MATERIALS SCIENCE

A fresh twist for self-assembly

Molecular helicity affects many of the bulk properties of materials. A study finds that helicity also controls the self-assembly of colloidal particles, opening the door to a new generation of functional materials. SEE LETTER P.348

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The next time you go to the supermarket, take a look at the pasta. You'll probably find everything from long, thin spaghetti to butterfly-shaped farfalle and twisted fusilli. On closer inspection, you'll see that the strands of spaghetti readily align and pack closely together, whereas the packing of the fusilli is considerably more complex. This complexity is due to the fusilli's chirality — its helical geometry. On page 348 of this issue, Gibaud *et al.*[1] report that such complexity of packing can be exploited to control the self-assembly of nanometre-scale particles, allowing the reversible formation of various architectures*.

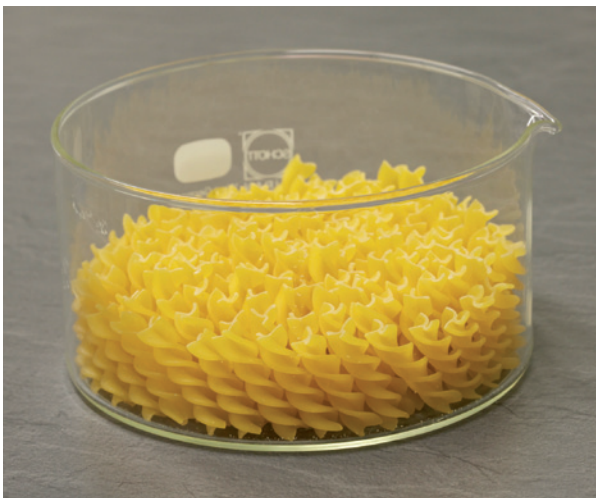

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Figure 1 | Pasta packing. When constrained in a circular container, fusilli pasta pieces mostly pack together so that their long axes are vertically aligned. But at the edges of the container, the pasta twists away from this alignment. This packing arrangement is a consequence of the pasta's helicity (chirality). Gibaud *et al.*[1] report that the chirality of colloidal particles affects the self-assembly of those particles.

To closely pack two individual pieces of fusilli, the pasta pieces have to twist with respect to each other so that their long axes are not parallel — this is an effect of their chirality. But when many fusilli are crammed together, this twist hinders the ability of the pasta to align in one direction, as required for efficient packing. The resulting competition between chirality and packing can have astonishing consequences for geometrically constrained chiral objects: if you stack fusilli upright in a beaker, the axes of the fusilli in the centre are perfectly vertical, whereas those at the edges of the beaker twist away from this alignment (Fig. 1).

This balance between geometric constraints and chiral interactions is at the heart of the unique properties of chiral liquid crystals. In 'blue' liquid-crystal phases, for instance, chiral molecules self-assemble into cylinders of twisted molecules that stack in a cubic lattice, giving rise to vividly coloured and reflective materials[2]. And in smectic liquid crystals, chiral interactions lead to a twisted, layered structure that is also manifested in the optical and mechanical properties of the materials[3].

Gibaud *et al.*[1] examined the balance between chirality and geometric constraints in the self-assembly of colloidal particles. Their model system was an ensemble of rod-like fd viruses, 7 nanometres in diameter and 880 nm in length, suspended in water. The chirality of these viruses depends on the ambient temperature: the rods are achiral at high temperatures, but chiral at low temperatures. The authors observed that, as for any other suspension of colloidal particles[4], the addition of an appropriate polymer that does not adsorb to the rods drove a phase separation of the mixture into a polymer-rich and a colloid-rich phase. At high temperatures, at which the rods are achiral, this led to the self-assembly of a circular colloidal membrane (a monolayer of vertically aligned rods[5]).

The authors observed that the rods at the centre of the membrane readily align parallel to each other, but at the perimeter of the membrane they twist gradually away from the vertical. This twist at the margin minimizes the interface between the polymer-rich and the rod-rich phases, and so reduces the interfacial tension that arises from the imbalance of forces between particles in this region. But twisting rods out of alignment with the other rods in the membrane has its own energetic cost, known as elastic energy. The formation of circular membranes with twisted margins is therefore the result of a trade-off between minimizing the phase interface and minimizing the elastic energy.

But what happens if the rods are chiral, so that twisted packing is preferred — just as it is for closely packed fusilli? Gibaud *et al.* addressed this question by performing experiments at lower temperatures, thereby 'switching on' the chirality of the viruses. They observed that increases in chirality — that is, increases in the contribution of chiral interactions to the energy balance of the system — reduce the elastic energy, thus lowering the energetic cost of creating a twist at the membrane's margin. This destabilizes the edges of the circular membrane and triggers the formation of ribbon-like structures that splay out from the circular membrane (see Fig. 3a of the paper[1]). The effect of increasing the chirality of the viruses in the colloidal membrane is therefore similar to that of adding surfactants to oil–water mixtures: it decreases the interfacial tension and so allows more interfaces to form.

The beauty of the authors' experimental set-up is that it allows all the parameters involved in the self-assembly of chiral colloids to be readily teased out and measured. Another advantage of the system is that the colloidal building blocks are much bigger than the molecules typically used in studies of chiral materials. This allowed Gibaud *et al.* to precisely quantify the colloidal self-assembly process at all scales, from the microscopic movements of individual viruses to the macroscopic properties of the resulting membrane. It also allowed them to exert well-defined local forces on the system, to affect the balance between twist and interfacial energy, and so to induce structural transitions — for example, by pulling on the membrane, they converted it into ribbon structures.

