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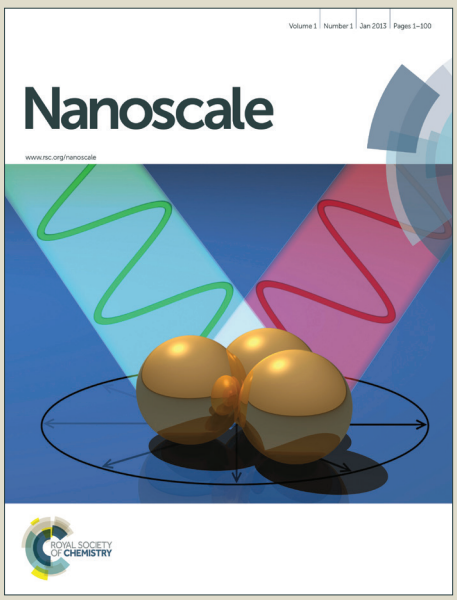

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DNA Nanotechnology for Nanophotonic Applications

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Abstract

DNA nanotechnology has touched the epitome of miniaturization by integrating various nanometer size particles with nanometer precision. This enticing bottom-up approach has employed small DNA tiles, large multi-dimensional polymeric structures or more recently DNA origami to organize nanoparticles of different inorganic materials, small organic molecules or macro-biomolecule, like proteins, RNAs into fascinating patterns that is difficult to achieve by other conventional methods. Here we are especially interested in the self-assembly of nanomaterials that are potentially attractive elements in the burgeoning field of nanophotonics that includes plasmonic nanoparticles, quantum dots, fluorescent organic dyes, etc. DNA based self-assembly allows excellent control over distance, orientation and stoichiometry of these nano-elements that helps to engineer intelligent systems that can potentially pave the path for future technology. Many outstanding structures have been fabricated that are capable of fine tuning optical properties such as fluorescence intensity and lifetime modulation, enhancement of Raman scattering and emergence of circular dichroism responses. Within the limited scope of this review we have tried to give a glimpse of the development of this still nascent but highly promising field to its current status as well as the existing challenges before us.

Key words: Self-assembly, plasmonic nanoparticles, quantum dots, DNA nanotechnology

Introduction

Nanophotonics is a burgeoning research area in the construction of well-controlled assemblies of photonic nanoparticles (NPs), including plasmonic NPs (i.e. noble metal NPs), photo-luminescent molecules and nanocrystals (i.e. quantum dots), and the investigation of their emerging properties that may lead to future functional devices. For example, carefully designed assemblies of plasmonic NPs allow interactions of their surface plasmons, which result in new collective optical and electronic properties, such as shifting of the surface plasmon resonance peak that maybe used in colorimetric assay,[1] enhancing the local electric field at the nano-gap between the particles that upon photo-excitation results in surface enhanced Raman scattering of molecules sitting in the gap,[2-4] and modulating the photo-luminescence of fluorophores in close distance for sensing and energy transduction.[5] Occurrence of these prominent new properties of the NP assemblies requires precise control of the inter-particle distances, stoichiometry, and their relative orientation and positioning, which are difficult to achieve using conventional solution based deposition or top-down electron beam lithography methods.

Currently we still face a gap between these excellent nanophotonic elements and creating useful devices in real applications. The challenges are multi-folds that require a good fundamental understanding of the interactions between the nanophotonic elements, and to develop reliable strategies to organize them with precise spatial control. DNA nanotechnology provides the unique opportunities in meeting both the challenges.

DNA nanotechnology is a fast developing field, where DNA molecules are used as the building material (rather than genetic material) for construction of nanostructures with well-designed geometry and connectivity. The specific recognition and sequence

programmability (due to the predictability of Watson-Crick base pairing), considerable rigidity of the double helix, feasibility of diverse functional modifications and automated synthesis on commercial scale, have made DNA a versatile and affordable construction material. Since Ned Seeman proposed the idea of using DNA tiles as building blocks to assemble nanoscale objects,[6-9] lattices[10] and devices,[11, 12] over the years there have been numerous progresses of designing and constructing DNA nano-architectures with ever growing dimensions and increased complexity that have been carefully reviewed elsewhere.[13-15] Currently, there are three different assembly strategies, 1) tile based assembly through sticky ends associations, 2) scaffolded assembly or called DNA origami,[16] and 3) single stranded tile assembly. The first one is powerful in generating regular 1D and 2D repeating patterns, and the latter two are powerful in generating 2D and 3D structures with arbitrary shapes of fixed sizes. Many of the DNA nanostructures have been used as molecular scaffolds to direct the assembly of photonic elements or biomolecules with good control of their spatial arrangements.[17-21]

In this review, we briefly summarize the recent progresses in the active field of DNA directed assembly of nanophotonic elements, especially metallic nanoparticles and quantum dots, which establish the great potential of using DNA nanostructures for organization of these nanophotonic elements and provide the opportunities for fundamental studies of their interactions and observation of emergent properties. At the end we will also give prospective view of the future directions.

DNA directed assembly of metallic nanoparticles

Nanometer scale photonic materials, like plasmonic NPs or quantum dots (QDs), can be linked to DNA nanostructures in two ways (Figure 1): 1) by hybridizing the NP

containing one or multiple copies of single stranded DNA attached at its surface with one or multiple "capture strands" of complementary sequences that protrude from the DNA nanostructure; 2) by replacing a selected component strand of the DNA nanostructure with a DNA modified NP (or QD) that has a 1:1 DNA:NP ratio, which carries the NP to grow into the DNA nanostructure during the annealing process. In both cases, reliable functionalization of the individual NPs with DNA strands and improving their colloidal stability is of utmost importance.

