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DNA-controlled assembly of an NaTl lattice structure from gold and protein nanoparticles

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Abstract

The formation of a non-compact diamond structure from tailorable building blocks is an important goal in colloidal crystallization because the non-compact diamond lattice is an essential component of photonic crystals for the visible light range^{1–7}. However, designing nanoparticle systems that self-assemble into non-compact structures has proven difficult. Although several methods have been proposed^{7–10}, single-component nanoparticle assembly of a diamond structure has not been reported. Binary systems, in which at least one component is arranged in a diamond lattice, provide alternatives^{7,11,12}, but control of interparticle interactions is critical to this approach. DNA has been used for this purpose in a number of systems^{13–18}. Here we show the creation of a non-compact lattice by DNA-programmed crystallization using surface-modified Q β phage capsid particles and gold nanoparticles (AuNPs), engineered to have similar effective radii. When combined with the proper connecting oligonucleotides, these components form NaTl-type colloidal crystalline structures containing interpenetrating organic and inorganic diamond lattices, as determined by small-angle X-ray scattering (SAXS). DNA control of assembly is therefore shown to be compatible with particles possessing very different properties, as long as they are amenable to surface modification.

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Author Contributions. P.C., A.K.R.L.J., D.A., and M.G.F. were responsible for the synthetic components of the project. P.C. and M.G.F. designed the structure of DNA-linked virus capsids. A.K.R.L.J. and S.Y.P designed DNA-linked nanoparticles and the DNA sequences. S.Y.P. was responsible for the theoretical components and the overall experimental design of the project. S.Y.P. performed SAXS experiments and analyzed the SAXS data. All authors contributed to the writing of the manuscript.

The self-assembly of binary systems (as precursors for creating a diamond lattice by the post-assembly removal of one component) can produce one of two alloy lattices, displaying MgCu_2 or NaTl -type structures. The former should be favored when component particles of two different sizes are used, but these materials tend to be mixed with other unwanted alloy structures. Surface patterning has been proposed to solve this problem, but has not yet been experimentally demonstrated⁷. The NaTl lattice^{11,12,19,20} is more likely to be formed when the building blocks are of similar size; here, the two components each form an interpenetrating diamond structure in which next nearest neighbor interactions are crucial²⁰.

DNA base pairing is an effective way to engineer inter-particle interactions in a well-controlled manner. For example, it has been demonstrated with DNA-linked gold nanoparticles that changing the “sticky ends” of the DNA from a self-complementary sequence to a pair of binary sequences induces a switch in crystalline aggregate structure from face-centred cubic (f.c.c.) to body-centred cubic (b.c.c.)¹⁷. This DNA-based crystallization method is applicable to colloidal particles from nanoscale to micron-size¹³⁻¹⁸, and allows for the incorporation of different types of core materials.

We chose to combine organic virus-like protein nanoparticles (VLPs) and inorganic gold nanoparticles (AuNPs) in this way, as shown in Figure 1. While their properties are very different, both are radially symmetric building blocks of well-controlled size. Modification of these core particles with the same non-interacting DNA sequences allows particle assembly to be induced by Watson-Crick hybridization using the appropriate linker sequences, creating a binary system (Figures 1 b and c). Core particle interactions leading to phase separation behaviour would otherwise be expected to be significant, especially when the component particles are composed of different materials.

We further minimized this possibility by constructing particles of very similar effective radii. The distance of the DNA “sticky ends” from the center of the nanoparticle is relatively well-defined, mainly as a consequence of the rigidity of the double helical DNA and the dense loading of DNA strands on the surface. The effective radii of the DNA-linked nanoparticles, a crucial parameter in determining the crystalline structure, include the DNA corona and can therefore be controlled by changing the DNA length (Figure 1b).