By including chiral interactions in their system, Gibaud *et al.* have added a new degree of freedom to the self-assembly of colloidal particles. Transferring their results to other

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materials opens the door to the hierarchical assembly of functional materials that could react sensitively to changes in ambient conditions or to mechanical stimuli. One way to extend the functionality of their system could be to make colloidal particles that are not only chiral, but also have surfaces patterned with microscopic domains that attract or repel each other. Such patterned colloidal particles have recently been shown to self-assemble into useful functional structures such as 'kagome' lattices[6].

Chiral interactions between particles occur in all kinds of materials, from liquid crystals[2,3] to cytoskeletal filaments in cells (for which the hierarchical assembly of bundle-like structures is dependent on, and sensitive to, the helical twist of the filaments[7,8]). Most of the chiral materials studied so far are passive or in thermal equilibrium. This means that their structural assembly is governed only by diffusion and by local interactions between the constituent particles. But most naturally occurring materials are far from passive. Instead, they constantly consume energy so that their particles self-organize into higher-order structures — the cytoskeletons of cells are prime examples of this[9,10].

The next step, therefore, is to apply the principles identified by Gibaud and colleagues[1] to active systems. Imagine replacing the viruses used in this study with self-propelling chiral bacteria — would they still pack together in a two-dimensional membrane, and, if so, would the membrane move, or rotate, across mesoscopic or macroscopic distances? Could actively beating ribbons form, or would the noise stemming from active movement of the bacteria prevent the formation of such structures? All we can say for certain is that chiral interactions will add a new twist not only to the self-assembly of colloids, but also to the self-organization of active materials. ■

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GENOMICS

The path to retinoblastoma

Genomic analyses of tumours of the childhood cancer retinoblastoma reveal a low mutation rate, challenging the view that genomic instability is crucial for its progression. The work also identifies a new therapeutic target. SEE ARTICLE P.329

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Retinoblastoma is a rare tumour that affects retinal cells in the eyes of children. Analyses of familial and sporadic cases of this cancer, backed by studies in genetically engineered mice, have shown that loss of function of the tumour-suppressor protein RB1 (also known as RB) is required for the development of most, if not all, tumours of this type. However, it is not clear how RB1-deficient retinal cells progress to malignant tumour cells[1]. In addition, emerging evidence that loss of RB1 function can induce genomic instability[2] has raised the tantalizing possibility that RB1-deficient retinal cells might be predisposed to accumulating many additional mutations, further complicating the identification of mutations that contribute to the development and maintenance of retinoblastoma. On page 329 of this issue, however, Zhang *et al.*[3] demonstrate that retinoblastoma genomes have very few recurrent mutations in genes other than *RB1*. Instead, the expression of cancer-related genes is affected by epigenetic modifications on chromosomes, which do not affect DNA sequence but are inherited after cell division.

To identify mutations that could cooperate with loss of RB1 function in tumour development, Zhang and colleagues[3] sequenced and compared the genomes of normal tissue and retinoblastoma tumours from four patients. The researchers found that *RB1* was the only known cancer-related gene consistently mutated, and that the retinoblastomas had 15-fold fewer total mutations than other types of solid tumour whose genomes have been sequenced[4].

Next, the authors searched for epigenetic alterations and for abnormal gene expression in retinoblastoma cells. They identified the gene that encodes the protein kinase enzyme SYK as a potential oncogene whose expression is consistently higher in retinoblastoma cells than in normal immature retinal cells. Moreover, the activity of SYK was essential for the growth of retinoblastoma cells. The authors also show that certain small molecules that selectively inhibit SYK activity induce the death of retinoblastoma cells in a mouse model of the disease.

These findings[3] indicate that SYK may be a promising target for treating patients with retinoblastoma. *SYK* was not identified in previous searches for genes with a role in this cancer because it is not mutated or structurally rearranged in retinoblastoma. Therefore, Zhang and colleagues' study emphasizes the importance of high-throughput approaches that integrate genome sequencing with gene-expression analysis and epigenomics to identify cancer genes.

Low mutation frequency has also been observed[5] in medulloblastoma (a type of brain tumour that affects children), suggesting that it could be a general feature of childhood cancers. A possible explanation for this difference between the cancers of children and adults is that childhood tumours arise in cells that are naturally undergoing rapid developmental growth, with fewer brakes on their proliferation than cells in adults. An alternative explanation is that, in children, these cells are negotiating crucial developmental checkpoints that are susceptible to corruption, leading to incomplete or abnormal maturation. In both cases, only a few mutations would be needed to trigger the cellular changes associated with cancer.

Furthermore, epigenetic changes in children and excessive mutations in adults may have similar roles in cancer development. Another childhood cancer, Wilms' tumour, also has a relatively stable genome and displays an increased variation in DNA-methylation patterns compared with normal cells[6]. RB1-deficient retinal cells may be particularly susceptible to this tumour-formation mechanism, because RB1 interacts with the machinery that controls the epigenetic status of cells, including enzymes that remodel chromatin (DNA–protein complexes) and other enzymes that add methyl groups to DNA[1]. Thus, childhood cancers such as retinoblastoma may carry epigenetic abnormalities that change gene expression and are stably propagated through subsequent cell divisions, helping to maintain tumour-associated features.

If this model is correct, it is possible that RB1-deficient tumours in adults — such as small-cell lung cancer and some breast,