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Applications of DNA Nanotechnology in Synthesis and Assembly of Inorganic Nanomaterials

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In addition to its inherited genetic function, DNA is one of the smartest and most flexible self-assembling nanomaterials with programmable and predictable features, for which, more and more scientists combine DNA with nanomaterials and put them into designing, synthesizing and assembling. In this review, four modes of action of DNA molecules are introduced in a figurative and intuitive way, based on the four different roles it plays in synthesis and assembly of nanomaterials: (a) smart linkers to guide nanoparticle assembly, (b) 2D or 3D scaffold with well-designed binding sites, (c) nucleation sites to directly facilitate Au/Pd/Ag/Cu nanowires, nanoparticles, nanoarrays and (d) serving as capping agents to prevent crystal growth, and control size and morphology. To be sure, this state-of-the-art combination of functional DNA molecules and inorganic nanomaterials greatly encouraged step towards the development of analytical science, life science, environmental science, and other promising field they can address. DNA-guided nanofabrication will eventually exceed expectations far beyond our scope in the near future.

Keywords inorganic nanomaterial, DNA nanotechnology, DNA origami, assembly

Introduction

For over half a century, the basic biological role DNA plays in carrying genetic information has been studied extensively.[1-3] Apart from that, many unique properties, such as easily labeling or modification, rigidity and address ability on the nanoscale, pH responsive, exact biomolecule binding and fantastic metal ion recognition, attract scientists to exploit DNA as a functional chemical molecule in inorganic nanofabrication beyond genetic blueprints for life.[4] And nowadays, DNA is being regarded as a masterpiece in the field of nanotechnology for the creation of diversiform structures and the placement of functional materials at nanoscale.

In the synthesis and assembly of nanomaterials, DNA molecules can play diverse dissimilar roles, four of which are introduced as follows. Based on the inherited complementary base pairing,[5,6] DNA can be a smart linker to guide nanoparticle assembly, which is one of the most convenient methods of inorganic nanofabrication. In the mid-1990s, Mirkinand his co-workers[7,8] made the first attempt to assemble nanoparticles (denoted as NPs) into well-defined predetermined constructions by using DNA oligomers to connect NPs into useful geometries. Subsequently, some discrete nanostructures have also been elaborately designed. Another kind of method is based on the successful synthesis of a four-way branched junction and a double-cross-over motif by Seeman.[9,10] And the tile-based method has come into use with the generating of numerous branching building blocks. This branching building blocks can be broadly classified as being planar tiles, branched junctions, discrete building blocks, or helix bundles.[1,11] Another tremendous progress took place when the high-impact paper was reported by Rothemund in 2006.[12] He proposed a new method called "DNA origami". Compared with the tile-based method in the earlier studies, DNA origami is a modern approach and it is applied more frequently in the construction of larger and more complicated DNA structures since only a few staple strands need to be designed for the change of orientation of DNA chain. A long single-stranded DNA (denoted as ssDNA) molecular is folded to create structures of arbitrary shapes with the help of some smaller staple strands as pins to change the trend of linear long strands and fix the shape. To some extent, these staple strands are scientists' hands in the nanoscale, which can move and fold the long single-strand DNA molecule into desired pattern.[13,14] In recent years, DNA origami tech-

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nology has frequently been applied in the synthesis of designed DNA motifs.[15,16] And the methods of assembling 3D origamis have also been researched. One method is based on folding flat surfaces against one another. The links between the helices could be coaxial, non-coaxial, orthogonal or at any angle.[17] Another strategy is to make 3D structures out of multiple layers.[18] In addition, the arising of some multifunctional softwares for designing and predicting the DNA stuctures, such as SARSE,[19] caDNAno,[20] canDo,[21] helps this field attain maturity.

Any desired DNA structure can be synthesized flexibly. Since DNA origami has different sequences at all position on the surface, DNA-modified multifunctional nanomaterials can be organized onto specific predesigned positions on this 2D or 3D scaffold with well-designed binding sites.

