Using shape for self-assembly

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A 1980 poem by Alan Mackay outlines his aspiration ‘to see what all have seen but think what none have thought’: a daunting task, which he accomplished not once, but several times. A ‘truly myriadminded, manysided man—a veritable triacontahedron’ in the words of his colleagues and friends, Alan Mackay pursued a lifelong interest in the problems of morphogenesis and form, a comprehension of which necessitated him crisscrossing the borders of the inanimate and animate world of soft and hard materials, through the integration of concepts and methods of chemistry, physics, mathematics and biology. In other words, he realized in his time a genuinely interdisciplinary approach to complex problems that still to this day remains beyond much of the academic community. Being invited to contribute a paper on the theme ‘beyond crystals’, we naturally wondered how Alan Mackay would think about the world of nanoscale self-assembly where so much depends on shape and form.

Keywords: nanochemistry; self-assembly; nanocrystals; nanowires; shape

1. Introduction

A 1980 poem by Alan Mackay outlines his aspiration ‘to see what all have seen but think what none have thought’: a daunting task which he accomplished not once, but several times [1–4]. A ‘truly myriadminded, manysided man—a veritable triacontahedron’ in the words of his colleagues and friends, Alan Mackay pursued a lifelong interest in the problems of morphogenesis and form, the pursuit of which led him to crisscross the borders of the animate and inanimate worlds of soft and hard materials, integrating concepts and methods of chemistry, physics, mathematics and biology. In other words, he realized in his time a genuinely

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interdisciplinary approach to complex problems that still remains beyond much of the academic community. In the spirit of the theme ‘beyond crystals’, we naturally wondered how Alan Mackay would think about the world of nanoscale self-assembly where so much depends on shape and form [5].

This review discusses the role of shape as a mediator of self-assembly, especially at the micro- and nanoscale. Specifically, we attempt to define and collect under one ‘roof’ the general principles and concepts that define the shape-based design rules for the self-assembly of ‘small’ objects.

By self-assembly, we refer here broadly to the process by which multiple components spontaneously organize to form a larger entity [6]. Self-assembly remains important for two primary reasons.

— The potential of ‘bottom-up’ manufacturing to improve the economics and performance of certain technologies. It is conceivable that, even if ‘top-down’ manufacturing is never displaced from the production of high-tech devices, there will be an increasing demand for simpler devices (e.g. disposable sensors, batteries, solar cells and flexible displays) that are incompatible with the capabilities and/or the cost of top-down fabrication techniques. While it is still very interesting to apply self-assembly to improve the performance of current devices, it is our impression that greater opportunities lie in using self-assembly to expand the accessibility of certain technologies and capabilities to new, less affluent, markets.

— The creation of new functions and capabilities that will provide a basis for future technologies. Here, inspiration comes from living organisms—themselves a product of spontaneous organization. By virtue of their complexity (carefully engineered by evolution), living organisms are capable of chemical processes and functions (e.g. metabolism, respiration, thought, self-awareness, reproduction and self-correction) that we only dream of replicating in the laboratory. Guided by selective forces (natural or otherwise) or genetic engineering, these processes create new functions—for example, the metabolism of certain bacteria has been genetically engineered to produce petroleum [7]. Can we design from scratch spontaneous processes that yield systems capable of similarly complex functions? While we presently do not know the answer to this question, we do expect that self-assembly will play a role in its pursuit.

Owing to its generality and broad usage, the term ‘self-assembly’ (and all its ancillary concepts—e.g. interactions, building blocks, divalent versus polyvalent) can be challenging to define in a way that is both broad enough to be all-encompassing and yet specific enough to be useful. Consequently, different scientific communities define—and think of—self-assembly and its related concepts in slightly different ways. In more extreme cases, what for some is clearly self-assembly is merely aggregation to others.

In the service of clarity, we provide here definitions for the key terminology that is used in this review.

— Types of self-assembly. Different types of self-assembly are distinguished on the basis of the thermodynamic description of the resulting structure [8]. In equilibrium self-assembly, interacting building blocks organize within a
prescribed environment to form structures that minimize the free energy of the system. By contrast, non-equilibrium self-assembly leads not to equilibrium structures but rather to long-lived, kinetically trapped states, which depend on the history (e.g. processing) of the system. Finally, dynamic self-assembly describes the formation of dissipative structures that organize and persist only in the presence of thermodynamic gradients and flows, which prevent relaxation to equilibrium.

