

(polymersomes) are quite a lot thicker than those of liposomes, and so they are correspondingly more hard-wearing. But this brings new problems: having wrapped our molecules inside these tough parcels, how do we get them out again?

The solution found by Bellomo and colleagues takes advantage of compositional and conformational differences in the materials. The block copolymers they used are one step more complex than the usual simple synthetic polymers used in polymersomes. The use of synthetic polypeptides (polymers having the same building units as proteins) allows another level of structure. Rather than simply adopting the tangled, random-coil configuration familiar from simple polymers, these synthetic polypeptide blocks adopt a helical conformation of the type familiar to proteins. Specifically, they form a tight spiral stabilized by hydrogen bonds. The units from which the hydrophilic block is made are derivatives of the peptide lysine, decorated with a few water-soluble ethylene glycol units. This ensures that the rod formed by this half of the molecule has a good affinity to water. The other half of the molecule also forms rods but, being made from the much more hydrophobic peptide leucine, have much less affinity to water. The result is a supramolecular structure in which similar rods pack parallel to each other to form extended layers. In water, three layers form a sheet, with the layer of hydrophobic rods in the middle, shielded from the water by two layers of hydrophilic rods (see Fig. 1a).

In this system, the nature of the supramolecular organization of the molecules is closely coupled to their conformation. It is this close coupling that allows one to achieve the apparently contradictory goals of having a vesicle that is tough but highly responsive to environmental signals and able to release its contents. If some lysine is added into the region of hydrophobic

rods formed by leucine, the vesicle becomes responsive to pH changes. At high pH, the lysine is uncharged and it sits quietly in the helix. But at low pH, the lysine takes a positive charge. This is enough to disrupt the helical structure and change the conformation from a rigid rod to a flexible coil. As a result of this the whole structure of the vesicle falls apart (see Fig. 1b).

This achievement is made possible by advances in synthetic chemistry that allow the living polymerization of amino acids to produce synthetic polypeptides with a high degree of architectural control (though of course rather crude compared with what nature achieves with proteins)³. It is this combination of block-copolymer self-assembly with protein-like secondary structure that adds a new dimension to the now familiar story of self-assembly in block copolymers. In a like vein, block copolymers with an isocyanopeptide block have been produced⁴, which itself can form a helix⁵, and copolymers combining peptides with simpler polymers have been created^{6,7}.

The system developed by Bellomo and co-workers is entirely made of peptides. Two different peptide blocks, each with their own secondary structure, make it possible to exploit the interplay between secondary structure and supramolecular assembly to produce a dramatic effect in the overall structure of the material. This approach offers us a foretaste of many more fascinating functional materials that may be obtained by synthetic chemists, taking their inspiration from nature.

References

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MATERIAL WITNESS

A tangled history

Two recent essays on the life and work of Hermann Staudinger (*Angew. Chem. Int. Edn* 43, 1054 & 1064; 2004) remind us that any attempt to tell the history of science as a linear narrative is usually futile or dishonest.

By the time of Staudinger's pioneering work on polymers in the 1920s, the word 'polymer' was already almost a century old (Berzelius, the doyen of chemical nomenclature, got there first in 1833). 'Polymerization', meanwhile, was introduced by Berthelot in 1863: he even spoke about "polyethylene".

But neither of these terms had much to do with the polymers that were already commercially valuable by then: half-natural materials such as vulcanized rubber, rayon and celluloid (reportedly the cause of exploding billiard balls), and synthetics such as Bakelite and polystyrene. For Berzelius, polymers were substances with different molecular weights but the same chemical composition, such as acetylene and benzene.

The battle Staudinger fought to establish that true polymers are giant, covalently bonded molecules, rather than loose colloidal aggregates of small molecules, was even acknowledged in his Nobel citation of 1953. The opposition was there excused as "understandable"; and much as we might be tempted to romanticize Staudinger's tenacity, it is true that there were good reasons for caution at the time. The idea, for example, that crystallographic unit cells could not be smaller than the molecules comprising them may have been wrong but was not foolish.

More revealing, perhaps, is the unwillingness to believe that chemistry could be so messy as to permit a monstrosity like the macromolecule.

"Purify your products", Staudinger was told, "they will crystallize and turn out to be low molecular weight compounds." One suspects he was really being told to purify his ideas.

Equally telling is how Staudinger's struggle left his own theories literally inflexible to later refinements. Convinced that his macromolecules were rod-like, he was reluctant to accept the work of Paul Flory and others that invoked the entanglement of much floppier 'filaments'. "It is difficult to know what one should admire more", comments Helmut Ringsdorf in his essay, "the creativity of the scientist or the constancy of his adherence to his original idea."

Maybe we must conclude that all ideas can be proved right if you wait long enough. It has taken all the ingenuity of modern chemistry to make truly rigid macromolecular rods; meanwhile, the self-assembling, non-covalent polymers proposed in 1905 by Carl Dietrich Harries to explain the structure of rubber are now provided by supramolecular science.

And several of Staudinger's own Nobel musings sound astonishingly prescient. Who would question that "the wonder of Life in its chemical aspect is revealed in the astounding abundance and masterly macromolecular architecture of living matter"? And who can fail to feel the frisson of his remark, in the year of Crick and Watson's epochal discovery, that "this stability of the macromolecules ... supplies the living substance with the necessary basis for so specific a process as that of heredity"?



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