Besides the whole structure of assemblies, multitudinous nanomaterials, such as nanowires, nanoparticles, nano-arrays have been synthesized directly through DNA-templated method.[5,6,22] In 1998, Braun and coworkers[23] succeeded in preparing DNA-templated metallic silver nanowire. This pioneering work indicated that DNA molecules can be used as a template to guide the growth of materials, which will be given a detailed introduction in a later section. Since the work, many scientists contributed to the DNA-templated assembly of nanomaterial. With the development of DNA self-assembly, different kinds of designed DNA motifs can be constructed easily, which facilitate the development of DNA-templated assembly of nanomaterial further.[24] When modified with specific sequences, nanomaterial can grow along the post-synthetic DNA template to form designed high-order structure. Recently, scientists try to research the influence of DNA towards the morphology of the nanomaterial, especially nanoparticles so that we can get the predicted shape by simply adjusting the sequences.

As discussed above, DNA nanotechnology has opened a new dimension in the science of controlled synthesis of nanoscale architectures. In order to achieve well-defined and diverse structures, DNA self-assembly is an indispensable path.[25-29] In the present review, we focus on the new advances in the burgeoning research area of DNA directed synthesis and assembly of inorganic nanomaterials, and briefly summarize four diverse roles of DNA when it meets inorganic nanofabrication: (a) smart linker, (b) 2D or 3D scaffold with well-designed binding sites, (c) nucleation site and (d) surfactant or capping agent. Meanwhile, some outstanding and representative works were introduced as examples.

Smart linker

DNA molecules have been seen as good synthetic materials because of their programmable sequences and well-defined structure. Nanomaterials can bind to DNA segments easily mainly through electrostatic force or coordination. By modifying DNA strands, nanomaterial can be linked with each other and become dimer, trimer, satellite *etc*.,[22] which facilitates the construction of various multifunctional nanodevices and biological sensors.[30]

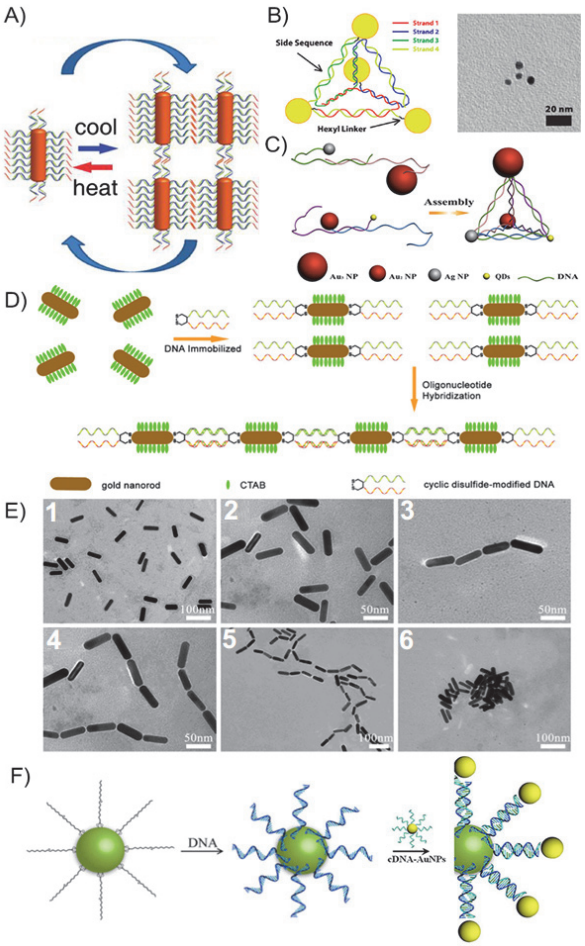

Figure 1 (A) Scheme of temperature-dependent reversible plasmonic circular dichroism responses based DNA modified AuNRs (yellow rod) (Reprinted with permission.[38] Copyright 2012, American Chemical Society). (B) Schematic (left) and TEM (right) image of simplest DNA-nanocrystal pyramids (Reprinted with permission.[36] Copyright 2009, American Chemical Society). (C) Scheme of the synthesis of Chiral NP Pyramid (Reprinted with permission.[37] Copyright 2012, American Chemical Society). (D) Scheme of the end-to-end assembly of AuNRs based on oligonucleotide hybridization of groups-modified DNA. (E) TEM images of the assembly of AuNRs with different DNA concentration: (1) 0, (2) 0.02, (3) 0.05, (4) 0.10, (5) 0.20, and (6) 2.0 μmol•L^{-1} (Reprinted with permission.[39] Copyright 2012, AIP Publishing LLC). (F) DNA-functionalized UCNPs synthesized from as-prepared hydrophobic UCNPs through ligand exchange strategy with merely one-step; DNA-directed assembly of oligonucleotides modified UCNPs (T30-UCNPs) and cDNA strands modified AuNPs (A27-AuNPs), forming a satellite structure (Reproduced with permission.[34] Copyright 2013, American Chemical Society).

