PATCHY COLLOIDS

Entropy stabilizes open crystals

Open crystalline configurations self-assembled from colloids with sticky patches have recently been shown to be unexpectedly stable. A theory that accounts for the entropy of the colloids' thermal fluctuations now explains why.

Michael E. Cates

Spurred by recent advances in microparticle synthesis, colloidal particles with 'sticky patches' on their surface have of late become a focus of interest. This is in great part because colloids with anisotropic, patchy interactions should allow better control of colloidal self-assembly so as to achieve specific target structures with tailored photonic, catalytic or mechanical properties[1]. Many such desired functional structures consist of 'open' crystalline configurations, whose maximum density is less than that at close packing. Only recently, patchy particles that self-assemble into stable open crystalline arrangements have been observed in the laboratory[2] and with simulation models[3]. However, the origin of the stability of such open lattices has not been explained. Now, Xiaoming Mao and colleagues report in *Nature Materials* that open crystals of patchy particles are stabilized by thermal fluctuations[4]. Specifically, the researchers show that the formation of such open arrangements increases the rotational and vibrational entropy of the patchy particles[4]. This result is surprising if one considers that for hard particles without sticky patches entropy favours the formation of close-packed lattices. The ability to understand and exploit these opposing entropic effects could thus prove to be an important addition to the growing toolbox for controlling colloidal self-assembly.

Entropy can be a subtle and elusive concept. Although in some sense it is the quantification of disorder, it has long been known that for hard spheres at high density an ordered crystal has higher entropy than a disordered fluid. This is attributed to the extra 'rattle room' that particles have when placed near — but not precisely at — fixed lattice sites. Put differently, the entropy loss caused by collective ordering of the mean atomic positions is more than compensated by the fact that each particle has more space to explore. For colloidal spheres, entropy also favours lattices capable of compression to the highest maximum density (which are the hexagonal close-packed or face-centred cubic lattices in three dimensions, and the hexagonal lattice in two dimensions). Although pure hard-sphere interactions are not realizable in atomic systems, the hard-sphere limit can be addressed in computer simulations, and approached in experiments on colloids. These two methods have long ago confirmed the existence of entropically stabilized, hard-sphere colloidal crystals[5,6] (which are synthetic analogues of natural opals).

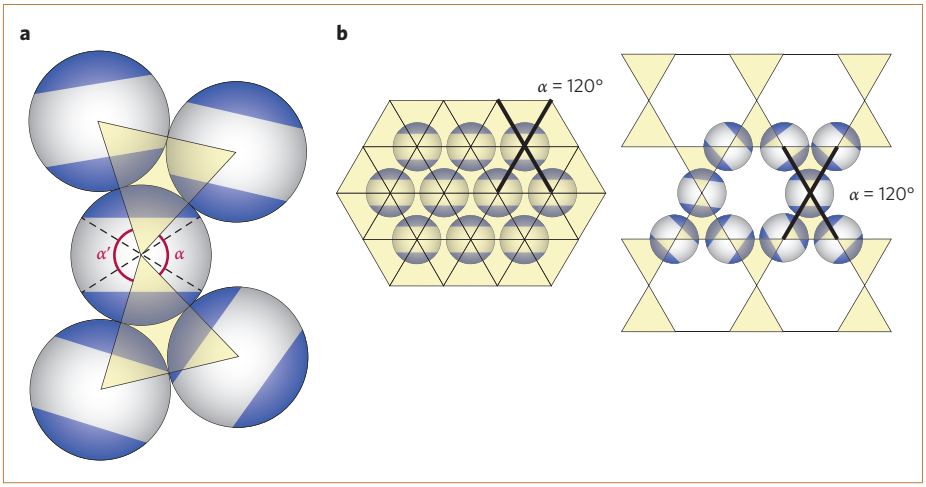

Figure 1 | The rotational 'rattle-room' of patchy colloids. **a**, Bonded contacts between triblock Janus spheres are maintained as long as the edges of the overlaid triangles cross the attractive blue patches. For a fixed particle configuration, the angular excursions that a particle can make without breaking any of its four contacts are independent of the corresponding excursions of neighbouring particles. In two dimensions such a rotational entropy can therefore be calculated one particle at a time, and depends only on the bond angles α and α'. **b**, The hexagonal (left) and kagome (right) lattices have the same number of bonded contacts and thus the same energy per particle. However, for moderate densities, particles in a kagome lattice have less room to rattle by translation, yet more entropy from rotational and vibrational motions, than particles in a hexagonal lattice at the same density. The latter effect dominates, which favours the formation of the kagome crystal over the hexagonal[4].

With patchy particles, however, this argument is partially reversed. A crucial new factor is the 'rotational rattle room', defined by the solid angle that each particle can rotate before any of its sticky patches lose contact with those of its neighbours (Fig. 1a). A lost contact would represent a 'broken bond', which is effectively forbidden by its relatively high energy penalty. Therefore, the rotational entropy of a patchy particle clearly depends on its environment, in contrast to what occurs for non-patchy hard spheres, which can always undergo complete rotation and for which entropy per particle is always a constant. At first sight, calculating the rotational entropy of patchy colloids looks like an intractable many-body problem of the sort that is only addressable by large-scale computer simulations. However, Mao and co-authors show that under well-motivated limiting assumptions the rotational-entropy contribution is calculable analytically. To see this, consider particles having two diametrically opposed sticky patches and held at fixed atomic positions. The existence of a bond between two particles in contact requires that the two involved patches cover the contact point, whose position is known. Each particle can therefore fluctuate independently within an angular domain set purely by the constraint that its patches cover all contact points with its bondable neighbours. This angular domain depends on the specified packing, but not on the orientation of neighbouring particles (Fig.1a).

