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DNA assembles nano-objects

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A programmable one-size-fits-all method builds lattices of nanoparticles, proteins, and enzymes.

Nanoscale objects are fundamentally different from either their atomic components or their bulk counterparts. Those differences extend across their optical, electrical, catalytic, and magnetic properties. For example, semiconductor nanoparticles efficiently emit light whose wavelengths, unlike in bulk semiconductors, depend on the particles' sizes. To put those unique properties to use—for example, as nanoscale pixels in TVs that save energy and enhance performance by emitting only the desired wavelengths—researchers are establishing methods to build the nanoscale particles and biomolecules into two-dimensional and three-dimensional systems. With top-down construction methods (see the article by Matthias Imboden and David Bishop, PHYSICS TODAY, December 2014, page 45), such as nanofabrication and 3D printing, researchers struggle to integrate different nanomaterial types and to provide small-scale spatial control, particularly in 3D. A promising alternative is self-assembly, in which building blocks organize themselves to minimize free energy. Self-assembly has the advantage that billions of nanoscale blocks can simultaneously assemble into a particular structure.

But designing the self-assembly process and the resulting nanomaterial is challenging. Unlike atoms, which come in a limited variety, nano-objects can be highly tailored and custom-made, with varied shapes and compositions and with surfaces covered by a range of organic molecules. Biomolecules in particular have complex shapes and surfaces with heterogeneity in both charge and chemistry. The resulting nano-objects are extremely diverse and too large for atomic-level computations. Therefore, even predicting the structures formed by assembled nano-objects is tricky and can only be done by limited coarse-grain descriptions. The situation is even more challenging if the end goal is not only to predict the assembled structure but also to prescribe and control its formation. Given the diversity of nanoparticles, a single approach is unlikely to address the challenge of building every desired system.

A solution for the one-size-fits-all assembly problem may lie in nano-blocks composed of DNA. Almost four decades ago, New York University's Nadrian "Ned" Seeman realized that single-stranded DNA (ssDNA) can serve as a programmable nanoscale building material. DNA's constituent nucleic acids bind in pairs: adenine (A) with thymine (T), and cytosine (C) with guanine (G). So a region of a DNA strand with the sequence CAT will bond with a so-called complementary region of another strand with the sequence GTA. Writing DNA sequences can thus prescribe which regions bond to form double-stranded DNA chains. By selecting and coding their joined regions, researchers can connect multiple single- and double-stranded DNA chains to form nearly any target shape.

In the past decade, researchers have used DNA's programmability and selective bonding to construct primarily 2D and increasingly 3D DNA lattices. Those engineered DNA architectures can serve as scaffolds for organizing inorganic and biological nano-objects regardless of shape or properties.

Building blocks

The addition of a DNA shell controls how nano-objects interact. In previous studies, nanoparticles repelled one another when coated with sufficiently dense polymers that have a neutral electrical charge. Particles covered with oppositely charged polymers could overcome that repulsion and bind together. Instead of such binary interactions, nanoparticles covered with short ssDNA bind with variable strength determined by the number and length of their complementary DNA sequences.

Using DNA-sequence encoding, my research group

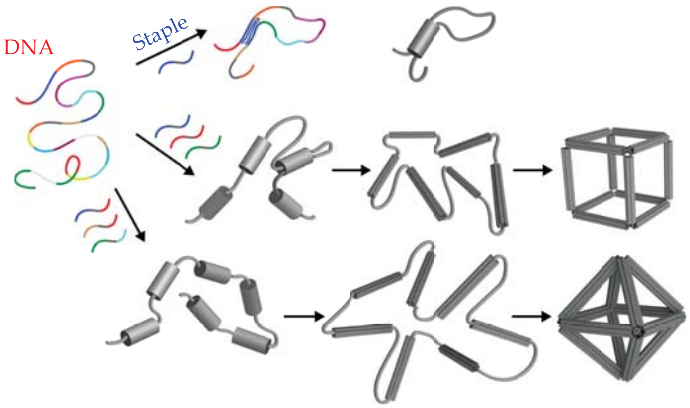

FIGURE 1. SINGLE STRANDS of DNA, left, bond to shorter DNA strands called staples in regions for which their nucleic-acid sequences are complementary (indicated by matching colors). The bonded regions fold the strand and form double helixes, indicated by the gray cylinders. With the right combination of staples, the double helixes bundle together and form a prescribed shape, such as a cube, shown at right. (Image by Oleg Gang.)

