Stuck on Mussels

A mollusk's natural grasp of adhesive science captivates biochemists

By IVAN AMATO

Isaac Newton himself floated the challenge in 1704. "There are agents in Nature able to make the particles of joints stick together by a very strong attraction, and it is the business of experimental philosophy to find them out," he wrote in his *Opticks.*

J. Herbert Waite, a modern-day experimental philosopher, took Newton's mandate to heart.

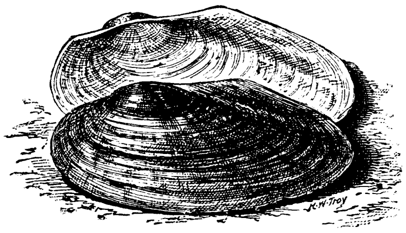
"Adhesives have become an integral part of our lives, extending from the cradle to the grave," observes Waite, a marine biochemist at the University of Delaware in Lewes. "As infants, we wear disposable diapers with tape closures, and as corpses, our orifices are sealed by undertakers with cyanoacrylates." On a less macabre note, manufacturers of everything from shoes to cars to furniture rely increasingly on glues. And as glue use spreads, adhesive failure causes far more headaches than it did in the days when nails, screws and welds did most of the joining.

For the past 20 years, Waite has made it his business to learn how the marine mussel *Mytilus edulis*—the indigo-shelled bivalve that often ends up in soups and appetizers — manufactures an underwater adhesive that ranks with the world's best. No synthetic glue designed for watery settings comes close to rivaling nature's own, he says. Sooner or later, water's many acts of adhesive vandalism cause synthetically bonded surfaces to come unglued, usually with the help of mechanical stresses. Water can chemically degrade or deform adhesive materials. Moisture can form a weak boundary between bonding surfaces. In cold settings, freezing and thawing can pry glued parts apart. Like oil and vinegar, adhesion and water just don't seem to mix.

And that makes biological adhesives all the more enviable, Waite says. "All living things in nature are exquisitely assembled from adhesively bonded parts," he noted in October at a meeting on biomolecular materials in Washington, D.C. Despite constant encounters with water, plants and animals need no nuts, nails or bolts to keep from falling apart.

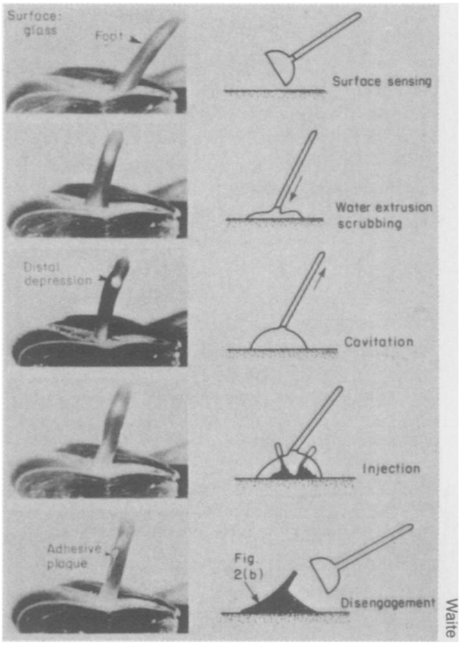
If nature can make underwater adhesives without human assistance, what might humans concoct with assistance from nature? Water abounds in many places where reliable adhesives would be quite handy. Doctors, for instance, have been eyeing surgical glue for use in tissue grafts, sutureless operations and dental applications (SN: 4/11/87, p.234), and the Defense Department could use environmentally sound, corrosion-resistant, slime-deterring, barnacle-repelling coatings and adhesives for marine applications. It costs a lot of tax dollars to drydock an aircraft carrier for hull repairs.

Yet Waite has found that mussels don't divulge their sticky secrets without plenty of prying.



To a mussel, adhesion means everything. Failure to cling to rocks or other stable surfaces in the turbulent ocean would doom these shelly creatures to rapid pulverization. For the past 300 million years or so, mussels and other bivalves have largely avoided that fate with a remarkable material called byssus, woven into tough, fibrous threads that enable the animals to anchor themselves—like rock climbers on a windswept cliff—to underwater strongholds. Neither wave, nor salt, nor tide of night can tear a mussel from its chosen site.

Byssus binds more powerfully, more rapidly and more persistently to more hard surfaces than any synthetic adhesive for underwater applications, Waite says. "This animal is at the cutting edge of marine adhesive technology."