Building on this simplification, Mao and co-authors construct an effective description of the interactions in a system of patchy particles with fluctuating lattice positions, and compare it with experimental data on the mode structure of lattice vibrations for triblock Janus spheres. Their calculations determine that in two dimensions the kagome lattice — a lattice with an open structure — is more stable than the close-packed hexagonal lattice. Both lattices have four bonds per particle and thus the same energy, but at close packing the latter has two additional non-bonded contacts (Fig. 1b). In a hexagonal crystal of the same density as the kagome lattice (whose maximum density is lower), patchy particles have more room to rattle translationally, but the combined entropy of rotation and vibration is reduced. For densities that are not too high, the latter effect dominates, and the kagome lattice is stabilized.

The work of Mao and colleagues has potential practical implications for the design and synthesis of self-assembled structures: a better understanding of the trade-off between different types of entropy contributions in colloidal systems should certainly lead to improved control in the design and realization of new functional materials, for example by providing guidance to experimentalists when exploring the parameter space for self-assembly. More generally, the work has also broader significance for statistical mechanics: the authors' findings add to a list of instances where the careful consideration of entropy effects has explained surprising experimental observations, such as the very existence of hard-sphere colloidal crystals[5,6], or the thermodynamic stability of small clusters of uniformly sticky spheres, whose relative abundances are similarly controlled (in large part) by rotational-entropy contributions[7]. We can certainly expect entropy to keep springing further surprises. ❐

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BIOENGINEERING AND REGENERATIVE MEDICINE

Keeping track

Assessing when cell death occurs following *in vivo* transplantation of stem cells is challenging. Now, pH-sensitive hydrogel capsules containing arginine-based liposomes are shown to act as magnetic resonance imaging contrast agents, allowing cell death to be monitored within the capsules.

Keren Ziv and Sanjiv S. Gambhir

The promise of regenerative medicine is to create living, functional tissues for the repair or replacement of damaged cells. This strategy, if eventually successful, could apply to many diseases and usher in a new era of therapeutics. To reach its full potential, however, researchers face several challenges including the prevention of transplanted-cell death and real-time assessment of cell fate. Poor transplanted-cell survival rate is primarily a consequence of inefficient delivery methods, lack of proper nourishment and integration into the tissue, and unwelcome immune responses. Methods aimed at improving cell survival are rapidly emerging, but assessment of cell fate after transplantation in a clinical setting remains a missing component.

Now, writing in *Nature Materials*, Chan *et al.*[1] report a nanosensor for the *in vivo* detection of transplanted-cell viability by exploiting the change in microenvironment pH that occurs during cell death. Chan *et al.* encapsulate cells (hepatocytes) in alginate-based hydrogel capsules, which are capable of generating a pH-sensitive magnetic resonance signal following cell death. An advantage of the nanosensor system is the potential to combine the functional signal of the transplanted cells with high-resolution anatomical images. Furthermore, the composite materials are all clinical grade, which should result in easier clinical translation.

In the preclinical arena there are several established ways to evaluate transplanted-cell fate[2]. These methods can be roughly divided into three groups. First, labelling a cell with reporter genes; second, labelling cells with a contrast agent prior to cell transplantation; third, using an imaging agent that is specific for a target naturally present on the transplanted cells. More specifically, the use of reporter genes — endogenous or foreign genes — relies on the monitoring of protein products. Reporter genes are usually used to detect the activity of a certain promoter, or — if expressed in a constitutive manner — to detect the viability of cells. Most reporter genes for preclinical *in vivo* use involve fluorescence or bioluminescence optical imaging and because of limited light penetration, clinical translation is problematic. Indeed, the only reporter gene applied in a clinical setting thus far, involves detection by positron emission tomography[3]. Also, the reporter genes method requires the introduction of genetic material, and hence introduces the hurdle of regulatory approval.

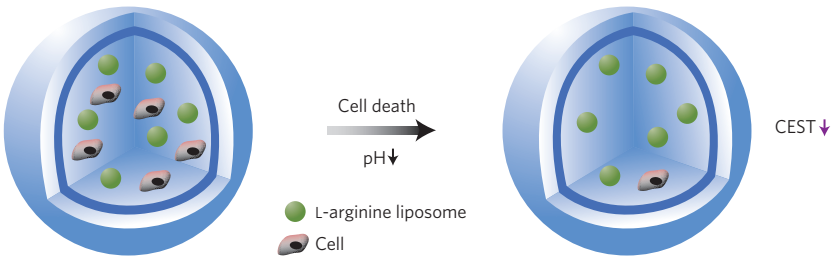

Figure 1 | A schematic of the structure of the LipoCEST microcapsules. Liposomes containing L-arginine are trapped in the alginate microcapsule together with hepatocytes. On cell death, the pH of the microenvironment decreases and subsequently the CEST contrast decreases.