ularly dated phylogenies will reveal whether any beetle clades shared their hosts' explosive radiation in the Miocene and whether this also occurred on several continents.

Cycads are a member of the "naked seed" plants or gymnosperms, which also include conifers and the *Ginkgo* tree. A recent analysis of the ages of extant gymnosperm genera (*11*) included most of the cycad genera dated by Nagalingum *et al*., albeit with much smaller species sampling. That study found that the average gymnosperm genus is 32 million years old, whereas the average angiosperm (flowering plant) genus is somewhat older. These results imply a high turnover of species and clades as lineages keep replacing each other. Neither molecular phylogenetics nor paleontology alone could have arrived at these insights, which required combining data and approaches from both disciplines.

Unfortunately, many living fossils, including the *Ginkgo* tree, have but one species, precluding molecular dating. For the two coelacanth species, *Latimeria chalumnae* and *L. menadoensis*, a molecular clock suggests that while they closely resemble their 360-million-year-old fossil relatives, they only diverged from each other about 30 to 40 million years ago (*12*). This example, and even more dramatically the cycads, illustrates that near-extinction need not be an evolutionary dead end. The diversification rate of most cycad genera, however, now seems to be slowing, and their relatively recent radiation is probably no guarantee against the next extinction wave.

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MATERIALS SCIENCE

Toward High-Throughput Zeolite Membranes

Thinner versions of highly selective membranes may allow for more energy-efficient separation processes.

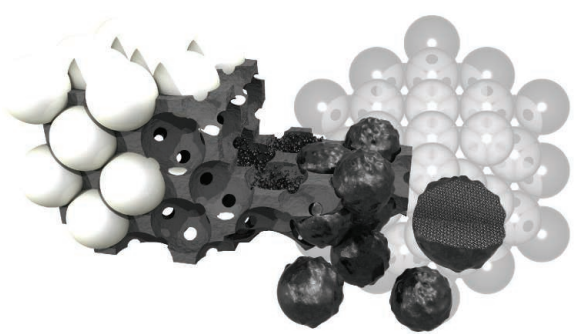
Michael Tsapatsis

Many energy-conservation strategies in manufacturing rely on replacing or combining thermally driven separation processes such as distillation with more efficient ones (*1*). Membranes made from zeolites, crystalline materials with precisely defined pores in the size range of molecules (angstroms to nanometers), are a promising material with which to achieve highly selective separations based on molecular recognition by the membrane pores (*2*). Although small-pore hydrophilic zeolite membranes for the dehydration of solvents and biofuels can be found in several small- to medium-scale industrial plants (*3*), zeolite membranes have been too expensive to replace competing technologies for many other applications. Competitive performance will likely come from creating thinner zeolite films with a hierarchical approach, in which nanoscale zeolite crystals or fragments of these structures assemble into larger porous networks.

Many notable improvements to zeolite membranes have been demonstrated recently, including record selectivities for separating certain mixtures by controlling preferential orientation of zeolite crystals (*4*, *5*) and the elimination of grain boundary defects (*6*) and cracks (*7*, *8*) that cause leakage. Moreover, zeolite chemical stability issues appear manageable; they can be used commercially in dehydration processes that put the membrane in direct contact with certain aqueous mixtures, an environment where zeolites are most vulnerable to dissolution. However, high costs per unit area of membrane ($5000 to $10,000 per square meter for an assembled module) have limited implementation to medium-sized industrial plants that use membranes with 400 m^2 or less of surface area; the major share of the cost (up to several thousand dollars per square meter) is actually imposed by the underlying porous support.

At current throughput levels, large surface areas and correspondingly high capital investment are required for many applications. As a result, despite the substantial energy savings, prohibitively long payback times (e.g., 10 years) are required. Unless costs per unit area decrease, a 10-fold increase in flux compared to the current state of the art appears to be the only way forward. For certain separations, this requirement would mean decreasing thicknesses to ~50 nm, a formidable task considering that the current state of the art is at least 10 times thicker.

How, then, can this leap to thinner films be achieved? One approach that has been pursued in the past decade is to prepare very small zeolite crystals or even molecules (fragments



Through thin, not thick. One process for making thinner selective membranes based on zeolites starts with the use of nanometer-sized silica spheres (shown in white) to template mesoporous carbon with precisely sized cages that are connected to neighboring cages through smaller openings. Zeolite crystals (shown in black) grow in these interconnected cages. Fragmentation can release individual zeolite particles that can be attached to a porous support, where they serve as templates for growing thin zeolite membranes.

