Heeding the Call of the Wild

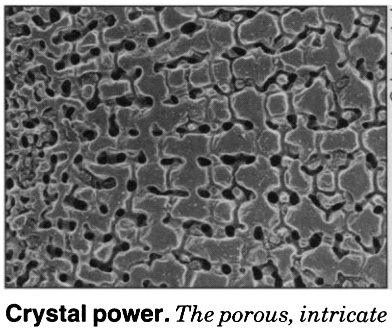
Drawn by the engineering brilliance embodied in biological materials, a growing number of researchers and entrepreneurs are getting into the business of biomimicking

IF NATURE COULD FILE PATENTS ON THE miraculous materials it has devised, materials scientist Joseph Cappello and his fledgling San Diego company, Protein Polymer Technologies, Inc., might end up paying out a lot of royalties. Biology has two prior claims on the company's very first product—an adhesive for gluing living cells to Petri dishes and other surfaces. The adhesive, which mates a molecular motif from spider's silk with one from a common blood-plasma protein that binds living cells to one another, could make lab technicians' lives a lot easier, Cappello believes. And he isn't alone in his debt to nature. A biology-savvy community of materials scientists is pirating its ideas from the living world—so much so that if species other than our own could demand intellectual tribute, a host of academic and corporate researchers would have to start crediting their best inspirations to mollusks, insects, and even rodents.

Some members of the tribe—known as biomimetic researchers—are unabashedly striving to reverse-engineer the ancient biochemical secrets that enable marine mussels to make some of the strongest adhesives in all of the oceans. Others are attempting to mimic the chemical and engineering virtuosity embodied in the tough, hard shells of abalones. Still others are filching ideas about making lightweight composite materials from beetle exoskeletons. "Nature has these wonderful solutions and exquisite structures that are far beyond anything we have now," remarks Michael T. Marron, molecular biology program manager in the Office of Naval Research (ONR), which has funded biomimetic materials research since the mid-1980s.

Not every materials scientist is sanguine that the lessons of biology can be translated to high-volume industrial processes (see box on p. 968). But Marron and his peers have dedicated themselves to proving the skeptics wrong. They hope to push the performance envelope of materials—creating, say, more capable armor, extra-durable textiles, or lightweight composite materials for advanced aircraft—by imitating the molecular makeup, microscopic architecture, and manufacturing processes of biological materials.

As biomimetic researchers see it, much of their basic R&D has been done for them—by the process of natural selection. "Nature has been developing materials for hundreds of millions of years," remarks Frederick L. Hedberg, program manager at the Air Force Office of Scientific Research (AFOSR), which oversees a modest biotechnology initiative that includes about \$500,000 for a handful of projects, among them the development of paint-stripping enzymes, marine adhesives, and aircraft materials based on biological models. Over the eons, evolutionary selection pressure has put millions of biological materials themes to the test, leading to today's long catalogue of durable, strong, fracture-resistant, elastic, energy-absorbing, lubricating, self-repairing, self-assembling materials. Inferior materials went the way of unsuccessful species, notes George Haritos, associate director of AFOSR.



Calvert, *et al.*

Crystal power. *The porous, intricate structure of a sea urchin spine is actually a single crystal of calcite.*

In that vast catalogue of biological materials, researchers have identified a common theme: They all reflect exquisitely precise control over composition and structure at every level, from atomic and molecular components through intermediate structures such as fibers and crystals on up to visible objects such as tendons, bones, and skin. That multilevel control is a skill that materials scientists are eager to acquire. "Learning from these complicated hierarchical material systems is the goal," explains chemist Eric Baer of Case Western Reserve University.

