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Programming nanoparticle valence bonds with single-stranded DNA encoders

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Nature has evolved strategies to encode information within a single biopolymer to program biomolecular interactions with characteristic stoichiometry, orthogonality and reconfigurability. Nevertheless, synthetic approaches for programming molecular reactions or assembly generally rely on the use of multiple polymer chains (for example, patchy particles). Here we demonstrate a method for patterning colloidal gold nanoparticles with valence bond analogues using single-stranded DNA encoders containing polyadenine (polyA). By programming the order, length and sequence of each encoder with alternating polyA/non-polyA domains, we synthesize programmable atom-like nanoparticles (PANs) with *n*-valence that can be used to assemble a spectrum of low-coordination colloidal molecules with different composition, size, chirality and linearity. Moreover, by exploiting the reconfigurability of PANs, we demonstrate dynamic colloidal bond-breaking and bond-formation reactions, structural rearrangement and even the implementation of Boolean logic operations. This approach may be useful for generating responsive functional materials for distinct technological applications.

The stoichiometry, orthogonality and reconfigurability of biomolecules or biomolecular complexes are often encoded within one-dimensional (1D) sequences of nucleotides or amino acids, characteristic of programmable biomolecular assembly and complexation for spatiotemporally regulated biological growth and reproduction at multiple scales including microtubule formation¹, nucleosome assembly² and viral packaging³. As exemplified by chromatin compaction, a highly conserved natural process in mammalian cells, the topology of chromosomes is defined by precise histone–DNA binding in nucleosomes and nucleosome repeat lengths (NRLs) that organize nucleosomes to compact metre-scale genomic DNA into a cell nucleus of tens of cubic micrometres⁴. By contrast, classic synthetic materials generally exhibit broad and continuous variations in structural parameters and rely on the use of multiple polymer chains to achieve patterning of single particles⁵. Thus, mimicking programmable interactions for error-free assemblies and functions remains a grand challenge in synthetic systems⁶.

During the past decade, a variety of engineering approaches have been developed to fabricate ‘colloidal atoms’ by conferring valence bonding to micro- or nanoparticles^{7,8}. Especially, colloidal particles with distinct small-molecule, polymeric or DNA patches (patchy particles) represent a rapidly emerging class of building blocks for rationally constructing biomacromolecule-mimicking three-dimensional (3D) supramolecular materials^{9–16}. In this non-covalent synthesis approach, sticky patches confer colloids with chemical/biochemical or topological specificity analogous to the valence bonds of atoms. The presence of short-ranged patch–patch inter-

actions in these ‘colloidal atoms’ allows the facile self-assembly of complex supracolloidal structures with low-valence and directional bonding^{9–16}. More recent progress to scale down patchy particles from a micrometre to tens of nanometres has been made by patterning nanoparticles with thermodynamically driven segregation of polymer patches¹⁷. However, designing ‘atom equivalents’ with atomic- or biomacromolecule-like interactions remains challenging due to the lack of ability to individually control the chemical/biochemical specificity of the patches (that is, the orthogonality). So, as a major step forwards, we envision the design of a single-strand encoder that provides orthogonality, directionality, stability and selectivity in a non-covalent synthetic approach to program, with high precision, nanoparticle assemblies.

The intrinsic programmability of DNA provides high design flexibility and sequence specificity to pattern colloids with directional patches¹⁸. Colloid atoms with fixed valences were fabricated with DNA patches, which led to the assembly of simple colloidal molecules^{10,19–22}. A variety of well-defined colloidal superlattices and crystals were also formed using spherical nucleic acids, or thiolated DNA-modified gold nanoparticles (AuNPs)^{23–25}. Especially, the use of a multi-component DNA tile or origami nanostructures provides a powerful means to endow colloids with the required anisotropy^{9,26–33}. Nevertheless, it remains a major challenge to pattern colloids with reconfigurability^{34,35}. Here, we exploit the highly specific consecutive gold–adenine (Au–A) coordination³⁶ to design single-stranded encoders (SSEs) containing alternating sticky polyA domains and non-sticky bonding domains. We find that polyA

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Fig. 1 | Programmable atom equivalents fabrication using single-stranded DNA encoders. **a**, SSE-based design of PANs with different valence bonds (I–IV). **b**, Agarose gel electrophoresis of PANs with individual valence bonds (I–IV). The plots show quantified band intensity of the gel, with blue peaks corresponding to unmodified AuNPs, and red ones to PAN with defined valences. **c**, Representative colloidal molecules formed with PANs. The clusters are denoted as $G^m G^n$, where m refers to the particle size level ($m=1$, 5 nm in diameter; $m=2$, 10 nm; $m=3$, 15 nm; $m=4$, 20 nm), and n refers to the particle number. Scale bar, 10 nm.

readily adsorbs to the surface of AuNPs, leaving bonding domains extending into the solution for specific and reversible hybridization reactions. By programming the order, length and sequence of these two domains, a range of SSE-encoded programmable atom equivalents (PANs) were synthesized with precisely controlled valence, orthogonality and reconfigurability for post-synthetic rearrangement of colloidal interactions. Using these PANs, we demonstrate the assembly of a wide range of low-coordination ‘colloidal molecules’ and monodispersed, linear or branched ‘colloidal oligomers’, and enable dynamic colloidal reactions.

