Multicolor and Erasable DNA Photolithography

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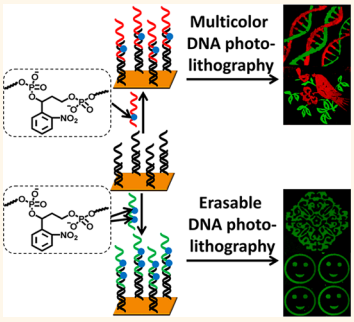
ABSTRACT The immobilization of DNA molecules onto a solid support is a crucial step in biochip research and related applications. In this work, we report a DNA photolithography method based on photocleavage of 2-nitrobenzyl linker-modified DNA strands. These strands were subjected to ultraviolet light irradiation to generate multiple short DNA strands in a programmable manner. Coupling the toehold-mediated DNA strand-displacement reaction with DNA photolithography enabled the fabrication of a DNA chip surface with multifunctional DNA patterns having complex geometrical structures at the microscale level. The erasable DNA photolithography strategy was developed to allow different paintings on the same chip. Furthermore, the asymmetrical modification of colloidal particles was carried out by using this photolithography strategy. This strategy has broad applications in biosensors, nanodevices, and DNA-nanostructure fabrication.



KEYWORDS: DNA photolithography · surface patterning · asymmetrical modification · colloidal particles · photocleavage · toehold-mediated DNA strand displacement

The biomacromolecule DNA has the characteristics of highly specific, predictable and thermoreversible base-pair interactions with its complementary DNA strand, easy chemical synthesis and modification, and precise sequence manipulation. Thus, DNA plays an important role in clinical diagnostics,[1,2] drug delivery,[3,4] biosensors,[5−7] and fabrication of DNA nanostructures and nanodevices.[8−11] Various devices, including circuits, catalytic amplifiers, autonomous molecular motors, and reconfigurable nanostructures, have recently been rationally designed to use toehold-mediated DNA strand-displacement reactions.[12−15] In some of these applications, DNA is required to be immobilized onto a solid support for the subsequent binding and detection of its complementary DNA chains or for the recognition of targeted small molecules and proteins.[16,17] In this case, the immobilization of DNA molecules onto the solid support is a crucial step in practical applications.

Many methods are used to immobilize DNA molecules onto different solid supports. A commonly used method for DNA immobilization is to functionalize it with a terminal reactive group that is selective for the surface of interest.[18−21] In practical applications, DNA molecules can be homogeneously immobilized over an entire surface or heterogeneously immobilized to form multifunctionalized DNA arrays. Fabricating multifunctionalized DNA surfaces is highly desirable for biomedical applications.[22] Photolithography, Dip-Pen nanolithography, and light-directed *in situ* DNA chemical synthesis are all used to fabricate multifunctional DNA surfaces.[23−27] Of these, photolithography is considered a versatile microfabrication tool in routine research laboratories to fabricate multifunctional DNA chip surfaces.[26] Chaikin *et al.*[28] recently reported a smart DNA photolithography method based on permanent cross-linking of cinnamate-modified DNA strands. In this method, microscale patterns are written on a surface using ultraviolet (UV) light, and the reversible attachment of conjugated DNA and DNA-coated colloids is demonstrated. Despite

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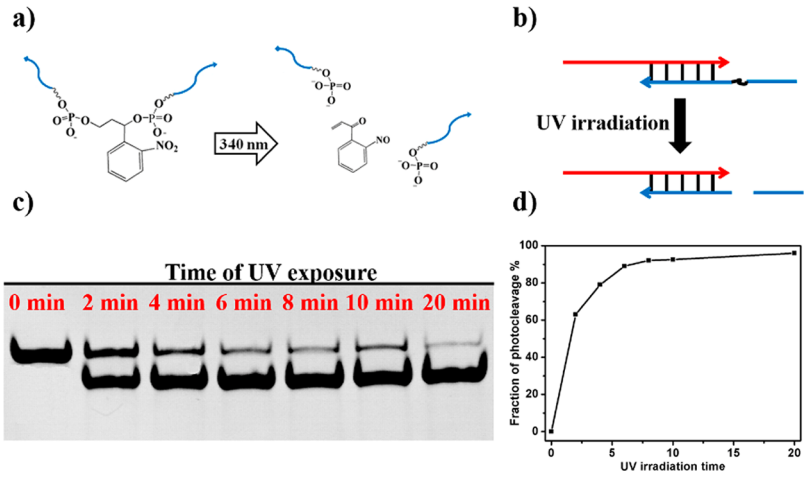

Figure 1. Chemical basis of DNA photolithography. (a) Structure of the photocleavable linker and reaction schematic. (b) Photocleavage process of DNA complex containing a photocleavable linker. (c) Cleavage kinetics of the DNA complex containing a photocleavable linker as observed by electrophoresis. (d) Plot of photocleavage fraction *versus* UV irradiation time.

success in this aspect, strategies for fabricating versatile functional surfaces are still urgently needed to fulfill the requirements of diverse applications.

