Treating the brain with
PSYCHEDELIC DRUGS

Energy savings through
BIOINSPIRED MATERIALS

Ticks spread the deadly
POWASSAN VIRUS

AMERICAN
Scientist

May–June 2025

www.americanscientist.org

Natural Forms, Surreal Sculptures

Art that explores the living world beyond human experience

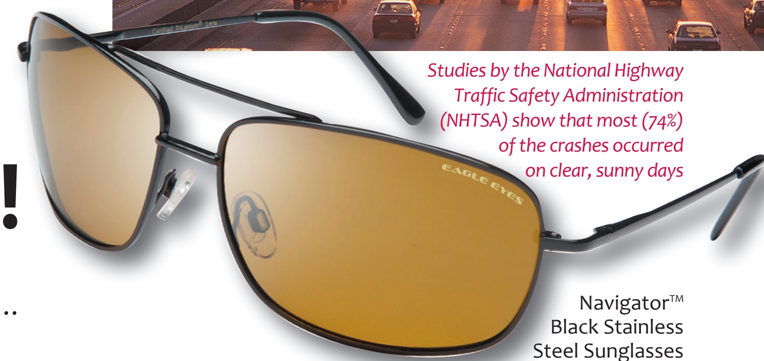
SIGMA XI
THE SCIENTIFIC RESEARCH HONOR SOCIETY

Urgent: Special Summer Driving Notice

To some, sunglasses are a fashion accessory…

But When Driving, These Sunglasses May Save Your Life!

Studies by the National Highway Traffic Safety Administration (NHTSA) show that most (74%) of the crashes occurred on clear, sunny days



Navigator™ Black Stainless Steel Sunglasses

Drivers' Alert: Driving can expose you to more dangerous glare than any sunny day at the beach can… do you know how to protect yourself?

The sun rises and sets at peak travel periods, during the early morning and afternoon rush hours and many drivers find themselves temporarily blinded while driving directly into the glare of the sun. Deadly accidents are regularly caused by such blinding glare with danger arising from reflected light off another vehicle, the pavement, or even from waxed and oily windshields that can make matters worse. Yet, motorists struggle on despite being blinded by the sun's glare that can cause countless accidents every year.

Not all sunglasses are created equal. Protecting your eyes is serious business. With all the fancy fashion frames out there it can be easy to overlook what really matters—the lenses. So we did our research and looked to the very best in optic innovation and technology.

Sometimes it does take a rocket scientist. A NASA rocket scientist. Some ordinary sunglasses can obscure your vision by exposing your eyes to harmful UV rays, blue light, and reflective glare. They can also darken useful vision-enhancing light. But now, independent research conducted by scientists from NASA's Jet Propulsion Laboratory has brought forth ground-breaking technology to help protect human eyesight from the harmful effects of solar radiation light. This superior lens technology was first discovered when NASA scientists looked to nature for a means to superior eye protection—specifically, by studying the eyes of eagles, known for their extreme visual acuity. This discovery resulted in what is now known as Eagle Eyes®.

Slip on a pair of Eagle Eyes® and everything instantly appears more vivid and sharp. You'll immediately notice that your eyes are more comfortable and relaxed and you'll feel no need to squint. The scientifically designed sunglasses are not just fashion accessories—they are necessary to protect your eyes from those harmful rays produced by the sun during peak driving times.

The Only Sunglass Technology Certified by the Space Foundation for UV and Blue-Light Eye Protection. Eagle Eyes® features the most advanced eye protection technology ever created. The TriLenium® Lens Technology offers triple-filter polarization to block 99.9% UVA and UVB—plus the added benefit of blue-light eye protection. Eagle Eyes® is the only optic technology that has earned official recognition from the Space Certification Program for this remarkable technology.

CERTIFIED SPACE TECHNOLOGY™ spacefoundation.org

The finest optics: And buy one, get one FREE! Eagle Eyes® has the highest customer satisfaction of any item in our 20 year history. We are so excited for you to try the Eagle Eyes® breakthrough technology that we will give you a **second pair of Eagle Eyes® Navigator™ Sunglasses FREE––a $59.95 value!**

That's two pairs to protect your eyes with the best technology available for less than the price of one pair of traditional sunglasses. You get a pair of Navigators with stainless steel black frames and the other with stainless steel gold, plus one hard zipper case and one micro-fiber drawstring cleaning pouch are included.

Your satisfaction is 100% guaranteed. If you are not astounded with the Eagle Eyes® technology, enjoying clearer, sharper and more glare-free vision, simply return one pair within 30 days for a full refund of the purchase price. The other pair is yours to keep. Don't leave your eyes in the hands of fashion designers, entrust them to the best scientific minds on earth. Wear your Eagle Eyes® **Navigators** with absolute confidence, knowing your eyes are protected with technology that was born in space.

Receive the Navigator™ Gold Sunglasses (*a $59.95 value*) **FREE! just for trying the Navigator™ Black**

Navigator™ Gold Stainless Steel Sunglasses

Certified EAGLE EYES® was developed from original NASA Optic technology and was recently inducted into the Space Foundation Technology Hall of Fame.

Fit-ons available for $39 +S&H
Black or Tortoise-Shell design

Two Pairs of Eagle Eyes® Navigator™ Sunglasses $~~119.90~~†

Offer Code Price **$49** + S&P **Save $70.90**

Offer includes one pair each Navigator™ Black and Navigator™ Gold Sunglasses

1-800-333-2045

Your Insider Offer Code: ENS245-01
You must use this insider offer code to get our special price.

Stauer®
14091 Southcross Drive W.,
Dept. ENS245-01
Burnsville, Minnesota 55337
www.stauer.com

ACCREDITED BUSINESS
Rating of A+

† Special price only for customers using the offer code versus the price on Stauer.com without your offer code.

Smart Luxuries—Surprising Prices™

AMERICAN
Scientist

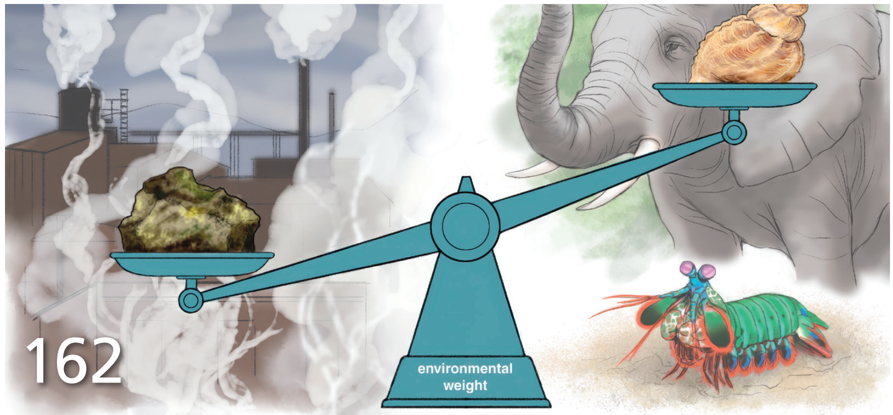
Volume 113 • Number 3 • May–June 2025

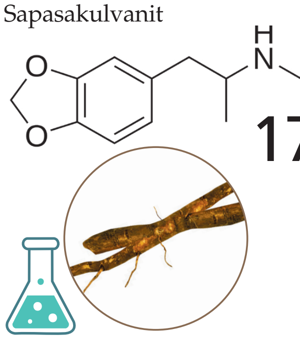
Departments

Scientists' Nightstand

From Sigma Xi

Feature Articles





170

The Cover

Sculptor Ellen Jewett brings together zoology, botany, ecological principles, and surrealism to explore human concepts of nature as familiar and comforting but also alien and indifferent. In "Creatures Both Serene and Deeply Strange" (pages 150–155), Jewett describes to contributing editor Sandra J. Ackerman her process of creating the plants and animals in her works through meticulous research and the techniques of medical illustration. Vulpes Anima (Soul Fox)*, created in 2024, depicts intricate relationships among a variety of life forms, both predatory and vulnerable. Using natural, local, and recycled materials wherever possible, Jewett invites human viewers to think more about conservation and our connections with the nonhuman world. (Cover image courtesy of Ellen Jewett.)*

From the Editors

Celebrating Science

During World War II, scientific research proved to be crucial. Even while the outcome of the war was uncertain, in 1944, U.S. President Franklin D. Roosevelt was certain of the essential contribution of science to the nation's security. He commissioned a report, spearheaded by Vannevar Bush, then the head of the Office of Scientific Research and Development, titled *Science—The Endless Frontier*. This influential white paper laid out the rationale for government support of science and led to the establishment of the National Science Foundation (NSF). Some of its main tenets were an emphasis on the open flow of scientific knowledge across international borders, the need for basic research, the discouragement of political favoritism in scientific appointments, and a focus on just educational opportunities. Bush and his colleagues employed the idea of science as capital, which provides the necessary fund of knowledge that could be drawn from to serve national security, health, and public welfare. (*For more, see "Frontier Values," November–December 2024.*)

Caught in the Moment Photography

Any number of accounting methods can show that the investment made in the NSF has paid off many times over. At a time when it appears that the proven reasons for institutions such as the NSF are being challenged by the current U.S. administration, it becomes imperative to emphasize the need for evidence-based research and decision-making at all levels of government and society. *American Scientist* and its publisher, Sigma Xi, The Scientific Research Honor Society, have always advocated for good science policy. Sigma Xi has submitted a request for clarification of the U.S. administration's plan for the future of scientific research. Keep an eye out for other resources from Sigma Xi, including mental health support, career aids for displaced federal scientists, and a webinar series featuring policy experts to help the scientific community navigate changes affecting federal science policy. The recent Stand Up for Science rally, held on March 7 in Washington, D.C., and with satellite events across the country, showed widespread support for research and the need for public celebration of science.

Art has always been another medium for both the celebration and critique of science, inviting a different viewpoint and a nuanced consideration of many angles on an issue or area of research. In this issue's Arts Lab column, "Creatures Both Serene and Deeply Strange" (pages 150–155), we feature an interview with Ellen Jewett, a sculptor who combines representations of often opposing organisms to examine ways that the natural world can be familiar and also indifferent. Her work was not created in response to current events, but in many ways, I feel it applies. In her 2017 work titled *The Burden of Motion and Ambition* (*below*), the artist says that the black bear speaks to the psychological real estate accrued from a life lived with great momentum. I feel that many scientists will resonate with this work, seeing in it the ways that researchers strive for answers in their data while dealing with the heavy weights of policy and funding. I hope that science and research remain strong and resilient. As always, join us on social media to let us know what you think. —*Fenella Saunders (@fsaundersamsci.bsky.social)*

AMERICAN Scientist
www.americanscientist.org
VOLUME 113, NUMBER 3

EDITORIAL
Editor-in-Chief Fenella Saunders
Managing Editor Stacey Lutkoski
Senior Consulting Editor Corey S. Powell
Associate Editor Nicholas Gerbis
Book Review Editor Jaime Herndon
Senior Contributing Editor Katie L. Burke
Contributing Editors Sandra J. Ackerman, Carolyn Beans, Emily Buehler, Christa Evans, Jeremy Hawkins, Flora Taylor, Michael Torrice, Sarah Webb
Editorial Associate Mia Evans

ART
Art Director Barbara J. Aulicino

DIGITAL
Digital Managing Editor Nwabata Nnani

ADMINISTRATION
EDITORIAL CORRESPONDENCE
American Scientist
P.O. Box 13975
Research Triangle Park, NC 27709
919-549-4691 • editors@amscionline.org

CIRCULATION AND MARKETING
NPS Media Group • Jamie Fallon, *account director*

ADVERTISING SALES
advertising@amsci.org • 800-243-6534

SUBSCRIPTION CUSTOMER SERVICE
American Scientist
P.O. Box 193
Congers, NY 10920
800-282-0444 • custservice@amsci.org

PUBLISHER
SIGMA XI, THE SCIENTIFIC RESEARCH HONOR SOCIETY
President Kathy Lu
Treasurer David Baker
President-Elect Daniel I. Rubenstein
Immediate Past President Marija Strojnik
Executive Director & Publisher Jamie L. Vernon

EDITORIAL ADVISORY PANEL
Richard Boudreault, *University of Waterloo*
Paula R. Buchanan, *National Center for Domestic Preparedness, Columbia Climate School*
René Fuanta, *East Stroudsburg University*
Simson Garfinkel, *AI2050, Schmidt Futures*
Sonya T. Smith, *Howard University*
Caroline VanSickle, *Des Moines University*

American Scientist gratefully acknowledges support for engineering content through the Leroy Record Fund.

Sigma Xi, The Scientific Research Honor Society is a society of scientists and engineers, founded in 1886 to recognize scientific achievement. A diverse organization of members and chapters, the Society fosters interaction among science, technology, and society; encourages appreciation and support of original work in science and technology; and promotes ethics and excellence in scientific and engineering research.

Printed in the USA

Stauer
Impossible Price
Entire Box For
LESS THAN
$20

Survive Just About Anything for Under $20

On any outdoor adventure, Mother Nature's job is to present you with challenges. Some days she's more demanding than others. And on those days, you'd better come prepared. **The Stauer Survival Box is a near-guarantee you'll be up to the challenge.** The stainless steel multitool offers wire cutters, knife, bottle opener, file, a set of screwdrivers, a pair of pliers and much more. The powerful flashlight has three different settings, and the tactical loop watch is a reliable, water-resistant timepiece that clips to your hip and never leaves your side. All told, opening the Survival Box gives you instant access to nine different tools for **JUST $19.50.**

Regularly sold for $99, we're offering this collection of survival essentials to you for **A FIFTH OF THE NORMAL PRICE!** Why? Because we've had an incredible year and we feel like giving back to our valued customers. As this kit has proven to be one of our all-time best sellers, we can only extend this offer while supplies last. Of our initial run of 1,737, **more than half have already sold.** Your move, Mother Nature.

Survival Box Specifications:
- Multitool: 3 ¼" x 1" folded
- Flashlight: 3 ½" x 1", 260 lumens, takes AA batteries (not included), three LED light modes: strong, medium and caution flashing
- Watch: 2 ¾" x 1", battery type SR626SW (included)

Survival Box ~~$99~~ **$19.50* + S+P** ***Save $79.50***
***You must use Insider Offer Code: SVB310-01 to get this price.**
California residents please call regarding Proposition 65 regulations before purchasing this product.

1-800-333-2045
Your Insider Offer Code: SVB310-01

Regularly priced at $99, take advantage of this special offer while supplies last!

Praise for Stauer's Survival Box
★★★★★
"[It] has everything!"
— Carol T., Anaheim, CA

Box includes flashlight, watch and multitool with wire cutters, knife, bottle opener, file, screwdrivers, pliers and more!

Stauer, 14091 Southcross Drive W., Dept. SVB310-01, Burnsville, MN 55337 **www.stauer.com**

Stauer® | AFFORD THE EXTRAORDINARY®

SIGMA XI
THE SCIENTIFIC RESEARCH SOCIETY
EXPEDITIONS
UNIQUE OPPORTUNITIES & SPECIAL OFFERS

Easter Island & the Leonid Meteor Shower
November 11 - 20, 2025
Archaeological wonders & a celestial lightshow *$4,995 + air*
***$200 off - book by May 15, 2025**

Magnificent Madagascar & the Total Lunar Eclipse
Aug 26 - Sept 10, 2025
Natural heritage, unique wildlife, & the southern sky! *$5,995 + air*

Flavours of the Scottish Highlands
October 6 - 12, 2025
History, archeology & culinary offerings of the Highlands & Islands
From $5,595 + air

Galápagos Islands
December 5 - 14, 2025 or
January 23 - February 1, 2026
Experience wonders & wildlife!
***5% savings for Dec** *From $6,275 + air*

Combine the Galapagos & Peru!
Machu Picchu & other Inca Sites of Peru
Nov 29 - Dec 5, 2025 &
Jan 17 - 23, 2026 *$3,995 + air*

Costa Rica at Christmas
December 20 - 29, 2025
Learn firsthand about the spectacular natural world *$4,595 + air*
***$200 off - book by May 15, 2025**

Panama Canal Expedition
January 9 - 16, 2026
with the Pearl Islands & Darien Jungle
***10% savings** *From $6,785 + air*

Discover the Islands of Japan
April 19 - 29, 2026
Explore iconic highlights & rarely-visited islands
***20% savings** *From $8,140 + air*
Must book by July 22, 2025
*All savings based on availability, conditions apply
Contact us for details
Call or email for Brochures
1 (408) 252 4910
Info@betchartexpeditions.com
BETCHART EXPEDITIONS INC.
17050 Montebello Rd., Cupertino, CA 95014

Online | @americanscientist.org

Now in its third decade, the American Scientist *lunchtime seminar series,* Science by the Slice, *invites scientists to share and discuss new results. The talks are available in person or hybrid online, and videos are posted on our website. Look on our social media for the talk schedule and for how to register for either virtual or in-person attendance. Below are summaries of two recent talks, now available as videos with social media highlights.*

Working Out for Better Gut and Heart Health

Studies have shown that if people have a family history of type 2 diabetes, they often show impairment in other physiological processes much earlier than they show signs of insulin resistance. For instance, they may have less metabolic flexibility—the ability of the body to switch the types of fuels it uses under stress—and they may have reduced blood flow in their extremities and capillaries. These impairments are exacerbated by high cholesterol, and are associated with low diversity in gut microbiota, which can also affect the permeability of the intestinal wall. Ryan Russell of North Carolina A&T State University discusses research results that look into how exercise can improve cardiovascular health, but consequently aid in gut microbiota composition, intestinal permeability, blood flow, and other metabolic factors that can reduce the cascade that leads to the development of type 2 diabetes.
www.amsci.org/node/5360

Breeding Fruits and Vegetables for Better Nutrition

A growing body of evidence supports the roles of *phytochemicals* from fruits and vegetables in meeting nutritional requirements and preventing chronic diseases. These phytochemicals are also appealing to consumers as natural food colorants or supplements. But breeding for nutritional value largely still relies on selection for the content of certain phytochemicals, and factors such as the actual activity of the phytochemicals is less known. For example, the chemical structure of phytochemicals (a trait under genetic control) can modulate their ability to be released from the plant and absorbed, and this trait is independent from total overall phytochemical content. Massimo Iorizzo of North Carolina State University and his collaborators have demonstrated that within the same crop, variation for traits exists across different cultivars and is often associated with chemical structure rather than total content. In this video, Iorizzo discusses the need for a DNA-based breeding strategy to develop new fruits and vegetable varieties that have improved health benefits.
www.amsci.org/node/5361

Check out *AmSci Blogs*
www.amsci.org/blog/

Find *American Scientist* on Facebook
facebook.com/AmericanScientist

Join us on LinkedIn
linkedin.com/company/american-scientist

Find us on Instagram
instagram.com/american_scientist/

Follow us on BlueSky
bsky.app/profile/amsci.bsky.social

American Scientist (ISSN 0003-0996) is published bimonthly by Sigma Xi, The Scientific Research Honor Society, P.O. Box 13975, Research Triangle Park, NC 27709 (919-549-0097). Newsstand single copy $7.95. Back issues $9.95 per copy for 1st class mailing. U.S. subscriptions: one year print or digital $33, print and digital $40. Canadian subscriptions: one year print $41, digital $33; other foreign subscriptions: one year print $49, digital $33. Print institutional rate: $75; Canadian $83; other foreign $91. Digital site license $200, print and digital institutional rate $275. Copyright © 2025 by Sigma Xi, The Scientific Research Honor Society, Inc. All rights reserved. No part of this publication may be reproduced by any mechanical, photographic, or electronic process, nor may it be stored in a retrieval system, transmitted, or otherwise copied, except for onetime noncommercial, personal use, without written permission of the publisher. Periodicals postage paid at Durham, NC, and additional mailing offices. Postmaster: Send change of address form 3579 to American Scientist, P.O. Box 193, Congers, NY 10920. Canadian publications mail agreement no. 40040263.

Cancer Fiends for Fructose

A diet high in this common sugar may lead to increased cancer cell growth, but in a roundabout way.

It's time to feed the fish at Gary Patti's lab. Patti, a chemist at Washington University in St. Louis, and his team keep their fish on a very specific diet: fructose dissolved right into the water of their tank. These zebrafish aren't just being given a little treat; the fructose is labeled with a chemical tracer that will allow Patti's team to follow the sugar through its metabolic journey. The zebrafish swimming through the syrupy tank all have tumors, and their sweetened environment might play a significant role in accelerating the cancer's growth. As Patti and his team reported in a recent issue of the journal *Nature*, they used these experiments to discover an unexpected way that high-fructose diets—at least in animal models like these—lead to increased tumor development, without changing body weight.

"Glucose and fructose have the same chemical formula, and we know that cancer cells are addicted to glucose," Patti says. "We've known that for about 100 years." With this understanding, he and his team expected cancer cells to have the same greed for fructose. The cancer cells did use the fructose to ramp up their uncontrolled proliferation, but not directly, like they do with glucose.

After confirming that fructose promoted tumor growth in the zebrafish, Ronald Fowle-Grider, a postdoctoral fellow in Patti's lab, tried to reproduce the result by giving fructose to human cancer cells in petri dishes. But he did not observe any increased growth in the isolated cells. "We had initially assumed that cancer cells would take up fructose and utilize it," Patti recalls. "But we were surprised to discover that the tumors didn't have the biochemical machinery to break down fructose."

It turns out that cancer needs a middleman for the job. "Fructose did not feed the tumors directly," Fowle-Grider explains. Instead, the body converts fructose into a different kind of nutrient, called *lysophosphatidylcholines* (or LPCs). "It's a type of lipid made by the liver, and those LPCs were then transferred to the tumors, and, as it turns out, tumors really like LPCs," Fowle-Grider said. The cancer cells could access only the by-products of fructose metabolism passed along by the organism's liver and intestines. The study of how small molecules such as LPCs move through the different tissues of our bodies is called *metabolomics*, and it's receiving more attention in cancer research.

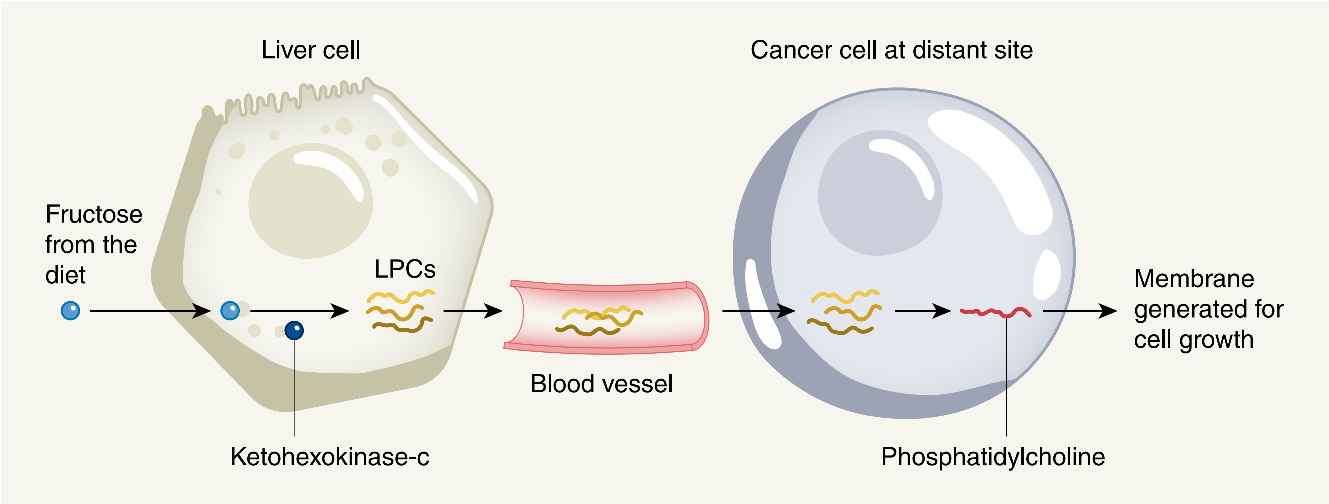
The cancer cells could access only the by-products of fructose metabolism passed along by the organism's liver and intestines.

To enable tumor growth, rapidly dividing cancer cells need a lot of resources. In addition to needing the energy that glucose provides, they also need the lipids that fructose provides in the form of LPCs to build the membranes of new cells. Cancer cells siphon what they need from their surroundings. When Patti reflected on their findings, it became clear why they had observed increased growth only in the animal models, but not in the isolated cells. "The small intestine and liver do a good job of clearing fructose so that little reaches systemic circulation," he says. Therefore, it has been considered unlikely that fructose would reach high enough levels in the circulatory system to drive the growth of tumors outside of these organs. However, Patti's findings suggest that LPCs could potentially reach more distant tissues, and that this potential for wider circulation might increase with higher fructose intake—meaning that fructose could affect more types of cancers than previously understood.

"We've cured cancer a million times over in a dish. But we haven't managed

Mark Smith/Science Source

Zebrafish like these were kept in a laboratory tank in which fructose was dissolved into the water. The fructose contained a tracer that allowed the sugar to be tracked once it was taken up by the fish. The laboratory zebrafish had tumors, and researchers were able to use the tracer to determine that the fructose was promoting tumor growth. However, the zebrafish tumors were accessing the fructose via the organism's metabolism, not directly from exposure.



H. C. D. Medeiros et al., *Nature* 636:580.

Ingested fructose is absorbed by liver cells, where enzymes such as ketohexokinase-c convert it to lipids, particularly ones called *lysophosphatidylcholines* (or LPCs). These lipids enter blood vessels, and from there they can be absorbed by cancer cells at distant body locations. Cancer cells convert LPCs into lipids called *phosphatidylcholines*, which are used to make the cell membranes required for the proliferation of cancer.

to in vivo," shares Rachel Perry, an endocrinologist at Yale School of Medicine. "This study really highlights that we need to think about fructose not really as a direct fuel for tumor cells, but rather as an indirect signaling molecule telling the cell to secrete components to make new cell membranes, which are required for rapid cell division. It forces us to have a systemic perspective in terms of what's going on, which jives with how physiology works."

Perry appreciated how Patti's group used tracers to reveal the mechanism behind fructose-fueled cancer growth, but because her lab also uses tracers, she emphasized that there are no simple interpretations of these types of studies: "The tracer studies were one of the strengths of the paper, but they also have to be interpreted with a great deal of caution. There are a ton of hormones and metabolites that are associated with fructose that could be altered here. And the same criticism can absolutely be applied to everything we've published as well. It's just a part of the game."

Nonetheless, both Perry and Patti are hopeful that this kind of metabolomics research will soon take a larger role in cancer treatment. The ability to affect cancer growth with something as simple as reducing dietary fructose intake would be a valuable intervention in the fight against the disease.

Patti has always viewed diet as a field in which we are all scientists. "In some sense, we do experiments with food all the time. I think everybody's tried some kind of diet, whether it be low-carb, vegan, Mediterranean, and so on," he says. "The idea that diet could be used as a way to modulate

The ability to affect cancer with something as simple as reducing dietary fructose intake would be a valuable intervention in the fight against this disease.

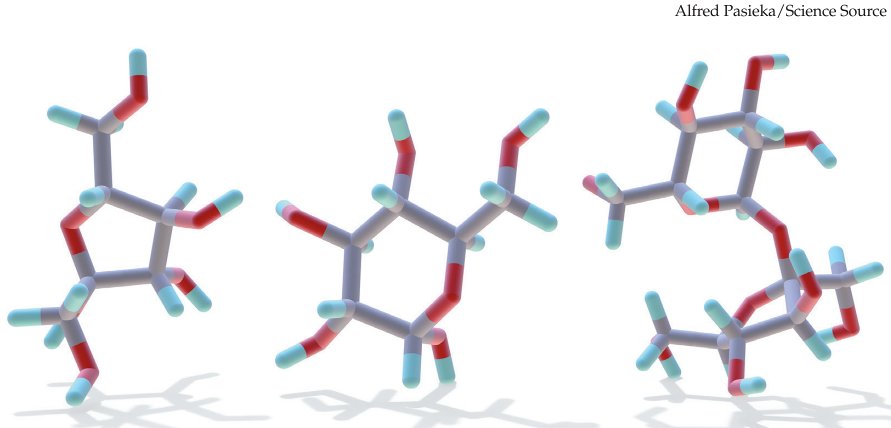
the response to cancer, or at least influence the development of the disease, is quite provocative."

Perry sees the potential for metabolomics research to give cancer patients greater control over their treatment. "I think there's a large opportunity for us to do studies in animal models, to generate those recommendations for people, because folks with cancer are very eager to have these recommendations," he says. "That means that we need to do the work to create them."
—*Jameson Blount*

Jameson Blount is a doctoral candidate in computational biology and bioinformatics at Duke University. He is also the deputy editor of the GeneBites website. Email: jb621@duke.edu

Glucose (*left*), fructose (*middle*), and sucrose (*right*), which is broken down into glucose and fructose molecules, are all common sugars, but cancer cells process them differently. Cancer cells can use glucose directly as fuel, but they must wait until fructose is converted by the liver before they can use its lipid products in the formation of cell membranes.

Alfred Pasieka/Science Source



Unlock Prehistoric Beauty and Flutter Your Way to Fabulous!

Over 44 million years ago in the Baltic region, a powerful force of nature was at work. Liquid Amber wept from the towering trees and slowly transformed over time, becoming what we know today as Baltic Amber. For centuries, this unique and beautiful gemstone has held a special place in the hearts and traditions of those who live in the region and is **often referred to as the "Gold of the North."**

With its rich history and natural beauty, it is no wonder that Baltic Amber has been used to create stunning jewelry pieces for centuries. And what better way to celebrate this natural wonder than by **pairing it with another symbol of divine beauty and grace: the butterfly.**

Our newest jewelry collection features exquisite Baltic Amber pendants and earrings - expertly shaped in the form of the butterfly to capture the intricate detail of these winged creatures. Each pendant and earrings set is crafted with the finest Baltic Amber, **designed by nature over 44 million years, creating a piece of jewelry that is not only stunning, but one which also holds the ancient energy of the earth within it.**

So whether you are looking for a special gift for a loved one or just want to treat yourself to something truly unique and meaningful, explore our Baltic Amber Butterfly collection today and let the beauty of nature inspire you. This stunning handcrafted set can be yours today for as little as **$79 (plus S&H) when using your unique code:** AS5YBB at checkout.

A. ***Baltic Amber Butterfly Pendant & 18k Gold Plated Chain***

~~$149~~ **$79** - *Save $70*

B. ***Baltic Amber Butterfly Earrings***

~~$149~~ **$79** - *Save $70*

** Exclusive Offer Price Using Discount Code*

C. ***Baltic Amber Butterfly Pendant & Earrings Collection***

~~$298~~ **$149** - *Save $149 (additional discount)*

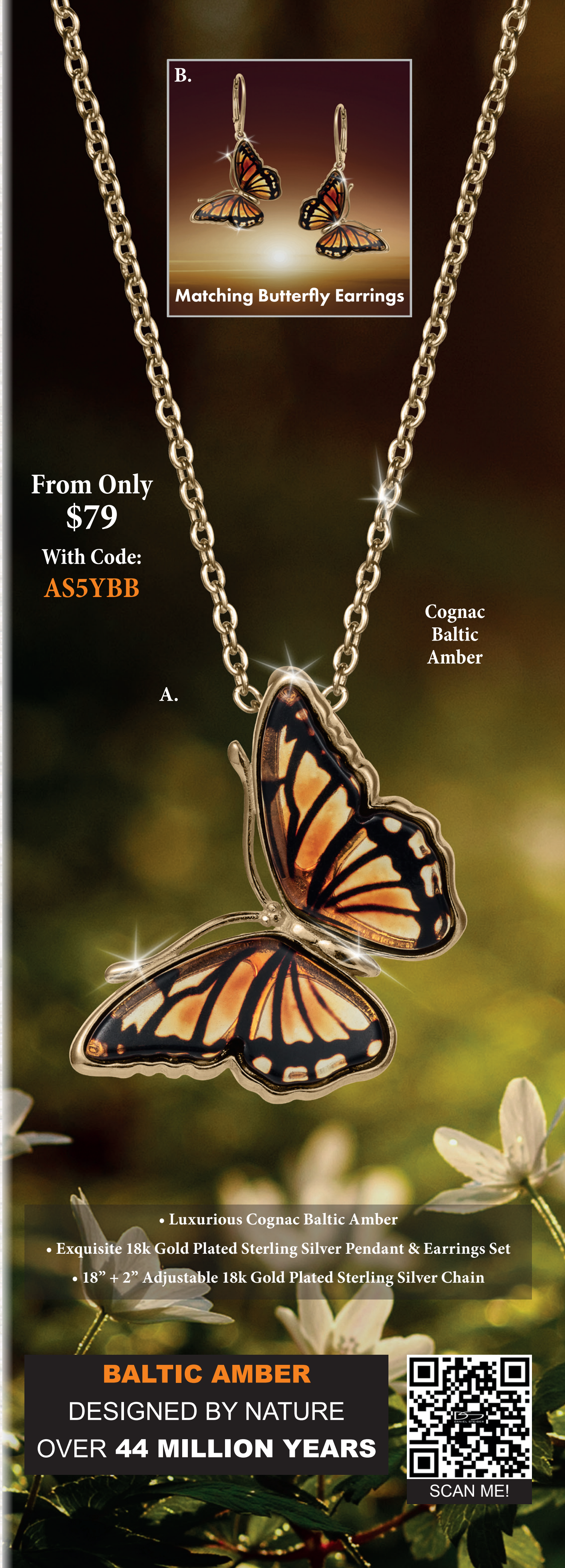
ORDER NOW TOLL FREE 24/7 ON:

1-800 733 8463

OR ORDER ONLINE AT: timepiecesusa.com

AND ENTER PROMO: AS5YBB

Pay By Check: Timepieces International Inc. 10701 NW 140th Street, Suite 1, Hialeah Gardens, FL 33018



Computer-Designed Antibiotics

César de la Fuente leads the Machine Biology Group at the University of Pennsylvania, where he and his team are applying computational power to try to accelerate discoveries in biology and medicine. He and his colleagues developed the first computer-designed antibiotic that showed efficacy in animal models. They also use artificial intelligence and other computational methods to mine existing biological information for new discoveries, and have found new classes of antimicrobial substances in the human proteome *(the complete set of proteins expressed by the human genome) using this methodology. De la Fuente's group also was able to find therapeutic molecules in extinct organisms, launching a field called* molecular de-extinction*. De la Fuente was a plenary speaker at the 2024 International Forum on Research Excellence (IFoRE), and spoke with editor-in-chief Fenella Saunders after the conference about his work. (This interview has been edited for length and clarity.)*

Martí E. Berenguer

You research antibiotics discovery. Why is finding new antibiotics so important?
Antimicrobial resistance is probably the top existential threat to humanity. There are more and more bacterial infections that are resistant to every antibiotic we have available—our entire antibiotic arsenal no longer works to treat some of these infections. They're associated with about 5 million deaths per year in the world. The projection is that by 2050 that number will increase to 10 million deaths per year in the world. If you run a quick calculation, that will be about one death every 3 seconds.

