

See discussions, stats, and author profiles for this publication at: <https://www.researchgate.net/publication/258850374>

Binding Assistance Triggering Attachments of Hairpin DNA onto Gold Nanoparticles

ARTICLE *in* ANALYTICAL CHEMISTRY · NOVEMBER 2013

Impact Factor: 5.64 · DOI: 10.1021/ac402908y · Source: PubMed

CITATION

1

READS

47

5 AUTHORS, INCLUDING:



[Cheng Zhang](#)

Peking University

25 PUBLICATIONS 77 CITATIONS

[SEE PROFILE](#)



[Jing Yang](#)

North China Electric Power University

27 PUBLICATIONS 79 CITATIONS

[SEE PROFILE](#)



[Shi Liu](#)

North China Electric Power University

87 PUBLICATIONS 670 CITATIONS

[SEE PROFILE](#)

Binding Assistance Triggering Attachments of Hairpin DNA onto Gold Nanoparticles

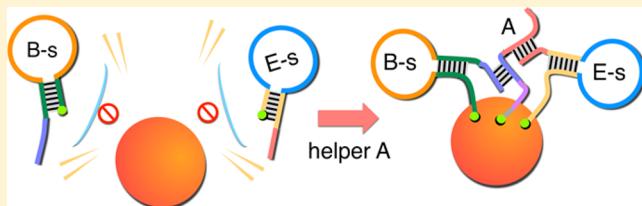
Cheng Zhang*,† Jingjing Ma,† Jing Yang,‡ Shi Liu,‡ and Jin Xu*,†

†Institute of Software, School of Electronics Engineering and Computer Science, Peking University, Key Laboratory of High Confidence Software Technologies, Ministry of Education, Beijing, China

‡School of Control and Computer Engineering, North China Electric Power University, Beijing, 102206, China

 Supporting Information

ABSTRACT: Here, we present a strategy to trigger monovalent attachments of thiolated hairpin DNA onto AuNP, assisted by molecular binding. Without binding helper strands, it is hard to control the attachments of thiolated hairpin DNA, because of spatial hindrance. By introducing a binding helper strand, the thiol-group can be brought into close proximity to the surface of AuNPs, which will greatly increase the local molecular concentration and attaching efficiency. In the experiments, the strategy is verified by the methods of DNA strand branch migration and dynamic assembly of AuNPs clusters. In addition, unique and complex AuNPs clusters with well-defined arrangements of DNA scaffolds are produced. Using this method, it is able to selectively manipulate and control different kinds and numbers of DNA attaching onto AuNPs. Our strategy also could be extended to assembling large complicated DNA/AuNPs programmable structures and nanodevices.



DNA is an ideal material for self-assembly of bottom-up nanosystems, because the specificity of strand interactions can be encoded in a DNA sequence. Recent progress and advances in DNA operations have shown great potential applications for molecular detection, information processing, and nanomaterials, such as nanomachines,^{1–4} computing systems,⁵ catalytic circuits,^{6–8} and assembly materials.^{9–15} Through delicate designs and implementations of different nanobuilding blocks, desired assembly structures can be achieved. Particularly, pioneered by Mirkin¹⁶ and Alivisatos,¹⁷ control of DNA/AuNP (gold nanoparticle) conjugates has become a rapidly evolving research focus, through which building blocks could be integrated into useful assembly cluster materials^{18–24} and functional devices.^{25–27} DNA, as a connection attaching to the AuNPs, is relatively simple and reliable and suitable to be used in constructing and assembling a variety of nanosystems. Combined with attachments of DNA strands, DNA/nanoparticle conjugations have been used extensively to detect and probe different molecules in various conditions.^{28–30}

For the purpose of assembling complex DNA/nanoparticle materials, it is essential that a precise number and kind of DNA strands per AuNP should be selectively controlled. Recently, to achieve monovalent functionalized DNA/AuNP conjugates, thiolated DNA attaching to AuNP is one of the key steps. Previous work has demonstrated that thiol-groups could well connect DNA with AuNPs, when generating multivalent DNA/AuNP conjugates.³¹ To obtain monovalent DNA/AuNP conjugates, a low DNA concentration is usually chosen to decrease the chances of multivalent attachments.^{32,33} Unfortunately,

