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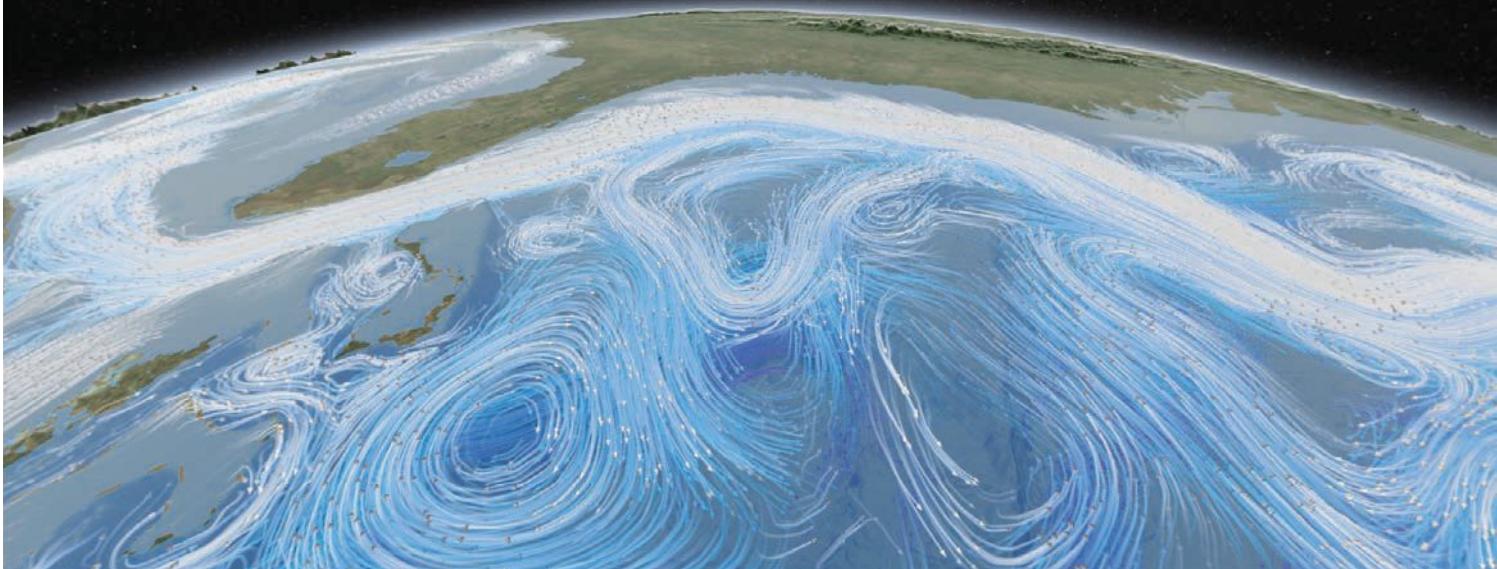
BIOLOGISTS CONSIDER THE
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RED TIDES

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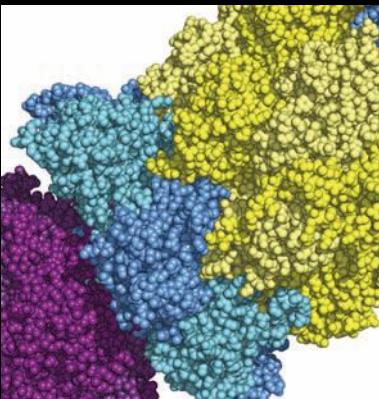
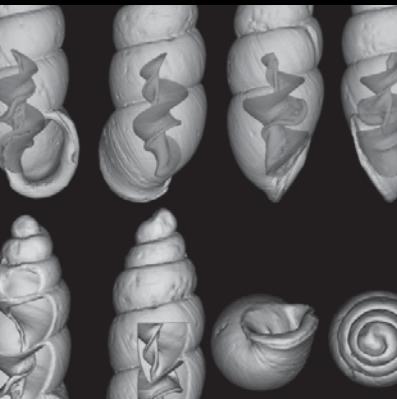
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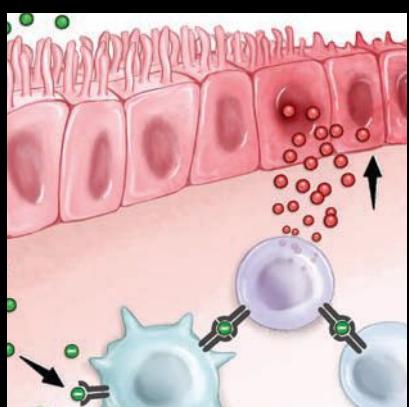
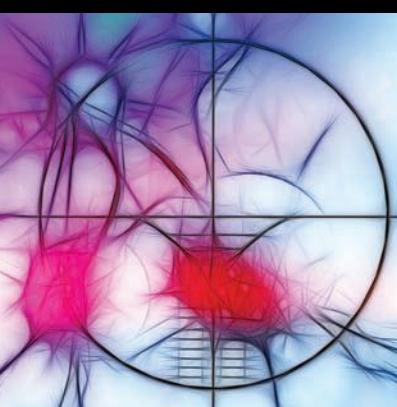
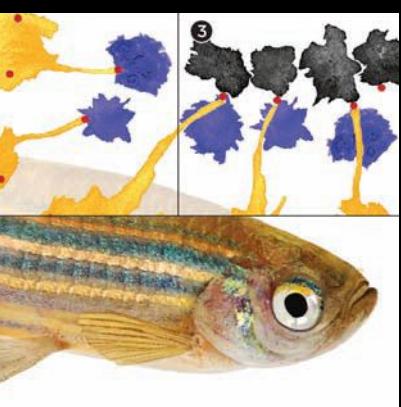
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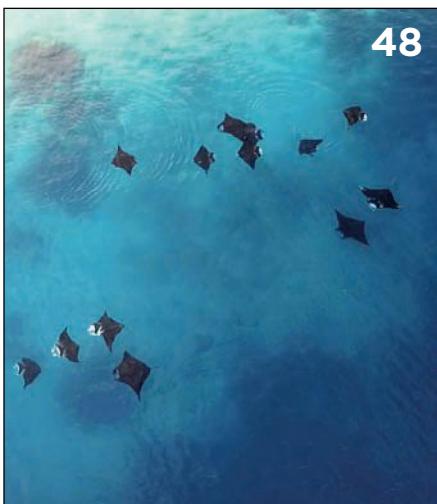


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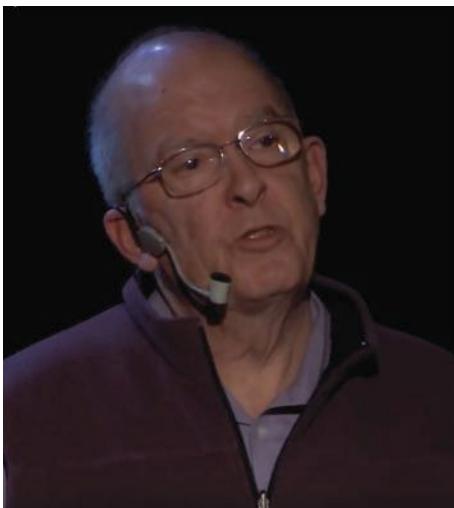
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VIDEO

Discovering Whale Song

Watch a TED talk by researcher Roger Payne, who was among the first scientists to hear and identify the complex vocalizations of whales.

AS ALWAYS, FIND BREAKING NEWS EVERY DAY ON OUR WEBSITE.

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- The latest findings on nuclear bodies called paraspeckles
- How language policies are affecting science laboratories
- The latest life-science game changers: 2019's Top 10 Innovations
- The importance of mitochondrial diversity in evolution

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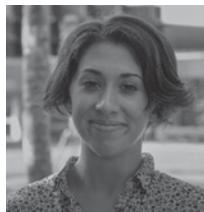
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Contributors



Growing up in Palmetto, Florida, **Nicoletta Lanese** dreamed of being a fiction writer. In high school, she found herself drawn to science. She was also an avid dancer, having performed in a variety of styles since age four. So she decided to attend the University of Florida (UF), where she could double major in dance and neuroscience. There, Lanese's interests started to collide, as she choreographed dances inspired by scientific illiteracy and locked-in syndrome, and blogged about what she was learning in her science classes. In her junior year, she got the idea of what she might do for a living when a neuroscience professor handed her back an assignment in which she'd summarized a research paper and told her that she would "make a good science writer," Lanese recalls. A quick Google search led to her to numerous resources on the profession, and she quickly realized that it bridged her interests in scientific research, writing, and creative forms of communication.

After Lanese graduated from UF in 2017, she enrolled in the University of California, Santa Cruz's science communication program, and while there she interned for two university press offices and two local newspapers. She topped it off with a six-month stint as the science communication fellow at the Okinawa Institute of Science and Technology Graduate University in Japan. In the spring of 2019, Lanese moved back to the US, and to New York City, where she began freelancing before accepting an internship at *The Scientist* this summer. "I was really grateful to get that dual experience of writing usual faster online articles and then more processed magazine pieces," Lanese says of her time with the publication. In this issue, find her stories on the brains of convicted murderers (page 15), the electrical activity of cable bacteria (page 48), and the work of young researcher Martha Munoz (page 53). In September, she accepted a job as a staff reporter at *LiveScience*.



Over the past two decades, **Richard Smith** has scuba dived about 3,600 times in the waters off of six continents. But growing up in the Cotswolds in rural England, his first dives were with his father in cold British waters. "It was not very much fun, I'll be honest," he tells *The Scientist*. "[It] almost put us completely off the whole idea." But he became hooked on the pastime once he visited the Great Barrier Reef, and ever since, he's been photographing underwater life and documenting animal behavior. He did his PhD research at the University of Queensland in Australia on pygmy seahorse biology, and now leads marine expeditions for experienced divers.

His first book, *The World Beneath: The Life and Times of Unknown Sea Creatures and Coral Reefs*, was released in September, and it showcases the diversity and history of underwater life. "There's just so much more to the oceans than people realize, and I wanted to bring that to people's attention," he says. He's hoping that by increasing awareness and appreciation of marine life, he can help protect it. On page 60 of this issue, he writes about his undersea observations.



Mark Colyvan, a philosopher at the University of Sydney in Australia with a particular interest in science, is currently focused on exploring the similarities and differences between different branches of physical and life sciences. He and his colleagues, University of California, Santa Barbara, ecologist John Damuth and retired theoretical ecologist Lev Ginzburg, are on a mission to raise awareness of the importance of making ecology a bit more like physics and mathematics. As the trio writes on page 20, the search for universal laws that undergird ecology is a controversial, but potentially game-changing, quest.

The three researchers posit that the curious correlations discovered by allometry, the study of how the characteristics of living creatures scale with body size, are keys to establishing ecological laws. For example, whether measuring elephants or mice, a given area of land will support the same absolute amount of metabolism exhibited by the organisms within it. "You might think of these as a different kind of law," Colyvan says, "like a law as yet to be underwritten by the big theory." A debate still ensues among researchers as to whether or not ecology can be described by overarching laws, with some scientists opining that biology is simply too complex for such an organization. "So the thought is that there are no perfect laws, in the sense that they perfectly describe biological systems," Colyvan says. "But it seems to us that that's putting too much emphasis on the noise and not enough on the correlations."

Ocean, Muse

The sea has inspired painters and poets for centuries. It has also spurred generations of scientists to plumb Earth's living mysteries.

BY BOB GRANT

The style and sensibilities of Impressionist painter Claude Monet emerged from the ocean. He is arguably most famous for his paintings of the ponds and water lilies that dotted his verdant home in landlocked Giverny, but *Impression, Sunrise*, the painting that christened an artistic movement, depicted the bustling port of the seaside town of Le Havre in Normandy. Monet was raised from the age of five in Le Havre, and it was there that he met Eugène Boudin, a marine painter who would teach the young artist to use oils and paint outdoors. The eager student would paint numerous seascapes throughout his robust career, and Monet once famously said: "It is extraordinary to see the sea; what a spectacle! She is so unfettered that one wonders whether it is possible that she again become calm." Monet's contemporaries, such as Vincent van Gogh and Paul Gauguin, and artists who came before, including Japan's Katsushika Hokusai, were similarly drawn to the ocean's dynamic charm.

Writers, too, have been moved to create throughout history by the salty waves. From poems such as Emily Dickinson's "I started Early—Took my Dog" and Samuel Taylor Coleridge's epic "The Rime of the Ancient Mariner" to timeless books by Jules Verne, Herman Melville, John Steinbeck, and Ernest Hemingway, literary figures of all stripes have committed the mystery, brutality, and potentiality of the sea to the page.

The same holds true for seminal works of science. Charles Darwin's dogma-shattering theory of evolution would not have arisen from the primordial ooze of creationism without his arduous, nearly five-year sea journey aboard the *HMS Beagle*, which ferried him around the globe and further changed his mind about the immutability of species. Even before that, as a student in Edinburgh, Darwin made some of his earliest forays into biology by studying marine invertebrates under the tutelage of Robert Edmond Grant (no relation, as far as I know).

Another paragon of scientific thinking referenced the unfathomability of the sea as a way to downplay his own unmatched contributions to physics. Sir Isaac Newton is said to have declared: "I do not know what I may appear to the world, but to myself I seem to have been only like a boy playing on the sea-shore, and diverting myself in now and then finding a smoother pebble or a prettier shell than ordinary, whilst the great ocean of truth lay all undiscovered before me."

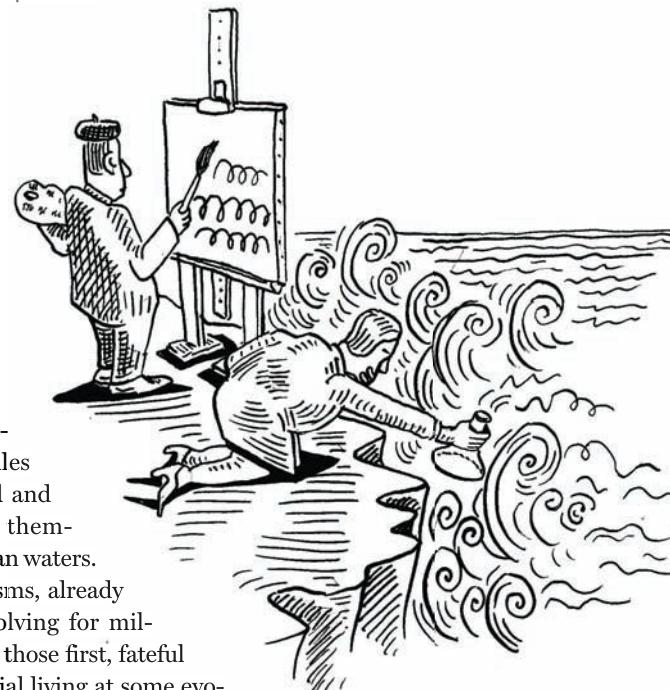
To me, this connection between the ocean and scientific inspiration makes perfect sense. After all, the con-

sensus among biologists is that the likeliest scenario for life's initiation and evolution is intimately entwined with our planet's seas. The first rudimentary biomolecules probably assembled and began replicating themselves in or near ocean waters. And marine organisms, already established and evolving for millions of years, made those first, fateful slithers into terrestrial living at some evolutionary launching pad situated where the sea met the land. My own journey through science was greatly influenced by the sea, and were it not for the allure of journalism, I would have finished my PhD and most likely would be a marine biologist today.

It is in this spirit of discovery that *The Scientist* decided some time ago to prominently feature stories of marine research in one issue per year. Over the years, never have we found any shortage of fascinating research or inspiring stories to be harvested from the ocean. From the confluence of literary and scientific currents highlighted by Rachel Carson's relationship with the sea (page 64) to the tale of the paradigm-shifting discovery that humpback whales sing songs (page 50), this issue is packed with salt-tinted tales to delight and challenge the mind. Reporting my feature story on Florida red tides (page 26) reinvigorated my own fascination with marine research, reminding me that there is so much we have yet to learn about the boundless waters that connect us all and about the organisms that make their homes in that vast expanse. ■

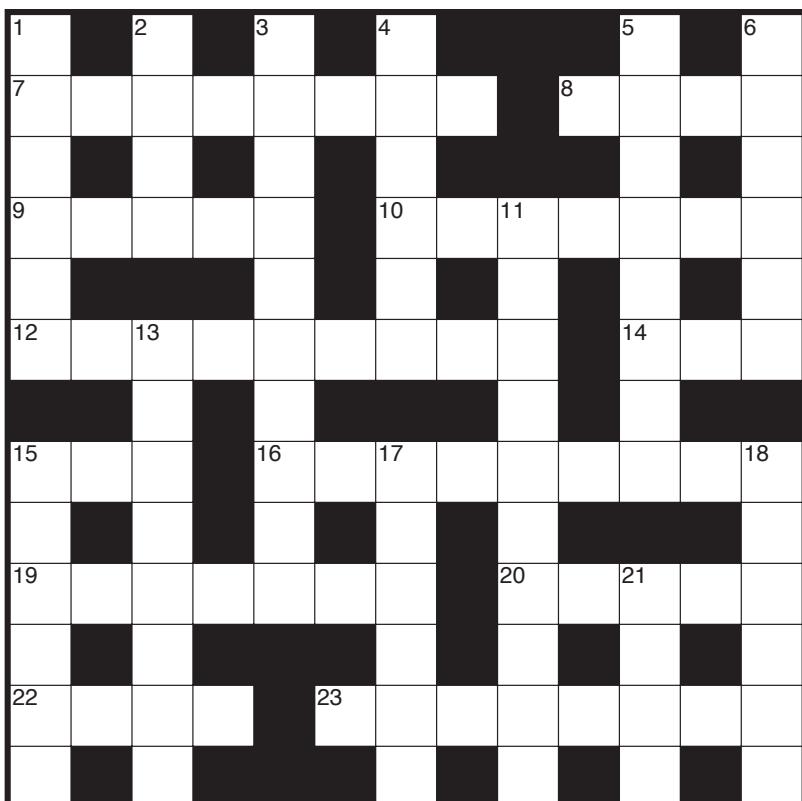


Editor-in-Chief
eic@the-scientist.com



Speaking of Science

Note: The answer grid will include every letter of the alphabet.



BY EMILY COX AND HENRY RATHVON

ACROSS

1. Ancient Greek who believed in atoms and promoted *ataraxia*—a life free of worry
8. One of three figures in a Douglas Hofstadter book
9. Like an animal affected by a lyssavirus
10. Immune response trigger
12. Study pursued by Davy, Bunsen, and the Curies
14. Chimpanzee, gorilla, or gibbon
15. Eye; planet
16. Touch-me-not's genus
19. Arthropod's posterior section
20. Archaeological site in Jordan called the "Rose City"
22. Articulation of the femur and the tibia
23. Chili pepper with a tilde in its name

DOWN

1. Containing element #26
2. Offshoot from a trunk
3. The four "mathematical arts" in medieval studies
4. Organism resulting from DNA replication errors
5. What's processed in Broca's and Wernicke's areas
6. Matter of probability
11. Amino acid much debated at Thanksgiving
13. Stuck like a bug in amber
15. Ha Ha Tonka State Park's highland region
17. Folivores partial to bamboo
18. Dugong or manatee (2 wds.)
21. Jurassic theropod, familiarly (2 wds.)

Answer key on page 5

I would like to have eyes on the deep ocean when hurricanes come by, that would be great to know.

—Rut Pedrosa Pàmies, marine biogeochemist and coauthor of a recently published study that suggested that hurricanes alter the oceans' "biological pump" by increasing the export of organic materials from the surface to greater depths (*Wired*, October 4)

Our ocean cleanup system is now finally catching plastic, from one-ton ghost nets to tiny microplastics! Also, anyone missing a wheel?

—A tweet from Boyan Slat, CEO and founder of The Ocean Cleanup project, a nonprofit that launched a 600-meter-long device designed to collect refuse from the Great Pacific Garbage Patch (October 2)



Notebook

NOVEMBER 2019



Crossing Species Lines

From a small inflatable boat in the Rangiroa atoll in French Polynesia, Pamela Carzon got her first glimpse of the “strange” trio of marine mammals she’d been told about: a bottlenose dolphin mother (*Tursiops truncatus*), her seven-month-old calf, and another young cetacean that was slightly smaller and looked to be not a bottlenose dolphin at all, but a melon-headed whale (*Peponocephala electra*).

It was April 2015, and Carzon and a colleague at the Marine Mammal Study

Group of French Polynesia, a nongovernmental organization dedicated to whale and dolphin conservation, were out for the NGO’s annual photo-ID survey, very much hoping to find animals that a former collaborator had seen while diving in the region the previous November. “[T]he sea was very calm, and there were many dolphins around,” Carzon, also a PhD student at the Center for Island Research and Environmental Observatory (CRIOBE) in French Polynesia and the École Pratique des Hautes Études in Paris, recalls in an email to *The Scientist*. “It took us maybe two minutes to spot them: the dark calf was easy to spot among the bottlenose dolphins.”

DOLPHIN ADOPTION: A female bottlenose dolphin in the South Pacific has been sighted with both her own calf and another young cetacean identified as a melon-headed whale.

The mother, dubbed ID#TP25 by the researchers, was known to tolerate divers and boats, and that April day she approached the inflatable with both calves. Carzon grabbed her underwater camera and slipped into the water. “I was able to get good underwater footage and to sex both calves,” she says. ID#TP25’s natural calf was a female; the second calf was male. “I also noticed that both were ‘gently’ pushing each other [in order] to remain under the

adult female's abdomen" in so-called infant position. Continued observation over the following months revealed that the dolphin mom was nursing the foreign calf, whose species ID remains to be confirmed with genetic testing, and otherwise treated him as one of her own (*Ethology*, 129:669–76, 2019).

