vitro from only a few components, although it remains to be established whether these in vitro clathrin-coated pits form with the same kinetics and have the same morphology as those formed in vivo. Exactly how AP180 and AP-2 stimulate clathrin coat assembly and vesicle budding is not known, but their ability to interact both with each other and with clathrin suggests that they may coordinate clathrin coat assembly through dynamic and complex interactions. It is likely that their interaction with PIP_2 tethers the clathrin lattice to the plasma membrane.

Given the importance of AP-2 and AP180 in clathrin coat assembly and vesicle budding in vertebrate cells, it is puzzling that the yeast homologs of AP-2 and AP180 are dispensable for clathrin-coated vesicle formation (*2*). In contrast, epsins are crucial for endocytosis in both yeast and mammalian cells (*2*, *13*). Like AP180, epsin is capable of interacting with both AP-2 and clathrin. In addition, it also interacts with several multidomain proteins, including Eps15, which in turn can interact with other proteins implicated in endocytosis. Itoh *et al.* (*5*) show in cultured mammalian cells that the overexpression of epsin containing a mutation in the ENTH domain, which prevents epsin from binding to PIP_2, blocks clathrin-dependent endocytosis. Moreover, the ENTH domains of the yeast homologs of epsin are essential for endocytosis (*13*). This indicates that binding of epsin to PIP_2 is critical for the formation of clathrin-coated vesicles in vivo, although exactly how epsin is involved remains to be established. It is possible that epsin is part of a complex protein network that can fine tune endocytosis in response to phosphorylation and other protein modifications (*1*).

As PIP_2 is a central player in the assembly of the endocytosis machinery, regulation of its formation and turnover are of great importance for endocytic vesicle trafficking. This is illustrated by the finding that synaptojanin, which dephosphorylates PIP_2, converting it into phosphatidylinositol 4-phosphate (PIP), is involved in the uncoating of clathrin-coated vesicles, a process that is required before they can fuse with other membranes (*12*). Future studies should reveal how the PI 4- and 5-kinases and synaptojanin are regulated, and where exactly PIP_2 is localized in cellular membranes. The focal assembly of clathrin lattices implies that there may be PIP_2-rich patches in the plasma membrane. Recent technological developments such as fluorescence resonance energy transfer microscopy and evanescent wave microscopy promise to reveal whether these patches exist.

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PERSPECTIVES: MATERIALS SCIENCE

The Simplicity of Complexity—Rational Design of Giant Pores

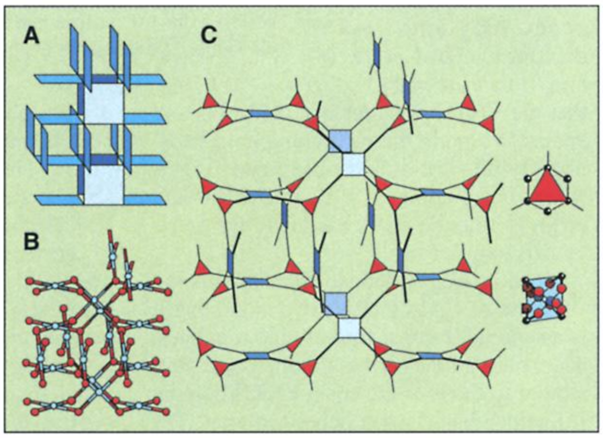
Gérard Férey

Porous materials with regular, accessible cages and tunnels are increasingly in demand for applications in catalysis, separations, sensors, and electronics. Depending on their structure and pore size, these materials allow only molecules of certain shapes and sizes to enter the pores. Furthermore, giant pores may act as nanoreactors. The confined volume may generate reactions that do not occur in the bulk. In this respect, the larger the pores, the wider the range of reactants that can be combined.

During the last decade, there has been a tremendous increase in the synthesis of new porous solids, both inorganic and organic (*1*, *2*). But researchers aiming to increase pore sizes have encountered two obstacles: a drastic decrease in material stability with pore size and the tendency of many materials to form two interpenetrated identical subnetworks by concatenation. Sometimes one strikes lucky, but usually these factors restrict the size and accessibility of pores, even if the accessibility can be optimized (*3*). Several design strategies have been pursued to circumvent these difficulties. Three approaches currently prevail. Müller *et al.* (*4*) and Khan (*5*) create linkages between isolated very large molecular moieties, such as $Mo_{72}Fe_{30}$ spheres. My group introduced the concept of "scale chemistry" (*6*), in which the size of the "secondary building blocks" (SBUs) in a structure is increased while maintaining the same connectivity between them; the larger the SBU, the larger the pores. Finally, the validity and power of a concept developed by O'Keeffe and Yaghi and co-workers last year (*7*) are demonstrated by Chen *et al.* on page 1021 of this issue (*8*).

The authors define three requirements: The final framework must be as thermally stable as possible, avoid or minimize interpenetration, and preserve the accessibility of the pores. To fulfill these conditions, they first choose a topology, select the tectons that are able to create this topology, and only then select a chemistry to reach the goal.

The originality of the concept is to start from very simple structure types, which are illustrated in every textbook and often correspond to thermodynamically stable structures, to describe them in terms of connected nets (*9*–*11*), and to decorate ("augment") these nets. In Chen *et al.*'s work (*8*), the simple structure is Pt_3O_4, a three-dimensional network of corner-shared square planes (see



How to design a porous solid. Chen *et al.* start from the simple three-dimensional network adopted by Pt_3O_4 (**A**), in which O and Pt atoms are three- and fourfold coordinated, respectively (**B**). They then replace the O atoms by triangles and the Pt atoms by squares (**C**). Any chemical species with the right connectivity (see examples to the right) can take up the places of these units.