despite its ease of controlling the number DNA strands per AuNP, it is still difficult to precisely control attachment of the DNA kinds. To achieve a function of selecting DNA attachment onto AuNPs, thiolated hairpin DNA may be a suitable candidate molecule, because of its structural variations and activities of thiol-group. In fact, researchers have well performed the attachments of thiolated hairpin DNA onto AuNP based on the method where the thiol-group is modified at the “protruding” end of the ssDNA.^{34–38} Interestingly, when it comes to hairpin DNA with a thiol-group modified at the “concaving” end, it has been found that the molecular secondary structure greatly hinders the monovalent attachments between thiol-groups and AuNPs, with a relative low DNA concentration (0.5–1.5 μM DNA, Figure 1). The reason may be that the spatial hindrance of hairpin DNA causes an effect of structural “embedment”, leading to the thiol-group being “inactive” (Figure 1a). Thus, taking advantages of such spatial hindrance, it is possible to trigger the activities of thiolated hairpin DNA and selectively control different kinds of hairpin DNA attaching onto AuNPs.

Here, we present a strategy to selectively trigger the attachments of the “inactive” thiolated hairpin DNA (a thiol-group modified at the “concaving” end) onto AuNPs, assisted by molecular binding. As shown in Figure 1b, the free thiolated hairpin DNA B-s can be captured to attach onto AuNPs, only through a specific capture by “helper” DNA A (it will bring the

Received: September 11, 2013

Accepted: November 18, 2013

Published: November 18, 2013



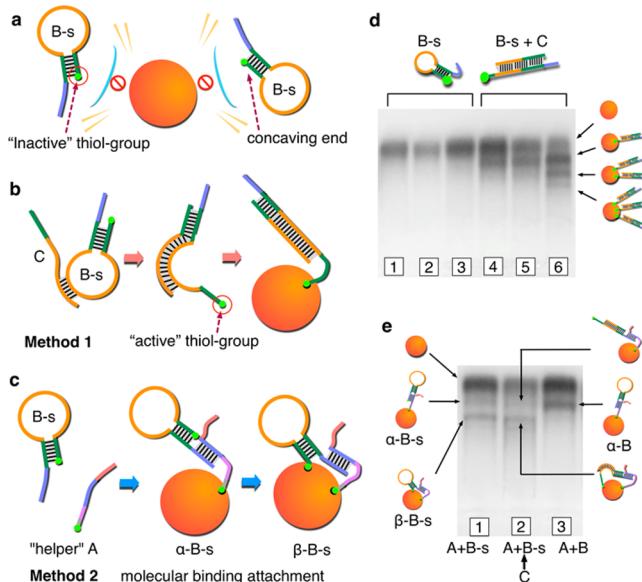


Figure 1. Illustrations of “inactive” thiolated hairpin DNA (a) and two kinds of monovalent hairpin DNA attachments: method 1 of opening loop (b) and method 2 of assisted binding (c). Electrophoretic results of 5 nm AuNPs were displayed in 3% agarose gel. (d) Lanes 1–3 correspond to AuNPs mixed with thiolated hairpin DNA B (concentrations 0.5 μ M, 1 μ M, and 1.5 μ M). The loop of hairpin DNA B was opened by adding equivalent C, and the results appeared in lanes 4–6. (e) Conjugate bands were produced by mixing AuNPs with DNA scaffolds (concentration 0.8 μ M): A+B-s (lane 1), A+B-s (lane 2, incubating with AuNPs for 4–6 h, then C was added for another 4 h), A+B (lane 3) (B-s: thiolated hairpin DNA B).

thiol group into close proximity to the AuNP surface to increase the connecting efficiency). This attaching method facilitates the building of large complicated DNA/AuNP programmable clusters, in which the number, placement, and relative orientation of AuNPs are specifically controlled in a predetermined arrangement by the geometrical hairpin DNA scaffold.

EXPERIMENTAL SECTION

Reagents and Materials. The main materials and chemicals used in our experiments are as follows: gold nanoparticles (AuNPs) with diameters of 5, 10, and 15 nm from Ted Pella; Bis (*p*-sulfonatophenyl) phenyl phosphine dipotassium salt dihydrate (BSPP) from Strem Chemical; Tris-Borate-EDTA buffer (TBE) and Tris-Acetic-EDTA buffer (TAE) from Solarbio; disulfide protected thiolated oligonucleotides by purification of HPLC from Sangon China; agarose from Biowest; methylenebisacrylamide and acrylamide monomer from TCI, Stains all from Sigma Aldrich.

