Controlled assembly of dendrimer-like DNA

YOUGEN LI[1], YOLANDA D. TSENG[1], SANG Y. KWON[1], LEO D'ESPAUX[1], J. SCOTT BUNCH[2], PAUL L. MCEUEN[2] AND DAN LUO*[1]

[1]Department of Biological and Environmental Engineering, Cornell University, Ithaca, New York 14853-5701, USA
[2]Laboratory of Atomic and Solid State Physics, Cornell University, Ithaca, New York 14853-5701, USA
*e-mail: DL79@cornell.edu

Published online: 21 December 2003; doi:10.1038/nmat1045

DNA possesses many desirable chemical/physical properties as a polymeric material. With the myriad of tools available to manipulate DNA[1], there is great potential for using DNA as a generic instead of a genetic material. Although much progress has been made in DNA computing[2–4] and DNA nanotechnology[5–19], the full achievement of DNA-based materials has not yet been realized. As almost all DNA molecules are either linear or circular, to rationally construct DNA materials one must first create additional shapes of DNA as basic building blocks. In addition, these DNA building blocks must be readily incorporated into larger structures in a controlled manner. Here, we show the controlled assembly of dendrimer-like DNA (DL-DNA) from Y-shaped DNA (Y-DNA). The synthesis of Y-DNA and controlled assembly of DL-DNA were robust and efficient; the resulting DL-DNA was stable and almost monodisperse. The multivalent DNA dendrimers can be either isotropic or anisotropic, providing great potential to link other entities.

Two strategies were used to synthesize the Y-DNA: stepwise synthesis and all-in-one (one-pot) synthesis (Fig. 1a). In the stepwise approach, two oligonucleotides with partial complementary sequences formed one arm of a Y-DNA; then the third oligonucleotide that was complementary to the first two unmatched portions of oligonucleotides, formed the other two arms of the Y-DNA. In the one-pot approach, equal moles of all three oligonucleotides were mixed together to form the Y-DNA. In both cases, the formation of Y-DNA was evaluated by gel electrophoresis (Fig. 1c), in which the mobility of a DNA molecule depends on its size, shape and extent of base pairing[20]. One major band appears on the gel (Fig. 1c, lanes 4–6), and its mobility is less than that of its components, the single-stranded DNA (lanes 1–3), indicating the formation of one arm of Y-DNA. The further shift of the mobility of the final annealing product of stepwise (Fig. 1c, lanes 7–9) and one-pot synthesis (Fig. 1c, lane 10) indicated the formation of Y-DNA. There is no difference in results between stepwise and one-pot synthesis. The estimated yield of Y-DNA is close to 100%, as estimated by densitometry. Other Y-DNA with different sequences were similarly synthesized. Synthesized Y-DNA were stable with no degradation observed after 30 days at 4 °C (Fig. 1d).

DL-DNA were assembled by ligation of Y-DNA molecules, whose sequences were specifically designed so that ligations between Y_i and Y_j DNA could only occur when $i \neq j$, where i and j refer to the generation number n (for example, G_1, G_2, etc., see Fig. 3a. The cohesive end of each oligonucleotide was non-palindromic, thus no self-ligations occurred, see Table 1, segment 1). In addition, the ligation could only occur in one direction, that is, $Y_0 \rightarrow Y_1 \rightarrow Y_2 \rightarrow Y_3 \rightarrow Y_4$ and so on. Furthermore, when Y_0 was ligated to Y_1 with a 1:3 molar stoichiometry, one Y_0 was linked with three Y_1, forming the first-generation DL-DNA (G_1, Fig. 2a). G_1 was then ligated to six Y_2 (one Y_2 for each of the six free branches of G_1), resulting in a second-generation DL-DNA (G_2, Fig. 3a). The third (G_3), fourth (G_4), and higher generation DL-DNA were assembled in a similar way (Fig. 3a). Note that the assembled DL-DNA (G_n) had only one possible conformation due to the unidirectional ligation strategy. The general format of the n^{th}-generation DL-DNA is $G_n = (Y_0)(3Y_1)(6Y_2)\ldots(3 \times 2^{n-1}Y_n)$, where n is the generation number and Y_n is the n^{th} Y-DNA. The total number of Y-DNA in an n^{th}-generation DL-DNA is $3 \times 2^n - 2$. The growth of DL-DNA from n^{th} generation to $(n + 1)^{th}$ generation requires a total of 3×2^n new Y_{n+1}-DNA.