The most common method to functionalize the surface of noble metals (Au or Ag) by organic molecule is through the strong interaction of Au or Ag with sulfur by adsorption of a thiol-containing molecule. DNA strands modified with one or multiple thiol-groups have been extensively used to conjugate to the surface of AuNPs, which provides sequence-specific recognition for NP assembly.[22-28] In addition, the saturation level of DNA strands covered on the surface also serve as negatively charged surface ligands to prevent aggregation of AuNPs in aqueous solution and confer a higher colloidal stability in aqueous solution containing relatively high salt concentration and elevated temperature, which are required for promoting sequence specific DNA hybridization. With low ratios of DNA added to the AuNPs, it results in a Poisson distribution of the number of DNA conjugated per NP. The relatively small sized AuNPs (< 20 nm) containing 1 or 2 long DNA strands (60+ nucleotides) can be purified by electrophoresis.[22] By varying the sequences of the DNA strands, discrete clusters (dimers, trimers) and 1D arrays have been achieved.[27] When multiple copies of DNA strands are present on the NPs, by tuning their surface density and distance of the complementary sequences to the particle surfaces, 3D crystals of NPs using DNA duplexes as association

forces have been successfully grown.[25, 26] The significant spectral change in the visible range due to plasmonic coupling of the AuNPs in the clusters has been used as a sensitive colorimetric detection method for short DNA strands of specific sequences.[1, 29-31]

The first report of programmed assembly of AuNPs on nanostructured DNA scaffold was in 2002 by Xiao at al.[32] With precise control over the inter-particle distance they produced 2D array of 1.5 nm AuNPs on rationally designed double crossover tiles. In 2004 Le et al. reported a slightly modified method of producing high-density 2D array of 6 nm AuNPs by hybridizing the DNA carrying particles on pre-assembled 2D DNA crystal.[17] Due to the presence of multiple copies of DNA of the same sequence on those particles, possibility of cross-linking cannot be ruled out. Sharma et al. (2006) came up with a strategy of producing 2D array of AuNPs on the 4x4 DNA tile array of square lattice by incorporating a single copy of DNA on each AuNP.[18] Distances between the particles are controlled by the dimensions of the unit tiles, which can be tuned by altering the design of the unit components of the polymerized structure (Figure 1b). More recently, Sleiman's group reported an alternative strategy of tile based assembly of AuNPs into small and discrete as well as long yet well controlled one dimensional architectures,[33] using a tile array organized on a long strand with repeating sequence that is generated by rolling circle amplification (RCA). Although there have been abundant reports of assembling AuNPs creating 1D, 2D arrays on DNA scaffold with nanometer precision of positional control (Figure 2), their direct technical application is scarce, mainly due to lack of the necessary range of control over inter-particle distances and versatility in geometric arrangement of the particles.

DNA origami based discrete assembly of nanomaterials has now emerged with significance in this field. DNA origami can be considered as a nanometer scale pegboard, with pixel resolutions 2-5 nm (distance between any neighboring staple strands). They also offer improved structural rigidity, enhanced addressability and high pixel density, thus better tunability for spatial arrangements of other nanomaterials. In 2008 Sharma et al. constructed AuNPs decorated rectangular shaped origami that can reliably place two AuNPs at pre-engineered positions with high positional accuracy and >95% yield of the dimer construct.[24] Since then numerous reports of varieties of DNA-plasmonic NP architecture are available in the literature. In 2010 Ding et al. fabricated a structure composed of three different sized AuNPs in a row with a specific size arrangement on one arm of a triangle-shaped DNA origami.[34] This kind of self-similar structure is predicted theoretically to generate strong electric field at the central gap that could be utilized for plasmonic application when the distance between the particles was close enough e.g. <10 nm. Zhao et al. extended 2D assembly of AuNPs to 3D on a specially designed DNA cage.[35] AuNPs of different sizes were placed on the sidewall of the cage as well as in the hollow central cavity. Pal et al. demonstrated assembly of gold nanorods on 2D DNA origami with controllable distance and angles between the rods, which was reflected in the resulting plasmonic absorption spectra showing a good agreement with the theoretical prediction.[36] Takabayashi and coworkers have studied extensively the factors that affect high density assembly of AuNPs onto DNA origami.[37] At elevated packing density, steric and electrostatic repulsion as well as cross bridging is a serious challenge that needs to be addressed especially for devices that would be based on near field coupling. They observed 4 tethers per binding site performed excellently in terms of

occupancy yield (97%) and positional precision (~1 nm) when they placed up to eighteen 10 nm AuNPs linearly onto a DNA origami tube with periodic center-to-center inter-particle distance of 14 and 29 nm. They also predicted that with increasing number of tethers, probability of site occupation would asymptotically approach towards 100%, and with 5 tethers it can be higher than 99%. These progresses in manipulation of the nanoparticle assemblies paved the way for further investigation of functional properties of these constructs.

Despite the fact that silver nanoparticles (AgNPs) have better plasmonic properties than AuNPs of the same shape and size, such as higher extinction cross section, reports involving DNA functionalization of these AgNPs and their employment is quite scarce in literature. SPR of AgNPs peaks around 390-420 nm depending on the size. They have good catalytic activity,[38, 39] interesting antibacterial activity,[40] and most importantly they are excellent candidate for enhancing Raman signal.[41-43] However there are several difficulties associated with DNA functionalization of AgNPs and limited their uses not as widely as that of AuNPs. AgNPs is chemically less stable and is susceptible to oxidation in the functionalization condition. Another reason is the lower Ag-S bond energy (217 ± 15 kJ/mol) compared to Au-S (254 ± 15 kJ/mol),[44] which makes it difficult to conjugate monothiol functionalized DNA to AgNPs. In the absence of a dense protective layer of DNA, the particles tend to aggregate in saline buffer. Mirkin's group demonstrated that instead of standard monothiol, a cyclic dithiol moiety can stabilize the particles that can stay suspended in NaCl concentration as high as 1 M.[45] Later Pal et al. introduced DNA with different numbers of phosphorothioate units (phosphorothioate modification is one P-O bond of the phosphate group in the DNA backbone is replaced

by a P-S) and came to the conclusion that 9 consecutive of such units provide best stability.[46, 47] The reliability of the method was further confirmed by constructing core-satellite type structure by hybridizing with DNA modified AuNPs. In a follow up paper AgNPs of diameter 30 nm were site-specifically organized on a triangle shaped DNA origami with precise control over inter-particle distances.[47] However, the usefulness of these DNA stabilized particles were not exploited further, which is partially attributed to the difficulties in obtaining pure constructs devoid of any free particles or free DNA origami. The gel electrophoresis commonly used for purifying AuNPs on DNA nanostructures tends to oxidize and destroy the particles during electrophoresis. Some further improvements of the assembly stability and purification protocols are required to enable the reliable and robust construction of AgNPs/DNA architectures.