We're heading toward a post-antibiotic era. The first antibiotic, penicillin, was discovered in 1928 by Alexander Fleming, but it was not incorporated into society until the 1940s. We've had antibiotics in our society for less than 100 years, which is a short period of time in the history of humanity. If you look, for example, at the average lifespan of humans, it has practically doubled in the past 100 years because of antibiotics, clean water, and vaccines.

Antibiotics are a huge pillar of human societies today, and a huge pillar of modern medicine. Indeed, a lot of contemporary medicine would essentially collapse without antibiotics, because they are essential in so many routine interventions—procedures such as surgeries and childbirth. If there's a complication from an infection, you need to have antibiotics that work so the health of the patient isn't threatened. People living with cancer and also undergoing chemotherapy treatments are immunosuppressed, so they have a high likelihood of dying from a potential infection. Statistics from cancer patients show that many patients end up dying from bacterial infections as opposed to the cancer itself.

My team and I feel this sense of urgency to think outside of the box about how we can come up with new antibiotics, and how we can do it using new paradigms that are different from those people have used before. This crisis has basically driven me for my whole career. Antimicrobial resistance is probably the most underinvested area of research, but it affects the greatest number of people in the world. The market incentives to create new antibiotics are not aligned with how for-profit companies operate. Labs like mine have a responsibility to try to do something about the problem.

Your laboratory group uses the term *machine biology*. What does it mean to be a machine biology lab?
In my lab, we use the power of machines to accelerate discoveries in biology. We bring together the realms of machine intelligence and human ingenuity to tackle big problems in biology, such as antibiotic resistance. We also have collaborations in other areas, such as cancer, immunology, and neuroscience research.

We've created a transdisciplinary environment in my lab. We collaborate with people from different parts of the world and different research backgrounds, so we approach problems in a heterogeneous way. Right now in my lab, we have people with backgrounds in computer science, chemistry, biology, microbiology, and engineering, all working together. Part of my role is as a translator so that there can be synergies that amplify our thinking. We tend to work between fields, because I think that's where the greatest breakthroughs will come—at the intersections where not a lot of people dare to explore because it's a lot harder than just focusing on one thing. But we try to do that hard work so we can bring concepts from one field into another to see if they might be useful.

How has AI accelerated methods of antibiotic discovery?
Over a decade ago, when I was finishing my PhD, I had the idea that with advances in computer power, perhaps someday we'd be able to apply machine intelligence to antibiotic discovery. In the past six years or so, I started conceptualizing biology as an information source—basically a bunch of code and information. Biology is just a bunch of nucleotides in DNA and a bunch of amino acids in proteins and peptides. With the right algorithms, we should be able to mine all of this code to find new molecules. In our case, we want to find new molecules that we can use to target antibiotic-resistant infections, but the same conceptual framework can be applied to finding anticancer molecules or other treatments.

Using this framework, we were able to mine the human *proteome* as a source of antibiotics for the first time. The human proteome is all the proteins encoded in our genome. With a simple algorithm, we're able to uncover thousands of previously unrecognized molecules encoded in our genome that have antibiotic properties.

That discovery sparked a lot of new questions in my lab, such as whether we might find similar compounds encoded throughout evolution and across the tree of life. We decided to look at our closest ancestors, Neanderthals and Denisovans, as potential sources of antibiotics, and in the process we developed a new framework that we call *molecular de-extinction*. The ultimate goal is to identify molecules throughout evolutionary history, synthesize those molecules in the lab, and learn how changes that occurred throughout time in those molecules affected their biological activity and function.

This research is new because traditionally, the molecule that we've used to learn about ourselves is DNA, which is a molecule of information. It doesn't have a functional role. But now, by identifying and resurrecting proteins and peptides throughout time, we can synthesize the molecules and make them in the lab using robots. We can see how the biological functions of these compounds evolved over time, which could include antimicrobial properties, anticancer properties, or properties in the immune system. We can, for the first time, look at evolution through this lens of molecular extinction and see how molecules evolved. In a way, molecules are documents of evolutionary history, like fossils, and we can learn from them and how they changed throughout time.

We developed an AI model to discover antibiotics in Neanderthals, for instance, and that was the first time that anybody had looked at ancient or extinct organisms as a source of therapeutic molecules. And that research was successful: We discovered antibiotics such as one called Neanderthalin, which comes from Neanderthals and was effective in preclinical mouse models.

That success encouraged us to ask a more ambitious question: Why not just mine every extinct organism known to science? To do that we needed a more powerful AI model. We developed a new deep learning model that we call APEX [*antibiotic peptide de-extinction*], which essentially opened a window into the past. It enabled us to sample every organism throughout evolution, including ones from the Holocene and the Pleistocene. We identified new molecules in ancient penguins that were extinct in the 1950s, and in magnolia trees that had disappeared over time. We moved on to woolly mammoths, giant sloths, and many other creatures—we've sampled the whole tree of life.

We've looked at not only ancient biology, but also living biology. We've looked at ancient and modern humans as well as bacteria and archaea. We've sampled representatives of each of these three branches of the tree of life, and we've identified millions of new antibiotic compounds. Using traditional methods, we would have had to go around nature and try to find preclinical candidates, which can take many years and is often unsuccessful. But today, in my lab, in a few hours with the computer, we can discover millions of compounds by mining biology at the digital level, instead of having to do it in the field.

"Molecules are documents of evolutionary history, like fossils, and we can learn from them and how they changed throughout time."

We take advantage of many years of sequencing data. People have sequenced genomes and proteomes over many years, and all of those data are available digitally in databases. We've developed algorithms that sort through that information and identify molecules that might be useful.

I'm very excited about the potential of AI in biology and antibiotic discovery. It is an incredibly exciting emerging field. It's what I have dreamed about for over a decade. And now in my lab we have this amazing playground combining computers, chemistry, and experiments and mouse models. We can discover something or design something on the machine, see it on the screen, and then within a week we can test it in mice. It's really incredible and incredibly fun.

Are sequences available for all these extinct organisms?

For a lot of them there's genetic information available based on sequencing methods that have been developed. Perhaps the pinnacle of that field was when, a couple of years ago, Svante Pääbo was awarded the Nobel Prize in Physiology or Medicine for developing sequencing methods for archaic DNA, which is very difficult because oftentimes in fossils and in ancient samples the DNA is mostly degraded. Early on, researchers developed ways of amplifying mitochondrial DNA, because we have a lot more copies of mitochondria. But more recently they've come up with methods of also amplifying chromosomal DNA. The amazing thing is that some of that information is available publicly. We can access it and then do everything digitally. Essentially the whole world of biology, or a lot of it, is at our disposal in databases.

Your team has developed algorithms to sort through immense quantities of biological information. What indicates to the algorithm that a certain sequence is antibiotic or antimicrobial?

It depends on each project. In the case of APEX, this new deep-learning model that we developed, it was trained using an in-house dataset that we generated painstakingly over several years. It contained experimental data of particular molecular sequences with their respective antimicrobial scores, all determined in experiments using standardized conditions. We started this years ago, at a time when AI had not been successfully applied in biology, or in molecules.

It was a big bet when I decided to invest a lot of money and effort into creating a dataset for antibiotic discovery. That dataset generation project has been unfunded in my lab, even today, because funding agencies typically want to fund hypothesis-driven projects but not dataset-generation projects. But if people want AI to be successful, we're going to have to do the hard work of building datasets.

It was an amazing experiment, because we didn't know how much data we needed to train an algorithm properly. We tested it iteratively. After one year of collecting data we tried to train APEX. It didn't work. After two years we tried again. It didn't work. It took about three and a half years to collect enough data to train APEX.

The project taught us that it takes about 1,000 molecules to train a model properly. And now APEX is a state-of-the-art model. Given an amino acid sequence, APEX predicts the antibiotic activity directly. It's a sequence-to-function prediction model; it doesn't take into account structure. It obviates that step. We're now working on APEX 2.0, building upon those discoveries and a lot of the hard work that we had to do early on.

Of course, every dataset is intrinsically biased. If people tell you otherwise, they're not telling the truth. One of the biases in our dataset is that the peptides that we work with tend to be alpha helical, so that means that APEX is biased toward trying to discover things that are alpha helical. A lot of those biases will be ameliorated over time as we grow the dataset, but there's always going to be inherent biases. That's just a limitation of AI models and how we train them, and I think it's better to just be completely up front about it.

None of this work is going to be perfect, but it's a great approach to discovering antibiotics. To ameliorate the biases, we're building novelty thresholds and filters to try to convince the algorithm to go in certain directions. But again, every algorithm is trained on a training set that is going to be inherently biased to some extent.

Do the antibiotic-resistant molecules found in older samples operate differently from those around today?

When we did a comparison of archaic humans versus modern humans, we saw a difference in the mechanism of action. Gram-negative bacteria [*a type of bacteria that tends to have high antibiotic resistance*] have two membranes: an outer membrane and a cytoplasmic or inner membrane. The ancient molecules tend to go after the inner membrane, whereas the modern ones tend to go after the outer membrane. It is an interesting example of applying the framework of molecular extinction and comparing molecules throughout time, and then being able to unlock new biological insights by applying that framework. We are also seeing differences when we compare the composition and the physical and chemical parameters of these ancient molecules to modern examples. We're still unpacking a lot of that information, but we are already finding interesting insights.

One of our goals is to learn about how molecules evolved in response to pathogens and infectious diseases or other stimuli. Infectious diseases are the greatest drivers of evolution in humans throughout history. They're the greatest killers of humanity, and so they've influenced many changes at the genetic level that then influence what kinds of molecules we make. By learning from that process we can inform better therapies that may be able to tackle resistance mechanisms in more effective ways.

“Infectious diseases are the greatest killers of humanity, and so they've influenced many changes at the genetic level that then influence what kinds of molecules we make.”

Are you finding molecules within the human proteome or microbiome that have antibiotic resistance? Could there be ways to amplify existing molecules already in the human body?

We find that a lot of molecules are produced by beneficial microbes. One potential approach in the future could be to engineer bacteria to overproduce some of these molecules. You could envision taking this engineered bacteria in yogurt or in supplements. They would colonize your gut, and then they would produce this beneficial molecule in an overexpressed manner.

There are vitamins that upregulate innate immune effectors in our bodies. For example, vitamin D upregulates a peptide called LL-37, which is part of innate immunity. In the future there might be other vitamins or supplements that you could take to specifically upregulate some of these compounds that we're finding. It could be a way of naturally upregulating our own defenses that we have intrinsically.

What ethical concerns does your de-extinction work raise, and how are you addressing these concerns?

When we were initially uncovering some of these compounds from extinct organisms, it was really exciting scientifically. But then I started worrying about whether it is okay for us to synthesize some of these molecules. When we do multiple sequence alignment for some of the ones we found in ancient biology, we can't find any overlap with any existing molecules, meaning they're not expressed in living biology. We're literally resurrecting them with chemistry. Is it okay for us to do that?

One thing we're doing is making sure we don't synthesize things with sequences that might be similar to biotoxins. In the last two or three years I've signed petitions on the safe use of AI in biology in order to prevent the potential design of bioweapons. In my lab we abide by those petitions that we've officially signed. We've also been consulting with bioethicists to make sure we continue innovating, but that we do so responsibly.

The sequences themselves are inert unless they're prion-like sequences, which could potentially be able to self-replicate. But typically they're inert. We keep them in test tubes. In our conversations with bioethicists and biosecurity experts, the recommendation has been to do what we're doing, which is to keep them in freezers. They're not living entities. It's not like we're engineering bacteria or human cells, particularly bacteria that then might be able to escape and self-replicate in the environment. In our case, we work with peptides, and they would simply degrade.

Another ramification of our work in molecular extinction is that natural compounds are not patentable. When I consulted with the patent office at the University of Pennsylvania, I asked about the ancient molecules that we're finding that used to exist in biology, but no longer exist. Are those patentable or not? It has opened up a new area of patent law, because patent lawyers are not sure. We take into account all of these things. ■

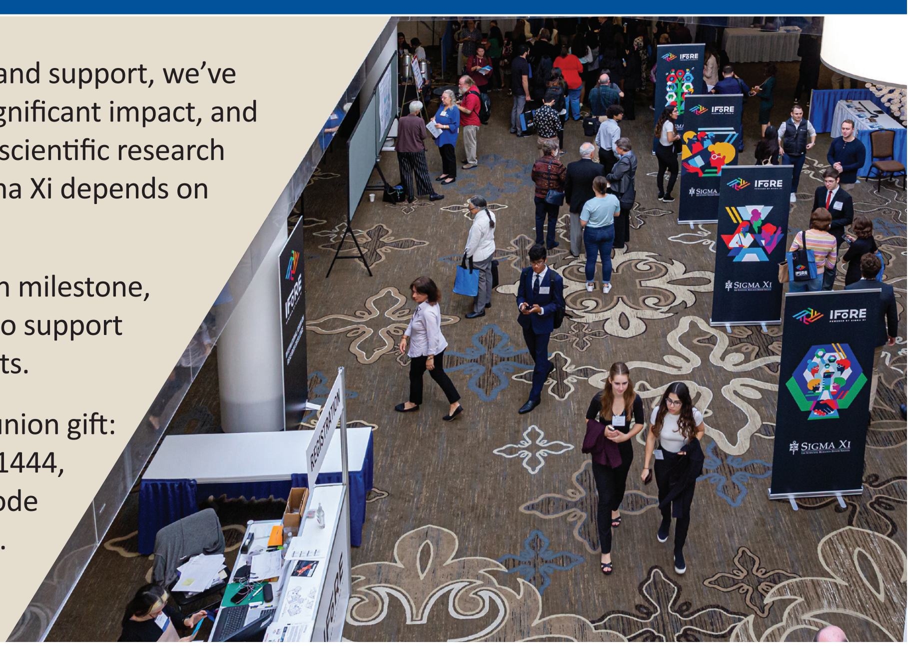
SUPPORT YOUR REUNION

2025 GIVING CAMPAIGN

Because of your membership and support, we've achieved many goals, made significant impact, and expanded our support for the scientific research community. The future of Sigma Xi depends on great members like you.

To commemorate your reunion milestone, please consider making a gift to support the next generation of scientists.

To make your reunion gift: Text sigmaxi to 41444, or scan the QR code from your phone.



AFRICAN PYGMY HEDGEHOG

LC NT VU EN CR EW EX Declining

IUCN Conservation Status: Least Concern

Animalia	KINGDOM
Chordata	PHYLUM
Mammalia	CLASS
Eulipotyphla	ORDER
Erinaceidae	FAMILY
Atelerix	GENUS
albiventris	SPECIES

LIFESPAN

2–3 years in the wild
up to 10 years in captivity

SLEEP CYCLE

nocturnal; very active at night
rest 12–14 hours daily

SOCIAL BEHAVIOR

quiet; sheepish
prefer to live alone

Hedgehogs have been known to snack on scorpions and small poisonous snakes.

Hedgehogs are often described as insectivores, but they are in fact opportunistic omnivores. The bulk of their diet does consist of insects and other invertebrates, but they also eat small vertebrates, plants, and even carrion.

WEIGHT

250–600 grams
9–21 ounces

When threatened, hedgehogs roll themselves into compact balls and erect their spines to protect their heads and bodies from potential predators.

LENGTH

17–23 centimeters
7–9 inches

Hedgehogs' quills lie flat against their bodies when they feel relaxed.

Unlike porcupine quills, hedgehog spines do not have barbs.

African pygmy hedgehogs have short tails that can be seen when they are relaxed.

A baby hedgehog is known as a *hoglet*.

To prevent injury to the mother, hoglets are born with their spines just below their skin.

Hedgehogs do not use their sight to hunt; instead, they rely on their hearing and sense of smell.

BREEDING AND PARENTAL CARE

MATING
- Polygynandrous short-term pairs
- Breed yearly from October to March

OFFSPRING
- 4–7 hoglets per litter
- Average gestation period: 35 days

African pygmy hedgehogs are solitary, but they do pair off frequently for what is typically a noisy courtship. While mating, both hedgehogs must work together to avoid unsuspecting attacks from hungry predators.

During courtship, hedgehogs circle one another while loudly snuffling, chirping, chuckling, and squeaking.

PREDATORS

carnivores; large birds
raptors, badgers, jackals, wild dogs

ECOLOGICAL ROLE

control pest populations
help balance ecosystems

Hedgehogs are popular pets. Some owners have even trained them to walk with a harness and leash.

RANGE

African pygmy hedgehogs are native to sub-Saharan Africa; however, as a popular pet, they are now commonly found worldwide. African pygmy hedgehogs have become an invasive species in New Zealand.

Habitat destruction and hunting remain the greatest threats to hedgehog populations.

Until recently, hedgehogs had been assigned to the order Erinaceomorpha; however, genetic evidence now classifies them in the order Eulipotyphla, along with shrews and moles.

Hoglets stay with their mothers for about five weeks before heading out on their own to live independently.

© Wandering Walden
Created by Abigail Lorincz
Source: Animal Diversity Web

In this roundup, associate editor Nicholas Gerbis summarizes notable recent developments in scientific research, selected from reports compiled in the free electronic newsletter *Sigma Xi SmartBrief*: www.smartbrief.com/sigmaxi/

Brain of Glass

The 79 CE eruption of Mount Vesuvius transformed the brain of one of its thousands of human victims into glass, retaining some of its neurons, axons, and other neural structures. The unique brain vitrification of the 20-year-old male in Herculaneum required high heat and rapid cooling conditions different from those previously inferred from volcanic deposits. Scientists at Roma Tre University in Rome suggest a hotter, briefer, and less substantial pyroclastic flow must have passed through the ancient Roman town earlier in the eruption, making the victim's surroundings hot enough to disorder his brain's crystalline structure, but not so hot that outgassing or other thermal forces would destroy it. The organ then had time to cool rapidly before the arrival of the heavier flows that famously preserved so many bodies in Herculaneum and Pompeii. The researchers' experiments show the necessary temperature topped 510 degrees Celsius—far hotter than the 315 to 465 degrees estimated by past studies of Vesuvius deposits.

Giordano, G., et al. 2025. Unique formation of organic glass from a human brain in the Vesuvius eruption of 79 CE. Scientific Reports *15:5955.*

Tracking Sea Turtles' Lost Years

A landmark study of sea turtles suggests they are more active during their juvenile years than once thought. Using tiny solar-powered satellite tags, scientists tracked 79 green turtles (*Chelonia mydas*), 26 Kemp's ridleys (*Lepidochelys kempii*), 5 loggerheads (*Caretta caretta*), and 4 hawksbills (*Eretmochelys imbricata*) during these "lost years," when sea turtles are difficult to observe. Findings by the team led by University of Central Florida researchers could affect conservation of the four threatened species amid human impacts, climate change, and pollution events by giving a fuller picture of rookeries and sea routes in need of protection, and of the potential effects of altered hurricane patterns on algal food sources. During their initial "oceanic stage," hatchlings were once thought to spend all their time drifting in protective and productive brown algae mats. Then, during their "neritic stage," juveniles were thought to permanently relocate to forage in the shallows near shore. But new studies show oceanic-stage turtles transiting to neritic environments and suggest they don't just drift, they swim. Also, rather than moving solely from one stage to the next, some turtles double back to revisit old haunts. In light of this more nuanced ecology, the authors argue for calling the "oceanic stage" the "dispersal stage"instead.

Jordi Chias/NaturePL/Science Source

Phillips, K. F., N. F. Putman, and K. L. Mansfield. 2025. New insights on sea turtle behavior during the "lost years." Proceedings of the Royal Society B *292:20242367.*

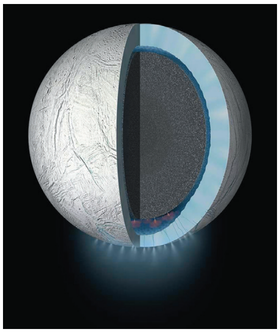
Poking Holes in Peto's Paradox

After almost 50 years, scientists have disproved Peto's paradox: the notion that bigger animals don't have higher cancer risks, even though logic suggests they should. Larger animals have more cells and cell divisions, which ought to create more opportunities for errors, mutations, and cancers. Yet in 1977, epidemiologist Richard Peto noted that, cell for cell, humans have a much smaller cancer risk than mice. Now researchers from Johns Hopkins School of Medicine, and from the University of Reading and University College London in the United Kingdom, have demonstrated that cancer is, in fact, more prevalent in larger species. Their results held true for all four major classes studied—amphibians, birds, mammals, and squamate reptiles (lizards and snakes). One of the most vexing ideas in comparative biology was resolved through access to larger datasets, statistical methods comparing numerous variables (such as age, lifespan, size, and mass), and improved modeling methods. So why aren't blue whales dropping dead from cancer? Researchers also found that larger species are often more likely to evolve anticancer adaptations.

Butler, G., J. Baker, S. R. Amend, K. J. Pienta, and C. Venditti. 2025. No evidence for Peto's paradox in terrestrial vertebrates. Proceedings of the National Academy of Sciences of the U.S.A. *122:e2422861122.*

Enceladus's Mushy Geysers

Saturn's moon Enceladus hides a global ocean beneath its icy shell and fires geysers hundreds of kilometers high from surface fractures. But instead of drawing from the subsurface ocean, as is commonly thought, the plumes might stem from melt pockets nearer the surface, driven by frictional heating and by Saturn's tidal forces. If true, then samples taken from the geysers by the Cassini spacecraft in 2008 might differ from the subsurface ocean in composition, which could hinder scientists' assessments of whether Enceladus or other icy moons—notably Jupiter's Europa—might support life. The oceanic plume hypothesis stems in part from the fact that the geysers contain dissolved salts and dust that could originate only from the subsurface ocean, and molecular hydrogen, which implies an interaction between water and a rocky seafloor. But models suggest that fracturing 6 kilometers of ice to reach the ocean would take larger forces than are available, and that such fissures would close within less than a year. The new model by the team led by Dartmouth College researchers suggests the surface might hold many of the materials detected in the Cassini flyby, retained either from Enceladus's formative years or in pockets that once received water from the ocean. In this mushy ice model, the lower melting point created by salt in the surface ice, combined with frictional heating, would cause melting inside the shell, resulting in plumes that match observed eruption rates and patterns.



NASA/JPL-Caltech

Meyer, C. R., et al. 2025. A potential mushy source for the geysers of Enceladus and other icy satellites. Geophysical Research Letters *52:e2024GL111929.*

Sightings

Fossils Saved by Fool's Gold

Mineralized animal remains from millions of years ago reveals new species.

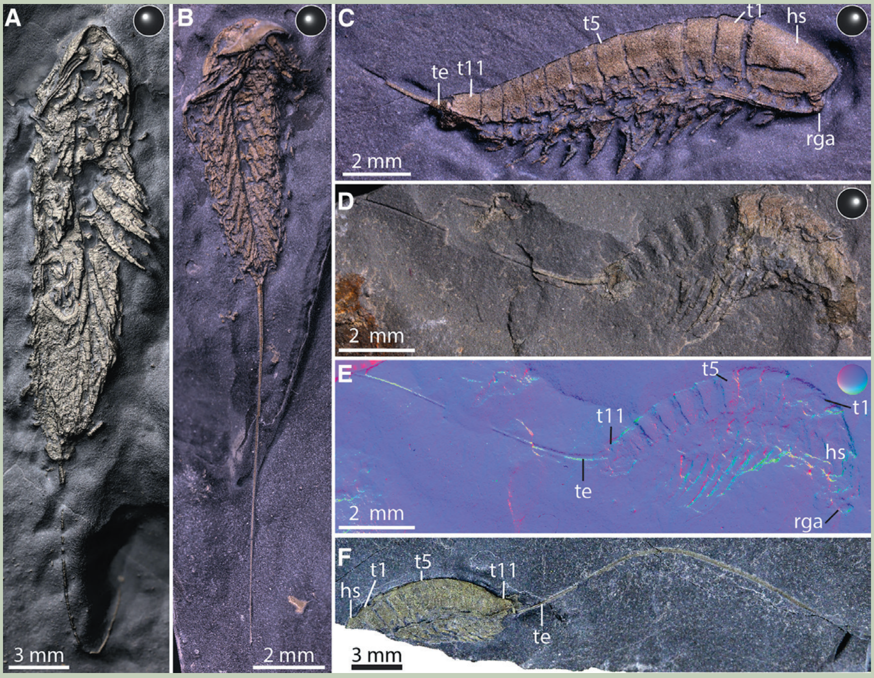
The glint of the mineral known as fool's gold used to be a blow for miners searching for the real thing. But for fossil hunters, this glimmering mineral, iron pyrite, is a priceless treasure. Under the right conditions, an organism's remains can be mineralized in pyrite, creating a fossil that is remarkably detailed and durable, providing evidence of extinct animal anatomy that is rarely preserved. A new pyrite fossil discovery, combined with advanced imaging techniques, has identified a previously undiscovered species that could help elucidate the evolution of arthropods, particularly the head appendages and mouthparts of horseshoe crabs and trilobites.

The set of five shimmering fossils was found in New York State at a famous site called Beecher's Trilobite Bed. The ocean floor there at the time these creatures died was low-oxygen and iron-rich, allowing for fast mineralization of the delicate tissues of these organisms. Sulfate-reducing bacteria break down organic material in these low-oxygen environments, producing hydrogen sulfide. This compound then reacts with iron to produce iron sulfide, or pyrite. Derek Briggs, a paleontologist at the Yale Peabody Museum who has worked on fossils from this site for decades, says that the fossils had to form quickly to preserve the structures before they decayed. "The cuticle of the exoskeleton provides a kind of enclosed space," Briggs says, "and the muscle tissue inside that decays but promotes the conditions that favor pyrite formation. The original cuticle decays in a matter of months, leaving the body and limbs preserved in pyrite."

Pyrite is dense, which lends itself to imaging with computed tomography (CT) scanning. Briggs's colleagues, Luke Parry of the University of Oxford and Yiu Lu of Yunnan University in China, conducted the imaging and modeling, as the team reported in a recent issue of the journal *Current Biology*. The fossils basically were imaged in digital slices that were combined by a computer into a detailed 3D model.

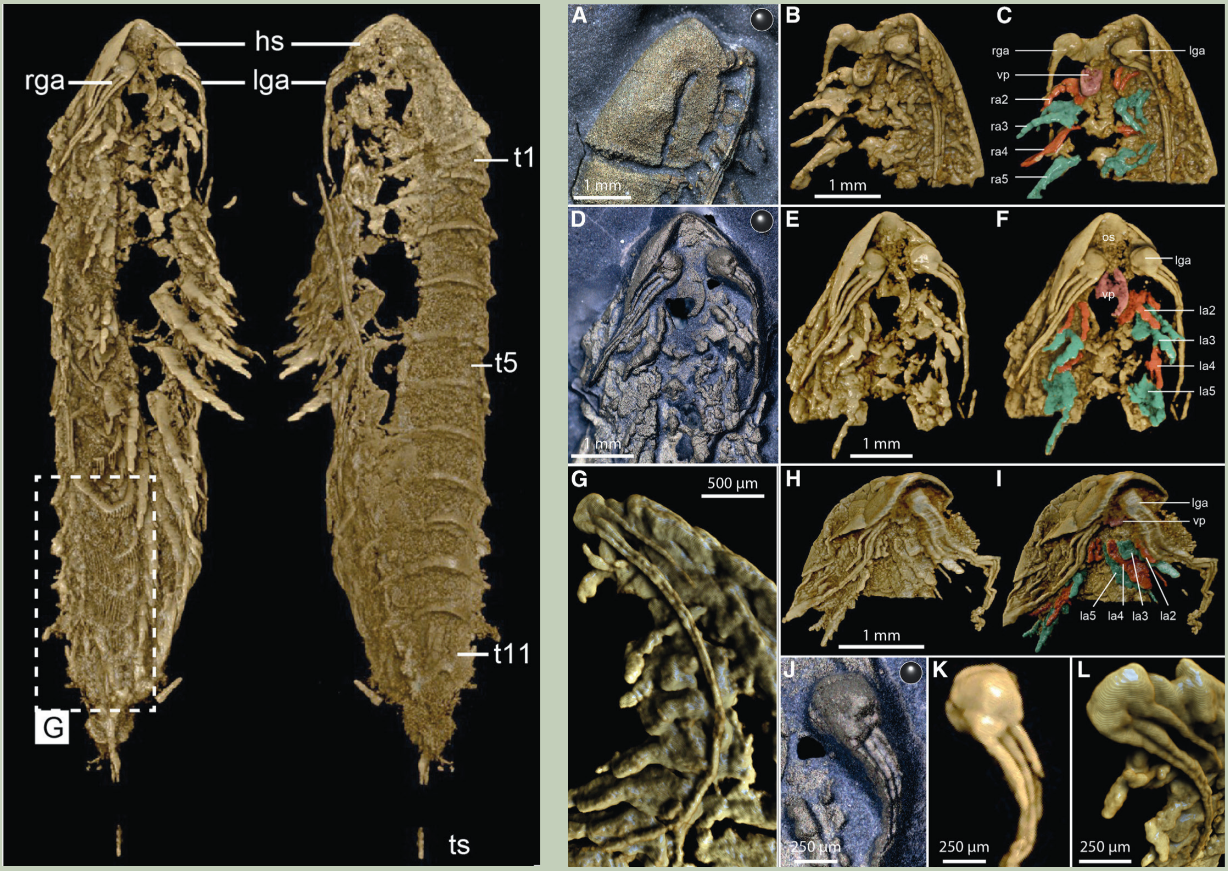
The vaguely shrimplike animal, which the team named *Lomankus edgecombei*, lived on the ocean floor during the Ordovician Period, about 450 million years ago. It belonged to a group of animals known as *megacheirans*, which thrived earlier during the Cambrian Period and were thought to be largely extinct by this time. Megacheirans had what's called a *great appendage*, a modified pair of limbs on the front of their heads. In earlier megacheirans, this great appendage was equipped for capturing prey. But in *Lomankus*, it was reduced in size and sported long flagellae. That, along with its apparent lack of eyes, indicates adaptation for a dark, murky environment. The placement of its great appendage also reflects that of later arthropod antennae and mouthparts, providing some further suggestion of an equivalency between these structures. "These fossils tell us about the range of form and diversity in arthropods, and indirectly inform the evolution of the group as a whole," Briggs said. "We knew very little about decay-prone arthropods from this part of the Ordovician, because we rarely get exceptional preservation of that age." —*Fenella Saunders*

A reconstruction of *Lomankus edgecombei* (*right, top*) shows that it apparently had no eyes, and that its head instead had appendages with attached flagellae that it likely used to navigate in murky environments. This reconstruction is possible because of pyritized fossils that preserved fine structures (*right*). Photographs of the fossils using different light sources and angles pick up on varying details (*below*). Details of the animal's head (*far right*) show photographs (*A, D, and closeup in J*), and CT scans rotated to show various anatomical details (*B–C, E–F, G–I*). The feeler on the front of the head, called the *great appendage*, and its attached flagellae are well preserved (*J, K, and L*).



Luke Parry, Yu Liu, and Ruixin Ran. From *Current Biology* 34: P5578.

Xiaodong Wang



Luke Parry, Yu Liu, and Ruixin Ran. From *Current Biology* 34: P5578.

The Case for Quantity in Science Publishing

Well-intentioned efforts that encourage researchers to produce fewer, higher-quality papers miss the many benefits of abundance in academic research.

David B. Allison and Brian B. Boutwell

In an influential 2016 editorial in the journal *Nature*, Daniel Sarewitz at Arizona State University warned that scientific research is being undermined by a glut of overpublishing. "Current trajectories threaten science with drowning in the noise of its own rising productivity," he wrote, adding that avoiding such an outcome "will, in part, require much more selective publication." This sentiment has since been repeated so often that it has practically become an accepted truism.

If we were forced to choose between quantity and quality in the production of research, quality seems the obvious choice. We reject the notion that improving the quality of scientific publishing requires limiting the quantity, however. On the contrary, we believe that rules and procedures designed to suppress quantity could end up harming the research community and hindering the emergence of new, creative ideas.

Most researchers already publish at a quite modest rate. One of the few studies to look systematically at the publication rate of individual researchers found no meaningful increase over the past century. The study's authors—Daniele Fanelli from the Meta-Research Innovation Center at Stanford and Vincent Larivière from the University of Montreal—concluded that "the widespread belief that pressures to publish are causing the scientific literature to be flooded with salami-sliced, trivial, incomplete, duplicated, plagiarized and false results is likely to be incorrect or at least exaggerated." A relatively small number of hyperproductive publishers create a distorted view of the situation.

The entire collective of scientific research should be thought of as a portfolio to be optimized.