G_1 DL-DNA were assembled by ligating Y_0 and Y_1 with a 1:3 stoichiometry (Fig. 2a). The ligation product migrated as a single band, and its mobility was slower than that of its building block, Y_0 (Fig. 2c). The presence of a single band indicated a new molecular species with a well-defined molecular weight. The estimated yield is close to 100%. To confirm that the ligation product was indeed G_1 DL-DNA, it was denatured (Fig. 2b) and examined by gel electrophoresis (Fig. 2d). Two major bands appeared in the electrophoresis: one with the same mobility as the single-strand DNA Y_{0a} (30-mer) and one with slower mobility (90-mer), which was exactly what one would expect from the G_1 DL-DNA structure according to the assembly scheme (Fig. 2b). Similar results were obtained from denaturation of G_2, G_3 and G_4, and the generation of newly ligated species were revealed by electrophoresis (data not shown). Assembled G_1 DL-DNA were stable with no degradation observed after 45 days at 4 °C (Fig. 2e). In addition, exonuclease III assays confirmed the absence of cyclic materials (data not shown).

The second-, third-, fourth- and fifth-generation DL-DNA were synthesized with a similar strategy and evaluated by gel electrophoresis (Fig. 3a and 3b). With increasing generation, the mobility of the ligated product decreased as predicted (Fig. 3b, see arrows). Furthermore, the yield and the purity of higher generation DL-DNA did not seem to decrease even in the absence of purification, suggesting that the assembly was very robust. To further confirm that the mobility-shifted species were indeed DL-DNA molecules, we examined the 4^{th} generation DL-DNA by atomic force microscopy (AFM) with both a

