As with monosodium urate, asbestos triggers an efflux of potassium from the cell. This event is required to activate Nalp3 (*9*), although the underlying mechanism is not known. Large crystals such as monosodium urate, or crystalline fibers such as asbestos, are subject to so-called frustrated phagocytosis and remain trapped at the cell surface, where cytoskeletal (actin) filaments form. Disruption of actin filaments with a pharmacological agent (cytochalasin D) inhibited the effect of monosodium urate and asbestos on interleukin-1β secretion. Asbestos also triggers the generation of reactive oxygen species in cells. Dostert *et al*. confirm this and further show that inhibitors of reactive oxygen species (such as *N*-acetylcysteine) block interleukin-1β production in macrophages. The source of reactive oxygen species in frustrated phagocytosis might be NADPH oxidase, an enzyme that is activated by the phagocytosis of microbes. The authors investigated a role for NADPH oxidase by using the inhibitor diphenylene iodonium, and by reducing the expression of the NADPH oxidase subunit $p22^{phox}$ by RNA interference. Both approaches diminished interleukin-1β secretion in response to asbestos. Reducing the expression of thioredoxin, a protein that detoxifies reactive oxygen species, increased interleukin-1β secretion, further implicating reactive oxygen species in the inflammatory response to this particulate.

When normal mice were placed in air containing chrysotile asbestos (which is found in building materials), an increase in total cell number was observed in bronchoalveolar lavage fluid, indicative of an inflammatory reaction. By contrast, fewer cells were recruited to the lungs of Nalp3-deficient mice exposed to asbestos, and production of multiple cytokines was impaired.

Nalp3 has already been implicated in the pathological increases in interleukin-1β that occur in gout and in autoinflammatory diseases such as Muckle-Wells syndrome (*10*). However, precisely how Nalp3 is activated is still not clear. The current model involves the binding and hydrolysis of adenosine 5′-triphosphate to a nucleotide-binding domain of Nalp3, which is thought to lead to a conformational change in the protein, allowing activation of caspase-1 within the inflammasome (*11*). How reactive oxygen species affect this process is unknown. Reactive oxygen species may be particularly important for crystalline activators of the inflammasome that are subject to frustrated phagocytosis, possibly pointing to multiple mechanisms to engage with Nalp3.

A crucial finding of Dostert *et al*. is that Nalp3-deficient mice are resistant to asbestos-induced lung injury. An important role for interleukin-1β in this process was already known, as was a role for this cytokine in the pathogenesis of asbestos-induced mesothelioma and in models of lung fibrosis (*12*, *13*). The present study therefore further highlights the importance of testing the interleukin-1 receptor antagonist anakinra, which has shown efficacy in patients with other Nalp3-mediated diseases such as gout and Muckle-Wells syndrome, as a therapeutic agent to slow the progression of asbestosis and silicosis. Nalp3 itself might prove to be an interesting drug target for these diseases as well.

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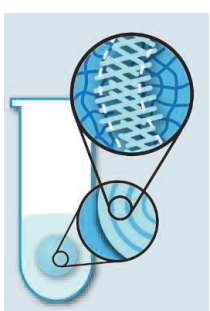
CHEMISTRY

Synchronized Self-Assembly

Building macroscopic containers from porous membranes may be easier because of advances in controlling the kinetics of self-assembly.

Jeffrey S. Moore and Mary L. Kraft

Self-assembly has long been recognized as a powerful synthetic approach to obtain dynamic structures exhibiting complex functions, such as those found in nature (*1*). By carefully regulating non-equilibrium self-assembly, two recent studies (*2*, *3*) demonstrate important progress, resulting in new porous membranes whose structure is controlled on several length scales.



Kinetic control of structure. Ladet *et al*. successively interrupt polymer densification by removing a molded hydrogel from neutralization bath to produce multimembrane hydrogels.

There are two main types of self-assembly (*4*). Static self-assembly deals with equilibrium structures; the shapes and interaction energies of the participating components are altered to achieve various organizations. For molecular components, noncovalent interactions—like hydrogen bonds, electrostatics, and van der Waals forces—are manipulated to encode building blocks with instructions that lead to the spontaneous generation of a desired target (*5*).

Dynamic self-assembly, on the other hand, is a non-equilibrium process in which energy is supplied to the system to maintain a steady-state population of ordered structures. Because dynamic self-assembly involves the added complexity of a sustainable driving force, only limited progress has been made in this area (*6*). Recognizing that non-equilibrium self-assembly may organize matter differently from that which occurs at thermodynamic equilibrium, chemists are challenged to bring kinetic control into their repertoire of methods. This is what the two recent studies achieved.