When DNA duplex interactions are dominant, without contribution from the core particles, the stable configuration is expected to be a CsCl-type b.c.c. structure, in which each particle has all 8 nearest neighbours composed of the opposite particle type (Figure 1a). The CsCl structure maximizes the number of DNA hybridization points, minimizing the free energy¹⁷. However, the core particle interactions (e.g. gold-gold, gold-virus, virus-virus) can contribute significantly if they extend beyond the inter-particle distance established by the DNA to the next nearest neighbor. Examples are found in atomic crystal systems where interactions between binary components reach to the next nearest neighbor in the b.c.c. lattice, forming an NaTl (B32) structure (Figure 2a)^{19,20}. In these arrangements, all atoms remain on a b.c.c. lattice, but the relative position of each atom type is different, such that two interpenetrating diamond lattices are formed. This type of NaTl structure has never before been observed in a colloidal system. The prospects for their formation were examined by quantitative modelling, considering relative binding energies of different lattice structures

and compositions. The results, given in the Supporting Information, define a set of conditions under which the diamond-like lattice pattern can self-assemble.

To further anticipate what should be observed while nanoparticle aggregates are forming an NaTl crystalline order, we simulated the aggregation process using the Dissipative Particle Dynamics (DPD) mesoscopic simulation method^{21, 22} and calculated the scattering intensities of the system over time (Figure 2b, c, d and the Supporting Information). With this simulation method, we obtained binary aggregates eventually leading to a b.c.c. lattice structure with a CsCl morphology. An NaTl morphology emerged when we introduced the interaction energies and minimized the binding energy with a multi-canonical annealing method²³ (Supporting Information). These simulations provide a basic understanding of the scattering intensities to be expected from the different crystalline structures.

The greatest difference between the scattering intensities of the simulated candidate morphologies is the relative positions of the first and second peaks (Figure 2c and d). The second peaks, corresponding to the (110) and (220) planes, respectively, for the CsCl and NaTl structures, are in the same position because the lattice spacing is twice as large for NaTl compared to CsCl. When we define the inter-particle distance as d , the value of the second peak in q space corresponds to $\sqrt{6\pi}/d$. The first peaks correspond to the (100) and (111) planes for the CsCl and NaTl structures, respectively, with relative positions of $1/\sqrt{2}$ and $\sqrt{3/8}$. Lastly, the (422) peak from the NaTl structure is present throughout the simulated aggregation process. As marked with arrows in Figure 2c, only the peaks (111), (220), and (422) are consistent while all others are merged with or fluctuate.

Experimental realization of the NaTl structure was obtained using DNA-modified VLPs and AuNPs (Figure 3), the latter in different core particle sizes. For the former, we turned to the icosahedral bacteriophage Q β capsid, in preference over the cowpea mosaic virus that had been used in previous studies²⁴, as an example of a stable, highly monodisperse, and controllable nanoscale building block (Supporting Information.). The Q β particle is approximately 28 nm in diameter and is composed of 180 identical proteins (Figures 3a and b), each of which display four amino groups accessible on the outer surface^{25, 26}. The requisite DNA oligomer was modified with a linker containing a dye for quantitation and a terminal alkyne group (2, Figure 3c) for attachment to the Q β capsid by Cu-catalyzed azide-alkyne cycloaddition “click” chemistry (Supporting Information)²⁷. The same oligonucleotide was attached to the AuNPs of four different sizes (10, 15, 20, and 30 nm) by a thiol linkage.

NaTl alloy structures were self-assembled by mixing DNA-decorated AuNPs and VLPs in equal concentration. By controlling the length of the spacer region in linkers X and Y, the effective particle sizes were brought to an average diameter of 48 nm (Figure 4a), thus driving the assembly onto a b.c.c. lattice (Supporting Information). The two-dimensional SAXS patterns (Figure 4b) for these systems clearly showed the unique characteristics of a diamond structure, including the expected $\sqrt{8/3}$ ratio between the position of the first (111) and second (220) peaks. The averaged scattering intensities $I(q)$, determined by integration

and normalization based on the q value and the strength from the second ring (the largest intensity), showed three consistent peak positions, indicated with arrows in Figure 4c, which are consistent with the theoretical calculations. Comparing two theoretical models (infinite perfect crystal as the green line, and finite-sized NaTl-type aggregates as the blue line) with the data for the 15 nm AuNPs shows that the peak positions and the relative heights of these three peaks match well with theoretical estimations (Figure 4d). The experimental results with the 10 and 20 nm AuNPs showed very similar features. The inter-particle distance d , estimated using the position of the second peak, was found to be 45.8, 44.9, and 47.8 nm for the assemblies involving the three AuNP sizes, which falls within the range of inter-particle distances (44.1–51.9 nm, 42.9–49.7 nm, and 45.4–52.2 nm respectively) predicted from the length of the DNA linkers.