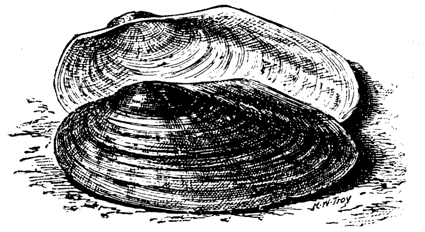
The mussel's plunger-like foot performs many jobs during the processing and deposition of byssus threads.

The mussel adhesive, which Waite likens to "externalized tendons," derives its material virtues both from its precursor ingredients and from the intricate processes the mussel uses to transform those precursors into byssus lifelines. Though the biochemical picture of byssus remains incomplete, it has already inspired BioPolymers, Inc., in Farmington, Conn., to make and market a research glue based on mussel-derived proteins, which biologists can use for attaching cells to surfaces in moist environments such as petri dishes. And Genex Corp. in Gaithersburg, Md., announced this summer it had cloned the mussel gene coding for a precursor of byssus' major protein component — an advance that might someday lead to mass production of synthetic byssus. Extracting and purifying the naturally occurring substance from mussels takes a great deal of time, effort and money.

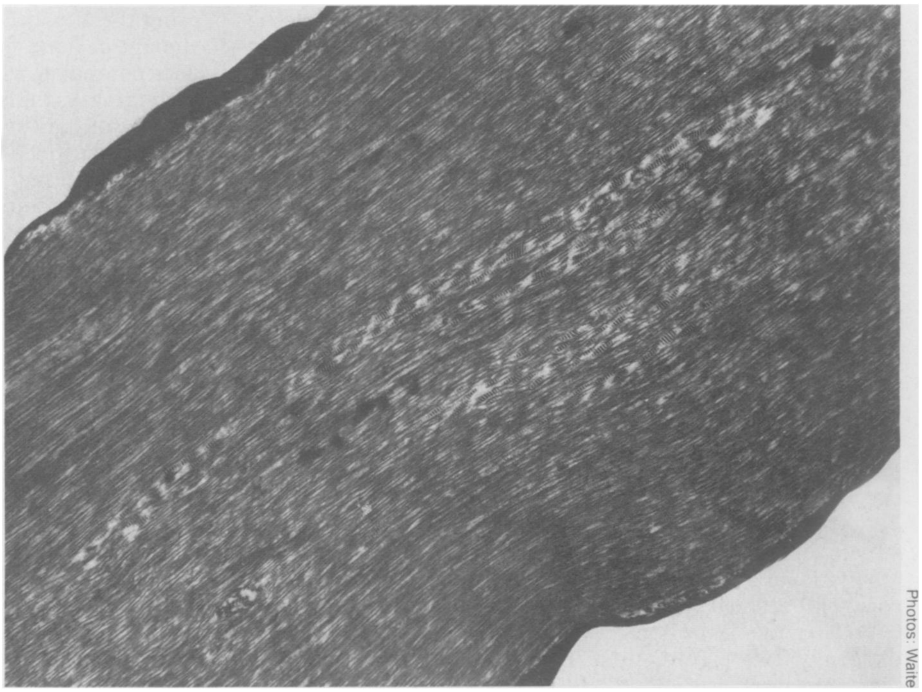
Like the silk threads of spiders and silkworms, mussel byssus consists of highly insoluble polymer fibers that form as liquid precursor ingredients get pushed through thin ducts. It also resembles the fiber-reinforced composite materials used in tennis rackets and aircraft. The bioadhesive fibers—made of keratin, the same rod-shaped protein molecules that make fingernails and hooves so tough — run through a resin component consisting primarily of a polyphenolic protein. Catalyzed by an enzyme called catechol oxidase, the resin's protein molecules link into an intertwined matrix that imprisons the keratin-based reinforcing fibers. The mussel coats each thread with a protective varnish, also made of polyphenolic protein molecules linked by catechol oxidase. With a varnish coat some 10 to 20 microns thick, each thread measures about 100 microns in diameter — about the same width as a human whisker.

After years of painstaking work, Waite and his colleagues have determined that the polyphenolic resin protein consists of nearly identical linked segments — each a string of 10 amino acids — repeated 80 times. The protein contains an abundance of specific amino acids, such as serine and threonine, that have "sticky" chemical appendages known as hydroxyl groups, which consist of an oxygen and a hydrogen atom. It is also rich in the amino acids tyrosine and proline. Enzymes modify the tyrosine and proline so that they, too, have hydroxyl groups or chemically related quinone components that allow the protein to link up readily with nearby resin molecules.

"It's a very unusual protein," says Robert L. Strausberg, director of research at Genex.

