaching the action sites and unevaluated genetic safety. These factors indicate that the functionalization of DNA structures for nanomedicine is in its early stages, and thus, intensive efforts are required to achieve practical therapeutic applications.

■ CONCLUDING REMARKS

The functionalization of self-assembled DNA nanostructures has advanced many fields through the developments in collective interparticle behaviors, controlled conductive polymer patterns, and chemotherapeutics. DNA nanostructures not only behave as templates but also contribute various intrinsic features to the functionalities. Progress in biology, chemistry, physics, and materials science will be integrated with DNA nanotechnology to bring about novel and exciting applications.

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Notes

The authors declare no competing financial interest.

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Zhen-Gang Wang received his B.S. in Chemical Engineering from Dalian University of Technology in 2003. He finished his Ph.D. in Polymer Chemistry and Physics under the supervision of Prof. Zhi-Kang Xu in Zhejiang University in 2008. Then he moved to the Hebrew University of Jerusalem and worked as a postdoctoral researcher in DNA functional self-assembly with Prof. Itamar Willner. In 2011, he became an associate professor in National Center for Nanoscience and Technology and focused on DNA-directed synthesis of functional nanostructures.

Baoquan Ding received his B.S. in Chemistry from Jilin University in 2000. He obtained his Ph.D. in 2006 from Department of Chemistry, New York University, under the supervision of Professor Nadrian Seeman. He then joined the Molecular Foundry, Lawrence Berkeley National Laboratory, as a postdoctoral research fellow. He worked as a research assistant professor at Biodesign Institute, Arizona State University, from October 2009. Dr. Ding became a professor in the NCNST in 2010. His research interests focus on nanostructures and device fabrication with self-assembled biomolecules, especially nucleic acids, and nanoparticles.

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