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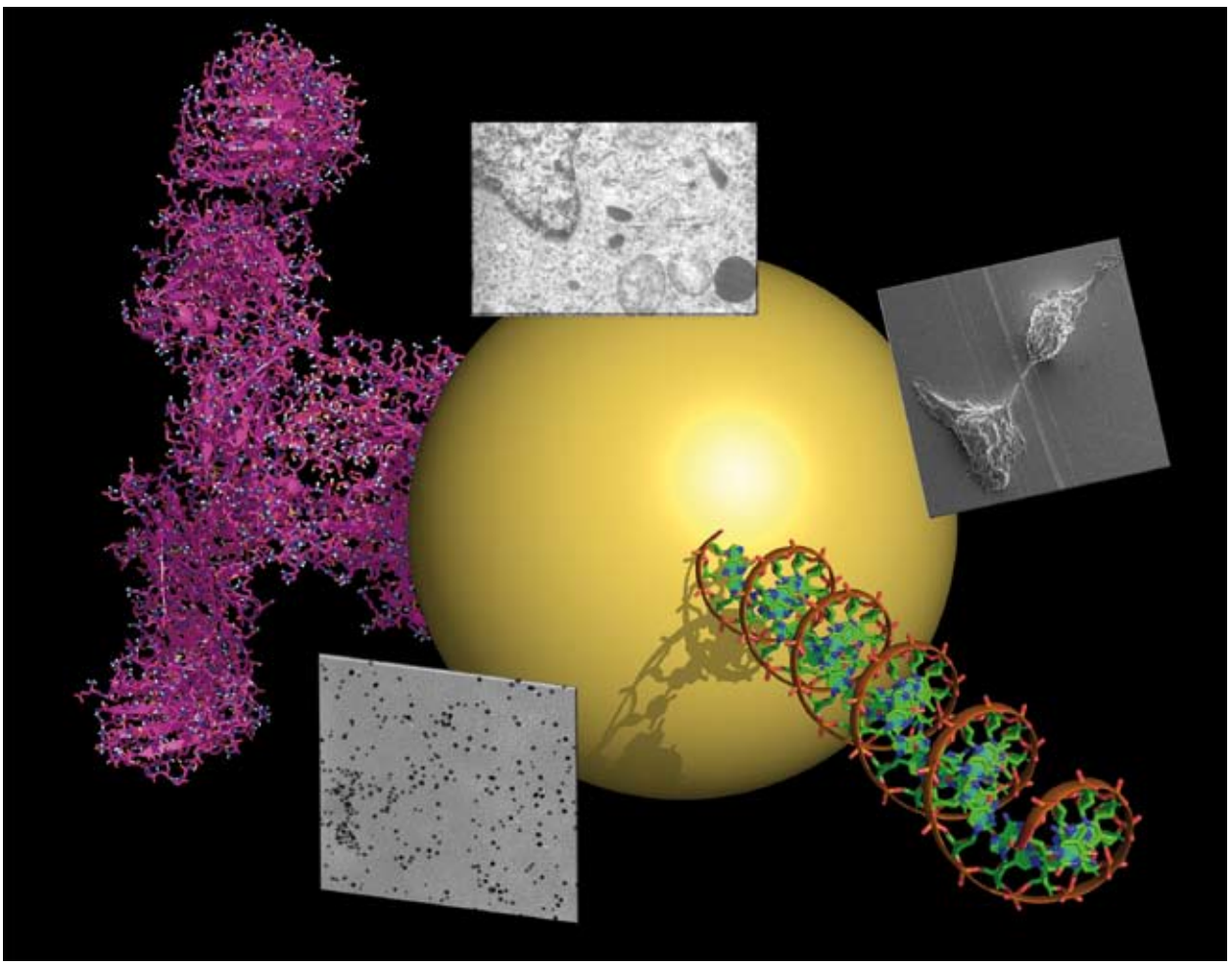

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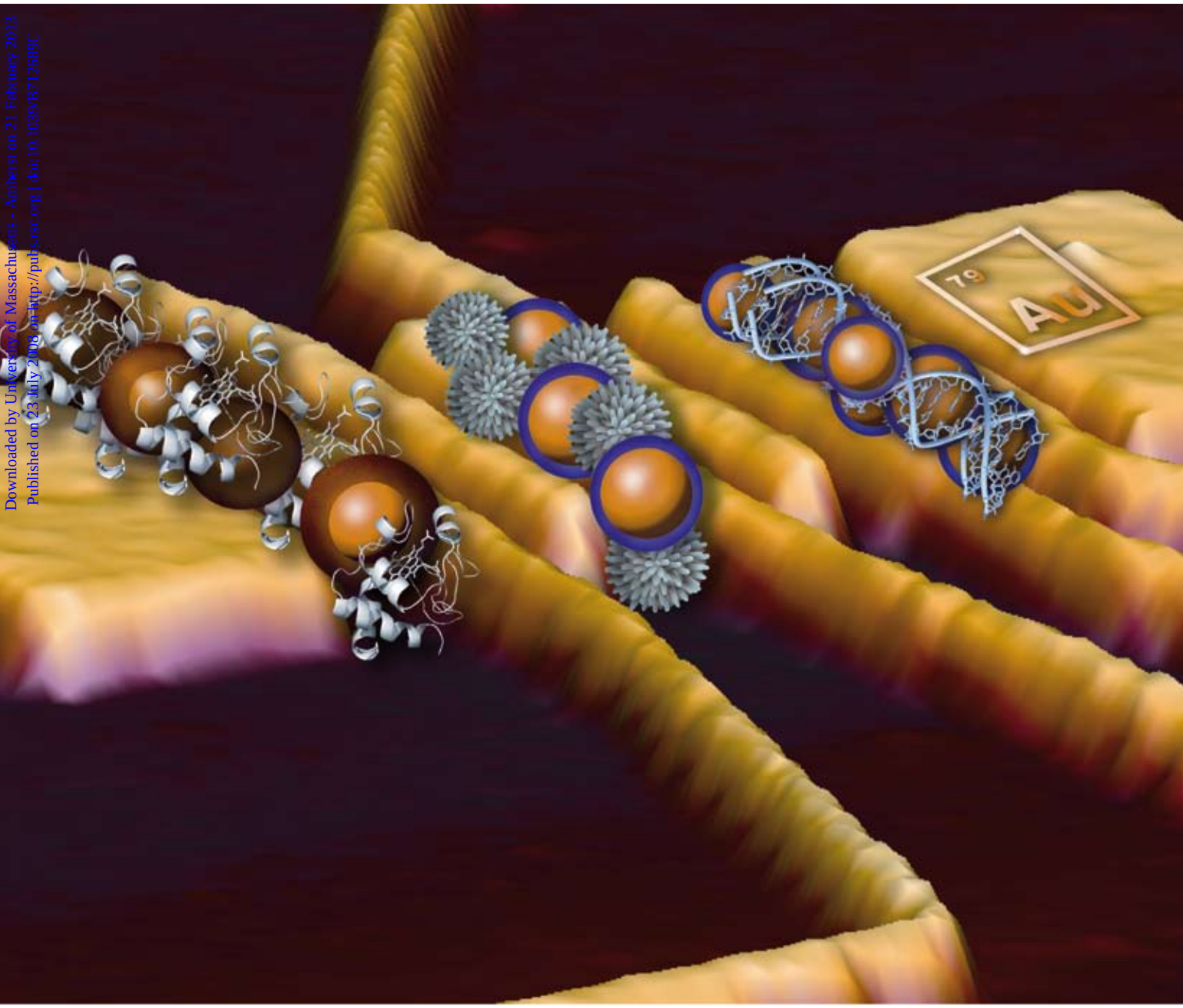

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Polymer and biopolymer mediated self-assembly of gold nanoparticles†

Yuval Ofir, Bappaditya Samanta and Vincent M. Rotello*

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Gold nanoparticle–polymer composites are versatile and diverse functional materials, with applications in optical, electronic and sensing devices. This *tutorial review* focuses on the use of polymers to control the assembly of gold nanoparticles. Examples of synthetic polymers and biopolymers are provided, as well as applications of the composite materials in sensing and memory devices.

1. Introduction and scope

Nanomaterials have a wide range of applications in the areas of sensors, electronics, and optical materials. The nanoscopic dimensions of these materials provide unique physical properties[1,2] that are often completely different than those observed for their respective bulk materials. Metal and semiconductor nanoparticles (NPs), in particular, feature interesting and useful quantum-confined properties including novel electronic, optical and chemical characteristics. Metal and semiconductor NPs are generally passivated by an organic monolayer that protects them from agglomeration while also facilitating tailoring of chemical properties through organic synthesis. The overall properties of NP-based systems can therefore be tuned *via* control of intrinsic features of the NPs such as shape, size and core material, as well as through environmental features like interparticle spacing and dielectric environment.