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panel A in the figure), in which oxygens and platinum atoms are three- and fourfold coordinated and build a 3,4-connected net (panel B). The decoration replaces Pt by squares and O by triangles and generates the topology of panel C. Squares and triangles may be referred to as the topological SBU; that is, they represent species whose connectivity is four for the squares and three for the triangles, whatever their chemical nature.

In Chen *et al.*'s macroporous material, the squares are taken up by a binuclear Cu carboxylate moiety, and the triangle is formed by 4,4′,4″-benzene-1,3,5-triyl-tribenzoic acid, with three corners of the benzene ring acting as the vertices of the inner triangle, the linkers being phenyl groups. The risk of interpenetration is lowered because the π–π interactions between the benzyl groups render the two equal sublattices interwoven instead of interpenetrating. This creates accessible pores with a free diameter of about 16 Å and windows with dimensions of 7 Å by 14 Å (corresponding to a surface area of 1500 m^2/g) after elimination of the solvents that reside in the cavities.

These properties are remarkable but are not as important as the new strategy described here. In this strategy, specific chemistry is only introduced after having chosen a desired topology and the tectons that may enable it to be formed. Moreover, the approach is general because it is independent of the nature of the reactants. It only depends on the connectivity of the tectons and thus allows every modulation of the chemical nature of topological SBUs, and every modulation of the linkers, within a given topology. The composition of a given solid is also known before synthesis because the ratio between the different topological SBUs is fixed by the choice of the initial structure type. With the success of such a strategy, the synthesis of porous solids will never be like it was before.

A final question arises. Many new solids have been reported recently that are crystalline and have giant pores, but what is the limit? Can we achieve crystalline materials with pores of the same size as in the so-called mesoporous solids (which have amorphous or disordered walls)? Progress can be expected to be rapid at this frontier between micro- and mesoporous solids, and new materials may soon exist that we cannot even imagine yet. The strategy demonstrated by Chen *et al.* is likely to play an important role in shaping this porous future.

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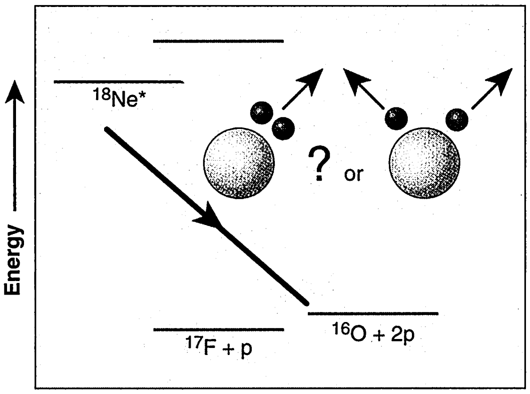
PERSPECTIVES: RADIOACTIVITY

Are Protons Leaving in Pairs?

Phil Woods

Nuclear physicists exploring the extreme limits of nuclear stability are discovering exotic phenomena not manifest in relatively stable nuclei. For example, a substantial number of neutron-deficient isotopes decay from their ground states through the emission of a single proton (*1*). Such proton radioactivity is, however, only observed for nuclei with an odd proton number, *Z*. In nuclei with even *Z*, the protons pair up, resulting in enhanced nuclear binding. As a result, single-proton emission becomes energetically forbidden or highly suppressed. But it turns out that an even more exotic decay pathway may be available in these cases.

Already in 1960, the Russian nuclear theoretician Vitaly Goldansky predicted (*2*) that nuclei with an even number of protons could decay from their ground states by the simultaneous emission of two protons. Since then, great efforts have been made to explore this exotic ground-state decay mode. Nuclear physicists have also searched for simultaneous two-proton emission from excited quantum states in nuclei. Simultaneous two-proton emission from an excited nuclear state was recently reported in *Physical Review Letters* (*3*). Tantalizingly, the two extreme theoretical descriptions of the decay process describe the present data equally well.



Unusual decay. The excited ^{18}Ne nucleus can only emit two protons simultaneously because there are no allowed pathways to the intermediate system, ^{17}F. It is not yet known, however, whether the two protons are emitted as a ^{2}He cluster or democratically (see text).

When Goldansky published his prediction, it was already known that the ground state of ^{6}Be was unstable to decay into two protons and an α particle (a $^{4}He^{2+}$ particle). However, the ^{6}Be isotope only existed as a short-lived state, the formation of which had to be inferred by observing its proton and α-decay products. This indirect evidence was not enough to nail the decay mechanism. In 1989, a group at the Kurchatov Institute in Moscow performed experiments that allowed the energy and angular distributions of the ^{6}Be decay products to be studied in great detail (*4*). On the basis of these studies, the group introduced the term "democratic decay" into the nuclear lexicon. It symbolizes the simultaneous breakup of a nucleus into three particles without passing through an intermediate stage. The authors demonstrated that the ^{6}Be decay process could be understood in terms of three basic competing patterns of decay: the "cigar mode," in which the protons are emitted from opposite sides of the α particle (spatial anticorrelation); the "di-proton decay mode," in which the protons are emitted in the same direction and are spatially correlated to the extent that the protons can be considered to exist as a metastable ^{2}He cluster; and the "helicopter mode," in which the protons are emitted with their spins aligned—a phenomenon that is not allowed by the proton-proton pair interactions but can occur prolifically because of the third body (the α particle). More recently, two-proton emission has been detected in the ground state decay of ^{12}O, which like ^{6}Be has too short a half-life to be observed directly (*5*). In this case, the protons were found to be emitted isotropically, but a sequential decay mechanism could not be ruled out and the exact

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