DNA Scaffolds Assembly. The DNA assembly scaffolds after hybridization which was accomplished in 80 μ L of 1 \times TAE buffer with each DNA strand in the concentration of 3 μ M for about 2 h in room temperature and were detected by nondenaturing polyacrylamide gels (acrylamide-bis 19:1, 10%) for about 2 h at the voltage of 10 V/cm in room temperature. The gel experiments were performed by a mini gel device (Bio-Rad) in 1 \times TAE buffer.

Phosphination of AuNPs. AuNPs and BSPP solid powder were mixed together in the ratio of 25 mL to 12.5 mg. The mixture was kept being shaken or stirred overnight at room temperature. NaCl solid powder was added to the mixture

slowly with continuous stirring until the color of the solution changed from red to purple. Then, the solution was centrifuged at 4000–7000 rpm for 15 min and the supernatant fluid was discarded. The AuNP sample was diluted in 300 μ L of 1 \times BSPP solution (10 \times BSPP solution, 1.24 mg of BSPP in 1 mL of deionized water).

Preparation of Monovalent AuNP/DNA Conjugates.

With the changing ratio of DNA to AuNPs initially used, the number of DNA strands that attach onto each AuNP varies greatly. With the increasing of the ratio, multiple strands will attach onto an AuNP, leading to a decrease of the conjugates gel running mobility. DNA strands modified by disulfide were incubated with a ratio of 1:1.5 or 2 of AuNPs, in 0.5 \times TBE buffer (89 mM Tris, 89 mM boric acid, 2 mM EDTA, pH 8.0) and a final NaCl concentration of 50 mM for 4–6 h at room temperature. When using 5 nm AuNPs, a concentration of DNA scaffolds was 0.8–1.2 μ M. When using 15 nm AuNPs, a concentration of DNA scaffolds was 0.15–0.25 μ M. After conjugation, 3% agarose gel was used to separate AuNP/DNA conjugates with different discrete DNA bands (running gel buffer 0.5 \times TBE, 70 V, 1.5 h). The product band of monoconjugates was run into a glass fiber filter membrane supported by a dialysis membrane (MWCO 14 000). Using optical absorbance at 520 nm, each sample of AuNP/DNA conjugate was quantified and preserved at 4 °C.

Hybridization of AuNP/DNA Conjugates. In a typical reaction, 6 μ L of purified ANP/BNP/ENP solutions was mixed with 6 μ L of suspension of 15 nm conjugates, in an excess concentration ratio. The mixed samples were incubated at room temperature for 6–8 h and then were electrophoresed for 1.5 h using 3% agarose gels (0.5 \times TBE running buffer).

TEM Analysis. Purified assembly conjugates were freshly isolated. A 3–6 μ L droplet of the sample was deposited on the TEM grids and excess solution was removed using a filter paper in 5 min. Then the grids were washed with Milli-Q water 1–3 times.

RESULTS AND DISCUSSION

Because the spatial hindrance of hairpin structures effectively hinder the direct binding between thiol groups and the surfaces of AuNPs, here we have two methods to make the “inactive” thiolated hairpin DNA attach onto AuNPs: (Method 1) open the DNA hairpin structures to eliminate spatial hindrance directly via DNA branch migration (Figure 1b); (Method 2) bring the thiol group into close proximity to the AuNP surface to increase the connecting efficiency by molecular binding of a helper strand (Figure 1c).

We first prepared the experiment of Method 1 to open hairpin DNA by DNA displacement, containing two kinds of DNA molecules: hairpin thiolated DNA B-s and DNA structure B-s+C (with hairpin structure of B being open, Figure 1b). As illustrated in lanes 1–3 (Figure 1d), it is easy to see that almost no attachments were produced even with increasing the DNA concentration to 1.5 μ M. However, when the loop of hairpin DNA B-s was opened in the presence of strand C, the hairpin structure was transformed into linear DNA structure B-s+C, with the spatial hindrance eliminated. Thus, the attaching efficiency of thiolated DNA to AuNP was greatly improved, leading to the attachments even at the low DNA concentration of 0.5 μ M (lanes 4–6, Figure 1d).