In 1996, a very classical work of Mirkin and his co-workers[7,8] opened the gate to assemble NPs into well-defined predetermined constructions. They use

DNA oligomers to connect the NPs into useful geometries, which has become the most general method of NPs organization. And Mirkin *et al.*[31] reported a method for asymmetric functionalization of AuNPs in a site-specific manner. The DNA-functionalized magnetic microparticles specifically bind the AuNPs with modification of complementary oligonucleotides, and assembly to unique nanoparticle heterostructures. Similarly, such satellite connecting type can be combined with the heated materials such as upconvertion nanoparticles (denoted as UCNPs) or quantum dots (denoted as QDs).[32,33] The general principle is attaching the oligonucleotides modified metal NPs (usually AuNPs) to the UCNPs or QDs which are modified by a complementary DNA (denoted as cDNA) strand to form a satellite structure. Lu *et al*.[34] reported a very simple strategy for fabrication of DNA-modified UCNPs from hydrophobic lanthanide-based UCNPs, which can be applied in bioimaging and DNA delivery because of their biocompatibility. As Figure 1F illustrated, after a ligand exchange progress, the DNA coated on the hydrophobic UCNPs, and then became the water-soluble DNA-functionalized UCNPs with the merit of no transfection agents modifying steps. The retained biorecognition ability of as-modified DNA can realize further assembly with other NPs modified by a complementary DNA (cDNA) strand. The T30 oligonucleotides (T30-UCNPs) modified UCNPs attached around with the AuNPs, which are modified by cDNA strand (A27-AuNPs) forming a satellite structure. Such combinations can make DNA play a role to a great extent in inorganic nanomaterial synthesis with multiple and desirable functions. A recently reported work is also mentionable. Yao *et al.*[35] reported a sophisticated way of combining an integrated DNA-strand-displacement circuitry with self-assembly of spherical nucleic acids, which may possess great potential applications in the fabrication of complex devices and architectures.

In addition, the discrete nonlinear geometries nanostructures, such as triangles, pyramids, cubes, and more complicated polyhedra have also been elaborately designed. The tetrahedral geometry DNA pyramids are especially surprising for the possibility of creating chiral nanostructures which have great potential in biological applications (Figures 1B and 1C). In this field, the smart double-stranded DNA (denoted as dsDNA) is commonly used as a scaffold to control the setpoint of nanoparticles. Mastroianni and his co-workers[36] successfully created chiral pyramids by using four different sizes of gold nanocrystals with 5, 10, 15, and 20 nm to conjugate to each tip. Beyond that, they stepped out of the limit of gold, finding multiple linker moieties for synthetic DNA, realizing the diversification of nanoparticle materials. In the simplest pyramid design, for example, each strand of DNA travels through three tips to form a side of the pyramid. Between any two tips, the dsDNA pair wise complemented and formed side sequences, and between these side sequences, three thymine bases are used to add sufficient flexibility to bend without straining the structure. Three thymine bases in side sequences make the bend more easily rather than straining the structure (Figure 1B). Similarly, In 2012, Yan *et al.*[37] created the preparation of heteroparticle chiral pyramids with plasmonic and semiconductor NPs modified with four different single-strand DNA (ssDNA). Since the synthesis can be scalable implemented, the study of chiral nanostructures will certainly be promoted greatly (Figure 1C).