Chiral arrangement of AuNPs leading to circular dichroic effects

In the recently years, complex DNA directed AuNP structures that display interesting optical properties have been reported. In 2011, Na Liu and Baoquan Ding groups in collaboration achieved producing distinct circular dichroism response by organizing AuNPs in a helical fashion.[48] They used a 2D rectangular origami and organized 10 nm AuNPs at specific locations along the diagonal direction, which was finally rolled up by connecting the opposite edges to obtain a tubular structure with the array of AuNPs arranged in helical architecture. In 2012, Tim Liedl's group achieved the same goal in a similar way by arranging AuNPs in a helical fashion on a tube-shaped DNA origami.[49] Both the right- and left-handed constructs showed distinct circular dichroism (CD) that matched quite well with the theoretically predicted values. They also

showed that when 16 nm particles were used, more red shifted and stronger CD signal was achieved compared to that using 10 nm AuNPs. This was attributed to the closer surface-to-surface distance between the adjacent particles that causes stronger near-field plasmonic coupling. It was further shown that upon deposition of a silver shell on the AuNPs the CD response could be further tuned. In 2013, Na Liu and Ding groups demonstrated another ways of producing chiral nanostructures[50] by placing identical AuNPs on both faces of the 2D rectangular origami in a tetrahedral fashion. Both right and left-handed structures were achieved as confirmed by CD spectra. Furthermore, Lan et al. demonstrated tailored CD response by building 3D nano-architectures composed of AuNRs on a 2D DNA origami.[51] The CD response was tuned by changing spatial configuration of the AuNRs, which, they claimed, could potentially serve as future chiral plasmonic ruler. The Liedl group reported switchable CD responses by toggling the orientation of the same construct as shown in their previous paper with respect to incident light.[52] Earlier this year, Liedl and Na Liu groups in collaboration fabricated a reconfigurable plasmonic nanostructure with AuNRs placed onto two interlinked DNA origami bundles at specific angles.[53] This smartly designed dynamic system is capable of switching between two conformations to tune the angle between the two bundles by DNA strand displacement, which was reflected in distinctive alteration in the CD spectra. They envisioned this to be an in situ probe for monitoring dynamic biological process.

Modulation of fluorescence by monomeric or dimeric AuNPs

As mentioned earlier, due to localized surface plasmon resonance of the metallic nanoparticle, upon interacting with visible light there is an enhancement in surface electric field that affects the local environment of a molecule localized close to the

surface. This effect is highly dependent on the shape, size and material of the plasmonic particles. The intensified electric field can enhance photoluminescence intensity if a fluorophore is placed in close proximity of the plasmonic NP. On the other hand, the fluorophores interact electronically with the localized surface plasmon, and open up faster non-radiative decay channels, resulting in severe quenching of fluorescence. The nature and mechanism of fluorescence enhancement or quenching has aroused curiosity among researchers for years. Although several theoretical models have been proposed,[54-57] their experimental validation, which requires well-controlled geometry and proper stoichiometry, was difficult. DNA origami directed assembly offers rigidity, addressability and sub-nanometer accuracy at the same time that provide unique opportunities.

Tinnefeld's group studied distance dependent quenching behavior of organic dye fluorescence in presence of AuNP on DNA origami.[58] In the single molecule measurement set up they observed energy transfer from ATTO647N to AuNP that follows an inverse fourth power dependence, in contrary to the traditional FRET that follows the inverse sixth power rule. Our group performed similar experiment between a 20 nm AuNP and fluorescent dye TAMRA,[5] although measured in bulk, and reinforced the possibility of analogous surface mediated energy transfer mechanism.

Enhancement of fluorescence has attracted considerable attention recently due to its potential applicability in single molecule detection system. Some major concerns with the increasingly popular single molecule detection systems are brightness and photostability of the fluorophore. Theoretically it is predicted that placing a chromophore in close proximity to a plasmonic NP or in the hot spot of two or more particles can

intensify fluorescence. Lithographically such nanogap has been generated before, but it is not only expensive but also incompatible to biological systems. Recently Tinnefeld group fabricated a system by incorporating two relatively large AuNPs (100 nm in diameter) ~ 23 nm apart onto a DNA origami, which eventually created a plasmonic hot spot and observed fluorescence enhancement up to 117 times from an ATTO647N placed between them.[59] This fluorescence intensity enhancement is accompanied with a substantial decrease of its fluorescence lifetime, reflecting a higher radiative decay rate constant, which means the fluorophore spends shorter time in its excited states.

As stated earlier photo-bleaching is one of the major problems in single molecule detection technique using dyes. Photo bleaching of a dye molecule happens in the excited electronic state due to the breakage of some chemical bond within the dye's molecular structure that disrupts the pi-electronic resonance network and results in a permanent dark state. It is attributed that spending less time at the excited state reduces the possibility of this mechanism and more photons can be harvested before the dye dies out. Indeed very recently Tinnefeld group observed reduced photo-bleaching of Cy5 in the presence of AuNPs.[60] When a dye is placed near an AuNP on the docking site of a DNA origami, they reported, smaller AuNPs like 20 nm hardly has any effect but interestingly larger AuNPs, such as 80 nm, by average can increase the number of harvested photons about five times from a single molecule before it stops fluorescing.