In the first study, Ladet *et al.* (*2*) formed chitosan gels by slowly removing the water from aqueous alcohol solutions of a chitosan polyelectrolyte. This alcohol gel can be molded into shapes such as tubes and spheres of various sizes. When the gel object was bathed in a solution of an aqueous base, hydrophobic interactions within the network dominated, causing the polymer molecules to contract and form a membrane-like skin around the original object. The rate of membrane formation via densification typically

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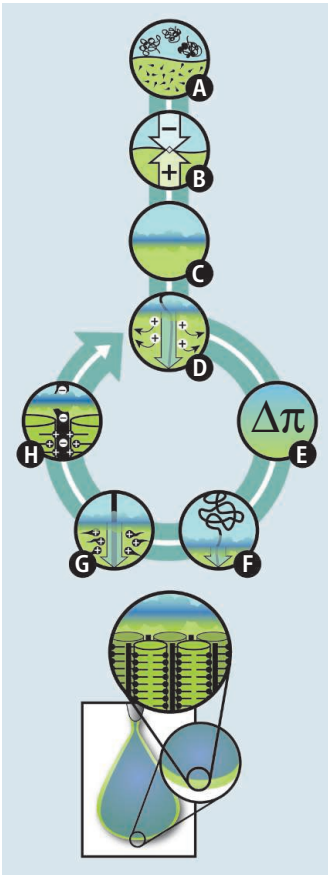
occurred on the time scale of minutes. Simply removing the object from the neutralization bath interrupts membrane thickening. Insertion of the object back into the bath initiates formation of a second membrane layer between the gel-core and first membrane. Interestingly, this process results in an intermembrane space that can accommodate payloads such as chondrocyte cells. Repetition of this sequence produced concentric shells of hydrogel membranes extending inward toward the core (see the first figure).

The process used to create these layered hydrogels exploits a simple type of kinetic control. Another way to drive new modes of nonequilibrium structure would be to time the release of the potential energy stored in the self-assembling components. A recent report by Capito *et al.* elegantly demonstrates such a regulated process, in which ordered structures rapidly self-assemble at the interface of two chemically distinct electrolyte solutions. This process produced functional porous membranes with complex hierarchical structures (*3*).

The authors assemble membranes instantly when two liquids come in contact, establishing a physical barrier that hinders dissipation of the ion imbalance between the small molecule electrolyte and the polyelectrolyte solutions. High osmotic pressure within the polyelectrolyte solution and the requirement for electroneutrality impels the megamolecules to extrude through pores in the structured barrier and enter the electrolyte solution. This leads to the growth of perpendicular nanofibrils in a dynamic process that is sustained by osmotic pressure (see the second figure).

The study shows that membrane-enclosed sacs of macroscopic sizes can be rapidly formed upon contact between the two liquids; moreover, the presence of polymeric electrolyte in the sac interior imparts unique self-healing function to these compartments. The resulting membranes are permeable to proteins and could be used to entrap cells by simple liquid-liquid contact to create mini-cell biology laboratories. These could then be used as controlled environments for cell expansion, stem cell differentiation, or studies of bio-signaling from neighboring sacs entrapping colonies of other cells. By tailoring the small molecule electrolytes, the structures might be customized for a diverse array of applications in biomedicine, catalysis, and energy generation.



Synchronized self-assembly. In the study by Capito *et al.*, macroscopic sacs and membranes are prepared when a solution of macromolecules contacts a solution of self-assembling molecules (**bottom**). Upon contact (**A**), the components are attracted by electrostatics (**B**) and instantly form a diffusion barrier (**C**). Sustained membrane growth proceeds by release of counterions (**D**), enhancing the osmotic pressure imbalance between the two liquids (**E**) that drives the polymeric electrolyte to uncoil and extrude through the barrier (**F**). New polyelectrolyte is then exposed (**G**) onto which new nanofibers assemble (**H**) causing further release of counterions (D).

These recent findings point to new synthetic concepts whereby the final supramolecular structure depends on the mechanistic pathway of the assembly, rather than the thermodynamic endpoint. Ladet *et al.* show that even a relatively simple kinetic scheme can produce intriguing structures from simple components. Capito *et al.* identify the possibility of a self-sustaining pathway in which static self-assembly and a kinetically regulated mechanism combine to generate diverse architecture and functions. This finding opens the way to exciting opportunities for novel materials that may stem from incorporating pathway-directing information into the constituents and processes of self-assembly.

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ECOLOGY

How Reefs Respond to Mass Coral Spawning

James Guest

A mass coral-spawning event at the Great Barrier Reef provided a natural experiment for studying energy and nutrient dynamics of the coral reef.

Coral spawning followed by successful larval recruitment is a crucial link in the persistence and recovery of reefs. Recent studies (*1*–*3*) have investigated the effects of a mass spawning event on coral reef biogeochemical processes. The research reveals how the fertilization pulse caused by spawning initiated a cascade of biogeochemical processes.

Hermaphroditic broadcast spawning is the most common reproductive strategy for reef-building corals. Broadcast spawning involves the release of buoyant, lipid-rich gametes (known as egg-sperm bundles) into the water column for external fertilization (see the figure). For sessile broadcast spawners such as corals, synchronous spawning within species is crucial to ensure cross-fertilization. Not only do populations exhibit synchrony, but it is common for different species to have overlapping spawning times. The first such "multispecies mass spawning event" was documented on the Great Barrier Reef (*4*), and similar events have since been witnessed in many locations (*5*). The most plausible explanation is that different coral species respond similarly but independently to timing cues and selective pressures to achieve maximum fertilization success within species (*4*, *6*, *7*).

Alternatively, spawning at the same time may saturate predators. Embryos and larvae

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