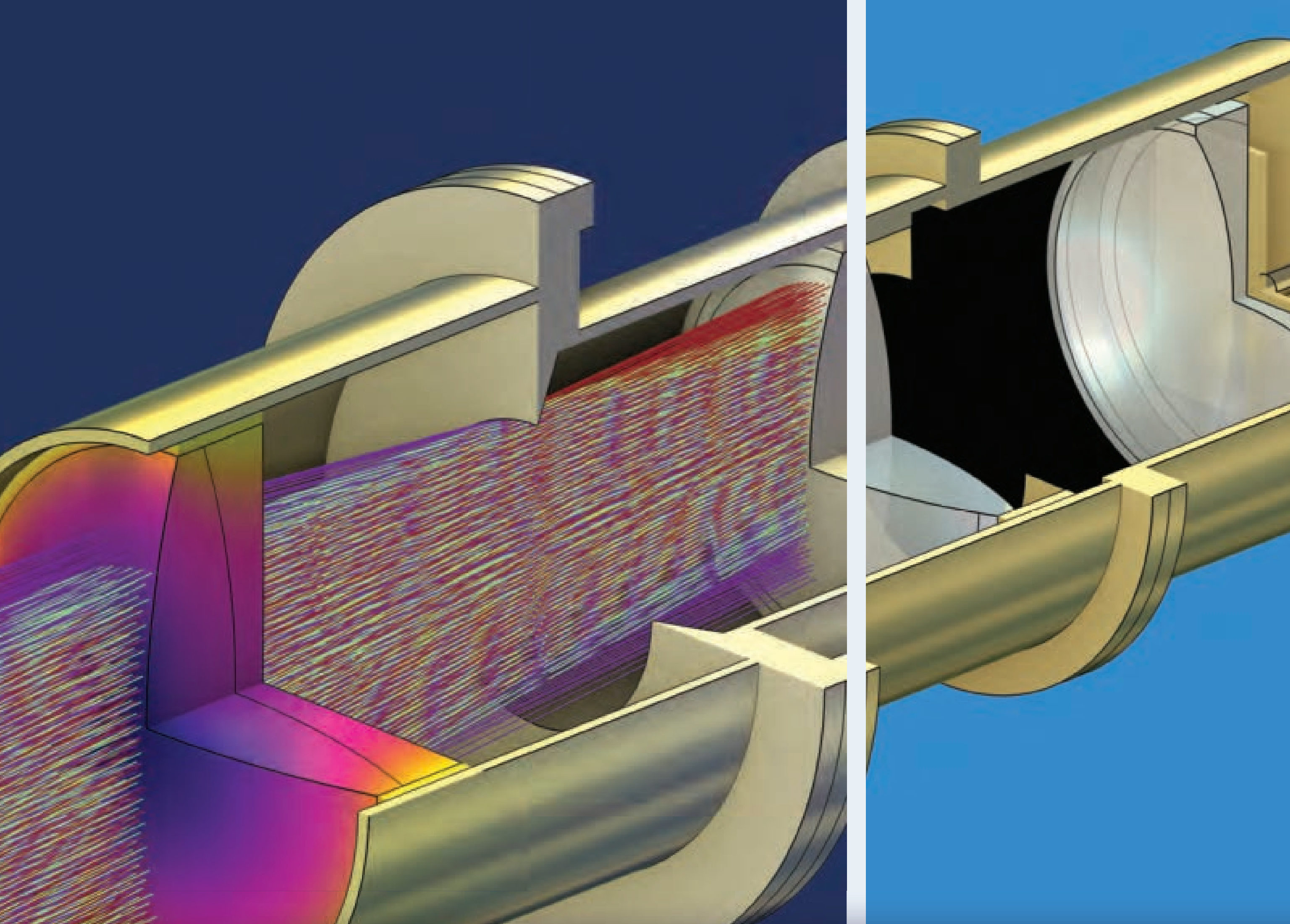


PHYSICS TODAY

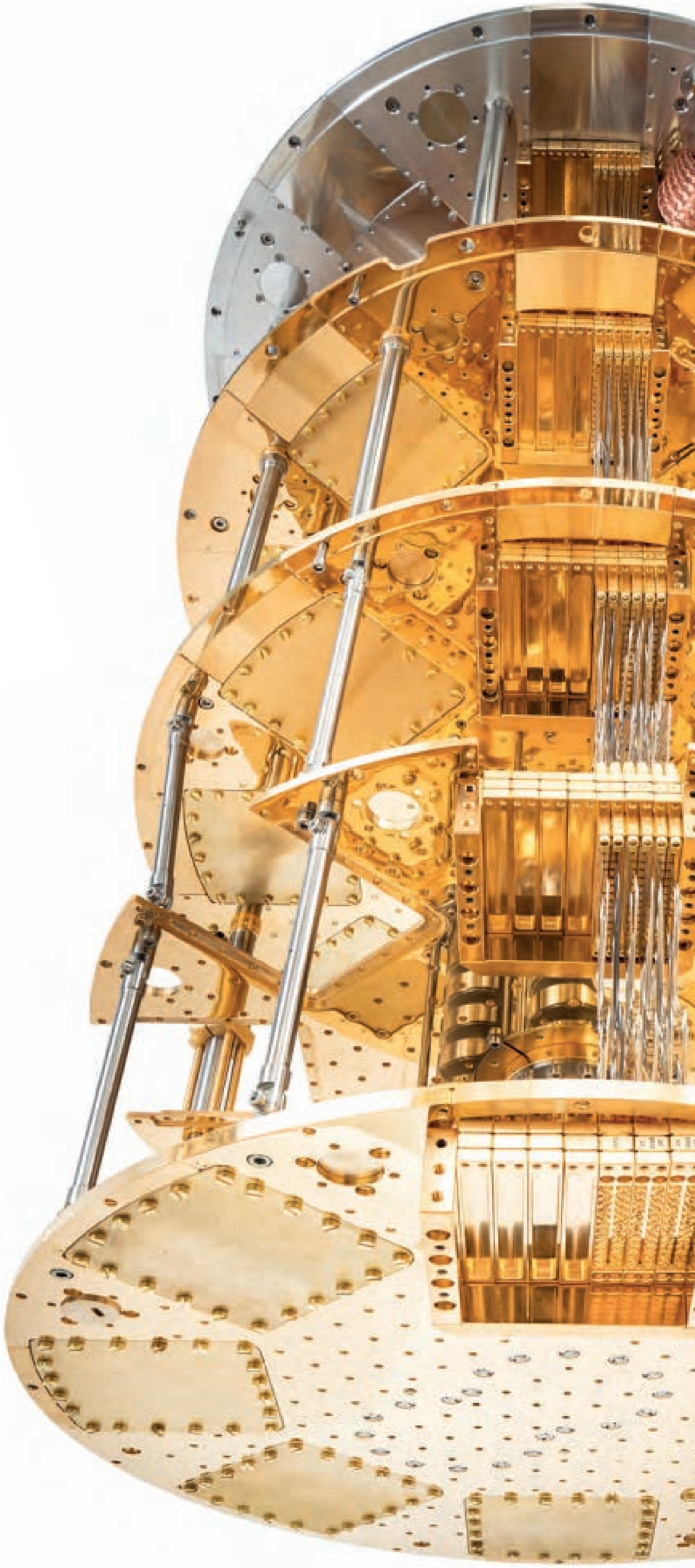
December 2022 • volume 75, number 12
A publication of the American Institute of Physics

TISSUE engineering

Animals' rheological toolbox

Removing petro- from petrochemicals

Compton effect centennial



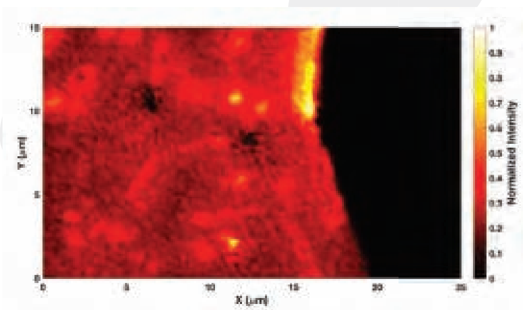
Excellence in Low Temperature Imaging

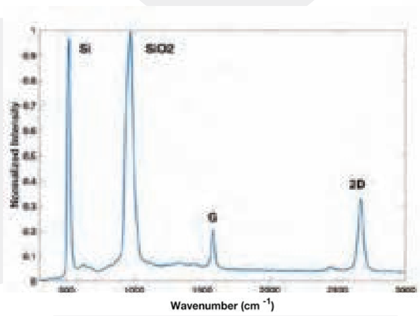
LT - NV Centre/Confocal Raman Microscope

High NA LT-APO Objective
0.82NA / 0.95mm WD
Scan Area
15x15µmx2µm @ 4K
Temperature Range
10 mK - 300K

- ☑ 48mm Outer Diameter
- ☑ XYZ Nanopositoner / Scanner for sample
- ☑ Z Nanopositoner for Cold objective
- ☑ XYZ Nanopositoner for NV/QTF Sensor