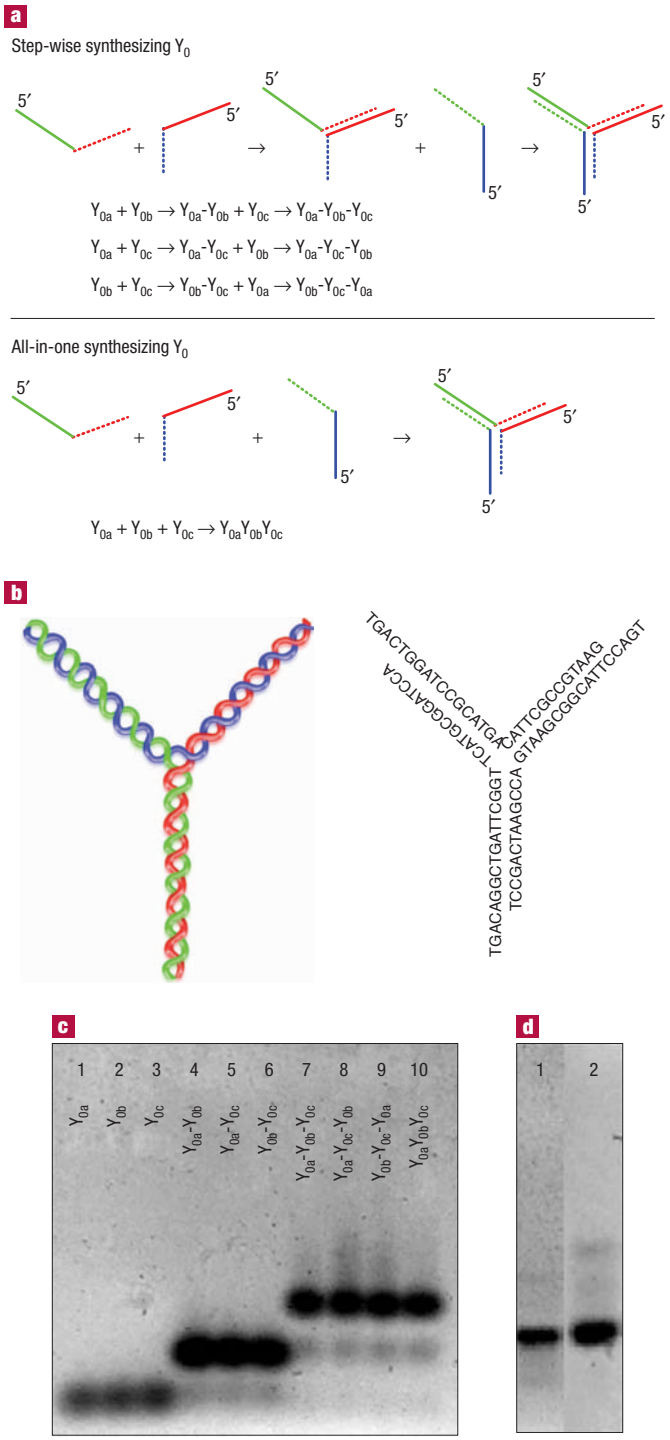

Figure 1 Y-shaped DNA (Y-DNA). a, Strategies of Y-DNA synthesis. **b**, Schematic drawing (left) and sequences (right) of Y-DNA. **c**, Evaluation of Y_0-DNA formation. Lanes 1, 2 and 3 are oligonucleotide Y_{0a}, Y_{0b}, Y_{0c}, respectively. Lanes 4, 5 and 6 correspond to the hybridized products of (Y_{0a} and Y_{0b}), (Y_{0a} and Y_{0c}) and (Y_{0b} and Y_{0c}), respectively. Lanes 7, 8 and 9 are stepwisely hybridized final products of (Y_{0a}, Y_{0b} and Y_{0c}), (Y_{0a}, Y_{0c} and Y_{0b}) and (Y_{0b}, Y_{0c} and Y_{0a}), respectively. Lane 10 is all-in-one (one-pot) hybridized final product of (Y_{0a}, Y_{0b} and Y_{0c}). **d**, Evaluation of Y-DNA stability. Lane 1 represents freshly made Y-DNA and lane 2 is the same Y-DNA stored at 4 °C for 30 days.