Carzon had been studying the bottlenose dolphin community inhabiting the northern part of Rangiroa atoll for a decade and knew that the cetaceans had a history of bringing young animals of other species into their group. In 1996, researchers observed a newborn spinner dolphin (*Stenella longirostris*) swimming in the slipstream of an adult male bottlenose—a behavior known as echelon swimming and a common interaction between mothers and calves. Scientists also regularly spotted a juvenile spinner dolphin over the next two years, often with a particular adult female bottlenose, Carzon says, although it's not clear whether it was the same individual they saw as a newborn. Then, in November 1998, a newborn melon-headed whale spent a few weeks in the area and was filmed swimming in echelon position with the same female bottlenose that had associated with the young spinner dolphin.

More recently, another adult female bottlenose in the same community has twice been seen with young of a different species. In January 2011, she was spotted with a neonate spinner dolphin for a few days, and in February 2018, she was photographed with a newborn Fraser's dolphin (*Lagenodelphis hosei*), which swam alongside her in echelon position. With such behaviors apparently relatively common within this social group, ID#TP25 may have picked up a thing or two from her conspecific companions, speculates Carzon. "The evidence that bottlenose dolphins are capable of imitation is very strong," she says. "[S]ocially transmitted ideas or practices from cultural models may have influenced [ID#TP25's] behavior."

As is the case with most animal adoptions in the wild, how the mother bottle-

nose came to acquire the melon-headed whale calf is unknown. The calf's natural mother may have died, or the bottlenose dolphin group may have "kidnapped" it, a behavior that was once observed in a dolphin group in the Bay of Gibraltar, Carzon notes. Whatever scenario landed the outside calf in the care of dolphin ID#TP25, the adoption was stable, lasting more than two years. ID#TP25's natural calf disappeared by early 2016, suggesting it died or weaned early, possibly joining another social group.

There is only one other published case of intraspecies adoption by animals in the wild: for about 14 months in the early 2000s, researchers documented the integration of an infant marmoset (*Callithrix jacchus*) into a group of

The adoption was stable, lasting more than two years.

capuchin monkeys (*Cebus libidinosus*) in woodland savanna of central Brazil. A female monkey that the researchers had thought was pregnant but who perhaps lost her own baby cared for the infant marmoset, carrying it on her back and appearing to nurse it (*Am J Primatol*, 68:692–700, 2006). "It was amazing because when she appeared, she was tiny tiny tiny," says Patrícia Izar, a primate ethologist at the University of São Paulo in Brazil who observed the adoption. "She was really a newborn, and she survived." Izar says she was particularly astonished because she knew that some groups of capuchin monkeys eat young marmosets. Care for the young animal was eventually assumed by another female capuchin, and all group members appeared to tolerate the marmoset's presence.

As for why intraspecies adoptions do—rarely—occur, wildlife conservation professor Robert Young of the University of Salford in the UK suggests that animals may not recognize that they're caring for young of another species. In the case of the dolphins, the presumed

melon-headed whale is similar in size to the adoptive mother's own bottlenose dolphin calf, and the dolphins have not evolved a strong ability to differentiate their own young from those of another species. "There's good reason to think it's just an identification problem," says Young, who says he has observed a handful of intraspecies adoptions among black-fronted titi monkeys (*Callicebus nigrifrons*) in Brazil.

The high levels of oxytocin coursing through mammalian mothers' bodies and the abundance of resources are also likely to be relevant factors. Indeed, in the case of the capuchin group that took in a marmoset baby, Izar and her colleagues had been providing coconuts to study the animals' use of stones to crack the fruit open, meaning that the monkeys had plenty of food to eat, and so looking after additional young might have been less costly. Interspecies adoptions are also much more common among domestic and captive animals, for whom food is often plentiful, than they are in the wild, Young notes. "If you've got a lactating female dog, you can just about get it to rear any other mammal."

Documented cases of interspecies adoption among the Rangiroa dolphins and Brazilian monkeys "shows that it's not impossible," says Izar. "I think that in time we will have other cases in the wild."

—Jef Akst

Notes from Underground

Carolyn-Monika Görres laughs at the seeming improbability of her own research. She never expected to find herself eavesdropping on beetle grubs living in the soil, much less to be planning a project she now calls Underground Twitter.

Görres, an ecologist at Hochschule Geisenheim University in Germany, is interested in how insects that munch on plant roots can contribute to greenhouse gas emissions from the soil. But in trying to tackle this question three years

ago, she was presented with a problem: it's hard to know what soil insects are munching on, or even how many of them are in the ground, without digging up the soil and destroying the very ecosystem she wanted to monitor.

This dilemma isn't unique to Görres' research; monitoring soil insects is notoriously difficult. "There is so little work being done with soil insects, and it's because it's really hard," says US Department of Agriculture researcher Richard Mankin, who has spent much of his career studying the subterranean critters. For farmers whose fields are threatened by soil pests such as white grubs, the voracious larvae of beetles in the Scarabaeidae family that frequently devastate harvests, the only way to confirm an infestation is to excavate their fields.

One approach to monitoring soil insects that scientists such as Mankin and David Chesmore, an acoustics researcher at the University of York, have explored is to listen for the sounds the larvae make. Acoustic monitoring is common among ornithologists surveying rare bird species, wildlife biologists

following hard-to-track fauna such as chimpanzees, and entomologists studying above-ground insects such as crickets and cicadas. Soil scientists have spent decades trying to detect white grubs and other crop pests by the sounds they make while moving or feeding, but "sounds in soil don't travel far," says Chesmore. As a result, most of the noise that reaches underground microphones, such as the ones Chesmore has spent his career developing, are quiet and indistinct.

Still, Görres needed a way to monitor soil insects for her research, so she teamed up with Chesmore to devise a way to record the sounds of white grubs in the lab. The pair's experiment consisted simply of "boxes with soil with some larvae in them," as Görres describes it, with stick-shaped microphones designed by Chesmore pushed down into the dirt. Listening to the initial recordings, Görres heard not only feeding sounds but a series of unexpected chirps. "I heard these strange sounds, so I went to David and he said, 'Oh my god, those are stridulations.' We didn't expect that at all."

Stridulations are most commonly associated with above-ground insects such as crickets, which produce the noises by rubbing their legs over a hardened, comb-like organ on their bodies. But these sounds are rarely heard in the soil, and haven't been well studied in white grubs. For Görres, it was a lucky break that completely changed the trajectory of her research. "When I started out, I wanted to measure greenhouse gas emissions. Acoustics was supposed to be just a very minor part of the project, and then it turned into a whole research area itself."

Follow-up recordings and analyses that Görres and Chesmore published this summer demonstrate for the first time that two species of white grubs, *Melolontha melolontha* and *M. hippocastani*, can be monitored by their stridulations. Importantly, the researchers were able to distinguish between the two species just by listening to the patterns of their sounds—*M. hippocastani* stridulations came in short, staccato bursts, while *M. melolontha* stridulations were slightly more elongated. They also found that the average stridulation rate per larva increased with increasing abundance of grubs in the container of soil (*Sci Rep*, 9:10115, 2019).

The ability to differentiate species within the soil based on their stridulations could be a major step forward both for researchers and for farmers, notes Kyle Wickings, a soil ecologist at Cornell University. An infestation of one particular species of white grub may become problematic for farmers once there are 100 or more larvae per cubic meter of soil, while another species may threaten crops at an abundance of only 10 larvae per cubic meter, he explains. Using stridulations to "not only detect the presence of pests, but also to tell [species] apart and relate that to a management decision is a pretty big deal."

Görres is hopeful that placing microphones in agricultural fields could one day offer farmers a cheaper and less destructive method to monitor infestations. Wickings says he supports that



ANDRZEJ KRAUZE

idea, although he cautions that Görres and Chesmore have yet to attempt to detect stridulations beyond their controlled lab experiment and have not yet demonstrated that it's possible to accurately estimate the abundance of larvae from the frequency of their stridulations.

In addition, Görres wants to record and analyze stridulation sounds in order to improve estimates of insect biodiversity. As part of her upcoming Underground Twitter study, which aims to determine when and why insects in the soil communicate with one another, she plans to bury multiple microphones in a field to record around the clock for six months. "There are all these insect studies about how biomass is dropping and species are endangered, but these are all about insects above the soil," she says. "We don't know much about biodiversity in the soil because it's so hard to monitor." Mankin agrees, although he notes that because many soil insects aren't known to stridulate, relying on stridulations alone could also skew estimates of insect diversity.

He said, "Oh my god, those are stridulations." We didn't expect that at all.

—Carolyn-Monika Görres
Hochschule Geisenheim University

Another hurdle in moving acoustic monitoring from the lab to the field is how to deal with the sheer quantity of data the approach generates. For the lab study, the researchers manually analyzed all of the recordings they made—about 12 hours' worth of audio—by listening for the occasional stridulation and deciding which sounds belonged to which species. "This is the one disadvantage of audio recording," Görres says. "It produces so much data, at [some] point you cannot analyze it manually anymore." However, she says she's confident that automated data analysis, perhaps enabled by machine learning, will be able to pick out stridulations from the recordings and identify

which sounds belong to which species in a matter of hours.

Ultimately, Görres hopes to return to the questions about greenhouse gas emissions that she initially set out to answer. "My hypothesis is that the acoustic activity [of white grubs] somehow relates to their metabolic activity," she says, "so maybe I can use acoustic activity to model greenhouse gas emissions. But right now, it's just a crazy idea of mine."

—Michael Graw

Murderous Minds

Kent Kiehl and his research team regularly park their long, white trailer just outside the doors of maximum-security prisons across the US. Inside the vehicle sits the bulky body of a mobile MRI machine. During each visit, people from the prison make their way to and from the vehicle in hourly shifts to have their brains scanned and help to answer an age-old question: What makes a murderer?

"It's not an uncommon thing for [incarcerated people], while they're getting a scan, to be like, 'I've always been different. Can you tell me why I've always been so different?'" says Kiehl, a neuroscientist at the University of New Mexico and the Albuquerque-based non-

profit Mind Research Network (MRN) who helped design the mobile MRI system back in the early 2000s.

The author of *The Psychopath Whisperer: The Science of Those Without a Conscience*, Kiehl has been fascinated by the criminal mind since he was an undergraduate at the University of California, Davis. Now, as director of mobile imaging at MRN, he oversees efforts to gather brain scans from thousands of people held in US prisons to learn what features, if any, might differ from scans of the general population.

This massive dataset recently allowed Kiehl to examine the brain structures of more than 800 men held in state prisons in New Mexico and Wisconsin in an attempt to distinguish incarcerated people who have committed homicide from those who have committed other crimes.

First, Kiehl and his colleagues laboriously sorted the pool of people who had volunteered for the study into three categories based on their crimes: homicide, violent offenses that were not homicide, or non-violent or minimally violent transgressions. The team relied on official convictions, self-reported homicides, and confidential interviews with participants to determine who

SCAN-MOBILE: Kiehl and his colleagues made more than 75 modifications to a trailer and the MRI system inside to outfit both for the team's unique research.



attempted or committed murder—both offenses that got a “homicide” label in their dataset.

People charged with felony murder—meaning that they had committed a serious felony that was in some way connected to a person’s death, even though they hadn’t intended to kill the victim—and people whose cases indicated considerable doubt about a judgment of homicide were not counted among murderers. And occasionally, people were moved from another category into the homicide group, Kiehl says. The researchers excluded people with abnormal radiology reports, traumatic brain injury, or diagnosed psychotic disorders from the study.

Controlling for substance use severity, time in prison, age, and IQ, the team analyzed the MRI data to look for differences among the study participants. Compared with the other two groups, the 200 men who had committed homicide showed significantly reduced gray matter in several brain regions that play important roles in behavioral control and social cognition (*Brain Imaging Behav*, doi:10.1007/s11682-019-00155-y, 2019).

“I think that the intriguing thing was, first, that they found a difference,” says Hannes Vogel, a neuropathologist at Stanford University Medical Center who was not involved in the work. “And second of all, that it correlates with some of the brain centers that deal with behavior and social interaction.”

Lora Cope, a neuroscientist who studies substance disorders at the University of Michigan, notes in an email to *The Scientist* that the team’s mobile MRI system has now been used in correctional facilities all over New Mexico and Wisconsin, and “has really revolutionized this area of research.” Indeed, the MRN has now used the equipment to collect roughly 6,500 scans from

more than 3,000 research participants since its first outing in 2007.

Although Cope wasn’t involved in the current project, she worked with Kiehl a few years ago while earning her doctorate at the University of New Mexico. After speaking with members of the Avielle Foundation, named for a six-year-old victim of the 2012 Sandy Hook Elementary School shooting, the two researchers spearheaded a study of more than 150 incarcerated young males, 20 of whom had been convicted of homicide, held at a maximum-security detention facility within the state. “Jeremy, [Avielle’s] father, really wanted to know if there was anything neuroscience could tell us about boys who commit homicide,” says Kiehl.

As in the current study, Cope and Kiehl deployed the mobile scanner to collect MRI scans of the incarcerated teens in New Mexico and discovered differences between those who had committed



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homicide and their imprisoned peers. The homicide offenders “had significantly less gray matter volume in parts of their temporal lobes,” Cope says (*NeuroImage: Clinical*, 4:800–807, 2014). When Kiehl compared the data from that study with the results of his latest project, he found a high degree of overlap. “Lo and behold . . . we found and replicated every region that was different in the boys and was different in the adult males, and in the same way,” he says.

The latest study’s finding that MRI data can distinguish homicide offenders not only from people who committed non-violent crimes, but also from those who performed other violent crimes, is particularly interesting, says Harold Koenigsberg, a psychiatrist at Icahn School of Medicine at Mount Sinai. “I would have thought there would be more of an overlap between [homicide and violent non-homicide offenders],” he says. “I’m surprised that it was so specific to homicide.”

Koenigsberg notes that homicidal violence can itself be split into two cat-

egories: impulsive and instrumental. Impulsive violence is born of unbridled emotions and overblown reactions, a brand of behavior linked to poor frontal lobe functioning and abnormal serotonin levels. Instrumental violence, on the other hand, is premeditated and is associated with other brain changes, such as reduced amygdala activation during emotion processing. “These two groups, we think that they have different biologies,” says Koenigsberg. Kiehl’s dataset could be enriched by adding measures of neurotransmitter release and electrical activity, along with related behavioral assessments, he suggests, and with both functional and structural data, psychologists might learn more about what gives rise to these distinct behavioral phenotypes.

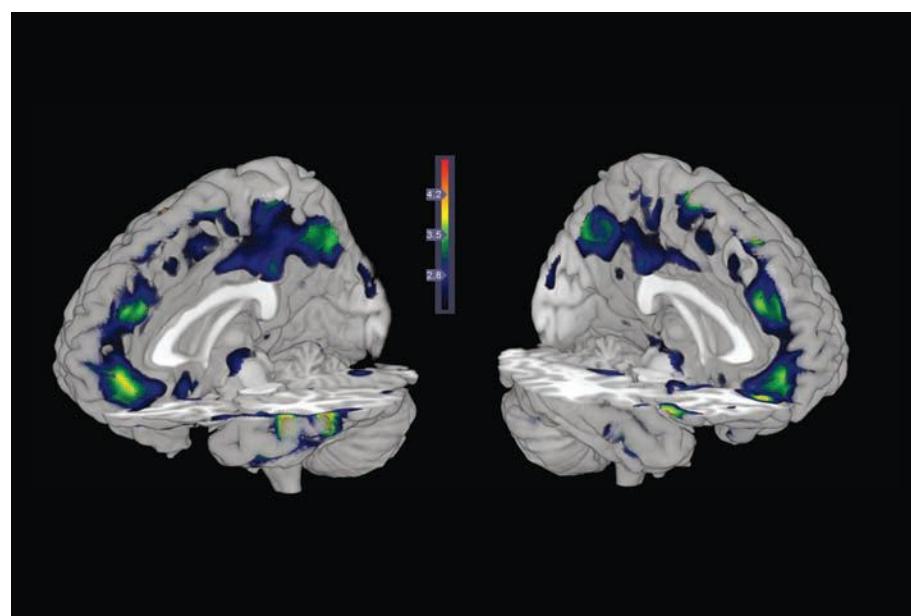
Koenigsberg, Vogel, and Kiehl all note that the structural data collected in the current study cannot on its own be used to predict who has committed homicide, let alone who might in the future. Nonetheless, the paper may find its way into the courtroom, says Vogel. If lawyers felt so inclined, they could try to “find an expert on one side who will quote this [paper]” in defense of someone who has committed a homicide, by arguing a client’s actions were due to brain abnormalities and thus out

Men who had committed homicide showed significantly reduced gray matter in several brain regions.

of his or her control. Or, a prosecutor could potentially use the paper to argue that MRI findings should be admissible as evidence that a defendant has committed a homicide, says Vogel, who has served as a consultant for court cases in California and Nevada, and helped investigate the brain of the Route 91 Harvest music festival shooter in 2017. “But then you’re [also] going to find an expert that will tear that [testimony] to pieces.”

Kiehl notes that his MRI study could also someday contribute to new evidence-based measures of homicidal risk. These measures could supplement current measures of violent behavior, such as psychological questionnaires, if future studies demonstrated they carried predictive weight, he says. Beyond courts of law, he also suggests that understanding how violent behavior arises could pave the way to better psychological treatment aimed at both rehabilitation and prevention.

— Nicoletta Lanese



A. SAJOUS-TURNER ET AL. (2019)

Snow Blanket

About a two-hour drive south of Fairbanks, Alaska, near the northern tip of Denali National Park, stands a series of fences. In the winter, snow piles up behind each fence, creating drifts roughly a quarter-meter high. These drifts, which insulate the tundra soil by preventing the chilly winter air from stealing its heat, are part of an experiment interrogating how permafrost—soil that remains frozen even as snow melts in the tundra—might be affected by global warming.

“Permafrost is one of the most unique kinds of soil,” says Neslihan Taş, an environmental microbial ecologist at Lawrence Berkeley National Laboratory. (See “Neslihan Taş: Digging Microbes,” *The*



SNUG BUGS: Snow fences in Alaska help keep patches of soil insulated as part of an experiment on microbes' emissions of greenhouse gases.

Scientist, December 2017.) “It contains more carbon than any other soil on Earth and twice as much carbon as is available in the atmosphere.” Because permafrost tends to maintain temperatures close to freezing, even in summer, microorganisms inhabiting this soil tend to be relatively inactive, so carbon is used up more slowly here than it is in warmer soils. But as global temperatures rise, microbes thaw and start to eat more, researchers hypothesize, transforming carbon stored in the soil into greenhouse gases such as carbon dioxide and methane that can then diffuse into the atmosphere.

In previous attempts to test this hypothesis, scientists took soil samples from the Arctic, warmed them in the lab, and found increases in emitted CO₂. However, these lab studies were limited in their ability to simulate the complex interactions of microbial communities, so Northern Arizona University ecosystem ecologist Ted Schuur and colleagues

decided to set up a field experiment. In the winter of 2008, Schuur and his colleagues erected the six fences in Alaska, where they have been insulating the same patches of permafrost over the last decade of winters.

The team collected soil samples from around each fence—both from behind the fence, where the snow had accumulated during the winter, and in front of it, where the soil was uninsulated—about a year and a half after the fences were installed, and then again three years later. The researchers analyzed the microbial DNA extracted from the soil to reveal the community’s range of lifestyles and metabolic activity. After 4.5 years, the average temperature of the insulated soil was roughly 1°C higher than that of the uninsulated soil, and the composition and activity of the microbial communities living there had changed rapidly as a result, the researchers reported in July (*PNAS*, 116:15096–105, 2019).

Specifically, the team found that the abundance of species and genes associated with carbon dioxide and methane production was greater in the insulated soil than

in the uninsulated soil, implying that tundra microbes may indeed release greater amounts of greenhouse gases from the soil as the climate warms. The researchers also found that the scale of the differences in microbial composition between the uninsulated and insulated soil seemed to accelerate over time. After roughly one year of warming, microbial communities in the insulated soil still resembled those of the uninsulated soil, but after 4.5 years, the contrasts were substantial.

“We were surprised by how quickly the microorganisms responded to warming,” says study coauthor Eric Johnston, who worked on the project as a graduate student at Georgia Tech and is now a post-doctoral researcher at Oak Ridge National Laboratory (ORNL) in Tennessee. Particularly noticeable was the increase in abundance of methane-producing microbes deep in the insulated soil. For example, at the end of the study period, the team found that soil that was between 45 and 55 centimeters under the surface in the insulated plots contained around three times as many microbes in the order *Meth-*

If old carbon that has been locked up for hundreds or thousands of years is being respired, this will cause a long-term increase in the concentration of carbon dioxide in the atmosphere.

—Eric Johnston, ORNL

nosarcinales as the uninsulated soil did. Methane warms the atmosphere 30 times more than carbon dioxide does over the same period of time, so it’s a “somewhat alarming” finding from a climate perspective, Johnston says.

Dave Graham, a microbial ecologist at ORNL who was not involved in the study, says he finds the changes in microbial composition in insulated tundra compelling because the result aligns with data that he and others have collected on permafrost microbes in the lab. “Cer-

tain microbial populations take a long time to establish after permafrost thaw,” he explains. “Methane producers, for instance, seem to be very sensitive to freezing.” Based on his team’s lab results, Graham and colleagues predicted that a long stretch of warmer temperatures would allow a large population of methane-producing microbes to grow—just as Schuur, Johnston, and their colleagues found. “It’s neat to see these kinds of [microbial] behaviors happening in the lab and all the way to the field.”