Surface enhanced Raman scattering

Another major application of plasmonic NPs is in enhancing resonance Raman signal. It was discovered decades ago that rough surface of silver or gold can induce significant enhancement of Raman signal, a phenomenon called surface enhanced Raman

scattering (SERS). Raman spectroscopy is especially appealing because of its capability to obtain unique fingerprint signals from distinct fluorescent or non-fluorescent molecules. But due to poor scattering cross section, the Raman signal without amplification from a surface molecule is hard to separate from the background noise. With the help of DNA nanotechnology directed assembly, recently several groups have achieved significant increase in Raman signal from fluorescence or non-fluorescent molecules.[4, 61-64] The main concept here is similar to the fluorescence enhancement: two or more large Au/AgNPs placed in close proximity behaved as a nanoantenna, creating a plasmonic hot spot with an intense local electric field at their junction. Without the unique addressability of DNA origami, this kind of nano-gap would be either randomly generated or orderly engineered with a high cost. Three recently published papers used the afore mentioned strategy using DNA templated assembly by placing fluorescent dyes (TAMRA, Rhodamine or SYBR-Gold) in between two AuNPs and showed several magnitude folds enhancement of SERS signal.[65-67] Pilo-Pais and coworkers used a slightly different strategy to improve Raman signal from a non-fluorescent molecule, 4-aminebenzenethiol.[67] Instead of using two particles, they employed four particles to create the plasmonic hot spot. However, it is challenging to assemble four particles in close proximity due to steric and electrostatic repulsion. They came up a rather clever strategy to accomplish that. At first, four 10 nm AuNPs were placed at the four corners of a rectangular origami (60 nm × 90 nm). This can be achieved relatively easily with a very high yield. In the next step the particles were grown larger by nucleated growth of a Ag shell on the top of the AuNPs surface by reducing silver nitrate. This created a tightly

packed cluster of four Ag/Au core-shell particles that generated a huge electromagnetic field enhancement at the center.

Besides the aforementioned important photonic applications, self-assembled noble metal NPs have the potentiality to replace conventional waveguides or photonic crystals. Klein et al. demonstrated that DNA origami directed assembly of AuNPs into linear, semi-rigid array can work as a waveguide transporting electromagnetic energy and converting it into nonradiating surface plasmon resonance.[68] The waveguide here works at sub-diffraction regime and is possible only when the NPs are placed close enough so that strong plasmonic coupling can take place between them. They produced DNA origami nanotubes that are nearly 400 nm long with a diameter of 6 nm, which were used to fabricate linear arrays of 10 nm AuNPs with varying inter-particle distances. The scattering spectra of the waveguides under white light illumination were examined with dark field microscopy, which showed significant shift of the plasmonic resonance especially in the longitudinal mode and the results were in good agreement with theoretical predictions. This kind of DNA driven waveguides can open new avenues toward large scale plasmonic circuitry that may serve the purpose of light focusing or light guiding in the sub-diffraction limit.

DNA directed assembly of quantum dots

Fluorescent semiconductor quantum dots (QDs) are another kind of NPs that are especially interesting in the field of nanophotonics. Their broad absorption but narrow and symmetric photoluminescence emission spectra, high quantum yield, excellent photostability, and resistance towards chemical degradation are some of the reasons behind their widespread application in bioimaging, labeling and sensing. In the past few

years, significant progress has been made in the area of conjugating QDs to biomolecules. In the literature, generally two different methods have been reported to decorate DNA nanostructures with QDs. One involves the biotin-streptavidin chemistry where commercial streptavidin coated QDs are self-assembled on pre-engineered DNA nanostructures displaying biotin molecules at specific locations. The other method is hybridizing DNA functionalized QDs to DNA structure carrying capture strands of complimentary sequence. Both processes have their respective merits and limitations. The first one is comparatively simpler but the polymer shell and large streptavidin proteins make the QDs considerably large and bulky. This is not desirable keeping in mind the importance of precision in distance between two particles in nanophotonics. However this can be overcome in the second method where short, linear DNA molecules are attached directly onto QD surface, but this generally involves multiple steps, including QD synthesis and ligand exchange or modification. Additionally the DNA oligomers have to be linked to the QD surface robustly so that during normal annealing process at high salt concentration they do not dissociate from QD surface resulting aggregation.

Sharma et al. from our group first reported streptavidin functionalized CdSe/ZnS QDs organized in periodic fashion on DNA tile based 2D array.[7] Due to lack of control over the size and specific boundary of these structures, DNA origami is more preferred in recent times. Bui et al. first reported assembly of streptavidin functionalized QDs on DNA origami tube at predetermined locations with full control over the number of QDs on each origami and the separating distance between them.[69] Ko et al. investigated the binding kinetics of these QDs to DNA origami quantitatively and established some thumb

rules that affect binding efficiency.[70] The same group further studied the binding process with single particle tracking system and evaluated the diffusion coefficient of fully formed or partially formed constructs without any additional purification.

On the other hand, our group reported a simple yet robust general method of DNA functionalization during shell synthesis on a pre-synthesized core QD. Deng et al. prepared a library of DNA conjugated QDs with emission maxima spanning wavelengths from UV to near infrared.[71] The DNA conjugated QDs were stable at high salt concentration and capable of retaining their high QY. They were further assembled on DNA origami with very high yield. Following this strategy QDs of multiple colors can potentially be organized on the same DNA structure just like a fluorescence bar code, which is tricky to achieve by the first method. Samanta et al. further extended it to real IR emitting QDs at 1200-1300 nm that were assembled on DNA origami as well, with decent yield.[72]

