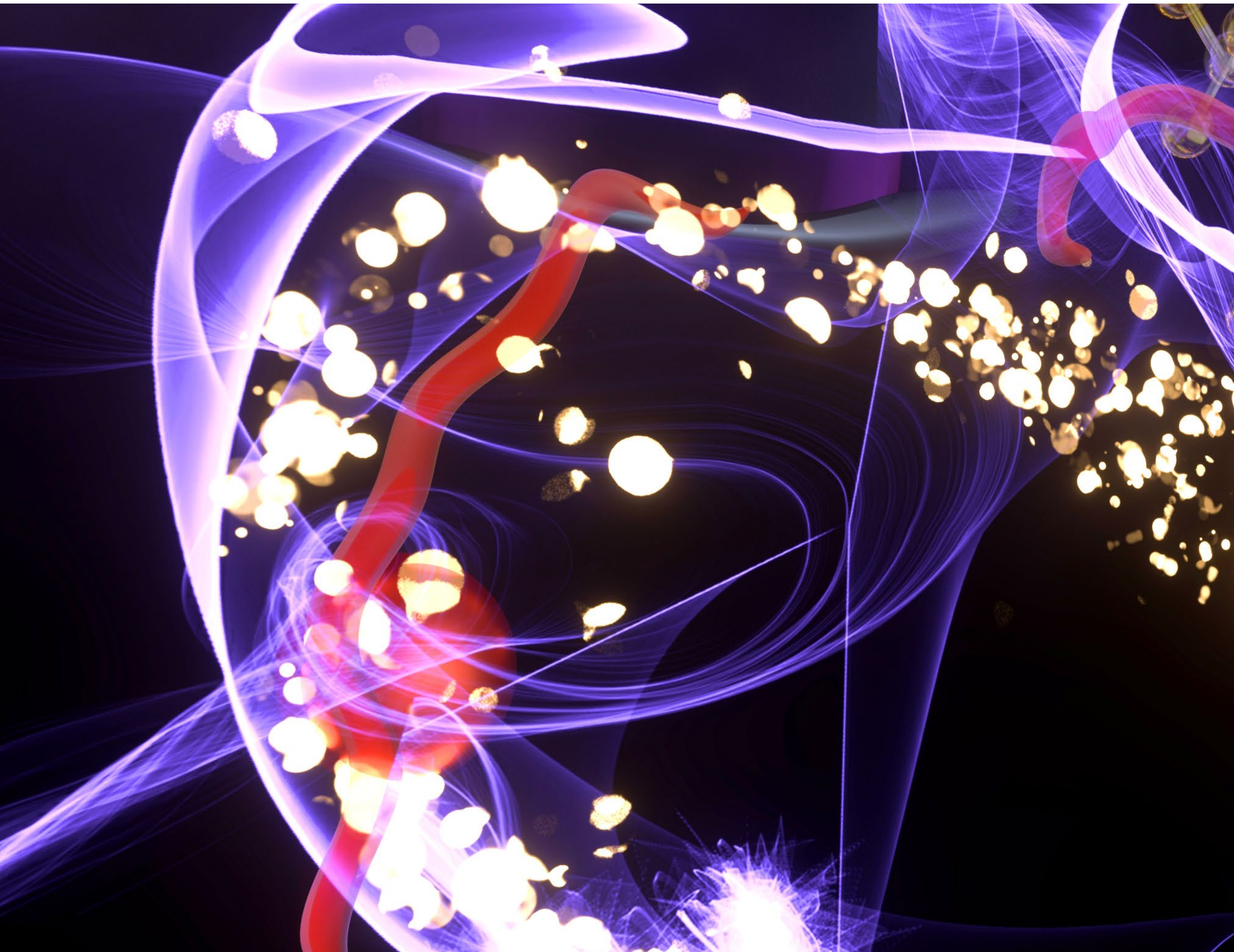
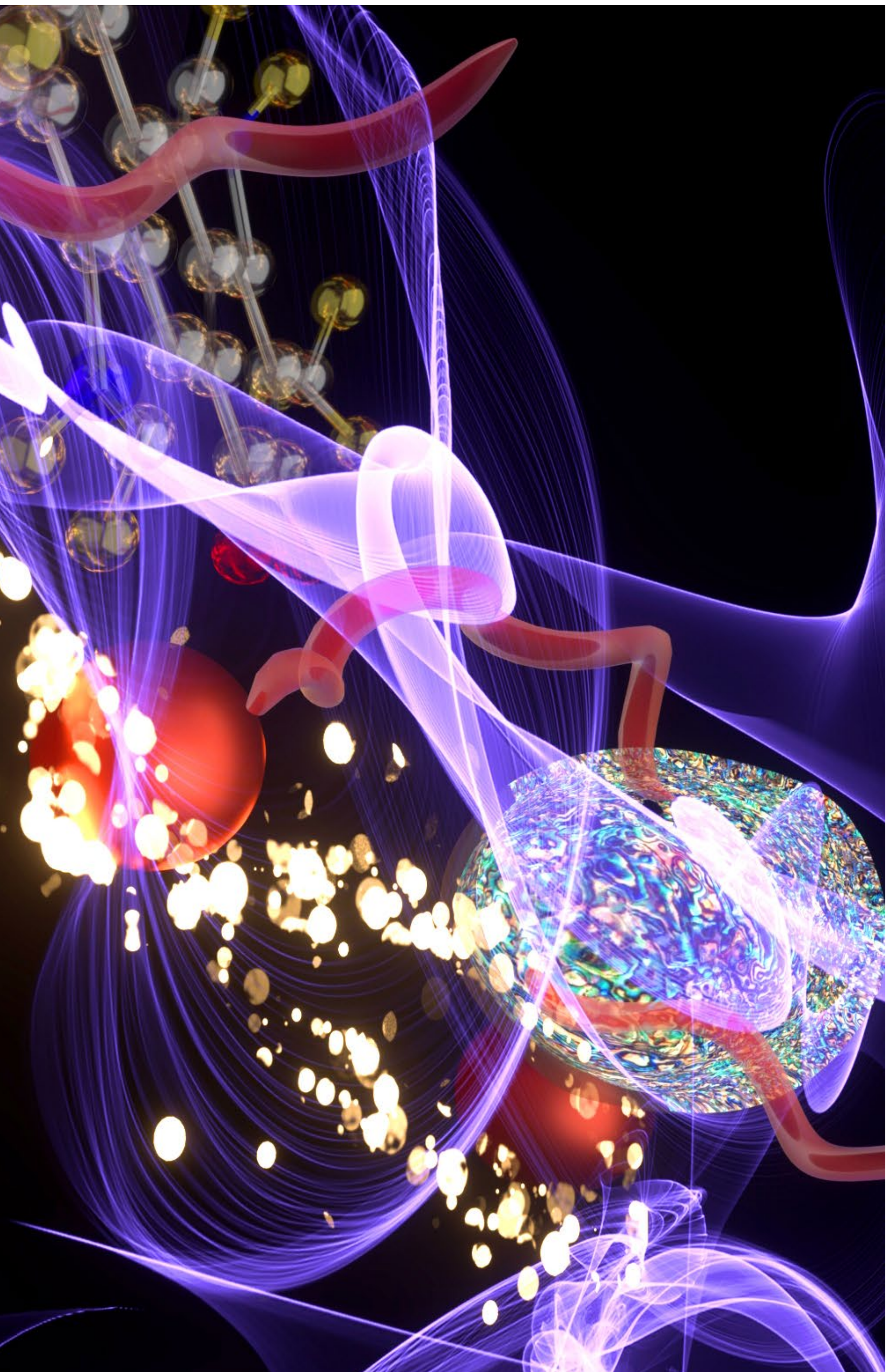
THE **BLOODWORM** ... AND OTHER **MARINE MAGICIANS** OF **BIOMINERALIZATION**



