DNA's New Avatar as Nanoscale Construction Material

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DNA is fast taking on a new aspect utilizing it's physical property of persistence length and chemical property of base pairing to build architectures in 1D, 2D and 3D. This field is called structural DNA nano-technology and is poised to revolutionize several areas ranging from materials science to cell biology.

DNA is the hereditary material in almost all life forms and carries the information for the cell to build and sustain life in the organism. A molecular level understanding of how DNA functions to store and impart genetic information emerged soon after its structure was elucidated in 1953 by Watson and Crick. Apart from its well-known role as the cellular storehouse of information, DNA is now being used to construct rigid scaffolds in one, two and three dimension on the nanoscale. This field is termed '*Structural DNA Nanotechnology*' [1]. It seeks to use double helical, Watson–Crick base paired DNA (i.e., B-DNA) to create ordered patterns in 1D, 2D and 3D on the nanoscale. Putting it simply, structural DNA nanotechnology is about specially choosing a set of DNA sequences, which when mixed together, self-assemble into regular, well-defined shapes on the nanoscale.

Keywords
Nanoscale, rigid scaffolds, DNA, double helical rigid rod.

B-DNA resembles a rigid rod at the nanoscale. Because the DNA double helix has a regular diameter of 2.3 nm and a pitch of 3.4 nm, it is an attractive building block on this length scale [2]. This inherently nanoscale object has a persistence length of ~150 base pairs, which implies that up to lengths of ~50 nm, the DNA double helix essentially behaves as a rigid rod [3]. Now, if you were given a set of rigid rods on the macroscale and asked to construct grills or shapes with them, then you would need some kind of glue such as a welding device or hammer and nails, with which to precisely join the ends of a preferred rod at a location of your choice. So given that B-DNA is a rod on the nanoscale, what kind of glue can be used to similarly 'weld' a set of DNA rods to give a 2D pattern or a 3D shape?

This 'welding' is achieved through the elegant rules of Watson–Crick base-pairing. A single strand of DNA binds with highest affinity another strand that has the complementary sequence, to give a double-helical rigid rod, or B-DNA (*Figure* 1a). Thus, if this B-DNA were to have a single stranded overhang, (*Figure* 1b), then only a particular rigid rod bearing a complementary overhang would selectively bind and bring about the 'welding' of these two double helices in space. It therefore becomes possible to program a set of linear DNA molecules by encoding as sequence information, instructions to self-assemble into predicted structures on the

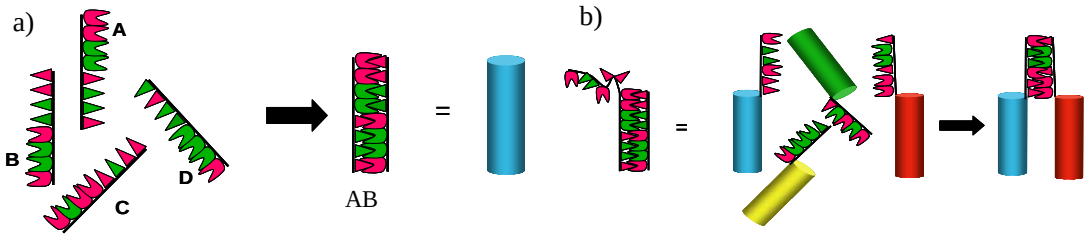

Figure1. (a) By complementary base pairing, DNA sequence A, is capable of binding selectively, sequence B, which is the exact complement from a solution of DNA sequences A-D. AB is a B-DNA duplex that behaves as a rigid rod.
(b) Similarly, a set of duplexes with single stranded overhangs are capable of recognition such that two duplexes rods bearing perfectly complementary overhangs are 'welded' selectively to each other at a pre-designated location.

nanoscale using simple base-pairing logic. The end result of such programming in the context of structural DNA nanotechnology is the self-assembly into double helices in specific spatial orientations, whereas the end result of programming DNA in the cellular context is the reading and translation of the DNA code into protein by cellular machinery.

