Communication

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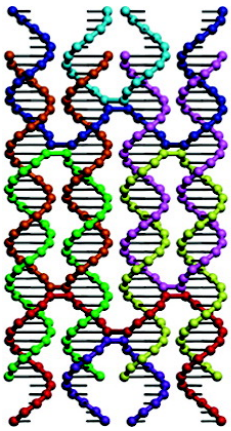

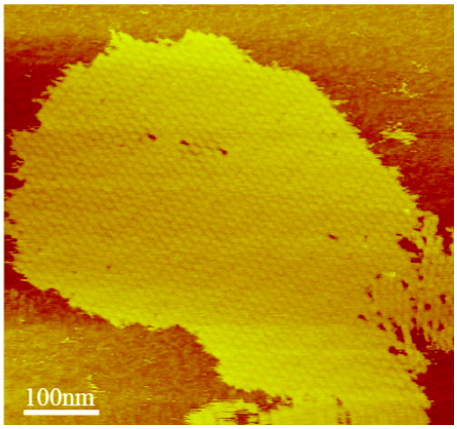

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Self-Assembly of DNA Double-Double Crossover Complexes into High-Density, Doubly Connected, Planar Structures

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In 1993, Fu et al.[1] described the double crossover (DX) DNA complex consisting of two DNA double helices connected by two reciprocal exchanges (crossovers). In 1998, Winfree et al.[2] used DX complexes to self-assemble regular planar structures. Subsequently, several other DNA complexes have been designed and used to self-assemble organized structures.[3−5] In this paper, we present a new complex based on the DX, the double-double crossover (DDX), consisting of four DNA double helices connected by a total of six reciprocal exchanges. We use DDX complexes to self-assemble high-density, doubly connected, planar structures. We also briefly describe a potential modification of the DDX complex that may permit the self-assembly of three-dimensional structures.

Structures self-assembled by Winfree et al.[2] and LaBean et al.[3] are singly connected (adjacent complexes are held together by a single pair of complementary sticky ends), while structures self-assembled by Yan et al.,[4] Chelyapov et al.,[5] and Ding et al.[6] are doubly connected (adjacent complexes are held together by two pairs of complementary sticky ends). Doubly connected structures may have greater structural integrity than singly connected ones. However, the doubly connected structures that have been created to date lack the high density (DNA mass per unit area) that is found in structures self-assembled using DX complexes. Watson-Crick base pairing endows DNA with the capacity to self-assemble into a wide variety of shapes and patterns.[7] This capacity, together with double connectedness and high density, may make structures created with DDX complexes desirable. For example, such structures might be useful as scaffoldings for the deposition of nanomaterials in the creation of high-density electrical and quantum devices.

Figure 1a shows the expected structure of the DDX complex, with two reciprocal exchanges connecting each pair of adjacent helices. Figure 1b shows how the complexes might tile the plane with individual complexes connected to neighbors via two pairs of sticky ends.

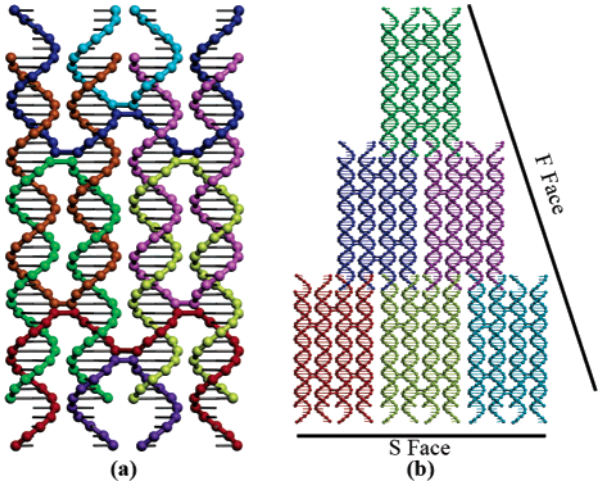

Figure 1. (a) Diagram of the DNA double-double crossover (DDX) complex consisting of eight strands forming four double helices connected via six reciprocal exchanges. (b) Diagram of the DDX complexes tiling the plane while connecting every pair of adjacent complexes via two pairs of sticky ends.

