interfere with inhibition of the desired protein–protein interaction. In other systems researchers have introduced cleavable bonds between the CPP sequence and the inhibitory peptide (see for example, ref. 8), which could provide one route to avoid this problem. There is also a fine line between CPP and AMP activity, so it is possible that bicycles containing CPP sequences may also possess (or could be developed to include) antibacterial activity[4].

The availability of general intracellular delivery methods based on CPPs should greatly expand the utility of biomolecular constructs, especially cyclic peptides in drug discovery and biomedical research. As the number of non-small-molecule biologics is increasing, this is certainly an important research area to pursue. The area faces great challenges, not only because of an increasing number of intracellular targets, but also because of the requirement to penetrate difficult barriers — including the challenge of passing through the blood/brain barrier. In view of the increasing number of people being diagnosed with neurological disorders it is imperative to study this area and approaches like the one described by Pei and co-workers provide significant first steps. ❐

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SELF-ASSEMBLY

Served on a nanoplate

Self-assembled cylinders can generally be extended only from their ends — growth that is considered to be 'one-dimensional'. Now, platelet-like structures with controlled size and composition have been constructed by growth in two dimensions of self-assembled structures, starting from crystallite seed micelles.

Chunhua Cai and Jiaping Lin

Polymeric nanostructures have potential applications in various fields, including nanomedicine, micro-devices, semiconductors and optics. The self-assembly of block copolymers — where covalently linked distinct polymer segments are dissolved in a selective solvent for one of the blocks — is a versatile technique for generating such nanostructures. The insoluble segments collapse into cores and the solvated polymer blocks form coronas that stabilize the structures in solution. By tuning the compositions of the polymer blocks and the assembly preparation conditions, a diverse range of nanostructures, including spheres, cylinders and more complex structures such as super-helices, can be precisely fabricated[1,2].

However, when compared with nanoscale spheres and cylinders, the preparation of well-defined platelet-like nanostructures remains a challenge. Nanoplatelets have a lamellar structure, but under lamella-forming conditions, it is energetically more favourable for most block copolymers to self-assemble into closed lamellae (vesicles) than flat lamellae (platelets). So far, there have only been a few examples of the self-assembly of block copolymers into platelet-like — or 'two-dimensional' — nanostructures[3,4].

Now, writing in *Nature Chemistry*, Ian Manners, Mitchell Winnik and co-workers report that the self-assembly of block copolymers into 2D nanostructures can be controlled in a manner akin to 'living' polymerizations[5]. Key to the process is the use of short cylindrical micelles as seeds. These seed micelles are assembled from a crystalline block of poly(ferrocenyldimethylsilane) (PFS), which forms the core of the seed micelles, and a block of amorphous poly(dimethylsiloxane) (PDMS) that forms the corona.

In previous studies, Manners, Winnik and co-workers have shown that through crystallization-driven self-assembly from similar seeds, PFS-based block copolymers can grow epitaxially. Such epitaxial growth leads to structures that include cylindrical micelles, scarf-like structures and branched star-like structures[6–8]. In all of these cases, the formation process is essentially the same and is based on a single growth direction of PFS-based block copolymers from various shapes of PFS-based seed crystals.