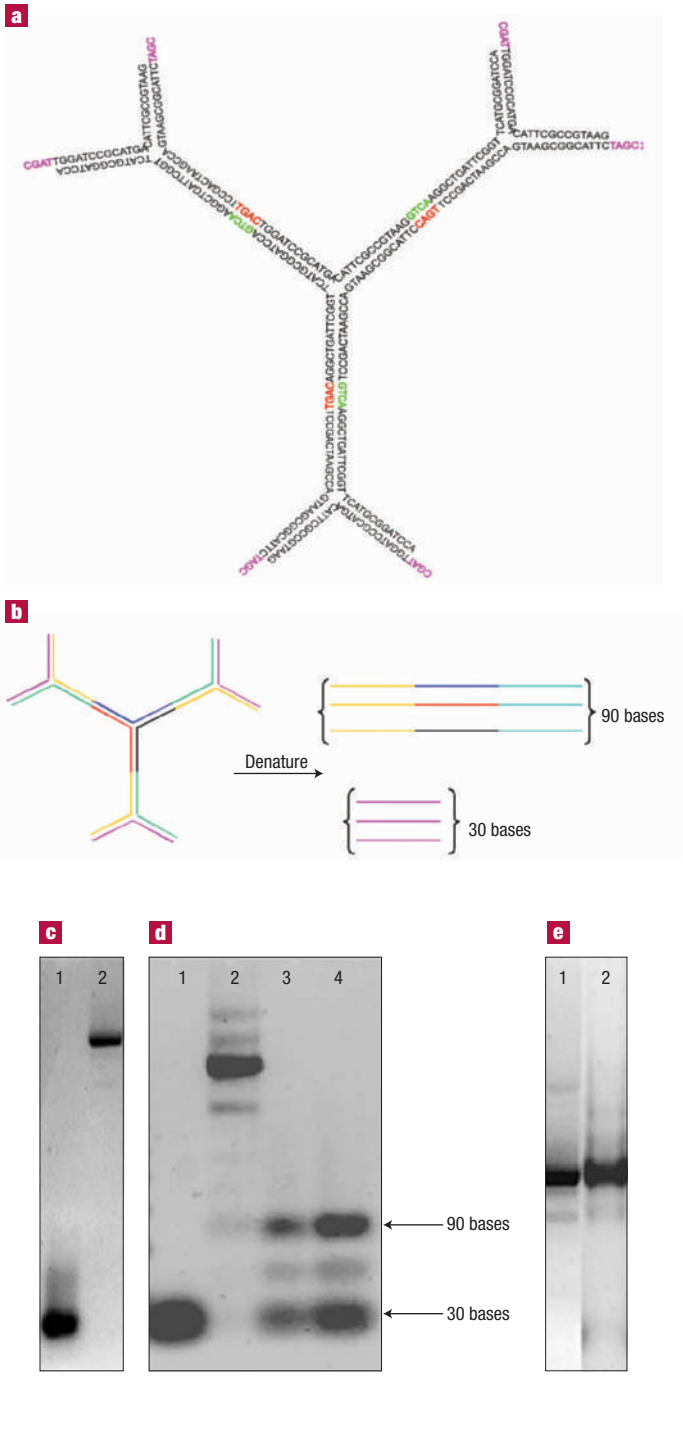

Figure 2 The first-generation dendrimer-like DNA (G_1 DL-DNA). a, Sequences of G_1 DL-DNA. **b**, A schematic drawing of denaturation strategy to confirm the G_1 DL-DNA structure. After G_1 DL-DNA denaturation, six oligonucleotides were generated; three of these six oligonucleotides were new species with a unique length (90 bases). The rest three were 30 bases. **c**, Evaluation of G_1 DL-DNA formation. Lane 1 is Y-DNA and lane 2 is G_1 DL-DNA. **d**, Evaluation of G_1 DL-DNA denaturation. Lane 1 is a molecular marker (oligonucleotide Y_{0a}). Lane 2 is G_1 DL-DNA without denaturing. Lanes 3 and 4 correspond to 0.25 μg and 0.5 μg of the denatured G_1 DL-DNA, respectively. **e**, Evaluation of G_1 DL-DNA stability. Lane 1 represents freshly made G_1 DL-DNA and lane 2 is the same G_1 DL-DNA stored at 4 °C for 45 days.

