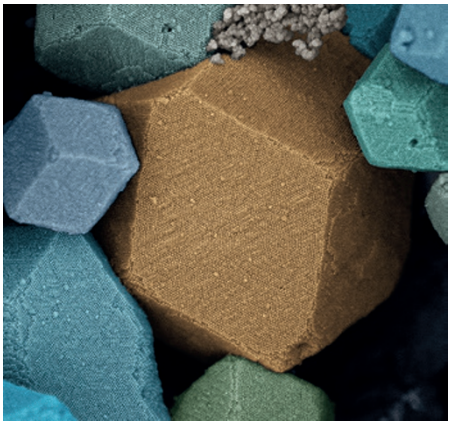
Mighty linkers

The versatility of DNA linkers as selective binders is accelerating the rational design of the assembly of nanoparticle crystals with unprecedented structural complexity.

Much has been achieved in the almost 20 years since the chemistries of DNA and inorganic colloidal nanoparticles were first harnessed to reversibly bond nanoparticles into assemblies[1,2]. Owing to protocols for coating nanoparticles with organic shells and to advances in DNA synthesis, as well as to the ability to design multiple DNA 'recognition' sequences with equivalent binding energy and flexible DNA 'spacers' with varied lengths, it has become possible to exert control over the distance between DNA-linked nanoparticles, and their placement and periodicity within ordered arrangements. Such control over the length, flexibility and recognition properties of DNA linkers, as well as linker density and placement on nanoparticle surfaces, has enabled the effective fine-tuning of the balance of attractive and repulsive interactions between the nanoparticles, and thereby their assembly into two- and three-dimensional arrangements with prescribed long-range order[3,4].

One main advantage of using DNA as a 'glue' to link nanoparticles is the degree of predictability and control of crystal stability and architecture that DNA linkers afford. Indeed, a set of recently described basic design rules for designing DNA–nanoparticle superlattices[5] have no counterpart in nanoparticle lattices held by electrostatic, covalent or other non-covalent interactions. These rules offer independent control of lattice parameters, crystallographic symmetry and nanoparticle size, and allow the properties of the nanoparticle's metallic core to be disentangled from those of its DNA shell (which control the assembly). Moreover, clever synthetic schemes wrap dense DNA shells around nanoparticles regardless of their composition[6], and uniform microcrystals with the thermodynamically expected equilibrium polyhedral shapes (pictured) can be obtained by slow cooling (over the course of days) through the temperature at which the bonds between the linkers break[7].

The last few months have witnessed further developments in the rational design of ordered nanoparticle assemblies. Both Chad Mirkin and Oleg Gang, and their respective collaborators, have recently shown that nanoparticles with vastly



Polyhedral crystals of DNA-linked nanoparticles. Image courtesy of Jessie Ku, Mirkin Group, Northwestern Univ.

distinct shape and/or moderately different size can be co-crystallized (for example, octahedra and spheres of similar size[8]; or cubes and disks of different diameter[9]). As noted by Jean-Philippe Sobczak and Hendrik Dietz in a News & Views article[10], to achieve large co-crystals with long-range order, one can either use nanoparticles with a high degree of shape complementarity together with stiffer (double-stranded) DNA linkers, or more flexible (single-stranded) linkers that compensate for a low degree of structural complementarity between nanoparticles.

Another advantage of using DNA linkers is the possibility to judiciously 'reprogram' the structure of a DNA–nanoparticle superlattice. This has been demonstrated by Gang and colleagues, who report[11] the design of different types of 'input' DNA strands that can be used to switch the structure of a 'mother' crystal into a selected number of 'daughter' crystalline structures. In a nutshell, owing to the reversibility of the DNA bonds, such input strands shift the attractive and/or repulsive interactions between the nanoparticles to those corresponding to a different crystal structure. In a News & Views article, Erika Eiser notes[12] that if a similar approach can be eventually applied to microparticles, these selective and on-demand transformations could form the basis of bulk materials with switchable photonic properties. Moreover, both the nanoscale structure of a nanoparticle crystal and its mesoscopic shape can affect the crystal's plasmonic and photonic properties[13].

Besides bridging nanoparticles, synthetic DNA can also be programmed to make origami frames that bind nanoparticles and arrange them into arrays[14]. This approach to using DNA as a rigid scaffold (rather than as a flexible linker) to place nanoparticles in ordered arrangements has barely been explored. In fact, as Bert Nickel and Tim Liedl argue in a Commentary[15], DNA-origami cages enclosing nanoparticles could make unit cells with the directional bonds that are needed to assemble open (that is, non-close-packed) lattices. They also point out that achieving large, high-quality crystals remains a bottleneck that could be overcome with a systematic exploration, supported by theoretical modelling, of the conditions that favour crystal growth.

Ultimately, DNA-mediated nanoparticle assembly is the most versatile approach to not only tailor the plasmonic and photonic properties of metal–nanoparticle aggregates, but also to build dynamic, functional nanostructures comprising individually addressable building blocks arranged in predetermined patterns (analogously to complex biomolecules such as proteins). Structures with such addressable complexity may form the basis of future nanomachines for gene regulation, biological imaging, drug delivery, or diagnostic applications. ❐

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