In this paper, we report a DNA photolithography method based on the photocleavage of DNA strands. Different from the permanent photo-cross-linking method,[28] we use a commercially available photocleavable 2-nitrobenzyl linker[29−32] (PC linker) to connect two DNA strands. This engineering design results in the formation of one long single-stranded DNA. The linked DNA strand forms two pieces of short DNA strands upon UV light-induced photocleavage of the 2-nitrobenzyl linker. Introducing these PC linker-modified DNA strands onto surfaces enables photolithography. With the use of this photolithography strategy, the asymmetrical modification of colloidal particles was carried out.

RESULTS AND DISCUSSION

First, the efficiency of UV light induced photocleavage of PC linker-modified DNA strand was evaluated. To accomplish this, the PC linker group 2-nitrobenzyl was first incorporated into the assigned position in the oligonucleotide probe sequence, as shown in Figure 1a. Subsequent UV irradiation caused cleavage of the PC linker and release of the two connected short DNA strands. To determine whether photocleavage proceeded as designed, a PAGE experiment was carried out. In a typical experiment, SS DNA was hybridized with PC linker-modified LS DNA (sequences are shown in Table S1) to form a DNA complex with two single-strand tails. UV irradiation caused cleavage of the PC linker and subsequent release of one tail, as shown in Figure 1b. As indicated in Figure 1c, the band with the small migration in all lanes corresponded to the DNA complex with two single-strand tails. Conversely, the band with large migration in all lanes corresponded to the newly formed DNA complex with one tail after UV irradiation. With increased UV irradiation time, the bands with small migration became less intense, but the bands of the newly formed DNA complex with one tail became more intense. These results proved that photocleavage indeed proceeded as designed and that the photocleavage fraction of the PC linker could be controlled by regulating irradiation dosage.

To determine the exact amount of cleaved PC linker, the band intensities of DNA complexes with two single-strand tails and newly formed DNA complexes with one single-strand tail after different UV irradiation times were analyzed with ImageJ software. The fraction of cleaved PC linker for different irradiation times was then calculated according to the band intensities. As shown in Figure 1d, the fraction of cleaved PC linker increased with increased UV irradiation time. After 10 min of UV irradiation, 93% of the PC linker was cleaved in solution. The photocleavage of PC linker modified DNA on gold-coated glass surfaces was further studied and the results are shown in Figure S1 and Figure S2. As the irradiation time increased, increasingly more PC linker modified DNA on the gold-coated glass surface was cleaved, as demonstrated by the decreasing fluorescence intensity in Figure S1. The fluorescence intensities after different UV irradiation times were analyzed with ImageJ software. The fraction of cleaved PC linker on the surface for different irradiation times was then calculated according to the fluorescence intensities. As shown in Figure S2, the photocleavage process on a surface is slightly slower than that in solution. For subsequent DNA photolithography studies on the surface, we used 10 min as the optimum time, because this short irradiation time sufficiently cleaved the PC linker.

Next, DNA photolithography was first attempted by generating a pattern with one color on the surface.

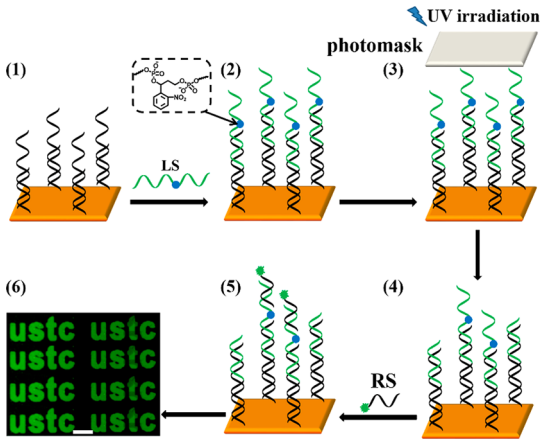

Figure 2. Schematic of DNA photolithography with a photocleavable 2-nitrobenzyl linker-based DNA strand to generate a pattern with one color on the surface (1−5) Procedure of DNA photolithography and (6) green fluorescent pattern on the surface after photolithography. The scale bar is 200 μm.

Toward this end, PC linker-modified short DNA (LS in Table S1) was introduced onto the DNA (SS in Table S1) coated gold surface by hybridizing with preimmobilized SS DNA, as shown in Figure 2. The SS DNA strand used in this study consisted of two major parts: an inert section and a sticky end. The inert section can hybridize with its complementary strand (CSS in Table S1) to form a double-stranded duplex. The sticky end was used as the directing and recognition unit to bind to the LS DNA. The SS DNA strand was first annealed with an equal number of CSS DNA strands to hybridize and form a construct with a 49-bas-pair rigid duplex, followed by a 22-nucleotide sticky end. The annealed DNA was then incubated on the gold surface to enable attachment. Afterward, LS DNA was hybridized with SS DNA by incubation on the SS DNA coated gold surface (Figure 2, steps 1 and 2). Then, a photomask with "USTC" patterns, as shown in Figure S3, was placed on the surface and exposed to UV light (step 3). UV light could penetrate the transparent film, but not the dark patterns on the film. In this way, LS DNA in the exposed regions was cleaved, whereas that in the pattern regions remained intact (step 4). After UV light exposure, the green fluorescently labeled RS DNA (Table S1) was incubated on the surface to hybridize with the remaining LS DNA strand in the pattern regions (step 5). After hybridization with the RS DNA strand, the pattern was imaged by confocal microscopy, and the result is shown in Figure 2 (6).