Besides the NPs organization, the combination of gold nanorods (denoted as AuNRs) and DNA has recently become the favorite feast of scientists for the unique shape-dependent optoelectronic properties and the high reactive end surfaces of AuNRs. With the help of the hydrogen bonds formed between the complementary strands or sticky ends, Tang *et al.*[38] reported a work combining DNA assemblies with AuNRs. In his research, the programm ability of DNA provided an excellent platform for constructing the hybrids with AuNRs in a controllable way. Single-stranded-DNA stabilized AuNRs are incubated with its complementary DNA containing the sticky end of four extra bases to form double-strand DNA modified AuNRs. By adjusting temperature, these nanorods can assemble into a high-ordered structure (Figure 1A). Based on another coordination-oligonucleotide hybridization, Zhang *et al*.[39] came up with a novel and feasible approach to generate a highly stable end-to-end assembly of AuNRs (Figure 1D). In this work, groups-modified DNA of cyclic disulfide immobilized on the end faces of AuNRs, and directed the end-to-end assembly through oligonucleotide hybridization. These short cyclic disulfide groups and ring structures formed a rigid structure in DNA molecules, which guarantees the stability of assembly. And the TEM images further confirmed that the assembly of AuNRs behaves differently with diverse DNA concentration, and the desirable end-to-end assembly was organized when DNA remained at 0.2 $\mu mol \cdot L^{-1}$ (Figure 1E). Another more creative work was reported by Kotov *et al.*[40] They connected NPs with NRs of selective modification with DNA oligomers to form three types of regiospecific assemblies denoted as End, Side, and Satellite NP-NR assemblies, which displayed high synthetic yield and a new level of control of NPs.

Using DNA as a smart linker is an easy and effective method for nanofabrication. Through such a facile way, our ability to engineer novel nanomaterials certainly will continue to advance.

2D or 3D Scaffold with Well-Designed Binding Sites

In 2006, Rothemund[12] first proposed and implemented DNA origami as a new approach to generate DNA nanostructures, which fueled the rise of DNA nanotechnology largely as mentioned above. Since DNA origami has different sequences at all position on the surface, nanomateirals modified by oligonucleotides

with complementary sequences can be organized onto specific predesigned positions on the addressable 2D or 3D scaffold with well-designed binding sites.[21] By combining nanomaterials with complex and subtle structures fabricated by DNA origami, scientists have scored remarkable achievements.

The most frequently-used method for origami modification is related to the hybridization of DNA to terminal extensions of selected staples, which stretches out of the origami plane.[15] This method was mainly used for the decoration of origami with different-sized nanoparticles. A kind of ingenious design is the programmable positioning of well-defined metal nanostructures, including gold and silver nanoparticles, as well as quantum dots. When excited at their plasmon resonance, the high local-field enhancement they generated can be used for detectors, optical wave guides, and resonators. For example, In 2010, Yan *et al.*[41] demonstrated a method to form a linear structure with well-controlled orientation within 10 nm spacing (Figure 2B). Thiolated ssDNA was used to functionalize the nanoparticles to hybridize to complementary sequences of DNA origami, with different sets of capture strands, different-sized Au nanoparticles could be selectively bound to an origami structure, generating extremely high field enhancement. Based on a triangle origami structure like wise, in another work, the same group[42] developed well-ordered Au nanorod dimers with controlled inter-rod angles, distances, as well as orientations on a DNA origami scaffold, providing an efficient way to manipulate the geometry of anisotropic material multimers, promoting the study of plasmon interactions (Figures 2D and 2E).

Another reported application about DNA origami in the synthesis of inorganic nanomaterials was a label-free RNA sensor by Yan and co-workers.[43] A rectangular DNA origami tile was used as the chip, multiple ssDNA probes were precisely patterned on the origami scaffold to target specific RNA sequences as shown in Figure 2A. They simply extended the end of specific staples with sequences designed to bind RNA segments of biological interest. The hybridization between the staple extensions and the RNA targets created local protrusions from the origami surface that were readily imaged by AFM. They also incorporated a barcode system that enabled the one-pot, simultaneous detection of multiple targets. Yan's group[44] also used DNA origami to study distance dependent aptamer-protein binding. Aptamer modified staples were displayed on the surface of rectangular DNA origami, with precise control over the distance between two lines of aptamers, which enabled the researchers to determine the optimal distance for bi-valent binding.

The programmability DNA origami has also been used in fabricating nanotubes. Kuzyk *et al.*[45] obtained origami-scaffolded chiral helical AuNP chains on the surface of origami cylindrical nanostructures with defined circular dichroism and optical rotatory dispersion effects (Figure 2C). Such optical response is tunable.