Non-covalent synthesis of programmable atom equivalents

Figure 1a shows the general design principle for SSE-based non-covalent synthesis of PANs. A typical SSE contains alternating polyA (usually 30 consecutive adenines) and non-polyA domains (sequences listed in Supplementary Table 1). As established in previous studies^{36,37}, polyA can irreversibly adsorb to the surface of AuNPs (sticky domains), which repels non-polyA oligonucleotides without consecutive adenines and exposes them to the solution phase for hybridization (bonding domains). We envisioned that the use of multiple sticky polyA and non-sticky polyA domains may encode AuNPs with a defined number of valence-mimicking hybridizable oligonucleotides. For example, a monovalent PAN, PAN(I), is encoded by a two-domain SSE; a divalent PAN, PAN(II), is encoded by a three-domain SSE containing two bonding domains spaced by a polyA domain; trivalent and tetravalent PANs, PAN(III) and PAN(IV), are encoded by five and seven domains, respectively (Fig. 1a).

To fabricate PANs, we mixed AuNPs that were 10 nm in size with SSEs with various domains under ambient temperature (details

shown in Supplementary Information, Supplementary Fig. 1). After a 15 min incubation, we analysed the products with agarose gel electrophoresis. As shown in Fig. 1b, we generally observed two sharp red-coloured bands, with one band corresponding to unmodified AuNPs and the other representing PAN(I), (II), (III) or (IV). Interestingly, the bands of the PANs show decreased migration rates in accordance with the increased number of SSE domains. The yields of PAN(I), (II), (III) and (IV) were estimated to be 45%, 48%, 60% and 82%, respectively (Fig. 1b). This design strategy is applicable to AuNPs with various sizes (5 nm, 10 nm, 15 nm and 20 nm, denoted as G^1 , G^2 , G^3 and G^4 , respectively). For example, we obtained tetravalent PANs from these AuNPs with distinct sizes (5 nm, 15 nm and 20 nm) using the same SSE sequences, with yields of 88%, 38% and 30%, respectively (Supplementary Fig. 1). To evaluate the bonding ability of PANs, we hybridized them with oligonucleotides complementary to their bonding domains. The retarded mobility shown in gels reveals that these PANs are hybridizable for bond formation (Supplementary Fig. 2). Small-angle X-ray scattering (SAXS) studies confirmed that two PAN(I)s with complementary bonds could be hybridized into dimers with interparticle spaces of ~4–7 nm (Supplementary Fig. 3).

Synthesis of colloidal molecules and oligomers

Having established the basic assembly method, we employed PANs to synthesize multi-particle colloidal molecules. Using 10-nm PAN(I), (II), (III) or (IV) as the core atoms to bind with a satellite PAN(I) with a complementary sequence in the bonding domain, four representative colloidal molecules I–IV with mono-, di-, tri- and tetravalent binding modes were prepared. Both gel electrophoresis and transmission electronic microscopy (TEM) imaging confirmed the

Fig. 2 | Schematic representation and TEM images of colloidal molecules. **a**, Colloidal molecules. The valence and size of PANs increase from left to right, and from top to bottom, respectively. **b**, PANs with different compositions (AuNPs, grey; QDs, yellow). **c**, Hierarchical assembly of branched molecules. Scale bar, 20 nm.

formation of colloidal molecules (Fig. 1c and Supplementary Fig. 4). The yields of these four types of colloidal molecules were 85%, 79%, 69% and 63%, respectively (Supplementary Fig. 5). We also found that the bond angle distribution of PANs could be tuned by varying the length of the polyA. Using three-particle colloidal molecules as an example, we synthesized colloidal molecules with varied bond angles (Supplementary Figs. 6–10), mimicking molecules staying in different states with different vibrational energies.

We next performed all-atomistic molecular dynamics (MD) simulations to study the interactions between the polyA domain and the Au surface. An outstretched polyA on the Au surface was found to be thermodynamically more stable than a highly coiled one (Supplementary Fig. 11), suggesting that optimizing the sequence of the polyA domain might improve the ability to control bond angles. To experimentally test this, we tuned the kinetics of the binding of DNA strands and AuNPs by introducing fixed numbers of thymine (T)-base mutation in the binding domain (A40) of the SSE. The decrease of the polyA–Au affinity arising from the introduction of low-affinity Ts prevented kinetic trapping during the DNA–AuNP binding. As a result, the control over bond direction was significantly improved, as manifested by the reduced distribution of bond angles (Supplementary Figs. 12 and 13).