DNA directed assembly of heterogeneous hybrid nanomaterials

As mentioned before, DNA nanotechnology allows integration of diverse types of nanoparticles into the same platform. DNA functionalized QDs of different colors have been brought together that resembles formation of a molecule with atoms. Tikhomirov et al. observed efficient unidirectional energy transfer between QDs that are placed together with the help of double stranded DNA with controlled geometry, distance and stoichiometry.[73] AuNPs were also assembled with QDs by simple hybridization of the DNA on their surfaces.[74, 75] This method of preparing hybrid nanostructure is relatively less appealing since they produce a mixture of all possible products with divergent stoichiometry that are difficult to separate. More recently, Schreiber et al. constructed a

planet-satellite type structure consisting DNA functionalized QD as planet and AuNPs as satellites that are held together by DNA origami, however no photonic interaction among them was investigated.[76] Ko et al. constructed a more sophisticated system by bringing together different sized AuNPs and streptavidin appended QDs of two different colors on rectangular DNA origami.[77] By utilizing the unique plasmonic properties of AuNPs, they produced a smart system that is capable of engineering fluorescence lifetime. Recently Samanta el al. from our group integrated 30 nm gold nanoparticles and DNA functionalized QDs onto DNA origami with variable distances and showed the quenching effect of the large AuNP that works at long distances in the range of 10-50 nm.[78] This effect could potentially be used for long-range spectroscopic ruler.

Well-controlled quenching of fluorescence intensity and significant reduction in fluorescence lifetime are useful for sensing applications. However scientists are trying hard to achieve enhancement of fluorescence that could be very useful for imaging applications, where a stronger signal can subdue the background of auto-fluorescence in cells and tissues. Maye et al. reported an encouraging way to enhance fluorescence of CdSe/ZnS QD when it is linked to a AuNP of diameter 60 nm.[79] A 30 nm long double stranded DNA linked the two particles leading to 20-fold enhancement of QD fluorescence. Theoretically many more fold enhancement is possible if the QD can be brought closer to a large AuNP. The experimental realization of this still remains challenging.

Conclusions and perspectives

DNA directed self-assembly of nanomaterials has advanced fast in the past few years and has established its position on its own merit. Some highly sophisticated nanostructures now in our hands were only in imagination a decade ago. However along with its elegance and opportunities, challenges are intertwined, as always. Plasmonic nanostructures have tremendous potential to be used in biological systems. Plasmonically enhanced fluorophores can be of great use for bioimaging with better signal-to-noise ratio. IR emitting fluorophores are advantageous for tissue imaging, since tissues are transparent in the IR spectral region. But IR emitting dyes or QDs suffer from low QY, which can potentially be improved by plasmonic NPs. Nanostructures with plasmonic hot spot can be assembled on microfluidic devices that will be useful for detection of a diverse analysts. It has been also speculated that these types of nanoconstructs are capable of second harmonic generation (SHG).[80] SHG imaging technique is a burgeoning field but suffer from even lower cross-section than Raman scattering. DNA directed assembly of plasmonic nanostructures could provide more prospective to it. In addition, reconfigurable DNA nanostructures with external stimuli (such as small analysts or DNA or RNA strands) have already been reported. One challenge will be to employ these smart systems *in vivo* to monitor cellular processes. There is another emerging area of research where DNA solid matrices are being used in field effect transistor as gate insulator, as waveguides or for producing laser.[84, 85] Recently it has been demonstrated that DNA based solid film doped with rhodamine 6G on the nano- imprinted silica template can work as a distributed feedback laser (DFB).[86] The imprinted grating turned the broad emission of rhodamine into a sharp peak with very narrow line width at the pumping threshold fluence of just a few mJ/cm^2. This kind of biodegradable and water soluble

devices can be very useful in stimulating cellular components or in the areas where physically transient light emitting device is necessary. Instead of random matrix of genetic DNA, DNA tile based periodic assembly of nanoparticles or dyes can be a beneficial addition to this field.

Many unique hybrid nanomaterials have been synthesized recently. Their functionalization with information bearing biomolecules and consequent directed self-assembly into well-controlled nano-architecture can open up new directions of research. There are endless possibilities and we are all poised to explore more into this fascinating arena.