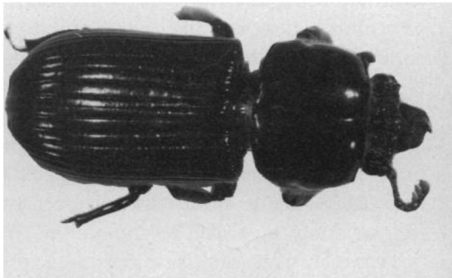
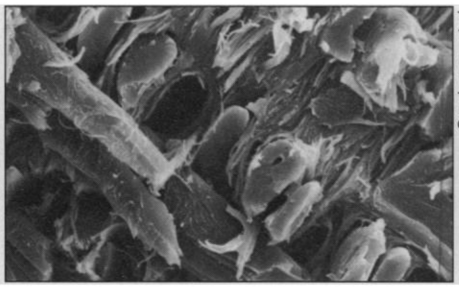
As an example, Baer cites collagen, a protein-based material found in connective tissue, tendon, tooth, and bone. Collagen fibers are structured rather like cables made up of bunches of twisted wire strands, with each strand a protein molecule. Thanks to that structure, they are strong, flexible, and tough, since the breakage of individual strands or bunches leaves the structure as a whole intact. Materials scientists could build better properties into their products by imitating that sort of microscopic hierarchy, Baer says.

He isn't preaching slavish imitation, however. Biomimickry most often involves borrowing nature's design principles but executing them in quite different materials (see opposite page). Stephen Gundersen of the University of Dayton Research Institute, for example, has been trying to imitate the multilayer construction that toughens the cuticle of the bess beetle, a biological composite turned up by one of Gundersen's colleagues during a literature search. But the resulting biomimetic materials—possible prototypes for strong, failure-resistant, and lightweight aircraft composites—would be made of decidedly unbiological materials such as epoxy resin and carbon fibers. Similarly, Paul Calvert and his colleagues at the University of Arizona are using synthetic ceramics and polymers to mimic the intricate architecture of mineral and protein found in rat's tooth.

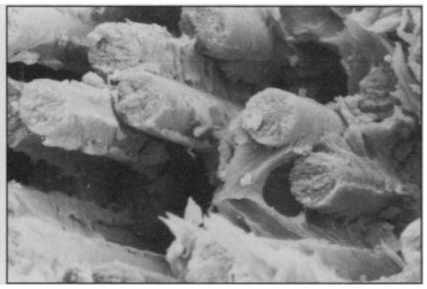
Translating such natural microstructures into lab-made materials, Gundersen, Calvert, and other biomimickers are finding, takes painstaking work. Standard laboratory techniques for making materials are ill-suited to giving researchers the kind of molecule-to-macromaterials control that results in something like collagen or insect cuticle. In making a material as simple as calcite (a form of calcium carbonate), for example, chemists and sea creatures couldn't be further apart at the moment. Chemists make calcite—the stuff of chalk and over-the-counter antacid pills—by precipitating it in bulk from a solution. The ions crystallize willy-nilly, most often into simple cubes. In sea urchins, a favorite object lesson for biomineralization researchers, calcite crystallization takes place within individual cells, which control the process to produce crystals with extremely intricate architectures: Witness the urchins' arrays of predator-deterring spines, each spine a single calcite crystal.

And that inspires biomimickers to learn not just what nature has done but how it does it, notes Stephen Mann, a chemist at the University of Bath who studies how organic structures resembling cell membranes can serve as precise templates for forming minerals. Mann, Ilhan Aksay and Mehmet Sarikaya

Biomimetic Materials and Their Natural Models

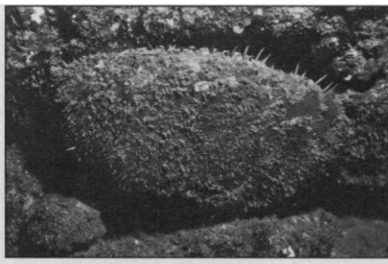



Gundersen, et al.



Sturdy as a VW bug? A bess beetle goes through life armored with an exoskeleton consisting of a protein matrix riddled with layers of chitin fibers, as shown in an electron micrograph *(center)*. The chitin layers are criss-crossed like the reinforcing plies in an old tire. The structure inspired a strong, lightweight composite *(right)* of epoxy polymer matrix with carbon reinforcing fibers.

Abalone architecture. In the tough inner layer of its shell *(center right)*, an abalone lays down calcium carbonate crystals in a bricklike pattern with a mortar of organic polymers such as chitin. The resulting material is not only strong but also fracture resistant, since a fissure is forced to take a tortuous path through the layered structure. The synthetic analogue *(far right)* consists of multiple layers made of a boron-carbide/polypropylene mixture alternating with thinner layers of polypropylene.