Second, the experiment of method 2 was implemented, in which molecular binding assisted attachment can be triggered by adding “helper” DNA (Figure 1c). In the case of this

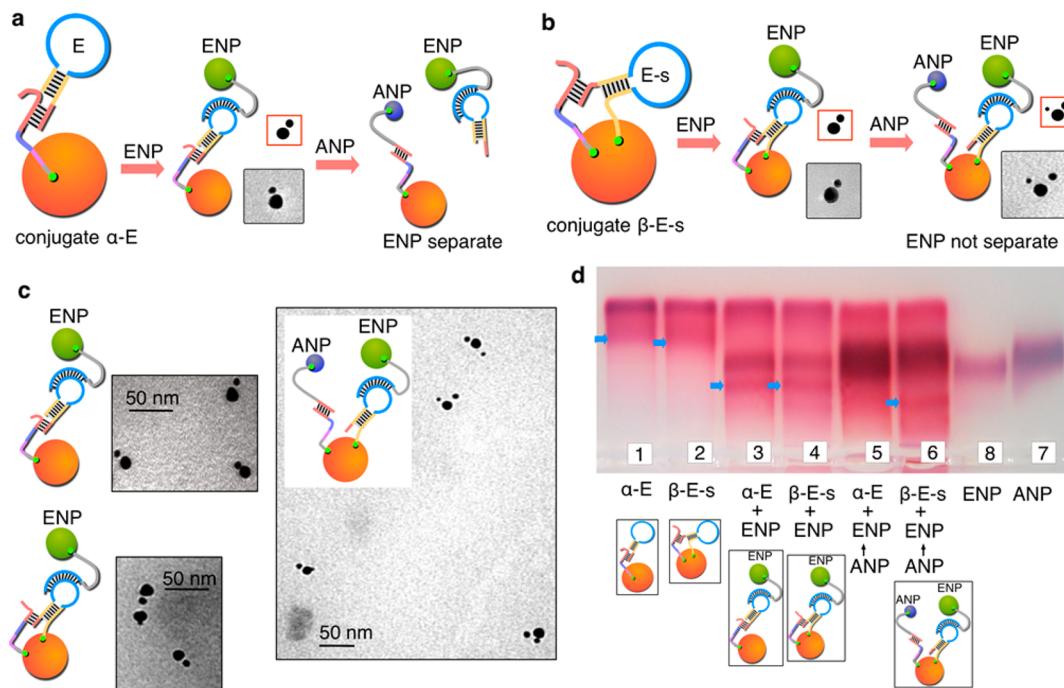


Figure 2. Schematic representations of the dynamic assembly of AuNPs clusters in parts a and b. Molecular geometry of AuNPs clusters was visualized by TEM in parts a, b, and c. (d) Electrophoretic analysis of dynamic AuNPs assembly. Products in lanes 1 and 2 (indicated by a blue arrow) correspond to 15 nm conjugates α -E and β -E-s, respectively. Adding 10 nm ENP conjugate to the solutions of conjugates α -E and β -E-s (lanes 3 and 4). Lanes 5 and 6 correspond to adding 5 nm conjugate ANP to lanes 3 and 4 for hybridizing. Lanes 7 and 8 correspond to DNA multivalent conjugates ENP (10 nm) and ANP (5 nm) (E -s: thiolated hairpin DNA E).

strategy, thiolated “helper” DNA A attached onto the AuNP in the first place and meanwhile captured free “inactive” thiolated hairpin DNA B-s. This specific molecular binding can lead to a monovalent attachment between an “inactive” thiol-group and one 5 nm AuNP. Gel results in lane 1 (Figure 1e) show that three product bands were generated, which indicated free unconjugated AuNPs, DNA monofunctionalized conjugates α -B-s and β -B-s, respectively. Clearly, the gel results of conjugates mixed with thiol-free hairpin DNA B (lane 3, Figure 1e) or thiolated hairpin DNA B-s (lane 1, Figure 1e) are different.

In our study, the molecular binding attachment of hairpin DNA can be confirmed by comparing the structures of monofunctionalized conjugates α and β (Figure 2a,b). To further test the capabilities of this attachment strategy and discriminate the structural differences between monofunctionalized conjugates α -E and β -E-s, a method, employing dynamic assembly of discrete AuNPs clusters (AuNPs with diameters of 15, 10, and 5 nm) is introduced. Before achieving hybridization, the multivalent DNA functionalized conjugates ANP and ENP were synthesized using 5 and 10 nm AuNPs, respectively.