Interactions. We consider an interaction to be any force (often described by the gradient of a scalar potential) acting between two or more objects. In the case of pair-wise interactions (see below), the magnitude of this force depends on the distance between (and mutual orientation of) the interacting components. Depending on how the force decays with distance, the interaction is considered to have a long (e.g. coulombic potential) or short range (e.g. van der Waals) relative to the size of the objects. The interaction can be highly localized between two objects (e.g. H-bonds) or rather extended among any number of objects (e.g. via magnetic fields).

Assembling objects (components, building blocks). We define the building blocks as the largest participants in self-assembly which do not fragment or break during assembly (the internal connectivity does not need to be rigid—e.g. a polymer molecule can be a building block in spite of its flexibility). If the assembly happens in multiple stages (e.g. where each stage assembles a higher order of a hierarchical construct), the building block will be different in each stage.

Multiple interactions (e.g. many body, polyvalency). Describing multiple interactions is especially complicated. The building blocks will often have internal components (e.g. atoms in a polymer) which can interact independently from each other (e.g. charges on a polyelectrolyte). If a building block has several of these ‘foci’ of interaction (e.g. H-bond donor–acceptor groups, or ions), which are able to interact with one or more components of another building block, then we consider the interaction to be polyvalent. Even when the building blocks are simpler (i.e. with a single ‘focus’ of interaction, like a smooth and spherical particle of amorphous silica in water), they can still interact with their neighbours with multiple kinds of interactions simultaneously (e.g. in the case of a silica colloid in water, via capillary, electrostatic, van der Waals interactions).

In describing the multitude of relevant interactions, it is often convenient to decompose the total force/torque on an object into pair-wise contributions acting between all pairs of components within the system. Importantly, this decomposition is approximate and depends on the desired ‘level’ of description (e.g. Born–Oppenheimer approximation, classical molecular dynamics, coarse-grained molecular dynamics and Brownian dynamics). While these approximations work fairly well most of the time, they raise the following questions: (i) Is the decomposition accurate and/or appropriate (e.g. can many-body effects be neglected)? (ii) Assuming it is (or even if it is not), what are the consequences of many such interactions? (iii) How do these many pair-wise interactions give rise to the next level of the description?
The path towards understanding and applying self-assembly is only at its beginning. Five major milestones mark our progress towards the ambitious goal of self-assembling life-like structure and function (figure 1): (i) make the building blocks; (ii) understand and control their binary interactions; (iii) predict the consequence of many components interacting in a prescribed environment; (iv) identify the components and interactions that will organize to form a desired product (‘reverse self-assembly’); and (v) create new functions using self-assembly. Below, we discuss our interpretation of where we stand on achieving these five milestones.

— Making the building blocks. The chemistry of creating components for self-assembly has been, from many points of view, successfully developed. We can now synthesize molecules, clusters, nanocrystals, colloids and bulk crystals in a fairly large variety of compositions, shapes and sizes. These building blocks already allow the creation of simple self-assembled systems (typically binary [9], ternary [10] and/or periodic [11,12]).

From another perspective, much remains to be done: the nanoscale species that we can synthesize from scratch lack ‘complexity’ and ‘perfection’, especially when compared with the components of living systems.

Traditional synthetic strategies can effectively synthesize relatively small (tens of atoms) molecules, but do not seem equally well suited to the synthesis of macromolecules or crystals whose composition and chemical functionality are arranged heterogeneously and deterministically—e.g. we cannot yet generate mass quantities of high-molecular-weight polymers composed of a specific and a complex sequence of arbitrary monomers. While we can synthesize milligrams of relatively large sequences of amino or nucleic acids, these approaches do not routinely and easily lead to molecules of a size comparable to that of most proteins.

It is also increasingly recognized that the traditional synthetic strategies may not be ideally suited to the preparation of truly monodisperse (‘perfect’) species at the $10^3–10^4$ nm scale (it is unclear if this is a fundamental limitation of our general approach towards chemical synthesis or just ‘a question of time’). The molecular chemistry that has given us synthetic drugs and fairly complex natural products [13] is challenged to create monodisperse structures of arbitrary complexity and nanoscale dimensions in ways that are simple, cheap, sustainable and scalable. The colloid chemistry that has given us nanocrystals of myriad compositions with remarkably low (approx. 2–5%) polydispersity is hard pressed to create analogous species that are truly monodisperse. While soft interactions between components can indeed reduce the detrimental effects of size/shape polydispersity on their self-assembly (as further discussed below), the most complex self-assembled systems (i.e. living organisms) often rely on the perfection and purity of their component proteins to perform many of their essential functions. For example, one wrong amino acid can compromise the behaviour of an entire protein, which can (not always, of course) then cascade into systemic disease (e.g. sickle cell anaemia [14]). In artificial systems, our reliance on ‘imperfect’ building blocks may severely limit the potential complexity of future self-assembled
Figure 1. The milestones towards the self-assembly of complex functional systems: (a) to make truly monodisperse building blocks from molecular or atomic species; (b) to control and understand their basic binary interactions; (c) to understand and control the consequences of many interactions mediating the assembly of multiple objects; (d) to understand how to predict which building blocks, interactions and processing steps are required to obtain the desired structure; (e) to understand how to best make use of the unique traits of self-assembly as a fabrication platform. (Online version in colour.)
systems. There is therefore an interest in developing a chemistry of nanoscale ‘perfection’ (and of ‘self-correction’), which strives to create and characterize atomically defined building blocks at the nano- and microscale [15].