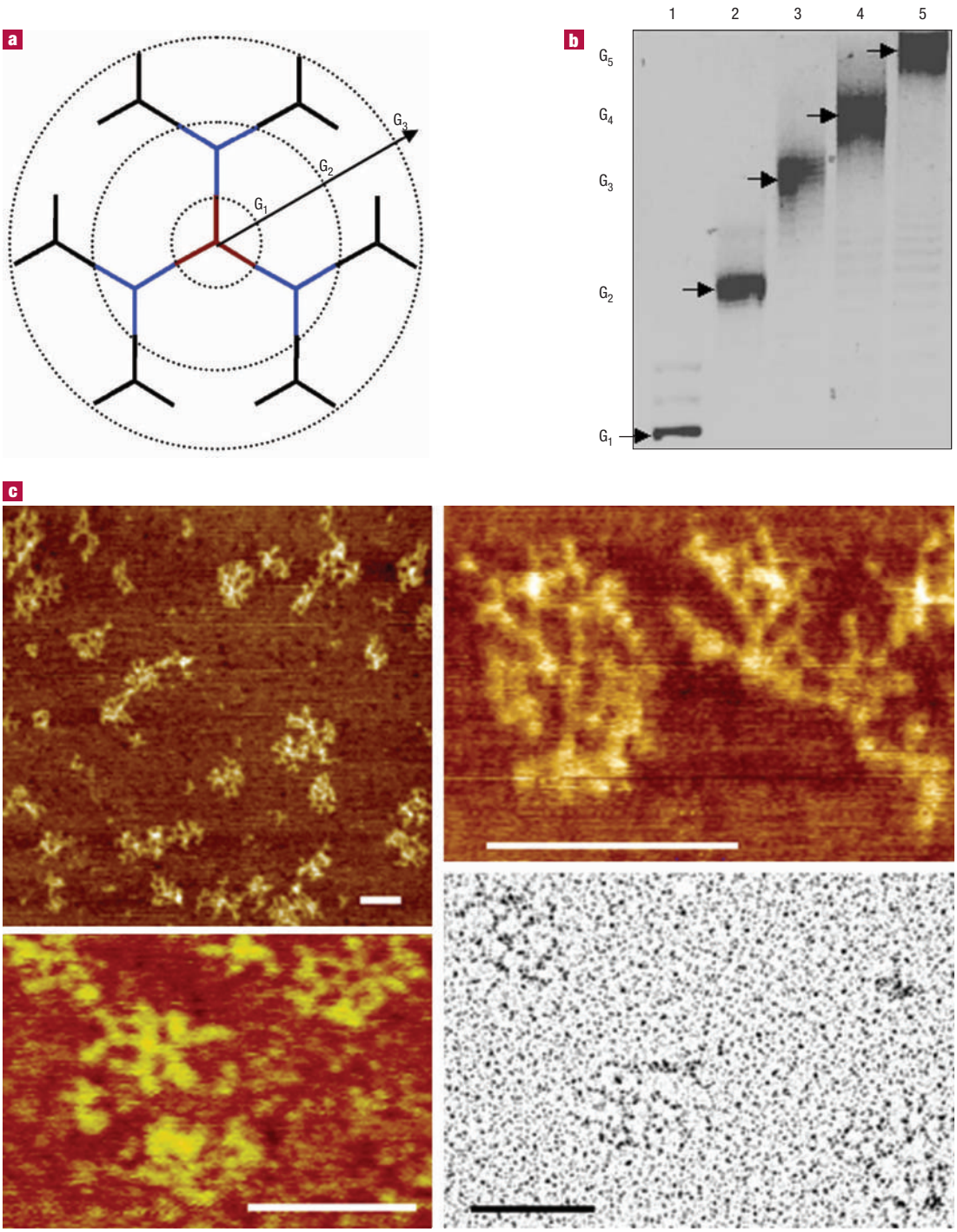

Figure 3 Higher generation dendrimer-like DNA. a, Schematic drawings of higher generation DL-DNA. **b**, Evaluation of higher generation DL-DNA formation. Lanes 1, 2, 3, 4 and 5 correspond to G_1 DL-DNA, G_2 DL-DNA, G_3 DL-DNA, G_4 DL-DNA and G_5 DL-DNA, respectively. The arrows indicate the decreasing mobility with increasing generation. **c**, Images of DL-DNA: AFM images of G_4 DL-DNA on mica surface using standard tip (lower left) and SWNT tip (top, left and right), and TEM image of G_4 DL-DNA (lower right). Scale bars correspond to 100 nm.

standard tip and a single-walled carbon nanotube (SWNT) tip, which revealed DL-DNA's highly branched dendritic nanostructure (Fig. 3c). The measured width of the G_4 DL-DNA nanostructure was 71.2 ± 6.7 nm, which was very close to the theoretically calculated value based on a B-DNA structure (69.0 nm) considering the relative flexibility of DNA molecules.

Although the AFM pictures revealed the dendritic shape of DL-DNA, they were not suitable for determining the distribution of sizes

due to many commonly occurring problems associated with AFM, including sample damage by AFM tips, cleanliness of the substrate, dehydration of DNA, contaminants during the preparation and so on. To further explore the size distributions, the 4th-generation dendrimer-like DNA was also visualized by transmission electron microscopy (TEM), which indicated the highly branched shape of DL-DNA (Fig. 3c). The size (diameter) of the DL-DNA was measured at about 80 nm, and the width of each branch was estimated at 3 nm, consistent with the theoretically calculated values. More than 20 TEM experiments were performed, and a total of 146 G_4 DL-DNA particles were measured. From such a large number of results, we believe that these TEM measurements are likely to reflect the nature of the dendrimer-like DNA. We measured the size of each particle in four directions: horizontal, vertical, diagonal 45° (relative to horizontal) and diagonal 135° (relative to horizontal). The average size of all 146 particles was 83.9 nm ± 9.8 nm, very close to the theoretical calculated value (considering the Pt/Pd coating). More interestingly, the average size of horizontal, vertical, diagonal 45° and diagonal 135° measurements were 84.9 nm, 85.1 nm, 82.1 nm and 83.9 nm, respectively, suggesting that the particles were circular in shape. Further examination of particle-size distributions of these 146 G4 DL-DNA particles revealed that 84% of the particles are within a size range 74.1 nm and 93.7 nm (one standard deviation of the average), consistent with our gel electrophoresis results, which suggested that 87.68% and 92.99% of the G_1 and G_4 DNA, respectively, had essentially the same mobility. Taking AFM, TEM and gel electrophoresis results together, they strongly suggested that DL-DNA molecules were very pure, and confirm their nanoscale dendritic structures.

In another study, seven dangling-ends of double-stranded DNA were annealed to construct dendrimer DNA, and the structure fixed through a non-specific crosslinker, psoralen[21,22]. The yield, purity and images were unknown. The dendrimer-like DNA presented here is very different from previously reported products. First, the building blocks were Y-shaped DNA with specially designed sequences. No self-ligation and cyclic products could occur, making dendrimer growth unidirectional and stepwise. Second, the growth of dendrimer was enzyme-catalysed, making the synthesis non-reversible, specific and efficient. And third, the final products, dendrimer-like DNA, were still true DNA that could be manipulated further with DNA enzymes.

We are aware that different motifs of a variety of geometric arrays were successfully (and impressively) constructed using rigid, linear 'crossover' DNA as building blocks[23–25]. A DNA mechanical device was also created[9,10]. Note that the building blocks used and motifs created are perfect for growing nanoscaled arrays and scaffolds[11,26], some of them (such as the DNA tiling system[11]) also provide a method for non-isotropic growth.