The fabrication of multifunctionalized DNA surfaces is highly desirable for some biomedical applications.[22] Therefore, we further extended the photolithographic technique to the fabrication of patterns with two different colors, accomplished with the aid of toehold-mediated strand displacement.[29] The photocontrolled toehold formation for toehold-mediated DNA displacement reaction was proven by fluorescence tests in solution and the result is shown in Figure S4. As can be seen, with increasing irradiation time, increasingly more hidden toehold was released, as demonstrated by the increasing fluorescence intensity after toehold-mediated DNA displacement reaction. For the subsequent multicolor DNA photolithography, we slightly changed the position of the PC linker in the linking-strand DNA (LS-1). Similar to the procedure of generating a pattern with one color, LS-1 DNA was first hybridized with the SS DNA-coated surface (step 2, Figure 3). After hybridization, the photomask with part of the pattern (Figure S5a) was placed on the surface and exposed to UV light (step 3). After irradiation, LS-1 DNA strands in the pattern regions remained intact, whereas LS-1 DNA strands in the transparent regions were cleaved to form the toehold (released single-strand section in SS DNA shown in step 4, Figure 3) for subsequent toehold-mediated strand displacement reaction. LS DNA was then incubated on the surface. In this way, the cleaved LS-1 DNA in the transparent regions was displaced by LS DNA through toehold-mediated strand displacement reaction (step 5). After displacement, the photomask with the remaining part of the pattern (Figure S5b) was placed on the surface and then exposed to UV light again (step 6). Upon irradiation, the LS DNA in the pattern regions remained intact, whereas LS DNA in other regions was cleaved (step 7). Finally, the target material (in this case, green fluorescently labeled reporter DNA strand (RS) and red fluorescently labeled reporter DNA strand (RS-1)) was hybridized with the remaining LS DNA and LS-1 DNA in the pattern regions to develop the pattern (step 8). After developing, the patterns were imaged by confocal microscopy. The patterns in the green and red channels were carefully merged using software, and the merged patterns are shown in (9), (10), (11), and (12) in Figure 3.

Finally, to repeatedly fabricate different patterns on the same chip surface and make the chip reusable, an erasable DNA photolithography strategy was developed. Different from current nonerasable methods based on permanent cross-linking of DNA strands,[28,33] we developed erasable DNA photolithography based on the photocleavage of PC linker and with the aid of toehold-mediated strand displacement. The entire process is shown in Figure 4. In a typical process, LS-2 DNA was first hybridized with the SS DNA-modified gold surface to form a homogeneous LS-2 DNA surface (step 2). Next, the photomask (Figure S6) was placed on the surface and irradiated with UV light (step 3). During UV irradiation, LS-2 DNA in the pattern regions remained intact, whereas most of the PC linkers in the exposed LS-2 DNA strand were cleaved, releasing the single-strand part (toehold) in SS DNA (step 4). After irradiation, RS DNA was used to develop the pattern (step 5) that was then imaged using a confocal microscope. To erase the pattern on the surface and

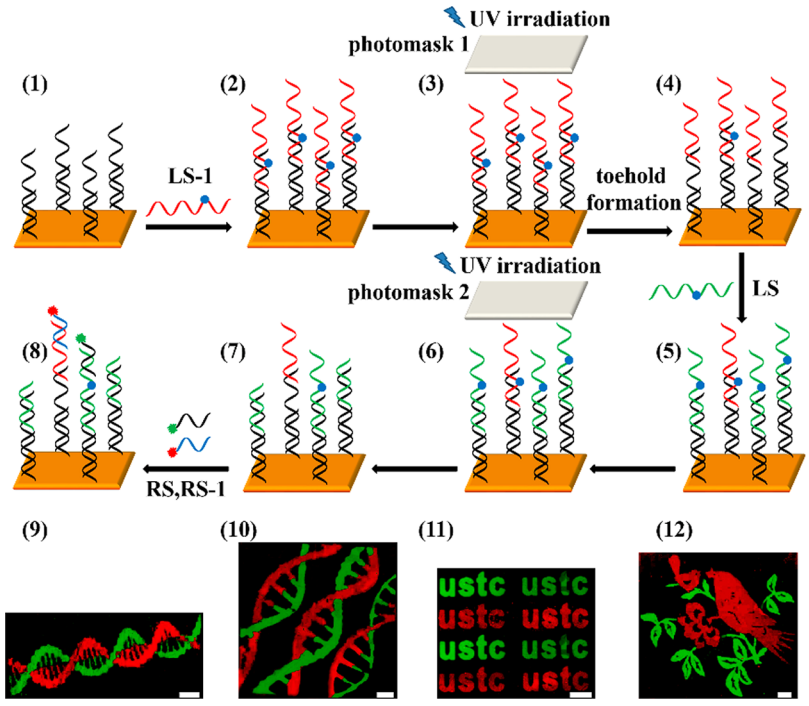

Figure 3. Schematic of DNA photolithography with a photocleavable 2-nitrobenzyl linker-based DNA strand to generate patterns with two different colors on the surface. (1−8) DNA photolithography procedures for generating the multifunctional surface and (9−12) fluorescent patterns with two different colors on the surface after photolithography. The scale bars are 200 μm.