Substantial effort has been devoted to organizing NPs in one, two and three dimensions. The ability to create NP networks, arrays and composites, however, depends on our ability to fully understand and control the assembly process of these materials. Incorporation of both "bottom-up" (*e.g.*, self-assembly) and "top-down" technologies (*e.g.*, lithographic techniques) in patterning and controlling spatial assembly of NPs and their composites is a growing field of research. Synergy between these two approaches provides new directions for the creation of functional materials and devices.

Gold nanomaterials have attracted particular interest owing to their ease of synthesis and functionalization, chemical stability, low inherent toxicity (biocompatibility), and tunable optical and electronic properties (absorption, fluorescence and conductivity).[3] In this review, recent progress in the field of polymer-mediated 'bricks and mortar' assembly of gold NPs (AuNPs) will be described, summarizing assembly using linear, branched, and block copolymers, as well as recent studies using biopolymers such as proteins and DNA (Fig. 1). We will also discuss emerging applications of these composite materials in sensors and devices. Since this tutorial review is a part of the special issue on gold, we will focus on the assembly of AuNPs using polymers, with synthesis of the particles covered by other reviews in this issue.

The polymer scaffold in AuNP–polymer composites can serve three purposes: (1) assembling the NPs into composite material, (2) serving as a matrix that induces ordering and anisotropic orientation in clusters and on surfaces, and (3) acting as a functional element (*e.g.* possess an electronic property). The chemical approach for the construction of these composites allows the polymers to serve any or all of these functions.

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(top) Vincent M. Rotello; (bottom) Bappaditya Samanta (left) and Yuval Ofir

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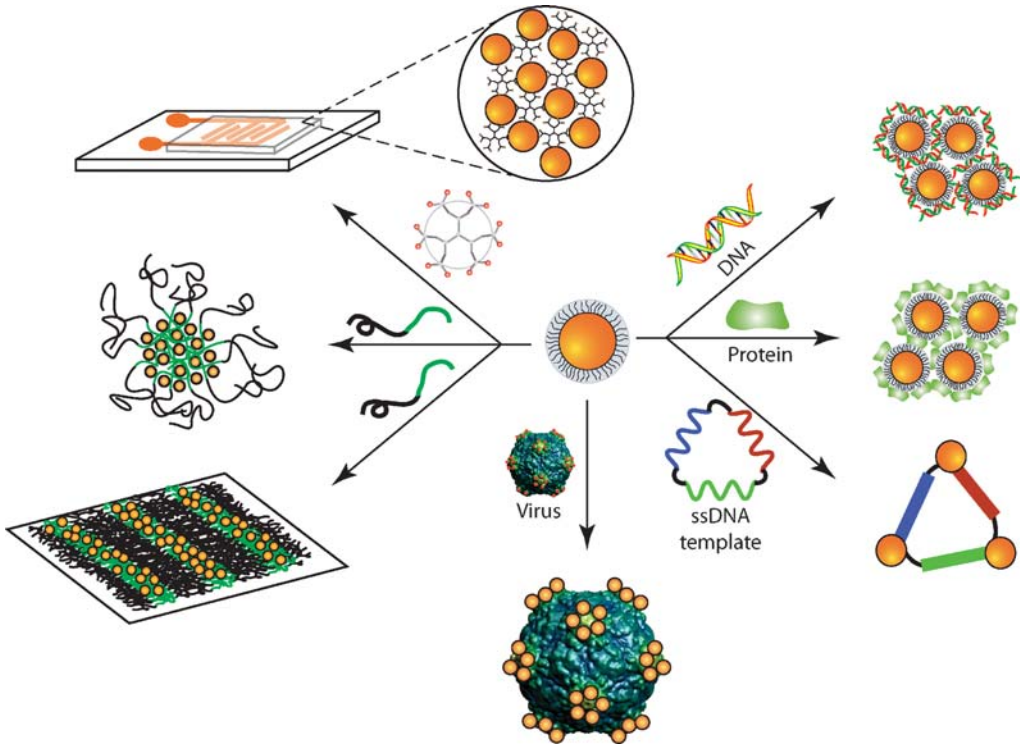

Fig. 1 Schematic representation of polymer-mediated assembly of AuNPs.

Chemical synthesis and post-modification of both the polymer and the AuNP organic monolayer can enhance the affinity between the building blocks, rendering the components compatible and facilitating self-assembly. For the polymer component, both polymerization of functionalized monomers or post-polymerization functionalization can be used.[4] For the AuNPs, either direct synthesis or place exchange reactions of functional/complex organic ligands can used to install the required properties, as described elsewhere in this issue.

Self-assembly requires interactions favorable enough so that stable equilibrium or near-equilibrium structures are formed, but not so strong that materials become trapped in unstructured energetic local minima. The intermolecular toolkit of interactions include hydrogen bonding, metal coordination, electrostatic attraction/repulsion, dipolar interactions, Van der Waals forces, and hydrophobic interactions.[5,6] These interactions can both induce NPs into controlled structures and modulate their physical responses.[7,8] Biomolecular assembly[9] can likewise be utilized to incorporate the intrinsic properties of biomolecules into nanocomposite structures.

2. Assembly of AuNPs using synthetic polymers

Supramolecular chemists have developed numerous synthetic methods to attach non-covalent host–guest dyads to nanoparticle 'bricks' and a wide variety of 'mortars' *e.g.* dendrimers, polymers, surfaces, proteins, nucleic acids and drug molecules. Each of these systems brings both structural and physical properties for the creation of functional nanosystems.

2.1 Layer-by-layer assembly processes

Layer-by-layer (LbL) assembly is a simple and elegant technique for fabricating structural and functional thin films on both flat and curved substrates. LbL uses sequential adsorption of complementary materials using electrostatics, hydrogen bonding and other complementary interactions. As an example, Crespo-Biel *et al.* developed various patterning strategies to create polymer-assembled NP films on cyclodextrin (CD)-functionalized self-assembled monolayers (SAMs) through host–guest (CD–adamantyl (Ad)) interactions.[10] CD modified AuNPs (CD–AuNPs) and adamantyl-terminated poly(propylene imine) dendrimers (Ad–PPI) were used for supramolecular LbL assembly process in two separate processes (Fig. 2).

The first approach of Crespo-Biel *et al.* used nanotransfer printing from poly(dimethyl siloxane) (PDMS) stamps that were pretreated with UV–ozone, resulting in a slightly negatively charged surface. This weakly charged surface was used for the formation of a LbL supramolecular assembly consisting of CD–AuNPs and Ad–PPIs. Due to the stronger interaction of Ad–PPI and CD-SAM, adsorbed LBL assemblies on the PDMS stamps were completely transferred onto a full CD-SAM on top of a silicon substrate by microcontact printing. In the second approach (Fig. 2) nanoimprint lithography and a lift-off process were integrated to directly form the LbL multilayer on a silicon substrate. The pre-patterned poly(methyl methacrylate) (PMMA) structure obtained through nanoimprinting lithography served as physical barrier for the formation of the CD-SAM. The CD-SAM was formed on the exposed native silicon oxide through a three step functionalization process. The LbL assemblies of CD–AuNPs and Ad–PPIs were printed over the entire area, followed by a lift-off process in acetone that yielded the patterned LbL film.

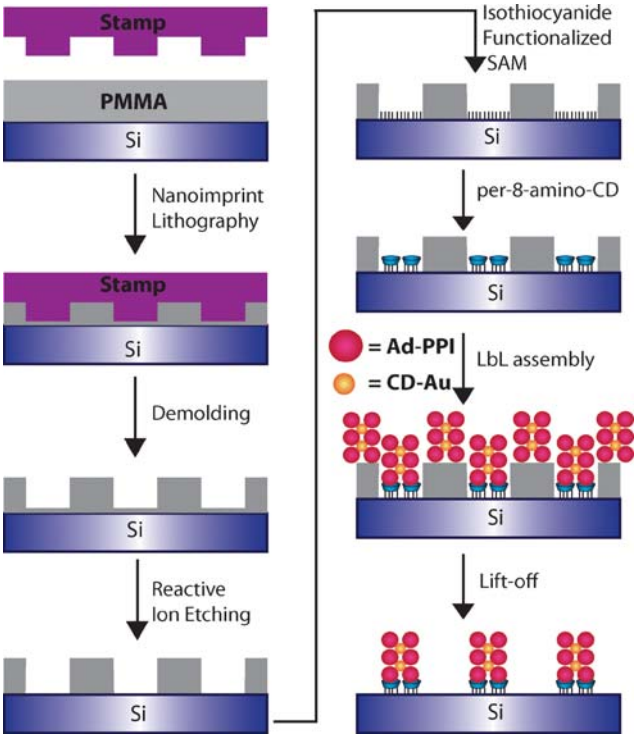

Fig. 2 Preparation of patterned LbL assemblies using nanoimprinting lithography, CD-SAM formation, and lift-off process (Adapted from ref. 10).