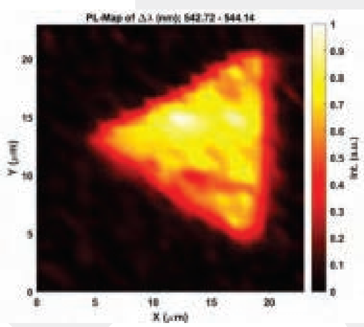
Single Layer Graphene Raman map*

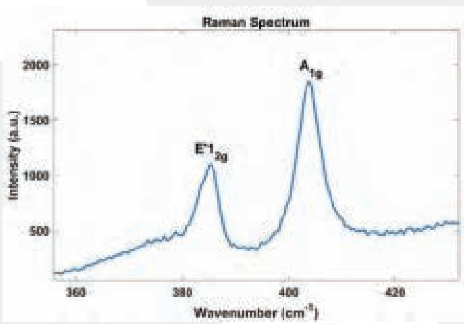


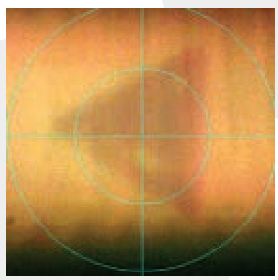


Can be customised to fit in any cryostat

Single layer MoS2 Raman map*







* Data courtesy of Furkan Ağlarcı, Çağlar Samaner, Serkan Ateş @ İzmir Institute of Technology, Turkey & Feridun Ay, Nihan Kosku Perkgöz @ Eskişehir Technical University, Turkey

NanoMagnetics Instruments
/NMInstruments
+44 7906 159 508
sales@nanomagnetics-inst.com
Suite 290, 266 Banbury Road Oxford OX2 7DL, United Kingdom

PHYSICS TODAY

December 2022 | volume 75 number 12

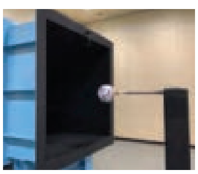
FEATURES

SPECIAL FOCUS ON PHYSICS AND BIOLOGY

ON THE COVER: Bioprinting, illustrated here, is a promising technology for fabricating human tissues and organs. But unlike ordinary 3D-printed objects, which are ready immediately, bioprinted objects must undergo additional processes before they can be implanted. In bioprinting, a machine dispenses bioinks—materials made of cell aggregates. When deposited next to each other, the segments fuse and self-assemble into mechanically robust tissue. On **page 38**, Ashkan Shafiee, Elham Ghadiri, and Robert Langer discuss the physics behind the self-assembly process. (Image by Ella Marus Studio/Science Source.)

Recently on PHYSICS TODAY ONLINE

www.physicstoday.org



JOHN ERIC GOFF

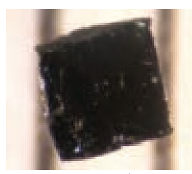
Physics of soccer

Each World Cup features a new ball, which has a distinct texture and distinct panel shapes. Those elements must be carefully calibrated to yield the desired performance. John Eric Goff of the University of Lynchburg explores how this year's ball, Al Rihla, compares with previous ones on such key metrics as the drag coefficient.
physicstoday.org/Dec2022a

NASA/ESA/SSC/CXC/STSCI

Galactic archaeology

Increasingly powerful telescopes and analytical tools help scientists determine the ages, chemical compositions, and motions of the 400 billion stars in the Milky Way. Rachel Brazil reports on why the past five years have been a particularly fruitful time for exploring the galaxy's past.
physicstoday.org/Dec2022b



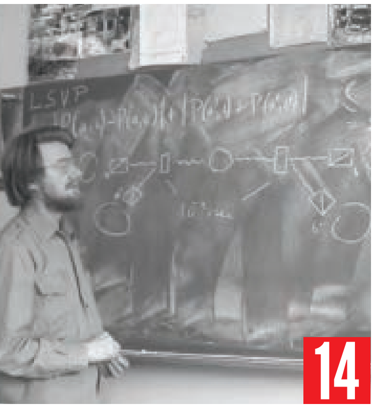
JAMES SLEZAK/CC BY-SA 3.0

Cuprate pairing

Since 1986, cuprate superconductors have been intensely investigated because of their unusual electronic behavior. But the mechanism behind that behavior is still unknown. Recent theoretical and experimental works point to a possible explanation: superexchange, in which copper-atom spins couple.
physicstoday.org/Dec2022c

PHYSICS TODAY (ISSN 0031-9228, coden PHTOAD) volume 75, number 12. Published monthly by the American Institute of Physics, 1305 Walt Whitman Rd, Suite 110, Melville, NY 11747-4300. Periodicals postage paid at Huntington Station, NY, and at additional mailing offices. POSTMASTER: Send address changes to PHYSICS TODAY, American Institute of Physics, 1305 Walt Whitman Rd, Suite 110, Melville, NY 11747-4300. Views expressed in PHYSICS TODAY and on its website are those of the authors and not necessarily those of AIP or any of its member societies.