— *Understanding and controlling the interactions.* The task of understanding the forces acting between assembling components is progressing steadily. Our understanding of pair-wise interactions is particularly advanced: we can predict them and use them reliably to form simple self-assembled structures based on simple building blocks [16]. Our control over these interactions is limited more by our ability to create the right components (e.g. size, shape and surface chemistry) than by our understanding.

The main challenge in this area (as well as in many other areas of science) is to obtain a quantitative and predictive understanding of the consequences of these pair-wise interactions on the assembly of many components (or systems with many degrees of freedom). In particular, with respect to biochemical systems, is overcoming the limitations in predicting the free energy of interactions occurring in aqueous solution. Although computational methods that treat water as an explicit participant in interactions fare well in predicting the free energy of interaction, they are computationally intensive, and no accurate potential functions for predicting water and solvation thermodynamics exist.

Other many-body challenges, like multivalency, seem to offer new routes towards the self-assembly of nano- and microsized materials, and are beginning to be exploited for that purpose [17,18]. Understanding the energetic consequences of clustering recognition elements will be part of this thrust: at present we do not have firm control over the enthalpic and entropic contributions that determine the free energy of multivalent association [19]. It is also important to acknowledge the limitations of the approximations which decompose the dynamics of a system into pair-wise contributions—e.g. even ubiquitous van der Waals forces can exhibit non-trivial many-body effects [20] that influence quantitative (and potentially even qualitative) aspects of self-assembly.

— *Predicting the consequence of many components interacting in a prescribed environment.* This remains a significant challenge. The effort in this direction is mostly concentrated on brute force approaches (e.g. all-atom molecular dynamics simulations [21,22] or mix-and-observe experiments). The arguments in favour of these approaches are that advances in computing power will enable the simulation of increasingly complex systems, and that trial-and-error experimentation is simple: progress is simply ‘a question of time’. The arguments against such approaches are that—while they allow certain problems to be solved on increasingly large scales (e.g. protein folding [23], synthetic hierarchical systems [24])—a ‘complete’ description of the experimental reality will always remain out of reach. Furthermore, when large simulations of a single set of conditions push the limits of computation, they are unlikely to be useful in the design and optimization of conditions necessary to create a particular, desired structure (reverse self-assembly).

The question is thus one of complexity: can we develop a hierarchy of understanding and control, whereby details at one level (e.g. length scale)
can be meaningfully ‘compressed’ at a higher level by simplifications and approximations? Molecular dynamics simulations do not need quantum mechanics if their most relevant consequences are captured by the force field. Protein crystallization does not require the details of the peptide sequence if a protein can be adequately described (for this purpose) as a semiflexible blob with a certain inhomogeneous surface chemistry. But can they?

— **Identify components and interactions that will organize to form a desired product (reverse self-assembly).** Our ability to identify the components, interactions and environment that yield a specific self-assembling system is strongly limited by the complexity of the resulting structure. Successes towards this task are largely restricted to cases of equilibrium self-assembly, where the resulting structure is either composed of few components (two or three) or spatially periodic.

For example, if our objective is to create a close-packed face-centred cubic lattice, we choose (largely from previous experience) to use hard spheres and, depending on their size, we now know how to self-assemble them quite well [25,26]. A notable extension of these intuitive design rules is the development of inverse statistical-mechanical optimization techniques, which offer solutions to the reverse problem for certain equilibrium systems—e.g. the identification of an isotropic pair-wise potential (albeit complex) that guides the formation of a diamond lattice [27]. Another important exception is DNA origami, where a detailed knowledge of the (highly selective, in this case) interactions guiding self-assembly is applied rationally to create a wide variety of nanoscale structures [28–31].

— **Knowing how to use self-assembly.** This remains the ultimate challenge. While it is possible and tempting to replicate existing functions and devices, realizing the full potential of self-assembly will require us to capitalize on its unique capabilities to build arbitrary three-dimensional architectures. As far as we can see, this puzzle remains largely unaddressed, and we are still developing the necessary understanding and—more importantly—intuition to make the next inspired advances.