Furthermore, the people who worry about overpublishing imagine a zero-sum game where none exists. Quantity does not need to come at the cost of quality, and there are significant upsides to quantity in publishing. More scientific papers and more scientific communication can contribute to the quality of the research enterprise as a whole, for a number of important reasons.

More Space for Good Ideas

Our first argument is that increasing the quantity of papers or publications leads to more opportunities for the law of large numbers to take effect, thereby increasing the chances of an important finding emerging. Nobel laureate Linus Pauling said that if one wishes to have a good idea, one must first have many ideas. Most ideas will flounder, a reality captured famously by the example of Thomas Edison. When asked about his repeated failed attempts to develop the light bulb, Edison responded, "I have not failed. I have just found 10,000 ways that won't work."

By extension, researchers cannot know ahead of time which seemingly inconsequential discoveries will turn out to be important. Reverend Thomas Bayes hit on the powerful concept of conditional probability in the 18th century partly as a way of understanding the shifting odds of winning a lottery. (Incidentally, his discovery of what is now known as Bayes's

QUICK TAKE

Widespread concerns that researchers are publishing too much, driving down the quality of their work, are misguided and potentially harmful to scientific progress.

Quantity is crucial in scientific publishing: It creates more opportunities for breakthrough ideas, error-correction, efficiency, communication, collaboration, and mentoring.

Methods for encouraging quantity can also safeguard quality, or even improve it. Reducing barriers that limit scientific output should benefit the research enterprise as a whole.

Yuki Murayama

Research thrives in an environment of abundance. When people work in an environment that encourages quantity—in the number of scientific studies, collaborations, and published reports—they are more likely to produce high-impact work over the course of a career.

theorem was never published during his lifetime.) Studies of Gila monster venom in the 1990s helped spark the development of today's GLP-1 diabetes and weight-loss drugs.

Roberta Sinatra of Northeastern University and colleagues analyzed data on the careers of scientists and the impact of their published work, ultimately concluding that "the highest-impact work in a scientist's career is randomly distributed within her body of work." Moments of great insight occurred with the same probability anywhere in the sequence of a scientist's publications. This random-impact rule held across disciplines, across careers of varied lengths, and over time. It applied whether authorship was solo or with a team, and whether or not credit was assigned uniformly among collaborators.

Rather than enjoining scientists to limit their quantity, expecting that reduced output will somehow provoke a hot streak, we should encourage steady productivity, patience, and perseverance. It's important, and entirely possible, to promote quantity while maintaining standards for quality and disincentivizing questionable research practices. For instance, we support having scientists make their raw data openly available and preregistering their plans for research and analysis. The goal should be to make those actions as frictionless as possible so that they don't harm productivity and output.

Visible Success and Failure

Another advantage of quantity is that greater numbers of studies and publications allow greater opportunities to observe both successful and failed replications.

Whether from random variations, subtle differences in methodologies, or statistical manipulations such as *p-hacking* (exploiting data analysis to produce desired results), what works in one study or lab is not guaranteed to work in other places and at other times. (*See "The Statistical Crisis in Science," November–December 2014, for more on p-hacking*.) Concerns about replication ability have surged among researchers, the public, and government officials alike. Members of Congress went as far as to request that the National Academies of Sciences, Engineering, and Medicine offer recommendations for improving rigor and transparency in research, which were published in 2019 as a Consensus Study Report titled *Reproducibility and Replicability in Science*. Brian Nosek at the Center for Open Science has conducted extensive investigations showing how a scarcity of replication can help conceal flimsy bodies of evidence.

More publications will naturally lead to more studies geared toward replication, with a positive impact for science as a whole. We argue that the entire collective of scientific research should be thought of as a portfolio to be optimized—that is, the incentives and evaluations that influence quality and quantity should lead to the best outcomes relative to available resources, as determined by new knowledge, novel applications, public interest, and support for the next generation of researchers. Such optimization will likely involve repeated shifts between focusing on novel studies and focusing more on replication attempts in subdomains of research.

Past a point, repeated replication attempts bring diminishing returns. More publishing is better when it is advancing knowledge and actively clarifying prior results; more is not better when it recapitulates robust results *ad tedium*. But overall, a greater volume of successful and failed replications not only weeds out individual flawed studies, it also highlights the insights from different areas of inquiry that time and again have resisted refutation.

The 19th-century scientist and philosopher William Whewell described a concept that is relevant here: *consilience*, a process of intellectual reinforcement that happens when demonstrated findings from one domain of inquiry accord with demonstrated facts or postulates from another. Consilience is akin to puzzle building. A single puzzle piece, like a single finding, could fit many different places, or it might not fit at all. The more pieces you have joined together, the easier it is to see where a new one can or cannot go. In this context, both success and failure become more evident.

The absence of consilience risks producing misleading results, as happened in 2011 when Cornell social psychologist Daryl Bem reported evidence for extrasensory perception (ESP), premised on ostensibly statistically significant results. The broader scientific community was rightly incredulous. The concept of ESP ran counter to our understanding of what physical laws permit within the construction of reality (that is, no consilience). Sure enough, further studies failed to replicate Bem's results.

Opportunities for Challenges

Quantity makes it easier for investigators to engage in competition and probe for weaknesses in an idea. In military and security training, one group will sometimes pose as an enemy "red team" to help the other team find and fix its weaknesses. A good red team personifies the notion of tough-minded but constructive criticism. A similar process happens in scientific research. In his book *The Knowledge Machine*, New York University philosopher Michael Strevens argues that science is at its best when honest but competitive investigators repeatedly search for flaws in their competitors' arguments in a collegial, constructive manner.

Rather than enjoining scientists to limit their quantity, expecting that reduced output will somehow provoke a hot streak, we should encourage steady productivity, patience, and perseverance.

A century ago, Albert Einstein intensely prodded Danish physicist Niels Bohr in this way over his interpretation of the statistical nature of quantum mechanics. Although Einstein's early work had provided much of the foundation for quantum mechanics, he had difficulties accepting core aspects of the fast-developing field. He repeatedly assailed Bohr's ideas, most notably at the Solvay Conference of 1927. The two physicists' attempts at refuting each other were frequently rebutted and, in some cases, found to contain mistakes. Their intellectual volleys rooted out flaws and strengthened the intellectual bulwark of quantum theory.

More recently, nutritionists David Ludwig of Harvard University and Kevin Hall of the National Institutes of Health have engaged in a series of vigorous debates over the connections among obesity, diet composition, and energy (caloric) intake. Their pointed critiques have elevated each other's thinking and prompted new insights into how physiologic and behavioral factors affect body weight. These red-team volleys were facilitated by numerous research papers as well as blog posts and other nontraditional forms of academic science communication.

Economies of Scale

Quantity in research can improve data collection as well. When individuals (or individual laboratories or teams) produce a great deal of a certain type of research, they become increasingly efficient and proficient over time. For instance, repeated use of expensive equipment and facilities can lead to a positive economy of scale and an increase in quality.

Fostering environments that encourage greater research productivity should lead to more publishing. At the same time, greater productivity implies increased use of the labs, research facilities, software, and databases required to generate the work. A 2017 review by a British team explored the effects of concentrating more work in one facility for biomedical and health research. The authors reported some direct evidence for "positive economies of scale" in universities and research institutes. Our personal experiences affirm such economies of scale, especially for research that depends heavily on repetitive use of complex procedures or instruments that are initially expensive to install or difficult to master.

In 1991, one of us (Allison) joined the New York Nutrition and Obesity Research Center as a postdoc under the mentorship of Steven B. Heymsfield, affectionately known as the "king of human body composition analysis." He seemingly had access to every new body composition device

Yuki Murayama

The puzzle of scientific problem-solving becomes easier when there are more pieces to work with. An abundance of published results, both successful and failed, clarifies which ideas and results can lead to important insights, and which ones are extraneous or misguided.

as it came out. Companies flocked to Heymsfield's lab to examine and validate the latest tools; health researchers from across the country likewise came to gather more precise measurements for their studies. As our team grew more experienced, the documented quality of our measurements improved and our databases of measurements expanded. Finally, the number of research papers generated by investigators with access to those databases grew as well, and continues to do so.

Openings for Collaboration

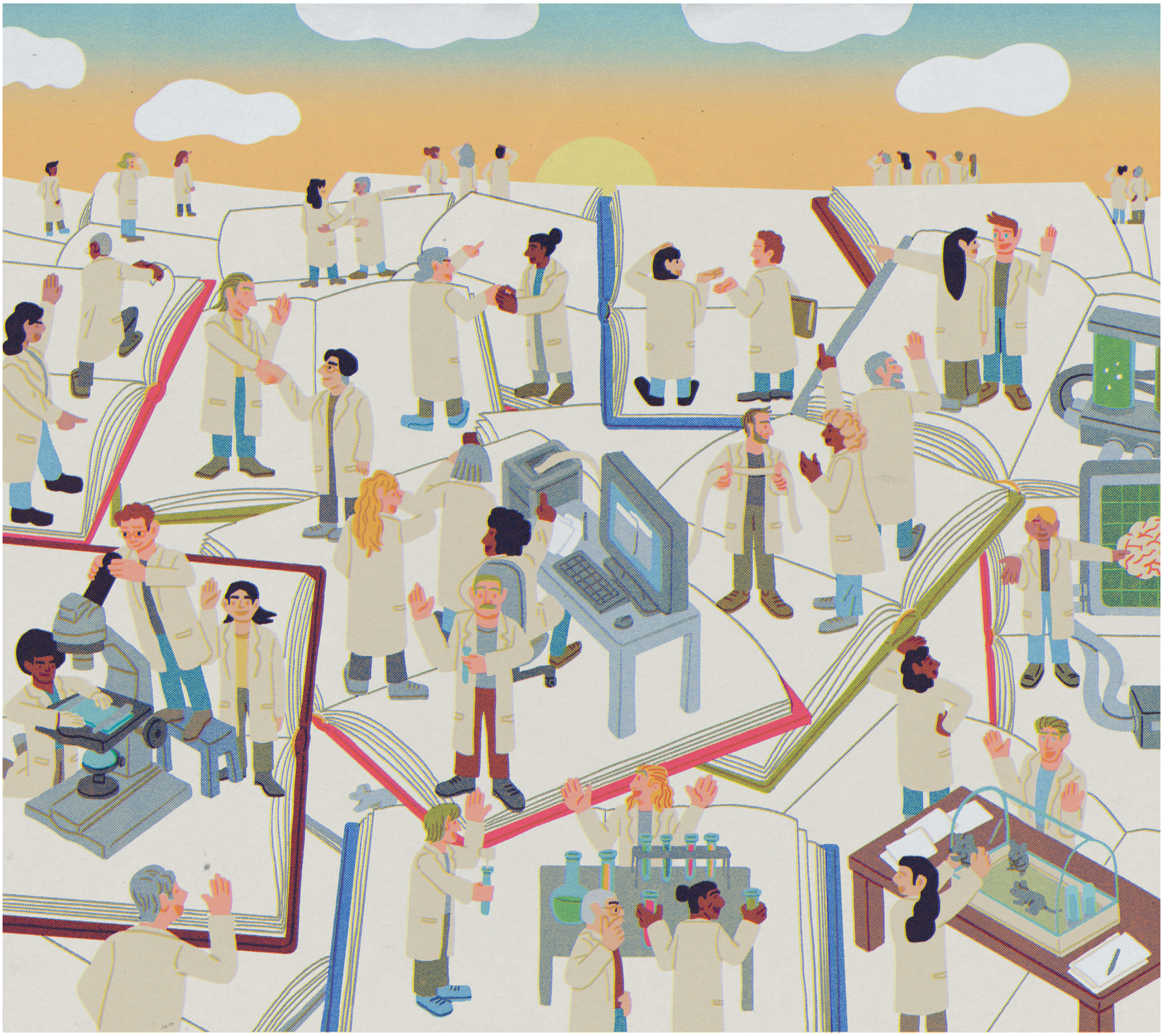
Multidisciplinary research has long been observed to increase insights from different fields of science. Increasing quantity can assist in this regard, because it can bring together individual scientists and their institutions, with benefits for science as a whole. More publishing, particularly of cross-disciplinary collaborations, increases the chance of exposure and creates more opportunities to draw on the knowledge of new collaborators.

When communicating their work to other researchers, both inside and outside their fields, scientists often inspire new collaborators who then bring fresh ideas and insights to the table. A famous example is that of the young Michael Faraday, later one of the greatest experimental physicists, who was drawn into the laboratory of the polymath Sir Humphry Davy after one of his lectures at the Royal Institution of Great Britain. Davy was mostly summarizing earlier research, but by exposing new people to his ideas, he helped to launch Faraday's career. Faraday subsequently developed the principle of the electric motor and identified the unified relationship between electricity and magnetism.

Both of us have attracted students, collaborators, and funders because our work was available for others to notice. We have also noted many other contemporary examples of research partnerships fostered through science publishing and communication. In the early 2000s, for example, immunologist Marta Catalfamo (then a fellow at the National Cancer Institute) attended a lecture about HIV patients by Clifford Lane, clinical director of the National Institute of Allergy and Infectious Diseases. As described on the George Washington University website, that lecture redirected Catalfamo's research toward understanding how HIV affects the human immune system, and led to her working alongside Lane to develop novel therapies for neutralizing HIV and suppressing secondary infections.

Potential for Communication

Public understanding of science is a critical factor in determining what research has a practical impact. At times it is necessary to bring an idea to many different audiences, both to convey its



Yuki Murayama

Scientific publishing in all forms helps build up a productive network of collaborations, constructive rivalries, and cross-pollination of ideas across teams. Popular communication, in particular, helps build bridges between fields of research and plays an important role in boosting public awareness of complex or controversial scientific concepts.

importance and to open minds to evidence supporting novel or controversial findings. Quantity creates openings for science to be applied more effectively, especially when an important idea is either not easily grasped or not easily accepted by others for social or emotional reasons.

We have on more than one occasion published a piece, such as a review article or perspective piece, in one journal, only to have another journal contact us afterward saying, "We saw your paper, and we'd like you to write a related piece for us." These days it is also common for major scientific societies to come out with a position statement that is created collaboratively with other journals and is then simultaneously published in more than one outlet. In the context of this article, we observe that quantity is important not just in academic publishing, but also throughout science communication more broadly.

Louis Pasteur regularly wrote letters to newspapers rebutting attacks against his ideas on germ theory and vaccines. In evolutionary biology, Thomas Henry Huxley earned the appellation "Darwin's bulldog" in the 19th century for his dogged promotion of Charles Darwin's ideas. Over the past few decades, scientists such as Stephen Jay Gould, Richard Dawkins, and Sean B. Carroll have continued Huxley's work, recognizing the importance of repeatedly articulating complex evolutionary ideas using different voices in journals, books, popular magazine articles, and videos. Public outreach is a separate type of quantity that could and should be encouraged through its own set of incentives.

Cultivation of Scientists

Promoting quantity can help cultivate the future workforce of science, encouraging diversity and equal opportunity. To make an analogy: The goal in professional basketball, or in any professional sport, is arguably to produce the best output for any unit of time and money spent, and to not spend time and money inefficiently. So, if we define the best version of the sport as the most technically proficient, and if we had just a single evening to spend watching, then it would seem best to have only the top performers or teams play, and only in the interval of their peak performance. Minor leagues, college basketball, children's leagues, or pick-up games would generally be eliminated so that we could promote quality and not quantity.

But hopefully we have much more time than just a single evening in our lives to enjoy basketball. Over time, it is also important to continuously draw new people into the game. If we value the abilities of a top basketball player, then justice requires that we allow others the opportunity to develop similar skills. By bringing in a diversity of players, we increase the pool to draw from, thereby increasing quality. We may also find that diversity adds complexity and creativity to the game. Thus, it is crucial to support developmental league games, college basketball, children's basketball games, and so on, if we value the future of basketball.

The same principles hold for scientific research. If we desire a strong scientific workforce, we must promote the careers of those who may not have attended the most elite universities or worked in the highest-profile laboratories. We should encourage people whose lives have given them a slower start by affording them opportunities to present results and receive encouragement, win awards, and obtain jobs. A vital way to do that is to provide more opportunities for junior researchers to publish their work, perhaps by adding journals that focus on student and mentee research. When established researchers publish more, they also have greater opportunities to take on junior researchers as coauthors.

The Larger Point

It seems useful to close by considering not just why it is important to promote quantity in science publishing, but how to do it effectively. Scientists often remark that there is never a good time to do research—you either find the time or you don't. But the system can make it easier for scientists to boost their productivity and increase their rates of publication while maintaining high standards. That is, we can optimize conditions for promoting both quality and quantity.

Journals could further streamline and automate the rules of publishing so that it takes less time to preregister research and analysis plans. Universities and funding agencies could work continually to reduce administrative burdens of tasks such as the submission of grant applications. Institutions of all kinds could provide more

The system can make it easier for scientists to increase their rate of publication while maintaining high standards: We can optimize conditions for promoting both quality and quantity.

infrastructure to help researchers be more creative and more productive. In particular, they could adjust the way money is allocated so that researchers experience periods of stable support, punctuated by periods of demand.

There is a body of literature supporting the idea that researchers work most effectively when they alternate through those conditions. During times of demand, researchers enter a state of high productivity: Get this grant, solve this problem, publish this paper. But researchers also need episodes of relative downtime, when they can think for a while and engage in open creativity. Einstein's seven years spent working in a Swiss patent office functioned as a (highly effective) creative escape from academic burdens. The Howard Hughes Medical Institute allocates creativity time to its grant winners and has been shown to produce a high level of creativity as a result.

A final thought about the current hand-wringing about overpublishing in science: The volume of research publications has been increasing exponentially for at least two centuries—for as long as institutional science has existed. The current growth should be viewed in that larger context, as a sign of the continued expansion of human knowledge. Making quantity a sacrificial lamb in the hopes of boosting quality will only impede the remarkable progress that is possible when science is functioning at its best.

Bibliography

Azoulay, P., J. S. Graff Zivin, and G. Manso. 2011. Incentives and creativity: Evidence from the academic life sciences. *The RAND Journal of Economics* 42:527–554.

Fanelli, D., and V. Larivière. 2016. Researchers' individual publication rate has not increased in a century. *PLoS ONE* 11:e0149504.

Forthmann, B., M. Leveling, Y. Dong, and D. Dumas. 2020. Investigating the quantity–quality relationship in scientific creativity: An empirical examination of expected residual variance and the tilted funnel hypothesis. *Scientometrics* 124:2497–2518.

Hernandez-Villafuerte, K., J. Sussex, E. Robin, S. Guthrie, and S. Wooding. 2017. Economies of scale and scope in publicly funded biomedical and health research: Evidence from the literature. *Health Research Policy and Systems* 15:3.

Kekecs, Z., et al. 2023. Raising the value of research studies in psychological science by increasing the credibility of research reports: The transparent Psi project. *Royal Society Open Science* 10:191375.

Michalska-Smith, M. J., and S. Allesina. 2017. And, not or: Quality, quantity in scientific publishing. *PLoS ONE* 12:e0178074.

National Academies of Sciences, Engineering, and Medicine. 2019. *Reproducibility and Replicability in Science*. National Academy of Science Press.

Nosek B. A., and T. M. Errington. 2017. Reproducibility in cancer biology: Making sense of replications. *eLife* 6:e23383.

Sarewitz, D. 2016. The pressure to publish pushes down quality. *Nature* 533:147.

Sinatra R., D. Wang, P. Deville, C. Song, and A. L. Barabási. 2016. Quantifying the evolution of individual scientific impact. *Science* 354:aaf5239.

Strevens, M. 2020. *The Knowledge Machine: How Irrationality Created Modern Science*. Liveright.

David B. Allison is dean and distinguished professor at the Indiana University School of Public Health in Bloomington. His studies focus on obesity, nutrition, and longevity, along with statistical methods and research rigor. Brian B. Boutwell is an associate professor of criminal justice and legal studies at the University of Mississippi, with a secondary appointment as associate professor and scientist educator in the John D. Bower School of Population Health at the University of Mississippi Medical Center. Email for Allison: allison@iu.edu

Arts Lab

Creatures Both Serene and Deeply Strange

The nature-based sculptures of Ellen Jewett blend the familiar with the fantastical.

***Ellen Jewett is a sculptor** whose naturalistic portrayals of plants and animals combine scientific accuracy with elements of the surreal. In her works, a white sea turtle sports a shell consisting of rich undergrowth, craggy rocks, and sweeping succulents, while long-tailed parakeets soar overhead between the limbs of a tree [*My Paradox, My Friend*, 2020]. A vibrant panther chameleon balances on its forelimbs, its hindquarters vanishing into the whorls of a snail shell that in turn supports a llama sporting a deer skull [*Our Emotional Imposters*, 2020]. A pink snake gazes calmly at the tiny green elephant on which it perches, the snake's curling body mirroring the curl of the elephant's trunk [*The Precautionary Principle*, 2025].*

Jewett studied fine art, anthropology, and zoology, but her sculpting methods were painstakingly self-taught. Her works use materials such as polymer clay, porcelain, resin, mineral powder, metal, and nylon fibers to create complex creatures and shapes. Jewett's sculptures have appeared in museum exhibitions and galleries around the world, as well as on television and in books, magazines, and online publications. From her home on Vancouver Island in Canada, Jewett spoke and corresponded with contributing editor Sandra J. Ackerman for this interview, which has been edited for length and clarity.

How does the idea for a new work usually come to you: As a theme? A visual image? A surprising combination of materials?

Although my process has evolved over time, it's usually an element of the narrative I want to capture in a given sculpture that sparks the planning phase. This element serves as the starting point for the sculpture and its accompanying narrative to unfold. It could be as simple as wanting to convey the feeling of grief or, more specifically, reflecting subversive parental roles in nonhuman species. From that initial idea, the rest tends to develop organically. My process is labor-intensive, so there's plenty of time while my hands are working for associations to percolate, and new ideas to emerge and take shape.

Does the balance between the biological and the metaphorical start to shift as you build outward from the skeleton?
Yes. I build in an additive manner, or from the inside out. In my current line of work, the base of each sculpture is usually the [sculpted] body of an animal. A lot of traditional sculptures that depict animals use a physical base to hold up the animal, often crafted to look like a piece of nature, such as a patch of grassy earth or rock for them to perch on. Sometimes the need for that base is an artifact of the casting or printing process, and/or is a matter of convenience; you can make a base any shape and size to counterbalance and accommodate the pose of the animal subject. However, in my work, the animal itself is usually the base, with most secondary details springing from it. So, the animal is no longer just the subject within the environment; the animal is the environment from which other subjects are projected. This is one subtle way I seek to move the animal from object to subject. While my work is, in some ways, an exploration of the human experience, I like it to be suggestively anthropomorphic as well, as I'm deeply fascinated by the nonhuman experience of being in the world.

The animal is no longer just the subject within the environment; the animal is the environment from which other subjects are projected.

To go back to the original question, as the base is an animal's body and the support structure, it is necessarily the most faithfully referenced part of each sculpture and the most grounded in biology. What springs forth departs further into the unfamiliar, psychological, or narrative-inspired territory.

Your sculptures are imaginative and almost hallucinatory in some ways, but also highly realistic. Where do you go for the information that enables you to work with such detailed accuracy?
I've always held the belief that the more personal the connection to the reference material an artist uses, the stronger the output will be. Whenever I give lectures to aspiring artists, I always reinforce that the worst thing you can do for personal growth is to look only at the work of other artists most similar to you or those that you envy. To make your own work authentic, look outside the art bubble and into the world. Seek primary sources and personal experiences. I believe there is a strong resonance in how I depict plants, animals, and fungi because I've worked with them my whole life—whether it's been propagating plants, working in animal rescue, or enjoying the rich environment around me through a super macro lens. I think

A Feral Antiquity I (_opposite_) and _A Feral Antiquity II_ (_below_) are complementary sculptures by artist Ellen Jewett that speak to the emotional resonance of older objects and how time can endow these objects with a sense of wonder and wildness. Drawing inspiration from natural history illustrations, these sculptures from 2015 initially began as a dialogue on grief, shrouded by the humbling beauty of age. (All images courtesy of the artist.)

the intimacy of connection directly impacts the sense of realism.

Is it true you don't use conventional sculpting tools in your work?

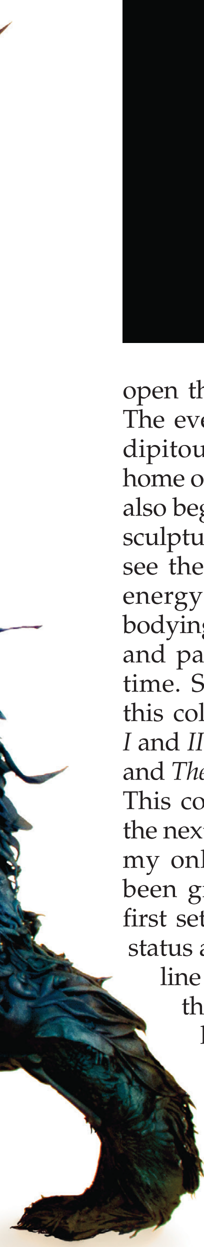
Yes. My approach to sculpting was self-taught and began in my early life at a time when I didn't have access to any professional tools, so I simply learned how to achieve my aims without them. I think some of the characteristic look of my sculptures is an artifact of this. At this time, the only tool that regularly comes into my practice is wire cutters for cutting metal armatures. I'm not against tool use, of course, and I certainly am open to using tools with materials I may work with in the future that aren't as conducive to being worked by hand. But in sculpting, I truly enjoy the tactile nature of the creation process. There is such rich biofeedback when using bare hands, so sculpting in ways too divorced from that isn't as appealing to me.

Looking back over all those years of creating art, do you see distinct stages of development or a more or less continuous course?

There is one collection of work that really stands out to me as a turning point in my early adult career. This came in 2015, when I decided it was time to

In *The Burden of Motion and Ambition* (2017), a black bear saunters forward with her gaze fixed and muscles primed. This sculpture, constructed from air-drying polymer and cold porcelain over metal, speaks to the psychological real estate accrued from a life lived with great momentum.

With *Of Mirth and Poetry* (2020) (*above*) and *Clever and Riddled with Secrets* (2015) (*below*), Jewett employs hollow interiors and flowing filigree to create the appearance of semipermeable windows that offer insight into the more private psychological depths of the subject. Symbolic plants and animals creep in and out of these windows, inviting us to conceptualize interior experiences.



open the next big chapter in my life. The events that followed were serendipitous. While searching for a new home on the other side of the country, I also began creating a new collection of sculptures. Looking back, I can clearly see these sculptures manifesting the energy of that transformation, embodying all the particular excitements and pains I was experiencing at the time. Some notable sculptures from this collection include *Feral Antiquity I* and *II*, *Clever and Riddled with Secrets*, and *The Burden of Motion and Ambition*. This collection really set the tone for the next decade of my work. Although my online presence and career had been growing steadily, this was the first set of my works to achieve viral status after being published in the online art magazine *Colossal*. Now, as the tenth anniversary of that collection approaches, it feels like the time for another big shift.

Do you think this shift will be a change in your process of creating a sculpture, or more in your choice of subjects?
I'm interested in experimenting with other types of

Scan For Free Magazines

With the drive of a great predator, as illustrated in *The Reliquary of Paths Unresolved* (2016), our minds may pursue paths never followed and ambitions never explored. However, like a tiger employing its great strength and cunning merely to chase a butterfly, this quarry yields no nourishment.

media and incorporating larger scales. I feel like the past decade of sculptures really encapsulates a specific line of work. I'm now planning the next chapter, but my process is applied and playful. At this stage, I'm really just experimenting. I believe that when seeking information, it's essential to keep experimenting, because the results will provide more insights to help inform how to move forward. This is where I am right now.

Do you see your art fulfilling any kind of social role? What has been your involvement in conservation, for example?

I see my sculptures as occupying multiple spaces. People often tell me why they were drawn to a specific sculpture and share their personal reading and interpretation of the piece. I always enjoy hearing these, especially because they usually involve superimposing personal narratives onto the sculptures in ways I could never anticipate. This is something I really enjoy as an artist. There are many things in this world best understood with objective truths, but art is something that naturally inhabits the subjective space. I see these personal interpretations as fascinating insights into the people sharing them, and they are valid as specific ways to enjoy the work. Often, these are narratives about their personal relationships with other people or animals in their lives, and I am happy my work can serve as a conduit to appreciate those connections.

But as the creator, I do, of course, have my own intentions as well, and one of them is to help bring curiosity to the human and nonhuman experience. I feel work like mine can be one such line, or window, to invite people to consider the nonhuman experience of being, and to look closer at the complexity of the relationships that all beings have to one another. So, that would be an indirect connection to thinking more about our role and connection with nature and the nonhuman world.

A more direct role my work has played toward conservation in particular is through fundraising. The donation of proceeds from certain sculptures and prints to rainforest protection, ocean cleanup, animal welfare, and wildfire charities is something I've always been happy to be able to do. I welcome other forms of engagement my work could have in the future to further these causes. ■

In *Of Illumination and Luck* (2024) (*right*) and *Hidden Medicine* (2024) (*below*), Jewett's palette ranges from muted tones that evoke subtlety and complexity to high chromas signaling danger, opportunity, and objects of value.

Spirit(s) of a Profession

Values are memorialized in the obituaries of three philosophers of biology.

Robert T. Pennock

The ways the dead are memorialized reveal both individual and cultural values. Some funeral practices emphasize personal mourning—some with wailing, some with quiet sitting. Other services accentuate religious tenets—some the cycles of birth and death, others the promise of an afterlife. Most rites combine both in some form of communal remembrance of the deceased through stories and songs, shrines and symbols, eulogies and obituaries.

Services for family members emphasize familial roles: devoted daughter, loving father, beloved grandmother. For people whose lives had broader influence and meaning, memorial services are structured to emphasize community roles: wise leader, courageous hero, patient peacemaker. Professional communities are typically smaller and more dispersed, so their memorials are necessarily more limited, with the scope expanding for more significant personages.

When philosopher of biology Michael Ruse died on November 1, 2024, at age 84, the news flashed through professional circles within hours. Always a larger-than-life figure, his death marked the end of an era. Ruse, together with Marjorie Grene (1910–2009) and David Hull (1935–2010), are credited as key figures who established the field of philosophy of biology itself. This generational turning point is an opportune moment to reflect on some aspects of the nature of philosophy of science and of professional communities generally that are often overlooked. By examining how such foundational figures are memorialized, we may glimpse some of the values that give a professional specialty its spirit.

A Proper Send-Off

Published obituaries mostly follow standard conventions. Guides for journalists, such as *The News Manual*, describe *obits*, as they are called, as stories that should sum up a person's lifetime work. Like a funeral speech, an obit "marks the proper respect due to the person" as a member of the community. A well-written one will "make the reader feel as though they have met the person." Certain basic facts of a person's career and achievements should be reported, but "much more important is to describe the person's character and personality." A person's faults are not to be ignored, so that their positive qualities are not inadvertently diminished by being falsely one-sided. Obits should give a fair account, but they are not meant to judge a life as though in court or at heaven's gate. What is interesting for our purposes is the way that obituaries indirectly highlight community values.

Deaths are especially meaningful events that focus the attention of community members. They naturally become public occasions to remind ourselves out loud of what we care about. Like other such normatively significant life occasions, funerals are part of a culture's internal regulatory mechanism. Funeral speeches express and reinforce community values through recounting the tale of a life. The end of a tale is where one hears "the moral of the story." Professional obituaries do something similar but from the special perspective of peers.

Community Spirits

Professional obituaries are typically published in specialized venues, such as the news-of-the-profession section of journals, society newsletters, or university and professional society websites. In a course I teach on the scientific character, one exercise I give students is to pick some famous deceased scientist and to compile and analyze their professional obituaries. Viewed with an eye to values, obits can provide an indirect view of the inner normative structure of a profession.

In my analysis of obits of scientists over time, I have found that current ones tend to focus mostly on scientists' affiliations and accomplishments, compared with those in an earlier period when it was more common to speak of scientists' character and the traits that the scientific community recognized as laudable. I have suggested that it would behoove us to nudge the pendulum back in that earlier direction, away from credentials to return toward character, as the latter is far more important to the normative notion of scientific identity. The same thing may be said

QUICK TAKE

The ways we memorialize the dead, especially in written professional obituaries, is directly about the individual's life, but indirectly reveals community values.

Analyzing the traits commonly noted in obituaries can give a sense of a field's values and the ways that its luminaries were viewed as exemplars of a profession's community spirit.

Obituaries of central philosophers of biology emphasize the value of being part of a long-standing, ongoing conversation, and passing that spark to the next generation.

Wikimedia Commons

Socrates held that an unexamined life is not worth living. Jacques-Louis David's 1787 painting *The Death of Socrates* is a visual obituary that artfully illustrates the philosopher engaged in that examination up to the moment of his execution, highlighting how he embodied the value of staying true to philosophical reflection and exemplified it for his community. Similarly, an examination of the obituaries of the luminaries of a field can highlight the values that give a professional speciality its spirit.

about obits in other professional fields, so this may be a general symptom of an age that is less comfortable with moral language and evaluation.

However, one may yet find value expressions today, as we may see when examining obituaries of these three founders of the field of philosophy of biology. For this analysis, I read every obit published for Grene, Hull, and Ruse; each was memorialized in about a dozen different venues. Befitting their importance, each received an obit in some major newspaper—the *New York Times*, the *Chicago Tribune*, the *Globe and Mail*—as well as various professional publications and websites. Their obits reveal the ways that they were viewed as exemplars of a profession's community spirit.

Legendary for Her Intellectual Ferocity

In addition to crediting her as a founder of philosophy of biology, all of Marjorie Grene's obits highlight her as the first woman to be included in the *Library of Living Philosophers*, a series conceived as a forum where senior, preeminent figures could reply to essays by their critics and interpreters while still alive. (To appreciate the significance of this honor, note that the first volume in 1939 featured John Dewey, with luminaries to follow including Bertrand Russell, Albert Einstein, Karl Popper, and Jean-Paul Sartre.) The volumes also include an "intellectual autobiography" and a complete bibliography of the subject's work. Well, almost complete. Grene's volume was published in 2002, when she was 92, but there were more publications to come before her death on March 16, 2009, at the age of 98.