In the first approach, 10 nm conjugate ENP was added to hybridize with 15 nm α -E and β -E-s (Figure 2a,b), respectively, for 4–6 h. It was expected that in the presence of 10 nm conjugate ENP, the furthest end of strand ENP would hybridize with the bulge region of hairpin DNA E/E-s connecting onto the surface of 15 nm AuNPs, forming a dimer of nanoparticles with asymmetric diameters. In Figure 2d, lanes 3 and 4 show hybridizing results corresponding to α -E and β -E-s, in which two bands were produced with almost the same gel running speed (indicated by blue arrows). TEM analysis of the indicated sample bands revealed that nearly each 15 nm AuNP was hybridized with one 10 nm AuNPs (Figure 2 and Figures S8a,b in the Supporting Information). In the second approach, after

mixing α -E and β -E-s with conjugate ENP for 4–6 h, 5 nm conjugate ANP was added for another 4–6 h hybridization. In the experimental design, the furthest 3' end of strand ANP could recognize and fully hybridize with the 5' end toehold region of A, which was previously bound with DNA hairpin E/E-s. Therefore, the ANP could displace the hairpin E/E-s for the longer hybridizing sequences.

For α -E (Figure 2a), adding conjugate ANP led to separation of conjugate ENP from α -E, due to no thiol-group in hairpin E connecting with the 15 nm AuNP. The gel analysis in Figure 2d lane 5 indicated that the band of the previous products with the asymmetric AuNP dimer (10 + 15 nm) disappeared, when compared with the product band indicated by an arrow in lane 3. For β -E-s (Figure 2b), although the ANP displaced hairpin E-s, the thiol-group in hairpin DNA E-s is still bound onto the 15 nm AuNP. Thus, with the addition of 5 nm conjugate ANP, the dimer of 10 and 15 nm nanoparticles did not separate but instead formed a trimer product consisting of 5, 10, and 15 nm nanoparticles. It was observed that a product band of trimer nanoparticles was generated (indicated by blue arrows, Figure 2d, lane 6), while no product band with the same gel running speed was generated in lane 5. The results of AuNPs dynamic assembly demonstrated the structural differences between conjugates α -E and β -E-s. In addition, the TEM images also showed that the typical structures of dimer and trimer were produced in the hybridization (Figure 2c and Figure S8 in the Supporting Information).

On the basis of the molecular binding attachment, the numbers and kinds of hairpin DNA onto AuNPs can also be selectively controlled. Here, to prove that this assisted binding method is suitable for a large and universal scale, both DNA hairpin B-s and E-s were introduced at the same time. Analysis of the gel results indicates that conjugate γ (Figure 3a, lane 3)

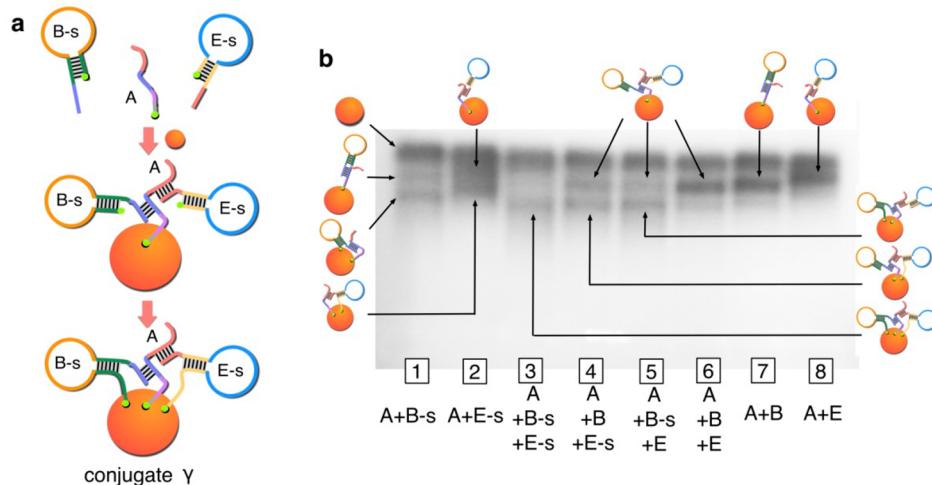


Figure 3. Illustrations of two thiolated hairpin DNA attachments (a). Lanes 1 to 8 in parts correspond to mixtures of different DNA scaffolds incubating with 5 nm AuNPs: (A+B-s), (A+E-s), (A+B-s+E-s), (A+B+E-s), (A+B-s+E), (A+B+E), (A+B), and (A+E), respectively.