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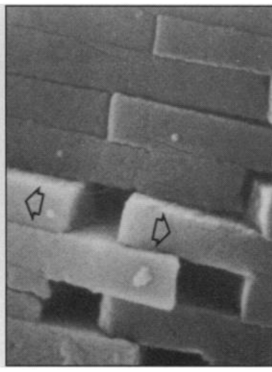
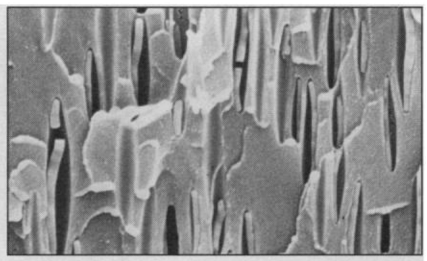


M. Sarikaya, *et al.*

I. Aksay *et al.*

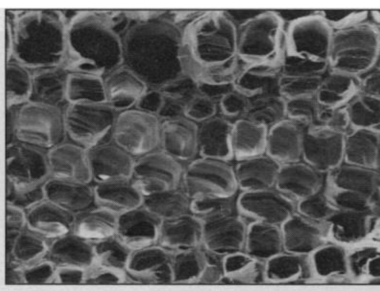
Animals Animals


Calvert, *et al.*



Rodent dentistry. Rats can gnaw through cans thanks to their tough, wear-resistant teeth. The secret lies in crossed rods of hydroxyapatite (a calcium compound that is also the main mineral in bone) embedded in collagen, a biological polymer. The structure *(center)*, has inspired a biomimetic material in which elongated particles of the mineral titania (TiO2) are distributed through a polymer matrix *(right)*.

Artificial wood grain. The cellular structure of Douglas fir wood *(right)* serves as a mold for depositing the ceramic precursor tetraethoxysilane. Water already within the cellulose of the cell walls hydrolyzes the precursor into a ceramic. Heating the preparation to 800 C gets rid of the cell material, leaving behind a cellular ceramic *(far right)* —strong but lighter than the monolithic material.



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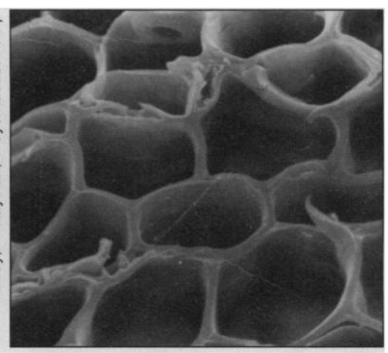


of the University of Washington, and others have been learning how to draw crystal precursors into tiny sacs or sheets made of phospholipids, the same kind of molecules that make up the membranes of living cells. The membranes serve as templates or, as Aksay prefers to call them, "nanoscale reaction vessels," for crystal growth. These scientists ultimately hope to use collections of such crystal-growing templates for controlling the size and shape of ceramic crystals and organizing them into technologically important forms—"elaborately structured ceramics, finely powdered catalysts, or single crystals of unusual shapes for electronic devices" are some of the possibilities Mann lists.

An important bonus, says Mann, is the fact that these tiny crystal factories work at normal temperatures and pressures. Indeed, that's typical for materials manufacturing modeled on biological processes. In contrast to the harsh conditions and toxic effluents of human manufacturing, living creatures make their own high-performance materials in aqueous environments, at low temperatures, and under physiologically friendly conditions. As a result, Calvert points out, biomimetic material making could lead to more environmentally sound manufacturing methods.

Still, the minuscule reaction vessels in which living things make the hard parts of their anatomies often cook too slowly for the purposes of modern industry, says Dan Urry, a University of Alabama materials scientist whose 10 years of work with protein-based polymers led to his founding of Bioelastics Research, Ltd., in Birmingham 2 years ago. "The clam makes its shell over a long period of time," he points out. So after discovering the rules by which animals slowly make bones, teeth, shells, and spines, biomimetic ceramic researchers need to learn ways of speeding up these biomineralization processes, he says. But Calvert suggests a simple remedy: using a feed solution more concentrated than the seawater from which marine animals extract the building blocks for their ceramics.