Grene did graduate work with major philosophers in Europe and the United States, and she held small academic jobs during World War II. She then spent a decade and a half working on farms with her husband in Illinois and then Ireland. She arose early to study and write before the day's farm work. Grene contended that such matters of her personal history had no place in an intellectual autobiography, though she did note that, as for many women, such family responsibilities held back her productivity and led her out of necessity to work on topics that were not her first choice. She was a major contributor in the introduction of existential philosophy, including that of Sartre and Heidegger, to the United States. But she thought little of their views and described having to write about existentialism during her time as "an Irish pig farmer's wife" as an unpleasant chore, perhaps not unlike slopping the swine, until she was able to return to an academic position. As she later wrote, "agricultural duties and critical philosophies don't mix."

Grene was one of the first scholars to focus on philosophical questions in the modern synthesis, which united Darwinian evolution with Mendelian genetics and molecular biology. She did significant work on issues of *reductionism* (asking if biology is reducible to chemistry and physics) and of hierarchies in biological classification. She also wrote on the role of chance in evolution, the role of nongenetic cellular components in organismal development, and boundary concepts between different species and between life and nonlife. These issues became topics of ongoing investi-

Lizzie Ruse, CC BY-SA 4.0

Michael Ruse was a prolific scholar who focused on explicating evolutionary science and stepping in the public sphere to defend it. Embodying intellectual fearlessness, but in the most amiable way, he did not hesitate to take on controversial subjects if he thought they were socially meaningful.

gation in the field. Later she delved into epistemology and cognition, articulating a relational, biologically rooted "ecological" view for which her slogan was "All knowledge is orientation."

All her obits highlight that in her philosophical work, she was a fearsome critic. She is described as "formidable," "uncompromising," and "a force of nature." Randall Auxier, who edited the *Living Philosophers* volume, wrote that she could "disarm or slay an opponent with a single phrase or question." Another colleague wrote that she "always managed to find fresh ways to impugn views she regarded as ill-founded, ill-argued, or just plain nonsense. And there were many such views." Some choice comments she made were, for instance, that Frankfurt School critical theorists were mostly just "unintelligible." Richard Rorty "just makes clever remarks that don't mean anything." Even Michael Polanyi, with whom she had worked closely, was not spared—he "hadn't a clue" about evolution and his work on it was "very bad." Such examples could be easily multiplied.

To temper this portrait of intellectual ferocity, most obits also play up a contrasting grandmother trope, noting that she was kind to young colleagues, baked cookies for the office, and walked the halls sharing Halloween candy.

I only got to see Grene in action once, at a session in her honor at a philosophy conference. Her professional reputation preceded her. She did not disappoint.

He Lived By His Own Standards

David Hull died less than a year after Grene, on August 11, 2010, at the age of 75. Like Grene, he pioneered philosophical investigations into topics ranging from reductionism to biological classification. He adjudicated the "taxonomy wars" among cladistics, evolutionary systematics, and phenetics. His most significant conceptual contribution was a detailed defense of biologist Michael Ghiselin's "individuality thesis"—conceptualizing biological species as individuals rather than as classes of things with essential features. He also contributed to the heated debates among evolutionary biologists about the units of natural selection, particularly the gene-centric view advanced by George C. Williams and Richard Dawkins. Not satisfied with Dawkins's view of genes as the only biological *replicators*, Hull distinguished these from what he termed *interactors,* to clarify what explains intergenerational continuity from what explains differential selection. He extended his ideas about hierarchies of selection in his best-known book, *Science as a Process*, which developed what its subtitle announced as "An Evolutionary Account of the Social and Conceptual Development of Science"—the thesis that scientific change occurs with the same sort of mechanisms of variation, replication, and environmental selection as those that drive biological change. His reflective paper "On Human Nature" shows him at his best, tying together many of the themes of his work to questions of statistical versus other notions of normality, and how species and other biological groupings compare to natural kinds in other sciences.

Hull had entered philosophy of science with a bang, with a call-to-arms paper delivered at the University of Pittsburgh that inspired Ruse and others. It was "a cry" and "a demand" that the philosophy of biology be based on a solid understanding of the pertinent science. Hull modeled this "hard-headed and empirically grounded" attitude, as one professional colleague put it, throughout his career. Obits point out that he mastered the science that he studied as a philosopher so well that he wound up contributing substantively to the professional societies he investigated. Indicatively, he served on the editorial board of some 15 professional journals in both philosophy and biology. He was president not only of the Philosophy of Science Association, but also the International Society for History, Philosophy, and Social Studies of Biology (ISHPSSB)—a mouthful of an acronym familiarly pronounced "Ishkabibble" or just "Ish"—and the Society of Systematic Biologists. He used systematic biology as a case for a detailed study of networks of scientific attribution. In his careful work on this topic, he avoided the ideological extremes of the internalist/externalist debates in sociology of science—which considered whether scientific progress is best understood in terms of internal factors (such as logic and methods) or in terms of external factors (such as society, economics, or politics). Instead, he held fast to the internal value of truth while acknowledging the importance of social networks and the desire for credit as contributors to science's development and success.

I was lucky to attend an invited talk he gave on this work at the Center for Philosophy of Science while I was a graduate student at the University of Pittsburgh. I never got to know Hull personally, but, like many others, I benefited from his professional largesse. My publisher approached him for an advance review of my first book and I still feel pleased by his praise not just of its philosophical content but that he recommended it as "also a very good read." He later invited me to contribute a chapter titled "Biology & Religion" to the *Cambridge Companion to Philosophy of Biology*, which he edited with Michael Ruse. Michael would have been a better choice for this chapter, but Hull insisted that neither of them be contributors to leave space for younger philosophers. While I was at the University of Texas in the 1990s, I tried to arrange for Hull to give an invited talk. He declined, explaining that he refused on principle to come to Texas until it overturned its then-active laws against homosexuality.

His obits all highlight Hull's work as a gay man against such discrimination. Colleagues noted how he mentored budding philosophers both gay and straight, but how the former especially appreciated him as a role model. The AIDS epidemic was an especially challenging time, and Ruse described how Hull took in and nursed many gay friends and acquaintances in their final days, calling him "the Mother Teresa of the gay community." Some people, concluded Ruse, are simply better than others: "All of 5′4″, David Hull was the biggest man I ever knew."

After his death, Ishkabibble established a biennial prize in his honor. Its purpose is to recognize an extraordinary contribution to scholarship and service that promotes interdisciplinary connections among these fields—the very contributions that professional obits highlighted that Hull had himself made.

Virginia Tech

Marjorie Grene, a philosophical pioneer in several areas, was lauded for exemplifying a core value of the philosophical community in her forthright and uncompromising critiques of weak positions, calling out bad arguments wherever she saw them. Publishing well into her 90s, she was equally critical of her own earlier errors.

No Fear of Controversial Subjects

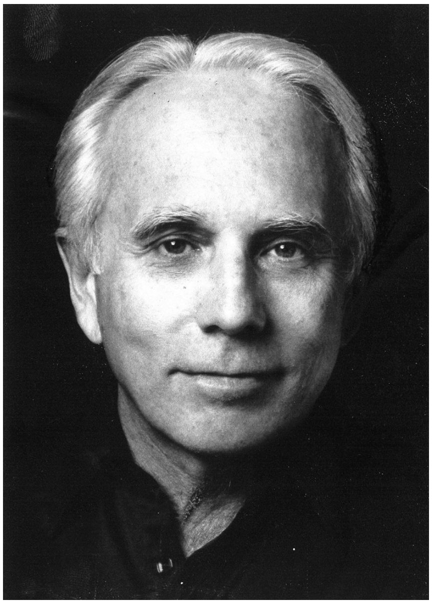
It is fitting that Michael Ruse won the Hull Prize in 2021 in recognition of his own lifetime contributions to the field. He was the author or editor of more than 70 books and many more articles, so calling Ruse "prolific" is enough of an understatement that some obits felt the need to add "incredibly." He continued to be productive until the end of his life, with at least one book in press when he died.

Ruse never shied away from topics that other philosophers found too fringy or controversial to tackle if he thought they were socially meaningful. He wrote books on the biological basis of homosexuality, on whether science is sexist, and even on ecologist James Lovelock's Gaia hypothesis that the Earth could be considered a living organism. Mostly, however, he focused on the philosophy of evolutionary biology. Nearly a third of his titles reference Darwin in some way, and consider the implications of his legacy and of the evolutionary advances that followed. Ruse considered his 1996 book *Monad to Man*, which examined the concept of progress in biology, to be his magnum opus. He followed it up in 1999 with *Mystery of Mysteries* on realism versus social constructivism, and in 2003 with *Darwin and Design*, which focuses on the concept of purpose in evolution. I reviewed the third book of this trilogy for *Science*, finding it to be one of his best, and one of the best ever written, on the subject.

The vast quantity of Ruse's published work in philosophy of biology tends to overshadow other ways in which he helped establish the field, especially in fostering its community and shaping its scholarship. I am proud that my first philosophy of science publication—"Moral Darwinism," a paper on how Darwin used ethics as part of his evidential argument for human evolution—appeared in *Biology & Philosophy*, the influential journal Ruse founded and edited from 1986 to 2000.

I had read Ruse's work in graduate school but didn't hear or meet him in person until I was a new professor. We both researched creationist attacks on evolution and then took the stand in two trials, he in an Arkansas case on so-called "creation science" and me a couple of decades later in a Pennsylvania case on "intelligent design." In the aftermath of the Arkansas case, he had edited an anthology titled *But Is It Science?* that focused on creation science, but generously proposed that I take over as lead editor for an updated edition to include intelligent design. Before his death, he asked the Stanford Encyclopedia of Philosophy to turn over responsibility for the entry on this topic to me, and though I had long ago moved on to other topics, I am honored to do so.

Though not a theist himself, Ruse was not hostile to religion and sought to promote a peaceful coexistence between religion and science. Obits note that he was as critical of the simplistic views of the "new atheists" as he was of creationists, but he was renowned for being convivial and friendly to all. Contrasting him to "Darwin's bulldog" (the moniker given to Thomas Henry Huxley), one scholar described Ruse as "more of a friendly cocker spaniel." Even creationists said they loved him. Many obits mention his upbringing in the Society of Friends and note that Quaker values remained with him. It is thus appropriate that the collection of memories offered about him somewhat mimicked the nature of a Friends memorial service, which consists entirely


Center for Biology and Society, Arizona State University/David L. Hull Collection

David Hull is lauded for setting high standards for the profession; philosophers who examined biology should be expected to know the science and engage with it seriously. Hull embodied this value in engaging his subject matter so well that he contributed substantively to it as well as to the philosophical community.

of individuals rising from the silence to share stories of some meaningful experiences that exemplify and celebrate the deceased person's unique spark of life. This structure seems somewhat reflected in the open comments section of the *Leiter Reports* philosophy blog, filled with tale after tale of his acts of professional and personal generosity, and is a testament to the impact his bighearted spirit had in the community.

Caveat Lector

Before drawing any lessons from this brief exercise of the reading of lives, one should note that this essay is not a history of philosophy of biology as a field, which would have included Morton Beckner's 1959 book *The Biological Way of Thought* and other pioneers such as Kenneth Schaffner and William Wimsatt, who were members of what is known as the first generation of the field. It is narrowly focused on a few notable personages who are widely recognized as its intellectual parents.

Nor is it a scientific study of values as revealed in obituaries. The obits I reviewed are exhaustive, but the three figures are not a random sample. A comprehensive study ought to cast a wider net. On the other hand, most members of a profession do not merit more than a simple death notice. Grene, Hull, and Ruse are significant in that they are seen by their peers as pioneers and, in some important senses, as models. That is one reason why looking at how they are memorialized reveals a profession's values.

Relevant to this point, however, neither is it assumed that obits are fully accurate or representative of their subjects. As baseball legend Roger Maris quipped of obituaries when he was still alive: "When you die, they finally give you good reviews." But these days it seems more common to see cynics and revolutionaries throwing stones to knock down an earlier generation's heroes. Some seem to take a zealous delight in calling out perceived biases and flaws of even the honored dead. A better attitude is a humble forbearance of flaws as a perhaps unavoidable part of human character and the slow improvement of culture. Either way, whether or not obits are representative of the person, they are useful as representative clues to cultural values.

Vocational Vices and Virtues

Vices are virtues taken to an extreme. We ought to aim for moderation, but we can find out something about virtue by identifying the ways in which exemplars may take things too far. Are philosophers sometimes too aggressively pedantic? Are we prone to fence-sitting and hair-splitting, endlessly postponing a conclusion? Do we occasionally play devil's advocate with a bit too much gusto? Such philosophical vices are perhaps best understood as overextensions of our profession's valued care about rational argument, where every assumption is subject to analysis and every claim to critical assessment. Such investigations help clarify concepts, bringing us closer to understanding and, we hope, wisdom.

Obituaries may help highlight the values that animated lives so as to inspire and motivate those who remain and those who are yet to come.

As we have seen, the obits of these philosophers emphasize their intellectual lives and their engagement with ideas—the concepts they investigated, the errors and infelicities of argument they identified, the theoretical clarifications they made—especially as seen in their prominent publications. They applaud intellectual fearlessness even for unpopular or controversial positions. They especially laud rigorous, perhaps even ruthless, analysis, so long as criticism or endorsement of a topic comes from a place of knowledge and aims at truer understanding. This is a core value in philosophy of science: It expects deep familiarity with, and serious treatment of, the scientific subject matter.

A second pattern seen in these obits is the value of humble self-reflection. It can be seen in myriad ways as philosophers describe the intellectual give-and-take of the profession. A constellation of related stories in the obits of these three philosophers gets to this point, as they pressed, dismissed, reassessed, and learned from one another. In his memoir of Hull, Ruse describes the different ways the two of them both challenged Grene on one of her early papers on the different evolutionary views of George Gaylord Simpson and Otto H. Schindewolf, and explains how he came to value Hull's critical yet sympathetic approach over his own fiery criticism. He describes rereading Grene's paper and coming to appreciate a pathbreaking aspect of it even though her basic thesis was wrong. For her part, Grene was dismissive of some of Ruse's views, especially his defense of E. O. Wilson's sociobiology. In a remembrance of Ruse, Grene's PhD student George Gale tells a story of how she whispered to him before one of Ruse's talks that she thought Ruse was "brusque, and, even worse, a positivist," but he adds that "she had no sooner gotten those words out of her mouth when Michael began to praise her as one of the founders of the philosophy of biology." Gale wrote that he glanced over at her face and saw it lit with a combination of surprise and abashment. The lesson is that even these great figures had to continually reassess themselves. Grene looked back on her early work and pronounced it "hasty and atrocious." Socrates said that the unexamined life is not worth living, and ideally philosophers should have a mindset that aims to constantly assess and improve their own thought processes as they assess those of others.

A third normative pattern to note relates to how philosophers see themselves as part of an ongoing conversation that began long before and may have stretched over decades or centuries. It is understood as valuable that this conversation should continue into the future. Obits of these seminal figures often end by highlighting ways in which they nurtured the seeds of the generation to come. They were praised for how they went out of their way to support younger scholars, by reading their papers, offering helpful improvements even with respect to positions they differed with, encouraging their research, and mentoring them in myriad ways.

Final Words

Obituaries, of course, are necessarily incomplete, abridging a life that has been truncated by death. Descriptions in words are always a step removed from the lives themselves. Nevertheless, if well-crafted, such descriptions may help highlight the values that animated lives so as to inspire and thereby to motivate those who remain and those who are yet to come. These obituaries of a small set of philosophers of science allow us to suss out some of that profession's values. A survey of obituaries of scientists would identify an overlapping but slightly different set of values. But the process would be the same; as reports of the lives of community exemplars, obits provide clues to the values that hold a community together and keep it going.

These three luminaries, having themselves been animated by the spirit of their vocation, now serve as tapers that the community holds up to remind its members of what ignites their common passion, and to pass that spark to others. Referring to a kind of candle, the term *taper* is etymologically derived from a phonetic alteration to *t* from *p*, taking us back through *papyrus* in late Middle English and Latin to the term's root in Greek, which stems (literally) from the pithy stem of the water plants that were used as the material for paper and for candle wicks. This is an appropriate symbol.

We, who yet live, use words on paper to convey what is more fundamentally a transfer of the flame by the wick of their lives. By such means, the natural spirit that lit their professional practice, lives on.

Bibliography

Auxier, R.E., and L. E. Hahn. (eds.) 2002. *The Philosophy of Marjorie Grene*. Library of Living Philosophers series. Open Court Publishing Company.

Falk, D. 2024. Philosopher of science Michael Ruse never shied away from controversy. *The Globe and Mail* (November 10).

Gale, G. 2024. Comment on In Memoriam: Michael Ruse (1940–2024). *Leiter Reports: A Philosophy Blog* (November 01). leiterreports.typepad.com/blog/2024/11/in-memoriam-michael-ruse-1940-2024.html

Ingram, D. 2008. *The News Manual: A Professional Resource for Journalists and the Media*. www.thenewsmanual.net

Martin, D. 2009. Marjorie Grene, a leading philosopher of biology, is dead at 98. *New York Times* (March 28).

Pennock, R. T. 2003. A Bridgewater treatise for the 21st century. *Science* 301:1051.

Ruse, M. 2010. David Hull: A memoir. *Biology & Philosophy* 25:739–747. doi.org/10.1007/s10539-010-9236-0

Robert T. Pennock is Sigma Xi Senior Fellow for Science and Engineering Values. He is a University Distinguished Professor at Michigan State University, where he is on the faculty of Lyman Briggs College, the departments of philosophy and computer science and engineering, and the ecology, evolution, and behavior program. His research involves both empirical and philosophical questions that relate to evolutionary biology, cognitive science, and the scientific character virtues. Email: pennock5@msu.edu

Science Policy Boot Camp

Information coming soon!

Join us for a four-day deep dive into state level policymaking with practitioners and leading experts in science policy, communications, and engagement.

SIGMA XI
THE SCIENTIFIC RESEARCH HONOR SOCIETY

sigmaxi.org/meetings-events/science-policy-bootcamp

Bioinspired Materials

Engineers are turning to biology for new ideas on developing high-performance composites that are more environmentally sustainable.

Hortense Le Ferrand, Rohit Pratyush Behera, and Slocha Sapasakulvanit

While you sit in your assigned seat casually scrolling on your phone or taking a short nap, an airplane's engines are enduring some wild conditions. Inside the engine, where the jet fuel burns, temperatures typically reach 1,400 degrees Celsius. Meanwhile, at cruising altitudes, the outside air temperature can drop to −60 degrees. Despite these extremes, the turbine blades keep spinning at many thousands of revolutions per minute, for hours at a time, enabled by resilient advanced materials. The blades are often made of nickel-based superalloys, which are coated with several layers of a thermal barrier to reduce temperature variations in the metal, preventing material fatigue and cracking.

Airplanes are not the only modern machines and devices that rely on the extraordinary properties of outstanding engineered materials. Spacecraft, satellites, underwater cables, and other high-tech equipment can operate in extreme temperatures, withstand severe shocks, and survive corrosive conditions thanks to high-performance materials—usually metals and alloys.

These impressive capabilities come with some significant downsides, however. Mining the metals used to make high-performance alloys comes with environmental and ethical hazards. For example, nickel mining in the Pacific Islands is a major cause of biodiversity loss due to harmful acids and toxic metals leaking into nearby waters. In addition, many nickel mines have been built on Indigenous lands, displacing people from their homes, and miners often endure poor working conditions. Meanwhile, rare earth metals such as indium, neodymium, and yttrium are used in minute quantities in alloys, and their mining generates radioactive waste.

And mining is just one source of problems. Once mined, metallic ores must be purified and melted to be shaped and transformed, which greatly contributes to greenhouse gas emissions. Nickel production emits 13 tons of carbon dioxide per ton of the metal produced, leading to about 35 million tons of CO_2 released into the atmosphere every year. And steel production accounts for 7 to 9 percent of global CO_2 emissions each year.

Because of these concerns, we and other researchers are seeking inspiration from nature to develop new, more environmentally sustainable high-performance materials that are based on substances made by living things.

At first glance, natural materials such as wood, bone, and seashells might not seem to meet high-performance standards. Yet natural materials allow redwood trees to climb 100 meters into the sky, support six-ton African elephants, and help mantis shrimp hammer their prey with appendages that strike at the speed of a 0.22 caliber bullet without breaking. These organisms' amazing feats suggest that we could create synthetic high-performance materials based on nonmetallic components if we can understand biology's secrets of materials science.

Our research and that of others have already identified structural elements that give natural materials strength, toughness, and other extreme properties. But simply learning these biomaterial secrets isn't enough. Researchers also need to figure out how to build materials in the lab that could someday be used as industrial components ready for mass production. The living cells that construct biomaterials operate on very different scales and conditions than what is required to produce airplanes or skyscrapers. Fortunately, our research has looked at and summarized a few principles concerning how nature grows these biological materials. We hope to emulate them.

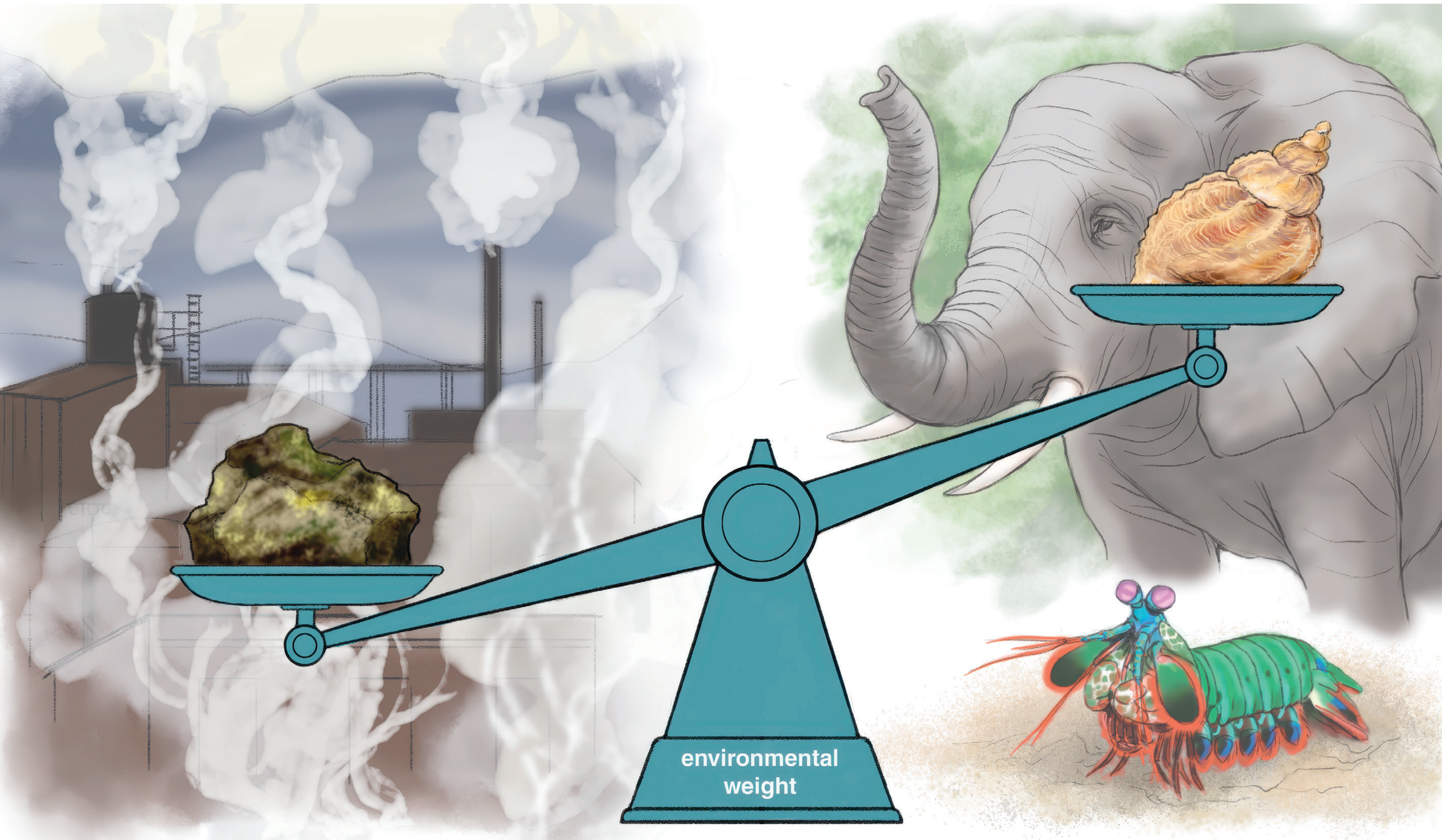
This research approach, known as *bioinspiration*, has been advancing slowly for a long time. Although we and other researchers have yet to build viable alternatives to high-performance metals and alloys, we have created bioinspired materials with interesting properties and promising applications. In our lab, we've made a boron nitride-based material that can help cool miniature electronics, aluminum oxide-based ceramics that could be used in dental implants, and a lightweight graphite material that could shield radars and satellites from electromagnetic interference. And we've constructed these materials using a process that doesn't rely on the toxic solvents and high-energy methods used in conventional ceramics and

QUICK TAKE

High-performance metals and alloys used in aerospace and other high-tech industries have large environmental footprints, leading materials scientists to search for alternatives.

Materials inspired by those found in nature, such as shells and trees, could be lighter-weight, more sustainable alternatives to traditional metals and alloys.

By studying how living organisms develop materials and structures, researchers are developing new ways to make synthetic composites with unique abilities.



Stephanie Freese

Metals and alloys are used in airplanes, satellites, and other high-tech equipment, but the mining and processing they require generates a heavy environmental footprint. Engineers are looking to materials made by living things—such as elephant bones, seashells, and mantis shrimp clubs—to find inspiration for new ways to construct high-performance materials that are more sustainable.

alloy manufacturing. These features could give our process a smaller environmental footprint.

Our goal is to adapt and improve this process to one day produce sustainable, high-performance, industrial use-ready materials inspired by nature.

Bioinspiration

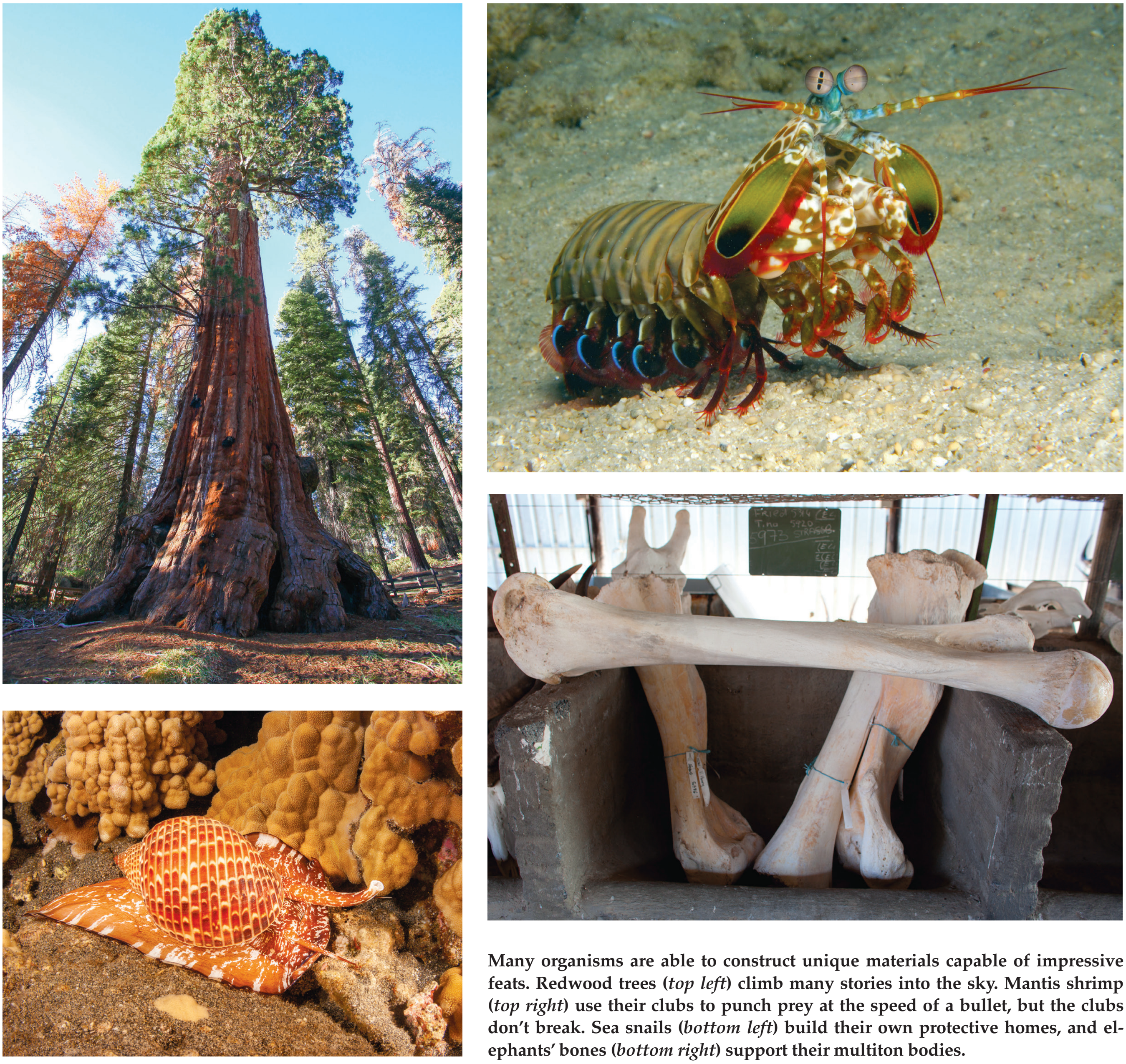
The inspiration for our new material-building process came from our studies of ceramic-based biomaterials in nature. Natural ceramic materials are found in the dense parts of our bones, providing strength and support for softer tissues, as well as in *nacre*, the substance in seashells and pearls that gives them their iridescence. These biomaterials are high-performance *composites*, which means they contain a mixture of organic substances, which are largely made of carbon, and inorganic ones, which usually aren't. Specifically, they mix an inorganic component made of ceramic particles and crystals within an organic polymer matrix.

Whether in human bone or nacre, natural ceramic composites exhibit high strength, stiffness, and toughness—coveted properties in commercial metal- and alloy-based materials. But unlike metals and alloys, these biomaterials are lightweight. Thus, these bioinspired composites could find applications where lighter weight is prized, such as in aerospace.

Other researchers have studied bones and seashells along with other biomaterials to learn how they achieve their structural feats. They've tested the materials' mechanical responses and analyzed how they fail. From these studies, researchers have determined that the strength, stiffness, and toughness of these natural composite materials comes from their internal microstructures—the way that their inorganic and organic components are arranged at the microscale. By comparing these results with other studies on how organisms build these biomaterials, we concluded that there is a strong correlation between these biocomposites' growth processes, the materials' microstructures, and their physical properties.

Natural Growth

When organisms grow bone or nacre, they rely on a porous organic matrix to create sites where ceramic minerals crystallize, leading to the intertwined formation of inorganic and organic components. In most cases, the matrix's chemical structure also directs the size and shape of the crystals. For example, the calcium carbonate minerals in the nacre of seashells have a plate-like shape. These specific non-spherical, also called *anisotropic*, shapes differ from what forms when calcium carbonate crystals grow in the absence of an organic matrix, like in a beaker of water. In that environment, the resulting crystals have undefined

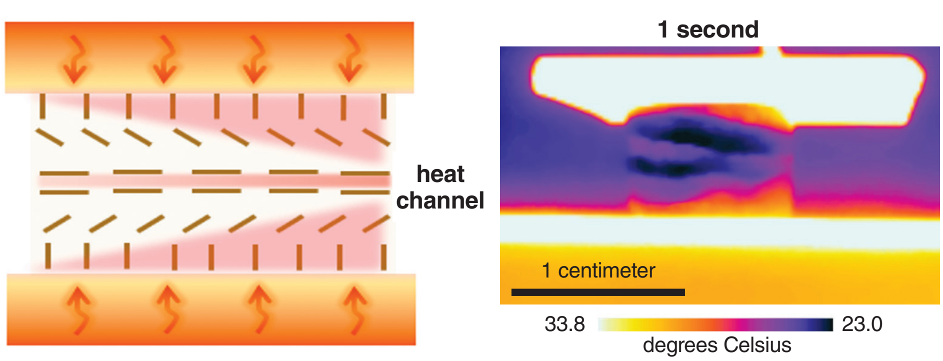


PHOTOSTOCK-ISRAEL; Ross & Diane Armstrong; Ton Koene, VW PICS; David Fleetham / Stocktrek Images / Science Source

Many organisms are able to construct unique materials capable of impressive feats. Redwood trees (*top left*) climb many stories into the sky. Mantis shrimp (*top right*) use their clubs to punch prey at the speed of a bullet, but the clubs don't break. Sea snails (*bottom left*) build their own protective homes, and elephants' bones (*bottom right*) support their multiton bodies.

shapes. Anisotropic-shaped ceramic minerals yield microstructures that can improve a material's toughness.

The organic material surrounding these crystals is a tightly packed matrix, which also plays a role in toughening ceramic biocomposites. This organic matrix is made of proteins, which are long chains of molecules. In the synthetic world, plastics are the main examples of long-chained organic materials. But unlike plastics, which arrange themselves randomly at the nanoscale like loosely entangled noodles, proteins fold into complex and tightly packed structures due to local molecular interactions that hold the chains in a specific shape. In biocomposites, the mineral crystals grow and push the molecules into even tighter spaces.