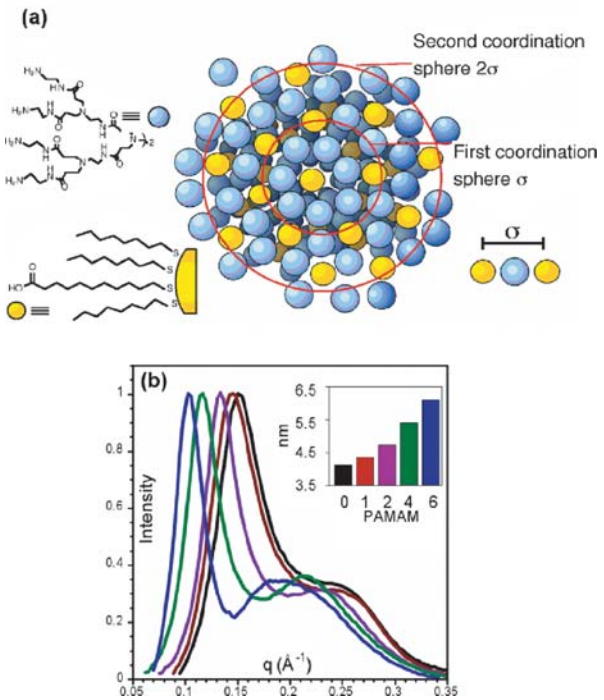

Fig. 3 (a) AuNPs assembly using PAMAM dendrimers. (b) Small-angle X-ray scattering plots, demonstrating increasing interparticle distances with increasing dendrimer generation.

2.2 Dendrimer-mediated assembly

A variety of assemblies between dendrimers and AuNPs have been reported. An approach developed by Crooks *et al*., uses poly(amidoamine) (PAMAM) dendrimers as a template for the synthesis of the AuNPs, which can later be extracted from within the dendrimers.[11] In a second approach presented by Astruc *et al*., a variety of dendrimers have been used as ligands on AuNPs after place exchange reactions. For example, tri- and nonaferrocenyl thiol dendrons were installed on AuNPs through place exchange reactions to create phosphate sensors.[12]

Dendrimers can also be used as integral components in NP assembly. The Rotello group has studied the self-assembly of AuNPs with PAMAM dendrimers using electrostatic attraction, demonstrating direct control of interparticle spacing based on dendrimer generation.[13] Salt bridge formation between the dendrimer surface amine groups and the carboxylic acid functionalized AuNPs provided thin films of AuNPs spaced by PAMAM dendrimers, providing a versatile means to control the interparticle spacing (Fig. 3).

The surface plasmon resonance (SPR) properties of metallic NPs have recently been exploited in optoelectronic materials and sensor applications.[3] In general, the wavelength of the SPR band is dictated by multiple factors including solvent, volume, and dipolar coupling. Through the self-assembly strategies described above, dendrimers were used as spacers to control interparticle spacing and hence modify dipolar coupling between the particles (Fig. 4).[14] UV-vis spectroscopy was used to analyze the SPR of each particle–PAMAM sample, demonstrating the modulation of dipolar interactions upon assembly.

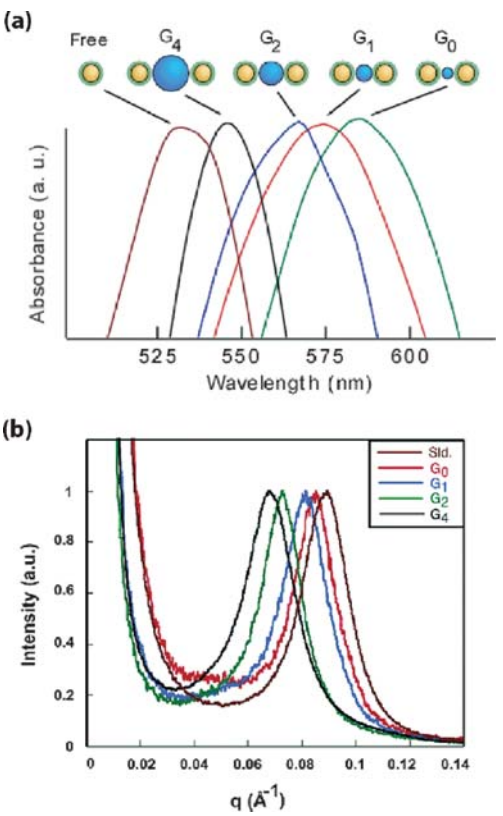

Fig. 4 UV-visible (a) and SAXS (b) studies on thin films of AuNPs assembled with G_0 through G_4 dendrimers.

The SPR showed a steady blue shift as the AuNPs were assembled with dendrimer G0 through G4, demonstrating the use of self-assembly to tune plasmonic properties.

2.3 Linear and diblock polymers and copolymers

Self-assembly of NPs in well-ordered 2D arrays represents a major goal in microelectronics, providing access to addressable components for high density memory devices and integrated circuits. Schmid *et al.* have reported on the ability to obtain both cubic and hexagonal packing arrangements of sulfonic acid-functionalized AuNPs using substrates coated with poly(ethylene imine) (PEI).[15] It was suggested that the two types of crystalline structures of the PEI were responsible for the templation, effectively ordering the AuNPs in arrays.

A different approach to the ordering of AuNPs using polymer thin films was demonstrated by Sita and co-workers,[7] using the periodic structure formation exhibited by phase segregated block copolymers. Polystyrene-*b*-poly(methyl methacrylate) (PS-*b*-PMMA) was thermally annealed to induce microphase separation, providing cylindrical PMMA features surrounded by a hydrophobic PS matrix. Alkanethiol-passivated AuNPs in toluene–ethanol solution placed on the film for 30 s resulted in selective deposition of the AuNP onto the non-polar PS domains, driven by the preferential interaction of the AuNP with the non-polar PS domain.

Balazs and co-workers have used simulations to predict the behavior of NP–polymer composites.[16] The work modeled mixtures of an AB diblock copolymer with hard NP spheres that are chemically compatible with the A blocks. The effects of NP size and volume fraction on the phase behavior of the system and the spatial segregation of the NPs within the A-type domains were explored. When the size of the NPs was comparable to the radius of gyration of the minority (A) block, the formation of new superstructures was predicted, where the NPs self assemble inside the copolymer micelles. The thermodynamic behavior was predicted to be governed mainly by entropic factors. These theoretical predictions were recently confirmed experimentally by Thomas and co-workers using poly(styrene-*b*-ethylene propylene) (PS-*b*-PEP) diblock copolymers that form alternating layers of PS and PEP.[17] It was shown that 3.5 nm AuNPs dispersed within the polymer matrix segregated to the interfacial boundary between the PS and PEP domains, while 21.5 nm silica NPs were concentrated at the center of the PEP domains.