Although the current study identified the genes present in the microbial community, it couldn’t detect which of those genes were producing proteins. “One of the critical [next] steps is understanding which genes are actually expressed: Which organisms are working hard, and what are they doing?” Graham says. “Another critical question is: What are they actually consuming?” The researchers note in the paper that the plant com-

munity in the experimental plots is becoming more abundant as a result of the insulation experiment. Plants can contribute fresh carbon to the soil for microbes to decompose, in addition to the older carbon already stored in the permafrost. Distinguishing between the two carbon sources is important, Johnston says, because if all of the carbon being metabolized by microbes is from fresh plant material, the resulting fluctuations in atmospheric carbon dioxide levels will be relatively minimal. On the other hand, “if old carbon that has been locked up for hundreds or thousands of years is being respired, this will cause a long-term increase in the concentration of carbon dioxide in the atmosphere.”

Schuur is starting to tackle these questions. In another paper published in July, he and his colleagues reported that, when analyzed together, the insulated and the uninsulated plots of soil lost an average of 5 percent of their stored car-

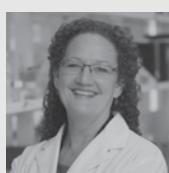
bon per year over five years, suggesting old carbon is indeed being used by resident microbial communities. Based on atmospheric warming predictions, that translates to permafrost losing up to 78 percent of carbon in its top 55 centimeters by the end of the century (*Nat Geosci*, 12:627–31, 2019).

The researchers note in their paper that they still need to see if the results hold true in other plots of permafrost around the Arctic, but the findings suggest permafrost warming will lead to significant greenhouse gas emissions, they conclude. “There is increasing recognition that the processes of soil microorganisms, and their responses to rising temperatures, need to be better incorporated into climate models in order to improve the accuracy of climate predictions,” Johnston says. “Research like this provides information for other researchers tasked with improving these models.”

—Ashley Yeager

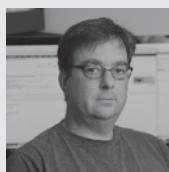
COMING SOON | Rare Genetic Disease: Models and Mechanisms

Establishing research models for any human disease is tricky business—more so for rare genetic diseases such as ataxia, telangiectasia, progeria, Paget’s disease, and Rett syndrome. Researchers who study model organisms such as *Caenorhabditis elegans*, *Drosophila*, mice, zebrafish, and yeast rarely connect with clinicians who report a rare genetic disease. Yet, studies on model organisms have provided pivotal insights into the mechanisms of several rare genetic diseases. For a detailed discussion on insights gained from model organisms used in understanding a wide spectrum of rare genetic diseases, *The Scientist* is bringing together a panel of experts to share their research, and to highlight the challenges and advantages of utilizing specific model organisms. Attendees will learn how model organisms can help scientists parse complex mechanisms underlying rare genetic disease from renowned experts in our interactive setting.



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The Dawn of Universal Ecology

Can science chart out laws that govern the interactions among living things even outside our solar system?

BY MARK COLYVAN, JOHN DAMUTH, AND LEV R. GINZBURG

There is a debate raging in ecology about whether there are ecological laws, analogous to the universal rules that underpin physics and mathematics. This discussion is important for a number of reasons. According to some, laws are the true mark of a scientific discipline, so ecology's status as a branch of science hinges on the outcome. The existence of ecological laws could also make a difference to the practice of ecology.

If there are no laws to be discovered, ecologists would seem to be in the business of merely supplying a suite of localized models. These models would be assessed for their empirical adequacy in specific contexts, but not for their ability to capture universal truths. If, on the other hand, ecology does have laws, this invites further exploration into what these laws are and what their utility might be in describing ecological dynamics.

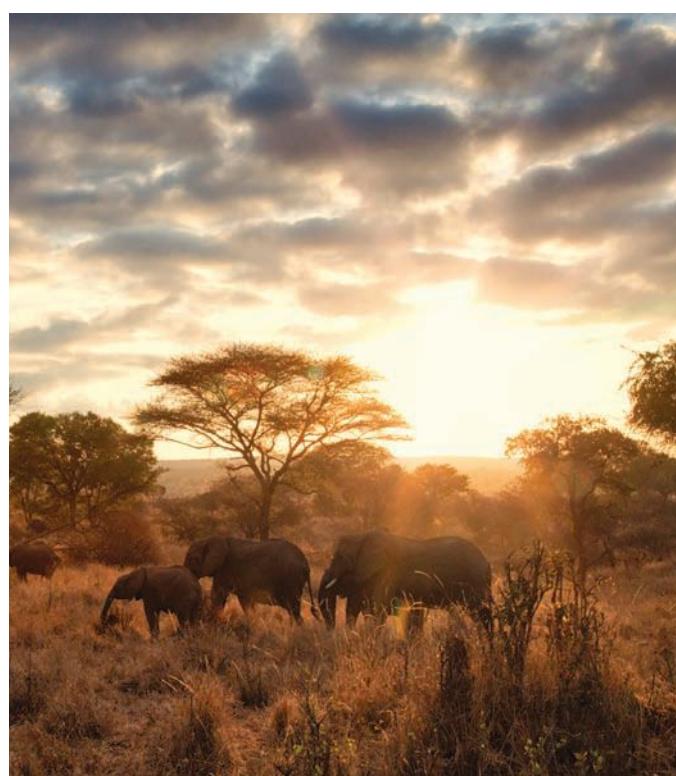
One way to approach the search for ecological laws is to consider what ecology on other planets would look like. If we expect that some aspects of Earth ecology would hold elsewhere in the universe, we would have good reason to suspect the existence of ecological laws (*Q Rev Biol*, 85:171–82, 2010).

On Earth, bacteria grow exponentially, lynx eat hares, and red panda populations decline due to habitat loss and fragmentation. How much of this ecology could we expect to find on other planets? Of course, we wouldn't find lynx, hares, red pandas, or Earth bacteria on a planet located outside our solar system. But might organisms there grow exponentially and respond to predators, prey, and habitat loss in the same ways as their Earthly counterparts? How could we tell?

Let's look to physics for some guidance. The laws of physics are the same throughout the universe. Local conditions, however, change: the acceleration due to gravitation on the surface of Mars is about 3.7 m/s^2 rather than the 9.8 m/s^2 here on Earth. But on both planets, acceleration due to gravity is proportional to the mass of the planet. In this example, looking beyond the superficial differences in the dynamics of a system reveals the scientific law that undergirds the differences. The same logic may apply to ecology.

Take the core ecological principle that, when resources are unlimited, populations grow exponentially. This principle, posited by Thomas Malthus in 1798, could be regarded as the cornerstone of population ecology. Ecologists have every reason to believe that this principle is perfectly generalizable. After all, it is a logical extension of the idea that every organism produces as many offspring as it can. A failure of exponential growth would require a systematic reduction in the overall reproductive output. In a system with limitless resources, such a decline would be inexplicable.

Exponential growth is thus an invariant principle; it codifies the idea that populations of reproducing organisms maintain a constant



reproduction rate regardless of time or place. The principle of exponential growth is one candidate for an ecological law. We argue that this principle plays as fundamental a role in ecological theory as Newton's first law does in physics (*Ecological Orbits: How Planets Move and Populations Grow*, Oxford University Press, New York, 2004).

But on any planet, resources are limited, and this changes things. Subject to this reality, a population grows (almost) exponentially at first, but the growth rate slows as the population approaches carrying capacity—the maximum population the environment can support. When approaching this limit, competition for resources among members of the population means that the density of the population becomes important, and the resulting reduction in individual resources causes a slowing of the population growth.

Population biologists chart this density-dependent growth variability using S-shaped population growth curves. The fact that no Earth-bound population grows exponentially forever testifies to the ubiquity of density-dependent limiting factors. So this principle, too, may fit the bill for universality. Now let us turn to some recent work on scaling relationships in ecology that suggest additional principles that could form the basis for ecological laws.

Ecologists have long known that metabolism scales allometrically with body size. That is, an organism's metabolism varies with its body mass raised to some exponent, and that exponent is usually less than one (*Hilgardia*, 6:315–53, 1932). As in all organismic allometries, the data may be noisy, but nonetheless the statistical relationship is clear. What has impressed ecologists in recent years is the degree to which other key ecological variables that also are known to vary allometrically with body size—abundances, productivities, and demographic characteristics—all seem to be interconnected in ways that ultimately appear tied to individual metabolic rates.

In general, the values of the exponents in question are clearly derived from the exponent for metabolism (*Size, Function, and Life History*, Harvard University Press, 1984; *Metabolic Ecology: A Scaling Approach*, ed. R.M. Sibly, et al., Wiley-Blackwell, 2012). But remarkably, two properties are invariant with respect to body size—in other words, they have exponents of zero. The maximum reproductive rate per generation is unrelated to species body size. Similarly, the energy use of populations of different species in a community is also not related to a species' body size. For example, the zebra (250 kg) and the wood mouse (35 g) can maximally produce about four offspring per female per generation, and their populations both use energy at an average rate of about 65 MJ per km² per day. (*Biol J Linn Soc*, 31:193–246, 1987; *Am Nat*, 169:621–31, 2007; *Biol Lett*, 6:850–53, 2010).

If the exponent of metabolic rate were different, all of the other exponents would change, except those for these two, which remain constant. Such invariance indicates that something is working the same way, on average, at all body sizes. These invariant relationships are like the laws discussed above: they are unaffected by local details, and we can expect them to hold true everywhere.

In Carl Sagan's novel *Contact*, an alien signal that was recognized as being sent by intelligent life consisted of a series of prime numbers in binary notation. The idea is that any intelligent civilization would have to have discovered the prime numbers and would recognize binary notation as fundamental. Indeed, mathematics is the same everywhere: $2+2=4$ is true on Earth as it is throughout the cosmos, and 7 is a prime number no matter where you live. Setting aside notation, extraterrestrial mathematics must be identical to terrestrial mathematics.

We have every reason to expect that the laws of physics and mathematics hold in far-flung corners of the universe. Recent work on ecological allometries suggests that researchers may be uncovering fundamental laws of biological interaction—universal ecology, if you like. Not only would we expect life on other planets to obey these allometric relationships, we could reasonably expect intelligent life forms to eventually discover these relationships. ■

Mark Colyvan is a professor of philosophy at the University of Sydney. John Damuth is an ecologist at the University of California, Santa Barbara. Lev R. Ginzburg is a theoretical ecologist who retired from Stony Brook University in 2015 and is the president of Applied Biomathematics, a private ecological research and software firm. All three were visiting scholars at the Stellenbosch Institute for Advanced Study in South Africa, where this article was conceived.



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Understanding T-cell polyfunctionality:

How single cell proteomics data drive CAR-T cell therapy research and development—an interview with Vladimir Senyukov

In CAR-T cell therapy, clinicians obtain T cell source material directly from a patient (autologous), or from a donor (allogenic), modify them, and re-introduce them to the patient. Working with autologous cells can be complicated by insufficient source material quality or quantity, and expanding the cells to the requisite number takes time that the patient may not have. Allogenic cells can be prepared in advance and mass produced, but they may be rejected by the patient, and in the worst case, begin attacking the patient's own cells.

Vladimir Senyukov is the Director of BioAnalytical Development at Precision Biosciences, where he investigates the development and manufacturing of allogenic CAR-T cell products. We spoke to him about working with allogenic CAR-T cells to unlock their therapeutic potential.

Using single-cell functional proteomics for CAR-T cell therapy development

Senyukov's goal is to learn what actually drives a cell to be polyfunctional – to produce multiple types of cytokines instead of a single cytokine – and to determine a way to apply that knowledge to improve CAR-T cell therapy in the future. Recent research found improved patient outcomes where polyfunctional T cells were present. For Senyukov, this indicates that genetic factors drive CAR-T cell heterogeneity, given that all the cells within a CAR-T product are ostensibly generated from the same starting material. But what is the relationship between these genetic factors and cytokine secretion profile? This is what Senyukov is trying to figure out with the help of single-cell functional proteomic approaches.

"My current project involves using IsoPlexis to profile the cytokine signatures of polyfunctional cells that we might have in a cell population," said Senyukov. "Then we take those cells and employ a single cell RNA sequencing approach where we can also try to identify



that polyfunctional cytokine signature in the RNAseq data. From there, we can try to identify what else—what other genes are associated with that signature—and then try to find the next genotype or other properties of a cell that makes them unique or different or better."

Testing and verifying edited and engineered CAR-T cells

Whenever cells have been altered in the laboratory—especially on a genetic level—researchers need to ensure that the edits function as intended. "To test CAR-T cells and figure out if they function properly," Senyukov said, "you usually test them against their targets." Researchers use three common metrics to evaluate T cell function and response: "When T cells are activated, they produce cytokines for the microenvironment and make it more pro-inflammatory. They [recruit] other cells and make the target cells more sensitive for killing, and that's one of the first responses usually from T cells when they encounter a target. The second way that a T cell responds is by killing, so we can measure how effectively CAR-T cells kill the target cells. The third expected response is that T cells will proliferate—when T cells recognize an antigen, they will increase the population of T cells that are responsive to that antigen."

Single-cell functional proteomics is valuable here as well, explained Senyukov. "When optimizing, or when changing manufacturing processes to make better cells, it can be used to monitor cellular changes. It is especially valuable in screening for polyfunctionality, which is key, because based on the literature, polyfunctionality is one of the most important factors driving clinical efficiency."

Unlocking the potential of allogenic CAR-T cells

Ultimately, Senyukov would like to break new ground for allogenic CAR-T cells, given that most of the existing research on polyfunctional T cells comes from cases of autologous cell transfer. "There haven't been too many studies on the importance of polyfunctionality for allogenic material, and there's a need to find specific signatures that could give us information about functional efficiency in a particular patient group. It's also about trying to find other pathways of gene expression associated with polyfunctionality that could allow future optimization of manufacturing processes."

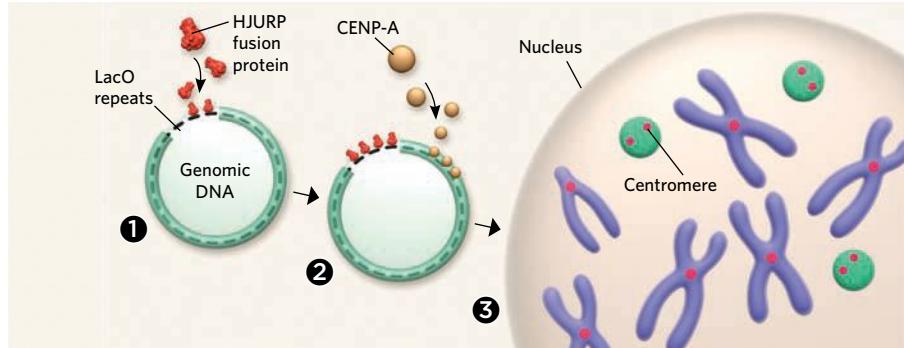
Streamlined Artificial Chromosome Creation

Recruiting an epigenetic instigator of centromere formation into large segments of cloned DNA facilitates their transformation into artificial chromosomes.

BY RUTH WILLIAMS

Artificial chromosomes are essentially miniature versions of real chromosomes that can replicate alongside their natural counterparts in host cells. They have the potential to be “incredibly useful for genome engineering, especially in cases where you want to put in a very large piece of DNA that, let’s say, [encodes] a whole cascade of enzymes involved in a particular pathway,” says chromatin researcher Gary Karpen of Lawrence Berkeley National Laboratory. However, this potential isn’t always realized because there’s a stubborn hurdle hindering artificial chromosome construction: creating centromeres.

Like natural chromosomes, artificial ones need centromeres to attach to mitotic spindles and separate sister chromatids during cell divisions. Centromeres are defined by the presence of a specialized histone called CENP-A that’s critical for connecting to spindles. But how CENP-A is initially recruited is not entirely clear. Centromeres tend to be buried deep in a jungle of repetitive DNA, known as α -satellite DNA in humans, and those repeats often contain binding sites for CENP-B, a protein thought to contribute to CENP-A loading. Researchers therefore generally include α -satellite DNA with CENP-B binding sites in sequences they wish to convert to human artificial chromosomes (HACs), but even with these seemingly appropriate sequences, centromere formation is hit-and-miss.



BUILDING A CENTROMERE: To convert a piece of cloned DNA into a centromere-containing human artificial chromosome (HAC), an array of repeated LacO sequences is incorporated into the DNA. The DNA is then transfected into human cells that have been engineered to express a fusion protein consisting of a LacO binding domain and a factor called HJURP. The fusion protein binds to the LacO domains 1, and incorporates the specialized centromeric histone CENP-A into and along neighboring chromatin 2. In turn, the region of CENP-A-containing chromatin forms a centromere, converting the cloned DNA into a functional self-perpetuating HAC 3.

Chromosome biologist Ben Black of the University of Pennsylvania and colleagues have now taken a more direct approach, essentially forcibly recruiting CENP-A into their chosen piece of cloned DNA. They first incorporate repeats of a 27-base-pair sequence called LacO in the part of the overall DNA molecule where they want a centromere to form. They then transfet the LacO-containing DNA into human cells engineered to express a fusion protein composed of a LacO binding domain and a protein called HJURP—an epigenetic factor responsible for incorporating CENP-A into chromatin. After binding to the LacO repeats, the fusion protein integrates CENP-A into and along the surrounding DNA, forming a centromere to support the stable replication of the HAC.

Using this method, the team was able to create functional centromeres in previously recalcitrant α -satellite-containing regions of cloned DNA. The researchers were even able to generate HACs using a region of chromosome 4 that entirely lacked α -satellite repeats. If other DNA sequences are similarly amenable to α -satellite-free HAC production, this could eliminate the added difficulties of handling highly repetitive DNA.

“I think the idea of preloading the DNA with CENP-A is a really good one,” says Karpen, who was not involved in the study. “It’s an important breakthrough. . . . [and] opens up new opportunities for creating artificial chromosomes.” (*Cell*, 178:P624–39. E19, 2019) ■

AT A GLANCE

HUMAN ARTIFICIAL CHROMOSOME FORMATION APPROACH	COMPONENTS	RATIONALE	STABILITY OF HAC CLONES
Sequence-based	40–200 kb of α -satellite repeats with a high frequency of the CENP-B binding sequence	α -satellite DNA is found at all human centromeres. CENP-B can facilitate CENP-A nucleosome assembly.	Varies considerably. At the low end, a HAC clone can be considered stable if the HAC is present in more than 20 percent of cells.
Epigenetic	A 10 kb array of LacO repeats that bind HJURP fusion proteins and approximately 200 kb of surrounding DNA	CENP-A is indispensable for centromere formation and function. Forced CENP-A seeding can generate self-propagating centromeric chromatin on plasmids in fruit fly cells.	The majority of clones have the HAC present in 80 to 100 percent of cells.



CONOR GOULDING/MOTE MARINE LABORATORY

TIDES, **RED** IN TOOTH AND CLAW

Red tide events strike Florida annually. Researchers are racing to understand and mitigate the potentially disastrous phytoplankton blooms.

BY BOB GRANT

Asingular scene from last year's red tide event in the Gulf of Mexico sticks in the memory of phytoplankton ecologist Vincent Lovko. "I got to go up in a helicopter with a news crew," Lovko says. "You could see the front of the bloom right along the coast"—a reddish cloud of millions of microscopic organisms called dinoflagellates floating in the water. "The striking part was all the little white dots, which were the dead fish."

Red tides are caused by the dramatic reproduction of *Karenia brevis*, a species of dinoflagellate that is common in Gulf waters. Every year when conditions turn favorable, populations of the unicellular alga grow rapidly, dyeing undulating patches of water a brown, green, or rusty

ment of Health noting a small uptick in the number of weekly emergency department visits statewide in July through November 2018 for people reporting respiratory symptoms and red tide exposure. Although a causal relationship was not formally established in these cases, brevetoxins are known to cause respiratory irritation when the compounds become airborne as wind and waves whipped the water into sea spray.

Currents first swept the 2017–2019 red tide near the Florida panhandle and then around the Florida Keys and up the Atlantic coast, dumping swaths of ruddy water into nearshore ecosystems as far north as Orlando. (See map on the opposite page.) The bloom "was in so many places at the same time," remembers Kate Hubbard,

evolved to produce brevetoxins, nor do they have a complete understanding of the environmental and ecological drivers of bloom formation, maintenance, and termination.

The factors at play are so numerous and dynamic that anticipating shifts in local conditions that might promote a bloom has proven difficult, to say the least. Broader concerns about how climate change might alter Florida's red tides add to the uncertainty. All of this makes for a vexingly complex soup of unknowns surrounding *K. brevis*.

But new insights are emerging all the time, and the scientists who study the phytoplankton and its blooms are getting closer each year to decoding the phenomenon. Hubbard, Lovko, several of his Mote colleagues, and other researchers throughout the state and beyond are taking advantage of new technologies—such as self-propelled underwater robotic gliders that sample water and track conditions in situ, and advanced genetic tools for detecting the presence of *K. brevis* cells—to try to understand what triggers the phytoplankton to undergo rapid population growths, why they make brevetoxins at all, and how best to mitigate red tides once they begin ramping up in the Gulf.

"The implementation of those tools is going to really help us address some of those key questions," Hubbard says. "I feel pretty optimistic that we are going to be able to make some new discoveries . . . to help us in our predictive models."

The bloom trackers

Historical accounts suggest that populations of *K. brevis* in the Gulf have been undergoing annual population booms since at least the 15th and 16th centuries, when Spanish explorers in Florida described fish kills in Gulf waters that bore a striking resemblance to the scene that Lovko noted last year.¹ In 1882, the first official, though anecdotal, documentation of fish kills, bird deaths, and human sickness caused by red tide blooms in the Gulf of Mexico—as far back as 1844—was published in the *Proceedings of the U.S. National Museum*.

I honestly do not know if *K. brevis* blooms can be “prevented” based on the level of our current knowledge.

—Karen Steidinger, retired phytoplankton ecologist
after whom *Karenia brevis* is named

hue. Sometimes these events come and go in a matter of weeks or months. But the bloom that Lovko, a researcher at the Mote Marine Laboratory in Sarasota, saw dotted with the corpses of fish lingered in the Gulf for more than a year. It started sometime in October 2017 and didn't dissipate until early this year. And the fish—most likely killed by potent neurotoxins called brevetoxins produced by *K. brevis*—weren't the red tide's only victims.