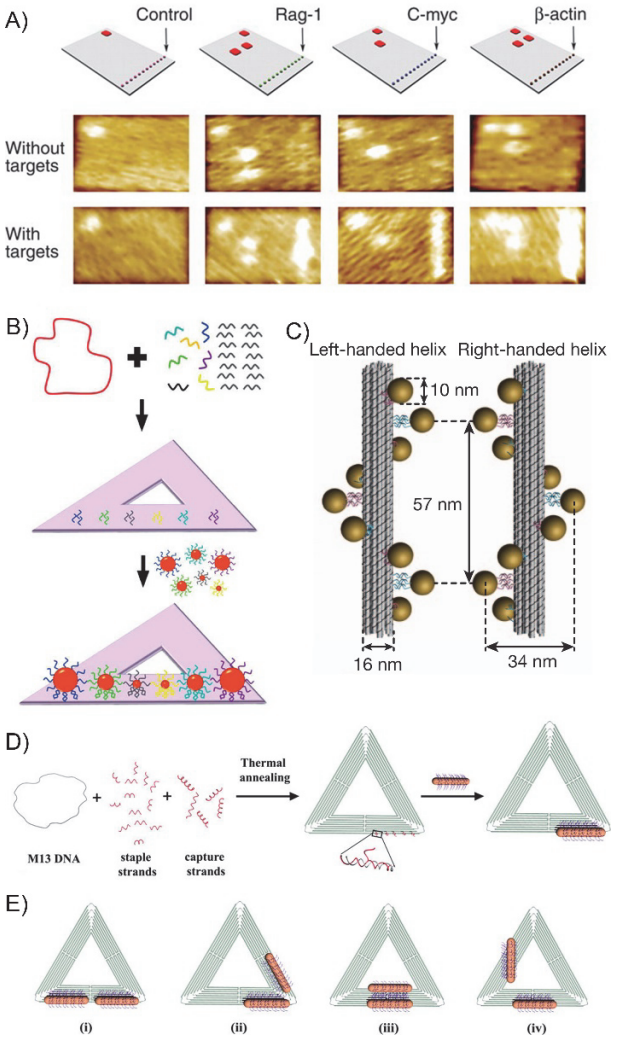

Figure 2 (A) The distinctive bar-coded tile designs and AFM images of the bar-coded tiles without targets (middle) and with targets (bottom) (Reprinted with permission.[43] Copyright 2008, American Association for the Advancement of Science). (B) Bowtie-like alignment of AuNPs with different sizes (Reprinted with permission.[41] Copyright 2010, American Chemical Society). (C) Origami-scaffolded chiral helical AuNP chains (Reprinted with permission.[45] Copyright 2012, Rights Managed by Nature Publishing Group). (D) Schematic of the assembly process of triangular origami with nanorod structure. (E) AuNR dimer structures with various orientation: (i) 180°, (ii) 60°, (iii) 0°, and (iv) 90°, respectively (Reprinted with permission.[42] Copyright 2011, American Chemical Society).

Also, the colour and intensity are consistent with the theoretical model. Shen *et al.*[46] introduced another simple method to construct 3D AuNP helices, leading engineerable plasmonic chiral nanomaterials. They utilized 2D rectangular DNA origami to organize AuNPs along two linear chains precisely. And then rolling the 2D sheets to obtain the 3D AuNP helices, the diameter and axial length, as well as the pitch of the 3D AuNP helices could be tuned by rectangular DNA origami template and the AuNP chain number on the origami. A

latest particularly outstanding study published on Nature by Zhou and co-workers[47] deserves to be mentioned. In an active plasmonic system, a gold nanorod can carry out directionally and progressively walking on DNA origami step by step, which triggers a series of conformational changes and activates subsequent near-field interaction changes, giving an optically immediate spectral response that can be read out. Thereby, a smart nanophotonic platform is provided for studying dynamic light-matter interaction at nanometer accuracy.

DNA as 2D or 3D scaffold with well-designed binding site, brings a new level of sophistication to nanofabrication.[48,49] Now DNA can be used to control self-assembly of subtle structures, arrange molecules and nano-components into any arbitrary shaped geometries with nanometer precision without any requirements of sequence design, hard time-consuming stoichiometry studies or control over the quality and quantity of the staple strands. It is important to believe that with the combination of DNA origami technology and inorganic nanomaterials, there will be more and more break throughs for more advanced applications.