The formation of a patterned surface through selective segregation of NPs onto one domain of a block copolymer film can be used to produce complex 2D NP arrays in a controlled fashion. However, the resulting NPs assembly is usually fragile and loses its structure. Shenhar *et al.* used an efficient and mild cross-linking protocol based on orthogonal self-assembly strategy to provide stable AuNP structures, which was applicable to a large variety of NP core and periphery functionality (Fig. 5).[18] Terpyridinyl (Terpy)-functionalized AuNPs were assembled onto PS-*b*-PMMA film. Similar to the findings of Sita and co-workers, these hydrophobic NPs preferentially bind to the relatively non-polar PS domains. Crosslinking of the assembled AuNP film was performed by immersing the sample into an ethanol solution of $[Fe(H_2O)_6(BF_4)_2]$, resulting in the formation of iron diterpyridine ($Fe(Terpy)_2^{2+}$) complexes between AuNPs. The robustness of the crosslinked film was demonstrated through solvent swelling experiments. It was shown that the sample dipped in the iron solution still maintained organized superstructure upon the swelling of the polymer film by chloroform vapor; whereas the AuNP structure of the control sample

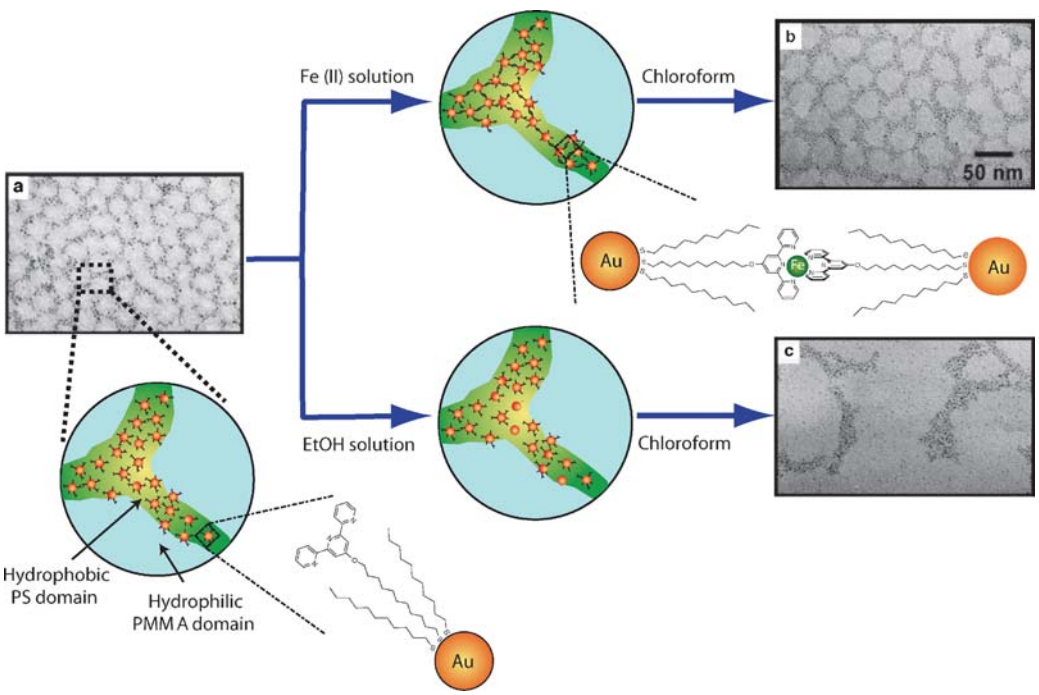

Fig. 5 TEM micrographs of (a) hexagonal patterns of Terpy-functionalized AuNPs on PS domain in a PS-*b*-PMMA film. (b) Fe-treated crosslinked samples, and (c) ethanol-treated samples after swelling in the chloroform vapor.

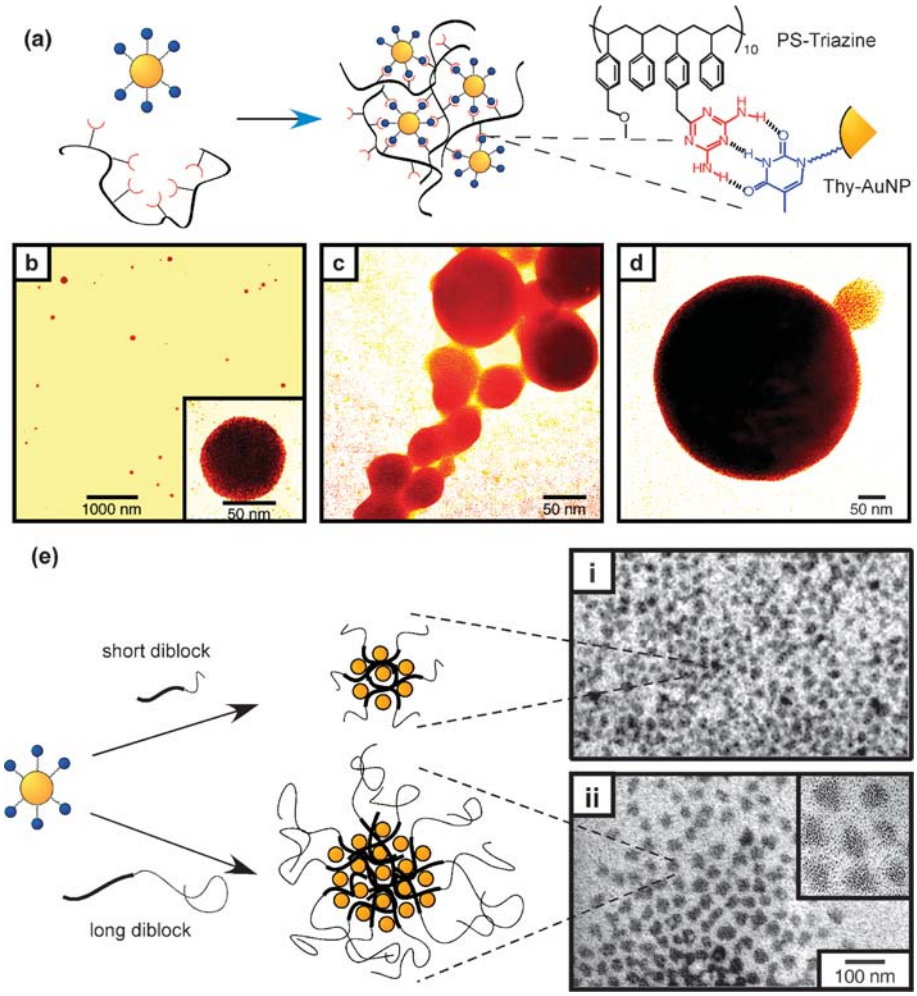

Fig. 6 (a) Schematic of recognition-mediated AuNP–polymer assembly. TEM of Thy–AuNP/Triaz–PS aggregates formed at (b) 23 °C, (c) 10 °C, and (d) −20 °C. (e) PS-*b*-Triaz-PS diblock copolymers used to control the aggregate size: (i) TEM of 13 nm size aggregates formed by assembly with short diblock copolymer (14k/14k), (ii) TEM image of 19 nm aggregates formed by assembly with long diblock copolymer (30k/28k).

dissociated due to the increased mobility of the underlying polymer film swollen by the chloroform vapor.

Molecular recognition based on multi-point hydrogen bonding interactions provides an effective means for assembling materials under near-equilibrium conditions. Rotello and co-workers have utilized AuNPs and polymer scaffolds functionalized with complementary hydrogen bonding recognition units (Fig. 6a–d).[19] Thymine-functionalized AuNPs (Thy–Au) were assembled in non-polar solvents with the complementary diaminotriazine-derivatized polystyrene (PS–Triaz) to form spherical aggregates. The diameter and morphology of these aggregates strongly depended on the temperature of the assembly process. When ambient conditions were used, discrete spheres of *ca.* 100 nm were formed; at 10 °C larger aggregates were obtained, forming interconnected networks, and at −20 °C discrete giant spheres were observed, measuring 0.5–1 μm in diameter and comprising 0.5–6.0 million individual NPs (Fig. 6b–d). In a later contribution, Frankamp *et al.* have shown the versatility of the system by using a diblock copolymer system.[8] The use of recognition-functionalized diblock copolymer provided not only the formation of nanometre aggregates but also precise control of the size of AuNP aggregates by changing the length of the diblock copolymer (Fig. 6e).

Another approach to control the structures of self-assembled block copolymers and AuNPs was recently shown by Wooley, and Pochan *et al.*[20] The authors kinetically manipulated the charged, amphiphilic triblock copolymers poly(acrylic acid)-*block*-poly(methyl acrylate)-*block*-polystyrene (PAA-*b*-PMA-*b*-PS) in solution to generate different nanoscale structures utilizing block copolymer chemistry (Fig. 7). The organization of the block copolymers relies on divalent organic counter ions and solvent mixtures to control the formation of complex one-dimensional structures using tetrahydrofuran (THF)–water mixed solvents and organic diamines. Amine-functionalized AuNPs were then incorporated into the PAA block based on electrostatic attraction, forming AuNP stripes (Fig. 7b and c).