To demonstrate the generality of this SSE assembly strategy, a spectrum of low-coordination colloidal molecules was synthesized using PANs with different sizes and compositions. PANs with sizes including 5 nm, 10 nm, 15 nm and 20 nm were used as mimics of congeners to synthesize colloidal molecules. We synthesized 32 types of colloidal molecules using a combination of 16 species of PANs (Fig. 2a and Supplementary Figs. 14 and 15), suggesting the nearly consistent binding ability of these PANs. Also, the use of this strategy to synthesize colloidal molecules with heterogeneous

compositions was demonstrated. First, monovalent core–shell CdSe/ZnS quantum dots (QDs) of 4 nm were prepared using a two-domain SSE with a phosphorothioate domain sticky to the QDs. Hybridization of monovalent QDs with 10 nm AuNP-based PANs resulted in the formation of multi-atom colloidal molecules (Fig. 2b), which are precisely controlled nanostructures that are potentially useful for nanocatalysis and nanomedicine.

In addition, branched colloidal molecules with higher-ordered structures were prepared (Fig. 2c). To accomplish this, first a two-atom colloidal molecule comprising a 5-nm PAN(I) and a 10-nm PAN(II) was synthesized. The empty valence bond in this colloidal molecule is available for further bonding with 15-nm PANs. TEM images revealed that the resultant structures possess a 15-nm core particle (as branch point) surrounded by defined numbers (2–4) of heterogeneous dimers. The ability to synthesize branched colloidal molecules with various-size nanoparticles (PANs) implies the potential to create multi-scale complexity based on colloidal molecules.

Having demonstrated the synthesis of colloidal molecules using PANs, we next explore the synthesis of high-molecular-weight colloidal oligomers. Linear colloidal oligomers were synthesized with two 5-nm PAN(II)s (types A and B) possessing complementary bonding domains. Polymerization occurred when A and B were incubated under ambient conditions, leading to the formation of G^n with a different number (n) of nanoparticles (Fig. 3 and Supplementary Fig. 16). Considering that the particle mass of 5 nm AuNPs is 760 kDa, we estimate that these colloidal oligomers are of high molecular weight, in the range of MDa.

An important question is whether PANs possess binding orthogonality endowing programmed anisotropy of colloidal molecules. To evaluate the orthogonality of PAN bonds, we fabricated a

Fig. 3 | Schematic illustration and TEM images of colloidal oligomers. Colloidal oligomers are formed by divalent PANs A and B, with n referring to the number of nanoparticles. The bonding domains of x and y are complementary to x' and y' , respectively. Scale bar, 20 nm.

trivalent PAN(III) of 20 nm carrying three independently encoded sequences (Fig. 4a). Next, the PAN(III) were hybridized with differently sized PAN(I)s (5 nm, 10 nm and 15 nm) carrying corresponding complementary sequences. On the addition of any one kind of PAN(I), even at excessive molar ratios, we observed exclusively the formation of ‘two-particle’ colloidal molecules (G^4-G^1 , G^4-G^2 , G^4-G^3) with one bond and two unoccupied bonds. This orthogonality remained for the ‘three-particle’ ($G^1-G^2-G^4$, $G^1-G^3-G^4$ or $G^2-G^3-G^4$) and ‘four-particle’ ($G^1-G^2-G^3-G^4$) colloidal molecules with two or three bonds (Fig. 4a and Supplementary Fig. 17), which established the individual controllability of PAN bonds.

Chirality is a fundamental property of the essential molecules and materials of life, most notable with the iconic tetrahedral structure of the asymmetric carbon atom as present in, for example, amino acids and proteins. Expected molecular and supramolecular chirality plays a key role in materials design, and the non-covalent assembly of chiral nanostructures would represent another major leap forwards. A PAN(III) hybridized with three differently sized PAN(I)s is intrinsically chiral. To test this, we measured the colloidal chirality of this anisotropic nanostructure (Fig. 4b). The type-A colloidal molecule fabricated with PAN(III) and PAN(I) of 5 nm, 10 nm and 15 nm exhibited a strong negative peak at the plasmonic absorption region (~ 530 nm) in the circular dichroism (CD) spectrum (Fig. 4b–d). Simulation studies further confirmed that the type-A structure with the expected spatial arrangements has asymmetric distributions of the electric current density corresponding to left- or right-handed circularly polarized (LCP or RCP, respectively) light at 530 nm (Fig. 4c). By contrast, the type-B colloidal molecule fabricated with PAN(III) and three equivalents of PAN(I) of 10 nm was CD-silent. Control measurements with solutions containing either free SSEs or mixtures of unmodified AuNPs with an equivalent

concentration and size combination did not show apparent CD activity within this range. These results confirm that we have made a homochiral colloidal ‘molecule’ by nanoparticle assembly and support the capability of using PANs to fabricate anisotropic colloidal molecules with plasmonic chirality. Given that chirality is a key feature of chemical and biological molecules, the construction of artificial chiral metamaterials with distinct optical effects in the visible wavelength range bears major potential in applications including photonic biosensing and photonic circuits^{19,38,39}.