The aspect ratios between AuNPs and VLPs in the three cases were found to be close to 1.0 (1:0.991, 1:1.03, and 1:0.912, respectively) by comparison to the inter-particle distance between virus capsid pairs in the capsids-only case (see Supporting Information). This is consistent with our assertion that the attached DNA linkers can be used to control the effective radii of the individual nanoparticles, independent of the core particle size or composition. When larger AuNPs (30 nm) were used, adjusting the effective diameter to 48 nm with a shorter linker X sequence, only a CsCl-type structure was observed when mixed with the VLPs, strongly suggesting that the core particle interactions are crucial determinants in the formation of an NaTl structure as predicted.

The ability to use both core particle and DNA base pairing interactions to assemble nanoparticles with such diverse properties opens the door to new and exciting possibilities for colloidal crystallization and materials assembly. As techniques for controlling the size and surface chemistry of nanoparticles improve²⁸, it is likely that more suitable materials for photonic crystal applications will become available for this type of programmed self-assembly. Extending the size range of such structures will then become an important challenge for the development of designed photonic materials for practical applications.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

DNA-programmable nanoparticle crystallization method: **a.** Different crystallographic arrangements can be programmed by changing the terminal part of the DNA linker sequence¹⁷. **b.** Matching of the effective radii of DNA-linked particles by adjusting the length of the spacer DNA linker to compensate for changes in the Au core particle diameter. Dark rings around DNA coronas indicate the sticky ends of linkers -X and -Y. **c.** Details of the binary-component assembly system in which AuNPs and VLPs are assembled using two different DNA linkers -X and -Y.

Figure 2.

a. Illustration of the NaTI structure, which features two independent and interpenetrating diamond structures. **b.** Example of morphology changes during aggregation simulation. (From left, $t=50.0$, 120.0 , and 190.0) As time goes on, the size of aggregates increases, and the crystalline structure becomes more well-defined. **c.** Calculated change in scattering intensity during the simulation. With increasing time the scattering intensity shows more distinctive peak structures, which indicates more well-defined crystallinity. Scattering intensities were calculated using the Debye formula with two different particles. In the calculations, we used the individual scattering intensities of the two different particles (AuNPs and VLPs), which were measured by SAXS experiments (Supporting Information).

Figure 3.

a. Rendition of the Q β virus capsid (from <http://viperdb.scripps.edu>). **b.** Interlocking dimer of coat protein subunits (black and gray); 90 such dimers form the capsid structure. The positions of surface-accessible amine groups are shown (orange = N-terminus, red = Lys2, blue = Lys13, green = Lys16); disordered sequences are not. **c.** Steps for surface derivatization of the Q β VLP. **d.** DNA oligomer attached to four different sizes of AuNPs used (10, 15, 20 and 30 nm in diameter) with average DNA loadings of 27, 60, 107, and 240 strands/particle, respectively.

Figure 4.

Assembly of an NaI alloy structure using DNA-linked AuNPs and DNA-linked VLPs. **a**. Schematic layout of effective particle size including both the core particle and the DNA. For larger core AuNPs, the length of the DNA spacer was decreased, resulting in a constant effective particle size, equivalent to that of the DNA-decorated VLPs. **b**. SAXS patterns of the NaI structure generated using this binary system of 10 nm AuNPs (top) and 15 nm AuNPs (bottom). The scattering pattern from 20 nm AuNPs was quite similar to the 15 nm case and is not shown here. **c**. Integrated data from b indicates the formation of NaI structures. The x and y axes were normalized to the height and the position, respectively, of the strongest (second) ring. These data show that DNA-directed nanoparticle assembly can combine two very different materials without phase separation behaviour. The integrated one dimensional data shows clear characteristics of an NaI structure. **d**. Comparison between the normalized scattering intensity of the 15 nm experimental results and theoretical calculations of the NaI (blue line) and CsCl (dotted grey line) structures. The relative positions and the relative heights of three peaks (indicated by arrows) are well-matched between theory and experiment.