Nucleation Site

Since the properties of nanomaterial depend largely on the organization within the assemblies, only using DNA molecules as a bridge to link nanomaterials cannot fulfill itself to the best. Therefore, using DNA as templates called "nucleation site" to guide the growth of the nanomaterial in a particular location has been hotly discussed. In this way, some groups have already facilitated crystal growth, and realized programmable nanoparticle position with DNA molecules inherent potential for sequence-based addressability.[50-53]

The methods for producing DNA-templated metallic nanowires consist of two steps. Firstly, metal cations are absorbed onto the negatively charged DNA backbone forming a DNA-metal ion complex. Secondly, the absorbed metal cations are reduced to metal that covers the DNA, thus forming metallic nanowires. In 1998, the group of Braun firstly achieved DNA-templated assembly of silver wires, which has great impact to the improvement of conductive DNA nanowires (Figure 3F).[23] The hybridization of the DNA molecule with surface-bound oligonucleotides was stretched between two gold electrodes. Silver ions were deposited along the DNA molecule to form complexes between the silver and the DNA bases. Then the silver ions were reduced to form nanometre-sized metallic silver aggregates bound to the DNA skeleton. As the template was a long and straight chain, silver aggregates become a long nanowire. This work demonstrated the potential of DNA for templated assembly. Then, DNA-templated gold, platinum, copper, and palladium wires have also been reported (Figures 3A and 3B).[54]

Besides, selective metallization can also be realized in this system. Mokhir *et al.*[55] made the first attempt on

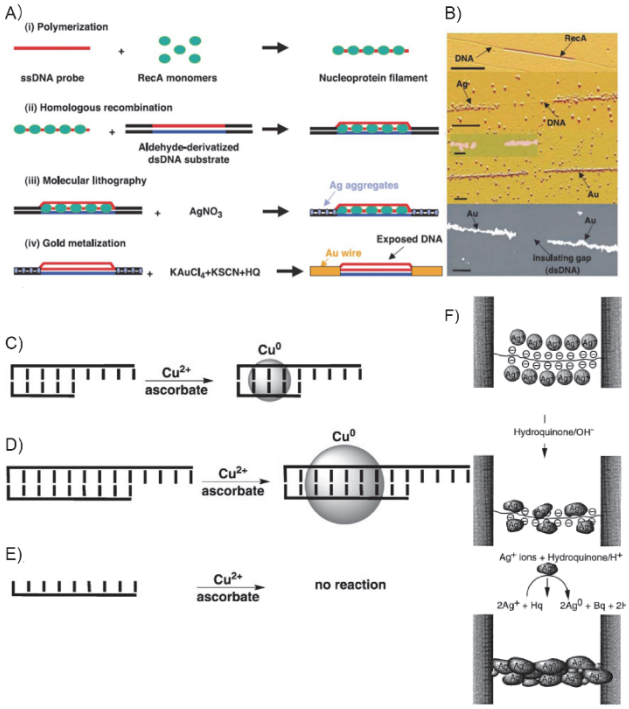

Figure 3 (A) A 16-μm-long strand of λ-DNA was positioned between two gold electrodes, then silver ions were localized onto the DNA backbone, after the reduction of the ions, silver aggregations were obtained, and formed 100-nm-thick silver wires (Reprinted with permission.[54] Copyright 2007, American Association for the Advancement of Science). (B) The images of metal deposited dsDNA by using atomic force microscopy (AFM) and scanning electron microscopy (SEM). (C, D, E) The schematic of selective metallization in ds regions of DNA with Cu (Reproduced with permission.[55] Copyright 2010, WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim). (F) Schematic process of an Ag nanowire's formation (Reprinted with permission.[23] Copyright 1998, Nature).

the selective metallization on dsDNA in solution which takes only a few minutes through the reduction of Cu^{2+} ions (Figures 3C—3E). Since the size of the CuNPs is dependent on the number of base pairs in the double stranded DNA template, it is a new way to control the size of copper nanoparticles by adjusting the length of the dsDNA templates. Recently, the sequence role in producing fluorescent CuNPs has been deeply studied, for the reason that such fluorescent CuNPs could serve as DNA-hosted Cu nanomaterials and promising fluorescent nanoprobes in biosensing. Using ssDNA poly-thymine (T) as a template is a popular method because other sequences do not induce the formation of CuNPs. Qing and co-workers reported a sequence-specific way to achieve the selective metallization on ssDNA.[56] The size and fluorescence of the CuNPs can be tuned just by the degree of poly-thymine (T); the size and fluorescence of these CuNPs could be tuned by the length of poly T. Liu *et al.*[57] demonstrated that the thymine base plays a dominant role in the formation of red-emissive fluorescent CuNPs through comparing and analyzing