Colloidal reactions

Next, we exploited the reconfigurability of PANs and colloidal molecules to implement colloidal reactions (Fig. 5), aiming at several basic synthetic transformations, that is, substitution, dissociation and condensation. A typical colloidal reaction involves a two-particle colloidal molecule serving as the initial reactant, and DNA hybridization or strand-displacement reactions (SDRs) mimicking electron or energy transfer^{40,41}. In an addition reaction in the form of $AB + C = AB \cdot C$, an unpaired DNA strand of PAN-B specifically hybridized with PAN-C, resembling the bonding of unpaired electrons, and resulting in the formation of the three-particle product $AB \cdot C$ (Fig. 5a). Furthermore, a decomposition reaction or a reduction reaction in the form of $AB + e = A + B$ was mimicked using SDR-triggered disassembly of a two-particle colloidal molecule AB (Fig. 5b). Mimicking more complex chemical transformation by using an external PAN-C or CD, we accomplished the single replacement ($AB + C = AC + B$) and double replacement ($AB + CD = AC + BD$) reactions (Fig. 5c,d). TEM imaging allowed the visualization of these reactions (Supplementary Figs. 18–22). Thermodynamics of these colloidal reactions can be semi-quantitatively analysed via gel electrophoresis. For example, in the decomposition reaction (Supplementary Fig. 18), equilibrium was reached when the molar ratio between the displacing strands and the two-particle colloidal molecules (AB) was close to 1/1 while dissociation of half of the reactant required approximately 0.5 times ($[e]/[AB]$) of the displacing strands.

We next performed colloidal reactions with four-particle colloidal molecules ($G^2_1G^2_3$, Fig. 5e–g). TEM images for a dissociation reaction showed that the PAN(I)s detached from the four-particle clusters in a stepwise process when triggered with specific sequences, which successively formed three-, two- and one-particle clusters (Fig. 5e and Supplementary Fig. 23). The yield of each step was 65%, 82% and 79%, respectively. We note that the loop domain and the sticky-end domain on PAN(III) work equally well for these reactions, suggesting that different domains of the SSE serve as equivalent bonds and can be rearranged.

We further implemented single- or double-replacement (substitution) reactions with the four-particle clusters (Fig. 5f,g and Supplementary Figs. 24 and 25). For the single-replacement reaction ($AB_3 + 3C = A + 3BC$), the two reactants, AB_3 ($G^2_1G^2_3$, in the form of 10-nm-particle tetramers) and C (G^1_1 , in the form of a 5-nm particle), formed two-particle (BC , 60%) clusters. For the double-replacement reaction ($AB_3 + 3CD = AC_3 + 3BD$), the reaction of AB_3 and CD ($G^1_1G^1_1$) resulted in four-particle and two-particle clusters. Product AC_3 (32%) was obtained when using a molar ratio of 10/1 for the reactants AB_3 and CD , as estimated from TEM analysis (Fig. 5g). Given the relatively high energy barrier of double displacement reactions⁴², it should be emphasized that apparently the SSE bonds on PANs are highly reconfigurable, which is an important finding for the realization of complex transformations.

Single-particle nanocircuits

Having established several basic colloidal reactions, we next explored the use of PANs for implementing Boolean logic operations. Previously reported NP-based logic gate systems generally employ isotropically modified DNA-NPs that often result in

Fig. 4 | Colloidal molecules with anisotropy and chirality. **a**, Schematic and TEM images showing bond orthogonality of the 20-nm PAN(III) with PAN(I) of different sizes (5 nm, 10 nm and 15 nm). Scale bar, 20 nm. **b**, Schematic and TEM images of the anisotropic (type A) or isotropic (type B) four-particle colloidal molecules. **c**, Simulated distributions of their electric current density at 530 nm of LCP and RCP light. **d**, Simulated and measured CD spectra of the structures.

intermediate NP aggregates⁴³. The use of PANs, as shown in the present study, holds the potential for generating true digital outputs that are adaptable for interfacing multi-layered complex circuits. In our design (depicted in Supplementary Fig. 26a), AND, OR, XOR and INH gates are constructed with two-particle PANs with toe-holds that can be dissociated by SDRs. In the presence of input strands that trigger SDRs, the decoupling of the two-particle PANs generates the ‘TRUE’ value (or 1). NAND, NOR and XNOR gates are constructed with a pair of one-particle PANs, the coupling of which (forming two-particle molecules) represents the ‘FALSE’ value. As an example, we introduced two independent toe-hold strands to implement a two-input OR logic gate. Two input strands were designed, each targeting one of the two toe-hold strands, each independently triggering the displacement of the bond. The dissociation of the two-particle PANs (output = 1) was imaged with TEM (Supplementary Fig. 27). Importantly, gel analysis also revealed that any single or two inputs (input = [0, 1], [1, 0] or [1, 1]) resulted in monomers (~75% yield) with higher gel mobility, and that without input (input = [0, 0]), the proportion of monomers (leakage) was

below 25% (Supplementary Fig. 26b–d). Hence, the use of PANs enables reliable replication of a single-particle calculation at the macroscopic level. Using a similar design, we implemented a set of Boolean logic operations including AND, OR, XOR, NAND, NOR and XNOR (Supplementary Figs. 26 and 27).