In sum, the task of understanding and applying self-assembly remains a daunting challenge, largely owing to the sheer amount of information that appears to be necessary to describe the various forms of organization in complex structures. Nonetheless, we believe that much can be gained by even qualitative generalizations, which help to simplify the problem, and, most importantly, build our intuition. Can we thus develop heuristic rules for the creation of self-assembling systems [5,6,8,32]?

The concept of shape presents a particularly attractive theme for the creation of such heuristics because (i) it is ubiquitous and (ii) it applies across all length scales. In the remaining discussion, we explore the general role of shape in self-assembly and its application at the nanoscale. The objective of this perspective is not to offer a comprehensive review of the global effort in the synthesis and use of shape for nanoscale self-assembly (several comprehensive reviews have appeared recently in the literature on this topic [16,33–37]). Our objective is rather to define, collect and discuss within a common context the general principles and concepts that drive the use of shape in the self-assembly process.
of nanoscale objects. The nanoscale is important in this context as it bridges the molecular scale with the macroscopic world: therefore, any self-assembly from molecular species will require an understanding of the self-assembly of nanoscale objects.

2. What is shape?

In the context of self-assembly and chemical systems, shape is a subtle concept. A conventional definition would define the shape of an object as the geometry of its surface. By this definition, shape is defined by the short-range repulsive interactions established by the atoms sitting at the surface. This definition is conventional and familiar because it is appropriate to the macroscopic scale of our sense of touch: to our hand, the shape of an object is the tangible one, the one that we can feel by touching its surface (i.e. the one that repels our fingers). This idea of shape is useful and works well for two reasons. (i) It typically gives results that are consistent with the morphological characterization of an object: a nanocube will look like a nanocube in transmission electron microscopy, atomic force microscopy and optical microscopy. (ii) It is directly defined by the position of the atoms, which is one of the key aspects of an object that is controlled by chemistry: when a chemist thinks of synthesizing a structure, he or she thinks about where the atoms need to be.

Nonetheless, when considering self-assembly, we are inevitably looking at the multitude of interactions between objects, not just at the short-range repulsion of the surface atoms. This is especially true at the nanoscale (and the molecular scale), where the importance of long-range interactions and surface chemistry are very important. For example, one can take a spherical colloid and coat half of it with one type of molecule, and the other half with another type. If I ‘touch’ this individual particle, I will ‘feel’ it to be a sphere. But if the two different molecules at the surface are able to form a bond with each other, these colloids will spontaneously assemble to form a necklace: hence, the symmetry (or ‘shape’) of their interaction is not spherical. The same is true for a ‘tangibly’ spherical colloid with a magnetic dipole moment: on its own it is a sphere, while with others of its kind it will form a chain.

If we consider these arguments, we can think of a more general definition of shape for the purpose of understanding its effect on self-assembly. It defines the shape of an object as the ensemble of the geometries of all interactions elicited by that object (figure 2). By this definition, an object could have multiple shapes, depending on the particular interaction of interest. An interesting challenge of self-assembly is thus to understand how these different shapes of the same object contribute to its assembly.

3. Synthesizing shape in nanostructures

Since its beginnings, the synthesis of shape has been an important part of nanochemistry. As mentioned above, any shape derives from the breaking of a spherical symmetry. We thus categorize the strategies for the synthesis of shape at the nanoscale in terms of the tools used to break the symmetry (figure 3).
Figure 2. The different shapes of nanoscale building blocks. (a) When considering ensemble interactions, even a simple spherical colloid can have various shapes, depending on the interactions that are dominant during assembly and the properties of the surface and bulk of the building block. (b) An isotropic repulsive potential coupled with confinement will lead to the maximization of the filling fraction and the formation of a face-centred cubic lattice of spherical colloids [26]. (c) How a magnetic dipole within a spherical colloid will confer on it an anisotropic interaction with its neighbours [38]. (d) How surface chemistry can be used to pattern the short-range attractive interactions between colloids, thus breaking the spherical symmetry of the tangible shape [39]. (Online version in colour.)