According to statistics kept by the Florida Fish and Wildlife Conservation Commission (FFWCC), the bloom killed more than 1,000 sea turtles, about 200 manatees, and nearly 190 bottlenose dolphins, in addition to countless fish and some economically important invertebrates, such as stone crabs. Humans may have also felt the effects of Florida's most recent red tide, with the Florida Depart-

head of the harmful algal bloom (HAB) research and monitoring program at the FFWCC's Fish and Wildlife Research Institute (FWRI). Phytoplankton biologist Cynthia Heil, director of the Mote Marine Laboratory's newly formed Red Tide Institute, adds, "Local currents do impact these blooms."

Red tides are nothing new to the Gulf. They've plagued the area for hundreds of years, and since the 1940s, when researchers linked *K. brevis* (then called *Gymnodinium breve*) to the Gulf's red tide events, the scientific community has been trying to learn more about the biology of the dinoflagellate species, hoping to more accurately predict blooms and mitigate the damage to local ecosystems and human health. But many critical questions remain. Scientists have not yet fully described *K. brevis*'s life cycle or plausibly hypothesized why the species

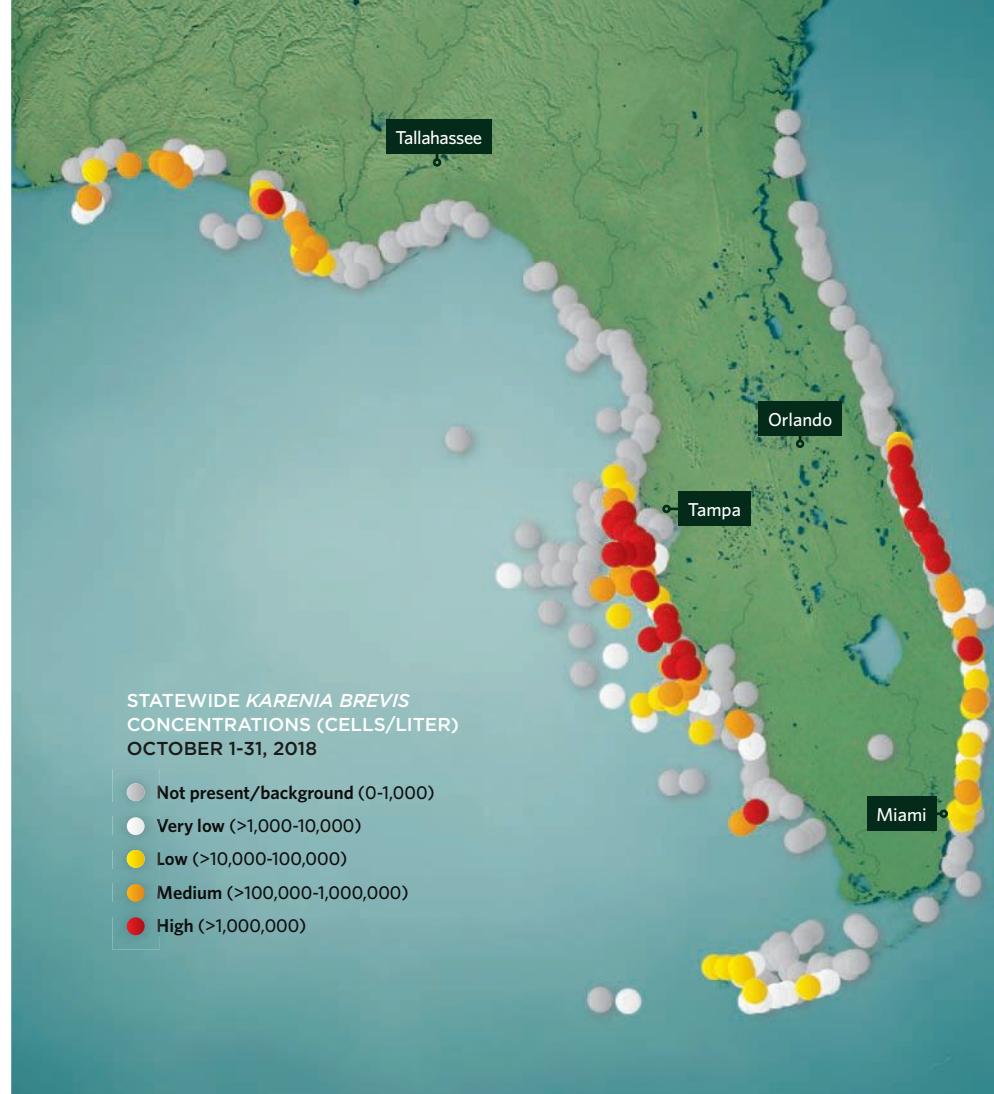
Since then, researchers have tracked the annual *K. brevis* blooms, which typically crop up in the late summer or autumn and vary in length.

In the FWRI lab in St. Petersburg, Hubbard's team of scientists is focused on monitoring *K. brevis* in the Gulf. They process water samples sent in by citizens or fellow researchers who notice something amiss—fish kills or discolored water, for example. FedEx shipments containing plastic containers of water are usually sparse in mid-summer, but during the 2017–2019 red tide event, Hubbard says, there was little letup. In total, her lab processed more than 14,000 of these samples over a 16-month period, she says.

Currently, Hubbard's team primarily uses manual cell counts for state-mandated estimates of *K. brevis* abundance. They also occasionally hook up a microscope to a submersible imaging flow cytometer, an automated machine that can process 5–8 mL samples in about 20 minutes, detecting a variety of phytoplankton species including *K. brevis*. The group also tracks toxins and phytoplankton cells in water samples using chemical analyses such as liquid chromatography and mass spectrometry. Now, in collaboration with other red tide researchers, Hubbard is working on refining a method that can detect *K. brevis* RNA in water samples, using a handheld device that is already showing promise in field trials for yielding quick and accurate measures of the phytoplankton's abundance.

"The genetic methods can be quite tricky," Hubbard says. "But I do foresee [the device] could be something that's used to quickly scan samples." Her team archives water samples so that they can be used to further develop this and other new methods of censusing *K. brevis*.

With the data they gather—which now includes inputs from an autonomous aquatic "glider" that samples environmental conditions in the Gulf—Hubbard's agency puts out twice-weekly bulletins detailing which Florida beaches are affected by red tide. People with lung conditions such as asthma are par-



ticularly vulnerable to serious adverse effects when winds blow airborne toxins onshore. Barbara Kirkpatrick, the executive director of the Gulf of Mexico Coastal Ocean Observing System (GCOOS), a nonprofit with a remit of providing information about the Gulf coastal and ocean waters, is working to refine that public-facing monitoring effort. "Blooms are patchy. Conditions can change day to day and beach to beach," she says. "We're trying to come up with a daily forecast that updates every three hours."

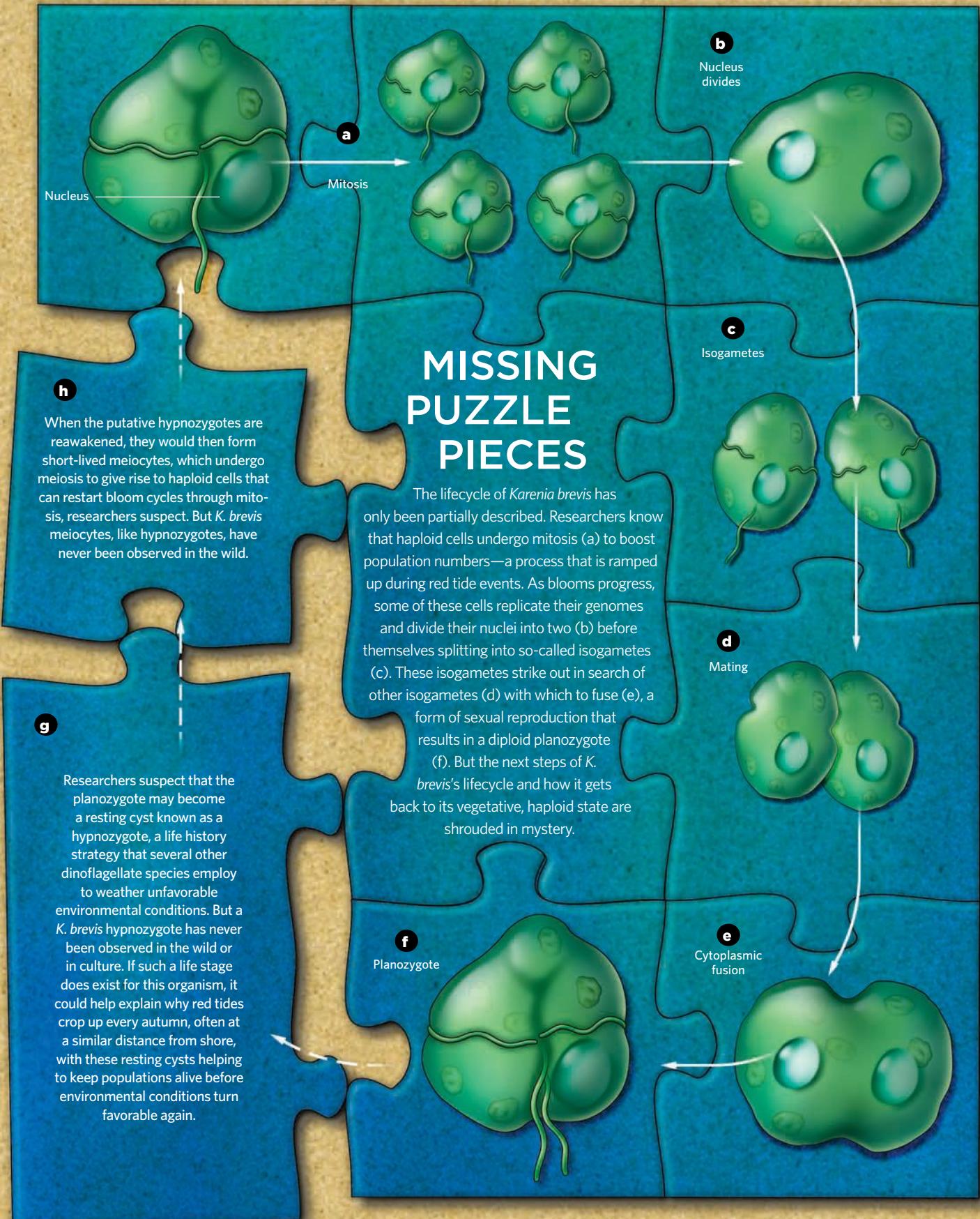
The complexity of the species' biology—and the gaping holes in scientists' knowledge of it—presents a challenge. "I honestly do not know if *K. brevis* blooms can be 'prevented' based on the level of our current knowledge," Karen Steidinger, the retired plankton ecologist after whom *Karenia brevis* was named when its Latin binomial was changed in 2001, writes in an email to *The Scientist*.

BICOASTAL BLOOM: In October 2018, at the height of the red tide that plagued Florida for more than 16 months, millions of the causative dinoflagellates teemed in waters off Florida's panhandle, as well as on the west and east coasts of the state.

Demystifying the red tide lifecycle

Dinoflagellate life histories are notoriously complicated, and *K. brevis*'s lifecycle in particular has been difficult to nail down. But by looking across more than 2,000 known species of marine dinoflagellates, scientists can identify common strategies that could start to fill in the missing details. For example, more than 10 percent of species employ a resting cyst stage,² and many phytoplankton scientists suspect that *K. brevis* does too. (See "Missing Puzzle Pieces" on page 30.)

Resting cysts are analogous to seeds in terrestrial plants: they afford dinoflagellates the ability to deposit their



Blooms are patchy. Conditions can change day to day and beach to beach.

—Barbara Kirkpatrick,
Gulf of Mexico Coastal Ocean Observing System

genomes in marine sediments or bottom waters as round, featureless cells, which lie dormant until favorable conditions trigger the transition back to a planktonic and highly reproductive stage of the lifecycle. The regular seasonality of Florida red tide blooms supports the existence of this type of strategy for *K. brevis*, with dormant “seeds” riding out the unfavorable conditions of the spring and early summer months, reawakening closer to fall, and transforming into so-called vegetative cells that multiply rapidly to cause the sometimes-catastrophic blooms. “Whether the cysts are in the sediments or in the water column, I do think it’s reasonable to suspect that there is a resting stage of some kind,” says Cary Lopez, a phytoplankton ecologist at FWRI. It’s also possible, however, that the species goes directly from reproducing more slowly during a period of sexual reproduction to more rapidly reproducing during asexual stages, without first transitioning into a cyst.

Determining whether the species has a resting stage could be a boon to managers seeking to predict and control red tide events as blooms in the Gulf begin to form, just as knowledge of resting cysts in other harmful algal species helps scientists manage blooms elsewhere. For example, researchers studying *Alexandrium fundyense*, a dinoflagellate whose blooms cause regular, toxic red tides that compromise ecological and human health along the northeastern coast of the US into Canada, have mapped out two distinct cyst beds—accumulations of resting-stage cells deposited by prior blooms. The research team that described these hideouts also noted that the size and distribution of those cyst repositories correlated with the extent of blooms that

followed.³ Finding similar cyst deposits in *K. brevis* would confirm that this part of the lifecycle exists, and would allow researchers to monitor dormant populations for signs of an impending bloom in the Gulf.

The opportunity to collect and study *K. brevis* cysts in the lab, or to generate them from an earlier life stage, could also help determine what precipitates the change from one life stage to another. “If we could identify this resting stage and then understand what drives the transition from a resting cyst to a vegetative cell, that would be very important,” says Lopez. She adds, however, that funding is often

funneled to more-pressing mitigation and monitoring research, so researchers aren’t scouring the Gulf for *K. brevis* cyst beds. Hubbard adds that while she and her team do keep an eye out for cysts when sifting through sediment samples, they are predominately relying on oceanographic measures, such as water temperature and the speed and direction of relevant currents, along with cell counts of *K. brevis*, to generate red tide forecasts.

“Right now, we’re using physical data to be able to predict what’s going to happen with blooms,” Hubbard says. “Not knowing whether there is some similar accumulation of *Karenia* cells and where that might be makes it really challenging to be able to predict exactly when and where blooms might start.”

READY TO BLOOM: *K. brevis* cells in the vegetative stage of their lifecycle are primed to undergo mitosis, increasing population numbers quickly and potentially leading to a red tide.



Sparking and sustaining blooms

While predicting red tide blooms remains tricky, it's clear that widespread and multifaceted factors drive their initiation each year. For decades, researchers have been amassing evidence that *K. brevis* blooms start near the seafloor about 10 to 40 miles offshore in the Gulf. This makes the species somewhat unique among bloom-causing algae, many of which begin to expand inshore or near-shore, flourishing in the high nutrient concentrations, warm temperatures, and sunlight that most phytoplankton require to survive and reproduce.

What may set *K. brevis* apart is its ability to thrive on a variety of nutrients and to get those nutrients in a number of ways. In several papers published in a 2014 special issue of the journal *Harmful Algae*, researchers including Heil documented that *K. brevis* can subsist

on nutrients from undersea sediments, decaying fish, atmospheric deposits, and estuarine water. They can consume other plankton species or use nutrients those species produce, and can absorb nutrients from the water following the decay of a filamentous cyanobacterial genus called *Trichodesmium*.⁴ "Karenia brevis is super flexible," Hubbard says.

The observation that the dinoflagellate can dine on rotting *Trichodesmium*, which occasionally also blooms in the Gulf, links red tides in the area to events that extend far beyond the state of Florida and the Gulf of Mexico. In 2001, scientists published evidence that dust storms in the Sahara Desert in early 1999 supplied nutrients that supported subsequent blooms of *Trichodesmium*, which requires high iron levels to thrive. Levels of dissolved phosphorus plummeted as it was consumed by the cyanobacteria, and dissolved nitrogen increased, potentially fueling a nitrogen-hungry *K. brevis* bloom that reddened Gulf waters in the fall of the same year.⁵

While it's not known whether large, sustained red tide events are caused by one or multiple dinoflagellate populations, once *K. brevis* gets blooming, the phytoplankton are sometimes swept toward shore by upwelling and prevailing currents into surface waters, where they continue to proliferate. This process involves yet another suite of drivers that include nutrient inputs from fertilizers in groundwater runoff, fish killed by the bloom, faulty wastewater systems, even air pollution—and, of course, local currents.

A recent study tracked the extensive movement of Florida's exceptional 2017–2019 red tide event and suggested that its movement into nearshore waters skirting the state's panhandle may have resulted from the passage of Tropical Storm Gordon across the Gulf from the southwest coast of Florida to Texas and Louisiana in early September 2018. The storm, the study reported, may have disrupted the upwelling that had brought the bloom into nearshore waters on the state's west coast, allowing the red tide to move north

A RISING TIDE: A *K. brevis* bloom dyed coastal waters off of Sarasota, Florida, in August 2018, during the 2017–2019 red tide event.



IN SEARCH OF SOLUTIONS: Amanda Muni-Morgan, a technician in Cynthia Heil's Mote laboratory, tests the effectiveness of compounds in killing *K. brevis* cells and neutralizing brevetoxins.

toward the panhandle. When the storm passed, upwelling resumed, and strong currents swung the red tide around the Keys and into coastal waters of the Atlantic along the state's eastern shore.⁶

Climate change and its effects on patterns of environmental conditions—rising sea surface temperatures increasing the frequency of intense hurricanes; changes in marine ecosystem function—add another layer of complexity. “In the 20th century, it was a question of looking at how are these local changes affecting red tide,” Heil says. In the 21st century, she continues, the focus has shifted to how climate change might be altering the longstanding ecological cycling represented by Florida red tides. “There are all these different, changing dynamics.”

“Just like anything,” Hubbard adds, “it’s not necessarily entirely predictable.”

Mitigating the effects of red tides

Although plenty of discoveries lie in wait for the scientists studying the basic biology and ecology of *K. brevis* and the nature and evolution of red tide events, funding these days is usually earmarked for monitoring and mitigation. Heil was the recipient of some of that episodic funding last October, when the Andrew and Judith Economos Charitable Foundation donated \$1 million to establish the Red Tide Institute at Mote, as the protracted *K. brevis* bloom churned in the Gulf and made its way around the state's southern tip.

On a rainy July day at the facility this year, Heil's head lab technician, Amanda Muni-Morgan, swirled several beakers filled with greenish water—it was chock-full of *K. brevis* cells. She added gramine, an extract from the giant cane plant (*Arundo donax*) that may help lyse the phytoplankton cells, but may also help mitigate the aftereffects. “Killing *K. brevis* cells is not difficult,” explains Heil.



“The problem is, you release the toxin when you kill the cells.”

Heil says she and her colleagues plan on testing a variety of other compounds as potential treatments to mitigate the toxicity and longevity of red tides. Currently, researchers and public health officials have no options at their disposal for effectively controlling blooms. Heil adds that she's focusing on naturally derived compounds such as gramine, as they are less likely than harsher, synthetic chemicals such as herbicides to perturb the environment when added to seawater in the field. This work is in its early stages, notes FWRI's Hubbard. “Right now, coming up with solid, robust strategies for testing those compounds is important.”

Unfortunately, funding for phytoplankton biologists seeking to untangle that complexity is patchy, says Kirkpatrick. Large and widespread blooms like the 2017–2019 red tide attract a lot of media and public attention, but only happen periodically, and “episodic events get episodic funding.”

The result, she says, is slowed scientific progress on the basic biological front. “Over the years, I've had people say

to my face, ‘Why don't you know more?’” she recalls. “It's not for lack of wanting to know more. It's for lack of the funding to do the studies to know more.” ■

Bob Grant is editor in chief of The Scientist. Email him at rgrant@the-scientist.com

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CONNECTED SEAS

To help conserve life in the ocean, researchers are following marine organisms' movements.

BY CATHERINE OFFORD

When it comes to telling manta rays apart, Asia Armstrong is an expert. The University of Queensland PhD student is studying populations of *Mobula alfredi*, the reef manta, in the Great Barrier Reef Marine Park off the northeast coast of Australia, and has spent countless hours poring over photos of the fish—snapped by citizen scientists as well as by Armstrong and her colleagues over several decades—with the aim of identifying individuals. “Manta rays have a unique spot pattern on their ventral surface—smudges, dots, stripes,” she explains. In a database of around 1,300 individual animals, “I’d probably recognize half of them now.”