A UCSB tale of curiosity-driven faculty, tenaciously applied expertise, and the pursuit of new materials via long-term collaborations that blur the lines of disciplinary divides



Last April, *The New York Times* ran an article about a marine creature known as the bloodworm, or *Glycera dibranchiata*. Upping the *Eek!* factor of the creature, which is not especially handsome or friendly, was a horror-film-fodder headline proclaiming that the roughly seven-inch-long worms, which burrow into intertidal-zone mud and are a favorite bait for New England fishermen, "grow copper fangs and have bad attitudes."

The article did eventually mention that copper makes up only one to ten percent of the worm's fanglike jaw, depending on location, and it quoted a pair of researchers from UC Santa Barbara, where the vast bulk of bloodworm research has occurred: **Herb Waite,** a renowned marine biochemist and a professor in the department of Molecular, Cellular and Developmental Biology (MCDB); and **William "Billy" Wonderly,** one of Waite's PhD students, who graduated in December 2021 after writing his dissertation on the composition of the worm's jaw. A chapter of that work, published last June in the journal *Matter*, inspired the newspaper article.

As a daily news outlet, the *Times* necessarily focused on only a tiny segment of what is actually a very long arc of interconnected research that began in the 1970s with investigations into materials produced by other marine creatures.

That longer story says a lot about the often-unpredictable evolution of scientific inquiry. It speaks to the brilliance of nature as creator and to the value of both the undiluted curiosity of people like Waite in bringing oddities such as the bloodworm into the scope of scientific investigation, and to the tenacious application orientation of engineers who build on that knowledge to develop new high-performing materials. And it sheds light on the kind of highly collaborative, long-term interdisciplinary scientific investigation, so prevalent at UCSB, that has allowed the College of Engineering (COE) and STEM disciplines across campus to develop top-tier international standing without enormous research endowments.

