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Not Just the Secret of Life: DNA in Nanotechnology

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Structural DNA nanotechnology uses the concept of reciprocal exchange between DNA double helices or hairpins to produce branched DNA motifs, like Holliday junctions, or related structures, such as double crossover (DX), triple crossover (TX), paranemic crossover (PX) and DNA parallelogram motifs. We combine DNA motifs to produce specific structures by using sticky-ended cohesion or by other interactions, such as PX cohesion. The major strength of sticky-ended cohesion is that it produces predictable adhesion combined with known structure.

From branched junctions, we have constructed DNA stick-polyhedra, whose edges are double helices, and whose vertices are the branch points of DNA branched junctions. These include a cube, a truncated octahedron, and an irregular graph. The cube was constructed in solution, as was the irregular graph. The truncated octahedron was constructed using a solid-support methodology. The cube is a hexacatenane, the truncated octahedron is a 14-catenane, and the irregular graph is a knot. Only in the irregular knot were the edges derived from separate double helices, rather than just resulting from the arms of the branched junctions at the vertices.

This approach has also rendered accessible several topological targets, such as deliberately designed knots. A half-turn of right-handed B-DNA is equivalent to a negative node in a knot or catenane, whereas a half-turn of left-handed Z-DNA is equivalent to a positive node. By varying solution conditions, we have produced a circle, trefoil knots of both chiralities and a figure-8 knot all from the same DNA single strand. The construction of an RNA knot enabled the demonstration that DNA topoisomerase III has an RNA topoisomerase activity, although topoisomerase I does not. The most elaborate topological target made is a set of Borromean rings made by combining B-DNA branched junctions and Z-DNA branched junctions. Recently, we have begun to template the topology of industrial polymers, such as nylon with DNA-like scaffolds.

Nanorobotics are key to the success of nanotechnology. To move in this direction, we have used two DX molecules to construct a DNA nanomechanical device by linking them with a segment that can be switched between left-handed Z-DNA with right-handed B-DNA. PX DNA has been used to produce a robust sequence-dependent device that changes states by differential hybridization topology. The sequence-dependent nature of this device means that a variety of them attached to a motif or to an array can all be addressed individually. Recently, we have constructed a protein-activated device that can be used to measure the ability of the protein to do work. The binding protein bends the DNA to which it binds; it must disrupt a varying number of base pairs if it is to bend the DNA. In addition, we have produced a precisely controlled bipedal walking device that moves along a sidewalk in response to externally provided signals in the form of DNA strands.

A central goal of DNA nanotechnology is the self-assembly of periodic matter. We have constructed micron-sized 2-dimensional DNA arrays from DX, TX and parallelogram motifs. We can produce specific designed patterns visible in the AFM from DX and TX molecules. We can change the patterns by changing the components, and by modification after assembly. In addition, we have generated 2D arrays from DNA parallelograms. These arrays contain cavities whose sizes can be tuned by design. Recently, we have used new motifs to produce honeycomb-shaped arrays. In studies complementary to specific periodic self-assembly, we have performed algorithmic constructions, corresponding to XOR operations. Algorithmic assembly is more demanding than periodic assembly, because correct tiles are competing for their sites with partially correct tiles, rather than with incorrect tiles.

The key challenge in the area is the extension of the 2D results obtained so far to 3D systems with a high degree of ordering. Numerous motifs have been produced that can produce 2D arrays in each of the three directions normal to the vectors that span the 3D space. Crystals with dimensions 20-100 microns of 10 Å resolution (as determined by X-ray diffraction) are relatively routine to produce. We have produced needle-like crystals longer than a millimeter. Thus, we are able to make connections between molecular design and macroscopic objects; this is a powerful way to understand the relationship between changes at the molecular scale and impact on the macroscopic scale. Ultimately, we expect to be able to generate high resolution crystals of DNA host lattices with heterologous guests, leading to well-ordered bio-macromolecular systems amenable to diffraction analysis.

Other challenges include the incorporation of DNA nanomechanical devices in periodic and aperiodic lattices. The positioning of different sequence-dependent devices at specific loci will lead to the positional control of surface or solid properties. Changing the configuration of the devices will lead to molecular pegboards. Another challenge to use the lattices to organize nanoelectronic components, such as metallic nanoparticles or carbon nanotubes.

Biology contains numerous lessons for the physical sciences. The existence of living systems with nanoscale structural components represents an existence proof that autonomous systems can build up and function on this scale, systems capable of energy transduction and replication. The overall challenge that biology presents to the physical sciences is to replicate this mode of behavior in other systems. Doing this in the most general fashion requires that we move from biokleptic systems to biomimetic systems, and ultimately to abiological systems that perform in this same manner. Structural DNA nanotechnology appears to be a good place to start in attempting to meet this challenge.

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