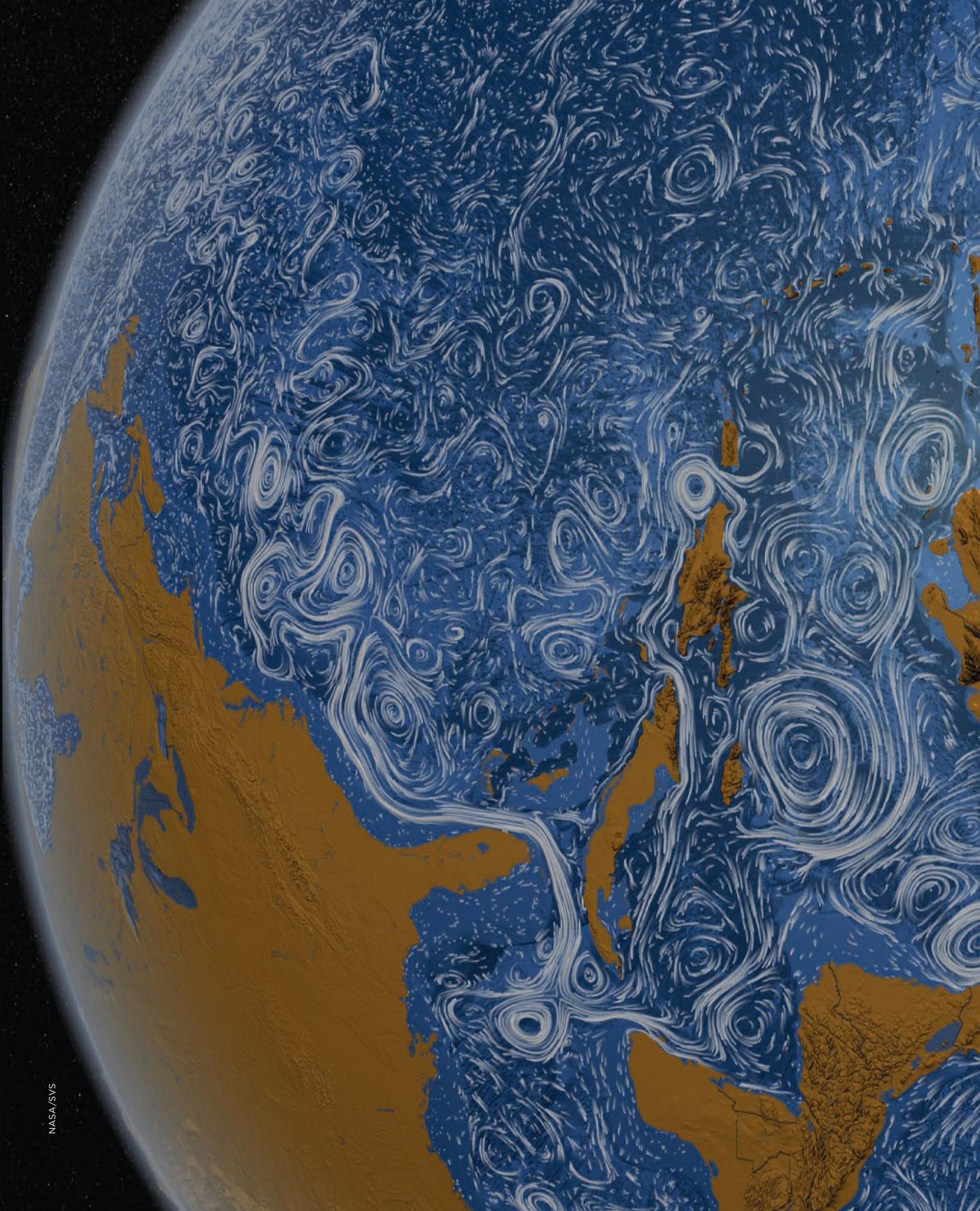
For the past few years, researchers have been working under the assumption that local manta populations are split between two main regions, a northern one and a southern one, separated by hundreds of kilometers. But a video Armstrong received last June from a dive site off the coast of northern Queensland in between the two supposed ranges threw that assumption into

doubt. The video showed two manta rays that Armstrong immediately recognized as members of a population inhabiting the southern region. Indeed, the rays had last been seen some 1,150 kilometers south of the dive site—a distance almost double that of the longest recorded movement for a reef manta. Photographs submitted a few weeks later confirmed the find: one of the two mantas had been spotted again swimming around the same site.

“Until this point, everything we had [on the mantas] from northern Queensland didn’t match anything from southern Queensland . . . and we didn’t have anything in between,” says Queensland marine scientist Christine Dudgeon, who coauthored the study documenting the finding in July.¹ Although it’s unclear whether the northern and southern populations overlap, the new data extend the southern population’s range by hundreds of kilometers to the north, she says. This information could help researchers devise better plans for worldwide conservation of manta rays, whose numbers are

decreasing in part due to the many threats they face from humans, including harvesting for use in traditional Chinese medicine.

The findings are a surprise to local manta researchers, but they hammer home the importance of considering marine organisms’ movements through the world’s oceans when trying to protect them. Research suggests that lots of animal species, many of them commercially, culturally, and ecologically important, could regularly traverse much larger areas than previously realized, whether as swimming adults, or, more often, at other life stages such as larvae or juveniles swept along by or propelling themselves within ocean currents. Until now, most species have been managed and conserved locally, often in marine protected areas (MPAs)—from strict “no-take” zones to areas with more-nuanced rules—overseen by national or regional governments. But the constant traffic of individuals from one place to another means that animals are often moving between areas with different levels of conservation protection and administrative oversight. Unless such



geographical links are taken into account, an organism's protection in one area could easily be undermined by its vulnerability in another.

Recognizing this, scientists and policy-makers are taking the concept of marine connectivity—a term biologists use broadly to refer to the exchange of individuals, genetic sequences, or food and other material between regions or populations in the ocean—into account as they wrestle with how best to protect marine ecosystems from overfishing, climate change, and other anthropogenic pressures. (See the Glossary on page 40.) Quantifying marine connectivity is consequently becoming a central focus of marine conservation research, with biologists developing new methods to assess species' movements and building management guidelines from the results.

"It is the next issue that policymakers are being faced with," says Anna Metaxas, a biological oceanographer at Dalhousie University in Halifax, Canada. "The science is telling us, 'Whoa, you have to consider [connectivity]. You can't ignore it if you want your MPAs to be viable.'"

The wild, wide ocean

Clumps of edible marine mussels (*Mytilus galloprovincialis*) are a familiar sight along the rockier parts of Portugal's Atlantic coast. Ecologically and socioeconomically important, *Mytilus* species help shape the structure and food webs of tidal ecosystems around the world. For the last few years, Henrique Queiroga and his colleagues have been studying the connectivity of wild populations of these mussels—specifically, the exchange of larvae between populations distributed along the coast. "In most marine species, dispersal takes place during the larval phase," says Queiroga, a marine ecologist at Universidade de Aveiro in Portugal. "Most of the marine species that we know and most of the marine species that we eat have a larval phase—tuna, cod, herring, clams, muscles, crabs, shrimps."

Because, completely unlike manta rays, these larvae are too small to see with the naked eye, Queiroga's team recently took advantage of an indirect method of assessing connectivity for a study of mussel populations around Lisbon. Right after it's

spawned, a mussel larva begins growing a calcium carbonate shell. For the next few weeks, the animal is ferried about by ocean currents until it settles on a rock or other surface along the shoreline to begin metamorphosing into a juvenile and later maturing into an adult. The chemical composition of each section of shell, Queiroga explains, depends on the seawater in which it develops, meaning that the base of a mussel's shell provides a permanent "elemental fingerprint" of where that animal started life.

To create a database of these fingerprints, the team harvested thousands of larvae spawned from mussels in the lab, and deposited them in batches of about 20,000 into larval homes—small PVC tubes with mesh covering either end. They then distributed these homes along more than 120 kilometers of Portuguese coastline, waited a few days for the larvae to begin making their shells, and then hauled them back into the lab for chemical analysis. The result was an atlas of chemical signatures of different spawning regions.



Making direct measurements of dispersal in the ocean is a hugely intensive effort.

—Simon Thorrold,
Woods Hole Oceanographic Institution

By comparing the shell bases of wild mussels collected along the shoreline to this chemical atlas, the researchers discovered that mussel larvae move quite a bit. Mussels in an MPA south of Lisbon seemed to have contributed offspring not only to their own population during the study period, but also to populations to the north, including another MPA more than 100 kilometers up the coast.² The findings underline the practical importance of considering connectivity. Often "you cannot just protect" one population, says Queiroga. "Because if this one is supplied by larvae that come

from the other population and the other population is not protected, then your management plans are worthless."

Such geochemical analyses can offer insight into many taxa beyond mollusks. For example, researchers often use calcium carbonate structures known as otoliths, present in the inner ear of many vertebrate species, to determine the origins of individual fish. One recent study that analyzed the otoliths of more than 100 Atlantic herring (*Clupea harengus*) demonstrated that measuring the relative concentrations of 17 chemical elements could pinpoint the specific bay or estuary where that fish had been spawned—serving as a "chemical 'birth certificate' of their natal origin," the authors write.³

But the approach is just one of many now being used to assess marine connectivity. Telemetry—using acoustic or satellite-based markers, for example—can offer more-detailed information about the peregrinations of organisms large enough to capture and tag. Work by Jay Rooker's group at Texas A&M University, for example, has used multiple types of tags to map the movements of sharks and commercially important fish across jurisdictional boundaries in the Gulf of Mexico,⁴ while Dudgeon and her colleagues have recently deployed satellite tags on their manta rays to track them in and around the Great Barrier Reef. DNA-based methods, meanwhile, can generate data not just about animals' journeys between populations, but the resulting exchange of genomic material as well.

Most of the genetics techniques used until now to study marine connectivity have focused on evaluating genetic diversity as a way to estimate gene flow between seemingly isolated populations. But an increasingly popular method is parentage analysis, which uses genetic markers such as single-nucleotide polymorphisms or repetitive, fast-mutating sequences of DNA called microsatellites to identify an offspring's parents. "What's amazing about the tool is that I can literally match [a larva] with the mother or father that produced it," says Mark Carr, a marine ecologist at the University of California, Santa Cruz. "As long as the adult doesn't move, we know where that larva came from."

Carr, along with a large group of colleagues, graduate students, and volunteers, recently carried out a parentage analysis for kelp rockfish (*Sebastes atrovirens*), an abundant species in temperate ecosystems. The team sampled 6,000 fish—clipping a bit of fin tissue from individuals caught with a hook and line, or nicking the skin of freely swimming fish with a customized pole spear while scuba diving—along 25 kilometers of California’s coastline that included multiple MPAs. Analyzing nearly 100 different genetic markers in the samples, the researchers identified eight parent-offspring pairs. At least two of those offspring had moved out of the MPA where their parents lived into areas where fishing is allowed. Four other offspring had also dispersed out of their parents’ MPA, but subsequently found their way into another.⁵

Unfortunately, such projects are expensive and time-consuming, notes Simon Thorrold, an ocean ecologist at the Woods Hole Oceanographic Institution whose group used parentage analysis a couple of years ago

TRACKING GIANTS: With the help of citizen scientists, researchers such as University of Queensland PhD student Chris Lawson have been photographing reef mantas for an online database that notes when and where the massive rays have been spotted.

to reveal high levels of connectivity among clownfish (*Amphiprion percula*) and butterflyfish (*Chaetodon vagabundus*) populations around Papua New Guinea.⁶ “[Mak-ing] direct measurements of dispersal in the ocean is a hugely intensive effort,” Thorrold says. Because researchers can’t study every species in the ocean using these methods, he adds, “we’re always going to be extrapolating from the few species we know considerably more about.”

Models of the sea

To aid in making such inferences, researchers turn to computer models. Simulations based on a species’ distribution and life history, combined with physical data such as ocean current measurements, can help labs predict the movements of marine organisms. Metaxas and colleagues, for example, recently modeled larval dispersal to assess connectivity between populations of deep-water corals, ecologically important but difficult-to-study organisms, in canyons in the ocean floor off the coast of Nova Scotia. Using physical data on ocean currents as well as the distribution of corals—which the team visually assessed using a remotely operated vehicle—the researchers estimated the movement of larvae from one population to another and found evidence for frequent exchange between Canadian and US waters.⁷

When possible, researchers complement physical data on ocean currents with biological data on larval behavior. Larvae of many species can swim up and down in the water column, for example, or toward or away from stimuli such as light, noise, and certain environmental chemicals. Nandini Ramesh, a postdoc in atmospheric scientist William Boos’s lab at the University of California, Berkeley, and colleagues recently developed one such biophysical model to estimate the larval movement of more than 700 commercially important fish species around the globe. Results generated by the model suggested that the world’s fisheries are highly interconnected, with many fish spawned in one country’s waters going on to be caught in another’s. Accounting for the species’ economic value to the fishing industry, the team estimated that this international connectivity helps generate more than \$10 billion a year.⁸

Such biophysical models can predict, on a large scale, both where individual animals might end up and how they get there. But the findings are difficult to validate, says Thorrold. “While [simulations] can produce quite compelling visuals, there really has been no way of determining how accurate those biophysical models are,” he says. “It’s going to come down to combining [them] with other methods.”

Back in Portugal, Queiroga and his colleagues have been working on just such a combined approach for their mussel populations. Last year, the researchers published a biophysical model of larval dispersal based on ocean currents along the coast and compared it to observations from their geochemical analyses. The results of the two approaches, the team found, were highly correlated.⁹ “If the different methods converge, [and their] estimates are similar to each other,” says Queiroga, “then we begin to be more confident about the description of the process.”

A protective net

As researchers continue to demonstrate the practical importance of marine connectivity, the concept is slowly being incorporated into conservation planning. Metaxas, who acts as an advisor to the Canadian government’s Department of Fisheries and Oceans, notes that policymakers around the world increas-



TRACKING

The most direct way of measuring marine movement is to record observations of ocean-dwelling organisms *in situ*. Those data can be collected through photographs, videos, or visual surveys or by using tags that store or remotely transmit location information to researchers. Tracking is particularly effective for large, migratory animals, but is practically infeasible for smaller species and larvae.

GENETICS

Tissue samples from marine organisms allow researchers to quantify genetic diversity within populations and gene flow between them. One particularly resource-intensive and time-consuming approach known as parentage analysis even allows researchers to identify which adults spawned a particular larva. For species that move relatively little in adulthood, such as many species of reef fish, researchers can then extrapolate to figure out where that larva was spawned.



BIOGEOCHEMISTRY

Calcium carbonate-containing structures such as fish otoliths and mollusk shells contain chemical signatures of the composition of seawater in which they formed. By comparing the otoliths or shells of wild organisms to a database of chemical signatures, researchers can establish where an organism developed.

SIMULATIONS

Researchers turn to computer simulations when fieldwork is impractical, or when they want to compare experimental data with a particular theory. This is an especially common approach for estimating the travel patterns of larvae or planktonic organisms, which can be moved great distances by ocean currents. More-complex models incorporate data on larval behavior to try to boost predictive power.



MEASURING MOVEMENT

Researchers study the movement of marine organisms using both direct and indirect techniques. Some methods are only appropriate for some species, and most groups try to use multiple methods to validate their results.

ingly use ecological data alongside social and economic information to guide the design of MPAs. But marine connectivity is “still the new kid on the block.”

Metaxas and Dalhousie University graduate student Arieanna Balbar recently reviewed nearly 750 MPAs in regions of the globe with advanced conservation initiatives. They found that just 11 percent included considerations of marine connectivity, and most of those that did were in Australia and California, which have the largest and second-largest networks of MPAs, respectively.¹⁰ New research guidelines take a while to trickle down into management plans, Metaxas says, and there’s still a lack of data for many of the marine areas that policymakers want to protect. “You have a disconnect between what managers *can* do and what scientists write in the literature that they *should* do.”

To help conservation planners consider marine connectivity even when data are sparse, Carr and others have promoted the idea of “rules of thumb” to guide the size and spacing of individual MPAs within a larger network of protected areas. According to these rules, developed in California after the state passed the 1999 Marine Life

Protection Act, each MPA should have an area of at least 50 square kilometers—large enough to contain all of the adults in most local reef or coastal fish populations. Furthermore, MPAs should be spaced closely enough that larvae from one MPA can disperse to an adjacent one—ideally, a distance of no more than 100 kilometers.



Connectivity may not always be necessary to include. But it should always be considered.

—Anna Metaxas, Dalhousie University

California’s MPA network is considered a model example, says Carr, and other managers, such as those in Oregon, have based their own marine protection plans on a similar framework. (See “Protected Area” on opposite page.) Yet some researchers argue that rules-of-thumb

approaches risk oversimplifying connectivity by ignoring factors specific to individual species or regions, and overlooking empirical data that may be on hand.

Metaxas and undergrad student Jenny Smith recently developed a decision tree that tries to incorporate more of that local specificity by walking conservation planners through a series of connectivity-relevant questions about a target species or habitat.¹¹ For example, according to the tree, a species with larvae that disperse over short distances would likely require that MPAs be large enough to capture that dispersal and ensure each population is adequately protected locally, but the spacing of the MPAs may not matter if dispersal outside the region is rare. The approach helps planners identify the aspects of marine connectivity that are most relevant and weigh them against other factors guiding MPA design—from ecological considerations such as a region’s existing biodiversity to socioeconomic factors such as the income and livelihoods of local fishermen, says Metaxas. Connectivity “may not always be necessary to include,” she explains. “But it should always be considered.”

Efforts to design effective networks of MPAs are made particularly tough by the

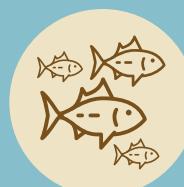
THE LANGUAGE OF THE SEA

A relatively young concept in marine biology, marine connectivity is loosely defined as the exchange of individual organisms, food, or other material between habitats or populations in the ocean. In addition to this umbrella term, researchers also use several non-mutually-exclusive subtypes of marine connectivity to describe species’ patterns. These terms have equivalents in research on connectivity in terrestrial habitats, too.



STRUCTURAL CONNECTIVITY

Movement due to the physical characteristics of the environment. Ocean currents and seafloor topography help determine structural connectivity.



DEMOGRAPHIC CONNECTIVITY

The effect of individuals’ movement on the size, growth, and other characteristics of a population.



FUNCTIONAL CONNECTIVITY

Movement due to the ecological traits of an organism. Dispersal ability plus habitat and food preferences influence functional connectivity.



GENETIC CONNECTIVITY

The effect of gene flow on evolutionary processes in a population.

fact that populations' interconnectedness is likely to evolve for most species and ecosystems in the coming years as anthropogenic pressures on the oceans intensify. With climate change, for example, altered weather patterns could drastically reduce the effectiveness of existing MPA networks by disrupting dispersal between areas, recent computational studies have found. "There are a number of things that are going to change," explains Ramesh. "Ocean circulation is going to change, but also the fish themselves are going to be responding to warmer waters and moving into habitats that they find most suitable.... This whole [connectivity] network is going to be shifting over time as the Earth warms." ■

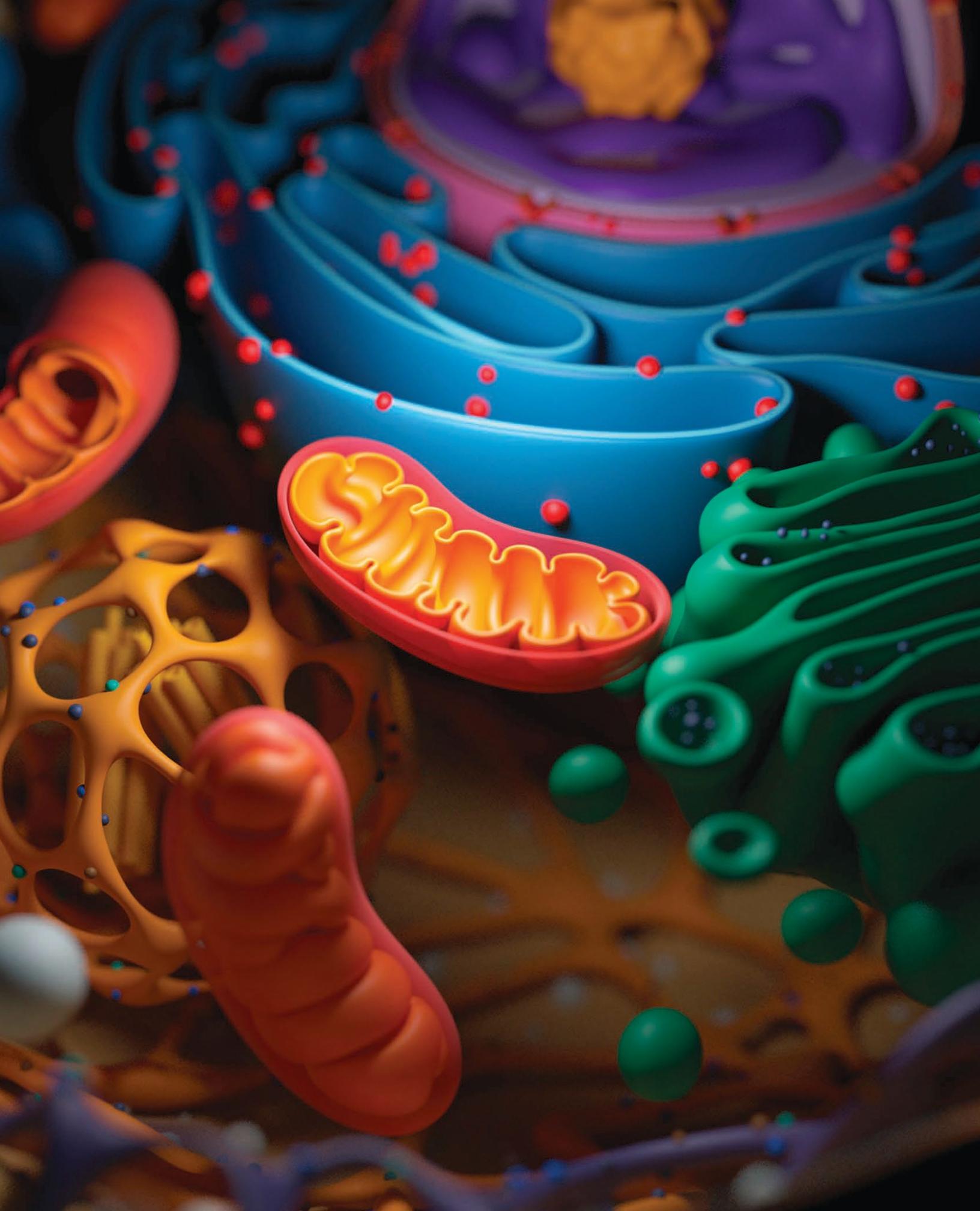
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PROTECTED AREA

California has one of the largest marine management programs in the world, with 119 marine protected areas (MPAs) and five state marine recreational management areas covering a total of 852 square miles. Marine connectivity is an important factor to consider during MPA network design, as the movement of organisms outside protected areas can render them vulnerable. In particular, connectivity influences how conservation planners decide the minimum area of an MPA, to make sure that most adults in local populations will be contained within it, and the spacing between different MPAs, as populations in different regions of coastline may depend on one another for long-term survival.





