makes this an attractive, more challenging game to play in the future. ❐

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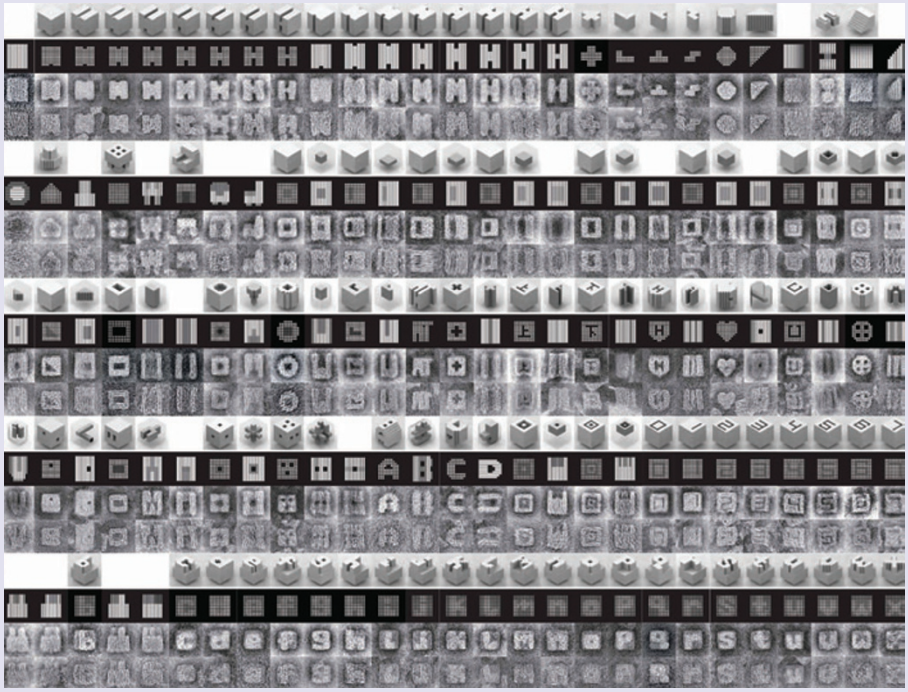
DNA SELF-ASSEMBLY

Effective by design

It shouldn't have been so easy. A couple of years ago, large numbers of short DNA strands or 'bricks' (pictured) were reported to have self-assembled into a target structure with unprecedented accuracy (Y. Ke *et al.*, *Science* **338,** 1177–1183; 2012). The implications were exciting: efficient drug delivery, novel imaging probes and templates for computer-chip fabrication, to name a few. But no one seemed to know quite why it worked — surely more strands would simply make for more mistakes. Aleks Reinhardt and Daan Frenkel have now determined theoretically that the odds actually favour the target structure over any incorrect assembly, and it seems the principle may be applicable to a broad range of molecular and colloidal systems (*Phys. Rev. Lett.*, in the press; preprint at http://arxiv.org/abs/1402.6228).

Previous attempts at DNA self-assembly — dubbed origami — used long pieces of single-stranded DNA, stapled together with shorter strands of DNA that folded them into a desired shape. This method proved fruitful, but required viral DNA and careful tailoring of bespoke staple strands for each new shape assembled. In contrast, the DNA bricks were made using short strands of synthetic DNA, interlocked to form modular units that looked rather like Lego.

The building-block analogy follows almost naturally from the chemistry of DNA: the molecule comprises four distinct nucleotides that bind preferentially in pre-determined pairings. But DNA crystallization isn't as straightforward as one might think — a single misincorporation can compromise the whole structure.



Somehow the DNA bricks were able to avoid this without explicitly excluding any unfavourable interactions.

There was some indication that their success might be related to a slow nucleation step preceding a faster growth regime, ensuring that incomplete structures were unlikely to encounter one another, and thus allowing the correct structure to form. Reinhardt and Frenkel ran extensive Monte Carlo simulations of a self-assembling DNA-brick cube, made up of nearly 1,000 DNA strand types, and found results that supported this idea. Their simulations revealed the existence of a narrow temperature window for which the target structure could self-assemble successfully.

The elegance of Reinhardt and Frenkel's system rests with its simplicity, which points towards its broader applicability. The pair made use of the fact that the geometry of the bricks was such that when assembled, their centres of mass formed a distorted diamond lattice. This enabled them to model the DNA bricks as lattice tetrahedra with attractive patches — a minimal description that suggests the principle may hold true for a wide range of nanoscale building blocks.

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