We emphasize here that this is the first time that almost monodisperse Y-shaped DNA and dendrimer-like DNA nanostructures have been synthesized in a highly controlled fashion with relatively high yield and purity. The synthesis was rather simple and robust; the 5th generation DL-DNA was close to being monodisperse even without any purification. The design strategies and assembly approaches can be easily used to construct other DNA building blocks, such as an X-shaped DNA (data not shown), that can be incorporated into even more complicated nanostructured material than those reported here. These DNA-based nanostructured materials can be manipulated at the molecular length-scale, providing an advantageous route for novel materials by design. In addition, it is unnecessary to protect and de-protect reactive ends of DL-DNA to achieve the dendritic structures. Furthermore, whereas chemical dendrimers are usually isotropic, DL-DNA can be easily assembled as anisotropic as well as isotropic through specific end design. The branch units of DL-DNA can also be either symmetrical or asymmetrical. With about 50 nm persistence length of double-stranded DNA[27], DNA basic building blocks can be at least as long as 50 nm, spanning the length scale of DNA nanostructured material (including DNA dendrimers) from the nanometre to even the micrometre range, which is very difficult to achieve from chemical dendrimers. The reported nanostructured DL-DNA molecules are envisioned to have great potential in nanotechnology by serving as templates for fabrication and synthesis, as their sizes, structures and morphologies can be changed through alteration of building blocks, and their interactions can be enhanced through conjugations with different functional groups. In addition, we believe that these water-soluble, dendrimer-like DNA nanostructures are versatile, and may find a myriad of applications in both biomedical and non-biomedical fields.

Table 1 Sequences of oligonucleotides.

Strand	Segment 1	Segment 2
Y_{0a}	5′-TGAC	
Y_{1a}	5′-GTCA	
Y_{2a}	5′-ATCG	TGGATCCGCATGACATTCGCCGTAAG-3′
Y_{3a}	5′-ATGC	
Y_{4a}	5′-GCAA	
Y_{0b}	5′-TGAC	
Y_{1b}	5′-CGAT	
Y_{2b}	5′-GCAT	CTTACGGCGAATGACCGAATCAGCCT-3′
Y_{3b}	5′-TTGC	
Y_{4b}	5′-GGAT	
Y_{0c}	5′-TGAC	
Y_{1c}	5′-CGAT	
Y_{2c}	5′-GCAT	AGGCTGATTCGGTTCATGCGGATCCA-3′
Y_{3c}	5′-TTGC	
Y_{4c}	5′-GGAT	

METHODS

MOLECULAR DESIGNS

The DNA sequences (Table 1) were designed according to the standards set by Seeman[28], and tested by trial-and-error. They were commercially synthesized and PAGE purified (Integrated DNA Technologies, Coralville, Iowa). Without further purification, oligonucleotides were dissolved in annealing buffer (10 mM Tris, pH = 8.0, 1 mM ethylenediaminetetraacetic acid (EDTA), and 50 mM NaCl) with a final concentration of 50 mM. Y-DNA was constructed by mixing three oligonucleotide components (1:1:1 molar ratio) in sterile Milli-Q water with a final concentration of 5 mM for each oligonucleotide. Hybridizations were performed according to the following procedures: (i) Denaturation at 95 °C for 2 min. (ii) Cooling at 65 °C and incubation for 5 min. (iii) Annealing at 60 °C for 2 min. (iv) Further annealing at 60 °C for 0.5 min with a continuous temperature decrease at a rate of 1 °C per min. The annealing steps were repeated a total of 40 times. The final annealed products were stored at 4 °C.

FORMATION OF Y-DNA AND DL-DNA

Y-shaped DNA (Y-DNA) were synthesized by mixing the same molar amount of corresponding oligonucleotide strands. The nomenclature is as follows: Y_{0a}, Y_{0b} and Y_{0c} are the three corresponding single oligonucleotide chains that form a Y_0-DNA (noted as Y_0 in short). Similarly, Y_{1a}, Y_{1b} and Y_{1c} are the three corresponding single oligonucleotide chains that form an Y_1-DNA (noted as Y_1 in short); and Y_{na}, Y_{nb} and Y_{nc} are the three corresponding single oligonucleotide chains that form an Y_n-DNA (noted as Y_n in short). The reactions are noted as the following: $Y_{0a}+Y_{0b}+Y_{0c}\rightarrow Y_0$, $Y_{1a}+Y_{1b}+Y_{1c}\rightarrow Y_1$, and $Y_{na}+Y_{nb}+Y_{nc}\rightarrow Y_n$, and so on. (see Fig. 1a). All the mixtures were first incubated at 95 °C for 2 min, then quickly cooled down to 60 °C, and finally cooled to 4 °C at 2 °C per min. For constructing DL-DNA, individual Y-DNA was ligated specifically to other Y-DNA. G_1 DL-DNA was obtained by ligating Y_1 to Y_0 (at a 3:1 molar ratio). Similarly, G_2 was formed by ligating 6 Y_2 with 1 G_1. Other higher generations of DL-DNA were constructed using the same strategy. Each ligation solution contains ligase buffer, 1.30 nmol Y-DNA monomer, and 0.235 Weiss unit of T4 DNA ligase (Promega, Madison, Wisconsin). The ligations were also performed with Fast-Link DNA Ligase (Epicentre Technologies, Madison, Michigan). The nomenclature of DL-DNA is as follows: the core of the dendrimer, Y_0, is designated as G_0, the 0 generation of DL-DNA. After Y_0 is ligated with Y_1, the dendrimer is termed the 1st generation of DL-DNA (G_1), and so on. The n^{th} generation of DL-DNA is noted as G_n.