Finally, the full, ongoing story of the bloodworm research, as well as related long-term investigations of other high-performing biomaterials, speaks to the value of the National Science Foundation's (NSF) Materials Research Science and Engineering Center (MRSEC) model and the Interdisciplinary Research Groups (IRGs) it mandates. (See sidebar on page 27.) As a PhD candidate, Wonderly presented regularly in IRG 3, "Resilient Multiphase Soft Materials," co-led by mechanical engineering professor and co-director of the California NanoSystems Institute (CNSI) at UCSB **Megan Valentine** and professor of chemical engineering **Matthew Helgeson,** who, with Waite, is listed as a co-author on Wonderly's paper in *Matter.*

UCSB has leveraged collaboration not only to generate numerous high-impact scientific breakthroughs, but also, increasingly, to attract multiple large awards from the NSF and other funding organizations to support a range of important centers and institutes built upon collaborative interdisciplinary models.

Collaboration and Diverse Systems

Like the *Times,* Waite, Wonderly, and their colleagues are interested in the copper in bloodworm jaws, but as part of an intricate system in which it interacts with other natural components — especially a melanin-like substance and a protein that has an unusually simple structure — to create an extremely hard and shatter-resistant functional biomaterial. UCSB materials scientists are interested in using that knowledge to develop new synthetic materials.

"Hardness is something you want in a blade or a tip that you use to penetrate something, but high hardness usually comes with high stiffness, which means brittleness," Waite explains. "The properties we saw in the worm jaw were really counterintuitive, a combination of high hardness but relatively low stiffness. A penetrating or cutting tool made from such material is going to be tougher and less brittle."

"A common denominator that interests us in all these materials is their amazing strength given their light weight," says **Paul Hansma,** UCSB emeritus professor of physics, whose innovations in atomic force microscopy (AFM) enabled it to become an indispensable tool for atomic-level characterization of biologically produced minerals.

Physicist Paul Hansma with an atomic force microscope he built. During years of biomineralization research, Hansma enabled multiple breakthroughs and developed innovative techniques that led to the instrument's widespread use among biologists.

> "Hansma developed an AFM technique to measure the step growth of a crystal — the deposition of atoms as it grows — and suggested using it to view the crystal structure of abalone shell."

Through the years, the bloodworm research has spilled over to, inspired and been inspired by, and occurred alongside of or in conjunction with related long-term investigations into an array of biomaterials, including human bone, spider-web silk, sticky mussel filaments, abalone shell nacre, the pigment cells that enable cephalopod bioluminescence, the silica-based glass spines of certain sponges, and the silica cell walls of diatoms (single-celled algae).

"What we're trying to do in IRG 3 is understand how the processing of the material occurs — not just what chemicals are there but how they have been put together and the order of operations and how they are mixed and handled," says Valentine. "We want to know how that piece of it leads to the mechanics. What's the recipe?"

Regarding the bloodworm, which was highlighted in the UCSB proposal for a previous six-year round of additional MRSEC funding, she says, "We knew that the extraordinary jaw material existed and that the organism could make it. Some of the components and some of the composition were known, but the details of exactly how this was done and, more importantly, how we might be able to think about leveraging them to work in an engineered environment — those were things we didn't know."

"If you can extract out and identify the critical components that an organism uses that are different, then you can understand how the natural system operates and how you can design synthetic systems to take advantage of that," says **Craig Hawker,** co-director of the CNSI at UCSB, the Alan & Ruth Heeger Chair in Interdisciplinary Science, and a Distinguished Professor in Materials.

Professor of materials and chemistry **Galen Stucky** brings yet another perspective to the topic. "The creation of life on Earth is based on the dynamical integration and cooperative assembly of inorganic and organic species into composite living biosystems," he says. "The interest for me is understanding the chemistry of that assembly, the functional interfacial relationship between the organic and inorganic components of the resulting biological systems, and how biosystems interact with their surrounding ecosystem. We're always asking, *How does a dynamic, functional system evolve from atomic and molecular parts?"*

"There's something really fascinating in an interdisciplinary way about what these organisms have evolved to do, but these biological systems are constrained to specific conditions or applications that can benefit from some evolution-selected advantage," says UCSB chemical engineering professor **Brad Chmelka.** "We want to understand the physicochemical origins of the biological processes that form such fascinating, often multifunctional, materials and their corresponding atomic-level compositions and structures. From there, we seek to exploit such insights to develop new synthesis strategies for preparing non-biological materials having novel properties. That's the biomimetic angle, which can liberate us from the requirements that are otherwise set by the physiology of an organism and the conditions it might need for survival. Such biomimetic approaches open new opportunities for expanding the conditions by which new multifunctional materials are formed,"

"It's research that brings together two different types of people," says Waite, who began working on the unique materials produced by marine organisms as a PhD student in the 1970s, conducting research on the byssal threads that mussels use to cling to rocks in turbulent tidal zones, a major focus of MRSEC-funded research at UCSB for more than a decade. "On the one hand, you have the creature people, and then you have the materials people. It's a meeting and a collaboration.