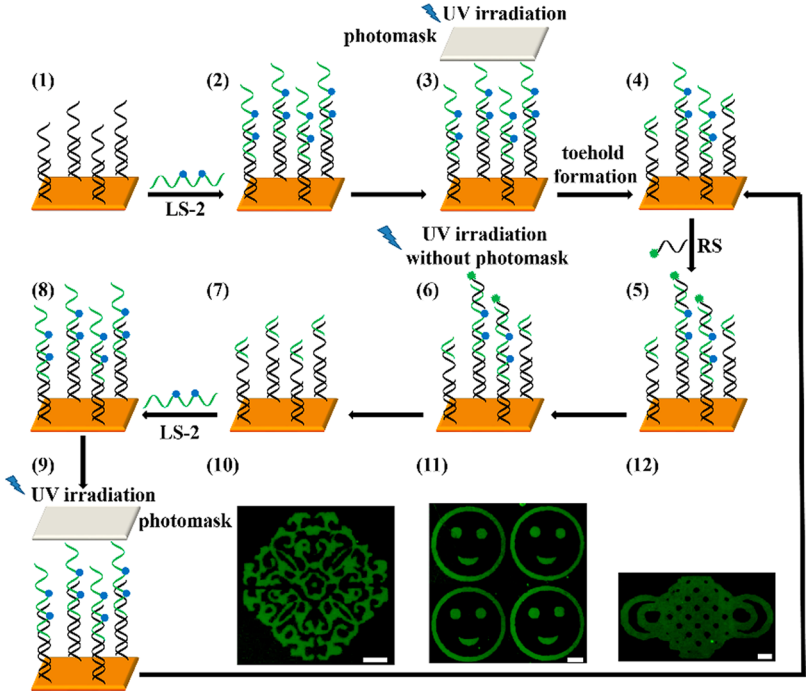

Figure 4. Schematic of erasable DNA photolithography. (1−9) Procedure of erasable DNA photolithography, and (10−12) green fluorescent patterns repeatedly generated using the same chip surface through erasable DNA photolithography. The scale bars are 200 μm.

repeatedly use the same chip surface to fabricate different patterns, the surface with a certain pattern was exposed to UV light without any photomask (step 6). In this way, all the LS-2 DNA on the surface was cleaved, forming the toehold (step 7) for subsequent toehold-mediated strand displacement reaction. To perform the toehold-mediated strand displacement reaction, LS-2 DNA was incubated on the UV light exposed surface to form a new homogeneous LS-2 DNA layer (step 8). This newly formed LS-2 DNA

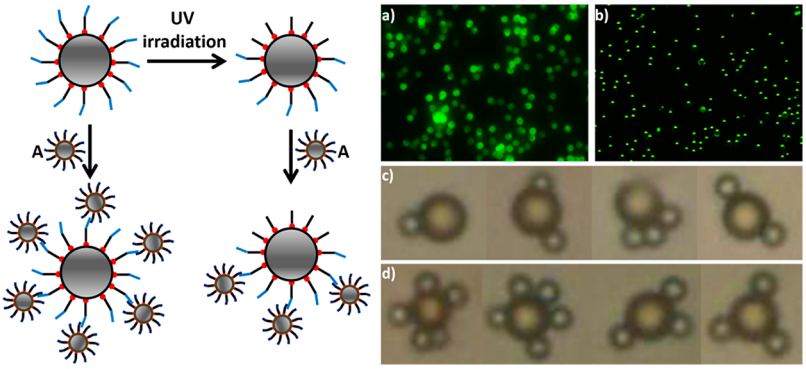

Figure 5. Schematic procedure for producing particles with one-side DNA functionalization. Fluorescent detection of the particles (a) before UV irradiation and (b) after UV irradiation. (c) Self-assembled structure of the one-side LS1 functionalized large particles with complementary small particles A. (d) Self-assembled structure of LS1 functionalized large particles with complementary small particles A.