Researchers trying to harness biological polymer-making methods may face fewer hurdles in trying to scale up to industrial production, notes synthetic chemist David Tirrell of the University of Massachusetts. For one thing, organisms, especially when working en masse, can churn out natural polymers such as proteins at a good clip. For another, the path has been smoothed by biotechnology researchers, who are already engineering bacteria to produce proteins. Now Tirrell and others are harnessing bacteria to make artificial materials—specialized biomimetic polymers. Equipped with genes for the chemical units of the novel materials, the bacteria act as minuscule polymer factories, working in parallel by the billions.

Two early fruits of this strategy are Protein Polymer Technologies' cell adhesion product and the candidate products of Urry's fledgling company. Urry and his colleagues are developing a series of epithelium-like materials with a molecular structure partially mimicking the elastin proteins found in blood vessels, lungs, and other tissues that repeatedly stretch and relax. The Navy is interested in trying out such materials as resorbable surgical implants; by providing a compliant layer between a patient's tissues, the implants might prevent the painful and sometimes dangerous "surgical adhesions" that often form after an operation.

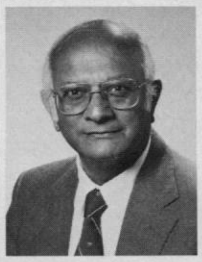
The small scale of these ventures emphasizes how far research and development on biomimetic materials still has to go. For now, many researchers are driven more by the thrill of uncovering and trying to imitate the exquisite match between biological form and function than by the lure of the market. "These are early days yet," Mann stresses.

And like any field in its infancy, this one faces threats to its future. For example, Marron of the ONR fears industry may not be willing to face development periods that could last 5 years or more, poor prospects for short-term gains, and the lack of any guarantee that biomimetic products will ever catch on in a marketplace raised on conventional synthetic materials.

Marron and like-minded scientists are biased, of course, but they see the potential payoffs of their work as more than making up for such uncertainties. Pursued to its limit, the most enthusiastic of the tribe will argue, the approach could even expand the definition of materials beyond the inert substances the word now conjures. Julian Vincent, an expert in biological materials at the University of Reading, puts it this way: "If some of the techniques of nature could be exploited, self-designing, self-adjusting, and self-repairing structures could be developed." Vincent and his fellow biomimetic researchers will have to pull off heroic feats to justify this dream, but if they do, they will have imitated not just the structures but the very dynamism of living material.

■ Ivan Amato

No Easy Lessons in Nature



Rustum Roy

A researcher's role in life might be described as pushing the bounds of optimism. That doesn't mean, however, that the materials scientists who are trying to imitate the products and processes of nature think their task will be simple (see main text). But their efforts to be pragmatic strike Rustum Roy, a veteran materials scientist at Pennsylvania State University who is known for his outspokenness, as pollyannaish. When it comes to the potential payoffs of biomimetic research, Roy also pushes the bounds—of pessimism. "Mimicking nature has the same chance as a snowball in hell," Roy told *Science*.

In a memo sent earlier this year to funding agencies—including the National Science Foundation, the Office of Naval Research, and the Air Force Office of Scientific Research (AFOSR)—and in other documents that have circulated throughout the materials science community, Roy has blasted the field. Exaggerated claims about the potential for mimicking biological materials and the technological promise it holds, he warns, can distort national goals for materials research.

Roy was prompted to write his memo by a research report and accompanying commentary that appeared in *Nature* on 24 January. He claimed the work—a biologically inspired experiment in which cadmium sulfide crystals were precipitated within a synthetic matrix—duplicated (without crediting) earlier studies published by him and others. The memo stressed that biomimetic materials researchers should scour the literature so as not to neglect crediting earlier researchers—a plea his fellow materials scientists mostly welcome. But Roy went on to question the concept of biomimetic materials as a whole.

As his complaint about credit shows, Roy himself has not been immune to the lure of biomimicking; in his ceramics research he has sometimes sought to duplicate natural mineralization processes. But those attempts, he says, taught him that the mild conditions biology uses—which enthusiasts tout as an added benefit of the biomimetic strategy—just don't allow materials to be synthesized fast enough for industrial purposes.

Many biomimickers acknowledge the need to find ways to accelerate natural processes, but they think it's too early to be discouraged. Besides, says AFOSR associate director George Haritos, "Nothing ventured, nothing gained."

■ I.A.