"There are very few engineers who are interested in the general idea of creatures making adaptive structures to survive in their daily challenges," Waite adds. "However, if you report a bizarre materials property, that's where they usually get hooked. UCSB is special in that there are a lot of engineers here who are at the cutting-edge of materials analysis and are fascinated by working on bio-inspired materials."

The Worm's Turn

When Wonderly began his doctoral work at UCSB, he entered something of a research desert. Even figuring out where to begin the search for the bloodworm-jaw "recipe" that Valentine spoke of above proved difficult, because Wonderly had to restart long-dormant research and find a direction for his own work on a subject about which little foundational knowledge existed. "It's such a complicated system; it took me years to really understand what was going on," he says.

The first paper relevant to the bloodworm jaw was published in 1980 by a pair of British researchers, who reported copper concentrations of up to thirteen percent in the jaws of a related bloodworm, *Glycerasp.*

Waite, a collector of such biomaterial-related oddities, kept the article. Then, in 2001, an Austrian postdoctoral researcher named **Helga Lichtenegger,** who for her PhD research had used high-resolution synchrotron X-ray scattering to study bio-nanocomposite materials, arrived at UCSB to study in the lab of Galen Stucky. He introduced her to Waite, with whom he had previously collaborated on a variety of projects related to biomineralization in marine organisms. Waite shared the jaw-copper paper with Lichtenegger and Stucky. "I kind of reached into my grab bag of zoological model systems and thought of the bloodworm, which is the only organic system apart from lichens to concentrate copper," Waite recalls. "We knew that, but no one had taken that knowledge further."

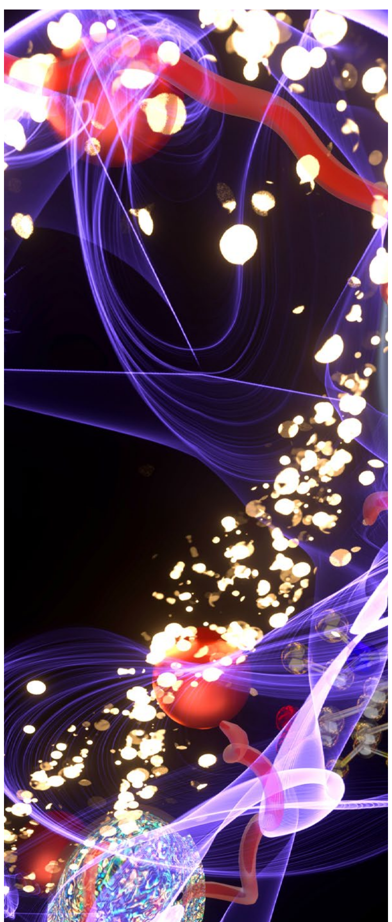
Lichtenegger got to work, and in 2002 she published a paper in *Science* that, Waite recalls, "received a huge amount of attention in the press."

"Helga did the first mechanical studies of the jaw, identifying the protein composition, showing a regional distribution of the copper, and determining that it is present primarily in mineral form, as atacamite," Wonderly says, adding that Lichtenegger, an expert in X-ray diffraction, did a follow-up study that was "more of a technical X-ray analysis of the jaw."

Waite notes, "There were informational tidbits that came out of that research period: that parts of the jaw contain a lot of copper in mineral form, that other parts, the best-performing parts, contain just a little bit of ionic copper, and that the other two components are protein and melanin."

After Lichtenegger returned to Austria, a PhD student in Waite's lab, **Dana Moses,** continued the bloodworm research, beginning in fall 2004. She identified the presence of the melanin-like material in the system and determined the composition of the jaw, as well as the role of a surprisingly simple protein — so simple that Waite initially hesitated to call it a protein — that makes up about forty percent of the jaw and that, unlike most proteins, which are far more complex, is composed almost entirely of just two amino acids: glycine and histidine.

When Moses graduated, there was no one to continue the bloodworm work, which then lay idle for about eight years, until 2016, when Wonderly arrived. He became part of a large interdisciplinary research family that had been growing and collaborating for several decades.



Mechanical engineering professor and California NanoSystems Institute and IRG 3 co-leader Megan Valentine wants to understand the "recipe" used to make amazing natural materials.

Beginnings

Back in the late 1970s, a group of UCSB professors began an unfunded ad hoc collaboration that had its beginnings in a field trip to the Channel Islands.

"A faculty colleague in another department took my wife and me to Santa Cruz Island for a weekend," recalls **Daniel Morse** (MCDB), a self-described naturalist who has studied biomineralization processes in marine creatures extensively, from the perspective of the genes and proteins that direct them. While on the island, he recalls, "I looked down into a tidepool and saw hundreds of abalone just bumper to bumper to bumper. It was a natural phenomenon, and I wondered, *what causes that?* I wanted to see if I could understand it."

