MOLECULAR SELF-ASSEMBLY

Another brick in the wall

Nature builds sophisticated materials and machines one molecule at a time with minimal energy. Scientists are now emulating these assembly processes to make artificial structures that are not found in the natural world.

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Figure 1 Self-assembly is common in the natural word, for example, when many fish congregate to form a large school.

Self-assembly phenomena are ubiquitous in nature[1], and are important for both 'soft' organic materials and 'hard' inorganic ones. In the latter case, consider the lattice packing in, for example, crystals and minerals, and the role this plays in the growth of teeth and the remarkable diversity of composite seashells. Self-assembly is also responsible for the formation of oil droplets in water: individual hydrophobic molecules come together to form spherical structures so as to minimize contact with the surrounding water.

Fundamentally, the same process governs the formation of complex biological systems, such as the two-dimensional arrays of S-layer proteins that form well-defined nanostructures in bacterial cell membranes[2]. Many components are precisely arranged into ordered arrays to perform tasks that are essential to life. Molecular machines such as ribosomes and light-harvesting photosystems are made in this way. Moreover, the structural properties of collagen — the main component of cartilage, ligaments and tendons — are a consequence of its assembly into a triple helix. Self-assembly goes far beyond chemistry, it is an essential part of all chemical and life sciences (see Fig. 1).

Advances in the fields of nanotechnology and nanobiotechnology will be achieved with the help of materials that can be used to fabricate hierarchical structures and ever more sophisticated devices[3]. The self-assembly of peptides, which are sequences of amino acids chemically bonded in a molecular chain, has been studied extensively over the last decade. A number of self-assembling peptide systems have been discovered and developed for diverse uses. These include 'Lego-peptides', which form nanofibre scaffolds, lipid-like peptide surfactants that form vesicles and nanotubes, biologically active peptides that can be printed as a molecular ink on surfaces to organize cells, and peptides that behave as molecular switches[4,5]. The organization of individual peptide nanostructures into regular arrays is another step along the road to functional systems. On page 195 of this issue, Meital Reches and Ehud Gazit from Tel Aviv University in Israel describe a simple method to self-assemble small peptide building blocks into nanotubes, which, in turn, form well-ordered vertically aligned arrays[6].

Peptide self-assembly is of general interest because the aggregation of some proteins (which are very long polypeptide chains) results in the formation of structures known as amyloid fibrils, which have been implicated in Bovine Spongiform Encephalopathy (BSE, mad cow disease) and degenerative human diseases such as Alzheimer's disease, type II diabetes and Creuztfeld-Jacob's disease. In earlier studies, Reches and Gazit systematically reduced large peptides into smaller and smaller fragments in order to understand the factors that govern the self-assembly process. They found that even very small fragments, that is, dipeptide building blocks — which consist of two amino acids bonded together — were able to organize themselves into nanotubes[7].

Reches and Gazit now study a range of dipeptides based upon the amino acid phenylalanine, which has an aromatic ring in its side chain. They look at the effect of size and electrostatic charge on the assembly process. It is thought that the assembly of amyloid fibrils, and also of these smaller fragments, occurs because of attractive interactions between the aromatic rings of the molecules. This kind of interaction is well known in molecules with delocalized π-electron rings and results in the attraction and stacking of individual units into extended arrays. In this study, it was found that the charge on the building blocks plays a significant role in determining if ordered arrays of nanotubes are formed, or if nanotube structures are formed at all.

The assembly process was achieved by dissolving the diphenylalanine building blocks in a fluorinated solvent, 1,1,1,3,3,3-hexafluoro-2-propanol (HFP). In this solvent, the peptides do not interact with one another and are easily dissolved. However, HFP is very volatile and rapidly evaporates, so the peptides are deposited from solution on to a surface. Gazit and Reches suggest that this process forms numerous sites from which nanotubes grow in a unidirectional fashion. Highly aligned nanotube forests were formed across the entire surface of the glass substrate on which the HFP solution was dropped. However, an alternative assembly mechanism, in which complete nanotubes first assemble in the bulk solution and then arrange themselves on to the surface to form a forest-like structure, cannot be ruled out.

Although the precise pathway of the growth is not fully understood at this stage, these findings pave the way to grow, molecule by molecule, well-structured nanotubes that may be useful for a wide range of applications. For example, it was previously reported that individual dipeptide nanotubes could be used as templates, inside which metal nanowires could be grown[8]. Furthermore, dense nanotube arrays with large surface areas and the capability to interact with other biological molecules could lead to high-sensitivity sensors for both environmental and medical diagnostic applications.