— **Crystal lattice.** The use of the reduced symmetry of the crystal lattice (compared to that of a sphere) to generate shape is widely adopted (figure 3a). Any nanoscale building block composed of a crystalline material will have a specific symmetry associated with its atomic lattice.
This reduced symmetry (and its defects) can be used in three ways: (i) to control the habit of the crystal, (ii) to control its surface chemistry, or (iii) to generate an anisotropy in its physical properties (e.g. dielectric constant, magnetic permeability and index of refraction). Bi$_2$S$_3$, for
example, is a covalent semiconductor characterized by a highly anisotropic atomic structure composed of stacked covalent ribbons lying along the [001] direction of the lattice. In almost any growth condition, the (001) planes will grow faster than the other planes leading to the formation of rods elongated along the [001] direction [40,41]. This difference in the growth rate of different facets of the same crystal is a consequence of the different surface energies associated with them. Higher energy surfaces will be more prone to adsorb and bind organic or inorganic ligands. Upon binding, these ligands will substantially decrease the surface energy of the facet to which they are bound, thus changing the rate of growth of different facets of the same crystal. This principle has been used to grow nanorods of CdSe and then many other crystals [42,43]. Lattice polymorphs and defects have also been used to generate shape in crystals [44–46]. While this approach is increasingly understood, its versatility is strongly limited by the available lattice symmetries of the crystals involved.

— **Templates.** A brute force approach to create nearly arbitrary shapes uses templates (figure 3b). A template is a sacrificial mould in which the nanomaterial is grown or deposited. Two-dimensional templates can now be produced with essentially arbitrary shapes [47,48], while arbitrary three-dimensional templates are harder (yet not impossible) to fabricate, especially in large quantities [20,49–51]. Examples of templates used to synthesize nanostructures include micelles [52–57], membranes [58–64], colloidal crystals [65–69], zeolites [70–72], block copolymers [73–79] and directly written templates [80,81].

— **Instabilities.** This approach aims to create a highly symmetric yet metastable structure (e.g. a spherical colloid coated with a metal). Upon the application of a stimulus, the structure ‘relaxes’ towards one of its ground states by breaking its own symmetry (figure 3c). A classic example is colloidal dimers formed by dewetting of a two component system. A spherical colloid is coated with a wetting substance. Upon application of the appropriate stimulus (e.g. heat), the shell dewets, leading to the formation of a lower symmetry shape (i.e. the dimer). This general principle was used, for example, by the Whitesides group to form gold/silica dimers [82]. The Xia group used instabilities in a spherical colloid to form colloidal bowls [83]. The synthesis and folding of proteins are another classic example of instability used to create shape: every protein is synthesized in a stretched metastable conformation which will spontaneously fold into its equilibrium state which has a functional shape [84–87].

— **Protection–deprotection.** Protection–deprotection strategies are used—especially in organic chemistry—when a reagent must be directed to react with a specific functional group, in the presence of other competing moieties on the same molecule. By ‘protecting’ one or more functional groups on the molecule (e.g. reacting them with a labile ligand), one effectively prohibits those groups from reacting. After the reaction has proceeded on the desired functional group, the protected groups are ‘deprotected’, and the reaction is carried to the next step (figure 3d).

This approach has been adapted to nanochemistry with the purpose of controlling the shape of a nanostructure. An example is the use of ligands
which selectively bind to certain facets of a crystal in order to prevent their growth [44]. On a different scale, protection and deprotection schemes are essential to photolithography [88].

— Surface chemistry. Surface chemistry can be used to manipulate the shape of short-range interactions (figure 3e). For example, Stellacci’s group showed how striped patterns formed by mixed self-assembled monolayers on the curved surface of gold nanoparticles could be used to generate divalent nanocrystals that would associate to form chains [39]. In that case, the surface chemistry conferred a different shape on the short-range interactions of these colloids. A somewhat similar example was reported by Cho et al. who postulated and showed evidence that compositional fluctuations (enrichment of cations or anions) at the [111] facets of PbSe nanocrystals could lead to the formation of temporary electrical dipoles, which, in turn, would lead to the formation of very complex (yet single crystalline) shapes by oriented attachment [89].

Despite the progress of these approaches, there remain four main challenges to the synthesis of shape: (i) the creation of arbitrary and three-dimensional shapes (so far only DNA self-assembly has achieved this goal); (ii) the synthesis of nanostructures as pure and perfectly monodisperse compounds; (iii) the scale-up of these strategies to industrial scale; and (iv) the achievement of more universal strategies for the synthesis of arbitrary shapes in arbitrary materials.

4. The role of shape in self-assembly

The shape of assembling objects influences (i) the geometry of their close-packing, (ii) the directionality of the interactions, (iii) the selectivity of the interactions, (iv) the connectivity between objects in their assembly, (v) the attraction between them, and (vi) the dynamic aspects of their assembly, especially when the interaction is mediated by a fluid. In what follows, we discuss these effects individually and highlight examples of their use in self-assembly at the nanoscale.