Recently, Rubinstein and co-workers have used amphiphilic Au nanorods bound to PS to assemble the Au nanorods into structures with varying geometries (Fig. 8).[21] The hydrophilic nanorod body tethered with hydrophobic polymer chains at both ends provides what amounts to a triblock copolymer. The central rigid hydrophilic block is formed by a Au nanorod

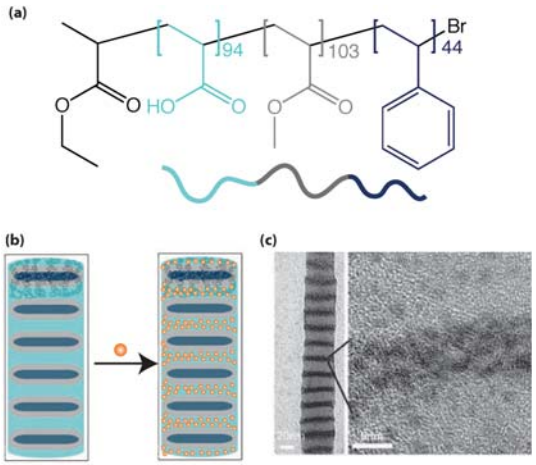

Fig. 7 PAA-*b*-PMA-*b*-PS polymer (a) that can kinetically self assemble into a striped nanowire structure (b) that can later be incorporated with cationic AuNPs interacting with the negatively charged PAA block (Reprinted with permission from ref. 20).

covered with a double layer of surfactant (trimethylammonium bromide (CTAB)), and the flexible hydrophobic side blocks are formed by thiol-terminated polystyrene molecules strongly anchored to the ⟨111⟩ gold facets at the ends of the rod. The self-assembly was solvent-controlled, and both tunable and reversible. The Au nanorod species could be organized into a range of different structures (*e.g.* rings, linear and bundled chains, and nanospheres with two dimensional walls), owing to the difference in triblock composition and structure.

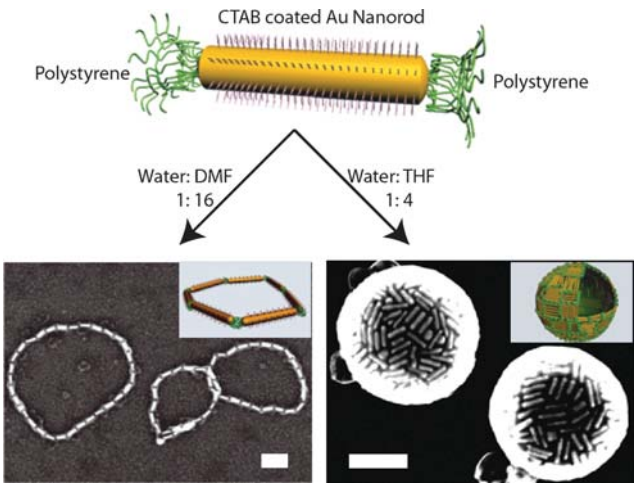

Fig. 8 (a) Self-assembly of polymer-tethered Au nanorods in selective solvents. An amphiphilic Au nanorod self-assembles into ring structures and nanospheres (Reprinted with permission from ref. 21).

3. Biopolymer-mediated nanoparticle assembly

3.1 DNA-mediated assembly

DNA provides a pragmatic platform for assembly of NPs into ordered nanomaterials because of its sequence programmability, selective molecular recognition ability, and the relative rigidity of its double-helical form. In this review, we will focus on assembly of AuNPs using two different approaches for the assembly process, namely DNA hybridization and electrostatic interaction.

NPs assembly based on DNA hybridization. Labeling AuNPs with ssDNA can be used to create multimeric networks and chain-like structures through sequence-specific DNA hybridization.[22,26] This approach leads to assemblies of AuNPs with controlled spatial arrangement of two or more distinct AuNPs.[23] Schultz *et al.* showed that AuNPs modified with ssDNA could be arranged into homodimeric and homotrimeric assemblies based on Watson–Crick base-pairing interactions.[24] In another report, they examined three other different possibilities in generation of heterodimeric and heterotrimeric AuNP aggregates (Fig. 9).[25] The first involved the use of two complementary 5′-ssDNA–AuNP conjugates to form a double-stranded AuNP–dsDNA structure (Fig. 9a). In the second approach, 5′-ssDNA–AuNP conjugates were assembled onto an unmodified template strand (Fig. 9b) resulting in dimers and trimers. In the third approach, two complementary oligonucleotides, synthesized with either one or two thiols extending from the C-5 position of deoxyuridine nucleotides, were used to create trimers. These oligonucleotides co-linearly arranged three AuNPs along one face of the double helix, with at least ten base pairs of dsDNA on each side of the modified nucleotides (Fig. 9c). More recently, Mao *et al.* have extended this method, and used longer linear DNA scaffolds containing repeating sequences, to template a linear array of AuNPs.[26]

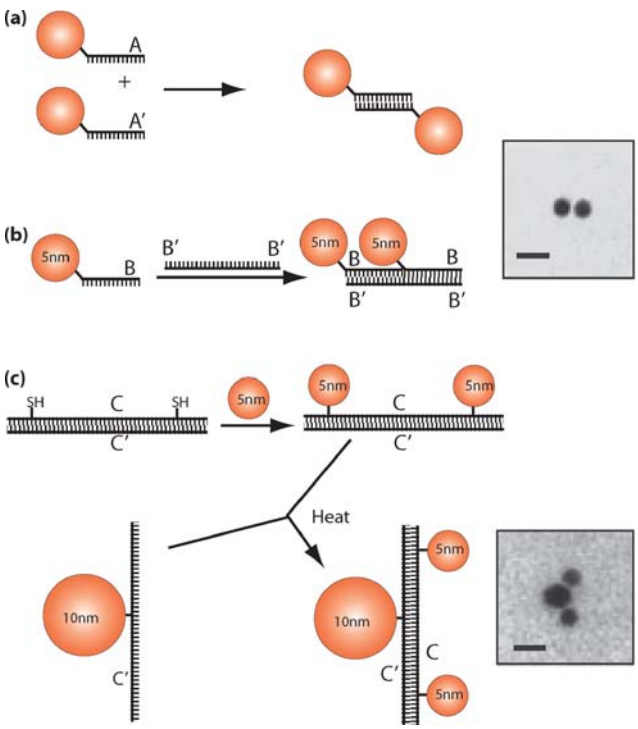

Fig. 9 Synthetic strategies (a–c) for AuNPs assembly based on DNA double strand formation. TEM images showing the dimer (b) and trimer (c) formation. The labels A′, B′, and C′ denote oligonucleotide sequences complementary to sequences A, B, and C, respectively (reprinted in part with permission from ref. 25).

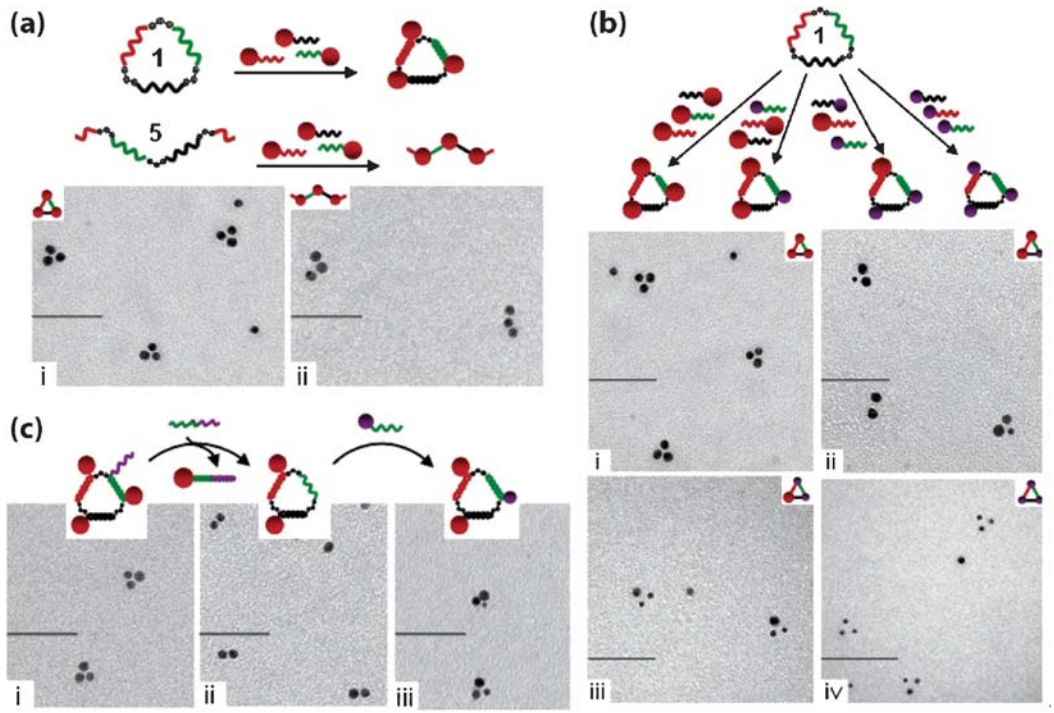

Fig. 10 (a) Organization of AuNPs with DNA cyclic oligomer **1** into triangles and linear oligomer **5** into open linear assemblies. (b) Use of **1** to generate triangles of (i) three large, (ii) two large and one small, (iii) one large and two small, and (iv) three small particles. (c) Write–erase function with **1** by (i) writing three Au large particles into triangles, (ii) removal of a specific particle using an eraser strand, and (iii) rewriting with a smaller particle. Bar is 50 nm (Reprinted with permission from ref. 27).