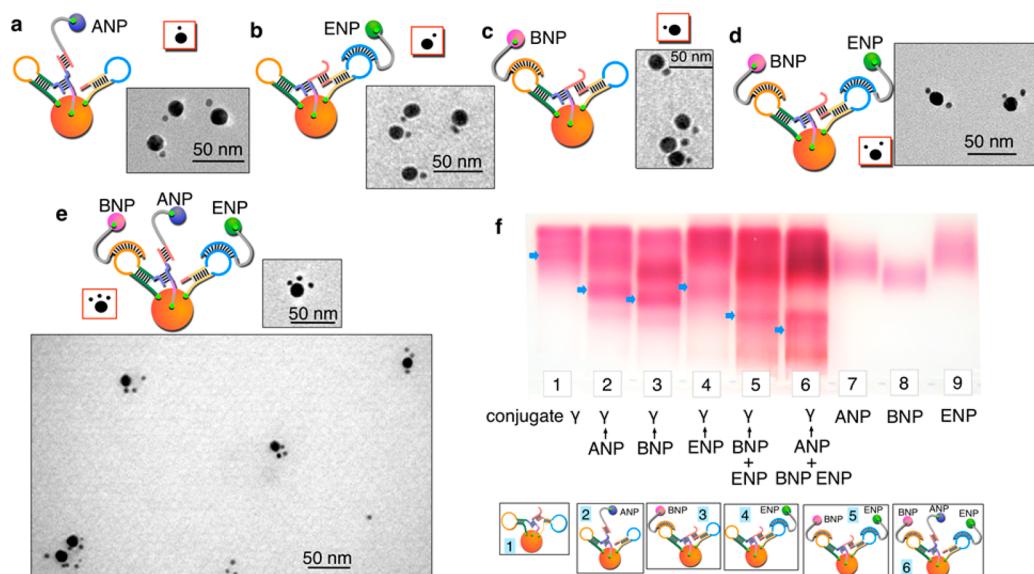


Figure 4. Molecular geometry of AuNPs clusters was visualized by TEM in parts a–e. (e) Electrophoretic analysis of DNA/AuNPs conjugates assembly: lane 1, conjugate γ . Adding either of the 5 nm multivalent conjugates of ANP, BNP, and ENP to conjugate γ (lanes 2, 3 and 4). In lane 5, both the 5 nm conjugates of BNP and ENP were added. In lane 6, all three kinds of 5 nm conjugates were added. Lanes 7, 8, and 9 correspond to 5 nm DNA multiple functionalized-conjugates ANP, BNP, and ENP.

with two thiolated DNA hairpins attaching on one 15 nm AuNP had a rather lower gel speed than those just attached with one thiolated DNA hairpin molecule (lanes 1 and 2). Interestingly, when adding either of thiolated hairpins B-s or E-s, a band of intermediate products (with thiol-group not attaching onto the AuNPs) was easily observed (indicated middle bands in lanes 4 and 5). However, when both of the thiolated hairpins were introduced, almost no such intermediate product was generated and, instead, only conjugate γ was found. It also should be noted that although the DNA scaffold structures of the conjugate with thiol-free hairpins B and E in lane 6 was almost the same as that of conjugate γ in lane 3, the gel mobility of the former was much faster than the latter.

We next sought to verify the monovalent hairpin DNA attachments by constructing complex hybridizing DNA/AuNPs clusters. For this purpose, a series of hybridizaiton were implemented based on a specific binding arrangement directed by geometrical DNA assembly structures. In the experiment,

multivalent 5 nm conjugates of ANP, BNP, and ENP (in an excess concentration ratio) were designed to specifically hybridize with the DNA scaffold of the 15 nm conjugate γ , at the 5' ends of A and the bulge regions of hairpin DNA B-s and E-s, respectively. To clearly distinguish the hybridized clusters' structures, different adding arrangements of multivalent conjugates ANP, BNP, and ENP were carried out. When mixing only one kind of conjugates of ANP, BNP, and ENP with conjugate γ for 6–8 h incubation, there were three newly generated bands in the gel (Figure 4f, lanes 2, 3, and 4, indicated by blue arrow). As expected, the TEM images of these bands indicated that clusters with asymmetric AuNPs dimers were produced, in which one 5 nm nanoparticle connected with a 15 nm one (Figure 4 and Figure S8 in the Supporting Information). Similarly, two kinds of 5 nm conjugates BNP and ENP were added at the same time. It is shown in Figure 4f lane 5 that a band of trimer product was generated (indicated by the blue arrow), with two 5 nm

nanoparticles connecting with a 15 nm one (Figure 4 and Figure S8 in the Supporting Information).