Gazit and Reches also show how these peptide nanotubes can be aligned horizontally. The high-yielding assembly of peptide nanotubes can be performed in the presence of magnetic particles, which end up coating the outside of the tubes. These magnetically modified structures were spread on to a surface where they adopted random orientations. However, the nanotubes were seen to realign in response to an applied field, resulting in both spatial organization and alignment. Altogether, Gazit and Reches have demonstrated how to control both the vertical and horizontal arrangement of self-assembled peptide nanotubes using quite simple, yet elegant, methods.

What makes this study especially interesting is the simplicity with which the well-defined nanotubes can be made. Although there have been reports concerning the production of nanotubes using other materials, this example uses a small, yet biologically relevant system, to grow large arrays of well-aligned high-integrity tubes. It is remarkable that such a basic building block can assemble into highly regular forest-like structures. Not only from small acorns do large trees grow, so do entire forests! It will be interesting to see if other aromatic dipeptides, either natural or man-made, can self-assemble into ordered nanostructures.

The authors' method is not just simple, but relatively inexpensive. As the basic starting materials are all commercially available and the methods are straightforward, this technology could be adopted widely and quickly. If nanotechnology is to lead to new devices and products, the development of the simplest methods is one of the most important factors. It must be emphasized, however, that going from milligrams of material to kilograms or tonnes is not easy and challenges still remain. New innovative approaches for the chemical synthesis of peptides or perhaps even cell-based production may play an increasingly important role for wider applications of self-assembling peptide materials.

Although nature can build numerous elegant structures and molecular machines, it is up to us to construct technological devices. We are now learning from nature and trying to do even better. As an old Chinese proverb says, "dark blue (qing) is derived from blue (lan) but is even better than blue". It is believed that these simple and versatile self-assembling peptides will provide us with new opportunities not only to study complex and previously intractable biological phenomena, but also to make novel materials and intricate molecular machines.

References

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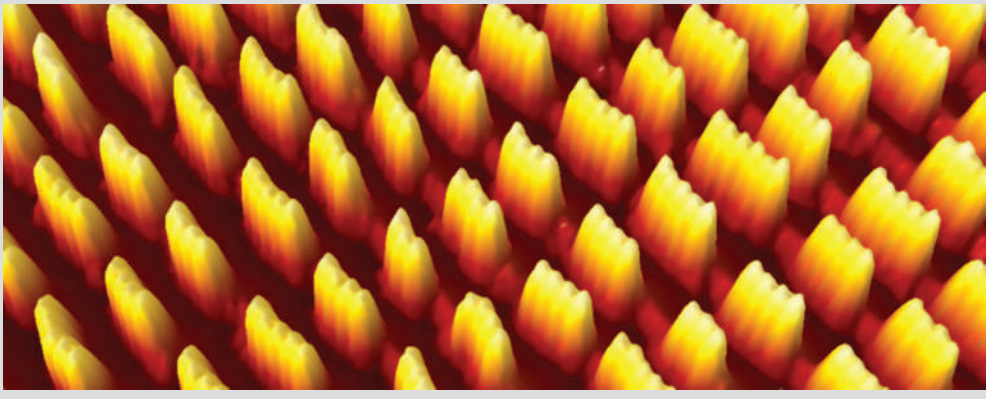
Surface patterning: Fullerenes line up

The ability to create arrays of organic nanostructures with long-range order and uniform size could have applications in electronic and optoelectronic devices. One of the most promising methods for making such arrays is to rely on the self-assembly of molecules on surfaces that already possess long-range order. Researchers at the Swiss Federal Laboratories for Materials Testing and Research in Thun and Liverpool University in the UK have now used this approach to grow ordered arrays of fullerene nanochains on a gold surface, as this image shows.



Gold surfaces are natural templates for growing nanostructures.

Roman Fasel and co-workers sublimated the fullerene molecules onto specially prepared gold substrates that naturally form a rectangular superlattice (*J. Phys. Chem. B* **110,** 21394–21398; 2006). Scanning tunnelling microscopy and low-energy electron diffraction revealed that the nanochains — which each contain just four or five fullerene molecules — only formed at the lower edges of the 'steps' that are found on the gold surface. It is thought that the electron-rich regions near these edges preferentially adsorb the fullerene molecules, which are electron acceptors, leading to the formation of arrays that perfectly reproduce the periodicity of the gold template.

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