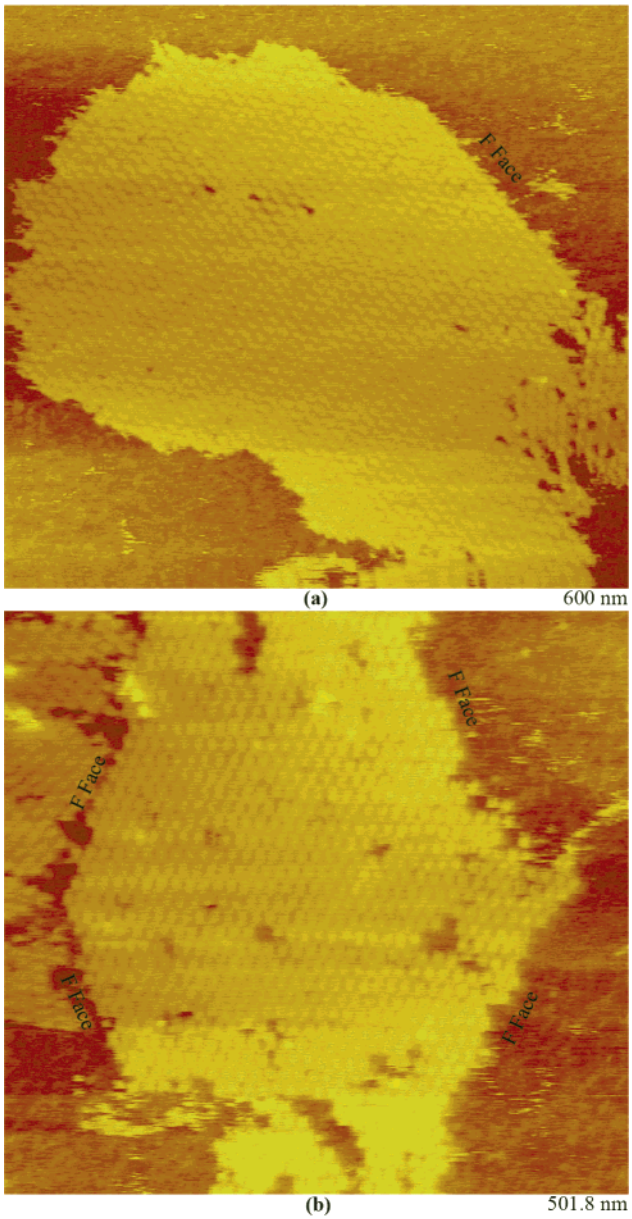

Figure 2. Atomic force micrographs of double-double crossover (DDX) complexes assembling into high-density, planar structures. Some F faces are labeled.

Complexes that are capable of periodically tiling a plane are also theoretically capable of forming tubular structures. Rothemund et al.[8] presented evidence that one of the factors that affects the

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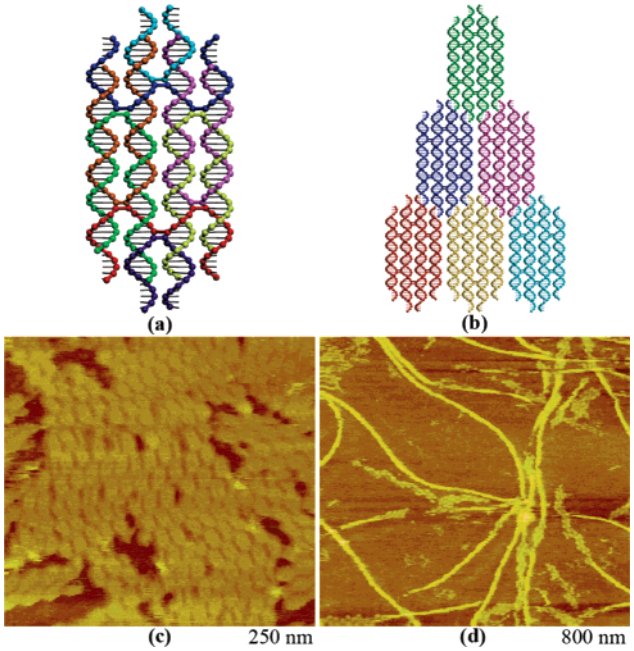