Morse and Waite had been collaborating since the early 1970s, when Waite was still at the University of Delaware and would come to UCSB to work with Morse on research related to another marine protein. As a spinoff from Morse's abalone research, he discovered the trigger molecule that makes worm larvae settle and metamorphose. The worms use that same molecule as glue to build the tubes where they live. Waite elucidated the structure of the glue protein, discovering it to be very similar to the chemical in mussel glue.

Back in his UCSB lab, Morse started trying to generate baby abalone to see what controls were involved. He first discovered the trigger that causes them to spawn, releasing eggs and sperm, an investigation that became the cover article of the April 15, 1977 issue of *Science*.

April 15, 1977 cover of SCIENCE. Reprinted with permission from AAAS

The 1977 SCIENCE *cover from Daniel Morse's research, which unlocked the secrets of spawning abalone.*

"We soon had millions of larvae swimming in the plankton, cute little things," he recalls, "but they wouldn't settle out of the plankton or metamorphose. They would just die. They required a molecular signal to trigger activation of their genes to metamorphose, develop, and grow."

With that clue, he and his wife, **Aileen Morse,** discovered the natural trigger for their metamorphosis, a molecule produced by algae that cover the tidepool rocks, which the larvae recognize with chemo-sensors. "We isolated the molecule and found a simple substitute for it, so, now we could trigger one hundred percent of the larvae to settle, metamorphose, and start to grow as juveniles," he explains. (While Morse began the work as a way to study how genes control early development, the discoveries it yielded would prove critical in enabling abalone aquaculture, which saved the California abalone after the wild population was nearly eliminated by disease, pollution, and climate change.)

Some years later, in the early 1990s, Morse recalls, he heard a knock on his door at UCSB. "It was this tall guy who said, 'I'm Galen Stucky. I'm in chemistry. I understand you're studying abalone shell,'" Morse recalls. After explaining to Stucky that he was indeed "triggering the development of abalone to study tissue-specific gene expression and protein synthesis leading to development," Stucky asked, "Have you ever thought of the shell as a *material?*"

Stucky explained that he had been working with Hansma, making use of his advancements in atomic force microscopy to study how small organic molecules influence and control crystal growth, and that they were interested in studying more biological systems. Hansma's atomic force microscopy work in that realm would lead to multiple breakthroughs, including the first one in the abalone-shell research.

Soon, Stucky, Morse, and Hansma began meeting every week in the conference room in the Marine Biotechnology Lab. "At first, there were a few students sitting on the sidelines away from the table and three professors at the table," Morse recalls. "As we discussed how the shell might be built, we'd ask each other questions, and one of the professors would jump to the board and sketch out a possible answer. Soon, the graduate

Herb Waite, shown here as a young professor with mussels in an aquarium, brings a sense of wonder to his work. His files are filled with curiosities from the sea, like the bloodworm, the jaws of which may inspire new materials.

students were also going to the board. We were trying to get at the fundamental bio-physical mechanisms behind these materials. Some of us thought of the genes and proteins that must control the process, while others thought about how the minerals and crystal growth completed the picture. This always led to hypotheses, which grad students would test in the lab."

"It was a great learning experience for everyone," Stucky adds. "The discipline languages of physics, chemistry, and marine biology, and the different ways faculty thought became translated into a common universal scientific language that opened up new perspectives for all."

The process resulted in significant findings. "We started getting cover articles in *Nature* and *Science*, because we were making breakthroughs and overturning dogma that had stood for more than a hundred years in the field of biomineralization," Morse says.

Brad Chmelka soon joined the group, bringing expertise in nuclear magnetic resonance (NMR) spectroscopy and chemical interactions at the atomic level, and then came EEMB ecologist and marine oceanographer **Mark Brzezinski,** whose work on the biological synthesis of silica complemented the lab work of Stucky and Chmelka, and **Tim Deming,** a UCSB materials professor (now at UCLA) and an expert on functional polypeptide materials who was making synthetic proteins.

Eventually, the group secured a Multidisciplinary University Research Initiative (MURI) grant, with all six members co-equal PIs and funding from the Navy Research Office, the Army Research Office, and NASA, all of which focused on biological and bio-inspired materials.

"All of the projects were based on the remarkable properties of biomaterials, like the abalone shell, which is made so strong by nanocomposites, which are also intimately integrated in the bloodworm jaws," Morse says. "It's a similar underlying concept, with different materials. The organism has this kind of nanoscale machinery that temporally and spatially governs the differential secretion of the proteins that direct the final composition of the composite material."

During that period, Hansma developed an AFM technique to measure the step growth of a crystal — the deposition of atoms as it grows — and suggested using it to view the crystal structure of abalone shell. One of Stucky's graduate students, **Srin Manne,** did the microscopy and quickly discovered a conundrum: multiple layers but a single crystal. The mystery, Morse says, was "There's a very thin layer of protein between the crystal layers, so how could it be that each thin layer is capped by a protein but the crystal continues to grow?"