Using this method, a more complex nanostructure that resembles a dendrimer was produced. In Figure 4f lane 6, all three kinds of 5 nm conjugates of ANP, BNP, and ENP were added to 15 nm conjugate γ . It is easy to see a newly generated band (indicated by a blue arrow), which was formed by hybridizing the three 5 nm nanoparticles with the DNA scaffold on the surface of asymmetrically monofunctionalized 15 nm nanoparticles. As is clearly seen from the TEM image, the tetramer products of indicated bands in lanes 5 and 6 consisted of a central AuNP surrounded by two or three peripheral particles (Figure 4 and Figure S8 in the Supporting Information). Importantly, the TEM results showed that, in the typical structures, almost all of the peripheral particles only attached on the same half side of the central AuNPs (Figure S10 in the Supporting Information). The positions of peripheral particles were not randomly distributed on the surfaces of AuNPs. The reason for this phenomenon may be that, without the help of binding assistance from strand A, free thiolated DNA in solution was difficult to attach onto AuNPs directly. Only through strand A capturing two hairpin DNA molecules and bringing them together, the thiolated DNA hairpins can be attached onto AuNPs.

In summary, we have developed a method to trigger the monovalent attachment of “inactive” thiolated hairpin DNA onto AuNPs, assisted by molecular binding. Our method uses a linear DNA strand as a binding arm helper, providing a specific molecular recognition and selective regulations, such as triggering the monovalent attachments, and controlling the numbers and kinds of hairpin DNA onto AuNPs. In addition, a formation method of dynamic and modular assembly of AuNPs clusters is developed. Our strategy could also be extended to assembling large complicated DNA/AuNPs programmable structures, to offer a powerful manipulation method of nanosystems and nanodevices.

ASSOCIATED CONTENT

Supporting Information

Description of other experimental procedures and additional figures. This material is available free of charge via the Internet at <http://pubs.acs.org>.

AUTHOR INFORMATION

Corresponding Authors

*E-mail: zhangcheng369@pku.edu.cn. Phone: 86-010-62750359.

*E-mail: jxu@pku.edu.cn.

Author Contributions

The study was designed by Cheng Zhang and was carried out by Jingjing Ma and Cheng Zhang. The manuscript was written by Cheng Zhang, Jing Yang, and Shi Liu and was revised by Jin Xu. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

We thank Prof. H. Inaki Schlaberg for helpful discussion and manuscript revision. This work was supported by the National Natural Science Foundation of China (Grants 61272161, 61127005, 61133010, 61033003, 60910002, and 61370099),

Programme of Introducing Talents of Discipline to Universities (Grant B13009), and the National Program on Key Basic Research Project (973 Program: Grant 2013CB329600).