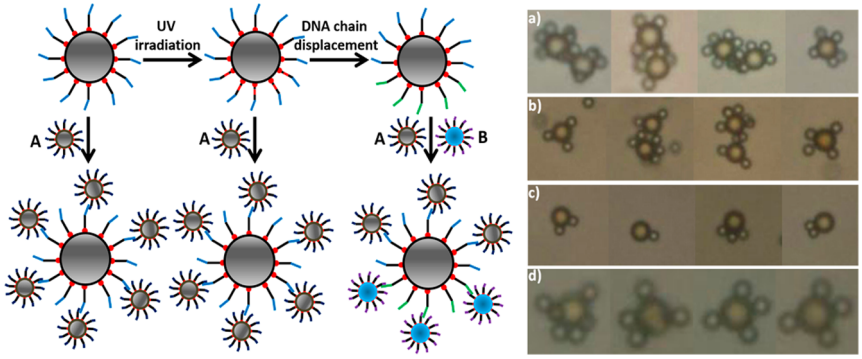

Figure 6. Schematic procedure for producing particles with two different DNA functionalization at different sides. (a) Self-assembled structure of LS2 DNA functionalized large particles with complementary small particles A. (b) Self-assembled structure of UV irradiated LS2 DNA functionalized large particles with complementary small particles A. (c) Self-assembled structure of LS2 and LS3 functionalized large particles with complementary small particles A or B. (d) Self-assembled structure of LS2 and LS3 functionalized large particles with complementary small particles A and B.

homogeneous layer could be used to fabricate a new pattern using a different photomask (from step 9 to step 4). With this erasable DNA photolithography method, three different patterns ((10), (11), and (12) in Figure 4) were fabricated on the same surface using different photomasks (Figure S6).

For the scientific applications of this method, the asymmetrical modification of colloidal particles was carried out by using this photolithography strategy and the results are shown in Figures 5 and 6. In Figure 5, LS1 (Table S3) coated magnetic beads were immobilized on the glass slide with the help of magnet (Figure S7). Then, the glass slide surface was irradiated with vertical UV light. In this way, the DNA chains on one side of the particles were cleaved by UV light, forming particles with one side LS1 DNA coating. The particles can further assemble with LS1′ coated complementary particles (particles A as shown in Figure 5), forming the self-assembled structure as shown in Figure 5c. Similarly, as shown in Figure 6, LS2 coated magnetic beads were immobilized on the glass slide and were irradiated with vertical UV light. After UV irradiation, the LS2 DNA on one side of the particles were cleaved to form the toehold for subsequent toehold-mediated strand displacement reaction. After that, LS3 was added and the cleaved LS2 on one side of the particles was displaced by LS3 through toehold-mediated strand displacement reaction. In this way, the particles with one side LS2 functionalization and the other side LS3 functionalization was obtained. The particles can further assemble with LS1′ coated particles A, LS2′ coated particles B or both of them. The self-assembled structures are shown in Figure 6c,d.

CONCLUSIONS

In conclusion, we presented a DNA photolithography method based on the photocleavage of PC linker-connected DNA strands. The PC linker can be efficiently cleaved upon UV irradiation. Our experimental results showed that 93% of the PC linker was cleaved after 10 min of UV irradiation. Using this methodology, we developed a photolithography method capable of functionally patterning surfaces by introducing PC linker-connected DNA strands onto the surface. With the use of this method combined with a toehold-mediated DNA strand displacement reaction, multifunctionalized DNA surfaces were fabricated and the erasable photolithography method was developed.

Our photolithographic technique showed potential for the repeated construction of different chemical and physical patterns on the same surface or for the fabrication of multifunctionalized DNA chip surfaces for genetic detection[34] or DNA computing.[35] This technique can also be used to asymmetrically modify microsized colloidal particles for medical and soft matter research purposes in a more controlled manner.[36−38]

EXPERIMENTAL SECTION

Materials. Ultrapure water with 18.2 MΩ·cm (Millipore Simplicity) was used in all experiments. All chemical reagents were analytical grade and used without further purification. Tris(2-carboxyethyl)phosphine hydrochloride (TCEP) was obtained from Alfa Aesar. All DNA oligonucleotides used were purchased from Sangon Biotechnology Co., Ltd. (Shanghai, China) and purified by HPLC or ultraPAGE. The DNA sequences are shown in Table S1. The buffer used in all experiments was TE buffer (20 mM Tris-HCl, 300 mM NaCl, and 5 mM $MgCl_2$; pH 7.4).

Native PAGE Analysis. A 5 μM mixture of SS and LS was annealed by heating it to 95 °C for 10 min and then cooling to 25 °C. The annealed mixture was irradiated for different times and observed using native PAGE gel. The gel was run in 20% acrylamide (containing 19/1 acrylamide/bisacrylamide) solution with 1× TBE buffer, at 100 V constant voltage for 3.5 h and stained for 20 min using GelRed (Biotium) to image the DNA position. Band intensities were analyzed with NIH ImageJ software to calculate the photocleavage fraction under different UV irradiation times. Origin 8.0 was used for data analysis.