To further demonstrate the potential of PAN-based reconfigurability, we constructed a single-particle nanocircuit with the three-input MAJORITY function (Fig. 6a and Supplementary Fig. 28). A MAJORITY circuit with multiple two-input logic gates generates an output of TRUE (or 1) when the majority of inputs (>(input number)/2) are TRUE; otherwise the output would be FALSE (Fig. 6a). To implement this circuit, we integrated three orthogonal AND gates (AND1, AND2 and AND3, each labelled with Cy3, FAM and Alexa647 fluorophores, respectively) onto a 10-nm PAN(III). In the absence of any input, the fluorophores on the gates are quenched by AuNPs. When three corresponding oligonucleotides (IN1, IN2 and IN3) were employed as inputs to AND1, AND2 and AND3, output fluorescence at different emitting wavelengths was observed (Supplementary Table 2). Figure 6b shows the fluorescence outputs

Fig. 5 | Programmable colloidal reactions based on atom equivalents. **a–d**, Schematic, representative TEM images and product statistics of the condensation (**a**), dissociation (**b**), single-replacement (**c**, exchange) or double-replacement (**d**, two-fold exchange) reaction with dimer colloidal substrates. **e–g**, Similar transformations with tetramer colloidal substrates. Coloured sticks represent reactant strands. The x in the product statistics represents unreacted reactants and other side products. Scale bar, 10 nm.

Fig. 6 | Programmable single-particle nanocircuits based on atom equivalents. **a**, Schematic of a PAN-based AND gate and a single-particle nanocircuit with the MAJORITY function. **b**, Fluorescence output for the MAJORITY nanocircuit in response to different inputs. **c**, Representative TEM images (from top to bottom: no input, IN1+IN2, IN1+IN2+IN3) and statistical analysis ($N=100$) of the circuit structures in response to different inputs. The dashed line indicates the decision threshold of the output. Scale bar, 50 nm.

in response to different input combinations, which reveal typical MAJORITY output.

To realize the MAJORITY function at the single-particle level, each gate was tethered with a 5-nm PAN(I), forming a colloidal

tetramer cluster that served as the circuit structure. In the presence of two or three oligonucleotide inputs, the release of one or three PAN(I) particles from the circuit structure (defined as 1) is expected; otherwise the tetramer structure remained intact (defined

as 0). TEM images (Fig. 6c and Supplementary Fig. 29) showed that with any single input, the circuit structure largely remained intact as tetramers (~60%, output = 0). With any two inputs, a large portion of trimer structures (~62%) were formed, suggesting the release of one PAN(I) from each circuit structure (output = 1). Likewise, the presence of all three inputs resulted in monodisperse PAN(III)s (~58%), suggesting the release of all PAN(I) particles from the circuit structure (output = 1). Gel electrophoresis analysis further confirmed the TEM imaging at the ensemble level (Supplementary Fig. 30). The successful construction of this single-particle MAJORITY nanocircuit suggests that all bonds on PANs are reconfigurable and can be dynamically rearranged. These findings hold great promise towards developing complex computation units at the nanoscale.

Fabrication of reconfigurable nanoparticle clusters with the ability to readily undergo post-synthetic rearrangement with control over the colloidal interactions, especially in higher-ordered nanoparticle suprastructures, represents a major advance towards future adaptive nanosystems, reconfigurable devices and ultimately developing dynamic nanomachines^{44–46}. In particular, the precision and simplicity in controlling the nanoparticle valence, orthogonality and reconfigurability as compared to previously reported systems^{34,35} provide a general route to adapt nanoparticle-based device systems and drive the transformation of nanomachines in response to external stimuli. For example, we envision that the multi-responsive single-particle circuits might mediate complex cellular/intracellular interactions for sensing, biomolecular imaging and therapy in cells or in vivo.

Outlook

We have demonstrated here a general single-stranded DNA encoder (SSE) approach for programming valence bonds of AuNPs in one step. Patterning of highly curved NP surfaces with desirable anisotropy is generally technically challenging^{30,31}. Whereas previous efforts to overcome this barricade have proven successful using thermodynamically driven polymer segregation¹⁷, this method does not possess programmability in the natural biomolecular complexation processes with genetic encoding. By exploiting well-established DNA–Au interactions, we demonstrated that the information required for the 3D spatial organization of DNA on AuNPs is reliably encoded within the 1D sequence of the SSE. Importantly, the sequence information of non-polyA domains encodes the orthogonality, and the length of Au–sticky polyA defines the bonding angle. The generality of this approach is confirmed by the synthesis of highly uniform PANs with different sizes and valences. Given the increasing understanding of DNA–NP interactions in quantum dots⁴⁷, silver NPs (ref. ⁴⁸) and upconversion NPs (ref. ⁴⁹), the SSE strategy might be further extended to encode other types of NPs.