Glycine

A Tale of Two Genomes

A revival of interest in mitochondrial biology is revealing the importance of their genetic interactions with the nucleus in many facets of physiology, and even in the evolution of species.

BY VIVIANE CALLIER

From Alaska down to the Baja Peninsula, the rocky tide pools of North America's West Coast are separated by hundreds of kilometers of sandy beaches. Inside those tide pools live *Tigriopus californicus* copepods, small shrimp-like animals that evolutionary biologist Ron Burton has been studying since he was an undergraduate at Stanford University in the 1970s. During those early days of DNA technology, Burton became curious how the genomes of the isolated copepod populations compared.

While still at Stanford, Burton sequenced the mitochondrial gene *cytochrome c oxidase subunit one*, the standard marker people used at the time for spe-

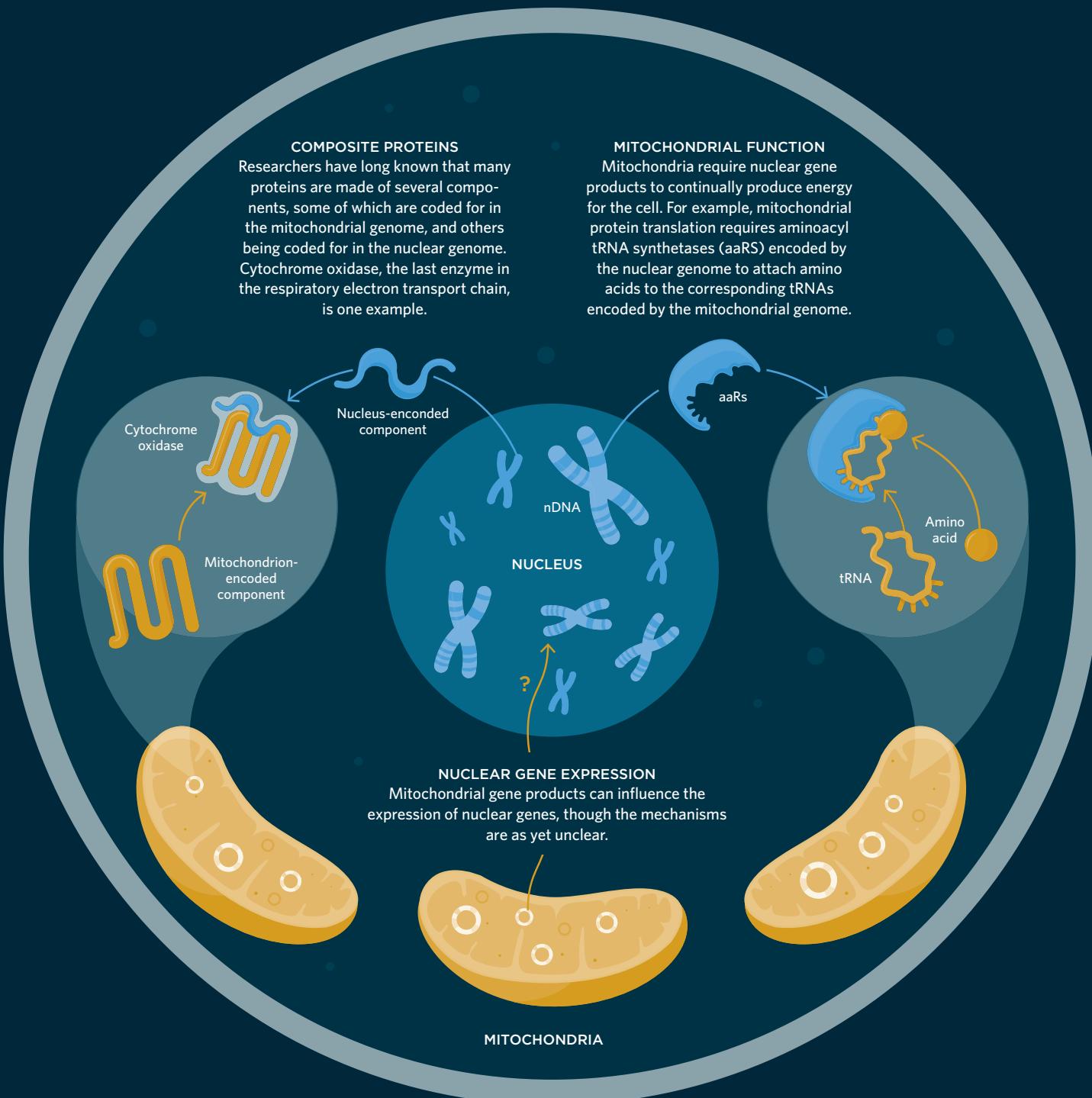
cies identification, and discovered that the copepod populations were strongly differentiated: on average, there was a 20 percent sequence divergence in this gene between populations. When he crossed Santa Cruz copepods with animals from San Diego, the hybrids did fine, but when he bred them to one another, their offspring did not do well, taking longer to develop, producing fewer offspring, and having lower survival.¹ "That was the first indication that there was some sort of genetic incompatibility developing between these isolated populations," says Burton, now a professor at the Scripps Institution of Oceanography in San Diego.

The first-generation hybrids have a full set of nuclear genes from each parent, but

among their progeny, genetic recombination has mixed and matched the parental genomes. This potentially creates mismatches between the nuclear and mitochondrial genomes that affect fitness. When Burton mated the second-generation female hybrids with male copepods from the parental Santa Cruz or San Diego populations, he found that the direction of the backcross made a difference. Breeding the second generation of hybrids with members of the paternal population produced no improvement in fitness. But a backcross to the maternal population produced offspring that were just as fit as the original natural populations. This happened regardless of whether the maternal popula-

TWO GENOMES, ONE CELL

For 1.5 billion years, the mitochondrial and nuclear genomes have been coevolving. Over this time, the mitochondrial genome became reduced, retaining only 37 genes in most animal species, and growing reliant on the nuclear genome to fulfill the organelle's primary function—to produce ATP by oxidative phosphorylation. Mitochondrial gene products interact with those encoded in nuclear genes, and sometimes with the nuclear genome itself. Because the mitochondrial genome mutates faster than the nuclear genome, it takes the lead in the mitonuclear evolutionary dance, while the nuclear genome follows, evolving compensatory mutations to maintain coadapted gene complexes. Researchers are now coming to appreciate that this has consequences for physiology and even macroevolution.



tion was from the north or from the south. (See illustration on page 46.)

"If you go to the maternal line, you're crossing to the population that matches the mitochondria, because mitochondria are maternally inherited," Burton explained. "That was pretty strong evidence that there was something going on between the mitochondrial and nuclear genes."

Mitochondria are ancient endosymbionts that over time lost many of their genes—some of which migrated to the nuclear genome—and increasingly came to rely on the nuclear genes to supply the basic raw materials necessary for mitochondrial function. In most bilaterian animals, the mitochondria's pared-down genome contains only 37 genes, 13 of which code for proteins, with the rest encoding various RNAs—all of which play roles in mitochondrial function. "For many years it was thought that all of the variation that we see in mitochondrial genomes had to be neutral because these genes are so important that any mutations that would have affected these functions would have been screened out," says Justin Havird, a biologist at the University of Texas at Austin.

In fact, that's exactly why mitochondrial genes are so commonly used to assess the genetics of populations: quantifying neutral variation serves as a molecular clock that allows researchers to estimate how long it has been since the populations diverged. When it came to genome analyses seeking to identify the genetic basis of adaptive change, mitochondrial genes were often ignored.

Over the past 20 years, however, researchers have begun to document the effects of variation in the mitochondrial genome on physiological functions such as growth rate and reproductive success in flies, copepods, and various fish species. Last year, for example, Brown University evolutionary biologist David Rand and colleagues found in fruit flies that the mitochondrial genome regulates the expression of hundreds or even thousands of nuclear genes, including genes that aren't related to mitochondrial function.² "On a per-nucleotide basis, the small mitochondrial genome is disproportionately influential given its very

small size," Rand says. "I think now people recognize that there's lots of functionally important stuff happening among different mitochondrial DNA. Crosstalk between the two genomes is probably an important part of a lot of physiology."

The evolution of the mitochondrial genome might also matter, the field has come to realize, for adaptation and speciation. "The big change that's occurred is just the way that people look at mitochondrial variation," says Havird.

A mitonuclear species concept

Mitochondria replicate their genomes more than once per cell cycle, and they do so in an environment full of DNA-damaging free radicals produced as a byproduct of the metabolic process that generates ATP within the organelles. These factors contribute to the rapid mutation rate of mitochondrial DNA, which greatly exceeds that of the nuclear genome. In the *Tigriopus* copepods, for instance, Burton has discovered that the mitochondrial genome evolves 50 times faster than the nuclear genome.

Moreover, mitochondrial genomes don't undergo recombination, so if a mutation arises in the mitochondrial genome, it's hard to get rid of it. Because mitochondrial gene products often interact with nuclear-encoded RNAs and proteins, such a mutation exerts a selective pressure for a compensatory mutation in the nuclear genome to keep the cell functioning properly. With mutations accumulating in both the mitochondrial and nuclear genomes, isolated populations drift apart, genetically speaking. Eventually, the mitochondrial genome of one population could become incompatible with the nuclear genome of the other and lead to reproductive isolation.

Ornithologist Geoff Hill at Auburn University in Alabama says he believes this process could explain speciation, and he has formalized this idea into the "mitonuclear species concept."³ In his view, a species is defined by a set of coadapted mitonuclear genotypes, "so if you mate outside a species boundary, you're creating bad combinations of nuclear and mitochondrial genes that lead to poor mitochondrial function," he explains.

For example, the closely related species of the golden-winged warbler and the blue-winged warbler, small songbirds that live in southeastern and south-central Canada and in the Appalachian Mountains, share 99.9 percent of their nuclear genome, but they have unique mitochondrial genotypes.⁴

Although the mitonuclear species concept is intriguing, it is far from universally accepted. Some consider Burton's copepods to be the poster child for the idea, but Burton himself says it's unclear at this point how important mitonuclear incompatibility is for speciation. "I think it can play a role, but I don't know that it is the organizing principle behind speciation," Burton says. The tight population structure of the copepods, with little gene flow between populations, is a key for creating the conditions for mitonuclear coadaptation, Burton says, and most species don't have such structured populations.

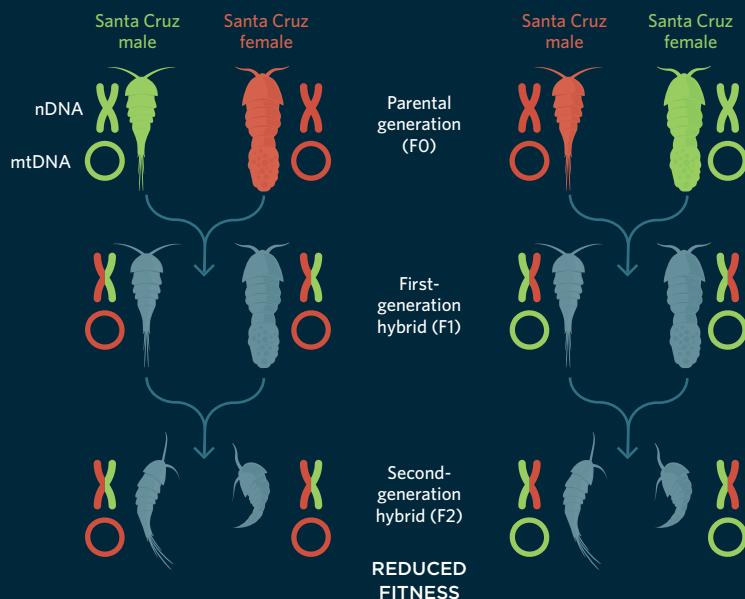
Burton is working to identify exactly which genes are responsible for the problematic mitonuclear interactions in the copepods from different tide pools. "We don't know if there's 10 different gene interactions that are responsible, or just one," he says. To explore this question, he is carrying out hybrid crosses that allow him to map the chromosomal locations causing problems. He then compares the incompatibilities arising between two pairs of closely related (recently diverged) populations with those between more distantly related (anciently diverged) populations to find out whether the same incompatibilities tend to arise repeatedly or if they are random and unpredictable. So far, preliminary findings point to the latter, Burton says.

Havird is intrigued by the mitonuclear species concept but says the jury is still out on how prevalent the phenomenon is. "In some cases, mitonuclear coevolution leads to reproductive isolation, and in other cases, mitochondrial genomes just seem to completely ignore species boundaries," Havird says. For instance, studies from the University of British Columbia found that Atlantic killifish (*Fundulus heteroclitus*) are differentiated into northern and southern populations whose mitochon-

CONSEQUENCES OF MITONUCLEAR INTERACTIONS

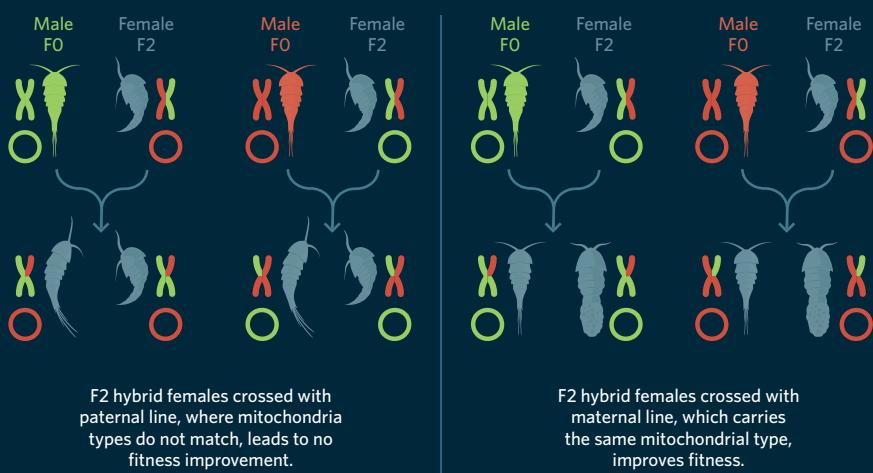
The intimate relationship between the mitochondrial and nuclear genomes comes into play as populations evolve. For example, the relatively fast mutation rate of mitochondrial DNA (mtDNA) means that the nuclear genome (nDNA) has had to evolve compensatory mutations to keep pace and maintain collaborative functionality. This process causes populations to drift apart due to mitonuclear incompatibilities.

Copepods on the Pacific coast of North America are the best-known example of this phenomenon. Researchers have successfully bred animals from different tide pools, and while the first-generation hybrids do fine, second-generation individuals develop slower and have fewer offspring.



MITOCHONDRIAL MATCHES

When F2 hybrids are backcrossed to the paternal line, they show no improvement in fitness. When they are backcrossed to their maternal line, however, their fitness is rescued, most likely because the backcross in this direction reintroduces the nuclear genome to the mitochondrial background it is co-adapted with.



dria are functionally divergent in ways that are clearly adapted to different water temperatures.⁵ In spite of this, there does not appear to be evidence of mitonuclear incompatibilities between northern and southern populations—studies show the two populations can mate without any untoward consequences.⁶

One of the challenges in studying mitonuclear interactions in the context of speciation is that it's difficult to establish a causal relationship: it is possible that mitonuclear mismatches could arise due to drift after a speciation event, rather than drive the reproductive isolation in the first place. These are questions that Michi Tobler, a biologist at Kansas State University, is trying to answer. His study system of choice: the fishes of the family Poeciliidae, several lineages of which have adapted to live in hydrogen sulfide-rich springs in Mexico.

Hydrogen sulfide is extremely toxic because it binds to and blocks cytochrome c oxidase, thus interrupting mitochondrial function. Tobler wanted to understand how the fish could survive in these conditions, and to figure out whether mitochondrial adaptations to sulfidic environments could cause mitonuclear incompatibilities that would promote speciation. He has discovered that in some lineages, one of the mitochondrial proteins in the cytochrome c oxidase enzyme has evolved a shape that cannot be inhibited by hydrogen sulfide.⁷ The modified protein, along with evolved changes in gene expression, allows the fish to survive the toxic environment. This should, in theory, exert selective pressure for compensatory changes in the nuclear components of cytochrome c oxidase—something he is currently trying to suss out across lineages that have been separated from their cousins in non-sulfidic waters for various lengths of time.

This is an ideal study system, he says, because “we basically get snapshots at different time points during speciation,” revealing clues as to how the animals evolved.

Asymmetrical inheritance

The fish adapting to sulfidic springs are a clear example of mutations in the mitochondrial genome leading to changes in

the physiology of the evolving lineages. But emerging evidence suggests that mitochondrial variation can influence the physiology of males and females differently. That's because mitochondria are maternally inherited, meaning that mutations that are harmful to males but ben-

"to revise my enthusiasm for the idea. I'd rather have allegiance to my data."

Moreover, from a physiological perspective, it's unclear whether mitochondrial mutations with different effects in males and females can arise and be maintained. A priori, one would not expect the

olites differently," Montooth says. "Even though the process of larval development and metamorphosis seems sexually uniform, it may actually not be."

Notwithstanding whether variation in the mitochondrial genome can have different physiological consequences in males and females, these and other experiments continue to unveil the organelle's substantial coordination with the organism's nuclear genome. "To me" says Rand, "this whole mitonuclear interaction is the really exciting stuff because that tells a story of a billion years of evolution, and how these two genomes make the cell and the organism work." ■

The big change that's occurred is just the way that people look at mitochondrial variation.

—Justin Havird, University of Texas at Austin

eficial or neutral for females could, in theory, accumulate in mitochondrial DNA.

Researchers first proposed this idea, dubbed "mother's curse," in 1996, but it's only in the last five years or so that researchers have begun collecting data to investigate the question empirically. The logic of this argument seems obvious: "It's inevitable that the mitochondrial genome will accumulate mutations that are exclusively male-harming," says Damian Dowling, an experimental evolutionary biologist at Monash University in Australia. But empirical tests have been equivocal, with Dowling's group finding some evidence for it under some circumstances,⁸ while Rand's work has yielded no support whatsoever.

For example, in a recent study,⁹ Rand's team generated 72 experimental pairs of mitonuclear genotypes in fruit flies to test for mitonuclear gene interactions, or epistasis. When these flies were then exposed to different dietary and oxygen environments, the researchers found evidence of many mitonuclear gene interactions—and these interactions changed depending on the dietary or oxygen treatments the fruit flies were exposed to. But they found no evidence that males were worse off, as would be predicted by the mother's curse hypothesis.

In another recent study, looking at the transcriptional responses to hypoxia in *Drosophila*, Rand found that females were generally more sensitive to lack of oxygen than males—a result that squarely contradicts mother's curse predictions.¹⁰ "Several years ago, I had several papers showing some support for [mother's curse]," he says, but the new results have forced him

fundamental cellular processes encoded in the mitochondrial genome to work differently in males and females. "What is the real capacity for [sexually antagonistic mutations] when the mitochondria is this really core organelle for physiology?" says evolutionary physiologist Kristi Montooth of the University of Nebraska. "You expect that there wouldn't be a lot of physiological capacity [for mitochondrial mutations that harm males but not females], and so even if we can make this evolutionary argument [for mother's curse], how pervasive do we really expect the phenomena to be?"

Like Rand, Montooth has found that sometimes the deleterious outcomes are stronger in females, counter to the predictions of mother's curse.¹¹ But she is also uncovering evidence suggesting that the physiology of males and females may be more different than previously realized. At the Society for Integrative and Comparative Biology meeting in Tampa, Florida, last January, Montooth presented evidence that mitochondrial variation can have sex-specific effects when fruit flies are reared under long daylight cycles that cause an increase in metabolic rate.

To investigate this further, Montooth and her collaborator Elizabeth Rideout at the University of British Columbia are exploring to what extent metabolism can differ between male and female flies by introducing sex markers to tell larval males from females and measuring their metabolic activity. "It may be that males and females are just really from the get-go using metabolites and storing metab-

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The Literature

MICROBIOLOGY

Living Cables

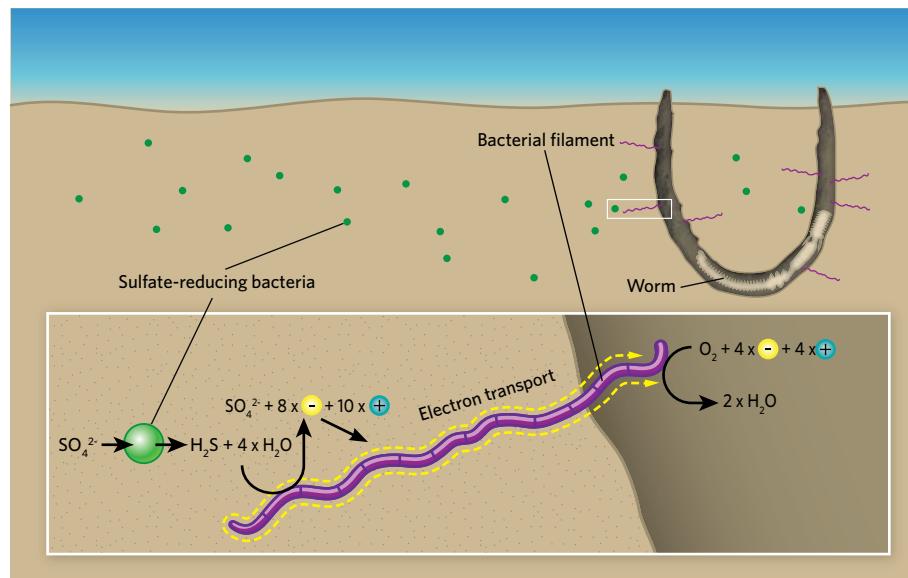
THE PAPER

R.C. Aller et al., "Worm tubes as conduits for the electrogenic microbial grid in marine sediments," *Sci Adv*, 5:eaaw3651, 2019.

