DNA NANOTECHNOLOGY

Geometrical self-assembly

DNA origami tiles with complementary shapes have been designed and assembled into large nanostructures through the geometrically controlled stacking of their helices.

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DNA provides one of the simplest yet most flexible platforms for the programmable assembly of molecular devices[1]. Its success as a construction material arises from the predictability of Watson–Crick base-pairing — which makes it possible to control interactions between strands of DNA through sequence design — and on the astonishingly low cost and high throughput of commercial DNA synthesis.

A small revolution in DNA self-assembly was triggered by the introduction of the 'DNA origami' technique by Rothemund in 2006 (ref. 2). At that time, a typical DNA nanostructure was constructed from fewer than twenty synthetic oligonucleotides, each containing a few tens of bases[3,4], resulting in structures smaller than 20 nm in size. Rothemund showed that a single, 7,000-base strand of genomic DNA could be used as a template to organize hundreds of synthetic 'staple' strands, through hybridization, into raft-like structures ('tiles') the side of which can reach 100 nm. Each staple strand is designed to hybridize with three different domains on the long template, stapling the domains together and forcing the template to fold into a rectangular raster of parallel lines that defines the shape of the tile (the folding of the template inspired the name origami). Each tile consists of parallel double helices, in which one strand of each helix is provided by the long template and the other by the short staples. The crossover of the staple strands from helix to helix holds the tile together. This 'template–staples' origami strategy has also been extended to three dimensions[5], and underpins much of the current research into self-assembled nanostructures based on DNA.

Writing in *Nature Chemistry*, Sungwook Woo and Paul Rothemund now describe a yet higher level of self-assembly. By structuring the edges of origami tiles to manipulate tile–tile interactions they were able to use them as building blocks[6] (Fig. 1) to induce assembly at a larger length scale.

They demonstrated the specificity of the interactions between these tiles by successfully assembling them into ordered chains, whose lengths reached the micrometre scale. The tile–tile bonds are based on helix stacking interactions: a blunt end — where the strands of a DNA double helix end on a base pair — at a tile edge can stack on the end of a helix in another tile to form a quasi-continuous helix that is only slightly disrupted by the discontinuities in the DNA backbones. This base-stacking interaction is the same one that makes a large contribution to the stability of a double helix — larger, in fact, than that of the base-pairing hydrogen bonds[7]. To ensure that, to a good approximation, the stability of a tile–tile bond depends only on the number of stacked helices (rather than on the details of the stacked bases), Woo and Rothemund designed each helix to terminate with the same C–G base pair.

They demonstrate two strategies for coding information in the structure of a tile edge: a binary code, in which '1' and '0' bits correspond to structured duplex ends (capable of stacking) and unstructured ends (which cannot stack), respectively, and a multi-level code in which helices are shortened or extended to shape the tile edge into something resembling a jigsaw piece (Fig. 1). In each case, a tile will bind preferentially to a tile with a complementary edge, and it is possible to find sets of approximately orthogonal edges within which non-complementary interactions are much weaker.

Woo and Rothemund point out interesting analogies between DNA strand–strand hybridization and their tile assembly experiments. The construction material in both cases is, of course, DNA, and in both cases the dominant contribution to the energy of the bonds is base stacking. In both cases, the strength of binding is programmed through information stored in structure: two strands of DNA hybridize if the strands have complementary base sequences, such that successive pairs of bases can pack together in the core of the double helix; similarly, two origami tiles will bind together if their edges are structured to maximize the number of stacked helices. Furthermore, the edge of an origami building block has a 'stacking polarity' — similar to the 5′–3′ polarity of a DNA strand. In both cases, binding between the fundamental structural motifs (either bases or helices) is cooperative, and the number of possible bonds between species increases exponentially with the number of motifs that they incorporate — that is, with the length over which they interact. This combinatorial scaling is particularly significant: the freedom to select sets of orthogonal bonds from a very large pool of possible sequences

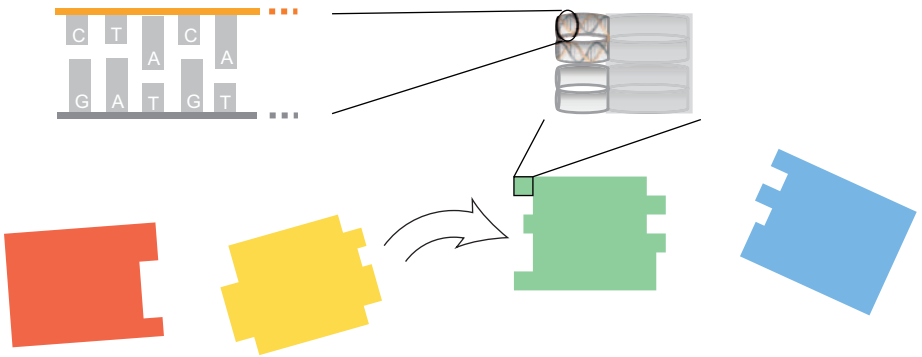

Figure 1 | Using shape to programme interactions between supramoleular assemblies. Attractive interactions between DNA origami tiles are coded in their complementary shaped edges, recapitulating the binding of complementary sequences of bases to form a DNA double helix.

underpins control of DNA hybridization through sequence design; combinatorial libraries of 'shape codes' may prove equally useful in controlling higher-order assembly.

This correspondence between DNA strand hybridization and DNA origami shape complementarity is elegant: although Woo and Rothemund's shape-coded bonds are an order of magnitude bigger than DNA base pairs, they use the same principles to achieve sequence-programmable interactions. There is a further interesting correspondence between synthesis techniques — origami tile assembly, which provides the building blocks of this higher-order assembly process, is relatively robust and efficient, analogous to the highly developed solid-support synthesis technology that puts together the building blocks of DNA itself.

DNA nanostructures can sense, compute and move[8], and provide breadboards on which other molecular components can be laid out with subnanometre accuracy. Every position on an origami tile can be distinguished by its own 'address' provided by the local base sequence of the template strand[2]. The methods of Woo and Rothemund now extend the size of DNA structures that can be created by self-assembly while maintaining nanometre-scale control and addressability. If DNA-based self-assembly is ever to become a commercial nanofabrication technology[9], techniques that bridge length scales, such as the shape coding demonstrated here, are likely to play an important role. ❐

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References

1. Seeman, N. C. *Nature* **421,** 427–431 (2003).
2. Rothemund, P. W. K. *Nature* **440,** 297–302 (2006).
3. Fu, T. & Seeman, N. C. *Biochemistry* **32,** 3211–3220 (1993).
4. Chen, J. H. & Seeman, N. C. *Nature* **350,** 631–633 (1991).
5. Douglas, S. M. *et al. Nature* **459,** 414–418 (2009).
6. Woo, S. & Rothemund, P. W. K. *Nature Chem.* **3,** XX–XX (2011).
7. Kool, E. T. *Annu. Rev. Biophys. Biomol. Struct.* **30,** 1–22 (2001).
8. Bath, J. & Turberfield, A. J. *Nature Nanotech.* **2,** 275–284 (2007).
9. Whitesides, G. M. & Grzybowski, B. *Science* **295,** 2418–2421 (2002).