This SSE approach endows synthetic NPs with the orthogonality analogous to that observed in the biomolecular complexation found in nature. We have shown that the orthogonality of PANs enables bottom-up construction of metamolecules, chiral colloidal molecules, colloidal oligomers and other higher-ordered suprastructures^{50–52}. Given that AuNPs possess various plasmonic, electronic or catalytic properties that are closely associated with their spatial arrangements, these structurally reconfigurable, colloidal Au nanostructures provide a rich toolbox for developing intelligent, environmentally responsive functional materials, which enriches the realm of synthetic materials for various photonic, electronic and biomedical applications.

Online content

Any methods, additional references, Nature Research reporting summaries, source data, extended data, supplementary information, acknowledgements, peer review information; details of author contributions and competing interests; and statements of data and

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Methods

Materials. All oligonucleotides were synthesized and purified by JieLi. The sequences used in this study are listed in Supplementary Table 1. Bis (*p*-sulfonatophenyl) phenylphosphine dihydrate dipotassium salt (BSPP) was obtained from Sigma-Aldrich. AuNPs were obtained from Ted Pella. Agarose gel was obtained from Bio-Rad.

Preparation of BSPP-protected AuNPs. The method for preparation of BSPP-protected AuNPs was adapted from previous studies⁵³. In detail, 3 mg of bis (*p*-sulfonatophenyl) phenylphosphine dihydrate dipotassium salt was added to 10 ml AuNPs (5 nm, 10 nm, 15 nm or 20 nm) and the mixture was shaken overnight at room temperature. NaCl (solid) was added slowly to this mixture while stirring until the colour changed from deep burgundy to light purple. The resulting mixture was centrifuged at 7,000g for 5 min, and the supernatant was removed. The treated AuNPs were then resuspended in 0.3 ml BSPP solution (0.3 mg ml⁻¹), and mixed with 0.3 ml methanol. The mixture was again centrifuged, the supernatant was removed and the AuNPs were resuspended in 100 µl BSPP solution (0.3 mg ml⁻¹). The concentration of the ~100-fold-concentrated AuNPs was estimated from the optical absorbance at 520 nm.

Preparation of SSE-PANs. For preparation of SSE-PANs of valence 1–4, AuNPs (100 nM; 5 nm, 10 nm, 15 nm or 20 nm; protected with BSPP) were mixed with a SSE (I-30A, II-30A, III-30A or IV-30A) at a molar ratio of 1/1. After 1 min, citrate-HCl buffer (500 mM trisodium citrate, pH 2.0) was rapidly added to the DNA–AuNP mixture (final citrate concentration, 10 mM) followed by mixing. This mixture was incubated for 15 min at room temperature.

Gel separation of SSE-PANs. Agarose gel (3%) was used for gel separation. An amount of 5 µl PAN products was mixed with 50% (w/v) sucrose and loaded in the gel. The electrophoresis separation was performed with a Bio-Rad electrophoresis system at 100 V for 30 min. The gels were photographed with a digital camera. The desired bands were cut out from the gel and were immersed into the electroelution buffer (0.5 × PBS). After the electroelution, the products were recollected and concentrated by centrifuging.

Assembly of PAN-based colloidal molecules. Modified PANs (modified with SSE I-30A, II-30A, III-30A or IV-30A, listed in Supplementary Table 1, together with all DNA sequences used) with complementary modified PANs (modified with I-C1, I-C2, I-C3 or I-C4) were mixed together with a proper ratio, and then the NaCl concentration of the mixture was increased to 100 mM by adding 1 M sodium phosphate buffer. The mixture was then annealed from 42 °C to 15 °C overnight with a thermoincubator.

Colloidal molecular reactions. Two monovalent PANs (10 nm) prepared with II-Synthesis and I-Syn-C were hybridized to form a dimer structure, which was verified and purified by gel electrophoresis. The purified dimer structures served as initial reactants of the following reactions.

To implement a synthesis reaction, the 5-nm PAN (prepared with Syn) was added to the initial dimer structure at different ratios. The mixture was incubated at 37 °C overnight.

For decomposition and single-replacement reactions, the dimer structures were prepared with I-Rep and I-Rep-C modified monovalent PANs (10 nm). The DNA strand (Dec) as energy or the 5-nm monovalent PAN (modified by Rep) as a replacement reactant was added to the dimer structure. The mixture was reacted at 37 °C overnight.

For the double-replacement reaction, 10-nm dimer structures were prepared with I-DR-1 and I-DR-2, and 5-nm dimer structures were prepared with I-DR-3 and I-DR-4; these two dimer structures were mixed and reacted at 37 °C overnight. Products of all reactions were checked by agarose gel electrophoresis and TEM imaging.

