

density of charge carriers is zero. Moreover, all the superconducting transistors made by the Delft group can support a supercurrent, making the ability to sustain a Josephson effect yet another robust feature of graphene.

The development of commercial graphene-based nanoelectronics will encounter a number of technological challenges. First and foremost, is it possible to produce high-quality graphene wafers in sufficient quantities? Options include dissolving graphite and depositing it as a monolayer on a substrate in a bottom-up approach, or burning off silicon in the top layer of silicon carbide crystals in a top-down approach.

Another problem in the transistors made so far is that there is a noticeable leakage current, even when the device is meant to be switched off. This is related to the unstoppable nature of the electrons in graphene (see Box 1) and can only be remedied by creating a bandgap. One way to solve this problem is to use bilayer graphene, because, according to theory, a voltage difference between the two layers will generate a bandgap. However, making bilayer graphene on a large scale is probably even more difficult than making single-layer graphene. SETs could circumvent the problems with leakage currents, but again

the large-scale manufacture of such devices with reliable characteristics will be a challenge.

The use of graphene 'nanoribbons' could be another solution because the electronic properties of the ribbon depend on the type of edge it has: simple theoretical considerations suggest that all ribbons with so-called zigzag edges are metallic, whereas those with 'armchair' structures can be semiconductors (with a bandgap) or metals, depending on their width. However, some theorists have recently suggested that all graphene ribbons are semiconducting⁷. At present the edges are naturally passivated by hydrogen atoms, but they could be functionalized by attaching different chemical groups, providing potential for sensor applications. Preliminary reports on graphene ribbons are appearing^{8,9}, but the challenge of routinely cutting and pasting graphene with the required level of precision will require the very best tools from nanotechnology.

Although graphene research is still in its infancy, the number of experimental breakthroughs in the past three years has been stunning: the observation of the quantum Hall effect at room temperature, the first graphene-based SET, and the bipolar superconducting transistor are just a few of many highlights. Moreover, the development

of graphene-based nanoelectronics looks possible, if difficult. The main obstacles concern large-scale manufacturing and the challenge of patterning graphene at the atomic level. However, it took 50 years for silicon technology to reach maturity, so the parents of today would not be irresponsible if they told their kids that when they grow up, they might well find themselves using devices made from carbon pancakes just one atom thick.

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NANOPARTICLES

A very versatile nanocapsule

Numerous copies of a pumpkin-shaped molecule can be linked together to form a nanocapsule shell that can trap compounds inside. The outer surface of this capsule can be decorated with other species by plugging them into the cavities of the hollowed-out pumpkins.

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In the past half-century, scientists have made enormous strides towards creating nanoscale structures and devices. Often these efforts are inspired by biology, not least because nature has been making functional nanosystems using the 'bottom-up' approach for millennia. Scientists have, with varying degrees of success, been attempting to mimic the basic capsid architecture of viruses in order to create nanoscale capsules for applications ranging from targeted drug delivery to functional materials development¹. Now, writing in the

international edition of *Angewandte Chemie*, Kimoon Kim and colleagues at Pohang University of Science and Technology in Korea describe an impressively versatile synthesis of polymer nanocapsules with surfaces that can be easily and reversibly decorated with other molecules².

One of the many different strategies for making synthetic nanocapsules takes advantage of self-assembly — the method by which well-ordered architectures are formed spontaneously from small molecules³ or polymers⁴. For example, convex aromatic compounds can be pieced together along their edges through hydrogen bonds to form hollow spheres that encapsulate small molecules⁵. However, these supramolecular assemblies are held together by relatively weak non-covalent bonds and their stability depends strongly on their environment

— under some conditions their presence can be somewhat fleeting, with dissociated components often observed.

One way to enhance the stability of these structures is to covalently link the constituent parts. In general, the crosslinkable groups are attached — either covalently or non-covalently — to a core template. The core is removed by chemical degradation, yielding architectures that will ideally retain the shape of the central template⁶. Such 'core-shell' approaches are now well established¹, as are hybrid construction approaches that use a combination of self-assembly and templating⁷. The new approach taken by Kim and co-workers to make a nanocapsule is fundamentally different from these strategies — the building blocks are simply stitched together using traditional chemical reactions (rather than non-covalent

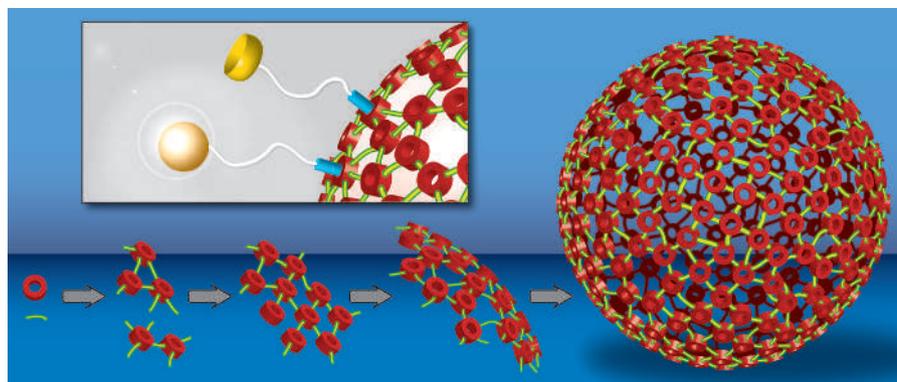


Figure 1 An idealized representation illustrating the proposed mechanism by which polymer nanocapsules are formed from cucurbit[6]uril units (red rings) interconnected by a chemical linking agent (green lines). The ability to tailor the surface through host–guest interactions is also shown, with a molecular receptor (yellow bowl) and a fluorescent tag (orange sphere) plugged into the surface CB array by linking ammonium ion chains (blue cylinders).

self-assembly) without the need for a templating core.