By controlling the orientation of boron nitride microplatelets (*left panel*), researchers were able to direct a flow of heat through a new composite material. Infrared photography (*right panels*) demonstrates how heat built up and moved through the composite over time.

Another way ceramic biocomposites achieve their high-performance properties is through the differences between the organic matrix and the inorganic crystals; the mineral crystals are stiff and strong, whereas the organic material in between is weaker. This weak interface between the crystals is important for toughening the composite. For example, when a crack starts to form, it does not propagate straight into the inorganic material, but instead stays confined to the weak organic layer and wraps around each mineral crystal. As a result, cracks follow a tortuous path, which prevents catastrophic failure. As a counterexample, consider a traditional ceramic such as a porcelain coffee cup, which is composed of small spherical grains strongly bonded together. When you inadvertently drop your cup on a difficult morning, it breaks instantaneously when hitting the floor, shattering into sharp pieces with straight edges because the cracks form and travel straight through each crystal. But in many of the biocomposites we have studied, even though the interfaces between crystals are weak, the growth of the inorganic crystals within the organic matrix leads to strong binding between the crystals and the matrix. This strong interaction prevents *delamination*, which is the separation of the two components upon cracking.

The way cells build biocomposites also helps them develop impressive structural properties through the cells' layer-by-layer action of secreting and depositing materials. For example, bone-forming cells called osteoblasts release proteins and mineral-containing vesicles to facilitate mineralization around them. This layer-by-layer growth of tissues creates local variation in each layer, ultimately leading to the formation of microstructures. Among the best-known microstructures in ceramic biocomposites are the brick-and-mortar assembly in nacre, where platelet-shaped crystals look like bricks stuck together by organic mortar; in the helical arrangements found in bones, where needle-shaped crystals are rotated by a minute angle between each layer; and in the layered structure of human teeth, which have vertically oriented mineral rods in the outer enamel layer and horizontal ones in the lower dentin layer. These microstructures provide the materials with specific localized properties, such as hardness in enamel and toughness in dentin.

All of the ceramic biocomposites we've investigated are grown in highly hydrated conditions. The presence of water is necessary for cells to live and function properly, as well as for the diffusion of ions and molecules that make up the materials. Water is not only present during the growth of biomaterials; it also remains afterward, albeit in small quantities. For example, our bones contain about 10 percent water. The water acts as a lubricant for the organic phase, providing molecular mobility and some ductility. The presence of water is also important for the toughness of our bones. As we age, our bones dehydrate, becoming more brittle and subject to fracture. Thus, the presence of water is clearly another important structural element of ceramic biocomposites.

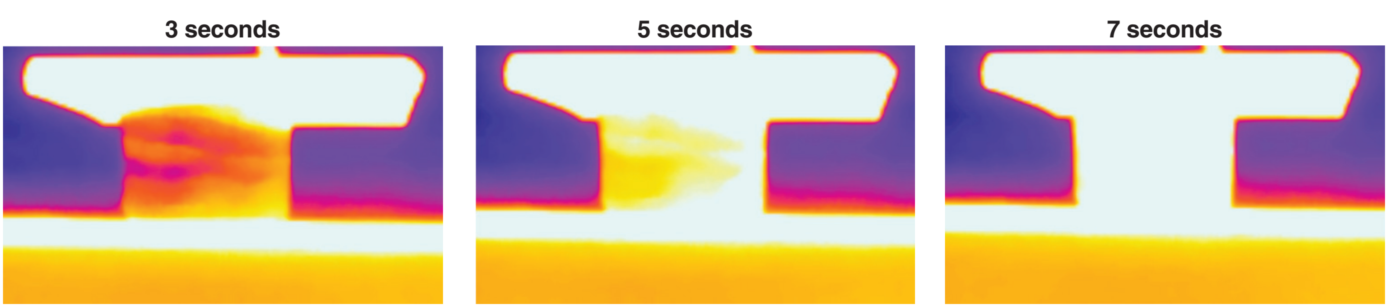
Nickel production emits 13 tons of CO_2 per ton of the metal produced, leading to about 35 million tons of CO_2 released into the atmosphere every year.

New Process for New Materials

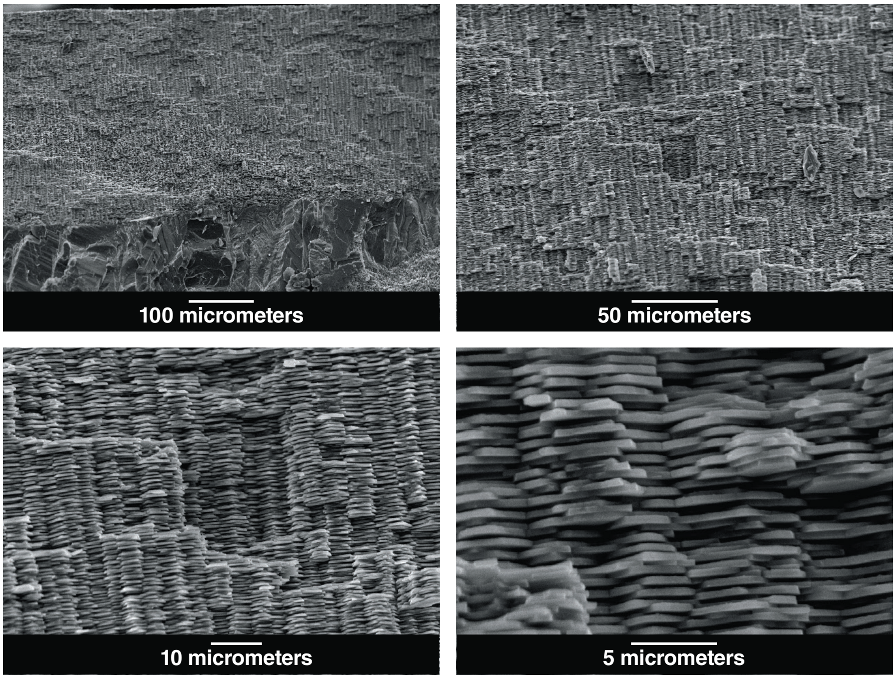
Researchers have found inspiration for new materials by studying many different organisms. For example, some researchers have studied mussels in order to develop polymers for use as nontoxic underwater adhesives that can glue cell tissues inside the human body or help restore corals in the sea. These polymers undergo a chemical reaction that occurs in the feet of mussels when they bind to rocks underwater. Unlike traditional glues, these bioinspired ones are efficient in wet environments, and they can self-heal.

In our lab over the past few years, we used the lessons we learned from natural composites to develop a new process for making composite materials. We wanted a method that allowed us to make structures similar to those we observed in nature. In particular, we needed to be able to control the arrangement of anisotropic-shaped minerals. We also wanted the method to be simple and environmentally friendly. For example, we use water as the solvent.

The process starts with small particles, called ceramic flakes or ceramic microplatelets, that are 2.5 micrometers to 50 micrometers (millionths of a meter) in diameter and about 0.5 micrometers to 2 micrometers thick. By using small particles, we can create samples with three-dimensional shapes. (Traditional composites, such

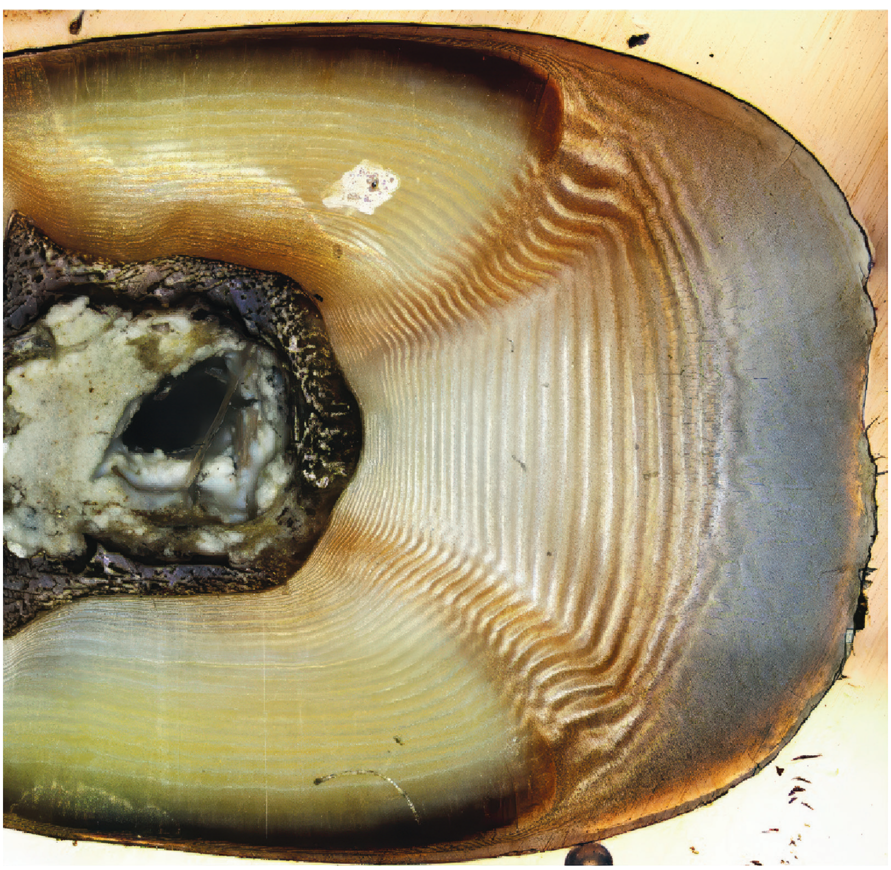


Reproduced with permissions from He, et al. 2022.



Xin Ying Chan

Electron micrographs depict the brick-and-mortar microstructure seen in nacre, the strong, iridescent material in seashells. Microplatelets of calcium carbonate are stuck together with a thin layer of organic material. This microstructure, which imparts strength and toughness to the nacre material, can be replicated in synthetic materials.



The Espinosa Group

Mantis shrimp clubs strike prey with astounding speed, but they don't break. These clubs have a repeating pattern created by *chitin*, which is a long chain of sugars, and calcium phosphate particles. This ripple pattern helps dampen the shock waves produced by the club.

as those made of long carbon fibers, are restricted to planar shapes.)

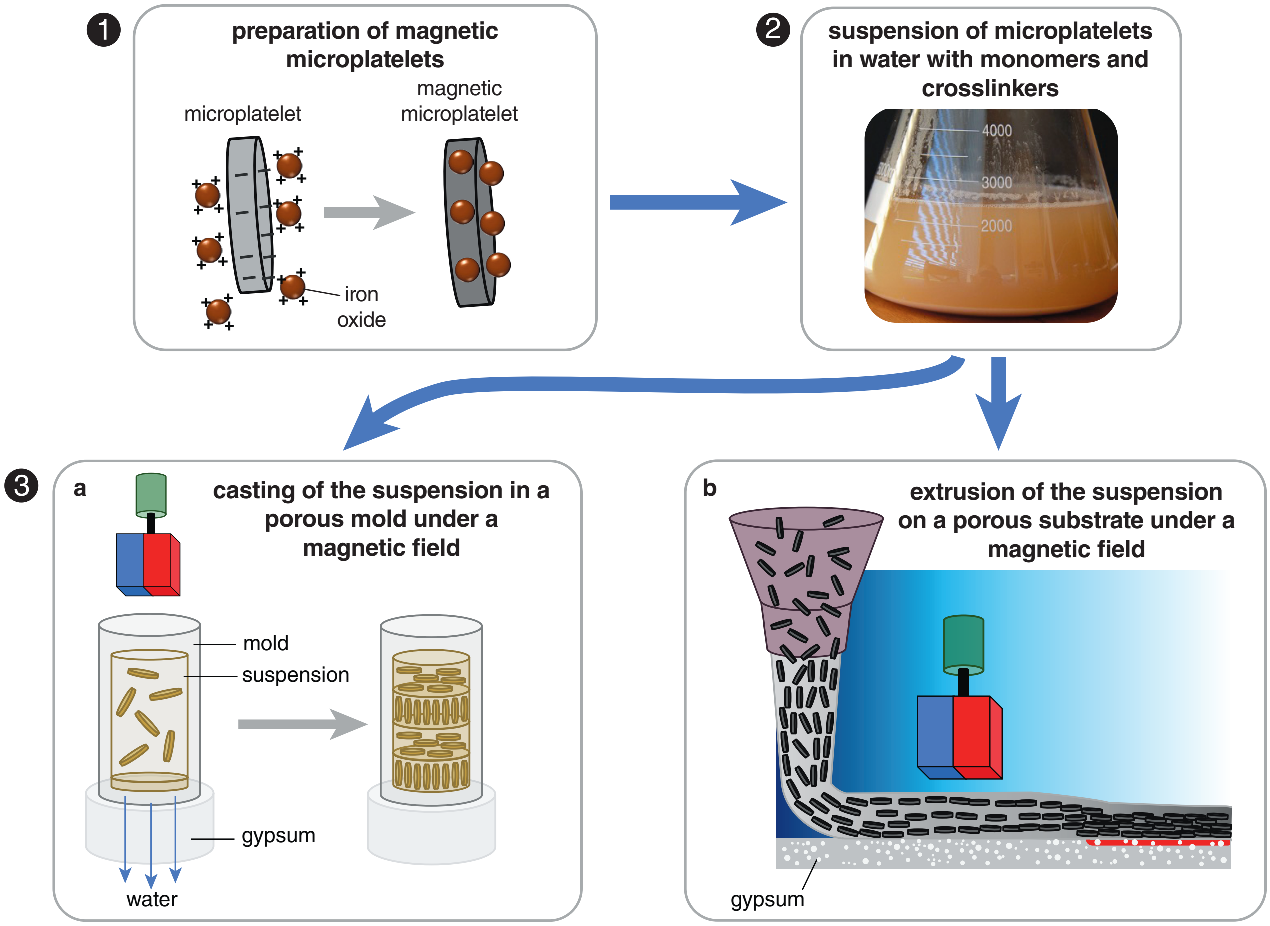
We disperse these microplatelets in water to create a suspension that can be cast in a mold or used as ink in 3D printing. Our goal has been to make a variety of shapes depending on the specific application we have in mind, such as simple shapes for dental implants or more complex ones for electronic components. We then use porous molds made of gypsum to suck water out of the suspension and concentrate the microplatelets. This manufacturing process of pouring a suspension into a porous mold is called *slip casting* and is already used industrially to make ceramic objects.

As with natural biocomposites, ours need an organic matrix to bind the ceramic microplatelets together. We add molecules called *monomers* and *crosslinkers* to the liquid suspension to construct this matrix. During the casting, those monomers can be joined covalently by the crosslinkers to form polymers. Since this matrix sets as the material is formed, it creates the weak interface between the inorganic particles and the strong binding between the organic and the inorganic phases that we observed in the natural composites.

To produce these intricate microstructures, we found a way to control the orientation of the microplatelets during casting. We add a small amount of iron oxide nanoparticles to the surfaces of the microplatelets to make them magnetic. By applying a low magnetic field during casting, we can orient the microparticles while the organic matrix forms and the water gets absorbed into the mold.

To make the more complex shapes with local microstructures, we skip the molds and instead use extrusion-based 3D printing, which is a method that involves depositing liquid inks onto a print bed by extruding them through a nozzle. By placing a magnet next to the nozzle to orient the microplatelets, we can print a complex 3D shape, while changing the alignment of the microplatelets.

One key advantage of this process is that it is chemistry-agnostic, so microplatelets made of various materials can be used. For example, using microplatelets made of aluminum oxide ceramics (Al_2O_3), we can produce composites with strong mechanical properties for dental im-



Hortense Le Ferrand

The authors' bioinspired process for making new materials starts by coating inorganic microplatelets with magnetic iron oxide particles (*step 1*). These microplatelets are then suspended in water with monomers and crosslinkers that will eventually form an organic matrix that will hold the microplatelets in place (*step 2*). Adding this suspension to a mold under a magnetic field (*red and blue block*) allows researchers to control how the microplatelets arrange themselves as the material sets (*step 3a*). Researchers can also use the same suspension as ink in a 3D printer, extruding the suspension in complex shapes under a magnetic field (*step 3b*).

plants, whereas using microplatelets made of graphite (a form of carbon) we can produce composites that also exhibit electrical conductivity for use as electromagnetic shielding. We can also use different monomers or other additives in the suspension, leading to various organic matrices, such as soft hydrogels and synthetic rubbers. Therefore, the process is highly tunable and customizable.

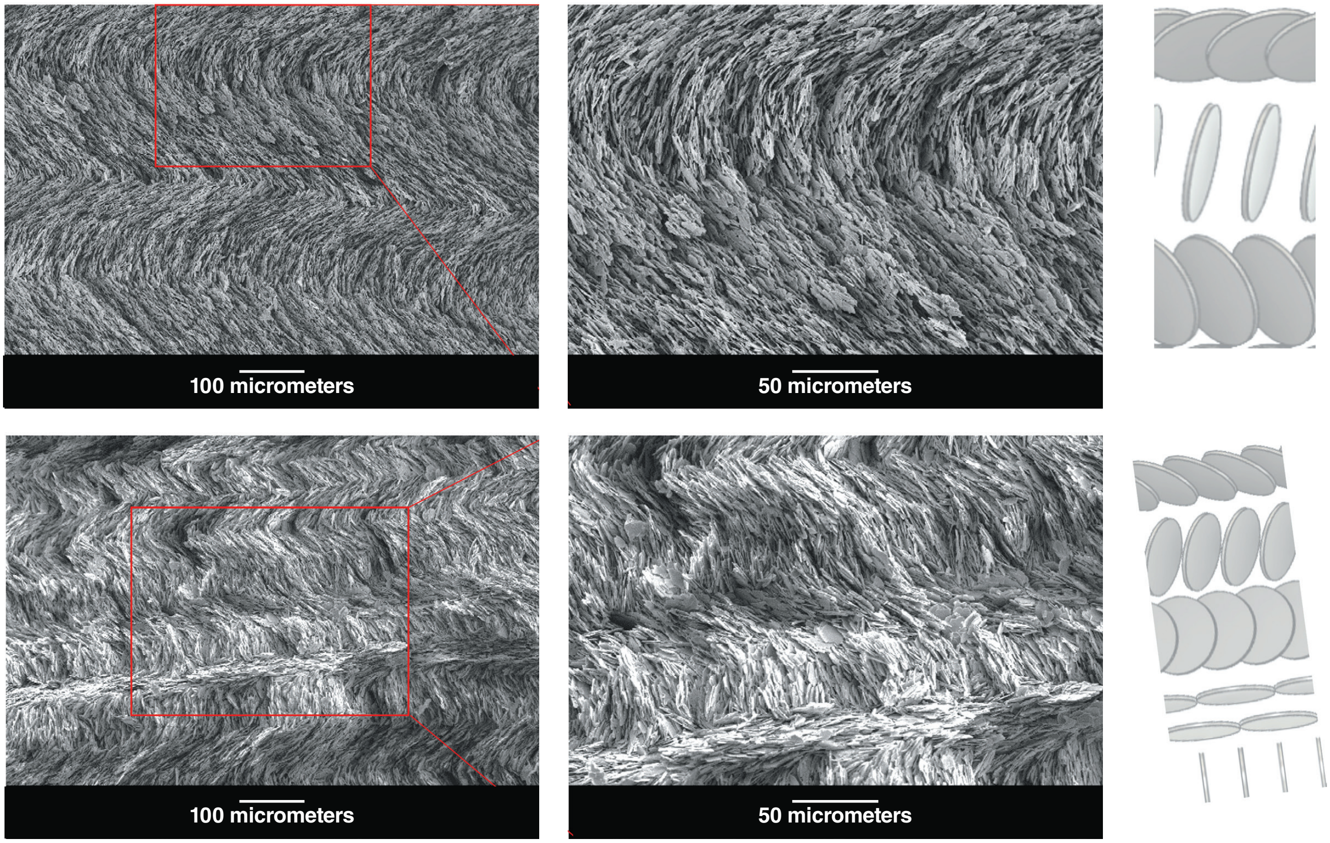
New Materials in the Lab

To test the capabilities of this bioinspired process, we have produced a range of composite materials with unique capabilities. We designed a material to help cool miniature electronic devices such as central processing units in desktop computers and vehicle control units in electric cars. These devices process a large quantity of data at very fast speeds, which means they generate a lot of heat and need to be cooled to avoid slowdowns, crashes, and system failures caused by overheating. Current cooling methods include fans, metallic heat sinks, and liquid cooling systems. These solutions are bulky for devices with serious space constraints, and can pose safety concerns if the water coolant leaks.

To produce smaller, safer cooling solutions, we used our bioinspired process to develop a material that channels heat in specific directions away from heat-sensitive components. The material is made from boron nitride microplatelets that exhibit unusually high thermal conductivity along their planes. These microplatelets get held together by a small amount of polymeric binder to create a material that is stiff and strong enough to perform in electronic devices without breaking. The material is lightweight like plastic but conducts heat 12 to 40 times better than plastic. And we can direct heat conduction in specific directions based on how we orient the boron nitride particles within the material.

Our process can also be used to construct electrically conductive composites. Materials made of graphite exhibit high thermal conductivity along their plane as well as electrical conductivity. Engineers are interested in graphite for shielding electromagnetic waves in radars and satellites, protecting the equipment from external interference. Currently, radars and satellites use metals like aluminum and copper to block these signals.

We wanted to develop a lighter-weight alternative, so we created a graphite-based composite by adding silica nanoparticles to a graphite suspension. Heating the suspension fuses the silica with the graphite, providing stiffness and rigidity to the composite. We can control how the material shields electromagnetic waves by manipulating the orientation of the graphite par-



Chan, X. Y., et al. 2022.

Controlling the orientation of particles, such as these aluminum oxide ceramic microplatelets (*micrographs, left column; close-ups of boxed areas, center column*), is a key step in creating bioinspired materials. Using a magnetic field, researchers arranged aluminum oxide ceramic microplatelets in specific microstructures (*illustrations, far right*). After adding a polymeric matrix, the ceramics' mechanical properties vary depending on the microplatelets' arrangement.

ticles. When an incident wave hits a graphite microplatelet perpendicular to its plane, the wave is mostly reflected back. If the wave hits the graphite on its side, the wave can penetrate through the composite. We created pillar-like structures with graphite microplatelets aligned along their surfaces so that electromagnetic waves bounced back and forth between the pillars. The total shielding efficiency of these materials reached 90 decibels, which is similar to that of most metals used in these applications. We can also tailor the microstructures to block the waves on one side while allowing them to pass through on the other side, which could be useful in antennas.

The strength, stiffness, and toughness of these natural composite materials comes from their internal microstructures—the way that their inorganic and organic components are arranged at the microscale.

Our bioinspired process can also be used to make mechanosensors for use in touchscreens, pulse monitors, and electronic skins that could give robots the sense of touch. These sensors are normally made with polymer-based materials. To make ours, we deposit drops of a suspension containing magnetic graphite microplatelets to build arrays of pillars, where each pillar is a sensor. By controlling the orientation of the microplatelets with a magnetic field, the sensors can detect pressure in different directions, and by arranging these particles layer-by-layer, we can increase the sensors' sensitivity.

After the pillars dry, we apply a polymer matrix, such as silicone, to make the pillars compressible. Graphite microplatelets are electrically conductive, so how much current each pillar conducts will depend on the pressure applied. Higher pressures will push the graphite particles into closer contact, leading to lower electrical resistance and higher electrical current. We also added a layer of droplets containing boron nitride microplatelets below each pillar to help cool the structures as current passes through them. To measure pressure, we simply need to pass an electric current through the pillars and observe their conductance. Our pillars can respond to a larger range of pressures than sensors currently used in touchscreens.

By combining our bioinspired method with a postprocessing step called *pressureless ultrafast high-temperature sintering*, we can also create strong, stiff ceramics in a short amount of time and with more tailorable microstructures than is possible with existing manufacturing methods. This sintering process converts a stack of ceramic powders into a ceramic block within minutes by heating the materials quickly to temperatures reaching 1,700 degrees Celsius.

To make these particular ceramics, we start with a suspension containing Al_2O_3 microplatelets and Al_2O_3 nanoparticles. During the sintering step, the nanoparticles fuse with the microplatelets and fill the gaps while maintaining the anisotropic nature of the grains. The presence of a small quantity of magnetic iron atoms at the surface of the Al_2O_3 microplatelets creates weak interfaces, which are crucial for preventing catastrophic failure. The resulting ceramic material has a bending strength almost similar to that of conventional Al_2O_3 ceramics, but ours is three times tougher. Thus, these new ceramics are as difficult to bend as others, but they take some time to break completely, and they do not break sharply with one straight crack. These ceramics could be useful in machining tools and dental implants, providing tough, lightweight alternatives to steel bearings and the zirconia in dental crowns.

Room for Improvement

Although our bioinspired process is versatile and allows us to tailor various useful properties, we are still far from manufacturing the next generation of composites appropriate for airplanes and other high-performance applications. For instance, the sizes and shapes of materials we can produce are still limited. The turbine blades of an aircraft engine are about 15 centimeters in length and 10 centimeters in width, and they have a twisted shape. Our bioinspired ceramic composites are lighter and more heat resistant than current alloys, but the largest piece we can make in the lab is only about 5 centimeters by 5 centimeters. Also, the twisted shape of the turbine blade is difficult to cast with our porous molds.

Meanwhile, 3D printing bioinspired ceramic composites is not a scalable, fast, and cheap process compared to conventional methods. This disadvantage means that we need to carefully evaluate which applications are best suited for our process in terms of the required material properties and an analysis of time and cost trade-offs. Right now, our process is best suited for small-scale applications such as cooling devices in miniature electronics and mechanosensors in touchscreens.

We also need to find a strategy to print our water-based inks to form structures that include overhangs and the helical structures inspired by bone. And, no existing commercial 3D printer can control the local orientation of ceramic microplatelets while printing, which means we will need to develop our own printer.

Finally, if we are someday going to offer more sustainable alternatives to conventional metals and alloys, we need to conduct a life cycle analysis of our process. This sort of analysis measures the environmental impact of each material and step in a given process. For example, our process relies heavily on water-based suspensions that are cast or printed at room temperature. The lack of toxic solvents means this aspect of our process would likely have a relatively low environmental impact. However, the ceramic microplatelets we use are sometimes made through energy-intensive processes. Additionally, although we have eliminated the need for high pressures, our method still sometimes requires heat to dry the composites, or high temperatures via sintering to produce ceramics. We would also need to investigate how readily our materials can be recycled.

Although our process requires significant further research and technological development, we see this work as a major step toward developing materials that leave a smaller environmental footprint while delivering high-performance capabilities.

There is a strong correlation between these biocomposites' growth processes, the materials' microstructures, and their physical properties.

Bibliography

Behera, R. P., A. Y. R. Ng, M. J. Reavley, Z. Du, C. L. Gan, and H. Le Ferrand. 2024. Rational design and fabrication of hierarchical ceramics using bioinspired microstructures for tailorable strength and toughness. *Cell Reports Physical Science* 5:102140.

Chan, X. Y., C. Chua, S. Tan, and H. Le Ferrand. 2022. Energy dissipation in composites with hybrid nacre-like helicoidal microstructures. *Composites Part B: Engineering* 232:109608.

Erb, R. M., R. Libanori, N. Rothfuchs, and A. R. Studart. 2012. Composites reinforced in three dimensions by using low magnetic fields. *Science* 335:199–204.

Guan, L., J. Fan, Z. K. Ng, E. H. T. Teo, and H. Le Ferrand. 2024. Modulation of the electromagnetic shielding effectiveness through micro/macrostructure design for electronic packaging. *NPG Asia Materials* 16:35.

He, H., W. Peng, J. Liu, X. Y. Chan, S. Liu, L. Lu, and H. Le Ferrand. 2022. Microstructured BN composites with internally designed high thermal conductivity paths for 3D electronic packaging. *Advanced Materials* 34:2205120.

Le Ferrand, H., F. Bouville, T. Niebel, and A. R. Studart. 2015. Magnetically assisted slip casting of bioinspired heterogeneous composites. *Nature Materials* 14:1172–1179.

Liu, W. C., V. Chou, R. P. Behera, and H. Le Ferrand. 2022. Magnetically assisted drop-on-demand 3D printing of microstructured multimaterial composites. *Nature Communications* 13:5015.

Sapasakulvanit, S., J. H. Teoh, and H. Le Ferrand. 2024. Bioinspired processing for the sustainable fabrication of high-performance bioinspired ceramic-reinforced polymer composites. *Matter* 7:3786–3810.

Wegst, U., H. Bai, E. Saiz, A. P. Tomsia, and R. O. Ritchie. 2015. Bioinspired structural materials. *Nature Materials* 14:23–36.

Hortense Le Ferrand is an associate professor of mechanical and aerospace engineering at Nanyang Technological University in Singapore. Rohit Pratyush Behera is a postdoctoral research fellow and Slocha Sapasakulvanit is a PhD student at Nanyang Technological University. Email for Le Ferrand: Hortense@ntu.edu.sg

Psychedelics Move Toward Mainstream Medicine

Humans have experimented with mind-bending substances since ancient times. Can these drugs become effective treatments for mental health conditions?

Gregory A. Fonzo and Charles B. Nemeroff

We sat in rapt attention while our patient, Jeff, described his brush with a suicide attempt. "I put the gun to my head and pulled the trigger . . . click. Nothing happened. The gun was empty. No bullets at all. I realized later that someone who cared about me more than I did about myself must have emptied the magazine." Jeff, a former marine and firefighter, went on to recount how that experience served as a wake-up call. He needed to do something different, and fast. But what?

Jeff, like millions of Americans, suffered from post-traumatic stress disorder (PTSD) and major depressive disorder. And like roughly 25 to 50 percent of patients with PTSD and 10 to 30 percent of patients with major depressive disorder, Jeff had found little relief from evidence-based psychotherapy or antidepressants. Nothing alleviated the intrusive memories of the war atrocities he had witnessed during his military service in Afghanistan. He felt dead inside, unable to experience any zest for life.

Back in 2020, when this conversation took place, we spoke with many patients in our clinical practice who described how available treatments had provided minimal improvements in their mental outlooks. As mental health practitioners, we wished we could offer more effective therapies. We were intrigued, however, when Jeff and others like him reported that they had found something that worked for them, even though it hadn't been provided by us or by any Veterans Affairs hospital: psychedelic drugs.

At the time, classic psychedelics such as LSD (lysergic acid diethylamide), mescaline, and psilocybin, as well as related drugs such as MDMA (3,4-methylenedioxymethamphetamine, commonly known as ecstasy), had not received much attention from academic researchers as potential mental health treatments in decades. But some research groups were beginning to explore whether these long-maligned drugs had medicinal merit.

Jeff, having read about this early work, was determined to find out for himself. In that same meeting in our office, he told us about how he had procured, on the black market, large quantities of the psilocybin-containing mushrooms commonly known as "magic mushrooms." He downloaded the music playlist used in clinical trials, set up a dosing room in his basement, and proceeded to take the mushrooms without professional guidance. We were fascinated by his journey but highly alarmed by the potentially dangerous situation. Here was a psychologically wounded warfighter taking massive doses of mind-altering fungi with ready access to firearms and no one to help him manage his psychedelic "trip."

Today, Jeff agrees that psychedelics should be administered by trained professionals. But he is adamant that his self-prescribed treatment ended his suicidal thoughts. Indeed, it changed his life: "I repeated the experience every few weeks for several months. I had mind-blowing, earth-shattering experiences that shook me to the core. But through it, I found a new identity for myself. I found a part of myself that I thought was lost forever."

As scientists, we were skeptical of such stories. Could someone really treat their mental health condition using trippy substances popularized in the 1960s? Yet we were also excited by what we were hearing from Jeff and many others. So we dove into studying the history of psychedelics and their current implementation in research.

First, we explored the history of human interactions with psychedelics, from the preindustrial Indigenous communities who had consumed magic mushrooms as a cultural practice to members of the 1960s counterculture movement who had embraced LSD. Then we reviewed the scientific literature to understand what was definitively known about whether and how these drugs affect mental health.

The data was limited and lacking in rigor, so we began producing our own research. In 2021, we established the Charmaine and Gordon McGill Center for Psychedelic Research and Therapy at the University of Texas at Austin. There, our goal is to conduct high-quality research to inform our understanding of psychedelic mechanisms and guide safe and effective clinical delivery of psychedelic treatments to patients suffering from serious psychiatric disorders.

QUICK TAKE

Psychiatrists began testing whether psychedelic drugs, such as LSD and mescaline, could be used to treat mental health conditions in the mid-20th century.

Until the past several years, clinical trials of psychedelic drugs did not deliver meaningful results because they were too small and lacked proper controls.

Studies today are approaching the size and rigor required to finally show us whether psychedelics can treat conditions such as depression, anxiety, and PTSD.

Amaringo Shuña, Pablo. *Conocimientos Curvos* (*Curved Knowledge*). 2003, Scott Olsen Collection, mysteriesoftheamazon.com

Psychedelic drugs have long been administered by traditional healers. The Peruvian shaman and artist Pablo Amaringo (1938–2009) depicted the experience of consuming ayahuasca, a psychedelic tea, in many works, including this 2003 painting *Conocimientos Curvos* (*Curved Knowledge*).

We, along with other psychedelic research groups around the world, are part of a burgeoning psychedelic renaissance. Much remains to be understood. But through larger studies with better designs, we are beginning to see that psychedelics really do have the potential to promote rapid symptom improvement in patients experiencing depression, PTSD, and a wide range of other difficult-to-treat mental health conditions.