Cable bacteria (family Desulfobulbaceae) are known for forming long lines of cells that stretch through underwater sediments and usher a stream of electrons through their ranks. It was thought that these living electrical wires couldn't grow in environments shared by animals such as brittle stars or mantis shrimp, which violently stir up the mud and might cut the microbial cables to bits. But it turns out that cable bacteria can withstand this upheaval—if they team up with parchment worms.

Cells at the sediment-embedded ends of these bacterial filaments collect electrons from sulfides and other donor molecules in the sediment and pass the particles up the cable to react with oxygen in the top-most layers of mud. The process releases energy for all the cells within the filament. Researchers had thought that cable bacteria must typically build filaments straight down through centimeters' worth of sediment to have access to both the electron-donating and electron-accepting environments, a feat that couldn't be achieved in agitated areas of the seafloor. But Stony Brook University marine biogeochemist Robert Aller wondered if they might still be found lurking somewhere in perturbed sediments.

Aller and his colleagues went searching for the microbes in the mixed-up mud of the Great Peconic Bay and Long Island Sound in New York. The team collected sediment cores, then used radiochemical analyses, light microscopy, and other techniques to learn how solutes and bacteria were distributed in each sample. The analyses revealed that cable bacteria aggregate in stable zones



PLUGGED IN: Parchment worms (*Chaetopterus variopedatus*) construct tubes in underwater sediment and constantly pump water through the structures to collect oxygen. Cable bacteria (Desulfobulbaceae) act like electrical wires, connecting to the tube lining and providing electrons that react with the oxygen, generating energy for the microbes. The bacteria extend radially in the mud to gather these electrons from sulfide—compounds often produced by nearby bacteria.

near parchment worms (*Chaetopterus variopedatus*), with filaments growing up to 650 μm length in these areas.

Parchment worms construct sturdy U-shaped tubes from carbohydrates and amino acids and continually collect dissolved oxygen from water that they pump through the fibrous structure. A tube can stay in place for months or more while its resident worm hunkers inside, providing bacteria with a shortcut into the mud. The results of Aller's study suggested that cable bacteria, which require both a reliable oxygen source and physically stable surroundings, cozy up to these worm tubes to survive.

Instead of growing straight down into the mud, the microbes radiate in all directions from the parchment worm tube "just the way people crowd around a luggage carousel at the airport," Aller says. Belinda Martin of the University of Western Australia and colleagues previously found

that cable bacteria form similar relationships with seagrasses, huddling around their roots for stability (*ISME J*, 13:707–19, 2019).

Because the sediment samples were only gathered from a few locations, it's not clear how widespread the phenomenon of the cable bacteria–worm partnership is, says Sairah Malkin, a biogeochemist and ecologist at the University of Maryland who was not involved in the work. Nonetheless, the findings suggest that cable bacteria may occupy a larger variety of environments than previously thought, she adds—including sediments that get disturbed by other organisms.

Beyond parchment worms and seagrasses, questions remain about what other species cable bacteria associate with, perhaps even as partners with which they exchange electrons. "A big exciting question could be, can other microbes plug into the cable bacteria?" says Malkin.

—Nicoletta Lanese



GET TOGETHER: Groups of reef manta rays in Indonesian waters have a more complex social structure than previously thought.

ECOLOGY & ENVIRONMENT

Manta Social

THE PAPER

R.J.Y. Perryman et al., "Social preferences and network structure in a population of reef manta rays," *Behav Ecol Sociobiol*, 73:114, 2019.

Reef mantas (*Mobula alfredi*) are some of the largest fish in the ocean, but much about their biology, particularly when it comes to their social lives, remains mysterious. Grad student Rob Perryman at Macquarie University in Australia has been trying to fill in the gaps by studying mantas around the reefs of the eastern Indonesian archipelago Raja Ampat, where the rays come to feed and be cleaned by smaller fish.

For Perryman and colleagues' latest study, the team observed hundreds of mantas at multiple sites between 2013 and 2018. The researchers counted how many times each individual appeared at each site, and noted an association between two rays if they visited the same place at the same time. Focusing on 112 mantas sighted 10 or more times each, the team plugged these associations into a computer model to construct social networks.

Even when controlling for individuals' site preferences, the researchers found that some mantas associated with particular individuals more frequently than would be expected due to chance. The network also revealed two distinct communities—one dominated by older females and the other comprising a more-even mix of sexes and ages. Evidently, "being social is a pretty fundamental feature of the species' biology that's going to affect reproduction, movements, habitat use," says Perryman—"all things that are really important for conservation."

The findings "suggest a complexity of social behavior in mantas that was suspected, or perceived as being possible, but as yet unproven," says Callum Roberts, a marine conservation biologist at the University of York who was not involved in the work. "It's quite a groundbreaking study in that respect." He adds that tagging studies could help collect data on manta behavior outside of the handful of locations studied here. "We need to try to unlock ... the lives of these animals away from the focal aggregation sites."

—Catherine Offord

© ROB PERRYMAN; FATMA DENIZ



HEARD, SEEN: Functional maps of brain activity show that the meaning of particular concepts or phrases is represented almost identically during reading and listening.

NEUROSCIENCE

Seeing Is Hearing

THE PAPER

F. Deniz et al., "The representation of semantic information across human cerebral cortex during listening versus reading is invariant to stimulus modality," *J Neurosci*, 39:7722–36, 2019.

Researchers know that similar brain regions become active in response to the semantic content, or meaning, of language, whether it is read or listened to. But brain-imaging studies haven't had the resolution to determine if it's the same neural circuits, or just adjacent ones, within those regions that respond to the two language modes, says University of California, Berkeley, neuroscientist Jack Gallant.

To find out, Gallant, postdoc Fatma Deniz, and colleagues transcribed several 10- to 15-minute clips from *The Moth Radio Hour*, in which speakers tell stories to an audience. The researchers had nine participants either read and then listen to the stories, or listen to them and then read them, while inside a functional magnetic resonance imaging (fMRI) machine.

Using the imaging data and computer modeling, the team created detailed maps of brain activity for each participant. These maps indicated that the brain circuits responding to the semantic content of each concept within the stories were almost identical within each individual, regardless of whether people were reading or listening. After discounting the different sensory areas of the brain that process sound and sight, says Gallant, "essentially you can't tell the difference between the semantic maps."

"It's a very impressive paper," says Rik Vandenberghe, a neurologist at KU Leuven who was not involved in the work. He highlights the team's "courage to address language in its full complexity" by using stories, rather than single words, as stimuli. While it's not surprising the brain uses common pathways to process meaning, "the beauty of this paper is more the way that they demonstrate this in a very convincing way."

The researchers are now studying how semantic concepts are represented in people who are bilingual. "If you have two language representations, are they the same?" says Gallant. "We think we might be able to answer that question."

—Catherine Offord

Watcher of Whales

Roger Payne used his discovery that whales sing songs to convince the world that the animals are worth saving.

BY DIANA KWON

The first time Roger Payne heard a whip-poor-will, a nocturnal bird named for its distinctive calls, was as a child while visiting friends of his family in New Jersey. He sat captivated by the sounds for hours, deeply moved by the boldness of the bird, whose seemingly endless song rang out fearlessly into the darkness. “In the dead of night, when one would have thought of all kinds of reasons not to draw attention to yourself, it nevertheless did,” Payne recalls.

Now in his 80s, Payne still vividly remembers that night. He’s only heard whip-poor-wills on a few more occasions since then—and opportunities to hear them have become increasingly scarce. Populations of the bird have steadily declined in recent decades and are expected to continue falling as climate change destroys their already scarce habitats, which are primarily the forests of the eastern United States. For Payne, this is just one example of the degradation of the natural world.

Whales are another example. Payne has spent decades studying these animals—their songs, behavior, and the harms caused to them by human activities. This work has taken him on more than a hundred expeditions in Bermuda, Argentina, and elsewhere. But the force that has driven him to conduct all this work can be linked back to the imperiled whip-poor-will, whose haunting song enchanted him as a young boy. “All my life I’ve seen the destruction of wild places and the destruction of beauty,” Payne says. “I became determined that I would try to do something.”

BATS, BIRDS, AND BUGS

Payne was born in New York City in 1935. With a mother who was a professional violinist and a father who was an engineer, both music and science naturally wove their way into Payne’s life. Though he chose science as a career, he has been a lifelong cellist, and his ear for music ended up playing a crucial role in his scientific discoveries. “Almost everything I’ve ever done traces back to music,” he says.

Payne initially considered following in his father’s footsteps and applied to an engineering program at MIT. After getting accepted, however, he realized that he was more interested in animals. He chose to study biology at Harvard University instead. There, he met Donald Griffin, a zoologist who, with neuroscientist Robert Galambos, had discovered that bats echolocate at a frequency humans can’t hear. Griffin was one of the instructors of Payne’s introductory biology class, and as part of the course, students were invited to Griffin’s laboratory. There, Griffin eagerly

played the group recordings of oilbirds, a South American bird that also echolocates, at a frequency that humans can hear.

“It was clear that [Griffin] was really interested in what he was doing,” Payne says. “He couldn’t hide that.” Intrigued, Payne joined Griffin’s lab, and then conducted his undergraduate thesis with the zoologist, investigating the directional sensitivity—the responsiveness to the location of sounds—of bat ears. Several years later, the pair would meet again and work together for almost two decades. “He became one of the two most important influences in my life,” Payne says.

The other major influential figure for Payne was Cornell entomologist Tom Eisner. Payne met Eisner during his doctoral studies at Cornell, working in the lab of ornithologist William Dilger. Payne also worked as a lab assistant to Eisner, who took Payne on after seeing him biking through campus with a cello attached to his back. Eisner was a pianist, and the two would occasionally play together, bonding over music as well as science. Eisner “was the man who really taught me biology,” Payne says, and instilled in him a fascination for insect biology, so much so that he went on to investigate moths for his postdoctoral studies with Kenneth Roeder at Tufts University. As he had done with bats and owls, Payne studied the directional sensitivity of hearing in moths—specifically, how they identify the location of an approaching predator using an acoustic system that consists of only a few cells (*J Exp Biol*, 44:17–31, 1966).

Despite his success, Payne says he wanted to find more meaning in his work. “I was doing stuff that interested me—and some other people—but it did not serve the purpose of stopping the destruction of the wild world,” he says. He wondered: What animal that depends heavily on hearing could he study while also contributing towards preventing its destruction?

The answer, he determined, was whales.

LISTENING TO THE SEA

One afternoon while he was still at Tufts, Payne heard a report that a dead whale had washed ashore on a nearby beach. When he drove there after work, he beheld a distressing sight. A dolphin had been mutilated—previous visitors had cut the animal’s tail, carved initials into its side, and stuck a cigarette into its blowhole. “It was at that moment that I thought that if there was any way I could find a way of doing it, I would try to learn something about whales that would make it less likely that people would do that to them,” Payne says.



ROGER PAYNE

Founder and president, Ocean Alliance, Gloucester, MA
Member, Scientific Committee, International Whaling Commission (1983-1989)
Adjunct Associate Professor, Rockefeller University (1971-1985)
MacArthur Fellowship (1984)
Research Zoologist, Institute for Research in Animal Behavior (1966-1983)
Scientific Director, Whale Fund of the New York Zoological Society (1970-1983)
Assistant Professor, Rockefeller University (1966-1971)
United Nations Global 500 (1991)
Dawkins Prize for Animal Conservation and Welfare (2008)

Greatest Hits

- Discovered that humpback whales sing songs
- Proposed that whale songs can be heard across oceans, a hypothesis that was later confirmed by one of his former students
- Developed numerous research techniques for studying whales in the wild
- Coproduced records of his whale songs and compositions that incorporate whale songs

Upon completing his postdoc, Payne received a job offer from Griffin, who had moved from Harvard to Rockefeller University in Manhattan. But Payne hated the thought of moving back to a big city, so he declined the offer and remained at Tufts as an assistant professor of biology. “The idea of ever having to return to New York was absolutely abhorrent,” Payne says. “I had four kids by then, and I couldn’t imagine trying to raise them in that environment.”

A few years later, Griffin managed to convince Payne to visit Rockefeller. This trip changed Payne’s mind. To his surprise, the campus was a green oasis hidden away from the hustle and bustle of the surrounding metropolis. At first, Payne’s family remained in Massachusetts, and he drove back to visit them on the weekends. But by a stroke of good fortune, Payne was eventually able to find the perfect home for his family near the city in a place called Wave Hill, a sprawling green estate in the Bronx. There, the Paynes lived in an unused underground gymnasium with four bedroom-size changing rooms, a kitchen, and a living room fitted with a massive glass wall of windows that looked out onto a stunning view of the Palisades, a line of steep cliffs along the western shores of the Hudson River.

The hair still goes up on the back of my neck when I remember thinking, ‘Holy shit, Roger’s right.’

—Christopher Clark, Cornell University

It was by this time the mid-1960s, and within a few months of making the move, Payne made the switch to studying whales. Commercial whaling was then at its peak—and unchecked hunting was causing several populations of whale species to steeply decline. However, other than the desecrated dolphin on the beach, Payne had never seen a whale up close, and he had no idea where to find one. Luckily, he received a tip from one of the New York Zoological Society’s trustees, the physician and millionaire Henry Clay Frick II. During one of the organization’s meetings, Frick mentioned to Payne that he and his family frequently sighted humpback whales at their estate in Bermuda.

So Payne went to Bermuda, where he met a man named Frank Watlington, who was on a secret mission for the US Navy that involved listening to the ocean. While eavesdropping on the seas, Watlington had picked up some usual sounds that he

suspected might have come from the humpback whales that would occasionally swim by the listening station. When Watlington played his recordings, Payne was awestruck by the sounds. "It was absolutely fantastic," Payne says. "I had never heard anything like it."

Immediately, Payne realized that he had stumbled onto an invaluable tool. These sounds, he thought, were the key to making the public listen to—and care about—these creatures. "It was clear to me that nobody would be able to hear these sounds without having them deeply affect them," Payne explains. Payne asked Watlington for a couple of his tapes, which he took home and played hundreds of times. As he listened to the recordings, he quickly realized that certain sounds would recur at regular intervals. This repetition suggested that the whales were singing structured songs.

Several years later, Payne worked with Scott McVay, who was then an administrator at Princeton University, to create detailed visual representations called spectrograms of the humpback whale recordings. The pair confirmed that the animals were producing a series of sounds that would last for up to 30 minutes, then repeat, verifying that humpback whales do indeed sing songs (*Science*, 173:585–97, 1971).

This discovery "opened the world's eye to the notion that [these whales] are not just swimming bags of blubber, that they have these extraordinary communication features, which, even then, hinted at complex social interactions," says Scott Kraus, the chief scientist for marine mammal conservation at the New England Aquarium, who met Payne while studying right whales off the coast of Argentina in the 1970s. "I would say that this was his most important contribution [to science]."

In 1971, Payne founded the Ocean Alliance, an organization dedicated to the protection of whales and their environment, and while continuing his research, spent time spreading the word about whale songs to anyone who would lend him an ear. "I figured that if you could build these sounds into human culture, you could maybe get a movement going to save the whales," he says. Payne's plan worked. Several musicians, including the singer Judy Collins and the saxophonist Paul Winter, incorporated Payne's recordings into their own music.

Payne also coproduced his own records of whale songs and has written, directed, and featured in numerous television and film documentaries about his work. This activity spurred many conservation organizations to action. It helped spark Greenpeace's "Save the Whales" campaign, which raised the public's awareness of whale hunting around the globe. After facing pressure from the global community, the International Whaling Commission voted to place a ban on commercial whaling in 1982.

Later that decade, Payne left the Rockefeller University to focus his research on conservation through Ocean Alliance.

WHALES IN THE WILD

Payne's first trip to Bermuda was one of more than a hundred field expeditions that followed. His research on whales brought

him back to Bermuda on numerous occasions, as well as to Hawaii, Mexico, Alaska, Argentina, and other destinations.

Payne's family joined him on almost all of his voyages. His former wife, Katy, assisted in his research. She created numerous spectrograms of whale vocalizations and coauthored papers about the animals. According to Payne, one of Katy's most important contributions was discovering how whale songs change depending on the season and location. (Later, Katy herself became famous for discovering that elephants use low frequency "rumbles" to communicate.) "I was determined that I wasn't going to have to go into the field without my family," Payne says. "It worked out beautifully in the end—the kids were good company to everyone, and that improved how people got along, which was the absolute essence of whether an expedition would be a success or not."

Payne's work didn't come without controversy, however. Together with Douglas Webb, an oceanographer at the Woods Hole Oceanographic Institute, he calculated how far whales' songs could be heard using variables such as the loudness and frequency of their vocalizations. The duo postulated that the songs of baleen whales, which are very loud and very low-frequency, could travel thousands of miles in the deep waters of a quiet ocean (*Ann NY Acad Sci*, 188:110–41, 1971). "That came closer to destroying my whole career than anything else I did," Payne says. "People said, 'This guy is just a whale enthusiast and of course you can't hear them that far.'"

Payne was certain of the calculations, though, and two decades later, Christopher Clark, a bioacoustics researcher at Cornell University and one of Payne's former students, experimentally confirmed this theory using data collected from the US Navy's undersea microphones. "I was listening to a whale singing in Ireland, and I was listening to it off of Bermuda," Clark says. "The hair still goes up on the back of my neck when I remember thinking, 'Holy shit, Roger's right.'"

The function of these ultra-long-distance songs remains a mystery, but Payne has a hypothesis: it allows whales to spread over entire oceans and still communicate with each other when necessary. For example, certain whale species, such as blue and finback whales, don't have any known mating grounds. One potential reason for this, according to Payne, is that they can call to each other across vast distances, making it unnecessary to have a designated meeting spot. This skill could also come in handy when hunting. Schools of krill, the main prey for some whales, pop up in unpredictable locations—so whales may also use their ability to transmit information about the location of food to relatives across the ocean.

Payne is currently working on three books, two about his research on whales, and one on the importance of wildlife conservation. All three are aimed at a broad audience. "I'm trying to write in a more general way about the world, because I feel heartbroken as to the current direction that everything seems to be headed," he says. "I think the biggest mistake we make now is failing to recognize that we are totally interdependent on the rest of life. That's the message I'm trying hardest to get across to the world." ■

Martha Muñoz: Exploring Evolution

Assistant professor of ecology and evolutionary biology, Yale University, Age: 34

BY NICOLETTA LANESE

Raised in Flushing, New York, Martha Muñoz fed her love of nature at the Bronx Zoo, the Queens Botanical Garden, and the American Museum of Natural History. "I was, on a regular basis, flabbergasted by the diversity of life," she says. As a teenager, the first-generation Cuban-American planned to become a wildlife veterinarian, but that changed when Muñoz started her undergraduate degree at Boston University in 2003 and took a biology course with Chris Schneider. On day one, Schneider lectured on the Cambrian explosion, and Muñoz says she remembers being "emotionally moved, physically to tears." She knew she wanted to answer the big questions that evolutionary biologists were asking.

After earning her undergraduate degree in 2007, Muñoz won a Fulbright scholarship to study population genetics using the collections at the National Museum of Natural History of Spain in Madrid. A year later, she began studying lizards as a graduate student in the lab of Jonathan Losos at Harvard University. Losos, Muñoz recalls, encouraged her to "find the thing that spun [her] spurs," which she discovered was learning how organisms interact with their environment to increase their evolutionary fitness.

During a research trip to the Dominican Republic, Muñoz noted that anole lizards there behaved differently depending on their ecological niches. Lizards closer to sea level clung to relatively cool tree trunks throughout the day, while lizards living two kilometers up in the mountains only emerged when the sun was high to warm themselves on sun-soaked rocks. In turn, populations of the high-altitude lizards adapted skull and limb shapes better suited to splaying out on boulders. Yet, even though the animals' behaviors and morphologies had changed to better suit their environment, they still had similar physiologies to tolerate heat, she found (*Am Nat*, 191:E15–E26, 2018).

Muñoz finished her PhD in 2014, and then joined Craig Moritz at the Australian National University in Canberra as a postdoc to study heat tolerance in some of Australia's rainforest lizards. The lizards with low heat tolerance hide away in the shade at midday, while those with high tolerance bask in the sun during that time. Surprisingly, the lizards have swapped their sunning behaviors repeatedly over evolutionary time; once-sun-loving species' heat tolerance dipped predictably as, over generations, they hid in the shade, while former shade-lovers' tolerance increased after their ancestors repeatedly sunned themselves at midday, Muñoz found (*Evolution*, 70:253–49, 2016).

"Behavior, morphology, and physiology are constantly in a delicate evolutionary dance, no part removed from the other," Muñoz explains.

After working in Moritz's lab, Muñoz joined Sheila Patek at Duke University for a second postdoc and began studying the evolution of animal biomechanics, and in 2017, she established her own lab at Virginia Tech. There, she launched a study on *anole* lizards descended from animals that had washed ashore on the Caribbean islands from mainland Latin America. The island lizards evolve quickly to occupy distinct ecological niches, such as the canopy, tree trunks, or bushes, which scientists assumed meant island organisms evolved faster than their mainland counterparts. But Muñoz found that this trend isn't uniform across all traits. Populations of the island lizards don't evolve physiologically to regulate their temperature because individuals don't have to contend with many predators, so they simply step out into the sun when they get a bit cold. Mainland lizards, on the other hand, must spend their days in hiding, and have rapidly adapted changes in heat tolerance over evolutionary time (*Evolution*, 73:1241–52, 2019).

Earlier this year, Muñoz moved to Yale University, where she says she hopes her research will reveal more about the core laws of evolution. "We're still in a major discovery phase . . . stitching together how it all works." Moritz suspects she will be successful. Muñoz is adept at using fieldwork to shape her research questions and is propelled by her "intellectual vitality," he says. "I expect great things." ■



Pharma's Orphans

Changes in the way Big Pharma operates are leaving dozens of research and manufacturing facilities empty. What happens to them?