Kim's capsules are built from cucurbit[6]uril (CB), itself a hollow container molecule that is capable of binding small molecules within its inner cavity (which is approximately $3 \times 9 \text{ \AA}$ in size). Its name is derived from the taxonomical family name for the cucurbits (Cucurbitaceae), or gourds, owing to the molecule's resemblance to the best-known member of this family, the pumpkin⁸. A more accurate description of the molecule, however, might be that of a hollowed-out pumpkin, with a hole carved in its top and bottom. Although first reported in 1905, it was William Mock who determined the CB structure some seventy-six years later — and gave it its name. CB and several of its larger structural analogues have gained widespread attention because of their ability to host, in a highly selective manner, certain types of guest molecules in their hollow interiors. In the supramolecular and nanotechnological age, this selectivity has been exploited in molecular switches, artificial enzymes and in the remediation of waste water⁹.

To form a nanosphere, Kim and colleagues first decorated the outer rim of the CB molecules with 12 alkene groups, which, in the presence of ultraviolet light, can react with thiols to form carbon–sulphur bonds. When reacted with linear molecules that have a thiol group at each end (dithiols), the modified CB units were stitched together to form the shell of a spherical nanocapsule. The nanosphere was constructed without the need for a template — a remarkable result given that there are many alternative structures that could potentially be formed from this polymerization reaction. Kim and co-workers suggest that the nanocapsules form by a sequential process (Fig. 1) in which,

initially, two or three CB units react with the dithiol linking agent to form covalently bonded dimers or trimers. These small building blocks then react with more dithiols to produce two-dimensional 'patches', which begin to curve to reduce their total energy. Finally, multiple curved patches join together to form a minimally crosslinked spherical capsule. Additional interconnections between proximal CB units in the structure result in a highly crosslinked structure.

A battery of analytical techniques was used to characterize the nanospheres, in addition to imaging by three different microscopy methods (atomic force, scanning electron and transmission electron microscopy). The data collected from these studies suggest that the shells of the capsules are about 2.1 nm thick, which corresponds to a single layer of linked CB molecules. The capsule diameters ranged from approximately 60 to 600 nm, depending on the length of the dithiol linker and the solvent in which the crosslinking reaction is carried out. When the capsules were formed in the presence of carboxyfluorescein, this fluorescent dye was trapped inside them and could not escape because it is too big to fit through the cavities of the CB molecules. At the same time, however, the fluorescence could be quenched when either acid or methyl viologen — molecules small enough to pass through the CB pores or the gaps between them — were added to a solution of the nanocapsules. This indicates that the capsule surface exhibits size-selective porosity — the small quencher molecules can enter, but the larger dye cannot escape.

To demonstrate potential applications of their nanocapsules, Kim and colleagues examined whether ammonium ions, which are known to form strong host–guest complexes with CB by threading into its

cavity, could be bound to the nanocapsule surface. To this end, a small polyamine, known as spermine, was chemically modified with fluorescein isothiocyanate — a fluorescent tag. A second surface binder was prepared by conjugating spermine to folic acid, a compound that can be used to target many types of human tumours. The modified spermine molecules were assembled on the surface of the nanocapsule by plugging their ammonium ion tails into the CB receptors (Fig. 1). It was shown, using fluorescence measurements, that this supramolecular assembly was taken up by human oral cancer cells (KB cells) via endocytosis.

The versatility of the nanocapsule is increased by the multiple CB units arrayed on its surface. Nonetheless, an obvious question is whether the synthetic approach is limited to this particular building block. A theoretical study was performed to model the nature of the spontaneous curvature thought to occur when the nanocapsules form. The results suggest that nanocapsules of the type described by Kim and colleagues can be formed using any building block with a simple flat aromatic core and polymerizable groups that are able to direct polymer growth laterally. A preliminary result using another monomer — a different planar core with six polymerizable groups around the periphery — also produced a polymer nanocapsule. Obviously, this is a remarkable step towards demonstrating a fully general approach to the synthesis of hollow nanocapsules that does not rely on templating or core removal.

For the nanosphere reported by Kim and co-workers to be clinically useful in drug delivery or diagnostic applications, it will have to be non-toxic, non-immunogenic, and have an appropriate biodistribution profile. The overall versatility of this particular nanocapsule — almost anything can be plugged into its surface if attached to a spermine chain — and the intriguing possibility that the synthesis can be generalized to multiple building blocks, guarantees that this exciting new system will be examined by others. A host of applications can be readily imagined and await discovery.

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