(a) Shape controls packing

The most obvious consequence of shape on self-assembly is purely steric (figure 4a). Even when objects interact only through ‘hard’ repulsive potentials (i.e. of a range much shorter than the characteristic length of the objects), they can assemble to form organized structures that fill space most ‘efficiently’. From a thermodynamic perspective, the resulting organization serves to minimize the relevant free energy of the system, which—for ‘hard’ systems—is dominated by entropic contributions. This leads to the somewhat surprising observation that ordered, close-packed structures are often more probable (i.e. they have higher entropy) than similar amorphous structures [90], in which ‘jamming’ limits the mobility of the assembling components. Importantly, entropic ordering of ‘hard’ components occurs only at high concentrations (e.g. owing to a reduction in volume or additional attractive forces) and typically results in the formation of periodic structures (there are interesting exceptions that lead to aperiodic structures [1,12,91]), in which the local (i.e. ‘point’) symmetry of the building blocks determines that of the larger assembly (i.e. the space group) [92].

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Figure 4. The roles of shape in self-assembly: (a) packing is controlled by shape since the symmetry of the resulting close-packed assembly will depend on the point symmetry of the building block; (b) shape can confer directionality on an otherwise isotropic interaction; (c) shape complementarity can be used to give selectivity to short-range interactions; (d) attractive depletion interactions arise in mixtures of large and small components; (e) shape can be used to generate interlocked structures; and (f) the shape of an object in motion can affect its dynamic interactions with its neighbours. (Online version in colour.)

For example, spherical particles (e.g. silica colloids [93–95]) typically organize to form either cubic or hexagonally close-packed arrangements [96,97] while nanoscale cubes assemble onto a simple cubic lattice that shares their cubic symmetry [98,99] (figure 4a).

The use of ‘hard’ repulsive interactions in the assembly of nanoscale components is often accompanied by strong, short-ranged attractive forces (e.g. van der Waals and solvation forces) that cause jamming or gelation and can inhibit self-assembly. Fortunately, ‘soft’ repulsive interactions that act over larger distances (e.g. electrostatic) can also be used to (i) induce organization upon confinement—driven primarily by enthalpic (not entropic) forces—and to (ii) make assembly less susceptible to the detrimental effects of component polydispersity. For example, in a widely studied example [96], like-charged colloids—hundreds of nanometres in diameter and interacting among one another through long-ranged electrostatic forces—are concentrated within a drying meniscus by evaporation and capillary forces [100]. Upon confinement, the colloids organize themselves so as to reduce the unfavourable electrostatic energy by maximizing the distances between neighbouring particles; in doing so, they form a typically periodic but non-close-packed array (i.e. a colloidal crystal), which is ultimately frozen into place when the liquid evaporates. This basic principle is gradually approaching large-scale industrial application, especially in relatively defect tolerant applications such as solar cells, random lasers and displays.
For nanostructures, the length scale of the relevant repulsive potential is often comparable to the dimensions of the assembling components. For example, the Debye length characterizing the range of electrostatic interactions is typically approximately 1–10 nm (in water); the range of steric interactions owing to surface functionalization with long organic molecules is also a few nanometres (roughly the length of the stabilizing molecules). Therefore, nanoscale colloids exhibit characteristics of both ‘hard’ and ‘soft’ particles. For example, nanocrystals stabilized by organic ligands—although non-spherical at the atomic level—may organize like ideal spheres. As the symmetry of the particle is reduced, the resulting structure remains the same, but the typical size of the ordered domains decreases [45]. Upon further reduction of the particles’ symmetry, there are two possibilities: (i) if the shape of the particles is compatible with periodic packing (e.g. rods), the assembly will adopt a new structure, whose symmetry is distinct from that of close-packed spheres [101] and (ii) if the shape of the particles is instead incompatible with periodic packing (e.g. decahedra [102]), order will disappear completely or almost completely.

In the simplest case, the essence of a particle’s shape is captured by a single parameter—its aspect ratio, which quantifies the deviation from spherical symmetry. The literature provides beautiful examples of the effect of aspect ratio on the packing structure: low-aspect-ratio dimers will pack very similarly to spheres [103], while high-aspect-ratio nanorods will show liquid-crystal-like (i.e. smectic or nematic) structures [101,104] and high-aspect-ratio platelets will stack in columns [105].

(4) Shape controls directionality

While shape alone, in the form of repulsive forces, provides an important mechanism for self-assembly, the possibilities grow enormously with the addition of attractive forces (figure 4b). In this context, shape provides a useful route to control the directionality of interactions mediating self-assembly—not only of bulk structures but also well-defined colloidal assemblies. For example, consider a collection of spherical particles interacting through a spherically symmetric, attractive potential (figure 4b); the resulting assembly is simply a close-packed, crystalline arrangement. Altering the shape of the components through the addition of a bulky spherical ‘group’ (by analogy to organic chemistry) gives directionality to the attractive potential through the steric repulsion between interacting particles. Depending on their shape, the particles assemble to form well-defined, ‘molecular-like’ clusters [106] or even one-dimensional fibres in direct analogy to the micellar structures of molecular amphiphiles (which indeed are also controlled by shape [107]).