BY KATARINA ZIMMER



The hallways of Pfizer's first-ever facility once swarmed with more than 1,000 workers tasked with making some of the most popular drugs of our time, including the erectile dysfunction treatment Viagra and the antibiotic Zithromax. Nowadays, the building in Brooklyn, New York, carries scents of chocolate, baked goods, beer, and a lingering waft of construction.

Pfizer began to wind down its production of drugs here decades ago, and the last of the company's Brooklyn employees had to leave in 2008 when the pharmaceutical giant closed down the site as part of a wave of modernizing changes. But Pfizer's birthplace has since become a much sought-after space in one of Brooklyn's most cramped neighborhoods, with about 1,600 people now working in the building.

The eighth floor, which used to be reserved for the offices of Pfizer's chief

executives, now hosts counterterrorism training run by New York City's Police Department for its officers. A vast space on the fifth floor, where half a dozen nine-foot-tall stainless steel mixers used to churn pulp that would be pressed into a variety of pills, spent much of the summer filled with construction debris—a result of the area's transformation into a soundproof recording studio for the Blue Man Group. Many of the building's old research labs are now used by local artisans to make a variety of food products, and in a spacious tent in the parking lot, acrobats train on a 40-foot structure built by the Trapeze School of New York.

"You can see how this [transformation] is adapting, reusing space, that was used by Pfizer fifty, sixty years ago," explains Jeff Rosenblum of Acumen Capital Partners, a real estate firm specializing in repurpos-

A NEW LOOK: An old GlaxoSmithKline campus in Upper Merion Township, Pennsylvania (photograph, opposite), is currently being transformed into what its developers, The Discovery Labs, call "the largest 'coworking' ecosystem for healthcare, life sciences and technology-enabled companies in the country" (artist's rendition, above).

ing industrial buildings, which bought the property in 2011 for \$26 million. Still the building's owner, the company now has an office there on the sixth floor.

The Pfizer site is not the only pharmaceutical facility to get a makeover in recent years. Dozens of giant drug-manufacturing and research facilities in the US and elsewhere have been abandoned by their parent companies. Some continue their stories in other realms of life science, some sit empty and unused, while others—like Pfizer's old facility—find new purpose in entirely different industries.



A change of hands

Pfizer was founded in Brooklyn's Williamsburg neighborhood in 1849 by German cousins Charles Pfizer and Charles Erhart. The company headquarters stayed there for well over a century as Pfizer grew into the pharmaceutical behemoth it is today. But when several of the company's best-selling drugs began to lose patent protection just over a decade ago, compounding difficulties the company was already facing in managing worldwide drug production, Pfizer launched a global push to cut its workforce and operating costs. That decision included letting go of its Brooklyn birthplace and the 600 or more jobs associated with it.

The move reflects a pattern of closures in the pharmaceutical industry since the late 1990s that has left empty hundreds of facilities once dedicated to drug manufacturing and research and development (R&D). Some of the earlier closures were prompted by changes in regional tax laws or other regulations. But now, most are likely driven by two key shifts in the industry over the last couple of decades, says biomedical industry expert Erik Gordon of the University of Michigan's Ross School of Business.

One is the increasing frequency of mergers and acquisitions among pharma companies. "The corporate management feels a lot of pressure to show that combin-

ing two companies gives you a company that is better and more efficient," says Gordon. Consolidation often means closing manufacturing or R&D facilities, as Pfizer did with 13 more of its sites after it acquired Pennsylvania-based Wyeth in 2009.

Big Pharma has also changed how it conducts R&D. To cut costs, companies are doing less of their own research and are instead relying on making deals with smaller companies or university research divisions that have already successfully developed drug candidates or therapeutics, and often working with contract research organizations on the continued development of those products. "The old 'make what you sell, sell what you make' is no longer the preferred strategy," says Bill Wiederseim, president and CEO of PharmaBioSource, a Pennsylvania-based consultancy firm that advises pharmaceutical companies on finding or selling facilities, among other matters.

These closures, in addition to often making hundreds or thousands of workers jobless, vacate enormous, expensive facilities that few companies need or can afford. "These sites are over a million square feet of R&D lab and sometimes manufacturing [spaces] that are really obsolete at this point in time on that type of scale," explains Shawn Straka, who co-directs the real estate firm Cushman & Wakefield's life sciences division in New Jersey.

Occasionally, abandoned facilities attract academic owners, or even other large pharmaceutical companies, thanks to building designs specialized for research. For example, in 2015, two years after Merck & Co announced it would vacate its headquarters in Summit, New Jersey, biotech Celgene bought up the 1,000,000-square-foot property as part of a rapid expansion in its R&D programs. Sometimes, smaller pharmaceutical companies or contract research firms looking to upsize will also express interest in these properties. But such deals are becoming rare, explains Straka, forcing pharmaceutical companies or the agencies that take over their properties to look further afield for buyers.

An alternative option that's becoming increasingly popular is selling sites to firms that specialize in redeveloping and parcelling old pharma properties out to smaller life-science companies. This new real estate ecosystem has given rise to several science and technology parks that offer affordable, convenient spaces for smaller companies that lack the capital to build their facilities from scratch.

Facilities that are old or in less attractive locations can remain empty for years. Some are simply torn down altogether.

A new ecosystem

Just an hour's drive from Pfizer's original headquarters in Brooklyn, New Jersey's biotech sector is experiencing a transformation. Once known as the "medicine chest of the world," the state is home to several massive R&D and manufacturing facilities, many of which have come on the market in recent years. Now, these properties are providing a new home for a multitude of smaller pharmaceutical firms, biotech startups, and academic institutions.

One such facility is Swiss drugmaker Hoffmann-La Roche's old 116-acre campus bordering the towns of Nutley and Cliffon, New Jersey. In its heyday, the complex churned out a variety of therapies, includ-



KITCHEN FITTING: Many of Pfizer's old laboratories at 630 Flushing Avenue in Brooklyn, some of which boast a view of Manhattan's skyline, have been converted into workspaces for local food manufacturers.

ing the anxiety treatment Valium and the melanoma drug Zelboraf—until the company decided to move its US headquarters to San Francisco as part of its takeover of Genentech. In 2012, Hoffmann-La Roche announced the closure of its New Jersey site, and four years later, New Jersey-based real estate developer Prism Capital Partners bought the campus for a reported \$88.5 million, according to real estate news outlet *The Real Deal*, after noticing the proliferation of smaller and mid-size biotech companies in the state. “We saw the R&D money flowing back in and recognized that there'd be opportunity,” says Prism Capital Partners founder, Eugene Diaz.

It didn't take the agency long to find tenants from various fields of life science to occupy parts of the campus, Diaz says. The Hackensack Meridian Health System is creating a health sciences-focused research campus there, and recently finished redeveloping an existing building into what is now the Hackensack Meridian School of Medicine. The former pharma complex, named On3 after the connecting state highway Route 3, will also house

several of Seton Hall University's graduate health sciences programs, plus a number of other life science facilities with focuses ranging from manufacturing biomaterials to developing diagnostic tools for disease.

Other real estate companies or developers are attempting to reposition former pharmaceutical sites as biotech incubator spaces with the potential to fuel the next generation of biologics-based therapeutics. For instance, The Discovery Labs, a company launched by real estate investor MLP Ventures, is currently redeveloping a former GlaxoSmithKline campus in the Pennsylvania township of Upper Merion. When it sold the property in 2018 to MLP Ventures, GlaxoSmithKline decided to lease one building as a cleanroom for developing one of its therapeutics. The rest will be taken up by a range of life science–focused tenants, including the Children's Hospital of Philadelphia and laboratory materials supplier Tosoh Bio-science. Unite IQ, The Discovery Labs's own biotech incubator, is to form the heart of the site, explains Audrey Greenberg, the company's cofounder and managing director.

Greenberg envisions the repopulated campus as a collaborative workspace that could help accelerate the development of new therapeutics by building a community of tenants, each of which specializes in a different aspect of the drug development pipeline. “Whether it be getting a viral vector,

getting a plasmid, getting [contract manufacturing organizations] to work with them on research development and outsourcing... intellectual property attorneys,” says Greenberg—“[they're] all housed under one roof.”

Such transitions don't come without challenges. For instance, in several buildings on Hoffmann-La Roche's former campus in New Jersey, each floor had a 3:1 ratio of lab to office space—considered a good split when the property was built during the 20th century. However, today's companies prefer a 1:1 allocation to allow more space for the computational equipment and personnel involved in research, Diaz says. Because the buildings had been built with unmovable block walls, they couldn't be adapted to a new ratio—one of the reasons why Roche and Prism eventually had them torn down.

Some of Wiederseim's clients also need tweaks to the laboratories to make them suitable for biologics-based research. For instance, fume hoods, designed to protect researchers working with potent reagents and chemicals, may need replacing with biosafety cabinets, which protect the integrity of the biological entity, such as cells or DNA. These challenges are often surmountable, however, and Diaz notes that several vacant pharmaceutical sites in the US have now successfully been redeveloped into life-science parks.

Leaving pharma

For sites that fail to find a purpose in new scientific projects, the future is far less certain. Facilities that are old or in less attractive locations can remain empty for years, Gordon says. Some are simply torn down altogether. For instance, after Schering-Plough closed its R&D facility in Bloomfield, New Jersey, in the 1990s, “no other company (large or small) wanted it,” science journalist Derek Lowe wrote in a 2014 blog post in *Science*. Eventually, the buildings were razed and the land sold. Since 1997, a Home Depot store has stood in its place.

Others get demolished “because they're contaminated and they're hard to repurpose,” says Wiederseim, who says he and his colleagues have recom-

mended the demolition of 20 pharmaceutical buildings in the last decade. Facilities that used to manufacture antibiotics such as penicillin and cephalosporins are particularly likely to meet this fate: without complete decontamination, there's a risk that antibiotic remnants could contaminate any future products made in such a building, posing a risk to customers allergic to these compounds. Testing for contamination is expensive, and drug companies are required by law to finance this, so "most Western companies choose to demolish and build anew," Wiederseim says.

But some facilities, such as Pfizer's Brooklyn building, find new lives outside of pharma. In 2006, biofuel company Xethanol Corporation decided to purchase a manufacturing plant owned by Pfizer in Augusta, Georgia, and retrofit the site with equipment to produce ethanol from biomass waste streams from industries in the surrounding area. And in

Pfizer's birthplace has become a much sought-after space in one of Brooklyn's most cramped neighborhoods.

2011, Florida-based Caribbean rum maker Club Caribe bought an old GlaxoSmith-Kline plant in Cidra, Puerto Rico, to use as a distillery. Wiederseim also has several clients looking to repurpose pharma facilities into ones that specialize in cannabidiol processing. However, such extreme repurposing is still unusual, Wiederseim stresses. Because pharmaceutical facilities were built for very specialized purposes, "they make very poor Walmarts."

Back in Brooklyn, the Pfizer plant is reaching the end of its transformation into a modern hub for local food manufacturers, performance artists, and small companies—a community that Acumen's Rosenblum says reflects the diversity of the surrounding neighborhood. The con-

struction debris and ancient steel pulp-mixers were finally removed from the fifth floor in August—a difficult feat, as construction workers had to blast through the formerly windowless brick walls to get some of them out—and the Blue Man Group moved into the space in September.

While overseeing the building's transition, Rosenblum has salvaged several trinkets in remembrance of Pfizer's legacy. A doormat bearing the company's logo is visible as one enters Acumen's office on the sixth floor. Near Rosenblum's desk sits a flattened, two-foot-wide ring of stainless steel—once part of a submarine-like hatch used to open up the pulp-mixers if anyone needed to go inside for cleaning, he explains. In an industry undergoing such rapid changes to the way it treats property, these are pieces of history. ■

Katarina Zimmer is a New York-based freelance journalist. Find her on Twitter @katarinazimmer.

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VERENA BRUCKLACHER-WALDERT, PhD
Principal Scientist
Horizon Discovery Ltd.

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Breast Medical Oncology Group
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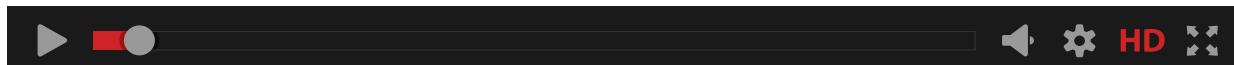
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ONDEMAND | QTY Code: A Tool for Designing Detergent-Free Membrane Proteins and Beyond

G-protein coupled receptors (GPCRs), a class of membrane proteins, are involved in critical cellular signaling pathways that have been shown to be linked to the onset and cause of many diseases. Determining the structure and function of membrane proteins can be challenging partly due to their hydrophobic properties, which make solubilization difficult. QTY variants, have 46-56 percent of their transmembrane α -helices altered, but are water-soluble, maintain stable structures, biologically functional and retain proper ligand-binding activity.

In this webinar, sponsored by NanoTemper Technologies, Shuguang Zhang, who created the QTY code technology, will share applications of his technology and the use of Prometheus to look at difficult to characterize targets such as amyloids and other disease-related molecules. Silvia Würtenberger of NanoTemper Technologies will share why Prometheus is the new gold standard for protein stability characterization as it tracks thermal and chemical unfolding as well as aggregation all in a label-free way.



SHUGUANG ZHANG, PhD
MIT Media Lab
Massachusetts Institute of Technology



SILVIA WÜRTENBERGER, PhD
Product Manager, Prometheus
NanoTemper Technologies

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- Examining protein stability using Prometheus

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The Underwater Paparazzi

Marine photographers are helping scientists to document the diversity of coral reefs before the imperiled ecosystems disappear.

BY RICHARD SMITH

I began exploring the aquatic realm at sixteen, learning to scuba dive with my father in a frigid British quarry surrounded by thickly frosted ground. My first time out, an icy November day packed with four dives, the only living thing I saw was a lone crayfish, but thankfully I persevered. Since then, my journey as a marine biologist and underwater photographer has given me unique access to the many overlooked creatures of coral reefs, culminating in my book *The World Beneath*.

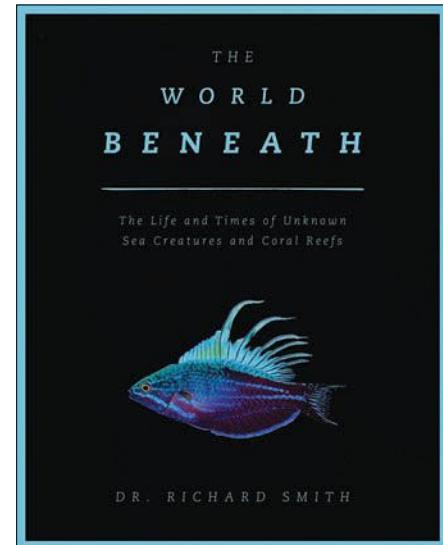
I captured some of my earliest photographs in the Maldives in 1998, when the first global coral bleaching event devastated many of the Indian Ocean's reefs. Although these photos were decidedly average, the subject matter sparked a fundamental shift in my consciousness, and my plan to become a terrestrial zoologist plunged beneath the waves. The following year, I spent several months on a conservation project in Indonesia working on nudibranch (sea slug) biodiversity. I struggled to identify and document the hundreds of different potential species of nudibranchs that inhabited the local reefs. The little sketches on my underwater slate weren't quite cutting it, so I started to take close-up images of these tiny slugs, most measuring less than a centimeter in length. My work expanded science's knowledge, documenting new species and greatly extending the known geographic ranges of some that were already known.

Several years later, underwater photography became a vital part of my PhD research on the elusive, but charismatic, pygmy seahorses. These unique fishes barely stretch across a dime, and the two species I studied spend their entire adult lives cryptically clinging to the surface of fanlike gorgonian corals. Through my photography, I was able to observe and record their reproductive cycle for the first time, taking

images to help sex the animals. Gaining this type of insight is only possible by taking a very close-up image of the base of the trunk to show a raised circular pore in females, or a slit-like opening in males from which young are released.

In 2002, when I saw my first pygmy seahorses on the coral reefs of Komodo, Indonesia, there was just one named species (*Hippocampus bargibanti*) in the area. Now there are seven, and I am working on describing another—the first from the Indian Ocean. Underwater photography continues to play an important part in furthering our knowledge of these animals, with many new pygmies coming to the attention of researchers through images taken by recreational divers. In 2017, the SyngBio conference held in Tampa drew the world's seahorse and pipefish researchers together for only the third time. I was invited to give a keynote speech one evening, and chose to speak about the huge diversity of these tiny fish. One of the images I showed was a pygmy seahorse measuring 1.6 cm in length that I had photographed a few years before in Japan. I was sure that it was a new species, but it wasn't until I chatted with seahorse taxonomist Graham Short after my talk that he trained his efforts on describing *Hippocampus japapigu* as a new species, a project we completed in 2018.

My background in natural history observation, photography, and marine biology has led me to photograph many new species. In 2014, I was diving in a remote corner of southern Indonesia with my friend Anna DeLoach when she spotted a stunning male flasherwrasse, an undescribed species that, two years later, would be named Alfian's flasherwrasse (*Paracheilinus alfianii*) after our dive guide and friend Yann Alfian. The rainbow of color, just a few inches long, flitted around above the reef, showing off like a frenzied



Apollo Publishers, September 2019

aquatic peacock to a harem of somewhat ambivalent females. The species is a vivid illustration that a surprising number of organisms now being discovered on coral reefs have tiny geographic ranges, possibly spanning only a few hundred square miles.

Through collaboration with researchers, my images of rare or previously undocumented behaviors and species have been published numerous times in the primary literature. But I hope these images can also reach beyond the scientific community to a wider audience. During the past 20 years, the coral reef fish identification books that I pore over have more than doubled in size with new species added thanks to the combined efforts of biologists and citizen scientists. These days, with the fabric of coral reefs changing before our very eyes, it's encouraging that new species continue to be discovered, but alarming how quickly their homes are disappearing. ■

Richard Smith is a British underwater photographer, marine biologist, and writer. See images from The World Beneath at the-scientist.com.



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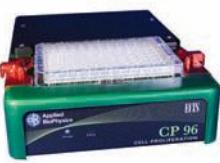
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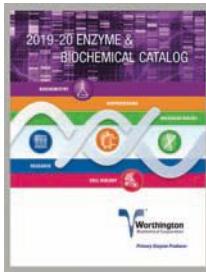
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Poet of the Sea, 1940s-1950s

BY SHAWNA WILLIAMS

The sea, Rachel Carson once wrote, is the “great mother of life.” Most know Carson for *Silent Spring*, an environmental manifesto that accused the chemical industry of spreading disinformation on pesticides. The book, published in 1962, contributed to the initiation of a federal ban on the use of the synthetic organic compound DDT, and to the creation of the US Environmental Protection Agency. But long before Carson’s carefully crafted prose helped to push the environmental movement forward, she introduced readers to the wonders of the sea.

To write *Under the Sea-Wind*, her first book, Carson lay on the beaches of Beaufort, North Carolina, and “felt the waves, listened to the birds, and imagined what was going on,” says Robert Musil, the president and CEO of the Rachel Carson Council, the legacy organization Carson envisioned before her death to carry on her environmental advocacy work. “She walked around at night with a flashlight and looked at the ghost crabs and became deeply involved with these creatures.” In the book, Carson follows a few of the animals—a mackerel, a pair of small shorebirds, and an eel—in their salty worlds.

For him, Musil says, the enduring appeal of Carson’s writing comes from her insight that “if you can’t identify with something, somebody, a species, or a people who are different than yourself, you’re inclined to destroy it.”

This ethic of environmental empathy was first instilled in Carson as she grew up outside of Pittsburgh, learning from her mother to listen to and identify the songs of birds and appreciate the wonder of the natural world. Carson made her first foray into writing at age eight with a story about two wrens searching for a house. She later enrolled at Pennsylvania College for Women, now Chatham University, to study English. A biology course taught by Mary Scott Skinker led Carson to a summer



TIDAL PROSPECTING: Rachel Carson with Bob Hines, an artist who illustrated *The Edge of the Sea*, collecting specimens from the surf in the Florida Keys in 1955.

research position at the Woods Hole Marine Biological Laboratory, where she combed the shore during the day, and at night peered into the water to watch what came to life under the moonlight.

Carson went on to study zoology at Johns Hopkins University, where she wrote a thesis on the development of a type of tissue that helps days-old fish embryos excrete waste, completing her master’s degree in 1932. She started her PhD in marine biology at Hopkins but left the program to take a job at the Washington, DC, office of the Bureau of Fisheries, now the US Fish and Wildlife Service (FWS), to support herself and her family during the Depression. She continued to write, first selling articles to *The Baltimore Sun*, and eventually submitting an essay to *The Atlantic*. After it was published, she began using her evenings to work on *Under the Sea-Wind*.

Published in November of 1941, the book was critically acclaimed, but because of the outbreak of World War II, it didn’t sell well. Drawing on her fish embryo research and her experience as an aquatic biologist and science writer at the FWS, Carson pitched a story on the detrimental effects of pesticides to *Reader’s Digest*, but it wasn’t accepted. Undeterred, she started on her second book, *The Sea Around Us*, which became an instant best seller, winning the National Book Award for nonfiction writing in 1952. Subsequently, Carson’s first book was republished and also became a best seller, as did the next book she wrote, *The Edge of the Sea*.

Ultimately, Carson did get her warnings about pesticides into print. And Musil says that the success of her first three books is part of the reason that *Silent Spring* had the impact that it did. ■

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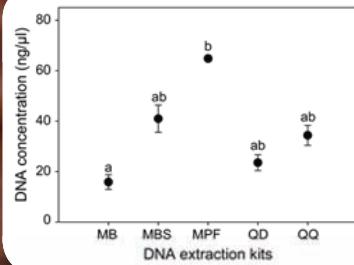
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