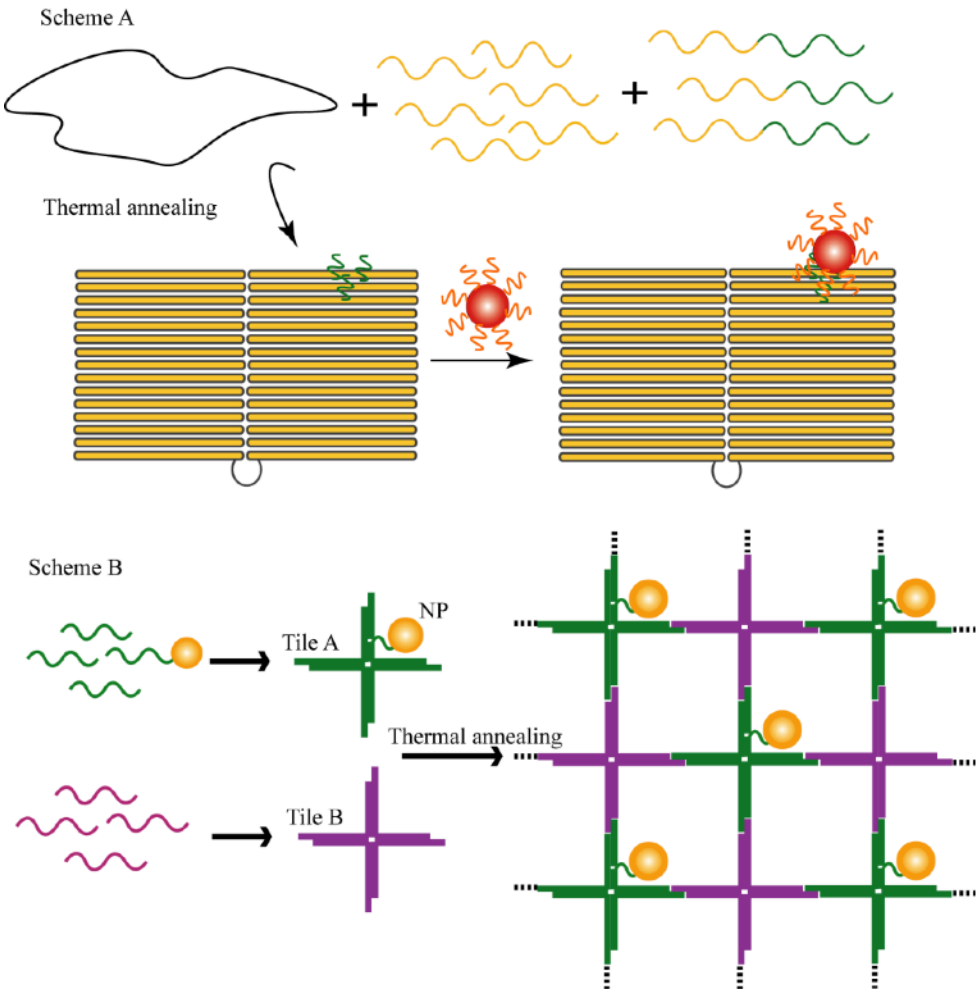

Figure 1. Schematic depicting two ways of NP incorporation into DNA nanostructures. Besides DNA functionalization of the particles (not shown here) both schemes A and B involve two annealing steps. In Scheme A, which involves DNA origami, the first step is to construct the origami replacing some of the staple strands with capture strands having complimentary sequence of the DNA displaying on the NPs. In the second step purified origami is mixed and annealed with the DNA conjugated NPs in buffer solution either at room temperature or annealed over a mild temperature gradient. In scheme B, which describes DNA tile based array, first small units composed of few ssDNA, called tiles, are formed that carries the NP where the single copy of DNA displaying on the NP is part

of the tile. Individual tiles are then annealed over a temperature gradient that ultimately forms the polymeric structure creating an array of NPs.

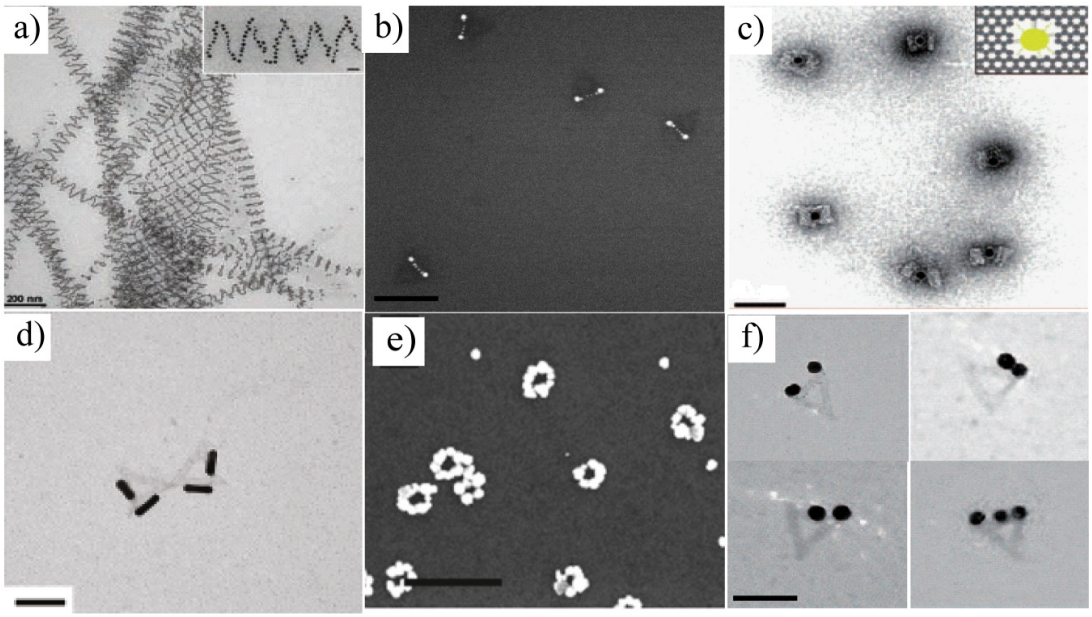

Figure 2. DNA tile and origami based assembly of plasmonic NPs in various fashions. (a) TEM image shows DNA tile based formation of tubular structures comprised of 5 nm AuNPs. Scale bar 200 nm. (b) SEM image displaying DNA origami based assembly of spherical AuNPs of different sizes into a self-similar chain. Scale bar 200 nm. (c) TEM image of 10 nm AuNP captured inside a 3D origami resembling a cage. Inset: design demonstrating the orientation of individual double helices and capture strands binding to the AuNP. Scale bar 50 nm. (d) TEM image showing two AuNRs (average length 42.6 ± 6.5 nm and diameter 12 ± 3.5 nm) organized on triangular origami at a 90° angle with controlled inter-particle distance. Scale bar 100 nm. (e) Representative SEM image of metal ring structure fabricated by self-assembly of AuNPs on rectangular DNA origami followed by nucleated chemical deposition of a silver shell. Scale bar 500 nm. (f) TEM image displaying 30 nm AuNPs placed site-specifically on triangular DNA origami with varying inter-particle distances. Scale bar 100 nm. (a) reproduced with permission from reference 81 © 2009, AAAS. (b), (d), and (e) reproduced with permission from