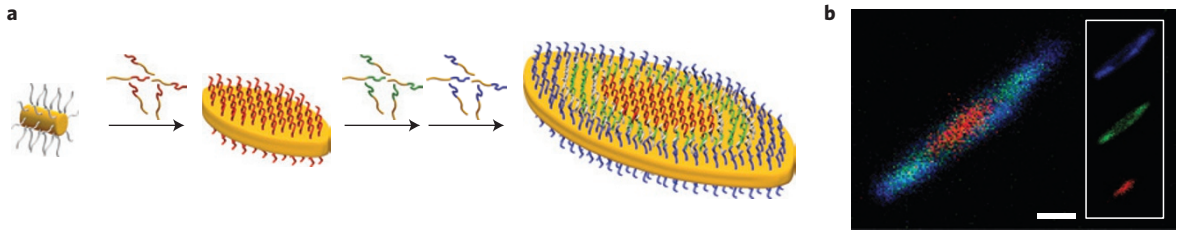

Figure 1 | Crystallization-driven growth of nanostructures in two dimensions[5]. **a**, Platelet nanostructures are formed by crystallization-driven self-assembly and growth in two dimensions of PFS-based block copolymers from a cylindrical crystallite seed. Subsequent addition of different dye-loaded copolymers leads to the formation of multicompartment nanostructures with concentric nanodomains. Yellow, PFS blocks; red, green and blue lines, PDMS blocks tagged with red, green and blue fluorescent dyes respectively. **b**, A laser scanning confocal microscopy image of a multicompartment platelet shows the different regions of red, green and blue-tagged copolymer that are incorporated into the self-assembly. Scale bar 500 nm.

However, as they describe in the present report[5], when PFS-b-PDMS block copolymers with a specific PFS:PDMS ratio were added to PFS-b-PDMS seed micelles, platelet-like structures were instead formed through the two-dimensional growth of the copolymers from the ends of the pre-formed seeds. The resulting platelets have a narrow area dispersity, and the area shows a linear dependence on the amount of added block copolymer, meaning that the size of the platelets can be predetermined and controlled in a manner analogous to living polymerizations.

The significant structural feature of the platelet-forming block copolymers is the symmetry between the core- and corona-forming block lengths (the core:corona block ratio is about 1:1). In comparison, for cylinder-forming block copolymers that grow one-dimensionally, the core:corona block ratio is usually between 1:6 and 1:20. For example, when PFS_{28}-b-$PDMS_{560}$ micelles are used as crystallite seeds, PFS_{50}-b-PI_{550} (with a core:corona block ratio of 1:11; PI, polyisoprene) grows epitaxially from the seed micelles to form long, 'one-dimensional' cylinders[7]. However, the addition of PFS_{114}-b-$PDMS_{81}$ (with a core:corona block ratio of 1.4:1) to the same seed micelle solution instead generates platelet-like nanostructures[5].

More impressively, the living nature of this 2D self-assembly and growth process provides a method for the preparation of multicompartment nanostructures in two dimensions. By sequential growth of several block copolymers from a seed micelle, concentric multilayered nanostructures can be formed with chemically distinct domains. This process is illustrated in Fig. 1a. Platelet-like nanostructures with up to five concentric nanodomains were formed by sequential addition of different PFS-based block copolymers to the solution of PFS-b-PDMS crystallite seed micelles. In order to monitor the growth processes of the 2D multicompartment nanostructures, block copolymers tagged with different fluorescent dyes (displaying red, green and blue fluorescence, respectively) in the corona blocks were sequentially added. Using laser scanning confocal microscopy, the multicompartment features of the formed nanostructures were clearly visible (Fig. 1b).

It should be noted that growth of the nanostructures from the addition of self-assembling block copolymers occurs at the 'living' ends of the cylindrical crystallite seed micelles, but not on the sides of the seeds, which are surrounded by corona-forming PDMS. Thus, when only a small amount of platelet-forming block copolymers is added, dumbbell-like structures are formed first, through growth from the two ends of the cylindrical seed micelles. As the amount of added block copolymer increases, continuous growth of the BCPs in two dimensions from the living edges slowly envelops the cylindrical seeds to form lenticular-shaped platelets. However, when the length of the cylindrical seed micelles is relatively long, this process is more difficult without large amounts of platelet-forming block copolymer and, as a result, structures that resemble double-headed spears can be produced. Because the length of the seed cylinders can be controlled, the distance between the two spearheads can be readily varied. Furthermore, by applying previously reported methods to block growth at one end of the seed micelle, non-centrosymmetric structures that resemble nanoscale arrows and spears can also be prepared.

Using the two-dimensional growth reported by Manners, Winnik and colleagues, we can envisage preparing complex hierarchical nanostructures either by sequential 2D crystallization-driven self-assembly of different crystalline block copolymers, or by using other forms of seed crystal. In addition, by introducing polymer blocks with specific functions — such as biocompatible or conducting polymers — these nanostructures may have great potential as biomaterials, and in photoelectrics and many other applications. ❐

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