From there, Morse recalls, "We discovered the presence of nanopores that are located randomly in each protein sheet. Their random placement causes the penetrance from the previous layer to be offset laterally, creating the interlocking brickwork of crystal platelets that contributes to the shell's incredible toughness, which is three-thousand-times more fracture resistant than chalk, which makes up ninety-five percent of the shell."

"The idea for a century or more had been that the protein

The day that Galen Stucky walked into Dan Morse's lab and asked, "Have you considered abalone shell as a material?" marked the beginning of a highly successful long-term collaboration.

> "In a paper published in *Nature* in 1999, Morse, Hansma, and their co-authors posited another enormously important hypothesis, describing "sacrificial bonds" and "hidden length" in proteins, which offered a new explanation for the toughness of natural composites like abalone nacre and bone."

Dan Morse examines the silica-based glass skeleton produced by a marine sponge "at low temperature, without the need for a furnace or acids or caustic solvents, so that it's benign and compatible with life."

sheet that covers the first layer of mineral acts as a kind of template to initiate the de novo growth of the next layer, in a repeating process," Morse explains. "But following Srin's microscopy work, we said, 'The new paradigm is this.'"

In a paper in *Nature* in 1999, Morse, Hansma, and their co-authors posited another enormously important hypothesis, describing "sacrificial bonds" and "hidden length" in proteins, which offered a new explanation for the toughness of natural composites like abalone nacre and bone. Their evidence, gathered by making use of Hansma's innovations in AFM, showed that some of the proteins are arranged in a tangled state, like a garden hose looped many times over itself, with short, fairly weak bonds connecting the various loops. When the polymer is stretched, such as under a potentially shattering force, those weak bonds break one at a time. When that happens, the energy that was stretching the composite material is dissipated as heat, and the shattering force is reduced back to zero, before it can approach a level that would break the backbone of the polymer, shattering the shell or bone. In this way, such short, "sacrificial" bonds provide resilience to the material. Further, they can reform once the stress on the backbone is relaxed, thus continually healing the material and regenerating that resilience. The "hidden length" is defined as the part of the molecule — the loop — that was constrained from stretching by the sacrificial bond but lengthens when it breaks.

"It's been like that ever since Galen knocked on my door," Morse continues, with collaborations leveraging disparate expertise and leading to important discoveries. "Nature has evolved such complex utilization of such simple ideas in ways you'd never think of, like this offset nanopore stenciling of continuous crystal growth generating all of these properties. There's the bloodworm, with copper, and there is silicatein, the name I gave to the enzyme that enables some marine sponges to produce a glass skeleton, and make it at low temperature without the need for a furnace or acid or some terribly caustic solvents, so that it's benign and compatible with life."

The work on sponges, incidentally, included the discovery of the first identified enzyme that catalyzes the synthesis of any mineral. It also led to major breakthroughs, such as the one resulting from a collaboration involving then-chemistry graduate student **Angela Belcher,** now the head of the Bioengineering Department at the Massachusetts Institute of Technology, who worked with Morse and **Evelyn Hu,** then a UCSB materials professor. Together, they developed a high-throughput commercial process for synthesizing designed inorganic nanoparticles using phage displays, a laboratory technique employed in the study of protein–protein, protein–peptide, and protein–DNA interactions.

In terms of engineered materials, further abalone studies informed the development of an external inorganic treated gauze that could control the blood-clotting cascade system of the human body. As of 2021, the resulting commercialized anti-coagulation product remained the most recommended first-responder hemostasis treatment of major arterial bleeding for all the uniformed services in the United States.

Teasing Out the Protein-Copper-Melanin Trio

Wonderly's doctoral research uncovered several previously unknown functions of what he called a "multi-tasking protein" (MTP) in the formation and performance of the bloodworm jaw, which is composed of fifty percent protein, up to ten percent copper — most in mineral form, with smaller amounts in solution as copper ions — and up to forty percent melanin.

Melanin has many desirable properties, but because experimental formation of it typically produces very small granules less than 100 nanometers in diameter, applications of melanin in synthetic materials remain limited. For instance, melanin has semiconductive properties, so it could be useful in, say, a solar panel, but it would have to be present at a much larger scale, as a continuous bulk material in crystal, not powder, form. "The worm jaws are amazing because they have contiguous melanin at the millimeter length scale, which is orders and orders and orders of magnitude larger than even most melanin found in a biological context," Wonderly says.

"And," Waite notes, "because the melanin and copper in *Glycera* jaws are correlated with impressive wear resistance, a deeper understanding of the mechanisms of their formation and function could lead to significantly expanded use of melanin in high-performance materials."

Wonderly achieved a key advance — Waite calls it his "first breakthrough" — when he figured out how to get *E. coli* to produce the protein, so that he would have enough for his experiments without having to harvest thousands of bloodworms. "Making recombinant jaw protein was a big deal," Waite recalls, adding, "Then, in playing around with it in solution, he found how tightly it bound with copper."