Figure 3. (a) Diagram of the alternative DDX complex. (b) Diagram of the alternative DDX complexes tiling the plane. (c) Atomic force micrograph of a planar structure self-assembled from the alternative DDX complexes. (d) Atomic force micrograph of tubular structures self-assembled from the alternative DDX complexes.

curvature of the structures formed by DX complexes is the number of bases between reciprocal exchanges. Certain choices favor planar structures, while others favor tubular structures.

To design DDX complexes that would self-assemble into planar structures, we wrote an algorithm that searches for a set of crossover positions that minimize interhelix strain in an idealized planar complex consisting of four parallel DNA double helices. On the basis of the output of the algorithm, we generated DNA sequences with 16 bases between outer reciprocal exchanges and 26 bases between inner ones (see Figure 1a). We designed sticky ends so that complexes of a single type would be capable of tiling the plane.

Images a and b of Figure 2 show atomic force micrographs of DDX complexes tiling the plane. We frequently observed crystals of this size and regularity. Each unit in the crystal is approximately 14 nm by 10 nm in size, which is consistent with our predictions of the size of the DDX complex.

While the correct placement of the reciprocal exchange points may be important in creating planar crystals, it appears that other factors are involved. When we generated an alternative DDX complex with the same distances between the reciprocal exchange points but different DNA strand lengths and sequences (see Figure 3a and b), the complexes sometimes assembled into planar structures (Figure 3c) and sometimes into tubular structures (Figure 3d). A preliminary report on this alternative complex can be found in Brun et al.[9]

Notice that in Figure 1b there are flat (F) faces and stepped (S) faces.[10] A new complex accretes to an S face via four pairs of sticky ends, but accretes to an F face via only two pairs of sticky ends. In theory, this suggests that F faces should be more stable than S faces of the same length and should be abundant at equilibrium. This

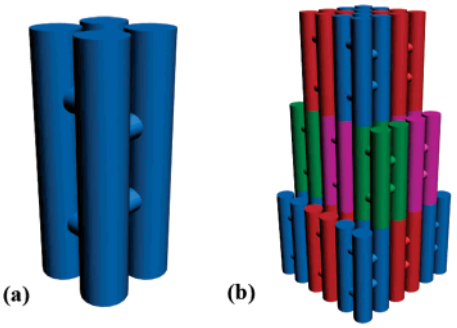

Figure 4. (a) Diagram of the four-helix bundle complex theoretically obtainable by connecting the left-most and right-most helices of the double-double crossover complex. (b) Diagram of a three-dimensional structure that, in theory, can self-assemble from these complexes. Colors added to distinguish individual units.

may explain the F faces in Figure 2a and b. However, it is also possible that these faces are the result of tearing along minimum-energy faults during the destructive processes of AFM sample preparation and imaging.

Several groups have considered the problem of using DNA to self-assemble regular 3-D structures: Winfree et al.[11] using two-helix bundles (DX), Park et al.[12] using three-helix bundles, and Mathieu et al.[13] using six-helix bundles. As a future direction, it may be possible to modify the DDX complex to form the four-helix bundle complex diagrammed in Figure 4a. Such complexes might self-assemble to form high-density, doubly connected, three-dimensional crystals, as shown in Figure 4b and are described in greater detail by Brun et al.[9]

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Supporting Information Available: Sequences for the double-double crossover complexes, nick placements, protocols for assembly, and sample preparation for AFM imaging. This material available free of charge via the Internet at http://pubs.acs.org.

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