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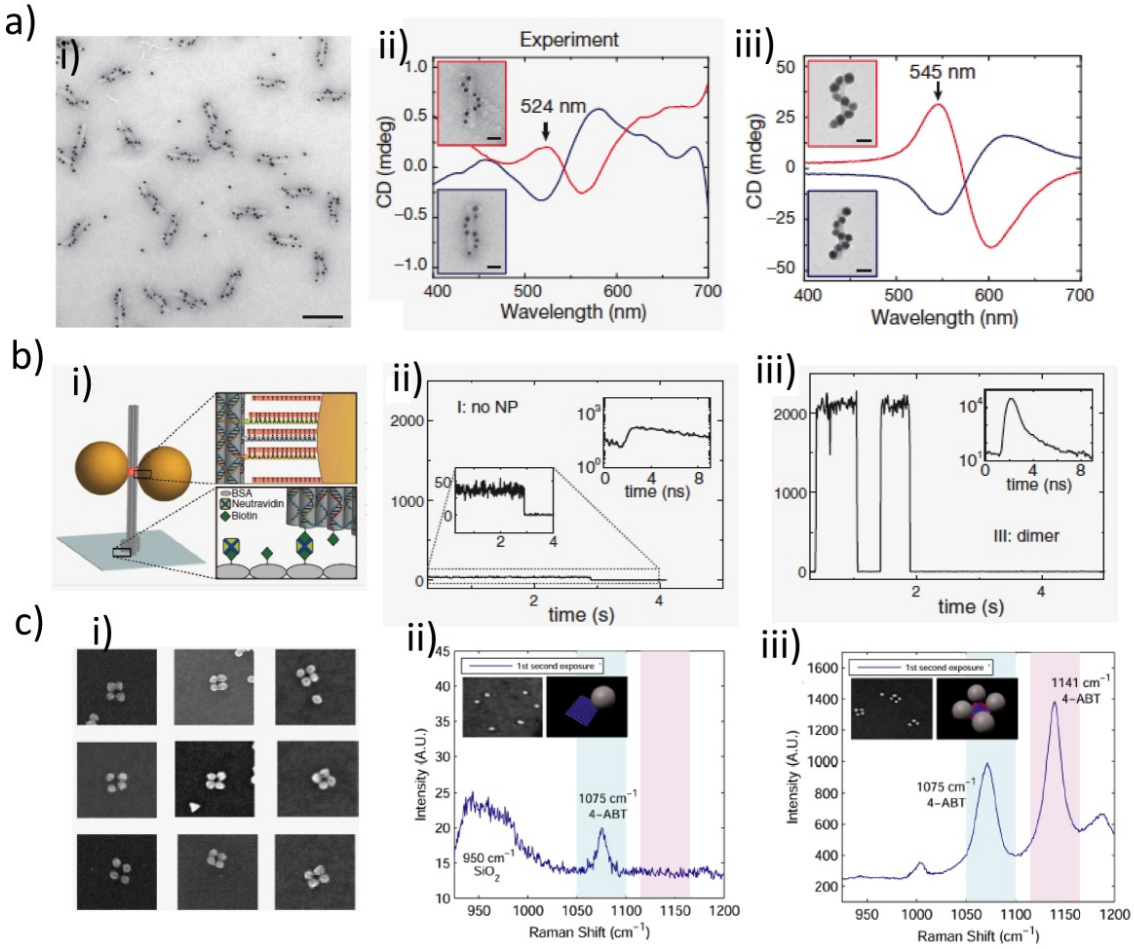

Figure 3. Several functional devices constructed with NPs assembled on DNA origami. Panel (a) (i) TEM image of DNA origami tube decorated with 10 nm AuNPs in a left handed helical conformation. (ii) and (iii) demonstrating the CD spectra obtained from two different handed constructs comprised of 10 nm and 16 nm AuNPs, respectively. In case of larger AuNPs the CD signal is much stronger due to intense plasmonic interaction among the particles. Reproduced with permission from Ref. 49 © 2012 NPG. Panel (b) (i) Schematic depicting arrangement of two AuNPs forming a plasmonic hot spot on a pillar shaped DNA origami. The red dot represents the fluorescent dye ATTO647N placed in the hot spot. In (ii) and (iii) fluorescence enhancement is quantitatively

presented. Photon count rate has increased nearly 50 times in (iii) compared the case of in the absence of the AuNPs shown in (ii). Reproduced with permission from Ref 59© 2012 AAAS. Panel (c) (i) SEM image exhibiting a tetramer of AuNPs attached on rectangular DNA origami then followed by chemically deposition of Ag. Proximity of multiple plasmonic nanoparticles helped to improve Raman signal of the pyrene molecule embedded onto the origami as displayed in (iii) compared to only one particle showed in (ii). Reproduced with permission from Ref 67 © 2014 ACS.

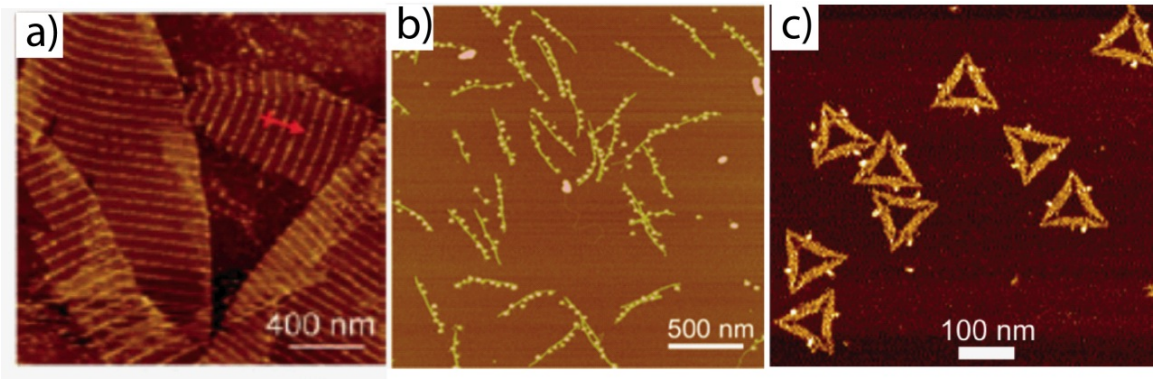

Figure 4. AFM images exhibiting self-assembled QDs onto DNA nanostructures. (a) Streptavidin functionalized CdSe/ZnS core/shell QDs are patterned on 2D DX DNA tile array displaying biotin at specific repetitive parallel lines. (b) Linear organization of the streptavidin functionalized QDs on 6-helix bundle DNA origami. (c) DNA conjugated core/shell CdTe/CdS QDs organized on triangular shaped DNA origami, one on each side. (a) reproduced with permission from Ref 7 © 2008 Wiley. (b) and (c) reproduced with permission from Ref 69 and 71 © 2010 and 2012 ACS, respectively.