That led to the hypothesis — which was then confirmed through observation and based on the fact that the copper-bound protein shares many characteristics with enzymes known to be involved in melanin synthesis — that the copper-bound protein is what catalyzes the chain reaction that

William Wonderly's PhD research on the bloodworm jaw has generated great interest among materials scientists.

An Argument for Long-term Research

Engineering and science require patience, and functional materials, like those that might one day be inspired by the jaws of the bloodworm, or others having no biological precursor, don't always arrive on schedule. While a new material may result directly from specific funded research, life-changing advancements, the kind that occasionally earn a Nobel Prize, typically come much later.

Last spring, the journal *Nature Synthesis* published an article by UC Santa Barbara professors emeritus **Anthony K. Cheetham** and **Fred Wudl,** together with **Ram Seshadri,** professor of chemistry, biochemistry, and materials and the director of the NSF-funded Materials Research Science and Engineering Center (MRSEC), which has funded diverse research into materials synthesized in marine organisms, like the bloodwarm jaw. The article tracks how and why the materials were initially synthesized, as well as how, and when, their utility was eventually recognized.

The authors identify several pathways to materials breakthroughs, with the most common appearing not to involve inventing something new at all. Rather, they tend to occur more often when an existing compound, often one that was synthesized out of simple curiosity, is repurposed in the application for which it becomes known.

"Our thesis is basically to encourage discovery synthesis of materials without worrying too much about the application space," Cheetham and Seshadri noted. "Funding agencies would like to think that if they give you one dollar, then they will get one dollar — or ten dollars — of utility out of it. Actually, they might get back a million dollars on the dollar, but twenty years from now and for something they never initially envisioned."

For example, polyacetylene was originally identified in 1866 and was first synthesized by a known polymer synthetic method in the 1950s. But it was only in the mid-1970s that UCSB professor (now emeritus) **Alan Heeger,** working with Alan MacDiarmid and Hideki Shirakawa, produced a revolutionary conductive thin film that earned each of them a share of the 2000 Nobel Prize in chemistry. That breakthrough would enable the entire field of conjugated polymers, with applications in such areas as thermo-electrics and wearable electronics.

Hybrid 3D perovskites are another example. Initially synthesized out of curiosity in Germany in 1978, it was not until 2009 that the work was done that led to their application as visible-light sensitizers in photovoltaics.

Another example, lithium-ion batteries, are the multi-generational result of research on lithium cobalt oxide. First synthesized in the 1950s, only much later did it find its way into service as the key compound in batteries used globally to power our electronic devices and vehicles.

As the unsurpassed creator of high-performance materials, Seshadri says, "Nature has had the luxury of evolving its processes over a very long period of time, and it has never had a funding agency breathing down its neck, requiring rapid results."

leads to formation of melanin and the bloodworm's tough jaw.

Wonderly then determined that once the protein binds copper, a phase separation occurs. That is, he explains, "When we have soluble protein, and we add copper to that solution, the protein binds the copper, but rather than remain soluble, it forms dense liquid protein droplets *separate* from the water. The copper-bound protein and water won't mix."

Wanting to figure out how exactly the protein droplets turn into a solid, Wonderly went to Matt Helgeson, whose group does a lot of rheological measurements, that is, measuring mechanical properties of complex fluids. "What we discovered," he says, "is that the copper not only causes the protein to condense into droplets, but the droplets then go to the interface and sort of spread to form a layer, but only in the presence of copper."

More lab work led to the discovery that "If you just have the protein sitting in a jar and add some copper and come back a little later, a film will have formed on top of the fluid where it contacts air," Helgeson says. "That means that somehow the protein is being recruited to that air-water interface and somehow solidifying. "

"It was super exciting," says Wonderly. "We went from this thing that we didn't think was really a protein to finding that, despite its low complexity, it has this high degree of functionality. The protein finds metal, it accelerates melanin formation, it phase-separates, and then that phase separation leads to this melanin formation concentrated at the air-water interface to form this solid melanin-reinforced solid: the jaw."

Wonderly says that a key challenge in the project was navigating the tension between "the desire to try to come up with something truly unique and the utility of that, while not wanting to miss something that should be included in the project and not wanting either to dilute my own insights or lean entirely on what came before."

In the end, he says, "Getting an idea of what was going on in this new system required a synthesis of paradigms from a lot of different systems."

Studying the polymerization process further, Wonderly found that it resembles the manner in which nylon polymer threads form at an air-water interface, suggesting possible material applications of the bloodworm's own polymerizing mechanism. And recently, Wonderly worked with Chmelka's lab on sophisticated NMR analyses of the jaws to understand the individual chemical interactions occurring at the atomic level. A paper on that project is in preparation.

"If I see a material that's interesting, I want to know why is has the properties it does," Chmelka says. "What is the atomic-level structure that underlies and accounts for those properties? If we can explain the origins of the properties, then, in principle, we can mimic, improve, or adapt them for diverse engineering applications. In this case, we got the jaws, did the NMR experiments and compared their analyses with those of related materials. From there, we could establish the atomic-level foundations that appear to account for their very different mechanical properties."