DNA-Coated Gold Surface. The DNA-coated gold surface was prepared as previously described[28] with slight modification. A coverslip (1.8 cm × 1.8 cm) was cleaned with 2% (w/v) Hellmanex solution (Hellma) for 30 min and coated with 10 nm titanium and 100 nm gold (99.999%, Sigma-Aldrich) using an SP-2 magnetron sputtering machine. About 2 μM end-functionalized disulfide surface strand (SS; 72 base pairs) with 60 μM TCEP was annealed to its complementary strand (CSS; 49 base pairs) by heating to 95 °C for 10 min and then cooling to 25 °C, resulting in the formation of a rigid double-stranded backbone. The sample was then incubated on the gold surface for 24 h under the following conditions: 25 °C TE buffer with a thiol DNA concentration of 2 μM. After incubation, excess strands were washed away using TE buffer at room temperature. The resulting surface had a DNA density of ~3000 μm^{-2} as reported previously.[28]

DNA Hybridization with a Coated Gold Surface. After it was coated with the SS DNA, the functionalized gold surface was further hybridized with the 2-nitrobenzyl (photocleavable linker, PC linker)-modified linking-strand DNA. About 2 μM of the linking-strand DNA (LS, LS-1, or LS-2) was incubated on the functionalized gold surface for 2 h at room temperature. In this way, the linking strand DNA could hybridize to SS DNA. After incubation, excess strands were removed using TE buffer at room temperature.

Photolithography Procedure. After the hybridization of LSs to SS, the 2-nitrobenzyl-modified DNA strand-coated gold surface was then exposed to UV light by photomasking for 10 min. All photomasks were designed using Coreldraw software and printed on transparent film. The UV power output was measured using a UV light meter with a peak sensitivity at 340 nm (LUYOR, UV 340B, China). For the external Hg lamp used for photolithography experiments (X-Cite 120Q), the UV power output at 340 nm was ~15 mW·cm^{-2} at the irradiated sample position. After exposure, the surface was washed three times using TE buffer at room temperature.

Toehold-Mediated DNA Strand Displacement Reaction on Gold Surface. To induce the second linking-strand DNA onto the surface or to reset the surface, 2 μM linking-strand DNA (LS or LS-2) was incubated on UV light-exposed LS-1- or LS-2-coated gold surface for 1.5 h at room temperature to perform toehold-mediated DNA strand displacement. After incubation, excess strands were washed away using TE buffer at room temperature.

Surface Pattern Development and Fluorescent Imaging. To develop the pattern on gold surface, FAM- or TAMRA-modified reporter (RS) DNA was incubated on the surface. For the pattern with one color, 2 μM 3′ FAM-modified RS DNA was incubated with surface for 1 h. For the pattern with two different colors, a 2 μM mixture of 3′ FAM-modified RS DNA and 3′ TAMRA-modified RS DNA (RS-1) was incubated on the surface for 1 h to hybridize with linking-DNA sequences. After pattern development, a Leica DM6000 CS confocal microscope (TCS SP5 II) was used to take all fluorescent images.

Surface Pattern Erasure Procedure. To erase the pattern on the surface, the entire gold surface with certain patterns was further exposed to UV light without photomasking for 10 min, and then the linking-strand DNA (LS-2) was incubated on the exposed surface to perform DNA strand displacement. In this way, the gold surface could be reset and further used to fabricate a new pattern.

Preparation of DNA-Coated Colloids. Streptavidin-covered magnetic beads (5.85 μm) and streptavidin-coated microspheres (3 μm) were purchased from Bangs Laboratories, Inc. (CM01N and CP01N). Biotin-SS DNA was first annealed with an equal number of LS DNA (LS1, LS1′, LS2 or LS2′) strands to hybridize and form biotinylated particles strands with a double-stranded backbone (detailed DNA sequences are shown in Table S3) and 11-nucleotide sticky end. Biotinylated particles strands with a double-stranded backbone were incubated with these particles for 1 h under the following conditions: 25 °C, light shaking, TE buffer, particle volume fraction 0.1% and a biotinylated strand concentration of 1 μM. Particles were washed by centrifugation and resuspensed in TE buffer.

Conflict of Interest: The authors declare no competing financial interest.

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Supporting Information Available: Detailed sequence information for all oligonucleotide probes; DNA sequences for the fluorescence characterization in solution; detailed sequence information for all oligonucleotide probes used in asymmetrical modification of colloidal particles; fluorescence images; plot of photocleavage fraction on gold surface and in solution versus UV irradiation time; photomask pattern used to generate a pattern with one color; photocontrolled toehold formation for toehold-mediated DNA displacement reaction; photomask patterns used to generate patterns with two different colors; photomask patterns used in erasable DNA photolithography; immobilized DNA-coated magnetic beads on the glass slide. This material is available free of charge via the Internet at http://pubs.acs.org.