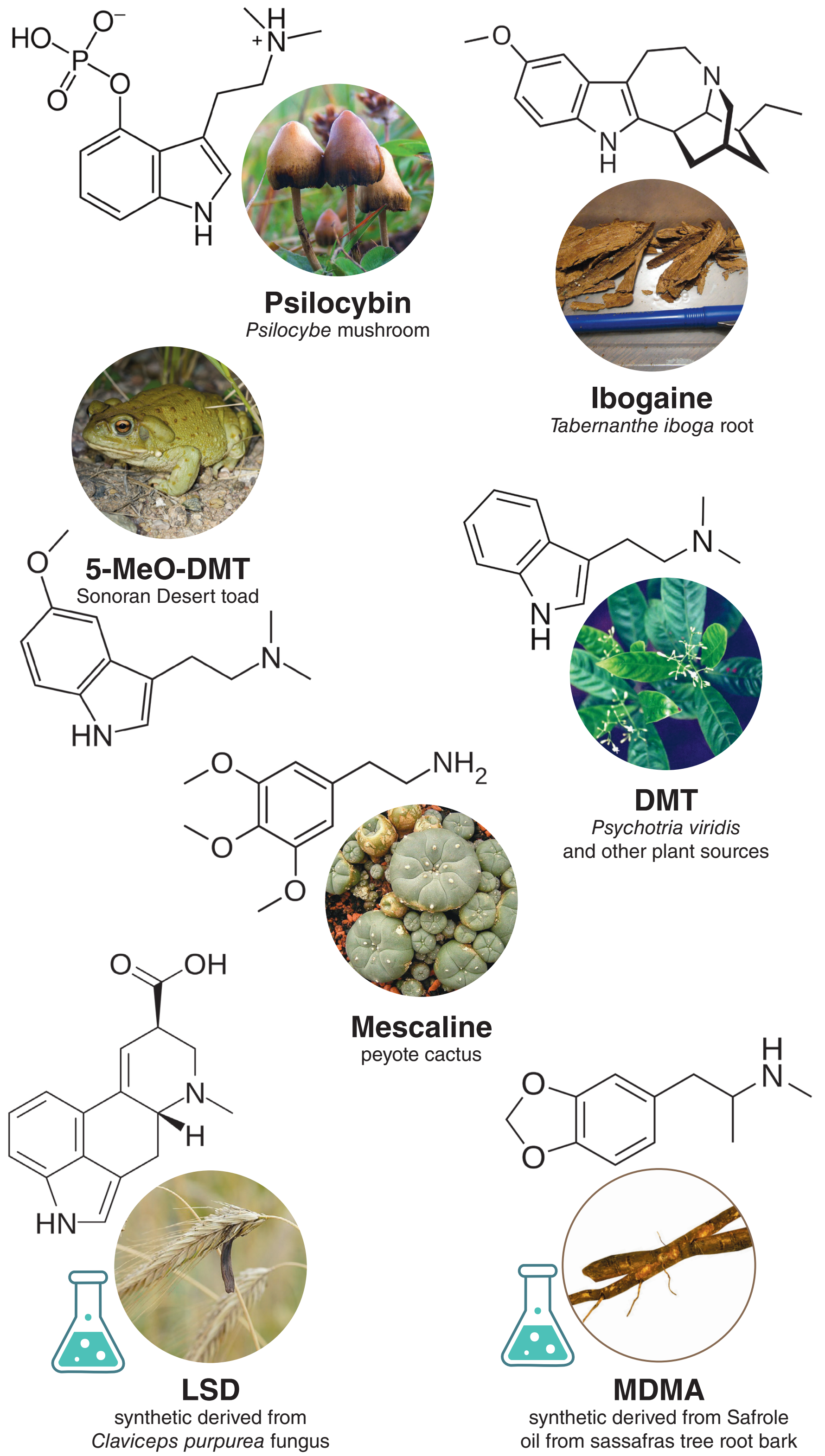
How Psychedelics Work

Psychedelics are psychoactive drugs that alter perception, thinking, and emotions. They can also cause hallucinations. Exactly how psychedelics cause people to "trip" in the short term, or change their mental outlook for the longer term, is not yet well understood. But research suggests that all classic psychedelic drugs, such as LSD, mescaline, and psilocybin, have chemical structures similar to that of serotonin, a chemical messenger that transmits information between neurons in the brain. Because of this similarity in structure, psychedelics can trigger a key serotonin receptor in the brain known as the *serotonin 2A receptor*. Setting off this receptor then puts into motion a cascade of downstream effects, including changes in neuronal firing, gene transcription, and protein synthesis, which researchers hypothesize may contribute to the psychedelic experience.

MDMA, a psychoactive drug and stimulant, is even less well understood. Researchers believe that it causes its psychedelic-like effects primarily by increasing the release of serotonin in the brain. It may also interact to some extent with the serotonin 2A receptor.

Recent studies by research groups across the globe suggest that both classic psychedelics and MDMA promote *synaptic plasticity*, the brain's ability to alter the strength of connections between neurons. After taking a psychedelic, the branches that form connections between neurons increase in number and size. These changes may, for a time, enhance the capacity for new neuronal connections to form and for old, unnecessary ones to be pruned. Many researchers theorize that this increase in synaptic plasticity could quickly enhance a patient's ability to adaptively alter patterns of thinking and behavior. Antidepressant medications can also enhance markers of synaptic plasticity, but typically only through prolonged use.

Whatever the mechanism, the immediate effect of ingesting psychedelics is a panoply of alterations in consciousness. A person experiences distortions



Barbara Aulicino; Images: Wikimedia Commons; Kim Gjerstad CC BY-SA; Bridget Spencer CC-BY-NC; Frank Vincentz CC BY-SA 3.0; Hossein Amir/Shutterstock

Psychedelic drugs come from a wide range of natural and synthetic sources. Even synthetic psychedelics are sometimes derived from compounds found in nature. LSD, for example, can be synthesized from ergot alkaloids produced by a fungus that infects grains.

in sight and sound. They may see strange visual hallucinations involving geometric patterns and colors, both with eyes opened and closed. Their emotions may range from euphoric to panicked. Their thoughts and cognitive processes become altered altogether, along with perceptions of time and even self. Many report mystical-type experiences characterized by a deep sense of unity, intuitive knowledge, and profound reverence for life.

Historic evidence indicates that people have sought out such experiences at least since the beginnings of civilization. Ancient artifacts and pictographs suggest that Mayan, Aztec, and Chavin cultures in ancient Mesoamerica all ingested psychedelic compounds. These practices continued until the early 1600s when Spanish missionaries demonized psychedelic use among Native cultures, believing it to be a form of witchcraft. In this way, the missionaries largely succeeded in suppressing both the culture and use of psychedelics.

As a result, these compounds remained relatively unknown in the West until the late 1880s, when outside observers became aware of the Native Americans' continued use of the psychedelic peyote cactus, commonly known as mescal buttons. Curious about the cactus, German chemist Arthur Heffter isolated its active ingredient, the alkaloid compound *mescaline*, from its dried flesh in the 1890s. By giving the substance to animals, and himself, Heffter confirmed that mescaline was responsible for peyote's mind-altering effects.

Into and Out of the Lab

The early decades of psychedelic research in the 20th century were complicated by contentious politics, cultural revolution, and military agendas. Initially, academic curiosity about psychedelics stirred quietly. The discovery of mescaline and its psychoactive properties was noted only by a niche group of researchers.

But the synthesis of LSD a few decades later awoke broad Western scientific and popular interest. Albert Hofmann, a Swiss-born chemist working for the pharmaceutical company Sandoz Labs, synthesized LSD in 1938 while researching drugs intended to stimulate the heart and circulatory system. In 1943, Hofmann accidentally absorbed LSD through his skin and experienced the world's first "acid trip." He then brought the discovery to his Sandoz colleagues. By 1949, Sandoz was marketing the drug in the United States for clinical and scientific applications, sparking a new interest in psychedelic research.

In the early 1950s, British psychiatrist Humphry Osmond first encountered mescaline and LSD while working in the psychiatric unit at St. George's Hospital in London. Osmond became interested in the potential for these drugs to induce positive or corrective mental health experiences in his patients. He coined the term "psychedelic" for these compounds, meaning "mind manifesting." One of Osmond's first test subjects was the English writer Aldous Huxley, who later recounted the consciousness-altering experience of consuming mescaline in his 1954 book *The Doors of Perception*.

A few years later, Robert Gordon Wasson, a vice president for public relations at J. P. Morgan and Company, published a story in *Life* magazine describing his experience with psychedelics at a traditional healing ceremony in Oaxaca, Mexico. His article brought psychedelics to the awareness of a much wider audience. Wasson is the first known Westerner to consume mushrooms of what we now know as the *Psilocybe* genus. These mushrooms naturally produce the compound psilocybin. On ingestion, psilocybin is converted to its active form, psilocin, which exerts the psychedelic effects. Wasson's article was titled "Seeking the Magic Mushroom," a term that remains popular to this day.

The world took notice of Wasson's story, including the future counterculture author and researcher Timothy Leary, whom President Richard Nixon later dubbed "the most dangerous man in America." But before that, Leary was simply a clinical psychologist on the faculty of Harvard University. A colleague of his had experimented with psilocybin mushrooms on a trip to Mexico after reading Wasson's article, and he told Leary about his experiences. Leary consumed psilocybin on his own trip to Mexico in 1960. He recounted that he learned more about the brain and its possibilities in the five hours after taking these mushrooms than in his 15 years of study.

Leary then began a research program known as the Harvard Psilocybin Project with a colleague, psychologist Richard Alpert, who later changed his name to Ram Dass. Leary and Alpert investigated psilocybin in a myriad of experiments and contexts, including one experiment that attempted to reduce recidivism in prison inmates. They also administered psilocybin and LSD to other faculty members, cultural figures (including beat poet Allen Ginsberg), and students. Leary and Alpert were eventually dismissed from Harvard, in large part due to concerns over the quality and integrity of their research.

Bettmann/Getty Images

Psychologist and psychedelics advocate Timothy Leary (*center*) in the custody of U.S. customs officials in New York City after being arrested upon reentering the United States in 1966. The U.S. government began criminalizing psychedelics use in the 1960s.

Leary's espousal of the benefits of psychedelics continued for decades and gained a wide following. As a figurehead for the psychedelic countercultural movement, he coined the phrase "Turn on, tune in, drop out." In the process, Leary made himself a glowing target for the federal government, which wanted to quell the antiwar and anti-federalist leanings of the countercultural movement that had become inextricably linked to the use of psychedelic drugs.

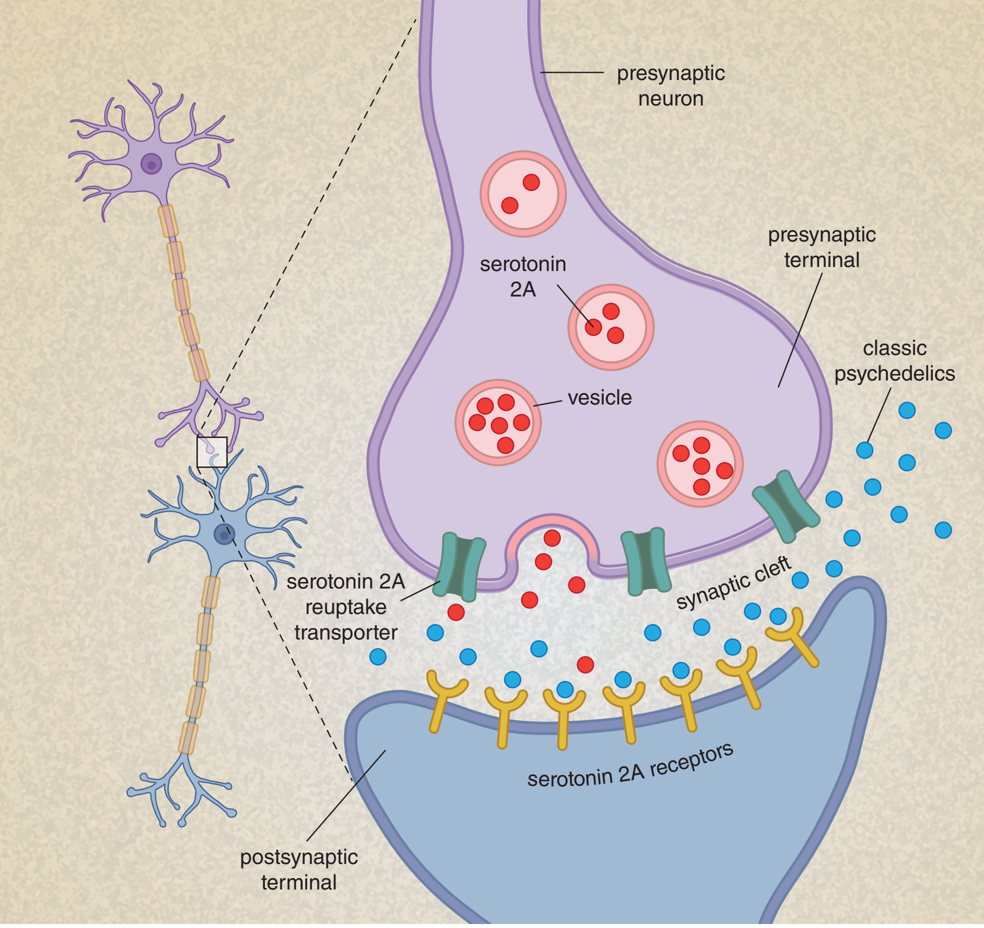
In truth, the U.S. government had been conducting its own psychedelic experiments since the 1950s, but not with therapeutic intentions. According to congressional reports released to the public in 1975, researchers working on a top secret government project called MKUltra dosed Americans with large quantities of LSD and other psychedelic compounds without their consent, while subjecting them to forms of coercion, such as electric shock, hypnosis, sensory deprivation, isolation, and verbal and sexual abuse. For 20 years, researchers drew unwitting participants from across American society—civilian and military, imprisoned and free, healthy and mentally ill. The government mistakenly thought that psychedelics might be a real-life "truth serum" that the military could administer to enemy combatants to elicit sensitive information.

In the early 1970s, President Richard Nixon declared a "War on Drugs." Congress enacted the Comprehensive Drug Abuse Prevention and Control Act of 1970, which in turn created the Controlled Substances Act and the five-tiered drug scheduling system we know today. Almost all of the widely researched psychedelic compounds—including LSD, mescaline, and psilocybin—were placed on Schedule 1, alongside heroin and cannabis, as drugs with no known medical or therapeutic value and a high potential for abuse. This act effectively halted all U.S. clinical studies of psychedelic compounds, a condition of stasis that the field remained in for nearly four decades.

Psychedelic Research Reemerges

Psychedelics slowly began to recapture scientific interest in the mid-1990s through the 2010s. In 1994, a team of researchers at the University of New Mexico published the first modern study in healthy volunteers of DMT (N,N-dimethyltryptamine), a psychedelic naturally found in many plants, and the active ingredient in the psychedelic tea known as ayahuasca. Small studies of psilocybin led by researchers at the University of California, Los Angeles, Johns Hopkins University, and New York University demonstrated beneficial mental health effects in terminal cancer patients. Then teams at Imperial College London and Johns Hopkins showed that psilocybin improved mental health for patients experiencing major depression.

Journalist Michael Pollan's bestselling 2018 book *How to Change Your Mind:*



Barbara Aulicino

Classic psychedelics, such as psilocybin, mescaline, and LSD, have a chemical structure similar to the neurotransmitter serotonin. These drugs trigger a serotonin receptor in the brain known as *serotonin 2A*. Researchers believe that this receptor plays a key role in eliciting a "trip" because experimentally blocking it prevents the psychedelic experience.

What the New Science of Psychedelics Teaches Us About Consciousness, Dying, Addiction, Depression, and Transcendence raised public awareness of psychedelic therapies. With the book's popularity, and with growing cultural interest in alternative therapies, legal attitudes toward psychedelics began to shift. Some local and state governments decriminalized psychedelic compounds for personal use. Oregon passed a bill that mandated a state-run program of dispensation of psilocybin mushrooms for personal or therapeutic use.

The genie had clearly come (back) out of the bottle. Military veterans in our clinic in the early 2020s described traveling to Mexico to undergo treatment with an African psychedelic known as ibogaine—a drug once studied for treating heroin addiction. Others recounted traveling with fellow veterans to retreat centers in Central and South America where they consumed ayahuasca. They reported intense autobiographical visions of past events. Many described the experience as 20 years of psychotherapy in one evening. Time and time again, we heard stories of a total disruption of addictive tendencies. "I completely lost the taste for alcohol" was uttered more than once.

We were encouraged by these positive stories, but also quite concerned that the hype might be exceeding the science. Therefore, we spent 2023 and 2024 systematically reviewing the evidence base for the most heavily researched psychedelic at the time: psilocybin. We searched through all of the 1,449 English-language clinical studies published in the past 25 years that mention psilocybin. From these, we assessed the 21 that reported outcomes of trained providers offering psilocybin to treat mental health conditions in controlled settings. Despite anecdotes from patients and the popular media's portrayals of psilocybin as a panacea for everything from stress to long-term limb paralysis, the scientific evidence we found presented a more sober picture.

One of our major concerns was limited sample size. Even most of the formal studies examining psilocybin as a psychiatric treatment contained only a small number of participants, with a mean of around 24. A few newer, randomized controlled trials for treating depression had combined sample sizes numbering in the hundreds. The field was just beginning to reach the point of scientific maturity.

Another issue was dosing. Most early studies used a weight-adjusted approach, with heavier individuals receiving higher dosages. Newer studies adopt a fixed dose, typically of 15 to 30 milligrams of psilocybin. No studies have tested the optimum dose for each individual and desired outcome.

Then there was the lack of true blinding. The gold standard for establishing a causal relationship between a treatment and a health outcome is the double-blind, randomized controlled trial. Individuals are randomly assigned to one of two or more treatment conditions, and both the participant and the experimenters are blinded—that is, they are unaware of the treatment assignment. But how can a person remain unaware that they are experiencing a psychedelic drug? That question stymied a lot of scientists.

Some researchers attempted to blind studies by offering inactive placebos. Others used active placebos such as niacin, a B vitamin that induces a tingling effect at high doses, but nothing similar to the psychedelic experience. Still others used low doses of the psychedelic, which exert minimal, if any, alterations in consciousness. Only a few studies had assessed the efficacy of blinding in psychedelic trials, and the ones that did displayed a clear flaw: The participants knew when they received the active treatment.

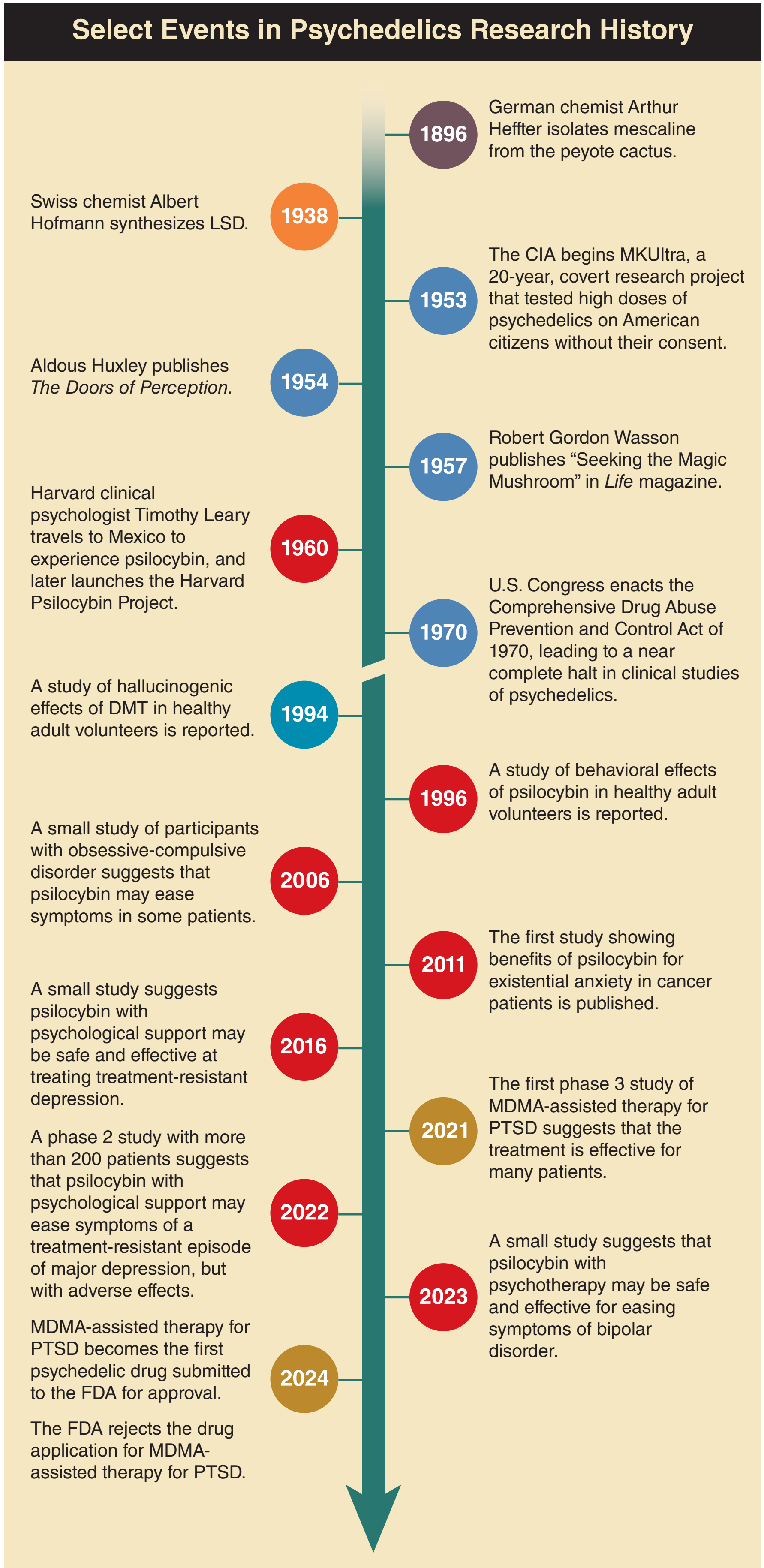
The durability of patients' mental health improvements was also not well established in most of these studies. Whereas some people (particularly those with major depression) clearly benefitted from psilocybin administration with psychological support, a subset of individuals did not respond at all. Many more experienced a relapse into their mental health condition weeks to months later. The few case reports and small pilot studies that described benefits for years after a single treatment of psilocybin were clearly not representative of all patients.

Lack of efficacy was only half of the problem. We also found that both the scientific literature and media coverage did not emphasize the risks of psychedelics nearly enough. In some studies, a small but concerning number of participants experienced suicidal ideation following dosing. This outcome is especially worrisome given that individuals who are already manifesting suicidality are typically excluded from participating. Also, few studies adequately tracked flashback phenomena, where individuals reexperience psychedelic-like perceptual alterations long after the drug has left their system. For some individuals, this experience can be highly distressing and can even lead to the diagnosis of hallucinogen persisting perception disorder.

Case studies reported in scientific journals also offered real-world examples of possible risks. For example, we recently published a report of an individual who used psilocybin mushrooms recreationally and then experienced a prolonged first episode of mania, psychosis, and severe depression that was difficult to treat. Case reports by other groups described similar adverse outcomes in individuals with no known prior history of such pathologies. Although these cases are clearly rare amidst the total number of individuals consuming psilocybin mushrooms recreationally, they underscore the potential dangers associated with efforts toward widespread availability, decriminalization, or legalization. We need to better understand how common these outcomes really are and if there are effective ways to mitigate them.

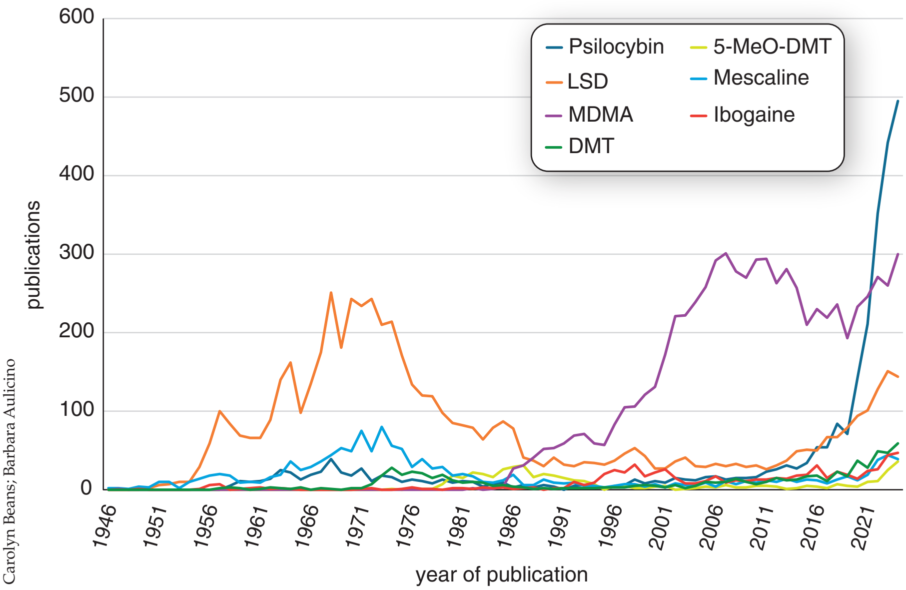
Another complication in understanding the true impact of psychedelics is the confounding factor of therapy. In most studies of psychedelics, therapists meet with patients before, during, and after the psychedelic experience. In the 1960s and 1970s, studies showed that offering this support generally improved outcomes, so the practice became standard. But our review revealed that nearly all studies of psychedelic-assisted therapy used psychotherapeutic approaches that contained few, if any, elements from the most effective forms of psychotherapy, such as cognitive-behavioral therapy. We agree that patients should receive support for safety and ethical reasons. But we believe that the therapeutic effects observed in modern studies are largely a function of the psychedelic itself, not this supportive therapy.

Jeff's story illustrates our point: He healed without any therapist present.



Barbara Aulicino

Over the course of the past 75 years, psychedelics research has moved from the fringe to the mainstream.



Carolyn Beans; Barbara Aulicino

This table presents research papers found in the U.S. National Library of Medicine's PubMed database published since 1946 that mention individual psychedelics. Since the late 1990s, the number of clinical studies of psychedelics published each year has steadily grown.

Furthermore, high doses of psychedelics typically incapacitate patients to the extent that normal therapeutic interactions with a therapist are minimal or absent. Yet symptoms are typically reduced even prior to follow-up psychotherapy. Whether these effects can be enhanced with evidence-based psychotherapeutic approaches remains an open and exciting question.

Maximize Healing, Minimize Risk

As a whole, the published clinical studies we reviewed could not definitively answer whether psychedelics are an effective form of psychiatric treatment. But there is now exciting new research underway to find safe, effective uses for psychedelics.

Several psychedelic therapies are now moving through rigorous clinical trials. In 2023, an MDMA-assisted therapy for PTSD completed the second of two phase 3 clinical trials. The therapy's developer, Lykos Therapeutics, became the first to submit a psychedelic to the U.S. Food and Drug Administration (FDA) for approval. Ultimately, however, the FDA denied approval. One issue raised by the FDA advisory committee was that the therapy portion was not well validated and potentially confounded the results.

Despite its recent decision on MDMA, the FDA sees potential in psychedelics. The agency has given "Breakthrough Therapy" status to three psychedelic-assisted therapies: MDMA for PTSD, LSD for generalized anxiety disorder, and psilocybin for treatment-resistant depression. This designation is intended to expedite drug development and review for treatments of serious conditions that have the potential to offer substantial improvement over available options.

Many psychedelics drug developers are now focusing on the drug effect as opposed to the combination of drug and psychotherapy, while still providing necessary but minimal psychological support. At the same time, many academic researchers are exploring combining psychedelics with more typical forms of evidence-based therapy, such as exposure therapy for PTSD and cognitive-behavioral therapy for depression.

Psilocybin for treatment-resistant depression—currently in phase 3 studies—may be the next psychedelic therapy submitted for FDA approval. A prior large, multisite phase 2 study demonstrated that 25 milligrams of psilocybin administered with psychological support improved symptoms of a treatment-resistant major depressive episode better than 1 milligram of psilocybin with the same support. Clinical trials of psilocybin have also demonstrated promise for the alleviation of anxiety and depression related to a life-threatening cancer diagnosis. Meanwhile, LSD is also beginning a phase 3 trial for the treatment of generalized anxiety disorder, a condition characterized by chronic, pervasive, and uncontrollable worry.

Other psychedelic therapies are moving through earlier phases of development, including LSD for various mood and anxiety disorders, and psilocybin for alcohol use disorder, tobacco use disorder, depressive episodes in bipolar disorder, anorexia nervosa, and obsessive-compulsive and related disorders.

In our own center, we are conducting clinical trials of psilocybin for treatment-resistant depression. We will also soon be studying MDMA-assisted therapy for PTSD using better controls, such as other psychoactive compounds, so that studies remain double-blind. In our observational studies of veterans and veteran family members undergoing psychedelic treatment in unaffiliated retreat centers, we have observed that some individuals show profound and sustained benefits, whereas others show little improvement or fail to maintain improvements over time. There is clearly no one-size-fits-all solution.

Our team is also now testing new ways to enhance psychedelic benefits. For example, rather than offer aftercare with psychotherapy alone, we are testing whether a form of magnetic brain stimulation—which is already used to treat depression—may further improve mental health outcomes in 100 individuals with treatment-resistant depression. Our hypothesis is that the synaptic plasticity caused by psychedelics may help the brain respond more malleably to the magnetic stimulation.

Our hope is that stories such as Jeff's will one day become more mainstream treatment triumphs in the personal lives of the many individuals afflicted with mental health conditions. One of the most critical remaining hurdles will be identifying who is and is not well suited to psychedelic therapy. Psychiatrists commonly proceed by trial and error until they find the right pharmaceutical treatment for their patients. But given the risks of psychedelic therapies, as well as their likely high cost of implementation, it is particularly important to get this right from the start. Researchers might be able to predict outcomes using brain imaging and electroencephalograms (EEGs), as well as biological and psychological measures, genetic and epigenetic tests, personality characteristics, and mental health–related symptoms.

Our experiences show that a personalized-medicine approach to psychedelic treatments could make the difference between a glowingly posi-

	psilocybin	MDMA	LSD	DMT	mescaline	ibogaine	5-MeO-DMT
phase 3	MDD, TRD	PTSD	GAD, MDD				
phase 2	AUD, binge eating disorder, MUD, OUD, GAD, demoralization syndrome, IBS, fibromyalgia, adjustment disorder, fragile X syndrome, depression with comorbid PTSD, depression and anxiety with comorbid PTSD	PTSD, social anxiety in ASD	MDD, existential distress in cancer patients	GAD, TRD			TRD, PPD, BDII, AUD, depression/anxiety in Alzheimer's disease, GAD
phase 1	OUD, OCD, PDD, neuropsychiatric disorders, headache disorder, metabolic disease	MDD, central nervous system (CNS) disorders, SAD, ASD	headache disorders, AUD, OUD	cocaine use disorder, TRD, stroke, undisclosed condition	obesity, AUD	OUD, AUD	psychiatric/neurological disorders, undisclosed condition, SUDs
preclinical	anorexia nervosa, MDD, IBS, binge eating disorder, fibromyalgia	PTSD, SUDs, AUD, eating disorders	MDD, anxiety disorder, neuropathic pain	glaucoma, undisclosed condition, anxiety, depression, and other disorders		SUDs, OUD, PTSD, TBI	psychiatric/neurological disorders, fibromyalgia, chronic pain, MDD, undisclosed conditions

ABBREVIATIONS: **ASD:** autism spectrum disorder; **AUD:** alcohol use disorder; **BDII:** bipolar 2 disorder; **GAD:** generalized anxiety disorder; **IBS:** irritable bowel syndrome; **MDD:** major depressive disorder; **MUD:** methamphetamine use disorder; **OCD:** obsessive-compulsive disorder; **OUD:** opioid use disorder; **PDD:** premenstrual dysphoric disorder; **PPD:** postpartum depression; **PTSD:** post-traumatic stress disorder; **SAD:** social anxiety disorder; **SUDs:** substance use disorders; **TBI:** traumatic brain injury; **TRD:** treatment-resistant depression

Data from Psychedelic Alpha Q1'25 Bullseye Chart: psychedelicalpha.com/news/q125-psychedelic-drug-development-pipeline-bullseye-chart

Psychedelic drugs are now moving through clinical trials testing their potential to treat a wide range of mental health conditions. Phase 1 trials test safety and side effects in a small group, typically 20 to 80 participants. Phase 2 trials test effectiveness and safety in a larger group. Phase 3 trials expand the study to a still larger group, confirm that the treatment is effective, compare results with other treatments, and track side effects and safety.

tive treatment outcome, such as Jeff's, and the prolonged case of mania, psychosis, and depression we also recently reported. Psychedelic mind expansion is a powerful but unpredictable method for treating mental illness. These drugs should be approached with caution and the utmost respect. They have the potential to manifest properties of the mind both healing and horrific. How to maximize the former and minimize the latter? That is the "trip" we are on.

Bibliography

Barber, G., C. B. Nemeroff, and S. Siegel. 2022. A case of prolonged mania, psychosis, and severe depression after psilocybin use: Implications of increased psychedelic drug availability. *American Journal of Psychiatry* 179:892–896.

Bogenschutz, M. P., et al. 2022. Percentage of heavy drinking days following psilocybin-assisted psychotherapy vs placebo in the treatment of adult patients with alcohol use disorder: A randomized clinical trial. *JAMA Psychiatry* 79:953–962.

Cassels, B. K., and P. Sáez-Briones. 2018. Dark classics in chemical neuroscience: Mescaline. *ACS Chemical Neuroscience* 9:2448–2458.

Fonzo, G. A., et al. 2025. Psilocybin: From psychiatric pariah to perceived panacea. *The American Journal of Psychiatry* 182:54–78.