For the decomposition reaction on trivalent PAN, 10-nm tetramer structures were prepared with III-Dec, I-Dec-1, I-Dec-2 and I-Dec-3. After gel purification, the decomposition strand (Dec-1, Dec-2 and Dec-3) was added to the tetramer, and the mixture was reacted at 37 °C overnight. Products of all reactions were checked by agarose gel electrophoresis and TEM imaging.

For single-replacement and double-replacement reactions on tetramer structures, 10-nm core PAN(III) was prepared with III-Rep, and was annealed with 10-nm satellite PAN(I)s modified with I-10-c. Then 5-nm PAN(I) modified with I-5-1 or 5-nm dimer (modified with I-5-1 and I-5-2) was added to the tetramer for the reaction at 40 °C overnight. Products of all reactions were checked by agarose gel electrophoresis and TEM imaging.

Logic calculations. Four logic gates, that is, AND, OR, XOR and INH, were implemented by dissociation of dimer structures via strand-displacement reactions with input DNA strands. The dimer structure for each gate was prefabricated with two monomers (respectively modified with corresponding DNA sequences listed in Supplementary Table 1). For each logic-gated reaction, input DNAs (10 µM, 1 µl each) were added to 5 µl corresponding dimer structure (100 nM). The mixture was allowed to react for 2 h at 25 °C. All resulting structures were checked by gel electrophoresis, and the yields were quantified by gel image analysis with ImageJ.

Three other logic gates, that is NAND, NOR and XNOR, were implemented by coupling PAN(I)s (respectively modified with the corresponding sequences listed in Supplementary Table 1) into dimer gate structures. For each reaction, the input DNA strands (100 nM, 5 µl each) were added to corresponding gate structures (100 nM each, 10 µl in total) at an equal molar ratio. All resulting structures were checked by gel electrophoresis. The yields of the resulting structures were quantified by gel image analysis with ImageJ.

For the MAJORITY circuit, the tetramer gate structure was achieved by mixing 10-nm PAN(III) (modified with III-Vote) and 5-nm PAN(I) (modified with I-V5-1, I-V5-2 and I-V5-3). After purification, different combinations of input strands (IN1, IN2 and IN3) were added to the gate structure at an equal molar ratio for an overnight reaction at 37 °C. The products were characterized by agarose gel electrophoresis and TEM imaging. For the fluorescent experiment, 10-nm PAN(III)s (modified with III-Vote) were mixed with DNA strands I-V5-FAM, I-V5-Cy3 and I-V5-Alex 647. After purification by centrifugation, different combinations of the input strands were added for an overnight reaction at 37 °C. The fluorescence outputs were read by an Mx3005P quantitative polymerase chain reaction system (Agilent Technologies).

SAXS measurements and analysis. SAXS experiments (adapted from previous studies⁵⁴) were carried out on bio-SAXS-BL19U2 at the Shanghai Synchrotron Radiation Facility. We used a flow-through cell with a cylindrical quartz glass capillary of 1.5 mm diameter and measured at 12 keV X-ray energy (wavelength 0.1033 nm). An evacuated flight tube was used to cover the sample-to-detector distance of 2.708 m. A motorized beam stop was placed inside the flight tube. A Dectris Pilatus 1 M CMOS Detector (172 × 172 µm pixel size) served as a detector. Silver behenate was used for the calibration of the sample detector distance and beam centre. The exposure time was 1 s for each sample. The beam size was 0.40 × 0.15 (horizontal × vertical) mm², and a conical mask was used to restrict the azimuthal integration to the direction with higher resolution. One-dimensional scattering intensity profiles $I(q)$ were obtained by circularly averaging the 2D scattering patterns and the corresponding structure factors $S(q)$ for the studied structures⁵⁵. $q = 4\pi\sin\theta/\lambda$, where 2θ is the scattering angle and λ is the wavelength of X-ray.

For SAXS data analysis, background (measurements of 0.5 × PBS buffer) subtracted scattering data were transformed with Bio-XTAS RAW 1.2.155 and fitted using SasView (Version 4.1.2)⁵⁶. The data were further analysed by the ATSAS 2.7.2 package. The built-in model 'linear-pearls' under the category of 'sphere' was used to fit the data of the DNA–AuNP dimers. This model provides the form factor for N particles (here $N = 2$ for dimers) of radius R linearly joined by short bonds (or segment length or edge separation) $L = (A - 2R)$. A is the centre-to-centre pearl-separation distance. The thickness of each bond is assumed to be negligible. Since we used only one DNA strand to modify an AuNP, the scattering intensity contributed by the DNA was neglected, and only the scattering of the AuNPs was considered. The scattering intensity was fitted with Equation (1):

$$p(Q) = \frac{\text{scale}}{V} \left[m_p^2 \left(N + 2 \sum_{n=1}^{N-1} (N-n) \frac{\sin(qnL)}{qnL} \right) \left(3 \frac{\sin(qR) - qR\cos(qR)}{(qR)^3} \right)^2 \right] \quad (1)$$

where the mass m_p is (scattering length density (SLD)_{pearl} – SLD_{solvent}) × (volume of N pearls), V is the total volume⁵⁷, Q is the total scattering intensity of the system and n is a set of natural numbers that begin with 1. We then calculated the pair distance distribution function (PDDF) $p(r)$ using SasView, r refers to the distance between two points that are incorporated in the bulk structure. The PDDF distribution for an AuNP dimer is expected to show two peaks. The location of the first peak is determined by the AuNP radius, while the second peak results from the centre-to-centre distance.