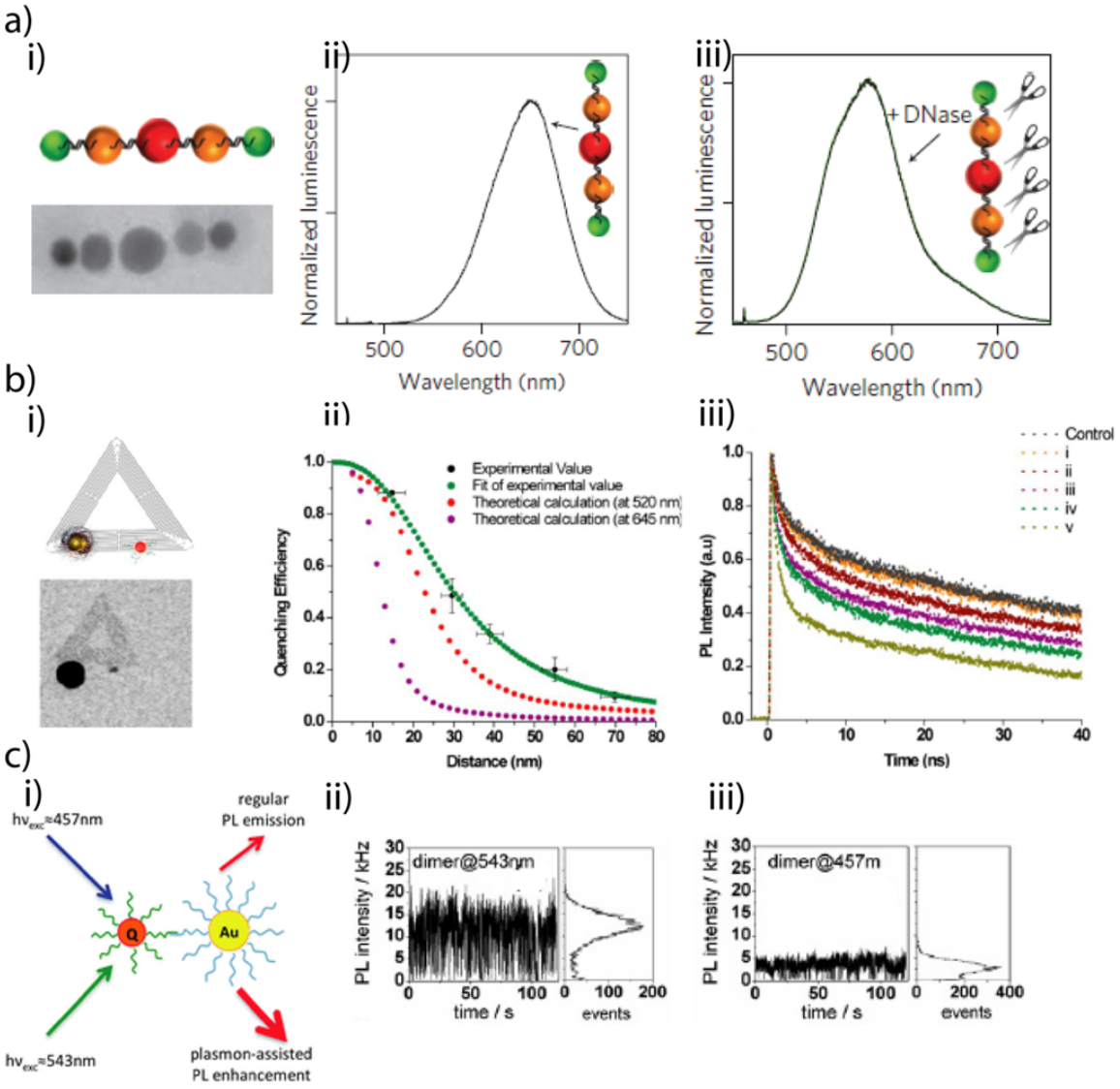

Figure 5. Panel (a) (i) Schematic depicting assembly of different colored QDs in a linear configuration and the corresponding TEM image. (ii) PL emission spectra of the linear construct showing efficient energy transfer from the green and orange QDs to the red QD. (iii) PL emission spectra of the constituent released QDs after DNase digestion. Reproduced with permission from Ref 73 © 2011 NPG. Panel (b) (i) Schematic illustrating 1:1 integration of 30 nm AuNP and DNA appended QD at varying distances on a triangular origami and one representative TEM image. (ii) QD Fluorescence quenching efficiency of the AuNP that is effective up to 60 nm. (iii) Time dependent

fluorescence decay that changes significantly by varying distances. Reproduced with permission from Ref 78 © 2014 ACS. Panel (c) (i) Schematic portraying construction of QD-AuNP heterodimer. (ii) Time trajectory of fluorescence intensity, the dimer was excited with 543 nm laser at the plasmon bands of the AuNP, which induced a higher fluorescence of the dye. (iii) The same dimer when excited at 457 nm, where the AuNPs have very low absorption, which did not affect the fluorescence of the QD, resulting much lower fluorescence intensity.

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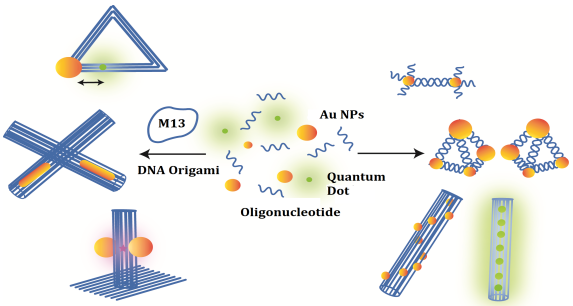
TOC figure



Description:

A comprehensive review of DNA nanostructure directed self-assembly of nanoparticles that have significantly contributed to the field of nanophotonics.

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