Incrementally, each of these related research projects contributes to unraveling the recipe, about which much is now known but which, to date, only a bloodworm can prepare.

Brad Chmelka employs his expertise in nuclear magnetic resonance spectroscopy to uncover "the atomic-level structure that underlies and accounts for" unique materials properties.

Researchers in Matt Helgeson's lab, who specialize in rheological measurements, were able to discover key processes in the formation of the bloodworm's melanin-based jaws.

The Collaborative Advantage: Why Working Together Works So Well

Without prompting, every faculty member interviewed for this section spoke to the importance of collaborative research in addressing large challenges. Collaboration is a cornerstone not only of UC Santa Barbara, but also of the National Science Foundation (NSF) MRSEC model and the interdisciplinary research groups (IRGs) that it mandates. The current (sixth) round of funding for the UCSB MRSEC supports three IRGs. IRG 3 — "Resilient Multiphase Soft Materials," led by mechanical engineering professor **Megan Valentine** and professor of chemical engineering **Matthew Helgeson,** is where **William Wonderly** (PhD '21) presented regularly on his bloodworm research and received, in return, feedback, ideas, and suggestions reflecting diverse perspectives.

Megan Valentine (Mechanical Engineering)

When UCSB submitted its proposal for renewed MRSEC funding, we wanted to broaden out beyond the mussel to look at a host of other types of organisms. The bloodworm was one of our showcase examples in our pitch to the NSF, because we thought it would allow us to answer a lot of questions about how organisms make materials that have these extraordinary properties.

Matthew Helgeson (Chemical Engineering)

For me, one of the most rewarding things about leading this big collaborative effort is that once you create a space for people to really work together to be creative and think outside the box of the typical training students receive, it's very autocatalytic in terms of their being able to generate their own research ideas and start pursuing them.

William Wonderly (PhD '21)

I can't say enough about how important it is to create these situations where people can interact. It gives them a voice. From my perspective, this project would have been impossible without the IRG.

Dan Morse (emeritus, MCDB)

You know what you know, but you also know what you need. A molecular biologist knows that she needs a hard-materials expert and someone to do electron microscopy. Projects require a lot of people who have varied expertise, so that one fact triggers a path of thinking that you never could have imagined. Many PhD students who participate in collaborative research that leads to groundbreaking discoveries get fantastic jobs at other universities and then nucleate the collaborative model there. The path of discovering the unknown is a delightful adventure, so, of course, this is how they work.

Galen Stucky (Materials, Chemistry)

Understanding the assembly, structure, and multicomponent networking of biosystems requires experiment and theory in the spatial and temporal continuum from atoms to macroscale and from milliseconds through the biosystem regenerative life cycle. It also greatly helps to have immediate access to real-life marine biology in the ocean and in the Marine Science Institute. Working in the interdisciplinary project environment has proved to be a great experience for researchers and faculty.

Herb Waite (MCDB)

We had dynamic meetings to talk about mussel adhesion, with equal participation from biology, chemistry, physics, and engineering. Although we knew a lot about chemical structures, the missing link was why the molecules were sticky underwater. You can make mimics easily enough, but the other disciplines and their tools — such as the surface-forces apparatus, atomic-force microscopy, NMR [nuclear magnetic resonance] spectroscopy, and modeling simulation — help you understand the structure-properties relationships and, in the hands of trainees, drive the evolution of the concept.

Ram Seshadri (Materials, Chemistry, MRSEC director)

Right from the beginning, our MRSEC has had an emphasis on looking at this interface between materials and biology, and trying to understand how nature makes materials. Initially, a lot of emphasis was just on finding out what the material was. Increasingly, it has been on how to reproduce the synthetic processes that nature uses to make the materials.

Craig Hawker (Materials, Chemistry)

It's subtle but important that we tell our students, "You need to attend every weekly IRG seminar. Even if you don't think the work is important to you, just absorb the ideas; expose yourself to them." Our junior professors and students are brought up in this culture, so they think it's normal, but it's not. There are places that try to mimic it and may get some way toward fulfilling the promise, but I don't think anyone does it as well as we do. And it's because people buy into the system. You need the initial buy-in to get the generational buy-in. I give credit to Ram [Seshadri], as leader of the MRL, and to all the others who lead and participate in multi-PI programs, because they practice what they preach.

Brad Chmelka (Chemical Engineering)

We're not all experts on all of these things, so we collaborate; it's the interdisciplinary culture at UCSB, and it allows each of us to reach beyond our specific expertise and expand the scope of our research to solve high-impact problems. The students become comfortable working beyond the boundaries between disciplines and receive training in the use and utility of different materials-synthesis techniques and instrumentation. This makes it possible to combine multiple methods or approaches, broadening and deepening the results of research and elevating its impact. And it presents fantastic educational opportunities.