Self-Assembly

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Multivalent Directed Assembly of Colloidal Particles**

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Nature's building blocks ubiquitously self-assemble into diverse structures in the world around us. In naturally occurring assemblies, directional interactions play a pivotal role in guiding structural complexity and functional specificity at various length scales. Yet, it is still a challenging task in materials science to create building blocks that predictably assemble into desired highly programmable suprastructures. Herein, we highlight an inventive concept for controlling the directional assembly of multivalent colloidal particles, which has recently been reported by Pine and co-workers.[1]

Micro- and nanoscale particles, made from organic, inorganic, or hybrid materials, represent an important class of building blocks for a range of applications, including optoelectronics, catalysis, biosensing, and drug delivery.[2] Well-defined integration of these materials into complex assemblies is a key step toward the realization of advanced functional materials. Recent progress in the synthesis of monodisperse colloidal particles with programmable sizes, shapes and compositions has paved the way for thermodynamically driven suprastructure assemblies with predictable morphologies.

The directional assembly of colloidal building blocks has been realized through the use of either anisotropic shapes (e.g., buckling,[3] faceting[4]) or controlled interactions (through creating single particles with regions of different surface roughness[5] or patterned hydrophobic domains[6]). The dimension-dependent physical and chemical properties of the particles, along with the reaction conditions, govern how these particles self-assemble, and the structures they form. Like artificial atoms, the controllable anisotropy of the particles allows for simulations of reaction kinetics.[7]

Although diverse structures have been formed from different classes of self-assembling particles, no single class of particles has afforded the three-dimensional (3D) directional bonding that mimics the entire range of atomic bonds. This was recently overcome by Wang et al. through the creation of patchy particles with "valency", that is, a controllable number of reactive sites per particle.[1]

It was previously shown that polystyrene particles reproducibly self-assemble into geometric shapes by an emulsion-evaporation method,[8] which is shown in Figure 1a. A discrete number of polystyrene particles (n) were trapped inside toluene emulsions in water. To minimize the second moment of mass distribution as toluene evaporates, the particles undergo dense packing into identical polyhedrons containing n particles. In a novel approach, Wang et al.[1] prepared clusters with amidine groups on their surface originating from the initiator (2,2′-azobis(isobutyramidine) dihydrochloride) used in the radical polymerization of styrene and converted them into atomistic building blocks with reactive patches (Figure 1b,c) using a two-stage swelling and polymerization process.[9] In this polymerization step, benzoyl peroxide was used as an initiator to partially mask the surface of the original clusters, leaving the extremities of the original amidinated clusters uncovered, which then serve as discrete reactive patches. These patchy particles required further separation and isolation to separate them into groups of n by density-gradient centrifugation. The amount of styrene monomer introduced dictates the size of the non-reactive polystyrene surface, and correspondingly the size of the reactive amidinated patches. The patches were specifically functionalized with biotin using amidine-*N*-hydroxysuccinimide (NHS) chemistry, and then further functionalized with DNA containing single-stranded "sticky" ends[10,11] through biotin-streptavidin-biotin linkages (Figure 1c), thereby creating "valency".[1]

The geometries of these patchy particles resemble the arrangements of bonds around atoms. Monovalent s and multivalent sp, sp^2, sp^3, sp^3d, sp^3d^2, sp^3d^3 hybridized orbitals were modeled by the assembled clusters adopting parallel symmetries (Figure 1b). Mixing particles with complementary sticky ends leads to analogues of molecules such as AB-type (for example, HCl), AB_2-type (CO_2), AB_3-type (SO_3), and AB_4-type (CCl_4) molecules. Furthermore, colloidal analogues of alternating copolymers were obtained from complementary divalent particles (Figure 1d). Divalent particles with a large patch size could also accommodate two monovalent particles per patch, forming ethylene-like structures.

