# Combinatorial self-assembly of DNA nanostructures†‡

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**Here we report a modular design of self-assembly of DNA nanostructures in a combinatorial approach; a square with ~25 nm cavity dimension, a chair with ~80 nm in height and a line with ~100 nm in length are formed through combinations of four cross-shaped DNA tiles which are kept constant and six variable linker tiles.**

Structural DNA nanotechnology is aimed at the design and construction of periodic or complex nanostructures using branched DNA building blocks (DNA tiles) through sticky-end cohesion.[1] The formation of different patterned lattices is usually achieved through variation of the structure and sequence of the component tiles. In recent years, there has been substantial progress in designing a variety of DNA tiles and self-assembly of these tiles have resulted in one-dimensional and/or two-dimensional arrays with different periodicity and cavity sizes.[2] These nano-patterned DNA structures can be used as scaffolds to construct nanoparticle arrays[3] with potential applications in nanoelectronic and nanophotonics or high density protein nanoarrays[4] for biodetection applications.

Modular design and reuse of DNA tiles in self-assembly allows efficient tuning of the lattice patterns without modifying the majority of the building blocks. For example, when only a small number of tiles are modified, large 2D DNA lattices with different cavity sizes have been produced.[5] We recently also demonstrated that, when only the sequences of the sticky ends are redesigned, DNA tiles can be directed to connect in a way leading to fixed size symmetric arrays.[6]

Here we report a new strategy of modular design using a combinatorial approach. By varying the connectivity and position of the 2-way linker DNA junction tile and keeping the 4-way DNA junction modules unchanged, simple objects such as a square, a chair and a line can be easily constructed through combinatorial tile self-assembly. Fig. 1 illustrates the schematic design of this approach. The formation of a square with a 25 nm cavity, a chair 80 nm tall and a line 100 nm long are achieved through combining four different cross-shaped DNA tile[2d] as the corners (Fig. 1Ai) and six different holiday junctions[5] as the linkers (Fig. 1Aii). The four corner tiles share five common strands (shown in blue color) and each have five different strands, and the linkers all share two common strands (in blue color) and each have two unique strands.

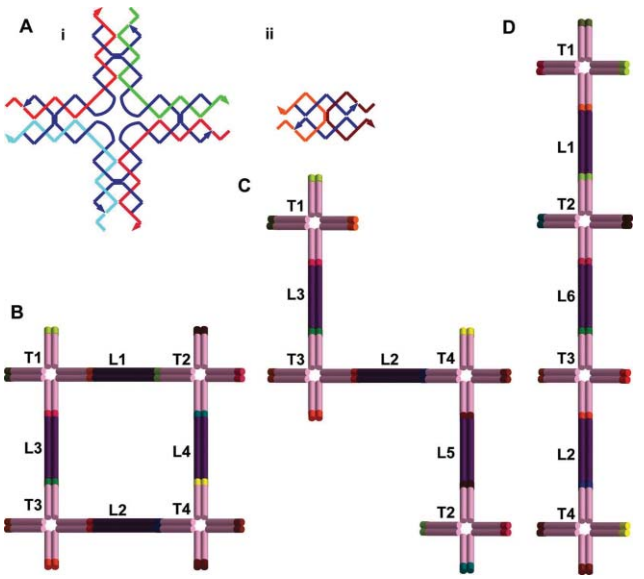


**Fig. 1** **A.** The two kinds of tiles used in construction. i. A cross-shaped tile acts as 4-way junction. ii. A holiday junction tile acts as a 2-way linker. **B**. A square from four cross-shaped tiles (T1–T4, in light purple) and four linker tiles (L1–L4, in dark purple). The unique sticky ends are labeled as short segments in different colors. **C.** A chair from four cross-shaped tiles and three linker tiles (L2, L3 and L5). **D.** A short line from four cross-shaped tiles and three linker tiles (L1, L2 and L6).

The sequences of the sticky-ends are designed to allow for the connection of the tiles in three different patterns. The square (Fig. 1B) contains four corner tiles and four linker tiles (L1, L2, L3 and L4). The chair structure (Fig. 1C) combines all the four corner tiles and three linker tiles (L2, L3 and L5). The line structure combines the same corner tiles and three linker tiles L1, L2 and L6 (Fig. 1D).

