DNA structural nanotechnology - a review

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1 - Introduction

Nanotechnology is above all a mindset, a way of thinking that is rooted in atomically precise perception.

As it is known, DNA is the molecule that nature uses as genetic material. The iconic antiparallel double helical structure assumed by its two strands facilitates high-fidelity recognition between the nucleotides of complementary molecules. Although every base can pair with every other base, including itself, the Watson-Crick pairing of adenine (A) with thymine (T) and guanine (G) with cytosine (C) appears to be the favoured type of interaction between polynucleotides if the sequences of the molecules permit it. Biology clearly exploits this form of interaction in the replication of genetic information and in its expression. Nevertheless, biology is no longer the only branch of science where DNA is finding a significant role: it is now possible to exploit DNA complementarity to control the structure of matter.

Structural DNA nanotechnology rests on three pillars: hybridization, stably branched DNA, and convenient synthesis of designed sequences.

1.1 - Hibridyzation

The self-association of complementary nucleic acid molecules, or parts of molecules, is implicit in all aspects of structural DNA nanotechnology.

1.2 – Stably branched DNA

Although the DNA double helix is certainly the best-known structure in biology, little biology would occur if the DNA molecule were locked tightly into that structure with an unbranched helical axis. For example, triply branched replication forks occur during semiconservative replication, and four–arm branched Holiday junctions are intermediates in genetic recombination. Likewise, branched DNA molecules (figures 1 and 2) are central to DNA nanotechnology. It is the combination on in vitro hybridization and synthetic branched DNA that leads to the ability to use DNA as a construction material.

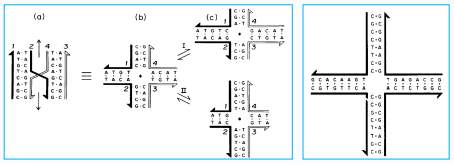


Figure 1. The recombinant junction. **Figure 2.** An immobile nucleic acid junction of rank 4

1.3 - Convenient synthesis of designed sequences

Biologically derived branched DNA molecules, such as Holliday junctions, are inherently unstable because they exhibit sequence symmetry. This symmetry enables an isomerisation known as branch migration that allows the branch point to relocate. Branch migration can be eliminated if one chooses sequences that lack symmetry in the vicinity of the branch point. Such sequences are not readily obtained from natural sources, which lead to the third pillar supporting DNA nanotechnology, the synthesis of DNA molecules of arbitrary sequence, which are synthesized within laboratories or centralized facilities since 1980s.

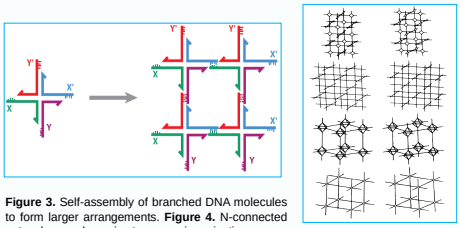


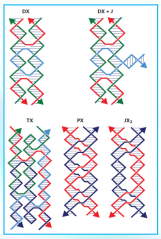
Figure 3. Self-assembly of branched DNA molecules to form larger arrangements. **Figure 4.** N-connected networks are shown in stereoscopic projection.

2 - Initial steps in the process

There are two fundamental steps needed to perform projects in structural DNA nanotechnology: motif design and sequence design.

2.1- Motif design

Motif design relies on the operation of reciprocal exchange, the switching of the connections between DNA strands in two different double helices to produce a new connectivity.



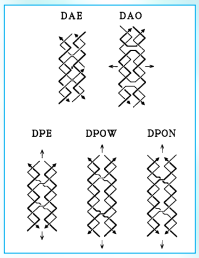
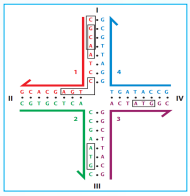


Figure 5. Motifs that can result from reciprocal exchange of DNA molecules. **Figure 6.** Schematic drawings of the five different structural arrangements of double-crossover (DX) structures

2.2 - Sequence design and symmetry minimization

The design of DNA sequences that do not adhere to the strict linear duplex DNA paradigm is likely to result in molecules that correspond to excited states of some sort. Sequence symmetry minimization would insist that each tetramer be unique.



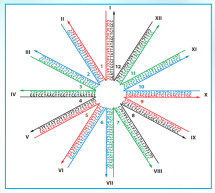


Figure 7. Sequence design. The four-arm junction shown contains four 16 mers that are each broken up into 13 overlapping tetramers. **Figure 8.** A 12-arm junction.

3 - Individual constructs

DNA can be used to construct specific target structures, which are self-assembled and then may be ligated into closed species. These molecules may be characterized only by their topologies, but some have been characterized geometrically

3.1 - Unscaffolded targets

The earliest DNA constructs were best described as topological species, rather than geometric species. This is because the earliest DNA motifs, i.e., branched junctions, were not robust but could be described as floppy if they were ligated. Idealized pictures of the first two structures, a cube and a truncated octahedron, each with two double helical turns between vertices, are shown in figure 9.

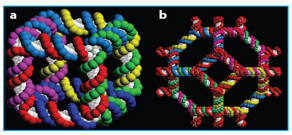


Figure 9. Early topological constructs built form DNA. a) A cube like-molecule. b) A DNA-truncated octahedron.

3.2 - DNA Origami

DNA Origami entails the use of a scaffolding strand to which a series of smaller staple strands or helper strands are added. The staple strands are used to fold the scaffolding strand into a well-defined shape.

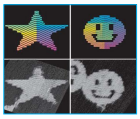


Figure 10. Atomic force micrographs of DNA origami constructs. A star and a smiley face.

4 - Crystalline arrays

The original goal of structural DNA nanotechnology was to produce designed periodic matter. The first stage of this effort was the assembly of two-dimensional crystals from robust motifs. These two-dimensional crystals could be readily characterized by atomic force microscopy.

4.1 - Two dimensional crystals

To generate periodic matter, it is necessary to have robust motifs that do not bend and flex readily; otherwise, a repeating pattern could fold up to form a cycle, poisoning the growth of the array.

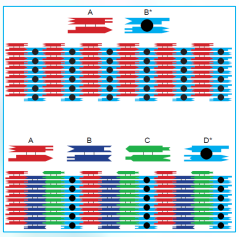


Figure 11. The top of this panel shows two DX molecules with complementary sticky ends shown as complementary geometrical shapes. The bottom of this panel shows a four-component array.

4.2 - Three-dimensional crystals

Control of the structure of matter would be incomplete without the ability to produce three-dimensional crystals of high quality. Although two-dimensional crystals are examined by AFM, the way to characterize the molecular structure of three-dimensional crystals is by X-ray crystallography.

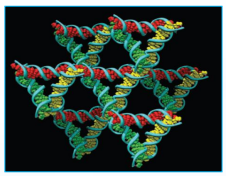


Figure 12. The three-dimensional lattice formed by the tensegrity triangle.

5 - Conclusions

DNA is one of the most powerful engineering materials available in nanotechnology.

DNA provides a platform for mechanical, chemical and physical devices.

The experimental results augur well for the use of DNA self-assembly to produce structural targets on the nanoscale.

The next step is to develop intelligent and refined structures that have viable physical, chemical and biological applications.

6 - Bibliography

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