In the above example, directional attractive forces were created by a process of elimination—that is, certain arrangements were prohibited owing to steric considerations. Shape also has a more direct influence on the magnitude and direction of attractive forces (e.g. van der Waals, electrostatic, magnetic, etc.). This is clearly illustrated in the case of short-ranged interactions, for which the interaction potential between two curved surfaces can be approximated using that between planar surfaces (by the so-called Derjaguin approximation [108,109]). From such analyses, one finds that the magnitude of the interaction depends on the relative position/orientation of the assembling components and is maximal when they ‘fit’ together with complementary shape (figure 4b).
Particle shape also influences the directionality of long-ranged forces such as electrostatic and magnetic interactions. For example, the curvature of a surface determines the distribution of surface charge (owing to ion adsorption or dissociation) and thereby the strength of electrostatic forces between two such surfaces [16,110]. Additionally, non-spherical particle shapes result in anisotropic electric and magnetic polarizabilities, which can be exploited to engineer directional interaction potentials (e.g. between nanorods and nanoparticles [111]).

(c) Shape controls selectivity

Closely related to the directionality of component interactions is the concept of selectivity (figure 4c). Selective interactions are those for which the free energy of two (or more) components in a specified configuration greatly exceeds that of the other possibilities (e.g. other binding partners and other configurations). At equilibrium, the probability of any such configuration is proportional to the Boltzmann factor, $e^{-E/k_B T}$; consequently, even moderate differences in interaction energies result in high selectivities for lower energy configurations. As demonstrated in the example above (figure 4b,c), shape complementarity—combined with short-ranged attractions—can provide an effective route towards the design of highly selective interparticle interactions.

While this idealized perspective—based on rigid, smooth surfaces and pairwise interactions—has proved useful in the assembly of micrometre scale colloids (e.g. ‘lock and key’ colloids [112]), the application of ‘lock and key’ principles to molecular—and by extension nanoscale—systems is often more nuanced. At the molecular level, surfaces are rarely ‘rigid’ but can reorganize dynamically upon changes in their surroundings. Furthermore, interactions are almost never pairwise but rather involve many components—namely, solvent molecules—that contribute in complex and often counterintuitive ways. Consequently, a purely enthalpic view of shape recognition based on the quality of the geometric ‘fit’ will fail to account for entropic contributions owing to molecular rearrangement and solvent effects—which can be comparable to or greater than enthalpic driving forces.

Despite the complexities of molecular recognition, there exists an increasingly diverse catalogue of molecular pairs—both natural and artificial—that interact reliably and predictably to form binary assemblies—e.g. host–guest, protein–ligand and nucleic acid complexes [113]. Importantly, these binary complexes can be combined to form larger multivalent constructs, which can be rationally designed to interact selectively with complementary molecules. This strategy is most clearly illustrated by DNA hybridization; however, it has also been used to prepare complex, binary assemblies of multivalent hosts and multivalent guests. In this case, the host–guest interaction acts as a selective ‘glue’ capable of binding nano- and microscale materials—even in water and even when the components are flexible [17,18].

As our ability to control the surface chemistry of nanoscale objects improves, we are increasingly able to pattern the chemistry of the surface of a nanostructure at the scale of a few angstroms. Therefore, multivalency and molecular recognition will become increasingly important in achieving control and complexity in self-assembly at the nanoscale and beyond.

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In addition to guiding the directionality and selectivity of attractive forces, shape—in the form of repulsive interactions—can also serve to bring components together even without such attractive forces. Long applied in colloid science, the so-called depletion effect \cite{114,115} relies on the use of smaller components (depletion agents) to induce the aggregation of larger components (figure 4d). The mechanism underlying this effect is primarily entropic in origin—that is, the ordering of larger components maximizes the total entropy of the system. While somewhat counterintuitive, the decrease in the number of configurations available to the larger particles is accompanied by an even larger increase in the number of configurations available to the smaller particles. Loosely speaking, ordering of the larger components allows for increasing disorder among the smaller components—and ultimately the entire system.

Because these depletion forces depend only on the repulsive interactions between components, they can be engineered by controlling the shape of both the components to be assembled and the depletion agents. For example, Sacanna et al. \cite{112} have demonstrated the selective interaction between shape complementary colloids using polymeric depletion agents. Alternatively, one can employ non-spherical, anisotropic depletion agents, which significantly increase both the range and the magnitude of the attractive depletion forces \cite{114,116,117}. The combination of these effects—that is, non-spherical components and anisotropic depletion agents—should allow for a variety of shape-based effects to be explored and applied in the context of self-assembly.