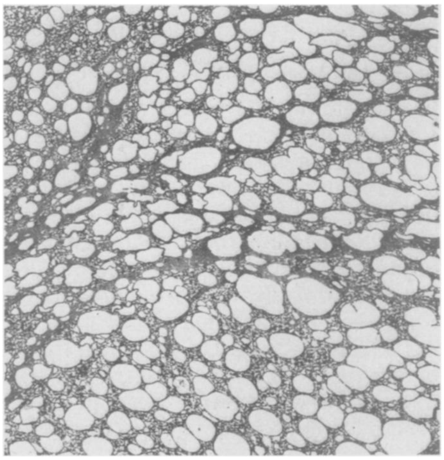


But an understanding of biochemical components does not an underwater adhesive make, Waite says. It's like trying to prepare a gourmet dish with an ingredient list but no recipe.



Cross section through the long axis of a byssus thread shows polyphenolic resin core (dark) with reinforcing keratin fibers, which appear as thin, striped inclusions.

Photos: Waite



Cellular, foam-like structure of the adhesive thread where it anchors to a polyethylene surface.

To find out just how mussels whip up their finished product from precursor ingredients, Waite has spent much of the last decade watching the shelly chefs at work.

Plucking mussels from a nearby bay and scrutinizing them in the lab, he has observed that they make and stockpile a "preadhesive" — the resin protein, fiber protein and catalyst — in a special gland, converting these raw ingredients into byssus as the need arises. But before that conversion takes place, the animal must tackle several chores, starting with the selection of a suitable anchoring site.

To assess a site, it scans the surface with its "foot," an incredibly versatile appendage resembling a rubber plunger. Waite suspects that as the mussel pulls its foot along the surface, it gets a "feeling" for the amount of resistance and can thus sense the potential for a secure bond.

Even if the surface passes the resistance test, moisture, grit, microbes and other undesirables can thwart adhesive bonding, either by physically blocking the surface or by chemically degrading the bonds that do form. So the mussel cleans house, using its foot like a broom to sweep away loose particles. Next, the water around the bonding site must go. That's a formidable task for a spineless creature surrounded by ocean, but the all-purpose foot paves the way. As the mussel presses its foot down, the flattening plunger squeezes water away from the surface. The mussel then contracts its foot muscles to enlarge the interior of the plunger, creating a vacuum in the expelled water's stead.

The preadhesive ingredients then surge through tubules connecting the storage gland to the plunger. From there they flow to a half-dozen injection ports located in the top of the plunger's bell until they finally reach the vacuum-surrounded anchoring site.

In less than a minute, the resin near the anchoring surface transforms into a foamy network of cell-like bubbles. Making foams usually requires some sort of gaseous blowing agent, but Waite says

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He points to other lines of research that support his argument. For instance, psycholinguists established nearly 20 years ago that people presented with true and false sentences generally take less time to determine the accuracy of the true statements. One research team wrote that when individuals read assertions, they "start with the truth index set to true."

Psycholinguistic work also suggests that the comprehension of a denial (say, "armadillos are not herbivorous") first involves grasping the concept under dispute ("armadillos are herbivorous"). A Spinozan mind employing this mental tactic should at times believe what has clearly been denied, Gilbert points out.

A 1981 study directed by psychologist Daniel M. Wegner of Trinity University in San Antonio, Texas, illustrates this paradox. In a finding of particular interest to journalists, students who read propositions such as "Bob Talbert not linked to Mafia" reported markedly more negative impressions of the fictitious Talbert than did students who read neutral statements such as "Bob Talbert celebrates birthday."

People also automatically tend to seek out evidence that confirms their beliefs about others. Studies have shown, for example, that volunteers led to believe in the outgoing nature of a young woman later asked her questions concentrating on the extent of her sociability, while neglecting to probe for shy or reticent aspects of her personality.

In related work, psychologists studying persuasion and lie detection have observed that people often believe what others tell them without question. Opinions about others, as well as autobiographical claims, often gain acceptance more readily when the listener performs a competing task that diverts attention from the speaker's message.

"People who sell used cars and vacuum cleaners have long known about the persuasive power of timed interruptions and diversions," Gilbert notes.

Many brainwashing and coercion techniques rely on extreme methods to fragment the attention of political prisoners, he adds. Interrogators often keep prisoners awake for days at a time and then browbeat the exhausted captives with an ideological barrage they find difficult to resist. Forced confessions also exert insidious effects: After writing and reciting a captor's message many times over, weary prisoners start to doubt their own opinions.