Both the structure and dynamics of nanoassemblies can be controlled by DNA hybridization. Recently, Sleiman and Aldaye[27] reported a straightforward method to mediate the assembly of discrete structures of AuNPs using single-stranded and cyclic DNA templates with rigid organic vertices (**1** in Fig. 10). Hybridization of this cyclic template with AuNPs monofunctionalized with DNA allows them to be directly positioned on the complementary arms of the templates. Control over geometry was demonstrated by facile creation of triangles and squares of AuNPs (Fig. 10a). Modularity of this approach provided precise control of the position and assembly of different AuNPs on these cycles (Fig. 10b). Write–erase functions were also demonstrated with these assemblies (Fig. 10c).

Another application of DNA templates is their use as programmable tiling lattices, providing an effective way to construct well-defined nano- to micrometre scale structures from simple DNA building blocks.[28] One approach of using DNA template to assemble AuNPs relies on biotin–streptavidin interaction.[29] In a representative work, Yan *et al.* utilized a linear DNA array consisting of biotinylated functionalized triple crossover molecules and incubated with streptavidin-functionalized AuNPs to create arrays with controlled spacing that is dictated by the periodicity of the nanostructured lattice.[30] Similarly, Simmel *et al.* obtained linear chains of NPs on longer scaffolds.[31]

Kiehl *et al.* has demonstrated the use of self-assembled 2D DNA lattices to organize AuNPs into periodic striped patterns (Fig. 11a).[32] AuNPs conjugated with multiple DNA sequences (T15) were assembled into closely packed rows by *in situ* DNA hybridization to provide a pre-assembled 2D DNA scaffolding with a precisely defined inter-row spacing of ~63 nm (Fig. 11a). Using the same strategy, Yan and co-workers created periodically patterned AuNP 2D square nanogrid lattices with well-controlled interparticle distances (Fig. 11b).[33] This approach can be broadly applicable to the manufacture of nanoscale integrated circuits for logic, memory, sensing, and other applications.

DNA-mediated NP assembly through electrostatic interaction. Another approach to create DNA–AuNP assemblies employs the strong electrostatic interaction between cationic NPs and anionic DNA, aligned along the DNA scaffold (Fig. 12). In these systems, the scale of the individual assembly depends on the length of the DNA templates allowing variation in assembly lengths from several nanometres to a few micrometres.

Murray and Wang explored the controlled assembly of AuNPs passivated with cationic trimethyl(mercaptoundecyl)-ammonium monolayers with anionic DNA,[34] affording one-dimensional water-soluble chains, with spacing between NPs determined by the monolayer thickness. These highly organized chains of metal NPs have potential applications as soluble conductive nanowires.

The controlled deposition of AuNPs on DNA-templated surfaces can be used to create nanoscale electronic materials. A variety of cationic AuNPs have been assembled on surfaces with DNA to afford AuNP wires and threads.[35] Network structures can be generated instead of linear structures by changing the NP : DNA ratio (Fig. 12a and b).[36] By

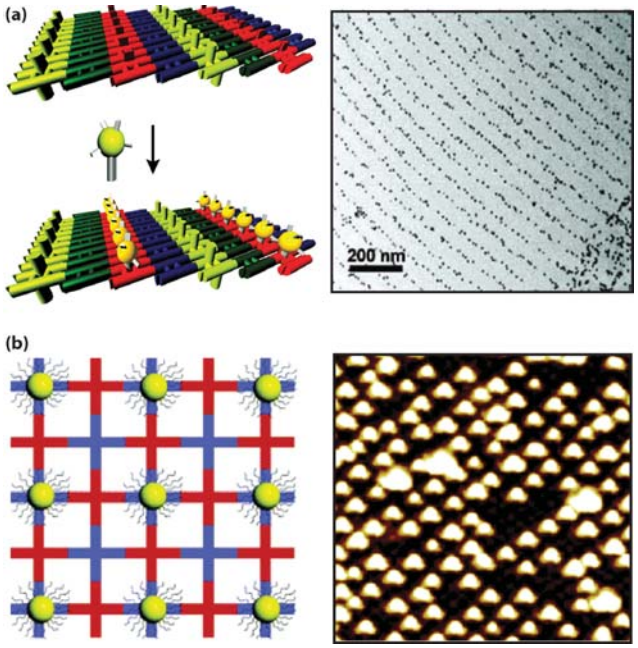

Fig. 11 (a) Use of 2D double crossover DNA tile lattice as a template to organize 5 nm AuNPs into parallel lines with an interline distance of ~63 nm. (b) Periodically patterned 5 nm AuNP 2D square nanogrid lattices with well-controlled interparticle distances (Reprinted with permission from ref. 32 and 33).

combining this approach with DNA-stretching technology, it is possible to generate highly ordered linear assemblies of AuNPs along stretched DNA molecules on substrates (Fig. 12c).[37]

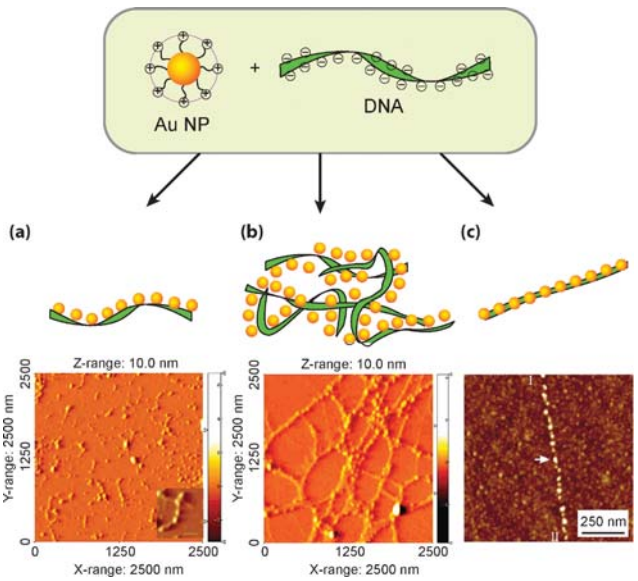

Fig. 12 Schematic representation and AFM images of assemblies between cationic NPs and anionic DNA molecules: (a) linear complexes of lysine-modified AuNPs and DNA at 10 : 1 NP : DNA ratio. (b) Network structures of lysine-modified AuNPs and DNA at 100 : 1 NP : DNA ratios. (c) Highly ordered assembly of oxidized aniline-coated AuNPs onto DNA molecules by DNA-stretching (Reprinted with permission from ref. 36 and 37).

The aforementioned assemblies involve complementary electrostatic interactions, however, the assembly between DNA and anionic AuNPs has also been reported. Wessels *et al.* found that negatively charged tris(hydroxymethyl)phosphine-capped AuNPs bind to calf thymus DNA immobilized on silicon. These complexes can subsequently undergo electroless plating to provide Au nanowires as narrow as *ca.* 30–40 nm.[38] The proposed driving forces for the assembly involve hydrogen-bonding interactions between the DNA and the AuNPs.

In a strategy combining supramolecular and covalent methods, Willner *et al.* incorporated psoralen onto the surface of AuNPs and investigated their assembly with DNA molecules.[39] The psoralen moiety intercalated with a double-stranded polyA–polyT duplex of *ca.* 900 nm length to generate a wire-like assembly. Upon UV irradiation, psoralen participated in a photoinduced $2\pi + 2\pi$ cycloaddition with the thymine residues, leading to a dense covalent attachment of the AuNPs onto the DNA. When λ-DNA was used, AuNP wires were also formed, but the density of the particles was substantially lower.

3.2 Protein-mediated assembly

Engineered interaction between proteins and monolayer-protected NPs can be utilized to generate highly organized assemblies with structural diversity. These superstructures combine tunable NP features with the unique physical and chemical properties of the proteins and, therefore, provide a potential route to a wide array of materials and devices.