REFERENCES

- (1) Bath, J.; Turberfield, A. J. *Nat. Nanotechnol.* **2007**, *2*, 275–284.
- (2) Ke, Y.; Lindsay, S.; Chang, Y.; Liu, Y.; Yan, H. *Science* **2008**, *319*, 180–183.
- (3) Venkataraman, S.; Dirks, R. M.; Rothemund, P. W. K.; Winfree, E.; Pierce, N. A. *Nat. Nanotechnol.* **2007**, *2*, 490–494.
- (4) Goodman, R. P.; Schaap, I. A. T.; Tardin, C. F.; Erben, C. M.; Berry, R. M.; Schmidt, C. F.; Turberfield, A. J. *Science* **2005**, *310*, 1661–1665.
- (5) Adleman, L. M. *Science* **1994**, *66*, 1021–1021.
- (6) Pei, R. J.; Matamoros, E.; Liu, M. H.; Stefanovic, D.; Stojanovic, M. N. *Nat. Nanotechnol.* **2010**, *5*, 773–777.
- (7) Omabegho, T.; Sha, R.; Seeman, N. C. *Science* **2009**, *324*, 67–71.
- (8) Seelig, G.; Soloveichik, D.; Zhang, D. Y.; Winfree, E. *Science* **2006**, *314*, 1585–1588.
- (9) Bath, J.; Green, S. J.; Turberfield, A. J. *Angew. Chem., Int. Ed.* **2005**, *44*, 4358–4361.
- (10) Rothemund, P. W. K. *Nature* **2006**, *440*, 297–302.
- (11) Yan, H.; Park, S. H.; Finkelstein, G.; Reif, J. H.; LaBean, T. H. *Science* **2003**, *301*, 1882–1884.
- (12) Zheng, J.; Birktoft, J. J.; Chen, Y.; Wang, T.; Sha, R.; Constantinou, P. E.; Ginell, S. L.; Mao, C. D.; Seeman, N. C. *Nature* **2009**, *461*, 74–77.
- (13) Han, D.; Pal, S.; Nangreave, J.; Deng, Z.; Liu, Y.; Yan, H. *Science* **2011**, *332*, 342–346.
- (14) Douglas, S. M.; Dietz, H.; Liedl, T.; Höglberg, B.; Graf, F.; Shih, W. M. *Nature* **2009**, *459*, 414–418.
- (15) Feldkamp, U.; Niemeyer, C. M. *Angew. Chem., Int. Ed.* **2006**, *45*, 1856–1876.
- (16) Mirkin, C. A.; Letsinger, R. L.; Mucic, R. C.; Storhoff, J. J. *Nature* **1996**, *382*, 607–609.
- (17) Daniela, Z.; Christine, M. M.; Wolfgang, J. P.; Daniele, G. A.; Alivisatos, A. P. *Nano Lett.* **2001**, *1*, 32–35.
- (18) Mathew, M. M.; Dmytro, N.; Marine, C.; Daniel, V. L.; Oleg, G. *Nat. Mater.* **2009**, *8*, 388–391.
- (19) Aldaye, F. A.; Sleiman, H. F. *Angew. Chem., Int. Ed.* **2006**, *118*, 2262–2267.
- (20) Sharma, J.; Chhabra, R.; Cheng, A.; Brownell, J.; Liu, Y.; Yan, H. *Science* **2009**, *323*, 112–116.
- (21) Sharma, J.; Chhabra, R.; Liu, Y.; Ke, Y.; Yan, H. *Angew. Chem., Int. Ed.* **2006**, *45*, 730–735.
- (22) Dmytro, N.; Mathew, M. M.; Daniel, V. L.; Oleg, G. *Nature* **2008**, *451*, 549–552.
- (23) Park, S. Y.; Lytton-Jean, A. K. R.; Lee, B.; Weigand, S.; Schatz, G. C.; Mirkin, C. A. *Nature* **2008**, *451*, 553–556.
- (24) Gu, H.; Chao, J.; Xiao, S. J.; Seeman, N. C. *Nature* **2010**, *465*, 202–205.
- (25) Lo, P. K.; Karam, P.; Aldaye, F. A.; McLaughlin, C. K.; Hamblin, G. D.; Cosa, G.; Sleiman, H. F. *Nat. Chem.* **2010**, *2*, 319–328.
- (26) Mastroianni, A. J.; Claridge, S. A.; Alivisatos, A. P. *J. Am. Chem. Soc.* **2009**, *131*, 8455–8459.
- (27) Hazarika, P.; Ceyhan, B.; Niemeyer, C. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 6469–6471.
- (28) Deng, Z. X.; Tian, Y.; Lee, S. H.; Ribbe, A. E.; Mao, C. D. *Angew. Chem., Int. Ed.* **2005**, *44*, 3582–3585.
- (29) Mao, C. D.; Chen, Y. *Small* **2008**, *4*, 2191–2194.
- (30) Sharma, J.; Chhabra, R.; Cheng, A.; Brownell, J.; Liu, Y.; Yan, H. *Science* **2009**, *323*, 112–116.
- (31) Kim, J. W.; Kim, J. H.; Deaton, R. *Angew. Chem., Int. Ed.* **2011**, *50*, 9185–9190.
- (32) Aldaye, F. A.; Sleiman, H. F. *J. Am. Chem. Soc.* **2007**, *129*, 4130–4131.
- (33) Feng, L. P.; Park, S. H.; Reif, J. H.; Yan, H. *Angew. Chem., Int. Ed.* **2006**, *42*, 4342–4346.

- (34) Cheng, Y.; Stakenborg, T.; Dorpe, P. V.; Lagae, L.; Wang, M.; Chen, H.; Borghs, G. *Analytical Chem.* **2011**, *83*, 1307–1314.
- (35) He, Y.; Zeng, K.; Gurung, A. S.; Baloda, M.; Xu, H.; Zhang, X.; Liu, G. *Anal. Chem.* **2010**, *82*, 7169–7177.
- (36) Song, S. P.; Liang, Z. P.; Zhang, J.; Wang, L. H.; Li, G. X.; Fan, C. H. *Angew. Chem., Int. Ed.* **2009**, *48*, 1–5.
- (37) Suzuki, K.; Hosokawa, K.; Maeda, M. *J. Am. Chem. Soc.* **2009**, *131*, 7518–7519.
- (38) Claridge, S. A.; Goh, S. L.; Jean, M. J.; Fre, C.; Williams, S. C.; Micheel, C. M.; Alivisatos, A. P. *Chem. Mater.* **2005**, *17*, 1628–1635.