The kinetics of AB_3, AB_4, and copolymer formation were investigated using real-time monitoring with optical microscopy. Because the hybridization of complementary DNA strands ($T_m = 50\,^\circ C$) is the driving force for bonding, the

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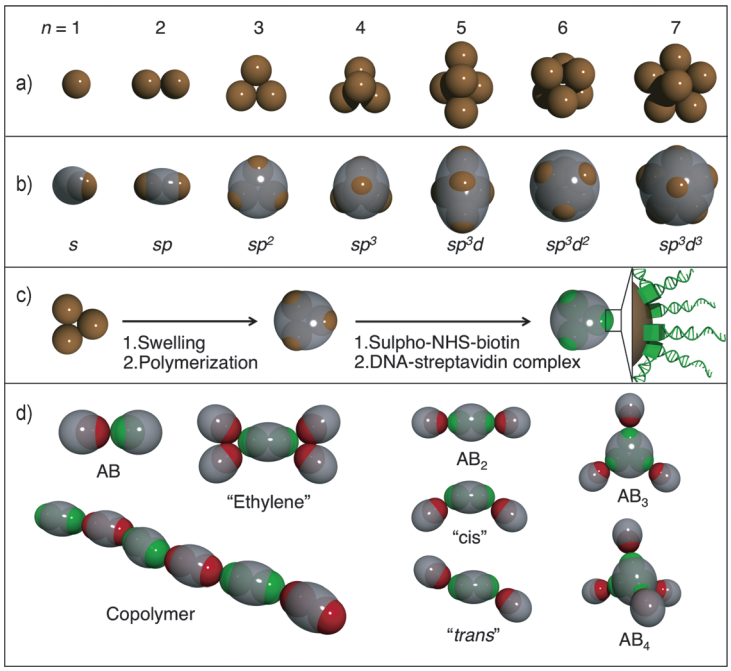

Figure 1. Multivalent directed assembly of colloidal particles synthesized by Wang et al.[1] a) The assembled clusters from n particles. $n=1$, singlet; $n=2$, doublet; $n=3$, triangle; $n=4$, tetrahedron; $n=5$, triangular dipyramid; $n=6$, octahedron; $n=7$, pentagonal dipyramid. b) The colloidal building blocks with the inherent symmetries of their parent clusters. Corresponding hybridized orbitals are shown below the diagram. c) Preparation of multivalent particles functionalized with DNA. d) Assemblies obtained from the multivalent particles, which are analogous to molecules.

assembly was monitored at 25 °C immediately after rapid quenching from dissociation at 55 °C. The estimated reaction times for AB_4 colloidal molecule formation from the Smoluchowski equation are 3.4 min, 6.5 min, and 16 min for the first, second, and third monovalent particles to attach, respectively, which is consistent with the real-time monitoring experiments.

As noted by Wang et al., improving the yield and separation methods for the patchy particles is of practical importance. They also suggest that colloids with different characteristics including size, color, chemical functionality, and electrical conductivity could be further linked to the patchy building blocks, as long as they can still be functionalized with DNA.[1] These patchy particles can be disassembled by heat, but future patchy particles could act as storage devices with electromagnetically controlled (dis)assembly, using light or an electric current. Wang et al. envision that assembled structures analogous to tetrahedrally coordinated diamond crystals with a full 3D photonic band gap could be formed by using patchy particles ($n=4$) with self-complementary DNA (palindromic strands).[1] Similarly, crystals with programmed distributions of 3D defects could be of interest for photonics, catalysis, or electronics, and could be built using metallic particles rather than polystyrene. To date, the method for creating patchy particles used by Wang et al. requires synthesis by radical polymerization,[1] but it is expected that this will be expanded to other methods to incorporate diverse materials in the future.

To extend this research toward more advanced molecular models, particle affinities paralleling electronegativity could be engineered by varying the number of mismatched base-pairs in between complementary DNA strands. Other non-covalent and covalent interactions such as hydrophobic, electrostatic, hydrogen bonding, antigen–antibody, sugar–lectin, thiol/disulfide, and alkyne–azide coupling should be candidates for controlling the equilibration kinetics, improving complex particle yield, or for tuning specificity and functionality. For example, it would be of interest to incorporate stimuli-responsiveness into the directional bonds in between particles, using pH, temperature, light, or ionic strength as stimuli. Anisotropic materials have received considerable interest in drug delivery,[12] and these multivalent patchy particles and their assembled clusters might possess distinct characteristics in the biological domain, such as directional cellular uptake or reducing phagocytic association.

The concept of particles with valency, introduced by Wang et al.,[1] represents a significant step forward in the field of directed assemblies. This simple, yet novel method will allow the scientific community to create molecule analogues that are, in many ways, potentially as useful and diverse as molecules themselves.

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