A variety of assemblies have been created using biotin–streptavidin and antigen–antibody interactions. In one example, Mann and co-workers employed antibody–antigen recognition to self-assemble AuNPs into macroscopic materials.[40] Streptavidin–biotin binding has been widely used for protein–substrate NP assembly due to its high stability and specificity.[30,41] In a representative example, multiple-biotinylated AuNPs were engineered to assemble with the tetrameric protein streptavidin.[42] The interaction of streptavidin with the AuNPs led to the aggregation of the NPs as evidenced by a shift in the surface plasmon resonance peak and broadening of the absorption spectrum (Fig. 13). The aggregates could be reversibly switched to the non-aggregated state by the addition of soluble biotin.

While biotin–streptavidin or antigen–antibody interactions provide a facile route to biologically programmed assembly of AuNPs, a higher level of structure is required for spacing-dependent modulation of collective optical and electronic properties of the assemblies. As an initial step in this direction, Rotello *et al.* have used carboxylate-functionalized AuNPs and two proteins, chymotrypsin (ChT) and cytochrome C (CC), to assemble them into controlled composites (Fig. 14a).[43] Circular dichroism studies revealed that ChT unfolds onto the NP surface and acts as a linear polymer, while the robust CC retains its native conformation. SAXS studies showed that upon assembly of the ChT-mediated NP composite, the interparticle spacing is smaller then the native protein size, suggesting a denatured form of the protein (Fig. 14b). In the case of CC-mediated assembly, the measured

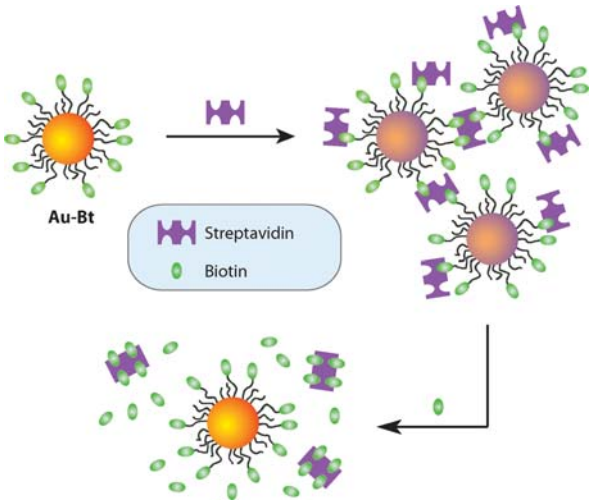

Fig. 13 Schematic representation of interactions of biotinylated AuNPs with streptavidin: assembly and disassembly.

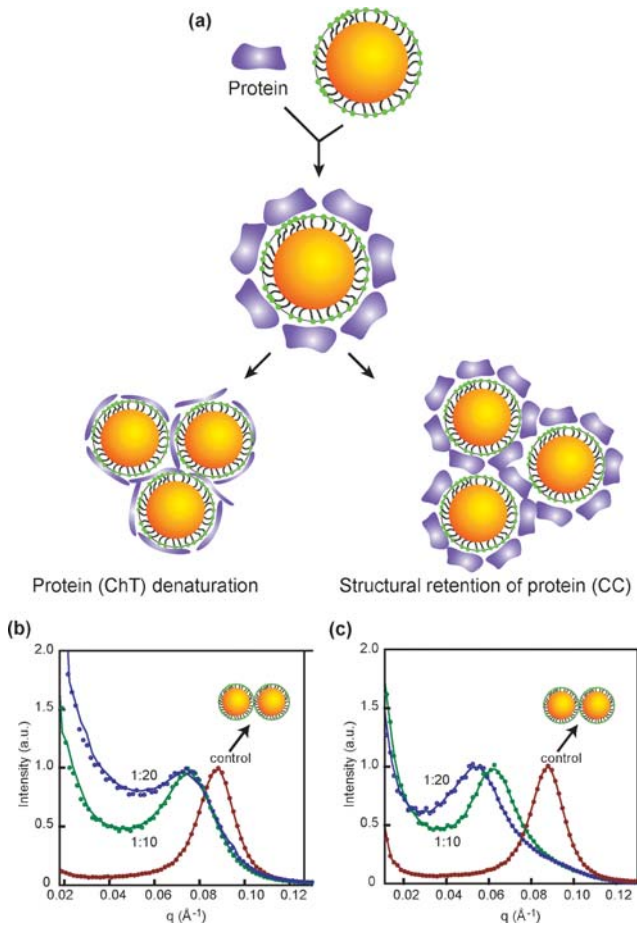

Fig. 14 (a) Schematic depiction of protein-mediated NP assemblies: protein denaturation upon interaction with AuNPs leads to a compact-packed assembly, while retention of protein structure results in an assembly with larger interparticle spacings. SAXS profiles of carboxylic acid-functionalized AuNP–protein assembly composites: (b) ChT and (c) CC at various AuNPs : protein ratios.

interparticle spacing is compatible to the native protein size, suggesting retention of the protein structure (Fig. 14c). In a subsequent study, the authors exploited the unique adsorption behavior of lysozyme on negatively charged surfaces for assembling the AuNPs into composites with a large range of tunable interparticle spacings and SPR behavior using this single protein spacer.[44]

Viral capsids and other multi-protein assemblies provide a useful tool for the assembly of nanomaterials. Ratna and co-workers utilized a mutant viral protein cage to control AuNP assembly onto virus capsids to generate 3D conductive molecular networks (Fig. 15a and b).[45] More recently, Hainfeld *et al*. have used His-tagged 20S proteasome as a building block to provide ordered assemblies, with AuNPs attached to the exterior of these large proteins (Fig. 15c and d).[46,47] In both cases, it should be noted that the protein was far larger than the particle, with the protein driving the ordering of the resultant material.

The aforementioned assemblies involved the outside surface of protein cages and proteins as templates for the NP assembly. Negatively charged AuNPs have been used as templates for viral capsid protein assemblies to create virus like particles (VLPs),[48] with the particles mimicking the anionic nucleic acid payload of the native viruses. Dragnea *et al*. reported the incorporation of AuNPs into Brome mosaic virus particles that feature an interior cavity of ~18 nm diameter.[49] The authors reported that several small AuNPs (3–5 nm) or one larger AuNP (16 nm) can be incorporated into the capsid (Fig. 16).[50] The formation of VLPs with high yield depends on the surface coating of the NP. The poly(ethylene glycol)

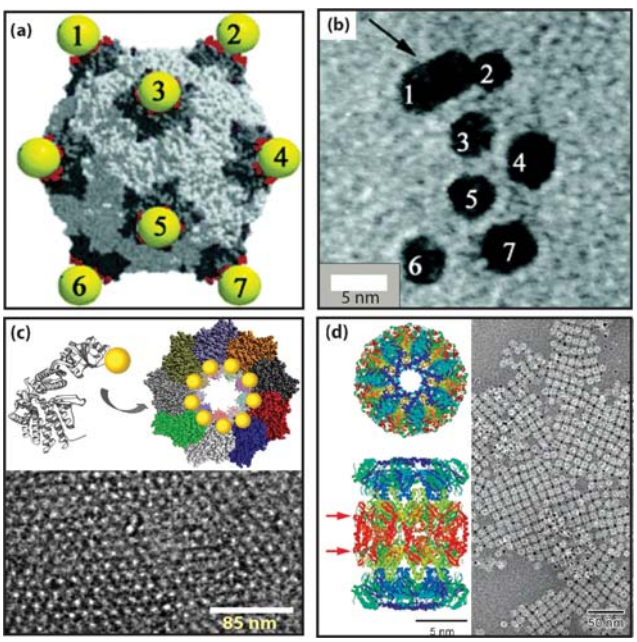

Fig. 15 (a) Model of the Cowpea mosaic virus mutant with one AuNP bound per 5-fold axis. (b) Unstained TEM image of eight AuNPs bound to an isolated mutant virus (Reprinted with permission from ref. 45a). (c) Proposed assembly of 1.4 nm AuNPs by genetically-modified HSP60 (Reprinted with permission from ref. 46). (d) AuNP assembly formed by conjugation to 20S proteasome *via* His tags (Reprinted with permission from ref. 47).