REFERENCES AND NOTES

1. Jayasena, S. D. Aptamers: An Emerging Class of Molecules That Rival Antibodies in Diagnostics. *Clin. Chem.* **1999**, *45*, 1628–1650.
2. Storhoff, J. J.; Lucas, A. D.; Garimella, V.; Bao, Y. P.; Muller, U. R. Homogeneous Detection of Unamplified Genomic DNA Sequences Based on Colorimetric Scatter of Gold Nanoparticle Probes. *Nat. Biotechnol.* **2004**, *22*, 883–887.
3. Zhu, G. Z.; Zheng, J.; Song, E. Q.; Donovan, M.; Zhang, K. J.; Liu, C.; Tan, W. H. Self-Assembled, Aptamer-Tethered DNA Nanotrains for Targeted Transport of Molecular Drugs in

Cancer Theranostics. *Proc. Natl. Acad. Sci. U.S.A.* **2013**, *110*, 7998–8003.
4. Bagalkot, V.; Zhang, L.; Levy-Nissenbaum, E.; Jon, S.; Kantoff, P. W.; Langer, R.; Farokhzad, O. C. Quantum Dot−Aptamer Conjugates for Synchronous Cancer Imaging, Therapy, and Sensing of Drug Delivery Based on Bi-Fluorescence Resonance Energy Transfer. *Nano Lett.* **2007**, *7*, 3065–3070.
5. Xiao, Y.; Lubin, A. A.; Heeger, A. J.; Plaxco, K. W. Label-Free Electronic Detection of Thrombin in Blood Serum by Using an Aptamer-Based Sensor. *Angew. Chem., Int. Ed.* **2005**, *44*, 5456–5459.
6. He, L.; Musick, M. D.; Nicewarner, S. R.; Salinas, F. G.; Benkovic, S. J.; Natan, M. J.; Keating, C. D. Colloidal Au-Enhanced Surface Plasmon Resonance for Ultrasensitive Detection of DNA Hybridization. *J. Am. Chem. Soc.* **2000**, *122*, 9071–9077.
7. Xiao, Y.; Piorek, B. D.; Plaxco, K. W.; Heeger, A. J. A Reagentless Signal-On Architecture for Electronic, Aptamer-Based Sensors *via* Target-Induced Strand Displacement. *J. Am. Chem. Soc.* **2005**, *127*, 17990–17991.
8. Modi, S.; Nizak, C.; Surana, S.; Halder, S.; Krishnan, Y. Two DNA Nanomachines Map pH Changes along Intersecting Endocytic Pathways inside the Same Cell. *Nat. Nanotechnol.* **2013**, *8*, 459–467.
9. Feldkamp, U.; Niemeyer, C. M. Rational Design of DNA Nanoarchitectures. *Angew. Chem., Int. Ed.* **2006**, *45*, 1856–1876.
10. Liu, D. S.; Bruckbauer, A.; Abell, C.; Balasubramanian, S.; Kang, D. J.; Klenerman, D.; Zhou, D. J. A Reversible pH-Driven DNA Nanoswitch Array. *J. Am. Chem. Soc.* **2006**, *128*, 2067–2071.
11. Seeman, N. C. Nanomaterials Based on DNA. *Annu. Rev. Biochem.* **2010**, *79*, 65–87.
12. Bath, J.; Turberfield, A. J. DNA Nanomachines. *Nat. Nanotechnol.* **2007**, *2*, 275–284.
13. Yurke, B.; Turberfield, A. J.; Mills, A. P.; Simmel, F. C.; Neumann, J. L. A DNA-Fuelled Molecular Machine Made of DNA. *Nature* **2000**, *406*, 605–608.
14. Zhang, D. Y.; Seelig, G. Dynamic DNA Nanotechnology Using Strand-Displacement Reactions. *Nat. Chem.* **2011**, *3*, 103–113.
15. Song, T. J.; Liang, H. J. Synchronized Assembly of Gold Nanoparticles Driven by a Dynamic DNA-Fueled Molecular Machine. *J. Am. Chem. Soc.* **2012**, *134*, 10803–10806.
16. Pavlov, V.; Xiao, Y.; Shlyahovsky, B.; Willner, I. Aptamer-Functionalized Au Nanoparticles for the Amplified Optical Detection of Thrombin. *J. Am. Chem. Soc.* **2004**, *126*, 11768–11769.
17. Baker, B. R.; Lai, R. Y.; Wood, M. S.; Doctor, E. H.; Heeger, A. J.; Plaxco, K. W. An Electronic, Aptamer-Based Small-Molecule Sensor for the Rapid, Label-Free Detection of Cocaine in Adulterated Samples and Biological Fluids. *J. Am. Chem. Soc.* **2006**, *128*, 3138–3139.
18. Khan, M. N.; Tjong, V.; Chilkoti, A.; Zharnikov, M. Fabrication of ssDNA/Oligo(ethylene glycol) Monolayers and Complex Nanostructures by an Irradiation-Promoted Exchange Reaction. *Angew. Chem., Int. Ed.* **2012**, *51*, 10303–10306.