Geyer, M. A. 2024. A brief historical overview of psychedelic research. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging* 9:464–471.

Goodwin, G. M., et al. 2022. Single-dose psilocybin for a treatment-resistant episode of major depression. *New England Journal of Medicine* 387:1637–1648.

Goodwin, G. M., E. Malievskaia, G. A. Fonzo, and C. B. Nemeroff. 2024. Must psilocybin always "assist psychotherapy"? *The American Journal of Psychiatry* 181:20–25.

Holze, F., P. Gasser, F. Müller, P. C. Dolder, and M. E. Liechti. 2023. Lysergic acid diethylamide-assisted therapy in patients with anxiety with and without a life-threatening illness: A randomized, double-blind, placebo-controlled phase II study. *Biological Psychiatry* 93:215–223.

Leone, L., B. McSpadden, A. DeMarco, L. Enten, R. Kline, and G. A. Fonzo. 2024. Psychedelics and evidence-based psychotherapy: A systematic review with recommendations for advancing psychedelic therapy research. *Psychiatric Clinics of North America* 47:367–398.

Mitchell, J. M., et al. 2021. MDMA-assisted therapy for severe PTSD: A randomized, double-blind, placebo-controlled phase 3 study. *Nature Medicine* 27:1025–1033.

Mitchell, J. M., et al. 2023. MDMA-assisted therapy for moderate to severe PTSD: A randomized, placebo-controlled phase 3 trial. *Nature Medicine* 29:2473–2480.

Murphy, R., S. Muthukumaraswamy, and H. de Wit. 2024. Microdosing psychedelics: Current evidence from controlled studies. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging* 9:500–511.

Petridis, P. D., et al. 2024. Psilocybin-assisted psychotherapy improves psychiatric symptoms across multiple dimensions in patients with cancer. *Nature Mental Health* 2:1408–1414.

Raison, C. L., et al. 2023. Single-dose psilocybin treatment for major depressive disorder: A randomized clinical trial. *JAMA* 330:843–853.

Vollenweider, F. X., and K. H. Preller. 2020. Psychedelic drugs: Neurobiology and potential for treatment of psychiatric disorders. *Nature Reviews Neuroscience* 21:611–624.

Gregory A. Fonzo is assistant professor and codirector of the Charmaine and Gordon McGill Center for Psychedelic Research and Therapy in the department of psychiatry and behavioral sciences at the University of Texas at Austin Dell Medical School. Charles B. Nemeroff is a psychiatrist at the University of Texas at Austin Dell Medical School. He is chair and professor in the department of psychiatry and behavioral sciences, where he directs the Institute for Early Life Adversity Research as part of the Mulva Clinic for the Neurosciences. He also codirects the Center for Psychedelic Research and Therapy. Email for Fonzo: gfonzo@austin.utexas.edu

Rare but Deadly

A perilous tick-borne illness is spreading—and it isn't Lyme disease.

Durland Fish

Many people remember Kay Hagan as the candidate whose upset victory against North Carolina Senator Elizabeth Dole allowed the Democrats to regain control of the U.S. Senate in 2008. For me, her name will always bring to mind the more personal health battle she fought a few years later against the effects of encephalitis, an inflammation of the brain that can cause neurological complications ranging in severity from mild to life-threatening. In Hagan's case, the condition quickly hampered her ability to control her muscles, arms, and legs, and made speaking difficult. In October 2019, she passed away unexpectedly at the age of 66—a former senator brought low by a creature the size of an apple seed: a tick carrying the Powassan virus.

When Hagan's face began to droop in December 2016, her husband assumed she had experienced a stroke. Even the doctors who diagnosed her with encephalitis took more than two months to identify the cause of her brain swelling, in part because Powassan was so rare: In 2015, the U.S. Centers for Disease Control and Prevention (CDC) reported only six U.S. cases of the virus, which its discoverers had named for the Ontario town where the virus killed a boy in 1958. Following the diagnosis, Hagan's husband reasoned that she had been bitten during a 2016 Thanksgiving trip to the Blue Ridge Mountains, likely when the couple picnicked on the grass at the picturesque Peaks of Otter. Powassan virus remains rare, but case counts are growing, and incidents are spreading geographically as an unintended consequence of reforestation. Today, there are nearly 300 known cases. The virus therefore offers an important case study in understanding and controlling the spread of new tick-borne diseases.

In my 40-year career as a medical entomologist and epidemiologist focusing on diseases spread by mosquitoes and ticks, I have studied diseases such as Rocky Mountain spotted fever and West Nile virus, as well as Lyme disease. I have been involved in the discovery of new tick-borne diseases such as human anaplasmosis and hard tick relapsing fever (*Borrelia miyamotoi* disease) and have studied Lyme disease since the identification of its causative agent, *B. burgdorferi*, in 1982. I have also studied the behavior, distribution, and ecology of vectors that transmit these diseases, and I have received grants from U.S. institutions such as the CDC, the National Institutes of Health, the Department of Agriculture, the Environmental Protection Agency, the National Science Foundation, and NASA to advance disease surveillance and prevention. My knowledge and experience in disease ecology (eco-epidemiology) provides insight into the causes of new disease outbreaks such as Powassan virus, and I am concerned.

Powassan Emerges

Powassan's capacity to cause severe neurological diseases such as encephalitis and meningitis places it among the most dangerous tick-borne diseases in the United States; until recently, it was also one of the rarest. Not all bites lead to active infection, and many Powassan cases are asymptomatic. However, the CDC estimates that, among those who are infected, Powassan results in a 10 percent fatality rate. That's comparable to untreated diphtheria and on par with the deadliest tick-borne diseases such as Crimean-Congo hemorrhagic fever (5 to 30 percent case fatality rate) and Rocky Mountain spotted fever (5 to 10 percent). The virus also has about a 50 percent chance of causing permanent neurological impairment in survivors, including paralysis, seizures, memory loss, and speech impairments—far higher than occurs in the better-known and more widely studied Lyme disease, in which 5 to 10 percent of patients experience longer-term difficulties with pain, sleep, and concentration. CDC data also show dramatic increases in U.S. cases of Powassan virus, from a single reported case in 2006 to 49 cases in 2023; this past decade saw more than 275 cases compared to just one-quarter that number during the preceding decade.

Driving this increase is a recent change in the ecology of Powassan virus that has enabled its transmission via the black-legged tick (*Ixodes scapularis*), commonly known as the deer tick and best known as the vector of Lyme disease. But unlike Lyme disease, which is a bacterial infection that takes up to 36 hours to set in, causes flu-like symptoms, responds to antibiotics, and allows full recovery in most cases, Powassan is a virus that infects within minutes of a tick bite, can cause severe neurological symptoms and death, has no treatment aside from symptom management (antibiotics do not treat viral infections), and can result in long-term impairments.

All of these factors indicate that Powassan virus is an important emerging disease that public health officials currently underestimate for numerous reasons. Because many Powassan infections present asymptomatically, or with symptoms like fever and headache that

QUICK TAKE

Powassan virus is a rare but potentially deadly tick-borne disease for which there is no vaccine. Its flu-like symptoms can progress to encephalitis and long-term neurological impairments.

Once confined to a tick species that seldom bites humans, it has since spilled over into the deer tick that spreads Lyme disease. These ticks can transmit infection during several life stages.

Now Powassan is spreading along with its deer hosts into areas reforested over the past century. Many cases go unreported, and improved tracking is needed.

Lauren Bishop CDC / Division of Vector-Borne Diseases, Rickettsial Zoonoses Branch

An adult female deer tick (*Ixodes scapularis*) *quests* for a host by extending her front legs, which contain an organ that can sense carbon dioxide, heat, and movement. Because ticks do not jump or fly, they also rely on these legs to grab onto passing mammals. These ticks can transmit Powassan virus, which doctors may mistake for other illnesses, delaying diagnosis.

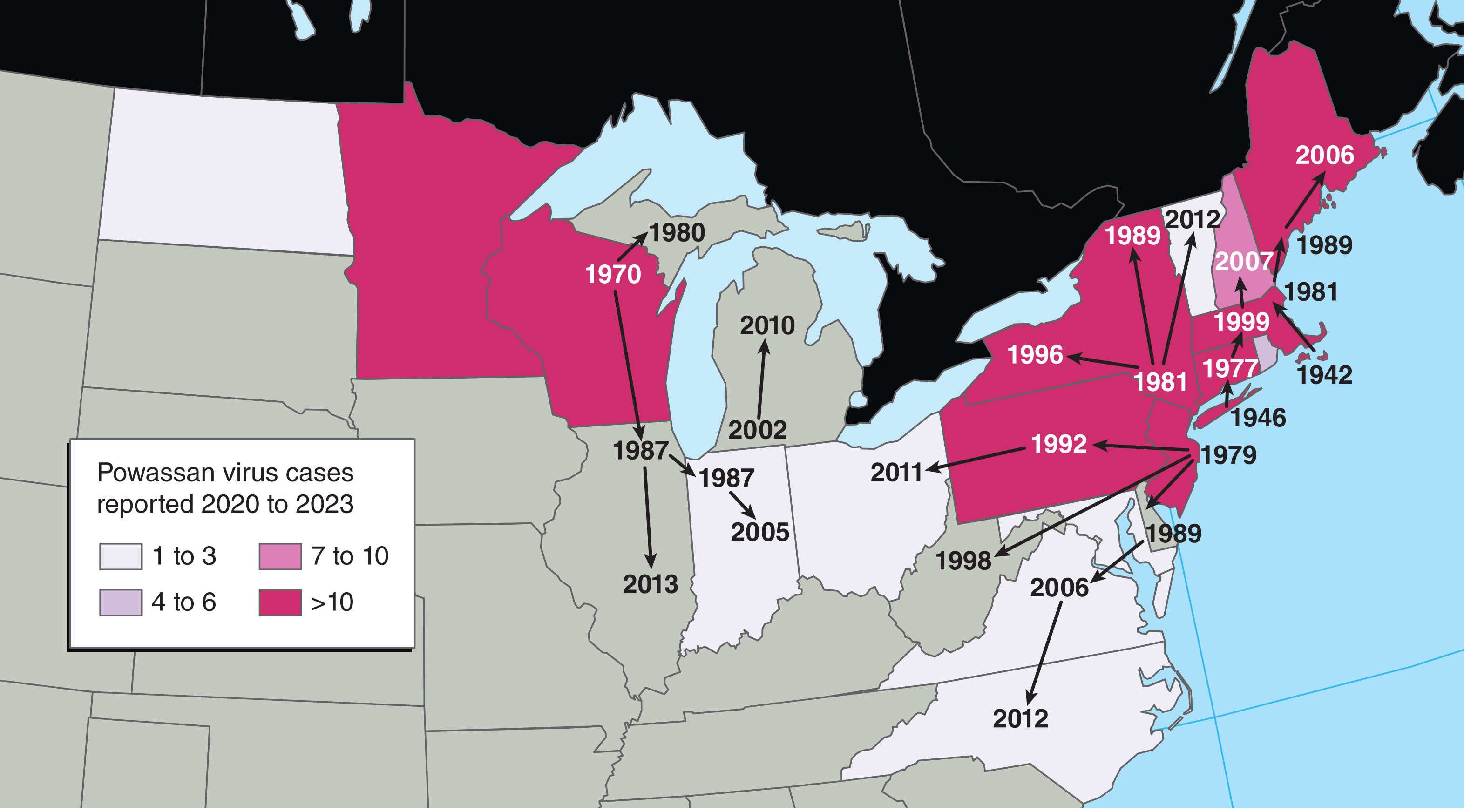
can easily be mistaken for other common illnesses, patients might not seek medical help. If they do, Powassan is likely to be far down the doctor's differential list of possible ailments, if the physician is aware of it at all. Diagnosis can only be confirmed via specialized laboratory tests. Meanwhile, unlike Lyme disease, field surveillance of Powassan remains limited. Thus the disease remains underreported.

Powassan entering deer ticks has vastly expanded the virus's potential range and incidence. When Donald McLean and William Donohue, both affiliated with the Hospital for Sick Children Research Institute in Toronto, Canada, investigated the previously mentioned index case in Powassan, Ontario, the picture was quite different. As explained in their landmark 1959 paper, a sudden onset of encephalitis usually stemmed from a viral infection, and late summer cases typically came from mosquito-borne viral encephalitis (encephalitis caused by ticks was then unknown in North America). That soon changed: After blood tests conducted for all known mosquito-borne viruses came back negative, the duo isolated a previously unknown virus in the deceased boy's brain tissue, thereby identifying the first North American case of a tick-borne *flavivirus* causing encephalitis. Flaviviruses are a family of viruses that copy themselves using RNA instead of DNA, are spread mainly via mosquitoes and ticks, and can cause serious diseases such as West Nile, dengue, yellow fever, and Zika.

Fearing the potential risk to others in the area, McLean and Donohue conducted a series of field studies that uncovered evidence of Powassan infection in wildlife near the boy's residence—specifically, in a groundhog tick (*I. cookei*) removed from its namesake animal. Indeed, further studies implicated a transmission cycle of Powassan virus maintained by groundhogs and groundhog ticks, which rarely bite humans and are much less widespread in North America than *I. scapularis* deer ticks. Further investigations by U.S. public health agencies in the 1970s identified more locations of Powassan virus infection in *I. cookei,* groundhogs, and skunks in upstate New York and Connecticut.

A North American TBE?

Powassan was the first tick-borne virus in North America known to cause neurological symptoms like encephalitis, but it should not be confused with the disease called *tick-borne encephalitis*, or TBE, which northern Europe and Asia have lived with since the 1930s and which is caused by the European castor bean tick or sheep tick (*I. ricinus*) and the East Asian taiga tick (*I. persulcatus*). In this serious and sometimes fatal relative of Powassan, a tick feeds on an infected animal, often a rodent, then



Barbara Aulicino; Map Resources; data from CDC and *Climate, Ticks, and Disease*, ed. P. Nuttall

Up to 5 percent of *I. scapularis* ticks carry Powassan virus, and the spread of the deer that host the ticks has created two geographically separated viral groups: one in the Midwest, where the original variant dominates, and the other in the Northeast, where the deer tick virus variant holds sway. The years on the map refer to the first recorded cases of Powassan in that area; the arrows reveal how disease-carrying ticks spread from relicts of colonial forests into regions reforested over the past century. This ecological shift, combined with the spillover of the virus into deer ticks sometime before 1997, is driving the rapid uptick in Powassan cases.

passes the virus to a human or other animal during its next blood meal. In rarer cases, people can contract TBE by consuming unpasteurized milk or cheese from infected cows, goats, or sheep. Locals know most of the areas affected by TBE, and residents of high-risk areas commonly receive vaccinations. Still, the World Health Organization reports around 10,000 to 12,000 clinical cases of the disease annually throughout Europe and Asia. In the milder European subtype, 20 to 30 percent of patients develop neurological symptoms, and mortality rates range from 0.5 to 2.0 percent, with up to 50 percent of surviving patients developing long-term neurological impairments.

Will Powassan become a North American TBE? The movement of the virus into deer ticks, a more widespread species that is more likely to bite humans, suggests a partial answer; indeed, one 2016 estimate reported *I. scapularis* in 1,420 (45.7 percent) of the 3,110 counties in the continental United States.

Trends in disease incidence and shifts in ecological patterns indicate the need for greater concern over Powassan virus.

There's another factor to consider, too. Epidemics caused by ticks and mosquitoes often spring from changes in the environment, which can create temperature, moisture, and habitat conditions that favor the vector, the host, or both. Once Powassan began to be transmitted via the deer tick, its fate, like that of Lyme disease, became more closely tied to the distribution of white-tailed deer (*Odocoileus virginianus*). To be clear, these deer are not the reservoirs for Lyme or Powassan; that role is filled by the smaller mammals upon which *I. scapularis* nymphs and larvae feed. Deer are the reproductive host for deer ticks, where mating occurs and female ticks engorge on blood to produce eggs.

Extensive reforestation of the Northeastern and Midwestern United States began in the last century, resulting in an explosive increase in deer populations and an expansion of the deer tick's range from isolated precolonial refuges on Long Island and in northern Wisconsin. Forests that were clear-cut for agriculture during colonial times are now reestablished over much of their former areas. Deer were reintroduced for hunting after 1900, but deer ticks were absent until the 1970s, the same decade Lyme disease was discovered. Since the 1980s, as deer have gradually expanded over much of their former range in areas of the United States and Canada, deer ticks have become the most common source of tick bites and the primary vector of the Lyme disease epidemic, as well as several other new tick-borne diseases such as human anaplasmosis, babesiosis, hard tick relapsing fever, and ehrlichiosis. This range expansion will march forward throughout its original precolonial range, while continued suburban development in forested areas will expose even more people to tick bites. We must therefore understand and prepare for the spread of this pathogen.

Dispersal Patterns

As deer ticks moved up the Hudson River Valley toward Albany, New York, during the late 1980s, an alert virologist, Margaret Grayson of the New York State Department of Health, wondered if the species could transmit Powassan virus. She knew of several cases of the virus in the Albany area and thought that, if deer ticks could transmit the virus, many more people could become infected. As a test, Grayson experimentally infected *I. scapularis* with Powassan in laboratory studies. Her findings showed that not only could the deer tick transmit Powassan just as effectively as the groundhog tick, but that a female could pass infection to her offspring through infected eggs. In addition to this *transovarian* route, we now know that deer ticks can acquire the infection by *cofeeding*, that is, feeding on noninfected wildlife adjacent to an already infected tick.

The following year, a paper in the journal *Emerging Infectious Diseases* confirmed the unwelcome news that Powassan-infected deer ticks had been found in the wilds of coastal New England. Sam Telford at Harvard University and Mark Wilson at Yale University identified what they initially thought was a new virus, but they soon discovered that their so-called "deer tick virus" was a variant of Powassan. Soon after, antibodies to Powassan virus were found in white-footed mice (*Peromyscus leucopus*) in Wisconsin and New England. This discovery was notable and concerning because the cycle of continuous passage of infection by the Lyme disease bacterium occurs between white-footed mice and deer ticks. Should Powassan virus follow a similar pattern in these mice—or, as described in a 2021 paper, in shrews—we might well expect many deer ticks and the people they bite to become infected.

Because deer ticks parasitize white-tailed deer so heavily, scientists monitor them both to investigate reports of expanding spread and rising incidence of deer-tick-borne diseases such as Powassan. When Louis Magnarelli and his team at the Connecticut Agricultural Experiment Station in New Haven tested a large collection of blood samples from more than 1,000 hunter-killed deer in Connecticut, Maine, and Vermont, the group found that the neutralizing antibody levels to Powassan virus increased from near zero in 1980 to around 80 percent by 2010, reflecting a consistent rise in infected deer ticks and consequently in risk of infection in bitten humans.

These findings offer convincing evidence of the increase in Powassan virus and of this expansion arising from ecological factors. We have seen a major change in the natural cycle of Powassan virus from groundhogs and groundhog ticks to small mammals and deer ticks. In epidemiological terms, this shift to a different branch of the rodent family tree (from the Sciuridae family of groundhogs and squirrels to white-footed mice and shrews) is known as a *spillover event*, which occurs when a pathogenic agent changes its host type, as when Ebola jumped from bats to humans. But in this case, the meaningful change occurred in the ecological shift—the rewilding of once deforested lands into forest ecologies more suited to white-tailed deer—and in how that shift affected the spread of the deer tick vectors, which are more likely than groundhog ticks to transmit Powassan to humans.

Once Powassan began to be transmitted via the deer tick, its fate, like that of Lyme disease, became more closely tied to the distribution of white-tailed deer.

We cannot say with certainty what caused this spillover event. The Powassan virus was not reported in deer ticks until 1997, about the same time that human cases began to increase. In the 1970s, during the investigation that later led to the identification of Lyme disease (and before deer ticks, infected or not, had spread from Lyme, Connecticut, to other areas of the Northeast), scientists at Yale University's Arbovirus Research Unit looked for a viral cause, or *etiology*, for Lyme disease by examining hundreds of deer ticks (they did not yet know Lyme is caused by a bacterium). The researchers did not find any viruses in deer ticks around Lyme. However, they did find Powassan virus in groundhog ticks in the town's vicinity.

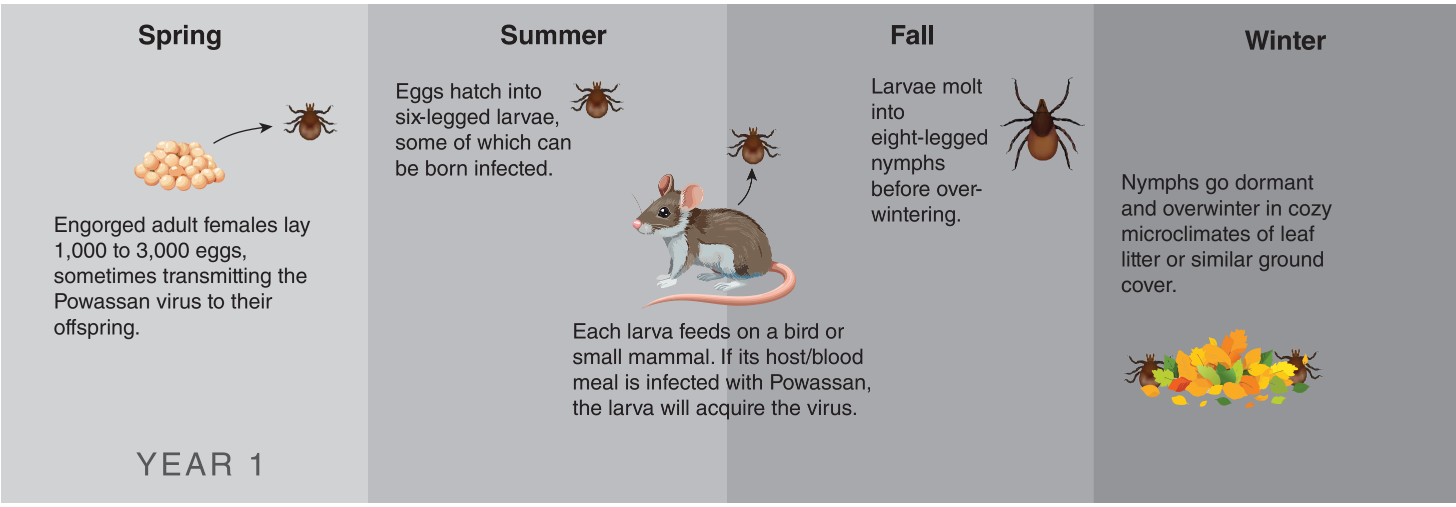
As the deer tick *I. scapularis* expanded its range through regions where Powassan was present or endemic, it's likely that it acquired the virus by feeding on groundhogs or other mammals infected by *I. cookei* groundhog ticks and then spread it to mice or the many other animals that deer ticks feed upon.

We now know that Telford and Wilson's 1997 report of a novel "deer tick virus" described a genetic variant of Powassan, the product of a genetic branching that could indicate the virus had long occurred in deer ticks and simply escaped detection until expanding deer and deer tick populations brought the virus in contact with humans. But other evidence suggests the variant developed more recently. Scientists did not find the deer tick virus in *I. scapularis* ticks until after they expanded beyond Lyme's environs in the early 1980s, which suggests that deer ticks acquired the deer tick virus variant of Powassan more recently. Also, the variant dominates recent cases of Powassan, whereas researchers have attributed cases prior to 2000 to the original Powassan strain, suggesting that the genetic change that produced the deer tick virus variant took place recently.

Regardless of the origin of the variant, we epidemiologists are seeking to understand what propelled the variant to recent dominance. Deer ticks have always possessed the capacity to acquire and transmit Powassan. Perhaps the genetic difference between Powassan virus and its variant represents an evolutionary adaptation to support more efficient transmission by deer ticks, much as West Nile evolved to be more transmissible by mosquitoes. From an epidemiological perspective, human infection with Telford and Wilson's deer-tick virus or with the original Powassan viral strain results in similar symptoms and mortality rates. The two infections are clinically and serologically indistinguishable and require molecular analysis to tell apart.

Missing Cases?

Recent field studies show that as many as 5 percent of deer ticks can be infected with Powassan virus. As a



comparison, consider Lyme disease: I have published several studies showing that around 20 percent of deer ticks carry *B. burgdorferi*, the bacterial agent for Lyme disease. This rate results in about 400,000 new Lyme disease cases each year. Should Powassan virus continue to expand throughout the range of deer ticks, one would expect that up to one-fourth as many Powassan infections as Lyme infections could occur each year. That would result in a whopping 100,000 Powassan cases annually compared with the less than 300 cases we now see spread across a decade. So why have we not seen more cases?

To grapple with the growing threat, we need more studies to determine infection rates and locations.

Two observations might help to explain the small number of case reports. First, the geographic distribution of Powassan virus doesn't compare to that of Lyme disease. Researchers find the Lyme disease bacterium nearly everywhere deer ticks occur, but (for now, at least) we cannot say the same for Powassan. Instead, isolated areas of Powassan virus lie scattered within the total range of deer ticks. We do not know the frequency of spread from the groundhog cycle to the deer tick cycle, and federal and state authorities make little effort to track it. The study of deer blood suggests a slow process that occurs steadily over decades. Nor do we know the geographic distribution of groundhog cycles, largely because experts discover them only after authorities identify human cases—too often, postmortem.

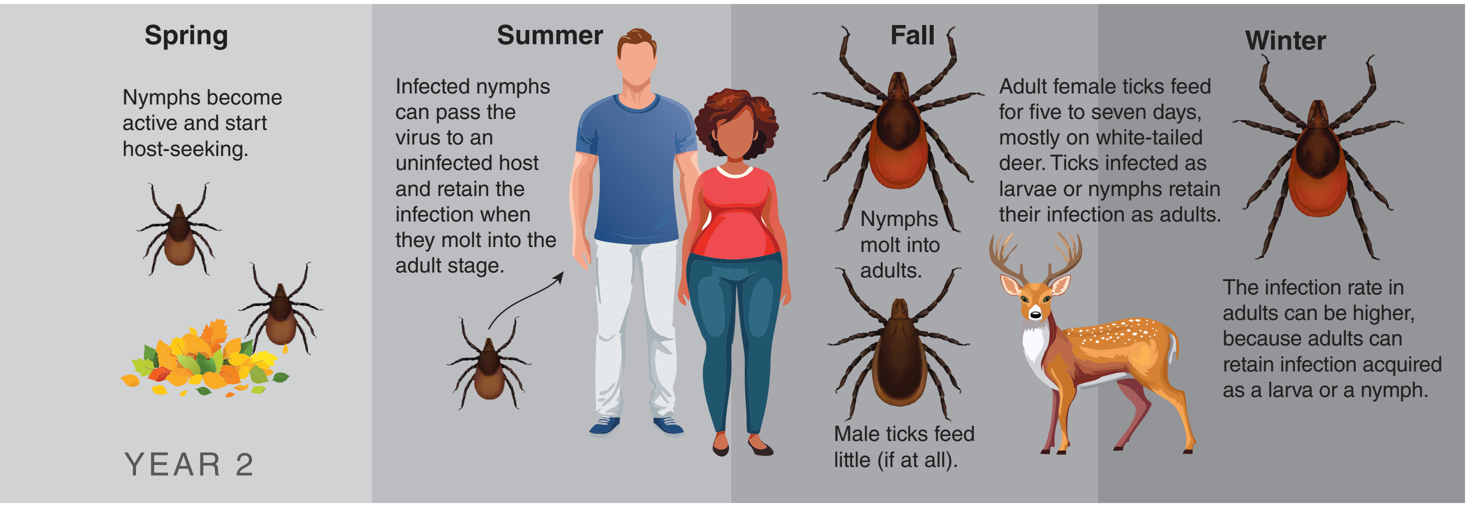
Europeans can access accurate maps of TBE for most of their continent, where public health agencies conduct field surveys to locate areas with infected ticks. Vaccine companies make maps that show recommended areas for TBE vaccination, and health officials use these maps to encourage people to take precautions against tick bites. Maps of areas at elevated risk for TBE in Europe differ from those for Lyme disease in the United States because TBE remains confined to certain ecological areas with specific combinations of ticks and wildlife. People in the United States can find maps showing areas of substantial Lyme disease risk, but no such maps exist for Powassan virus.

Another likely explanation for the low case reports is simply that Powassan may be vastly underreported. The virus is difficult and slow to diagnose clinically, and a diagnosis is made only if the patient gets sick enough to see a doctor who knows of Powassan virus and its symptoms. That doctor must also submit a blood sample to their state health department or to the CDC for analysis, and the relevant agency must officially recognize and report the case as Powassan. But Powassan cases have only recently joined the ranks of conditions reportable to state health departments and the CDC, and these reports remain voluntary. Moreover, people with mild symptoms are rarely reported and are not studied to see if they remain healthy.

The Challenges Ahead

If we hope to grapple with the growing threat Powassan presents, we need more studies to determine infection rates and to pinpoint where transmissions occur, especially in states where the virus is likely underreported. Only then will we understand the magnitude of the problem, and only then will we be able to develop actions that protect people from infection. High-profile and fatal cases like that of Senator Hagan make the news and raise temporary awareness of the disease, but interest soon fades. As for the more than $1 billion in funding allocated by Congress via the 2019 Kay Hagan Tick Act, I find no evidence that any of it has been directed toward researching the disease that actually killed the senator; instead, it has likely gone toward combatting all vector-borne diseases, including mosquito-borne diseases like West Nile and dengue fever. That these diseases are more prevalent and have higher incidence than Powassan may help justify this past oversight, but it does not reduce the urgency of tracking and combating the virus as its prevalence grows.

To understand the task ahead of us in battling Powassan, let us consider Lyme disease once again. Efforts to control



Barbara Aulicino

the current Lyme epidemic have met with only limited success, as evidenced by the steady increase in cases reported over the past several decades. Methods to control ticks in the environment have been only partially successful, and none have significantly reduced the number of Lyme disease cases. If we cannot control Lyme disease, how can we control Powassan?

To make matters worse, experiments show that the recently introduced Asian longhorned tick, *Haemaphysalis longicornis*, which feeds upon wildlife, domestic animals, and humans, can transmit Powassan virus both horizontally and vertically—that is, between hosts and from female ticks to their offspring. From its first detection in New Jersey in 2017, this invasive tick has spread across the mid-Atlantic states and into the Midwest. Nor should we ignore the potential effects of pathogens that coinfect vectors; for example, a recent study shows that deer ticks infected with both the Lyme disease bacterium and the Powassan virus develop elevated quantities of Powassan in their midguts and salivary glands, resulting in more efficient transmission to wildlife and humans.

We should be concerned. Incidence is increasing, and there is no vaccine in sight. Research on a vaccine for Powassan virus remains in its infancy, with only a few laboratory studies on mice being conducted by university researchers. Were a promising candidate discovered, the required clinical trials would take two to three years, after which the vaccine would enter the process for receiving approval for human use from the U.S. Food and Drug Administration. Because pharmaceutical companies balk at investing the substantial funds necessary to conduct clinical trials for a disease with low incidence, many more cases would be required to justify the investment. Europe, Russia, and China offer a few different vaccines for TBE, but none work on its cousin Powassan.

Yes, Powassan is rare, and we must weigh that. But if risk is calculated from both likelihood and harm then we must also weigh the stark reality that a single tick bite can deliver a fatal dose of Powassan virus within minutes, that survivors can suffer long-term neurological effects, and that the likelihood of getting bitten by Powassan-infected ticks is rising. This troubling reality should drive us to make greater efforts to prevent tick bites in areas where Powassan reports occur, especially where they affect the elderly (the average age for Powassan cases is 69) and the immunocompromised.

The spread of Powassan virus is a reminder of the importance of remaining vigilant as diseases appear, spread, and evolve. Protecting people is a chief duty of governments, one that cannot be shirked without dire consequences. As for Powassan, public health agencies should increase their efforts to detect the infection in ticks, actively report human cases, and create and distribute accurate maps of high-risk areas. The need for such proactive and protective measures will only grow as Powassan vectors continue to spread.

Bibliography

Campbell, O., and P. J. Krause. 2020. The emergence of human Powassan virus infection in North America. *Ticks and Tick-Borne Diseases* 11:101540.

Costero, A., and M. A. Grayson. 1996. Experimental transmission of Powassan virus (*Flaviviridae*) by *Ixodes scapularis* ticks (Acari: Ixodidae). *The American Journal of Tropical Medicine and Hygiene* 55:536–546.

Ebel, G. D., and L. D. Kramer. 2004. Short report: Duration of tick attachment required for transmission of Powassan virus by deer ticks. *The American Journal of Tropical Medicine and Hygiene* 71:268–271.

Fish, D. 2021. Range expansion of *Ixodes scapularis* in the USA. In *Climate, Ticks and Disease*, ed. P. Nuttall, pp. 176–182. CABI.

Hart, C. E., F. A. Middleton, and S. Thangamani. 2022. Infection with *Borrelia burgdorferi* increases the replication and dissemination of coinfecting Powassan virus in *Ixodes scapularis* ticks. *Viruses* 14:1584.

MacCleery, D. W. 1992. *American Forests: A History of Resiliency and Recovery*. FS-540. U.S. Department of Agriculture, Forest Service, in cooperation with the Forest History Society.

Nofchissey, R. A., et al. 2013. Seroprevalence of Powassan virus in New England deer, 1979–2010. *The American Journal of Tropical Medicine and Hygiene* 88:1159–1162.

Obellianne, C., P. D. Norman, E. Esteves, and M. E. Hermance. 2024. Interspecies cofeeding transmission of Powassan virus between a native tick, *Ixodes scapularis*, and the invasive East Asian tick, *Haemaphysalis longicornis*. *Parasites & Vectors* 17:259.

Vogels, C. B. F., et al. 2023. Phylogeographic reconstruction of the emergence and spread of Powassan virus in the northeastern United States. *Proceedings of the National Academy of Sciences of the U.S.A.* 120:e2218012120.