To give a simple example of how one can construct a two-dimensional array, consider a four-way junction as depicted in *Figure* 2. This four-way junction (4WJ) may be formed from four single strands of DNA where the 5' end of strand 2 is complementary to the 3' end of the strand 1. The 5' end of strand m, must be complementary to the 3' end of strand (m-1). One can form an *n*-arm junction, when 5' end of strand n is complementary to the 3' end of strand 1. If one appends one overhang each onto the four arms of the four-way junction or four-arm junction, we get the building block of a 2D array by specifying the overhang sequences or in other words, programming the overhangs. If we program the overhangs by specifying that the red overhang and green

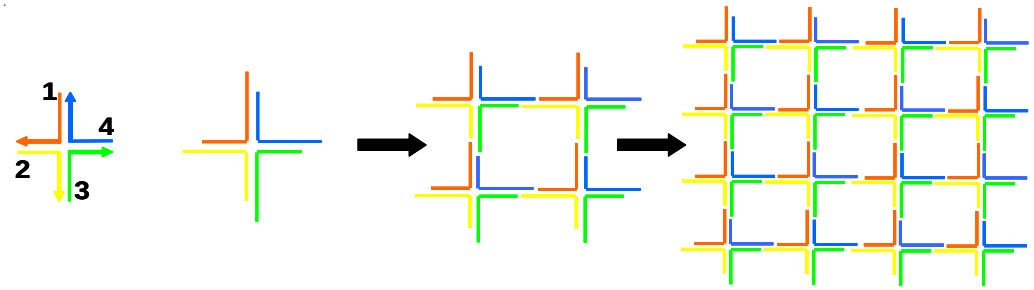

Figure 2. Making a two-dimensional array from a set of four DNA sequences that are programmed to assemble sequentially into a four-way junction, a quadrilateral tile and a 2D array.

overhang are complementary to each other, and that the blue overhang and yellow overhang are complementary to each other, then, four such 4WJs can assemble to form a quadrilateral tile as shown in *Figure* 2. This quadrilateral tile can assemble further, adding on 4WJs along the red-green sites as well as the blue-yellow sites to form a regular two-dimensional array with square patterns [4]. By changing the length of the sequences that form the 4WJ, one can change the length of the squares. Thus, one can obtain a 2D network with different pore sizes.

Structural DNA nanotechnology is still in an embryonic stage, where the underlying principles, the design and fabrication of building blocks, are still being explored. The programmability of DNA sequences aids their self-assembly into structures that are impossible to attain with other biomolecules. However, there are obstacles that limit the practical applications of such DNA assemblies. Errors in self assembly compromises function causing assembly defects that are not insignificant. Although it is theoretically possible to design several unique sequences for self assembly, the binding sites may still have moderate affinities for sequences that are not their exact complement. As a result, parts of a given sequence may be capable of hybridizing to multiple sequences, which could disrupt the overall assembly. Thus, the key issues in the area that would need to be addressed if structural DNA nanotechnology is to live up to its potential would be (i) to develop methodologies to achieve error-free assembly of components, (ii) to develop design concepts that control the size or confines 2D arrays to defined dimensions and (iii) to push the limits of the dimensions of rigid assemblies and scaffolds beyond what is currently achievable, into micron regimes. 2D scaffolds could also be made to extend into 3D and form a regular-periodic lattice which could potentially transform crystallography, as these scaffolds could present the desired protein periodically. There have already been reports of regular arrangements of proteins on 2D arrays [5]. 2D and 3D arrays also have regular cavities that could serve as super-accurate filters on the nanoscale [6]. Thus, despite the current limitations, structural DNA nanotechnology is well-placed to be a vehicle that could revolutionize nanoelectronics, macromolecular crystallography and nanorobotics.

Suggested Reading

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