The same principles extend beyond used car lots and dictators' dungeons, warns psychologist John A. Bargh of New York University. "My hunch is that control over automatic, unconscious influences on judgment and behavior is not usually exercised," says Bargh, who co-edited a compilation of research on the subject (*Unintended Thought,* 1989, Guilford Press, New York). "It's not that people are lazy. They tend to think these influences don't exist, and often don't have the luxury of extended thought about what they hear or read from moment to moment."

Moreover, Gilbert argues, just as healthy people immediately believe what they see, doubting their eyes only on rare occasions, so must they initially believe what they read or hear, if only for a fleeting moment.

Gilbert and his co-workers have yet to study whether distracted attention increases the likelihood of believing obviously outrageous assertions. Although Spinoza's theory holds that a statement such as "Hitler was a woman" meets instant acceptance and almost as quickly goes up in flames as contradictory evidence leaps to mind, that prediction proves difficult to study in the laboratory.

Despite gaps in scientific knowledge about belief formation, "the burden of proof has shifted onto Descartes' theory," Gilbert contends.

For now, though, a 1984 Gallup poll of a national sample offers a bit of comfort to the much-maligned Spinoza: One in five respondents referred to supermarket tabloids as "accurate."

Who knows? Tabloid believers may regularly suffer from attention meltdown in the checkout line upon hearing their grocery bills. ☐

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mussels manage to fabricate the sticky foam without any blowing agent. Just how they do this remains a mystery, he adds.

The bubbles, with walls just five-millionths of a centimeter thick and one-half micron in diameter, comprise very little material. Yet the foam's marshmallow texture enables it to withstand relentless compression from pounding waves, tugging from retreating tides, and virtually all other forces (except Waite's yanking when he harvests them) that would break the adhesive will of almost any other glue.

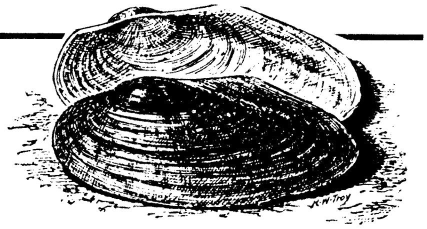
With its beachhead thus secured, the mussel uses its foot like an industrial injection-mold machine that shapes plastic products. Muscle action flattens the foot into a spatula and then curves the edges toward one another to form a hollow cylinder. The mussel pumps additional preadhesive into this foot cavity, where each dose of the viscous substance cures into a fine thread in just a few minutes.

By slightly varying the composition of the preadhesive, the mussel gives extra elasticity to byssus threads at the shell end. "It gives them a shock absorber," Waite says. Once the polymers have cured into several-inch threads, they get a coat of varnish.

Waite notes that catechol oxidase – the enzyme that links the protein molecules in both the resin and the varnish – is also used to cure or tan leather and other animal products. He has discovered that mussels possess an unusual abundance of the enzyme. In most catalytic reactions, a single enzyme molecule will process a million or more target molecules. But the mussel resin contains concentrations as high as one catechol oxidase molecule for every two or three polymer molecules.

Waite suspects that the catalyst, as part of "nature's sublime economy," does double duty as a structural component in the threads. He says he knows of no other case in nature where an enzyme also plays a structural role. Whether catechol oxidase actually does so awaits further study.

Waite also suggests that mussel adhesive might qualify as a "smart" material – that is, a material that can change some property, such as its color or stiffness, in response to changing environmental conditions (SN: 3/10/90, p.152). Catechol oxidase uses dissolved oxygen molecules to form the links between polymer molecules. Because turbulent waters provide more oxygen than calmer waters, the curing rate of freshly secreted threads is faster in rougher waters – just when the animal might need to get stuck most quickly.



As more of the mussel's adhesive secrets give way to scientific sleuthing, an industrial supply of mussel-inspired products seems closer to reality. Genex scientists have inserted the gene for the resin protein into yeast cells, which now churn it out in gram-sized batches. By using enzymes extracted from mushrooms or bacteria to mimic the tough-to-get mussel enzymes, the Genex researchers say they can elicit the polymer's adhesive properties.

Animal studies of sutureless wound healing using this recombinant mussel adhesive are encouraging, says Strausberg, who adds that plastic surgery and reuniting severed nerves rank high on the long list of potential applications. "This [adhesive] is one of our major projects," he says. "We think it has a lot of potential."

Synthetic mimics have yet to match the material marvels of natural byssus. But if Waite and others succeed in harnessing mussel power, their efforts could lead to a big, sticky business – a consequence unanticipated even by the far-sighted Newton. ☐