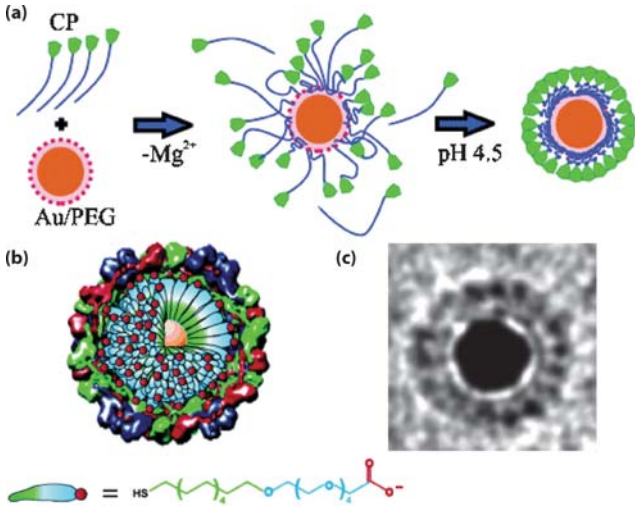

Fig. 16 AuNPs incorporation into Brome mosaic virus (BMV) like particles. (a) Proposed mechanism of viral like particle (VLP) capsid protein (CP) assembly; (b) schematic depiction of the encapsidated NP functionalised with carboxyl-terminated PEG chains; (c) cryoelectron micrograph of a single VLP. The regular character of the protein structure coating the 12 nm diameter AuNP (black disk) is evident.

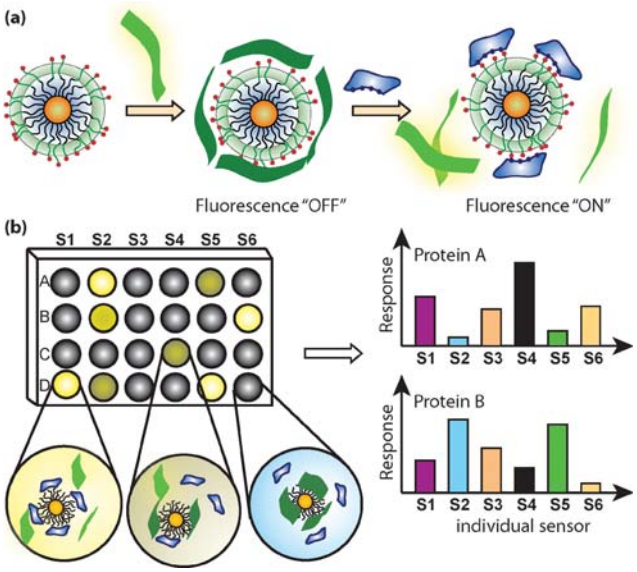

Fig. 17 Schematic illustration of 'chemical nose' sensor array based on AuNP–fluorescent polymer conjugates. (a) The competitive binding between protein and quenched polymer–AuNP complexes leads to the fluorescence light-up. (b) The combination of an array of sensors generates fingerprint response patterns for individual proteins.

(PEG)-coated particles were found to give best yield due to decreased hydrophobic interaction between NP and the protein shell in assembly media. These materials can be used as new optical and functional probes for biomedical imaging and sensing. Similar to the native virus, VLPs show their propensity for self-organisation to form multidimensional structures. Straightforward crystallization procedures lead to 2D and 3D crystals,[51] with potential applications in plasmonic metamaterials.

4. Application of AuNPs–polymer composites

The integration of AuNPs into thin films is particularly important for various applications including, biosensors and electronic/optoelectronic nanodevices. The incorporation of both polymers and AuNPs into films and devices provides increased flexibility and tunability of the resulting film properties. The polymer and the AuNPs can serve a variety of roles including: (1) Appended chemical functionality can be used for interaction with analytes and other environmental modifiers. (2) Crosslinking between the components can be used to provide reinforced films. (3) Control of interparticle spacing allows modulation of the film properties. This section of the tutorial will give some selected examples of recent applications of NP–polymer composites.

4.1 Sensors

Multilayered AuNP assemblies on electrode surfaces provide increased surface area, yielding enhanced electrochemical detection of redox analytes. Vossmeyer and co-workers have used dendrimers to produce composite films of dodecylamine-protected AuNPs for the selective detection of ppm levels of chemical vapors in a chemiresistor device.[52] Three different types of dendrimers were used: a hydrophobic, second generation polyphenylene (PPh) dendrimer; a hydrophilic, third generation PAMAM dendrimer; and a fourth generation poly(propylene imine) (PPI) dendrimer. All three dendrimers were functionalized at their periphery with end groups that can attach to the AuNPs by ligand displacement, allowing the assembly of a multiple layer device on top of a lithographically-defined interdigitated electrode structure. The different dendrimers provided varying solvent responses due to their polarity, and the sensing mechanism was attributed to swelling of the film upon analyte sorption, with the increase in the average interparticle distance leading to an overall increase in the electrical resistance.

A sensing mechanism on the basis of fluorescent indicator–displacement assay coupled with "chemical nose" approach, was developed by Rotello and collaborators who fabricated a sensor array composed of six cationic AuNPs and one anionic poly(*p*-phenylene ethynylene) (PPE) polymer.[53] As illustrated in Fig. 17a, the initially quenched polymer–AuNP complexes are disrupted by protein analytes through competitive binding, resulting in fluorescence restoration. Different AuNP–protein interactions, that are determined by their respective structural features such as charged, hydrophobic, hydrophilic, and hydrogen-bonding sites, lead to a fingerprint fluorescence response pattern for individual proteins (Fig. 17b). Linear discrimination analysis was used to differentiate the response patterns in high accuracy resulting in identification of seven proteins.

4.2 Memory devices

Building on the success of organic electronic devices, such as light-emitting diodes and field-effect transistors, researchers have also explored applications of organic materials and polymers specifically for the fabrication of non-volatile memory devices. Pioneering work in the field was demonstrated by Yang *et al.* that showed programmable electrical bistability in

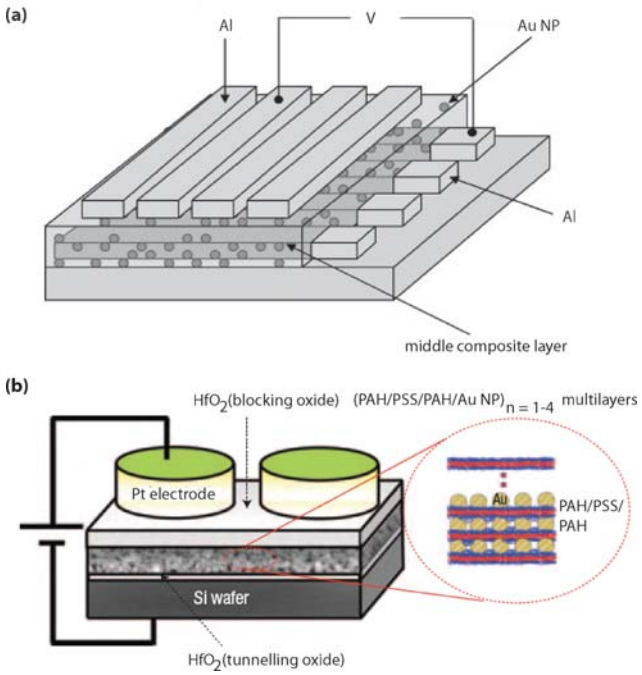

Fig. 18 (a) Polymer memory device incorporating AuNPs in a PS matrix (Reprinted with permission from ref. 54). (b) Schematic memory device incorporating LbL films with AuNPs (Reprinted with permission from ref. 55).

a PS film containing AuNPs and 8-hydroxyquinoline, sandwiched between two metal electrodes (Fig. 18a).[54] The low-conductivity state of the as-prepared device displayed an abrupt transition to a high-conductivity state ($\sim 10^4$-fold greater) under an external bias of 2.8 V. The device can be returned to its low-conductivity state by applying a negative bias of 1.8 V. The transition takes place in nanoseconds, and is non-volatile, indicating that the device may be used for low-cost, high-density memory storage, and was attributed to the electric-field-induced charge transfer between the AuNPs and 8-hydroxyquinoline. In a later work, Caruso *et al.* trapped anionic AuNPs in an LbL film of poly(allylamine)–poly(styrenesulfonate) to prepare a flash memory device.[55] Increasing the number of polyelectrolyte and AuNP layers was shown to influence the memory window and programming speed (Fig. 18b).

5. Summary

Polymer-mediated self-assembly of AuNPs provides a versatile and effective approach for the fabrication of new materials. This "bottom up" strategy couples AuNPs with diverse nano-sized building blocks, including linear, branched, and block copolymers, as well as biopolymers such as proteins and DNA. The flexibility and reversibility of self-assembly processes imparted by specific molecular interactions facilitates the formation of defect-free superstructures, and can be further explored in fields ranging from electronics and materials science to molecular biology.

The examples given in this review represent proof-of-principle demonstration to the creation of hierarchical structures. While great progress has been made in terms of controlling morphologies and the resultant physical properties of AuNPs assembly, deeper understanding of fundamental principles of self-assembly and advances in NP and polymer synthesis needs to be cultured to attain desired intricate nano-architecture, and convey promising nanotechnology into realistic devices.

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