Beyond mediating reversible interparticle interactions, shape can also bond objects together more permanently through mechanical interlocks or entanglements (figure 4e). Such ‘mechanical’ bonds have been demonstrated at the molecular scale (e.g. catenanes and rotaxanes \cite{118}) and at the microscale \cite{119} and offer several appealing characteristics. First and foremost, mechanical bonds are robust—the covalent, metallic and/or ionic bonds comprising nanoscale solids are often much stronger than intermolecular and surface forces (by analogy to woodworking, a dovetail joint is typically much stronger than glue alone). Despite their strength, mechanical interlocks can conserve much of the structure’s degrees of freedom (figure 4e)—by contrast, two or more chemical bonds between two nanostructures typically eliminate the rotational and/or translational degrees of freedom about the joint. Finally, owing to the rigidity of the interlocked components, mechanical bonds can potentially be used to transmit mechanical motion (as exemplified by gears) \cite{92}.

The application of these principles to the nanoscale has so far been very limited. Nonetheless, evidence for entanglement of nanoscale colloids has been observed \cite{120,121}.

In the systems described above, the resulting assemblies are ‘static’ structures (equilibrium or kinetically arrested states) that make no use of thermodynamic
gradients or flows to sustain their organization. Additional types of shape-dependent interactions arise (figure 4f) when a system is driven away from equilibrium [8] by an external energy supply (e.g. time-varying electric and magnetic fields and fluid velocity gradients). Among the most relevant to nanoscale assemblies are hydrodynamic interactions, which arise through the relative movement (rotational and translational) of components assembling within a fluid [122,123]. Unlike the interactions described above, such dynamic interactions depend not only on the relative positions and orientations of the objects but also on their velocities (and often their past trajectories [124,125]).

Although hydrodynamic interactions play no role in determining equilibrium structures, they can enable the formation of dynamic (dissipative) structures or potentially select among possible non-equilibrium states. For example, millimetre-sized components rotating under the influence of a magnetic field have been shown to organize under the influence of repulsive hydrodynamic interactions and magnetic confinement [126,127]. Interestingly, such interactions between rotating objects are highly sensitive to the objects’ shape—particularly, their chirality. In a similar system, chiral ‘spinners’ were found to attract neighbours of like chirality and repel those of opposite chirality—resulting in dynamic chiral assemblies of two types. Remarkably, similar effects have been reported for assemblies of chiral molecules, whose organization can depend on the orientation of the local fluid vorticity (i.e. clockwise flows versus counterclockwise flows) [128,129].

In the context of nanoscale colloids, the study of hydrodynamic interactions has typically focused on the rheological properties of macroscopic ‘complex fluids’, which in turn derive from the dynamic organization of colloidal components and their interactions [130]. The use of such dynamic interactions for the controlled assembly of nanoscale components far from equilibrium remains an outstanding challenge.

5. Conclusions

Shape will inevitably be a fundamental ingredient to our understanding and use of self-assembly. It affects the interaction between objects in ways that are often independent of scale (e.g. geometric packing and interlocking). As such, shape should be considered uniquely important for any inherently multi-scale process such as self-assembly.

The nanoscale represents a formidable playing ground to test a number of hypotheses on the effect of shape on self-assembly. Interactions at the nanoscale are affected by forces at the molecular (e.g. van der Waals interactions) as well as the near-macroscopic (e.g. capillary interactions) levels. Therefore, the molecular scale forces that control molecular self-assembly make way through the nanoscale to the macroscopic forces that control micrometre and millimetre scale self-assembly.

The challenges that, in our opinion, are most important in developing an understanding of nanoscale self-assembly are: (i) developing robust syntheses of ‘perfect’ or near-‘perfect’ building blocks (atomically defined constructs will be necessary to obtain complex chemical systems); (ii) understanding how to preserve the influence of shape in self-assembly when using long-range interactions.
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to mask the polydispersity of the assembling components; (iii) developing quantitative simulation platforms that span multiple length scales while remaining computationally feasible; (iv) creating efficient one-pot parallel serial assembly (the spontaneous assembly of large numbers of constructs by a predetermined sequence of steps occurring within the same environment); (v) controlling the self-assembly of non-symmetric, non-periodic constructs with function; (vi) understanding how to make use of the many shapes that the same object can have, when looked at via different interactions; and (vii) understanding and controlling defects in self-assembly, while defining error-correction and error-tolerant strategies to enable self-assembly as a fabrication platform for high-technology devices.

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