Durland Fish is emeritus professor of epidemiology at the Yale School of Public Health. He holds a master's degree in entomology from the University of Massachusetts Amherst, and a doctorate in entomology and ecology from the University of Florida. After receiving a U.S. National Institutes of Health fellowship to study vector ecology at the University of Notre Dame, he became assistant professor at Fordham University in New York, associate professor at New York Medical College, and professor at Yale. Email: durland.fish@yale.edu

Scientists' Nightstand

The Scientists' Nightstand, American Scientist's *books section, offers reviews, review essays, brief excerpts, and more. For additional books coverage, please see our* Science Culture *blog channel online, which explores how science intersects with other areas of knowledge, entertainment, and society.*

ALSO IN THIS ISSUE

ME, BUT BETTER: The Science and Promise of Personality Change. By Olga Khazan.
page 186

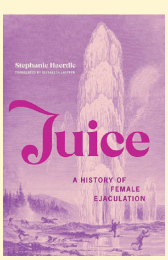
EINSTEIN'S TUTOR: The Story of Emmy Noether and the Invention of Modern Physics. By Lee Phillips.
page 187

ONLINE

On our *Science Culture* blog:
www.americanscientist.org/blogs/science-culture

The Demystification of Female Anatomy

Digital managing editor Nwabata Nnani reviews *Juice: A History of Female Ejaculation* by Stephanie Haerdle and translated by Elisabeth Lauffer.



Sweet Deceit

Kelly Brownell

SWEET AND DEADLY: How Coca-Cola Spreads Disinformation and Makes Us Sick. Murray Carpenter. 344 pp. The MIT Press, 2025. $29.95.

If the food industry established a Hall of Fame to honor companies that have compromised and co-opted both scientists and professional organizations, created pseudoscientific front groups, diverted attention from the harms of its products, distorted science, and undermined public health, Coca-Cola would surely be elected on the first ballot.

The company's manipulation of science is laid bare in journalist Murray Carpenter's new book *Sweet and Deadly: How Coca-Cola Spreads Disinformation and Makes Us Sick*. Carpenter explores how Coca-Cola has gotten away with these actions for so long and argues that not only does Coca-Cola significantly contribute to chronic disease, it has also actively and purposefully spread disinformation for decades to hide the health risks associated with its sugary beverages. These beverages are uniquely harmful, with "some scientists say[ing] they are the single item that most contributes to obesity and maladies such as type 2 diabetes and cardiovascular disease." Carpenter even goes on to say that drinking Coca-Cola and other sugar-sweetened drinks is one of the biggest threats to public health in the United States.

Carpenter notes that when previous corporate misbehavior by cigarette, opioid, and other industries has eventually come to light, it was often followed by policies, litigation, and other actions to protect the public. Coca-Cola, Carpenter says, is different, in that it "has countered its critics better than any other major corporation. The brand seems ever enshrouded in an aura of goodness and happiness. Its public relations campaigns are so effective that many Americans still have not gotten the memo about the health risks posed by sodas."

Drawing from court records, internal company documents, and investigative reporting, the book covers a range of related topics. Carpenter delves into the long-standing appeal of Coca-Cola products as well as their potentially addictive components; examines the disinformation campaigns intended to counter research linking sugared beverage consumption to diabetes, obesity, heart disease, and other ailments; and outlines Coca-Cola's systematic effort to undermine attempts at regulation and legislation, particularly soda taxes. He also illustrates the outsized effect of sugared beverages on communities of color, and how public exposure of Coca-Cola's disinformation campaigns has seemingly had no impact on its overall success.

Coca-Cola's disinformation efforts can be traced as far back as the 1940s, when alarms began sounding about sugar consumption and health. In the decades that followed, the science on sugared beverages expanded greatly and was joined by evidence on the addictive properties of certain foods, research on marketing (particularly to children), and concerns that pairing caffeine with sugar keeps people wanting more.

Carpenter describes Coca-Cola's highly sophisticated, well-funded, decades-long effort to convince the public, elected leaders, and bodies like the World Health Organization that its products do not cause harm and are actually good for people (hydration!). These efforts have included encouraging a focus on physical inactivity, rather than diet, to address obesity and diabetes.

In 2009, Coca-Cola partnered with two of the largest physical fitness organizations—the American College of Sports Medicine and the National Strength and Conditioning Association—to create a health program called Exercise is Medicine that emphasized exercise over diet. The beverage company was also the first corporate partner of the American Academy of Family Physicians (AAFP), which triggered the public resignation of more than a dozen doctors from the organization. Coca-Cola also went on to donate millions of dollars to the AAFP and the Academy of Nutrition and Dietetics (AND), formerly the American Dietetic Association. What did the donations buy? Silence for the most part, but also prominent speaking roles at national meetings, panels populated by industry-funded scientists, and in the case of AND, position statements on the benefits of sugared beverages (underwritten by Coca-Cola). The goal, of course, was to give credibility to the beverage company by masking the harmful effects of its products.

Carpenter exposes the Global Energy Balance Network (GEBN), which was created by two prominent researchers. GEBN was portrayed as a worldwide network of scientists doing credible work and became highly visible in the media. The organization issued reports, videos, and press statements that cast doubt on health research about diet, and the scientists involved spoke repeatedly to the press and were keynote speakers at major scientific meetings.

Two other facets of the debate about soda consumption and health are socioeconomic status and race. In lower-income and rural areas, good grocery stores are typically lacking, leaving only stores like Save A Lot, a discount supermarket chain, or convenience stores and bodegas. These stores are often filled with cheap, high-calorie, processed foods, which means people in these areas have fewer options and opportunities to eat nutritious diets. And sugared drinks are "the top items purchased with food stamps—generating about $6 billion in annual revenue for the beverage industry."

Yolanda Hancock, a pediatrician who studies obesity, states that Americans of color disproportionately consume Coca-Cola, and that this is not an accident. The soda industry targets people of color, she says, explaining that "on BET and these other 'Black channels' you're going to have the industry buying more ad time." Black children see twice as many soda ads as white children.

Eduardo Soares/pexels.com

Coca-Cola can be found almost anywhere, which is by design. Signage, product displays, and advertisements for the company are highly visible at sports events of all levels, airports, colleges and universities, and shopping venues. There is no other brand that is as ubiquitous as Coca-Cola. This is also not unique to America: Coca-Cola products are sold in more than 200 countries—and in developing countries, the brand is seen as a marker of wealth and sophistication.

By 2020, soda consumption among Americans was decreasing, with soda taxes playing a major role in the decline. However, although soda consumption may be declining, the sales of other sugar-sweetened drinks made by Coca-Cola and other companies are increasing. These include juice drinks and energy drinks.

Health professionals have long noted the striking similarities between the food industry playbook and tactics used by the tobacco industry. Carpenter observes that the tobacco playbook was, in fact, based on tactics developed by the sugar industry and refined during the years when major food companies were owned by tobacco giants.

Had Coca-Cola and other companies not acted this way for decades, the public would have known much sooner of the dangers of these products. Sugared beverage taxes might exist in many more jurisdictions. There would likely be much stronger labeling and warning requirements, along with strict boundaries on what can be marketed to children and pushed in schools. Companies might have been required to gradually reduce the sugar in their products. Would any of these changes have made a difference? What might the benefits have been on death and disability rates worldwide? If these potential benefits could be calculated, then the appalling impact of corporate influence on worldwide public health might finally become clear.

Kelly Brownell is dean emeritus and Robert L. Flowers professor emeritus in the Sanford School of Public Policy at Duke University. He cofounded the Rudd Center for Food Policy and Obesity at Yale University and founded the World Food Policy Center at Duke.

The Struggle Against Oneself

Daniel K. Mroczek

ME, BUT BETTER: The Science and Promise of Personality Change. Olga Khazan. 288 pp. Simon Element, 2025. $28.99.

Original: Anna Tunikova for peats.de and Wikipedia Vector: EssensStrassen/CC 4.0

The "Big Five" personality traits were derived from findings in early studies that used descriptors grouped together through factor analysis. Later research found a sixth factor, Honesty-Humility. Still, many people continue to refer to the Big Five when discussing personality traits and personal development.

Can someone change their personality? That question lies at the heart of Olga Khazan's newest book, *Me, But Better: The Science and Promise of Personality Change*. Khazan documents her attempts to alter her personality and become happier over the course of one year. Psychological research shows that personality does change for many people, but usually as a result of biological processes such as brain maturation or social changes such as new roles (for example, becoming a parent or starting a career). Khazan became motivated to try changing her personality after taking a personality test that showed her combination of traits were correlated with unhappiness and dysfunction. Tired of feeling "neurotic, introverted, and disagreeable," she set out to alter her personality.

Personality is thought by some to be made up of specific traits known as the "Big Five": neuroticism, extroversion, agreeableness, openness to experience, and conscientiousness. Taken together, levels of these traits are said to predict how a person will respond to situations.

Khazan opens the book with an exploration of what personality is, followed by a chapter on how personality changes. Then she dedicates a chapter to each of the Big Five before coming to conclusions about her year of personality change.

Before starting her project, Khazan consulted various academic experts on personality development and trait change, along with some nonexperts best described as self-help coaches. "The best personality-change interventions help people figure out what they want to change, tell them how to change, and remind them to continue changing," she writes. Khazan states early in the book that personality change might simply be a matter of remembering how you'd like to be and then acting that way—consistently. She then sets out to change her personality by focusing on each of the five traits for a few months, starting with extroversion.

After initially scoring "very low" on extroversion, Khazan decides to start her journey by trying something that would force her to leave her house and be social. Improv comedy is the first thing she settles on, because improv forces participants to interact and just say *something* in response to the other person. She then joins a sailing club and realizes that socializing in person provides the real-life interaction and contact she hadn't known she was missing, despite interacting with others all day on the computer. Later, at a party she decides to host, she realizes that, although she may be doing many of these things for the book, they also simply make her feel good. By the time she retakes the introversion section of the personality test at the end of the first part of her project, her score has gone up to "about average."

From there, Khazan tries a wide variety of other activities for the remaining traits, such as workshops on how to be a better conversationalist, a sensory deprivation tank, yoga, different kinds of meditation, and even surfing lessons. Some strategies Khazan tries seem questionable at first blush (such as using the drug MDMA (3,4-methylenedioxymethamphetamine, also known as ecstasy), whereas others are more established, such as cognitive behavioral therapy, which has almost 60 years of strong empirical support for its effectiveness. (By contrast, in the summer of 2024, a United States Food and Drug Administration advisory panel declined to approve MDMA-assisted therapy for the treatment of post-traumatic stress disorder.) Indeed, the activities Khazan chooses to participate in during her year of attempting personality change vary widely. In addition, she appears to give equal weight to both scientists who study personality change and untrained entrepreneurs who hawk untested, unvalidated techniques.

Still, the book shines whenever Khazan weaves her refreshingly honest tales of her often entertaining attempts at personality change into the narrative. Through sharing her personal and family history, as well as her experiences being a woman in America, she reveals a great deal about her inner fears and anxieties, expresses her vulnerabilities, and puts her experiences out there for all to see, making for a relatable narrator.

Khazan acknowledges that personality change requires sustained hard work and an ability to do things that make one uncomfortable: "But month after month, I dreaded the highway, or the improv showcase, or the stressful situation *du jour*, and ran into it anyway. This is what personality change looked like in the end: fits and starts, with the goal being for the starts to outnumber the fits."

The self-experiment in personality change laid out in *Me, But Better* is something very few professional personality researchers (including myself) would try on their own, and for this Khazan deserves praise. Ultimately, she comes to the conclusion that achieving large-scale change is not realistic, and instead she is satisfied by small but noticeable improvements. She wanted to reduce her neuroticism, which previously caused her large amounts of fear and anxiety. Although her core trait levels are still mostly where they were at the beginning of the experiment, they are altered in slight but important ways that make her life healthier and happier, such as not using alcohol to cope with anxiety. Though fear and anxiety are still present, her responses to these feelings and stressors have changed.

By the end of her endeavor, Khazan asks a question that many personality development researchers have asked in recent decades: How deep and lasting are the personality changes many of us work hard to make? Khazan's attitudes and behaviors did change over a year, at least based on her personality test scores, but does that qualify as a "new personality"? The personality changes that Khazan tried to produce—dramatic alterations that occur over a short period of time—rarely last. The transformation may look profound on the surface, but our inner selves may not have transformed much at all. Khazan herself considers this possibility near the end of the book: "Is it real, or is it all an act? Does a person's changed behavior mean they've truly changed? Or if it requires continual effort, does it mean they haven't really? And does it matter?"

Daniel K. Mroczek is a professor at Northwestern University, where he has a dual appointment across the Feinberg School of Medicine and the Weinberg College of Arts and Sciences. His research focuses on behavioral medicine, lifespan personality development, health psychology, cognitive aging, dementia, and mortality risk.

Hidden Genius

Megan Shields Formato

EINSTEIN'S TUTOR: The Story of Emmy Noether and the Invention of Modern Physics. Lee Phillips. 368 pp. PublicAffairs, 2024. $30.00.

From the very first page of *Einstein's Tutor: The Story of Emmy Noether and the Invention of Modern Physics*, physicist and science writer Lee Phillips asserts that mathematician Emmy Noether belongs among the most familiar names involved in the invention of modern physics, next to Albert Einstein and Erwin Schrödinger, to name a few. He quickly makes it clear that she doesn't belong there merely as Einstein's tutor, as the title of the book suggests, but as an equal.

The early pages of the book are filled with a dizzying array of Noether's accomplishments meant to unambiguously illustrate her exceptional mathematical talents and the singular significance of her contributions. Most strikingly, Noether's 1918 theorem provides the foundation for a unified theory of physics by showing a clear relationship between symmetry and the conservation of energy. Her theorem "supplied the methodology for constructing the most accurate theory in the history of physics: the standard model. This framework encompasses all the elementary particles and their interactions—it is our modern theory of matter." Her theorem also "provides the modern definition of the concept of energy and clarifies the importance of symmetry in nature." Furthermore, Noether's mathematics and "repeated and focused help" were essential for the completion of Einstein's theory of general relativity. At a critical time when Einstein was struggling with the mathematics required for his theory, he relied on Noether's work in abstract algebra and variational calculus to complete it. But despite her brilliant mathematics that continue to be applied across many areas of modern science—including physics, biology, and economics—Noether's name is still unknown to many.

Noether was a Jewish German mathematician who relentlessly pursued a mathematics education and research career in the face of significant gender barriers and, especially during Hitler's rise to power, religious discrimination. She earned her doctorate from the University of Erlangen and became a professor of mathematics at the University of Göttingen where she worked with some of the leading minds in mathematics at the time, including Felix Klein and David Hilbert.

A careful explanation of Noether's 1918 theorem and how it redefined the role of symmetry in mathematics is the heart of the book. The theorem is actually four theorems: two theorems and their converses. They establish that conservation laws can be derived from symmetry and that symmetry can be derived from conservation laws, showing that these two essential ideas for understanding the structure of the universe, which had previously been treated as mathematically and conceptually separate, were in fact conceptually linked.

Phillips describes how before Noether, "symmetry was a guide to the overall patterns of reality. It served as a concise description and sometimes as an aid to constructing the solution to a problem." After Noether's theorem,


Wikimedia Commons

When it became clear to Emmy Noether that she would likely never marry, she pursued teaching and became certified to teach French and English to girls. Her father was a mathematician, and she started auditing classes, including math and science. In 1903, Noether began postgraduate studies and would go on to be one of the greatest mathematicians of that era.

symmetry had a new role: It could and did "govern what could and could not happen wherever it was present." It was not just a pattern of reality anymore; it became a law.

Phillips spends a lot of time explaining Noether's theorem in detail, and he succeeds in making it accessible to a general audience. Complex ideas from mathematics and science are presented using intuitive and conceptual examples, and he makes few assumptions about his reader's prior mathematical knowledge. Some of the most elegant science communication in the book unfolds as Phillips walks us through what symmetry means in Noether's theorem. He carefully explains that symmetry for Noether goes beyond familiar examples like mirror images or the symmetry between butterfly wings. Instead, a thing had symmetry for Noether "if it is the same in every way after you apply a transformation." In other words, general symmetry describes any time you can make a transformation to something (such as by rotating or reflecting it) and change its meaning, but not its physical reality. Phillips helps his reader grasp this challenging idea with familiar examples. For instance, the ground floor of a building might be labeled the "1st floor" or the "lobby." This example describes symmetry because the name of the floor has changed, but the physical reality of the building has not.

Though Phillips recognizes Noether's remarkable skills and value as a mathematician, his clear assertions about Noether's foundational role in modern science are often paired with far more hesitant explanations about how or why her male colleagues failed to credit her work at the time. He makes sure to note that Noether did not care for self-promotion, freely gave away results to students and younger colleagues, and was happy to provide help to those who needed it. When it comes to pointing out that her work was not consistently credited by her male colleagues, Phillips almost seems to apologize for breaking the news to the reader. Before detailing how physicist Wolfgang Pauli cited the work of all of his male colleagues in an encyclopedia article on relativity while excluding Noether's essential contributions to the mathematics, Phillips writes that Pauli's actions will be "painful for physicists to contemplate." And there is a marked reluctance to his statement that "we must confront the apparent likelihood that certain authors suppressed or omitted her contributions where it would have been natural to do the opposite."

Throughout *Einstein's Tutor*, Noether emerges as a singular figure, capable of overcoming obstacles to contribute elegant and transformative solutions to thorny and significant problems in mathematics. Despite this insistence on Noether's individual genius, the book puts forward a remarkable story about the importance of collaboration in the construction of mathematical and scientific theories. Describing mathematics at Göttingen in 1915, Phillips creates a picture of mathematicians and physicists like Klein, Hilbert, and even Einstein, all of whom we are accustomed to seeing as individual geniuses, embedded in an "academic web" of interdisciplinary work, dependent on one another's ideas. And all of them are described as reliant on Emmy Noether's fluency in complex mathematics to move forward in their work. In this way, *Einstein's Tutor* asks us to reconsider who can be a genius, who is instead described as a collaborator, and how gender shapes the use of the trope of the scientific genius in the stories we tell about how modern science was made.

Megan Shields Formato is a historian of modern science and technology. Her research focuses on the history of scientific communication and the role of women in science. She is an advanced lecturer in Stanford's Program in Writing and Rhetoric, where she teaches courses in scientific communication and the relationship between technology and culture.

Sigma Xi Today

A NEWSLETTER OF SIGMA XI, THE SCIENTIFIC RESEARCH HONOR SOCIETY

Call for Leadership Nominations

Sigma Xi is seeking nominations for qualified candidates to fill positions for the Board of Directors, Associate Directors, and the Committee on Nominations for representation of regions and constituencies. The following positions carry three-year terms:

Board of Directors:

- Membership-at-Large Constituency
- Mid-Atlantic Region
- Northeast Region
- Research and Doctoral Universities Constituency

Associate Directors:

- Area Groups, Industries, State & Federal Labs Constituency
- Comprehensive Colleges & Universities Constituency
- Northwest Region
- Southeast Region

Committee on Nominations:

- Baccalaureate Colleges Constituency
- Canadian/International Constituency
- North Central Region
- Southwest Region

Nominations should be submitted to **elections@sigmaxi.org** by June 30, 2025. Active full members of Sigma Xi are eligible to run for office. An inactive member may become active at any time through payment of current dues. Sigma Xi seeks diverse and inclusive slates for all its elected positions. Self-nominations are welcomed. Visit **sigmaxi.org/elections25** to view a list of duties and responsibilities for each position, as well as full qualification criteria.

Sigma Xi Today is managed by **Jason Papagan** and designed by **Chao Hui Tu.**

From the President

A Year of Progress and the Road Ahead

As we approach the end of the 2025 fiscal year, I have been reflecting on my own year as Sigma Xi president with great pride. Our journey has been one of growth, collaboration, and commitment to scientific excellence. We have made remarkable strides in expanding our community, fostering interdisciplinary partnerships, and reinforcing our dedication to research integrity.

Over the past 12 months, Sigma Xi has strengthened its role as a beacon for research excellence. Thanks to the collective efforts of the entire Sigma Xi community, we have seen a historic 12 percent increase in membership, marking the first membership increase in decades. This surge reflects renewed interest in the Society's mission. We have also made significant progress in narrowing our budget gap, putting Sigma Xi back on a strong financial footing.

The 2024 International Forum on Research Excellence (IFoRE) brought together researchers from diverse fields to celebrate excellence, foster interdisciplinary collaboration, and emphasize ethical research practices. We provided opportunities for emerging scientists—high school, undergraduate, and graduate students—to present their work, gain valuable feedback, and engage with seasoned researchers.

Moreover, our international outreach efforts continue to grow, with new members and partnerships expanding our footprint beyond North America.

Despite these many clear successes, we must recognize the challenges that lie ahead—ones that we must meet with resilience, creativity, and a shared sense of purpose.

Misinformation and distrust in science have become widespread. Scientists must not only conduct rigorous research but also advocate for evidence-based decision-making. Cuts to funding could slow down groundbreaking discoveries, limit access to essential resources, and put increased pressure on researchers. This challenging environment may also disproportionately impact emerging scientists and underfunded research areas, exacerbating existing disparities in the scientific community.

Sigma Xi members have a responsibility to engage both the public and policymakers. We must continue to communicate our findings effectively, advocate for evidence-based policies, and inspire a deeper public appreciation for scientific inquiry. Sigma Xi is more than just a peer group organization. It is a community bound by shared values—research excellence, ethics, and honor. Our strength lies in our ability to support one another, to foster collaboration, and to champion the role of science in society.

As we move forward, I encourage each of you to actively engage in Sigma Xi initiatives, promote science tirelessly, mentor young researchers, advocate for responsible science, and contribute to our collective mission. And I encourage you to remember: Science is about the responsibility we bear to use knowledge for the betterment of humanity.

Kathy Lu **Kathy Lu**

2025 International Forum on Research Excellence

IFoRE POWERED BY SIGMA XI

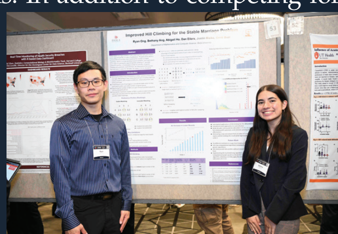
November 6–9, 2025 | Niagara Falls, New York

Sigma Xi's annual conference, the International Forum on Research Excellence (IFoRE), will take place November 6–9, 2025, at the Niagara Falls Convention Center in Niagara Falls, New York. Now in its fourth year, IFoRE is an immersive demonstration and celebration of excellence in research across all STEM disciplines. The conference is open to all researchers and supporters of science worldwide, including Sigma Xi members, students, educators, policymakers, and science communicators.

Visit **experienceIFoRE.org** to register.

Student Research Competition

One of the flagship components of IFoRE is the presentation of student research from high school, college, and graduate school attendees. Students will share their research with professional judges and attendees via oral or poster presentations. In addition to competing for cash prizes and awards in each discipline, all presenting students will gain science communication experience and mentoring opportunities through career workshops and professional networking events in their field of study.



Award-Winning Speakers

Keynote and general sessions will provide attendees with the opportunity to take part in lively discussions, interviews, and presentations of cutting-edge research. Many sessions will tie into the conference's theme, "Science and Society: Crafting a Vision for a Sustainable Tomorrow."

Awards Banquets

IFoRE attendees will be treated to prestigious speakers, special programming, and award ceremonies while they meet, greet, and eat at the Saturday evening awards banquet.

Friday Night at IFoRE

The Friday night party at IFoRE is the best time you can have at a STEM conference networking event! Take part in games, dancing, photo booths, food, and more as we roll into the IFoRE weekend.

Headshots

Free professional headshots for all IFoRE attendees!

Exhibitors

Learn about exciting new programs and find your next school or career opportunity by visiting the IFoRE exhibitor booths.

FACES of GIAR: Sarah Donaher

Grant: $1,000 in Spring 2022
Education level at time of the grant: PhD student

Project Description:
I investigated the response of an estuarine "sentinel" species after exposure to radioactive pollutants. The historical use of radioluminescent objects containing radium-226 (^{226}Ra)–based paint has resulted in contemporary environmental contamination of radioactive material, often near military-associated coastal sites. I conducted the first mechanistic study of the uptake and effects of ^{226}Ra in a marine mollusk, with the intention of informing biomonitoring schemes to ensure adequate protection of environmental health from legacy radioactive material. This grant supported travel to visit collaborators and to collect samples, as well as supplies for antioxidant assays in the lab.

How did the grant process or the project itself influence you as a scientist/researcher?
The grant process gave me one of my first opportunities to independently shape the future of my research by learning how to pitch my ideas, create and manage a budget, and justify the use of funds and the direction of the project. The grant really helped me take ownership of my own research, and it provided me with flexibility to pursue "high risk, high reward" research that resulted in publication in a high impact journal.

What advice would you give to future applicants?
Do your best to highlight the applications of your research, including future research lines and relevance to industry. And again, consider using this grant as a chance to pursue "high risk, high reward" research.

Where are you now?
In August 2024, I began as an assistant professor in the Department of Civil and Environmental Engineering at the University of Tennessee, Knoxville, with a joint appointment in the Department of Nuclear Engineering.

FACES of GIAR: Ryan Wang

Grant: $644 in Fall 2022
Education level at time of the grant: Undergraduate student

Project Description:
Neurological disorders are one of the world's leading causes of disability and loss of life. Neuromodulatory methods have improved scientific understanding of neural behavior and circuitry by precisely stimulating an area of the brain. Acoustically targeted chemogenetics (ATAC) is one method of neuromodulation that allows for high spatial and temporal specificity without the risks of surgery.

The project assessed the feasibility of targeting multiple sites with ATAC, thereby expanding its applications in science and medicine. Using focused ultrasound (FUS) and microbubbles to induce blood–brain barrier opening (FUS-BBBO), adeno-associated viruses (AAVs) can deliver genes for designer receptors exclusively activated by designer drugs (DREADDs) to a specific neuronal area. Cells expressing DREADDs are then activated or inhibited by specific synthetic drugs such as clozapine N-oxide.

How did the grant process or the project itself influence you as a scientist/researcher?
The grant helped validate my abilities as a scientific writer and thinker, inspiring my confidence to seek other research opportunities and affirming my aspirations to pursue a research career. During the grant process, I had to think very carefully about my past and future research work; by contextualizing the importance of my work, I am now more cognizant of the impact of my research. I also learned how to write an effective research statement and create a project budget. Financially, the grant allowed me to focus on my research project while helping to relieve its financial burden on my lab. Through the project itself, I have become more familiar with some of the in vivo neuroscience methods I may implement in future research.

What advice would you give to future applicants?
Start early and consult your mentors for feedback! Communicate your research idea in an understandable yet eloquent way for the benefit of the reader, who may have minimal background in your research area.

Students may apply for Sigma Xi research grants by March 15 and October 1 annually at sigmaxi.org/giar.

Sigma Xi Relaunches Emotional Support Program Through Happy Partnership

happy
FRICTIONLESS MENTAL HEALTH™

In March of this year, Sigma Xi announced a renewed partnership with Happy: Frictionless Mental Health™. The collaboration provides mental health services for Sigma Xi members, including a free hotline and monthly "Happy Hour" emotional support sessions.

The two organizations previously collaborated in 2021 to support the scientific research community with mental health concerns caused or amplified by the COVID-19 pandemic. Now, as the landscape of scientific research continues to evolve amid new uncertainties, Sigma Xi has reaffirmed its commitment to the emotional well-being of its members by reintroducing Happy's proactive peer-based support model—a first-of-its-kind solution designed to provide real-time human connection when it's needed most.

The renewed partnership educates Sigma Xi members on the benefits of emotional support and provides personalized, peer-based support services at no cost. The Happy platform uses advanced data and a unique vetting process to provide a network of on-demand services that connect individuals with uniquely qualified support givers.

"At a time when scientific research is more critical than ever, we must ensure that our members have the emotional support they need to thrive," said Sigma Xi CEO Jamie Vernon. "By renewing our partnership with Happy, we have reinforced our commitment to the well-being of researchers at all career stages, providing them with a proactive support system that meets them where they are."

Sigma Xi members can access services and learn more about Happy's frictionless mental health model by visiting **sigmaxi.org/happy**.

Standing Together for Science in Uncertain Times

The following is an excerpt from a letter sent to members from Sigma Xi leadership on March 7, 2025. Visit **sigmaxi.org** *to read the full letter.*

Scientific research is essential to addressing global challenges, expanding knowledge, and driving technological and economic progress. Since its founding at Cornell University in 1886, Sigma Xi has played a vital role in advancing the American research community and, in recent decades, has contributed to scientific progress worldwide.

However, recent actions by the Department of Government Efficiency (DOGE) and broader shifts in federal science policy have created uncertainty about the future of U.S. research funding. Delays, conflicting information, and funding disruptions are not only causing anxiety among researchers but also threatening vital discoveries and slowing scientific progress.

Sigma Xi is committed to standing with all our members, offering support, and working toward solutions. To help navigate these uncertain times, we are renewing and expanding initiatives to provide direct assistance to our members:

- **Mental Health Support**—We are relaunching our program to provide mental health resources for members experiencing stress and anxiety due to ongoing challenges in the scientific landscape.
- **Job and Career Support**—For those who have lost positions or resigned from federal agencies, Sigma Xi will create a dedicated platform for sharing job opportunities and career resources.
- **Informational Webinars**—We will host a series of webinars featuring policy experts, university leaders, and science advocates to help our community navigate the rapid changes affecting federal science policy.

We encourage you to contact your elected representatives to express your concerns about cuts to federal research funding and policies that undermine scientific progress. You can find your representatives and their contact information at **house.gov/representatives/find-your-representative**.

This is a pivotal moment for the scientific community. While the challenges we face are significant, so is our collective strength. Sigma Xi remains committed to advocating for research, supporting our members, and working with our partners to ensure a strong and stable future for science.

Sincerely,

Kathy Lu,
President

Dan Rubenstein,
President-Elect

Marija Strojnik,
Immediate Past-President

Jamie L. Vernon,
Executive Director

and the Board of Directors
Sigma Xi, The Scientific Research Honor Society

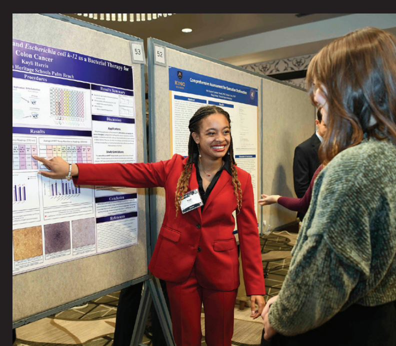
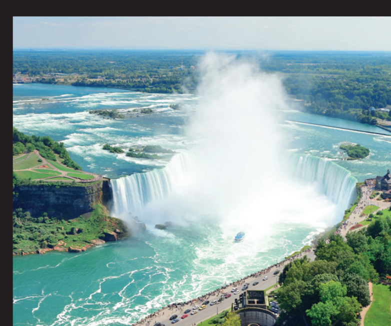
IFoRE

POWERED BY SIGMA XI

INTERNATIONAL FORUM ON RESEARCH EXCELLENCE

Science and Society: Crafting a Vision for a Sustainable Tomorrow



November 6–9, 2025

Niagara Falls, New York | Niagara Falls Convention Center

experienceIFoRE.org

How is this even possible? This necklace is FREE!

A Huge Carat Weight for the Incredible Price of F-R-E-E

JOIN MORE THAN 3 MILLION STAUER JEWELRY CLIENTS

Stauer® Impossible Price FREE Necklace

A.

You may think you know what "priceless" means—usually, it just means "astronomically expensive." But not at Stauer. Priceless means FREE.

Stauer is smashing luxury norms with our **FREE 77-Carat Durango Howlite Necklace.** That's right—zero dollars.* This genuine howlite piece, valued at $299, is yours for **FREE**—just cover $24.95 for shipping and processing. Plus, we'll send a **$25 Discount Coupon**, making shipping Better Than Free! No tricks, no obligation—though resisting our luxury deals won't be easy.

B.

C.

Why give away jewelry? Because once you see Stauer's rare gemstones and vintage-inspired watches, we know you'll fall in love. If not, keep your FREE necklace—no hard feelings.

Howlite, discovered in Nova Scotia, has been a gemologist's secret, often compared to turquoise. Our Durango Collection channels classic Southwest jewelry, featuring blue-green beauty in oxidized silver settings. Get nearly **160 carats** for just **$79!**

This deal won't last—we only have **2,500 left.** Call now to claim your **FREE** necklace and experience a new kind of priceless luxury!

Jewelry Specifications:

- Enhanced howlite.
- Oxidized silver finish.
- Necklace: 23" + 2", lobster clasp.
- Earrings: 3" drop, French wire.
- Bracelet: 7", elastic.

Durango Collection—Call In Only

A. Necklace (77 ctw)	~~$299~~	**FREE*** + S&P	*Save $299*
B. Earrings (23 ctw)	~~$199~~	$49* + S&P	*Save $150*
C. Bracelet (58½ ctw)	~~$299~~	$49* + S&P	*Save $250*
Set of all 3	~~$797~~	$79* + S&P	*Save $718*

**Special price only for customers using the offer code.*

1-800-333-2045

Your Insider Offer Code: DHC119-01

* This offer is valid in the United States (and Puerto Rico) except in TX, FL, CO, OK, RI, NH, WV, OR, SC, VA, CA and ID. These state residents will be charged one cent ($.01) + shipping & processing for the item. Void where prohibited or restricted by law. Offer subject to state and local regulations. Not valid with any other offers and only while supplies last. This offer is limited to one item per shipping address. *** Free is only for customers using the offer code versus the price on Stauer.com without your offer code.*

Stauer, 14091 Southcross Drive W., Dept. DHC119-01, Burnsville, MN 55337 | www.stauer.com

Stauer® | AFFORD THE EXTRAORDINARY®