Why nanotechnology needs better polymer chemistry

The self-assembly properties of block copolymers are primitive when compared with natural examples such as protein folding but, as **Richard Jones** reports, promising new approaches and ideas are being explored.

Why can't we create functional nanoscale machines and devices that are anything like as effective as the molecular motors, ion channels, ribosomes and the like that constitute the machinery of the cell? One reason is the fact that, despite the stunning recent developments of molecular biology and single-molecule biophysics, we are still only beginning to understand in detail how this machinery works. Moreover, efforts to develop a biomimetic nanotechnology, much less a wholly man-made bottom-up synthetic biology, are severely limited at the moment by deficiencies in the materials we have to work with.

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In the nanotechnology developed by nature, this sophisticated machinery is built from proteins (with occasional help from nucleic acids, as in the ribosome). The reason for this is partly because the structure of protein molecules includes some very useful structural motifs, such as the alpha helix and the beta sheet. However, the most fundamental advantage of proteins is the mapping between the information held in the one-dimensional sequence of amino acids that make up the protein and the precise three-dimensional structure that is made possible by the phenomenon of protein folding. This is the supreme example of self-assembly, and is possible for two reasons: first, the huge number of possible sequences that can be produced by combining the twenty different amino acids, even in molecules of modest length; second, the selection, by evolution, of those sequences that have a well-defined, single, native state from a huge range of possibile conformations.

In nanoscience and technology, we are seeing more interest in using synthetic peptides (short polymer molecules made from amino acids) as the building blocks for self-assembled structures such as tapes, ribbons and tubes[1]. These applications are, however, based on the propensity of these materials to assemble into the classic motifs of protein secondary structure (that is, the alpha helix and beta sheet), rather than relying on a true folding transition. The solid-phase synthesis techniques used to make peptides cannot make molecules long enough with enough sequence accuracy to construct truly foldable proteins, even if we knew how to design sequences to produce a particular three-dimensional structure from scratch. Indeed, understanding the relationship between the sequence of amino acids and the final shape of the protein is one of the outstanding challenges in modern biology.

In the world of synthetic polymer chemistry, on the other hand, the archetypal self-assembling systems are based on block copolymers — polymers made of two or more blocks, each of well-defined length and of different chemical character. A range of different self-assembled nanostructures can be made by exploiting the length differences and chemical interactions between just two blocks in a diblock copolymer, and structures of increasing complexity can be made by using three or more different blocks. But when one compares the amount of information encoded in even the most complex block copolymer (containing just a handful of different blocks and chemical types) with that encoded in a protein with perhaps a hundred amino acids (each chosen from twenty different possibilities), one can see straight away why the uses of self-assembly in synthetic nanotechnology fall so short in sophistication when compared with biology.

The fields of block copolymers and peptide self-assembly come together in peptide block copolymers. In these materials — consisting of a number of chemically linked lengths of polypeptide chain, each made from a single amino acid — the richness of protein secondary structure is added to the self-assembling propensities of block copolymers. However, the precision with which structures can be formed from peptide block copolymers still falls well short of that achieved in proteins. Aside from those areas of bionanotechnology in which whole complex biological structures such as molecular motors and light-harvesting complexes are used directly, the apogee of self-assembly in nanotechnology is reached in the field of DNA nanotechnology, in which the specificity of the base-pair interaction allows the design of sequences that self-assemble into quite intricate nanostructures (Fig. 1).

For many years this seemed like an academic curiosity, propelled by the enthusiasm and vision of the field's pioneer, Nadrian Seeman of New York University, but two developments should make one hesitate before dismissing DNA nanotechnology so lightly. First, researchers have moved beyond using DNA to make structures and are now making much more sophisticated devices, such as molecular motors and devices for information processing and molecular

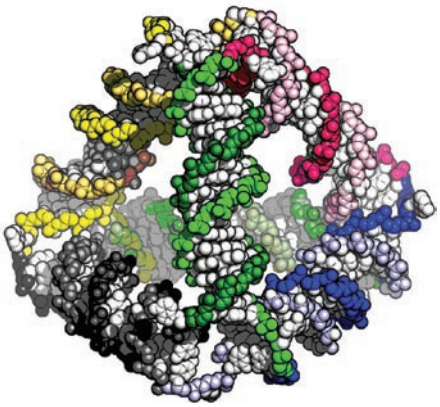

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Figure 1 DNA nanotechnology can be used to self-assemble quite complex nanostructures, such as this DNA tetrahedron[2]

logic[2]. Second, the cost of DNA synthesis has been falling steeply over the past few years, and there is every reason to suppose this will continue (see page 707 of this issue). It is my guess that some of the first synthetic complex systems of functional nanoscale machinery will be made from DNA, and that some of these may even turn out to be useful.

Yet for all its promise, DNA-based nanotechnology is going to have limitations. Even if the cost problem is overcome, the molecules are delicate, and the reliance on using rigid struts of double-stranded DNA as the main structural elements contrasts with the flexibility of protein-based construction. One interesting and as-yet little-explored possibility would be to use RNA rather than DNA[3]; RNA molecules combine the simplicity of the base-pair interaction with more flexibility, giving a wider range of more compact structures, some of which can have significant catalytic capability.

Is there any prospect of making fully synthetic systems that match the potential of nucleic acids or proteins for self-assembly? There would be considerable advantages if we could do this. Polymer chemistry has supplied us with some fascinating and useful examples of self-assembly, but there is a huge gulf to cross from diblock and triblock copolymers to sequenced copolymers synthesized with something approaching the complete control that a ribosome manages when making a protein. Polymer chemists have started to borrow some of the techniques that organic chemists have used to achieve precise molecular control in the synthesis of small molecules, but this is not easy[4]. What a wonderful challenge for synthetic polymer chemists — to close the complexity gap with nature.

References

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