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of zeolite structures smaller than the crystal unit cell) by control of nucleation and growth (*9*) and then form thin films by coating and assembling them on a support. However, the smallest zeolite crystals that can be achieved by systematic optimization of hydrothermal growth rarely go below the target size of 50 nm (*10*).

An alternative approach to zeolite nanocrystals is provided from a class of materials called hierarchical zeolites, which have mainly being pursued for their uses in catalysis. They consist of nanometer-sized zeolite domains connected to each other and separated by mesopores. Hierarchical zeolites include materials derived from layered zeolites (*11*) and materials made by confined synthesis in ordered mesoporous templates (*12*) or by use of dual-templating strategies (*13*). It is conceivable that through appropriate disassembly methods, hierarchical zeolites or their precursors can be fragmented to highly crystalline zeolite particles with one or more dimensions in the 1- to 10-nm range. Thinner films enabled by the disassembled structures allow the use of more expensive materials. Ten dollars or more per milligram of zeolite could be justified for thin films in the 50-nm range and allow for the use of expensive structure-directing agents and other sacrificial templates, such as ordered mesoporous carbons and polymers.

Recently (*12*, *14*), a very precise replication scheme starting from amorphous silica spheres to form crystalline zeolite particles as small as 10 nm was demonstrated. As depicted in the figure, nanometer-sized silica spheres are first used to template mesoporous carbon with precisely sized cages that are connected to neighboring cages via smaller openings. Next, zeolite crystals nucleate and grow in these interconnected cages, forming hierarchical zeolites. These hierarchical zeolites can then be fragmented into individual particles with a size similar to that of the carbon cages (and of the silica spheres used to template them). Selective membranes can be prepared by depositing these fragments as seed crystals on a support and creating a continuous film through a second round of zeolite growth (*14*).

Technical and fundamental challenges abound. In addition to isotropic particles, other shapes, like highly anisotropic lamellae, could conceivably be made and used in novel ways to form thin films (*15*). It may also be possible to tailor hierarchical zeolites and their precursors with disassembly in mind to obtain the desirable fragments in higher yield. Effective deposition methods should be developed, and mechanical and chemical stability of such thin films should be addressed. To harvest the high flux of the thin zeolite films, high flux supports and innovative module design will be required. Flux and selectivity in these films will likely be dominated by adsorption on the external surfaces and pore entrance rate processes rather than by transport in the zeolite pores. New experimental techniques (*16*) that could address these issues are emerging and will be powerful tools in understanding and tailoring nanometer-thin zeolite membrane performance.

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CELL BIOLOGY

Anatomy of Prostaglandin Signals

An enzymatic step in prostaglandin synthesis plays a key role in neuroinflammation in the mammalian brain.

Nephi Stella

Membrane metabolism generates many lipid signals that regulate diverse cellular processes. Although most membrane-metabolizing enzymes are specific to one lipid family, some act on a range of substrates and produce lipid signals with different bioactivities. These multisubstrate enzymes act as nodes that can change the flow of information carried by the lipid signaling network by, for example, boosting the production of one family of lipids while dampening that of another. On page 809 of this issue, Nomura *et al.* (*1*) show that the enzyme monoacylglycerol lipase (MAGL) (*2*) is a critical node within the lipid signaling network, coordinating the brain's defense mechanism to neurodegeneration. They also show that inhibiting MAGL prevents neurodegeneration and chronic neuroinflammation in a mouse model of Parkinson's disease, opening a new potential avenue for treating neurodegenerative diseases.

The brain is separated from the rest of the body by the blood-brain barrier, which insulates the central nervous system against toxins as well as peripherally circulating immune cells. It has its own specialized immune system orchestrated by microglia, a type of macrophage that constantly patrols brain parenchyma (*3*, *4*). Microglia become activated in response to pathogens and neuronal damage, rapidly changing into effector cells that initiate and control immune responses. Indeed, microglia are activated by HIV, malaria, tumors, ischemic insults, autoimmune events, and neurodegeneration. However, the phenotype of these activated cells varies depending on the pathology, from releasing toxins that harm adjacent cells, to decreasing the production of toxins and producing immune mediators that protect and repair adjacent cells (*5*).

The molecular mechanisms that determine the phenotype of activated microglia are controlled by lipid signals. For example, prostaglandins promote (*6*), whereas endocannabinoids dampen (*7*), microglia activation. Accordingly, modulating cannabinoid receptor and prostaglandin receptor activity can regulate the duration and outcome of the brain's innate immune responses. Unfortunately, the development of therapies based on synthetic receptor ligands is hampered by the compensatory desensitization or sensitization that follows long-term receptor activation or inactivation, respectively (*8*). Indeed, the intense search for therapeutic compounds targeting cannabinoid

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