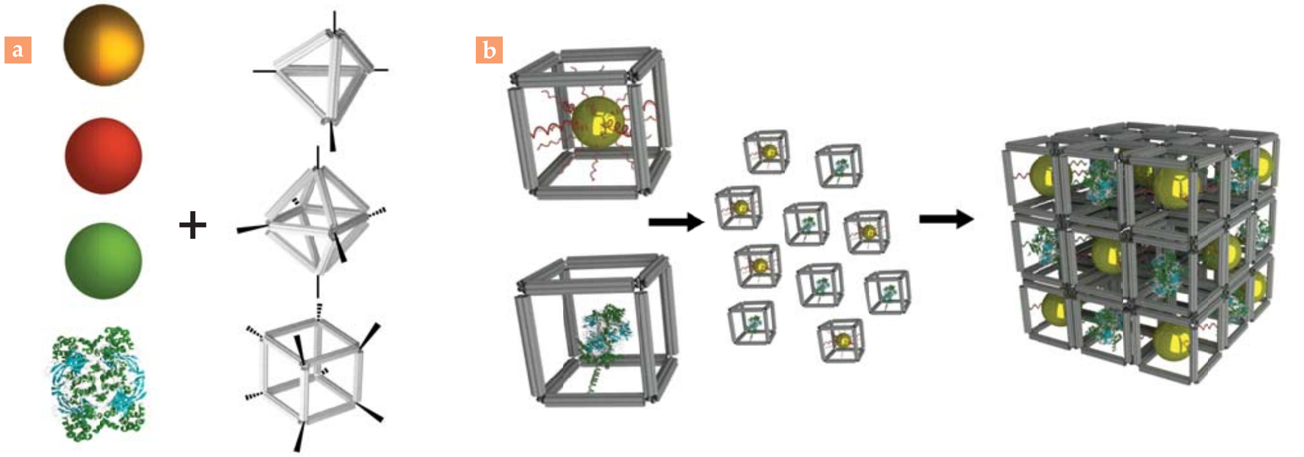

FIGURE 2. SELF-ASSEMBLY guided by DNA starts with a so-called voxel composed of **(a)** a nano-object—that is, one of the different types of nanoparticles (colored spheres) or biomolecules on the left—loaded into one of the DNA-origami frames on the right. (Adapted from Y. Tian et al., *Nat. Mater.* **19**, 789, 2020.) **(b)** The voxels (left) assemble into a lattice (right) as prescribed by DNA coding at each frame's vertices. The lattice's shape and symmetry are independent of the properties of the nano-object in the voxel. (Image by Oleg Gang.)

and others create a pool of particles in which only selected ones bond and the rest, without complementarity, repel. Such particles form various periodic organizations that mimic atomic phases, such as crystalline lattices, and that are determined by the particles' relative sizes and dynamic changes to the composition of their shells. But that assembly process is constrained by the nanoparticles' characteristics, such as their sizes, material types, shapes, and DNA shell properties.

Overcoming system specificity requires more complex DNA architectures and a technique called DNA origami, depicted in figure 1. Similar to traditional paper origami, the structure forms through folding. Using a long ssDNA chain, researchers can design short DNA strands, known as staples, that are complementary to two specific regions of the long ssDNA chain. Those staples bring together or fold the chain, and a specific set of staples folds the strand into a desired 2D or 3D shape.

Self-assembly

DNA origami shapes can encapsulate and assemble generic nano-objects, as depicted in figure 2. Although previous works used specific origami architectures to position nano-objects, my research group generalized the idea to different lattice symmetries and an array of nano-objects, including inorganic nanoparticles, proteins, and enzymes. In the approach, the lattice comprises what are called material voxels, a similar concept to the pixels that make up a TV screen. Each voxel has a 20- to 100-nm polyhedral DNA frame with one or more extra dangling strands inside. Those internal strands determine, through interactions with DNA attached to the objects, which inorganic or biomolecular nano-objects the frame carries. The frames also have external DNA strands that establish prescribed interframe bonds. Simple polyhedral frames—such as tetrahedral, octahedral, and cubic—with interframe DNA-encoded bonds located at their vertices self-assemble into diamond, simple cubic, and body-centered cubic lattices, as confirmed by x-ray scattering and computational methods.

Different kinds of nano-objects can organize using the same assembly platform. For example, an array of light-emitting quantum dot nanoparticles with two emission wavelengths could arrange with alternating colors through the lattice design. Because the voxels' dimensions were only about 1/10th the light's wavelength, the process patterned the nanomaterials at subwavelength scales. The same strategy forms, with nanoscale precision, a lattice of octahedral voxels loaded with six simple proteins called streptavidins. What's more, biomolecules preserved their biological functions. For example, when two enzymes arranged themselves in a specific order in a 3D lattice, they operated more efficiently because of their controlled spacing and mixing. The enzymes in question were a prototypical pair that demonstrate enzyme cascade, in which the products from one enzyme's reactions serve as the reactants for the next enzyme's reaction. The assembly approach enables a new class of chemically active nanomaterials that harvest their properties from the 3D organization of biomolecules.

The molecular-level programmability of DNA interactions opens opportunities for precision nanoscale manufacturing. DNA-guided self-assembly with billions of nanocomponents can form diverse material architectures with diverse functionalities. However, there's still work to be done to understand how to encode more complex structures through multiple DNA bonds and how to steer the assembly process through intricate thermodynamic landscapes.

Additional resources

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▶ S. Nummelin et al., "Evolution of structural DNA nanotechnology," *Adv. Mater.* **30**, 1703721 (2018).

▶ D. Nykypanchuk et al., "DNA-guided crystallization of colloidal nanoparticles," *Nature* **451**, 549 (2008).

▶ Y. Tian et al., "Ordered three-dimensional nanomaterials using DNA-prescribed and valence-controlled material voxels," *Nat. Mater.* **19**, 789 (2020). PT