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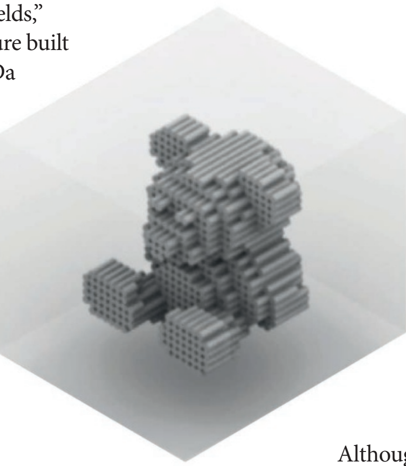
DNA NANOTECHNOLOGY

Building big with DNA bricks

> This study demonstrates new methods of molecular engineering and materials patterning that can go beyond patterning DNA

Despite progress in the field of DNA nanotechnology, the size and complexity of the DNA nanostructures that can be prepared in the laboratory are limited. Now, Peng Yin, Yonggang Ke, Gaetan Bellot and colleagues, writing in *Nature*, report a new one-pot approach that involves the self-assembly of DNA bricks — structural building blocks — for the construction of 3D DNA nanostructures of great size and complexity.

A DNA brick comprises a single strand of DNA with four short binding domains. These binding domains enable individual bricks to assemble through the formation of DNA duplexes at the brick/brick interface. "DNA bricks can be thought of as molecular Lego, with the bricks only fitting with specific and predefined partners," explains Luvena Ong, first author of the study. Whereas first-generation DNA bricks are 32 nucleotides long (comprising four eight-nucleotide binding domains) and can routinely assemble into megadalton-scale structures comprising hundreds of unique bricks, Ong *et al*. use 52-nucleotide bricks with longer binding domains of 13 nucleotides to build structures on the 0.1–1 GDa-scale from tens of thousands of unique bricks. The self-assembly of structures with the 52-nucleotide bricks is both faster and higher yielding, with these structures also showing higher thermal stability. "Additionally, we find that our structures assemble within a narrow temperature range, which enabled us to optimize the annealing protocol and thereby achieve higher yields," notes Ong. The largest structure built of unique bricks is a 536.4 MDa cuboid that contains more than 30,000 bricks with side lengths of more than 100 nm. Larger multimer structures can also be constructed, such as a 1 GDa tetramer built from four 262.8 MDa monomers.



Adapted from Ong, L. L. *et al*. *Nature* **552**, 72–77 (2018), Macmillan Publishers Limited.

The large size and number of components of the new structures combined with the unique sequences of the individual bricks — which can be carefully selected — open doors for the patterning of 3D shapes. The team has developed a software tool called Nanobricks that enables users to determine the DNA brick strands required for the synthesis of complex structures containing of the order of 10^4 bricks. To demonstrate the utility of Nanobricks, the team constructed a series of structures with complex cavity architectures, including a teddy bear and a bunny. "This study demonstrates new methods of molecular engineering and materials patterning that can go beyond patterning DNA," says Ong, with the team envisaging that DNA nanostructures could be used as 3D scaffolds for the precise functionalization of nanostructures, such as patterning gold nanoparticles or positioning proteins.

Although the present method enables the construction of larger DNA nanostructures, the cost of synthesizing thousands of DNA strands is prohibitive. But Ong is optimistic, suggesting that the current push to improve methods for amplifying DNA will lead to the method becoming more economically viable. The team continues to think big; "there is also the challenge of making even larger structures, for which we can focus on optimizing the assembly conditions and perhaps the strand sequences," adds Ong.

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ORIGINAL ARTICLE Ong, L. L. *et al.* Programmable self-assembly of three-dimensional nanostructures from 10,000 unique components. *Nature* **552**, 72–77 (2017)
FURTHER READING Seeman, N. C. & Sleiman, H. F. DNA nanotechnology. *Nat. Rev. Mater.* **3**, 17068 (2017)