TEM imaging. For TEM imaging, 5 µl sample solution was deposited on a copper grid for five minutes, after which excess solution was wicked away with filter paper. Imaging was performed using a Tecnai TF20 microscope operated at an acceleration voltage of 200 kV.

Cryogenic electron microscopy imaging. Samples for cryogenic electron microscopy imaging were prepared by absorption of 3 µl of AuNPs onto C-flat CF1.2/1.3 400-mesh grids (Protochips). Grids were prepared using a Vitrobot plunge freezer (FEI/ThermoFisher) with plunge freezing into liquefied ethane cooled by liquid nitrogen. Tilt series of images for A20 (II-20A), A30 (II-30A), A40 (II-40A), and A40-T (II-40A-T), A40-2T (II-40A-2T), A40-3T (II-40A-3T) were collected on a Titan Krios G2 (FEI/ThermoFisher) utilizing the Ceta2D camera at ×14,000 magnification from –60 to +60° alpha with a 2° increment between images. The IMOD package (Mastrorade) was used to reconstruct tomograms and visualize tilt series to determine angles between AuNPs.

Prediction of bond angles. For predicting the bond angles of divalent PANs resulting from different polyA lengths, the polyA block was assumed to wrap the AuNP like a geodesic line. The circumference of the 10-nm PAN was about 31.4 nm, and the lengths of 20A, 30A and 40A were about 6.6 nm, 10 nm and

13.2 nm, respectively. Therefore, the angles they formed were estimated to be 76°, 114° and 151°, respectively.

MD simulations. All-atomistic MD simulations were performed with the Amber16 program⁵⁶ for the adsorption process of the polyA segments (A20, A30 and A40) on the BSPP-protected Au(111) surface. The OL15 forcefield⁵⁹ was applied for DNA molecules. The van der Waals forces and electrostatic interactions for the DNA–Au interface were adopted with the CVFF-INTERFACE forcefield⁶⁰. The water molecules and counter ions were employed with the tip3P forcefield⁶¹. The NVT ensemble was used at the ambient temperature of 298 K, controlled by the Nosé method⁶². A time step of 1 fs was employed while the production time was set up to 5 ns after 1 ns pre-equilibration.

Based on all-atomistic MD simulations, we find that the polyA oligonucleotide tends to adsorb on the BSPP-protected Au surface in a stretched conformation rather than in a highly coiled conformation. Thus, the displacement length of the polyA oligonucleotides on the surface is positively correlated to the number of adenines (8.28 ± 0.05 , 10.90 ± 0.04 and 12.22 ± 0.03 nm corresponding to A20, A30 and A40, respectively), suggesting that the bond angle can in principle be tuned by adjusting the size of polyA.

CD theoretical calculations and measurements. Theoretical calculations were performed using the commercial software COMSOL Multiphysics based on a finite element method. The origin of the bisignate CD in the tetramer structures is a consequence of plasmonic interaction between the dipoles of neighbouring AuNPs. The CD signal was calculated as a difference in extinction for the LCP and RCP light. The incident light was polarized along the horizontal direction and normally irradiated on the models. In our calculations, the dimensions of the AuNPs were 20 nm, 15 nm, 10 nm and 5 nm, and the gaps between AuNPs were fixed at 2 nm. The refractive index of water is 1.34. The local electric current densities of the AuNPs were simulated by FEM under irradiating of the LCP and RCP light at 530 nm.

The CD spectra were measured by a Chirascan CD Spectrometer (Applied Photophysics) using the following parameters: wavelength range, 400 nm to 700 nm; optical length, 1 cm.

Data availability

All the data that support the findings of this study are available within the paper and its Supplementary Information files, and from the corresponding authors upon reasonable request.

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Author contributions

C.F. and B.L.F. directed the research. C.F., G.Y. and J.L. conceived the study. G.Y., Q.L. and X.C. performed experiments. R.P.N., D.W., G.Y. and H.Y. performed cryogenic electron microscopy imaging and analysis. F.W. and H.P. performed CD theoretical calculations. Z.Q. performed MD simulations. X.L. and X.C. performed SAXS experiments. Z.G. and H.P. assisted in the preparation of polyA–AuNPs. X.L., X.Z. and L.W. assisted with the TEM imaging. G.Y., J.L., Q.L., B.L.F. and C.F. analysed data and wrote the paper.

Competing interests

The authors declare no competing interests.

Additional information

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