CHARACTERIZING DL-DNA

The nucleic acid samples were evaluated on 3% agarose Ready-Gel (Bio-Rad, Hercules, California) at 100 V. For the denaturing experiment, single-stranded DNA was obtained by using NaOH. Briefly, gel-purified DL-DNA was denatured with a final concentration of ~40 ng ml^{-1} in a denaturing buffer containing 10 mM EDTA and 25 mM NaOH. The denaturing reaction was carried out at 95 °C for 2 min. The denatured products were immediately cooled down in a –20 °C freezer. Denatured DL-DNA was electrophoresed in 3% native agarose gel with ethidium bromide (0.5 mg ml^{-1}) in Tris-acetate-EDTA (TAE) buffer at 4 °C. Care was taken to make sure that the products were kept at 4 °C to keep the denatured status. Electrophoresis was carried out at 50 V for 10 min and then at 125 V for 65 min. For Exonuclease III assays, 1.0 μg of DNA were digested in 25 μl of Exonuclease III buffer with 30 units of Exonuclease III (Promega, Madison, Wisconsin) at 37 °C for 1 hour. The reaction was terminated by adding 2 μl of 0.25 mM EDTA.

AFM IMAGING

A 5 μl DNA sample was placed onto the surface of freshly cleaved mica (Ted Pella, Redding, California) functionalized with aminopropyltriethoxysilane (APTES, Aldrich) and allowed to adsorb to the mica surface for approximately 20 minutes. The mica was then rinsed in Milli-Q water and dried with compressed air. Tapping-mode AFM images were taken in air on both a Dimensions 3100 AFM and a Multimode AFM (Digital Instruments, Santa Barbara, California). Standard imaging was done with Pt/Ir-coated cantilevers with resonant frequencies of 60–100 kHz and force constants of 1.2–5.5 N m^{-1}. High-resolution imaging was performed using SWNT tips mounted on Pt/Ir cantilevers using the 'pick up' technique[29], whereby SWNTs are grown on a silicon substrate; during AFM imaging of the SWNT covered Si substrate a tube is picked up off the surface and then used as an imaging tip. All images were processed with a flattening filter.

TEM IMAGING

Approximately 0.5 μl of 0.21 mM G_4 DNA was mixed with 200 μl of Tris (30 mM, pH 8.0), and then 5 μl of 5% 2, 4, 6–Tri(dimethylaminomethyl phenol) (DMP) 30 was added to the mixture. A drop of the mixture (50 μl) was placed onto a sheet of parafilm at room temperature. The drop was covered with a petri dish for 11 minutes. After 11 minutes the DNA molecules were picked up by touching the drop with the formvar/carbon-coated grid (Electron Microscopy Sciences, Fort Washington, Pennsylvania) and left for 3 minutes. The sample was then stained with 2% uranyl acetate for 1 minute. The grid was then blotted with filter paper and allowed to dry in air, then rotary coated with Pt/Pd. Grids were analysed at a voltage of 100 kV using a Philips EM-201.

Received 19 May 2003; accepted 25 November 2003; published 21 December 2003.