Atomic force microscope (AFM) was used to demonstrate the formation of the designed structures (shown in Fig. 2A–C). Three representative figures are shown for each structure revealing the correct shapes as designed. The yield of the square was ~90%, however the yields of the chair and line were ~27% and ~66% respectively. This is because the unoccupied sticky-ends on the cross-shaped tiles are left open and sometimes allow for non-specific binding of tiles in different locations.

The dimension of the three structures can be precisely controlled. The edge to edge distance of two cross-shaped tiles linked with a holiday junction is ~37.5 nm. The AFM cross-section profiles of the square (Fig. 3A) and the chair (Fig. 3B) measured that the distance between the edges of two neighboring

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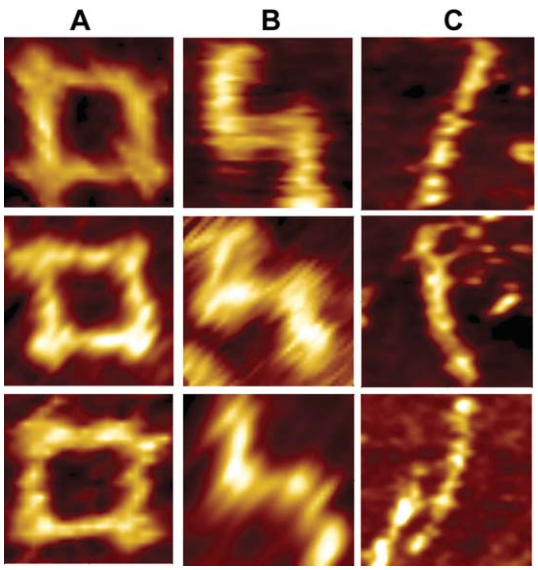


**Fig. 2** AFM images. **A**. Square. **B.** Chair. **C**. Line. The image sizes are 45 nm × 45 nm for A, 80 nm × 80 nm for B, and 95 nm × 108 nm for **C**.

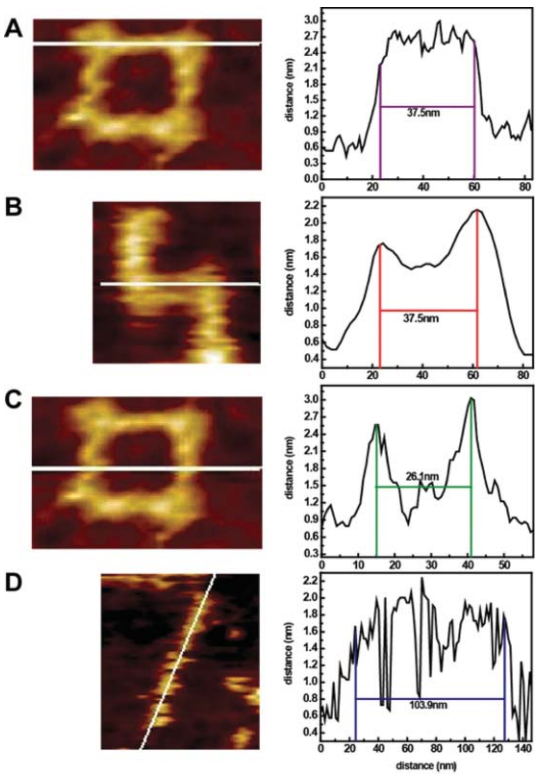


**Fig. 3** AFM image profile analysis. **A**. A square edge to edge distance. **B**. A square distance between opposite sides. **C**. The width of the chair. **D**. The length of the line.

cross-shaped tiles is ~37.5 nm. The predicted center to center distance between two opposite linkers on the square is ~26.1 nm, which is confirmed in Fig. 3C. The length of the line measured as 103.9 nm (Fig. 3D) consistent with the predicted 103.9 nm. The roughness of the line is partially due to the noise associated with AFM and also the cantilever force could remove some of the DNA.

In summary we have rationally designed and demonstrated the self-assembly of three structures (square, chair and line) through a combinatorial approach. By combining this approach with other strategies such as nucleated DNA self-assembly,[7] scaffolded DNA origami,[8] and step-wise self-assembly,[9] it opens us possibility to assemble more complex superstructures from the rich set of building blocks available.

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