materials update

DNA barcodes

The idea that DNA might provide the ideal fabric for nanoscale construction and for molecular computers, is bolstered by a demonstration that DNA building blocks can be assembled into microscopically visible strings of information.

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Philip Ball

DNA computers and complex scaffolds for nanotechnological construction are two of the objectives that John Reif and co-workers at Duke University in Durham, North Carolina, have in mind for the 'barcoded' DNA tapes they have created through a process of directed self-assembly[1].

The tapes are made from roughly rectangular tiles, which are themselves woven assemblies of short DNA molecules. The short ends of the tiles are programmed — through 'sticky' sequences of unpaired DNA bases — to stick to one another, end to end, in specified ways.

One- and two-dimensional DNA tiling patterns have been made this way previously, but these have generally been repetitive structures with crystal-like periodicity. Reif and colleagues have found a way not only to introduce an arbitrary, but pre-determined, aperiodicity into the assemblies, but also to make this aperiodicity immediately evident to microscopic probes. This provides a quick, convenient visual readout of the structure encoded in the tiling, which is revealed as a series of light and dark stripes — like a barcode.

The self-assembly of DNA tilings has previously been shown to be capable of embodying a kind of computational process: the tiles can serve as bits whose assembly represents a Boolean logic operation[2]. Reif and colleagues believe that their new approach might allow such

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operations to be programmed, and the outcome to be readily monitored in a DNA computer.

This particular manifestation of DNA computing is quite different from the proposal[3] made by Leonard Adleman in 1994, who showed that the massively parallel assembly of DNA single strands into double helices, according to the rules of complementary base pairing, could be used to solve computationally hard problems. Adleman's strategy involved a process of weeding out the 'wrong' answers embodied in some pairings until only the 'best' solution remained.

In contrast, the approach to DNA computing explored by Ned Seeman and his collaborators[2] is more deterministic, involving the assembly of sticky DNA tiles into patterns that encode sequences of bits. This proposal builds on demonstrations over the past decade or so that DNA-based supramolecular building blocks can be programmed to join together into all manner of topologically complex structures[4].

Seeman envisages some of these structures serving as templates around which nanoscale architectures can be assembled. DNA scaffolds might, for example, guide molecular-scale components into forming electronic circuits or mechanical nanomachines.

One of the most challenging problems, however, is to create structures that are not simply periodic or highly symmetric — in other words, to bring the building blocks together in an arbitrary arrangement. This is the question that Reif and colleagues have now begun to answer. The solution, they say, is to nucleate the nanoscale structure around a single-stranded template of DNA.

In effect, one might consider the formation of their barcoded assemblies to be a projection of Erwin Schrödinger's famous 'aperiodic crystal' from one level of a hierarchy to another: the aperiodic sequence of information encoded in a single DNA strand is transformed into an aperiodic 'bit' sequence in a pseudo-crystalline structure made by a repeated tiling arrangement of DNA-based building blocks.

Thus the single-stranded DNA acts as a template that directs the formation of a true aperiodic crystal. But the process happens in two dimensions. First, a single sequence of DNA tiles is laid down along the template strand, creating a (short, in the present case) string of tiles like so many threaded beads. But then these strings stick together side by side to form a tape that extends at right angles, like matchsticks laid out in a row.

The pattern encoded in the sequence of tiles in each string then becomes 'amplified' so that it is readily visible, as a barcode-like series of stripes, in atomic force microscope (AFM) images of the resulting assembly.

The DNA tiles are 'double-crossover' structures[4] formed by the interweaving of several — in this case, four — individual strands of DNA, with overlaps that provide the sticky ends. To distinguish between two types of tile, representing by the binary 1 and 0 (or the black and white barcode stripes), the researchers incorporate into one of the tiles two short hairpin loops of DNA that protrude from the main body, one on each side of the tile.

One of the strands that goes into making up each tile is the template strand: the string on which they become assembled. This strand too has hairpin loops along its length, defining the sequence of 1 and 0 that represents the barcode. The base sequences of the DNA tiles are such that a tile with a loop forms only where there is a loop in the template strand.

To demonstrate their strategy, Reif and colleagues made tapes encoding the sequence 01101. In other words, the template strand directs the assembly of a series of five tiles, about 75 nm long in total. Each of these five-tile assemblies then lines up side by side in tapes that can stretch for several hundreds of nanometres, in which the protruding loops show up under the AFM as bright, parallel ridges. The lattice spacing of this barcode — the distance between two adjacent stripes — is 16 nm.

The researchers have shown the programmability of these barcode sequences by using a different template to nucleate the inverse sequence 10010. They can also extend the hierarchy of self-assembly a stage further by giving the end tiles of each series sticky ends, so that individual tapes then stick together to form wider tapes in which the barcode sequence is repeated.

By using long scaffold strands that incorporate hairpin turns, Reif and colleagues propose that one might go beyond the effectively one-dimensional aperiodicity of a barcode: a scaffold that folds back on itself presents a two-dimensional template for constructing an arbitrary two-dimensional tiling pattern. The raised ridges on the tiles might, for instance, be arranged so as to spell out individual alphabetic characters at the nanoscale — or perhaps more usefully, a two-dimensional wiring pattern for a circuit.

References

1. Yan H., LaBean T. H., Feng L. & Reif J. H. Directed nucleation assembly of DNA tile complexes for barcode-patterned lattices. *Proceedings of the National Academy of Sciences USA* advance online publication (2003) | article |
2. Mao C., LaBean T., Reif J. H. & Seeman N. C. Logical computation using algorithmic self-assembly of DNA triple crossover molecules. *Nature* **407,**493–496 (2000)
3. Adleman L. Molecular computation of solutions to computational problem. *Science* **266,**1021–1024 (1994)
4. Seeman N. C. DNA in a material world. *Nature* **421,**427–431 (2003)