References

1. Luo, D. The road from biology to materials. *Mater. Today* **6,** 38–43 (2003).
2. Adleman, L. M. Molecular computation of solutions to combinatorial problems. *Science* **266,** 1021–1024 (1994).
3. Sakamoto, K. *et al.* Molecular computation by DNA hairpin formation. *Science* **288,** 1223–1226 (2000).
4. Benenson, Y. *et al.* Programmable and autonomous computing machine made of biomolecules. *Nature* **414,** 430–434 (2001).
5. Seeman, N. C. DNA engineering and its application to nanotechnology. *Trends Biotechnol.* **17,** 437–443 (1999).
6. Seeman, N. C. DNA components for molecular architecture. *Accounts Chem. Res.* **30,** 357–363 (1997).
7. Demers, L. M. *et al.* Direct patterning of modified oligonucleotides on metals and insulators by dip-pen nanolithography. *Science* **296,** 1836–1838 (2002).
8. Eckardt, L. H. *et al.* DNA nanotechnology: Chemical copying of connectivity. *Nature* **420,** 286 (2002).
9. Mao, C. D., Sun, W. Q., Shen, Z. Y. & Seeman, N. C. A nanomechanical device based on the B-Z transition of DNA. *Nature* **397,** 144–146 (1999).
10. Yan, H., Zhang, X., Shen, Z. & Seeman, N. C. A robust DNA mechanical device controlled by hybridization topology. *Nature* **415,** 62–65 (2002).
11. Winfree, E., Liu, F., Wenzler, L. A. & Seeman, N. C. Design and self-assembly of two-dimensional DNA crystals. *Nature* **394,** 539–544 (1998).
12. Alivisatos, A. P. *et al.* Organization of 'nanocrystal molecules' using DNA. *Nature* **382,** 609–611 (1996).
13. Niemeyer, C. M., Burger, W. & Peplies, J. Covalent DNA - Streptavidin conjugates as building blocks for novel biometallic nanostructures. *Angew. Chem. Int. Edn* **37,** 2265–2268 (1998).
14. Yurke, B., Turberfield, A. J., Mills, A. P. Jr, Simmel, F. C. & Neumann, J. L. A DNA-fuelled molecular machine made of DNA. *Nature* **406,** 605–608 (2000).
15. Watson, K. J., Park, S. J., Im, J. H., Nguyen, S. T. & Mirkin, C. A. DNA-block copolymer conjugates. *J. Am. Chem. Soc.* **123,** 5592–5593 (2001).
16. Braun, E., Eichen, Y., Sivan, U. & Ben-Yoseph, G. DNA-templated assembly and electrode attachment of a conducting silver wire. *Nature* **391,** 775–778 (1998).
17. Taton, T. A., Mucic, R. C., Mirkin, C. A. & Letsinger, R. L. The DNA-mediated formation of supramolecular mono- and multilayered nanoparticle structures. *J. Am. Chem. Soc.* **122,** 6305–6306 (2000).
18. Elghanian, R., Storhoff, J. J., Mucic, R. C., Letsinger, R. L. & Mirkin, C. A. Selective colorimetric detection of polynucleotides based on the distance-dependent optical properties of gold nanoparticles. *Science* **277,** 1078–1081 (1997).
19. Keren, K. *et al.* Sequence-specific molecular lithography on single DNA molecules. *Science* **297,** 72–75 (2002).
20. Kallenbach, N. R. *et al.* Fourth rank immobile nucleic acid junctions. *J. Biomol. Struct. Dyn.* **1,** 159–168 (1983).
21. Wang, J., Jiang, M., Nilsen, T. W. & Getts, R. C. Dendritic nucleic acid probes for DNA biosensors. *J. Am. Chem. Soc.* **120,** 8281–8282 (1998).
22. Nilsen, T. W., Grayzel, J. & Prensky, W. Dendritic nucleic acid structures. *J. Theor. Biol.* **187,** 273–284 (1997).
23. LaBean, T. H. *et al.* Construction, analysis, ligation, and self-assembly of DNA triple crossover complexes. *J. Am. Chem. Soc.* **122,** 1848–1860 (2000).
24. Yang, X. P., Wenzler, L. A., Qi, J., Li, X. J. & Seeman, N. C. Ligation of DNA triangles containing double crossover molecules. *J. Am. Chem. Soc.* **120,** 9779–9786 (1998).
25. Mao, C. D., Sun, W. Q. & Seeman, N. C. Assembly of Borromean rings from DNA. *Nature* **386,** 137–138 (1997).
26. Niemeyer, C. M. Progress in "engineering up" nanotechnology devices utilizing DNA as a construction material. *Appl. Phys. A* **68,** 119–124 (1999).
27. Smith, S. B., Finzi, L. & Bustamante, C. Direct mechanical measurements of the elasticity of single DNA molecules by using magnetic beads. *Science* **258,** 1122–1126 (1992).
28. Seeman, N. C. De novo design of sequences for nucleic acid structural engineering. *J Biomol. Struct. Dyn.* **8,** 573–581 (1990).
29. Hafner, J., Cheung, C. L., Oosterkamp, T. H. & Lieber, C. M. High yield assembly of individual single-walled carbon nanotube tips for scanning probe microscopies. *J. Phys. Chem. B.* **105,** 743–746 (2001).

Acknowledgements

This work was partially supported by the Cornell University's Innovation Grant administrated by Cornell Advanced Center for Biotechnology, and performed in part at the Cornell Nanofabrication Facility and Cornell Centre for Materials Research, which is supported by the National Science Foundation, Cornell University and Industrial Affiliates. We thank Francis Moran for preparation of Fig. 1b. Correspondence and requests for materials should be addressed to D.L.

Competing financial interests

The authors declare that they have no competing financial interests.