the results with different structure-types of DNA molecules as templates as well. Song and his co-workers[58] have also researched on this aspect. They developed a convenient method for regulating the formation of fluorescent CuNPs by changing the sequence combinations of dsDNA. The fluorescence intensity and the fluorescence lifetime of CuNPs can also be tuned by the length or the sequence of dsDNA, which can be confirmed by a sensitive and label-free fluorescence nuclease assay.

With the development of DNA self-assembly technology, many complex DNA templates can be synthesized easily. Specific DNA segments modified nanomaterial can grow along the template to assemble into a designed structure. In addition to diverse design of nanowires, 2D or 3D nano-arrays are also fabricated. One of the most common methods is combined with metal nanomaterials. Metal nanomaterials hold tremendous promise in nanoelectronics, sensing, catalysis, and nanophotonics.[59] In order to arrange them into well-designed and well-defined structure, structural DNA technology is a very important and efficient way.

Surfactant or Capping Agent

In the above discussion, the influence to the whole structure of assemblies has been discussed adequately, while the direct effect on the morphology, size or crystal structures of the independent nanomaterials, especially nanoparticles is not well understood. The size, morphology and shape of NPs greatly affect the properties and functions of themselves.[60] Also, since nanoparticles with complex shapes and rough surfaces have recently shown to enhance performance in SERS, catalysis, and cellular uptake, such shape-controlled nanoparticle synthesis based on DNA as the surfactant and capping agent could provide a new method for synthesizing nanoparticles with predictable structures for widespread applications.

In 2010, Lu *et al.*[61] pioneered the use of DNA to modulate gold nanoparticle from spherical to flower-shaped to realize some desired optical properties. Other groups of researchers such as Liu and his co-workers have been studying such aspects of DNA nanotechnology very thoroughly in these years as well, and have done lots of interesting and novel works especially in the shape-controll of Au/Ag NPs.[62,63] Actually, both the structure and function of nanomaterials can be tuned by the different sequences of DNA. Lu *et al.*[64] reported on the effect of varying DNA sequences on the morphology of gold nanoparticles comprehensively and systematically. They proposed the rules to govern the morphological of NPs with different DNA molecules and their various combinations. As the Figures 4A and 4B show clearly, different DNA sequences and combination have different shape-control effect. With this DNA-encoded nano-synthesis method, a number of nanoparticles with novel shapes were synthesized. By adjusting the sequences and combination, the synthesis of nanomaterial can be controlled more precisely. It is particularly gratifying that, recently some researchers utilized DNA as surfactants or capping agents to synthesize and control plasmonic nanostructures. Nanostructures with plasmonically coupled nanogap approximately equal to 1 nm or smaller are especially focused on for their outstanding optical properties. Herein, two notable works were introduced as follows.

