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Design Principles for Self-Assembling Colloids

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The holy grail of self-assembly is the spontaneous formation of an ordered multi-component structure from a solution of its building blocks. Living systems have mastered complex self-assembly, while human efforts to design nanoparticles that self-assemble into complex structures are just beginning. There are two critical design issues: first we need to functionalize nanoparticles such that the target structure is thermodynamically more stable than its competitors under experimental conditions. Second, the target structure should be kinetically accessible under the same conditions [1, 4], so that the system is not trapped in unwanted, metastable structures. These principles put constraints on the properties of the nano-sized building blocks.

In a recent publication [2] Hormoz and Brenner propose design rules for the building blocks of complex, three-dimensional structures, using concepts that were developed in the context of the random energy model (REM) [3] for protein folding [4]. Here a single, functional protein conformation (the native state) forms with high yield from a conformationally disordered denatured state. For efficient folding the free energy of the native state needs to be lower than the denatured state, and the potential and free energy landscapes need to be ‘unfrustrated’, which means that kinetic traps are absent [1, 4]. Hormoz and Brenner have now applied these concepts to the design of nanoparticles that can self-assemble to form specific structures.

The approach proposed in ref. [2] specialises to systems containing a fixed number of building blocks that have only nearest-neighbor interactions. The question then becomes: how many distinct building blocks are required to make a specific geometrical cluster with high yield and, secondly, what strength of interaction maximizes the yield? Hormoz and Brenner show that the REM puts bounds on the number of distinct building blocks that should be used. They also provide a simple answer to the question of how the strength of attractive and repulsive interactions should be tuned: high-yield self-assembly is expected if all the attractive interactions have equal strength with the same condition for all the repulsive interactions. Testing this prediction numerically for an eight-particle cluster reveals that the yield is lower when the variance in the attractive and repulsive interactions is larger [2].

However, there are limits to what can be achieved with nearest-neighbor interactions that do not depend on orientation. It is no coincidence that the building blocks of jigsaw puzzles typically have a low symmetry. The importance of orientation-dependence for self-assembly has been discussed in a series of papers by Winfree and collaborators (see e.g. [5]). For isotropic nearest-neighbor interactions certain patterns simply cannot self-assemble reliably from solution. An example is the face-centered cubic crystal structure, which consists of close-packed planes stacked in the sequence ABCABC⋯. In contrast, hexagonal close packing corresponds to the sequence ABABAB⋯. Clearly we cannot reliably enforce the formation of ABC sequences using isotropic nearest-neighbor interactions alone. Tindemans and Mulder have addressed this limitation for isotropic interactions by going beyond nearest-neighbour terms [6]. They found that formation of a unique pattern *can* be enforced if the building blocks have a repulsive interaction between particles of the same species, not just for nearest-neighbor interactions but also for next-nearest neighbors and—for some patterns— next-next-nearest-neighbors. The resulting rules rules are not much more complicated than those of ref. [2], and symmetry arguments can be used to prove that they are sufficient to program *any* extended 2D pattern. As in ref. [2], Tindemans and Mulder assume that all attractive/repulsive interactions have equal strength—the work of Hormoz and Brenner explains why such a choice might be optimal.

Design of high symmetry clusters for colloidal building blocks may be harder than experience with atomic clusters would suggest. The partition function for a given isomer of a cluster composed of N identical particles at temperature T can be written as $2N!\, z(T)/o$, where o is the order of the point group and $z(T)$ accounts for the energy of the structure and its internal degrees of freedom. The symmetry factor $2N!/o$ enumerates all the distinct permutation-inversion isomers, which all have the same partition function, $z(T)$. The factor of o accounts for permutation-inversions that are equivalent to overall rotations of the molecule, and do not entail an energy barrier. It reduces the probability of observing structures with high symmetry, acting against the lower potential energy that is expected from the principle of maximum symmetry [9]. For atomic clusters bound by medium- or long-ranged forces the lower potential energy of high symmetry structures often dominates. However, for the short-ranged interparticle forces corresponding to colloidal clusters the potential energy basically corresponds to the number of nearest-neighbour interactions at the optimal pair separation [8]. The abundance of structures with the same number of nearest-neighbour contacts is therefore determined by the symmetry factors if the vibrational frequencies and rotational constants are the same.

Of course, the particles from which colloidal clusters are built are not exactly the same. However, if the symmetry breaking effects are small then we expect the predictions obtained from the idealised analysis to be maintained. To show this explicitly, consider the number of distinct ways of arranging N different particles on a framework with N sites defined by the possible particle positions. If the framework is chiral then the o symmetry operations in the point group all correspond to pure rotations. The $N!$ arrangements over sites can therefore be partitioned into sets of size o, whose members are related by overall rotations, and there are therefore $N!/o$ distinct possibilities. The same argument applies to the mirror image framework, and so the number of distinct structures including enantiomers is $2N!/o$. If the framework is achiral then the same symmetry factor results because there will be $o/2$ pure rotations in the symmetry group and the number of possibilities is $N!/(o/2) = 2N!/o$ again.

Enumerating the number of distinct permutation-inversion isomers of a structure with o point group operations containing N identical particles is therefore isomorphic to asking how many distinct structures there are for N distinguishable particles arranged over the same sites. If all these arrangements have approximately the same partition function, $z(T)$, then we have the same result as for identical particles, namely $2N!\, z(T)/o$.

There remains the question of the practical implementation of the various design rules that have been proposed. The nearest-neighbor rules of Hormoz and Brenner are undoubtedly the easiest to realise experimentally, but the number of possible target structures will be constrained. The more complicated rules of Winfree et al. can in principle be implemented in colloidal systems, but synthesis of particles that repel selectively at a distance of more than one particle diameter has yet to be achieved. Hence the design of complex self-assembling systems will continue to be an active research field for both theorists and experimentalists.

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