19. Pirrung, M. C. How to Make a DNA Chip. *Angew. Chem., Int. Ed.* **2002**, *41*, 1276–1289.
20. Samanta, D.; Sarkar, A. Immobilization of Bio-Macromolecules on Self-Assembled Monolayers: Methods and Sensor Applications. *Chem. Soc. Rev.* **2011**, *40*, 2567–2592.
21. Balamurugan, S.; Obubuafo, A.; Soper, S. A.; Spivak, D. A. Surface Immobilization Methods for Aptamer Diagnostic Applications. *Anal. Bioanal. Chem.* **2008**, *390*, 1009–1021.
22. Xia, D.; Yan, J.; Hou, S. Fabrication of Nanofluidic Biochips with Nanochannels for Applications in DNA Analysis. *Small* **2012**, *8*, 2787–2801.
23. Fodor, S. P. A.; Read, J. L.; Pirrung, M. C.; Stryer, L.; Lu, A. T.; Solas, D. Light-Directed, Spatially Addressable Parallel Chemical Synthesis. *Science* **1991**, *251*, 767–773.
24. Pease, A. C.; Solas, D.; Sullivan, E. J.; Cronin, M. T.; Holmes, C. P.; Fodor, S. P. A. Light-Generated Oligonucleotide Arrays for Rapid DNA-Sequence Analysis. *Proc. Natl. Acad. Sci. U.S.A.* **1994**, *91*, 5022–5026.
25. Chow, B. Y.; Emig, C. J.; Jacobson, J. M. Photoelectrochemical Synthesis of DNA Microarrays. *Proc. Natl. Acad. Sci. U.S.A.* **2009**, *106*, 15219–15224.
26. Zhou, X.; Boey, F.; Huo, F.; Huang, L.; Zhang, H. Chemically Functionalized Surface Patterning. *Small* **2011**, 2273–2289.
27. Piner, R. D.; Zhu, J.; Xu, F.; Hong, S. H.; Mirkin, C. A. "Dip-Pen" Nanolithography. *Science* **1999**, *283*, 661–663.
28. Feng, L.; Romulus, J.; Li, M.; Sha, R.; Royer, J.; Wu, K. T.; Xu, Q.; Seeman, N. C.; Weck, M.; Chaikin, P. Cinnamate-Based DNA Photolithography. *Nat. Mater.* **2013**, *12*, 747–753.
29. Huang, F. J.; You, M. X.; Han, D.; Xiong, X. L.; Liang, H. J.; Tan, W. H. DNA Branch Migration Reactions through Photocontrollable Toehold Formation. *J. Am. Chem. Soc.* **2013**, *135*, 7967–7973.
30. Seo, T. S.; Bai, X. P.; Kim, D. H.; Meng, Q. L.; Shi, S. D.; Ruparelt, H.; Li, Z. M.; Turro, N. J.; Ju, J. Y. Four-Color DNA Sequencing by Synthesis on a Chip Using Photocleavable Fluorescent Nucleotides. *Proc. Natl. Acad. Sci. U.S.A.* **2005**, *102*, 5926–5931.
31. Ruparel, H.; Bi, L. R.; Li, Z. M.; Bai, X. P.; Kim, D. H.; Turro, N. J.; Ju, J. Y. Design and Synthesis of a 3′-O-Allyl Photocleavable Fluorescent Nucleotide as a Reversible Terminator for DNA Sequencing by Synthesis. *Proc. Natl. Acad. Sci. U.S.A.* **2005**, *102*, 5932–5937.
32. Qiu, L.; Wu, C.; You, M.; Han, D.; Chen, T.; Zhu, G.; Jiang, J.; Yu, R.; Tan, W. A Targeted, Self-Delivered, and Photocontrolled Molecular Beacon for mRNA Detection in Living Cells. *J. Am. Chem. Soc.* **2013**, *135*, 12952–12955.
33. Escorihuela, J.; Banuls, M. J.; Puchades, R.; Maquieira, A. DNA Microarrays on Silicon Surfaces Through Thiol-ene Chemistry. *Chem. Commun.* **2012**, *48*, 2116–2118.
34. Chee, M.; Yang, R.; Hubbell, E.; Berno, A.; Huang, X. C.; Stern, D.; Winkler, J.; Lockhart, D. J.; Morris, M. S.; Fodor, S. P. A. Accessing Genetic Information with High-Density DNA Arrays. *Science* **1996**, *274*, 610–614.
35. Liu, Q. H.; Wang, L. M.; Frutos, A. G.; Condon, A. E.; Corn, R. M.; Smith, L. M. DNA Computing on Surfaces. *Nature* **2000**, *403*, 175–179.
36. Pregibon, D. C.; Toner, M.; Doyle, P. S. Multifunctional Encoded Particles for High-Throughput Biomolecule Analysis. *Science* **2007**, *315*, 1393–1396.
37. Jiang, S.; Chen, Q.; Tripathy, M.; Luijten, E.; Schweizer, K. S.; Granick, S. Janus Particle Synthesis and Assembly. *Adv. Mater.* **2010**, *22*, 1060–1071.
38. Feng, L.; Dreyfus, R.; Sha, R. J.; Seeman, N. C.; Chaikin, P. M. DNA Patchy Particles. *Adv. Mater.* **2013**, *25*, 2779–2783.