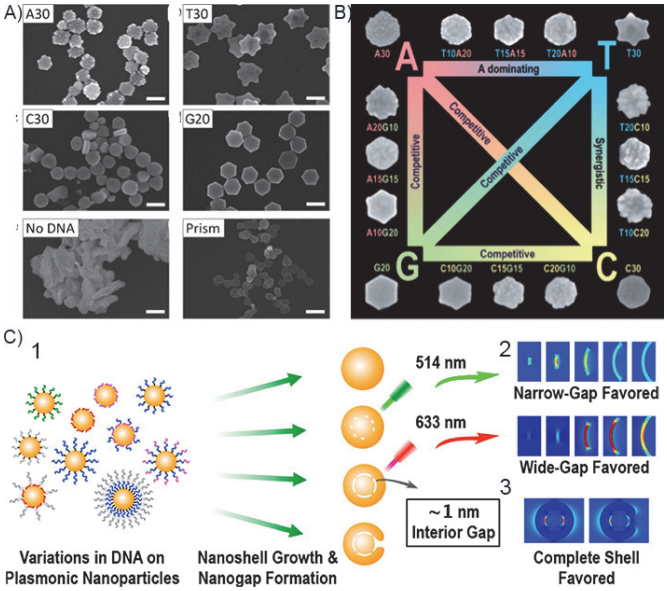

Figure 4 (A) SEM images of the gold nanoparticles synthesized with oligo dA30 (A30), oligo dT30 (T30), oligo dC30 (C30), or oligo dG20 (G20) and without gold salt. (B) Scheme of the shape-control effects of different DNA sequences and their effects in combination (Reproduced with permission.[64] Copyright 2012, WILEY-VCH Verlag GmbH & Co.KGaA, Weinheim). (C) (1) Schematic diagram for DNA grafting density-dependent formation of Au shell and interior gap. (2) Simulated diagram for near-field EM field distribution inside the shell structure at an incident laser wavelength of 633 and 514 nm. (3) Comparison diagram for EM fields of complete 11 nm Au shell and incomplete 11 nm Au shell with 633 nm incident light (Reprinted with permission.[65] Copyright 2014, American Association for the Advancement of Science).

Nam *et al.*[65] reported the thiolated DNA-based methods for designing and synthesizing a plasmonic Au core-gap-Au shell structures [Au-nano bridged nanogap particles (Au-NNPs)] with tunable interior nanogap and various Au shell structures by varying thiolated DNA base, length, sequence, grafting density, etc. They also studied the relationships between the SERS signal and interior nanogap widths, excitation laser wavelength, electromagnetic (EM) field distribution of Au-NNPs as shown in Figure 4C. Au-NNPs with various interior nanogap and shell structures were formed by varying DNA base, length and sequence (Figure 4C1). With 514 nm excitation, SERS signal strength of Au-NNP structures is negatively related with the width of nanogap. That is, the SERS signal strength is narrow-gap favored.

While the SERS signal strength is wide-gap favored at an incident laser wavelength of 633 nm (Figure 4C2). The EM field inside Au-NNP generated by the complete Au shell is stronger and more uniform than that generated by the incomplete one (Figure 4C3). Similarly, Lee and his co-workers[66] found the reaction parameters such as pH and NaCl concentration, have great influence on the DNA conformation, and thereby they obtained three anisotropic plasmonic nanostructures with different shell structures and adjustable intra-nanogap distance on a nanoscale. It is worth expecting that other materials such as Ag and Pt-NNPs can be synthesized, and then be applied to more scientific and engineering fields.

Such DNA-mediated control over the morphology or behaviors of metallic nanoparticles has stimulated the production of useful nanostructures to a large extent.[67]

Conclusions and Outlook

In the past, DNA was seen only as genetic codes for life. But today, the field of DNA nanotechnology has invited us to look at the code in a whole new perspective because of special features DNA molecules possess, and established its position on its own merit, such as the design flexibility, recognition function, responsiveness and easily labeling. Combined with the inorganic nanomaterials which possess amazing stability controllability and multifunction, DNA reaches value in analytical science, life science and environmental science, *etc*. In the review, four modes of action of DNA molecules are figuratively introduced based on four different ways it combines with nanotechnology. (a) Based on complementary base pairing, DNA can serve as smart linkers to guide nanoparticles to assemble to dimer, trimer, satellite, *etc*. (b) The addressable 2D or 3D DNA origamis can provide attachment sites for nanoparticles in nanomaterials assembly. (c) Be as nucleation sites, Au/Pd/Ag/Cu nanowire, Au/Ag NPs, 2D or 3D nanoarray can be directly facilitated. (d) Modificating on the surface of Au/Ag NPs, QDs, UCNPs, DNA can even prevent crystal growth, and control size and morphology of NPs. Without controversy, the outlook for functional DNA-guided assembly of inorganic nanomaterials is very promising. This perfect combination of functional DNA molecules and inorganic nanomaterials greatly encourags step towards the development in frontier science.

However, most studies so far focus on the theory research or the "toy" product limited in the laboratory. Therefore, the technical improvement is still called for. It's obvious that the next step will be investigating the possibilities for making practical materials with DNA nanotechnology. We will need to understand what our DNA assemblies are capable of and identify the important challenges of biology, chemistry, physics, drug delivery, and engineering that they can address. It is only by taking this path that DNA nanotechnology will evolve from an academic field to an applied, booming area of research.

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