PHYSICS TODAY
www.physicstoday.org


14


22


51

DEPARTMENTS

SUBSCRIPTION QUESTIONS? +1 800 344-6902 | +1 516 576-2270 | **ptsubs@aip.org**

Address
American Center for Physics
One Physics Ellipse
College Park, MD 20740-3842
+1 301 209-3100
pteditors@aip.org

PhysicsToday @physicstoday

Distinguished Postdoc Programs

The **INL Distinguished Postdoctoral Associate Program** is designed to attract, recruit, develop and inspire early-career researchers who have the potential to develop into INL's future scientific and technical leaders. These appointments are highly competitive and intended to recognize and provide Distinguished Postdoc Associates with a competitive award, research experience, mentorship, and training to develop their capabilities.

INL's Distinguished Postdoctoral Program Opportunity:

- Develop and build independent research while helping advance INL, Department of Energy and national agendas for energy and security
- Access to cutting-edge instrumentation and facilities
- Mentors include top INL researchers and leaders
- A prestigious and competitively compensated position

Glenn T. Seaborg Distinguished Postdoctoral Associate Program

The Glenn T. Seaborg Institute at Idaho National Laboratory has postdoctoral research positions available through its Distinguished Postdoctoral Research Associate program. The institute's mission is to nurture early-career Ph.D. scientists and engineers in the general area of actinide science. Outstanding applicants with research interests in solid state chemistry and physics, materials science, nuclear physics, solution chemistry and separations, radiation chemistry, and forensics and standards as related to the actinides are encouraged to apply. The Glenn T. Seaborg Distinguished Postdoctoral appointment provides up to two years of research support with a possible one-year extension.

Russell L. Heath Distinguished Postdoctoral Research Associate Appointment

Idaho National Laboratory has postdoctoral research positions available through its Russell L. Heath Distinguished Postdoctoral Research Associate program. The distinguished appointment is awarded to early-career scientists and engineers interested in advancing the fields of nuclear energy, critical infrastructure protection and clean energy. Outstanding applicants with research interests over a broad range of fields supporting INL's mission including, but not limited to, chemistry; physics; materials science; nuclear, mechanical and electrical engineering; earth/environmental science; separations science; biomass; geology; catalysis; advanced manufacturing; computational science; cybersecurity; electric vehicles and infrastructure; battery technologies; power engineering; wireless technology; systems analysis and design; or any related field are encouraged to apply. This appointment provides up to two years of research support with a possible one-year extension.

Deslonde De Boisblanc Distinguished Postdoctoral Appointment

This appointment will be awarded to early-career nuclear scientists and engineers to perform leading research and development for advanced reactor design and development as well as support operations, safety, fuel management, experiment management and other pertinent activities associated with INL research reactor facilities (e.g., the Advanced Test Reactor, used to support advanced reactor development). Outstanding applicants will have in-depth knowledge of computational and experimental reactor physics, core design optimization, nuclear instrumentation and thermal fluids science, and experience with established and well-validated reactor analysis tools such as, but not limited to, RELAP, MCNP, HELIOS, SCALE and Serpent. This appointment provides up to two years of research support with a possible one-year extension.

Apply Today! Scan the QR codes for more information or to apply online.

Applications will be accepted from Oct. 1, 2022, through Jan. 31, 2023, for positions starting in the 2023/2024 timeframe, although earlier appointments are possible. Notification of decision will be made within four months of receiving the application package. Applications should include a current CV, unofficial transcripts, a letter of interest including long-term professional goals, abstract of the doctoral dissertation, three letters of recommendation (one must be from a Ph.D. advisor), one peer-reviewed publication re/preprint, and a short research proposal.

Minimum qualifications include a doctorate degree in a field applicable to nuclear science and engineering research completed within the last five years; favorable recommendations; and demonstrated leadership, written and oral communication skills, and ability to work independently and as part of a team.

Equal Employment Opportunity: *Idaho National Laboratory (INL) is an Equal Employment Opportunity (EEO) employer. It is the policy of INL to provide equal employment opportunities to all qualified applicants without regard to race, color, religion, sex, sexual orientation, gender identity, national origin, age, protected veteran or disabled status, or genetic information. Women and People of Color are strongly encouraged to apply.*

ct.qmat
Complexity and Topology in Quantum Matter

ct.qmat – Complexity and Topology in Quantum Matter
Würzburg-Dresden Cluster of Excellence

Postdocs in Topological Condensed Matter Physics

ct.qmat is a strategic alliance of two of the world's leading quantum matter research institutions based in Würzburg & Dresden, Germany. Its aims are to develop a systematic understanding of topological phenomena in quantum physics, to find and design materials in which these phenomena can be observed in the laboratory, and to identify and test initial applications of these novel materials.

Applications are invited from new or recent doctoral recipients in the areas of **Electronic Quantum Materials**, **Quantum Magnetism**, and **Topological Photonics**.

Successful candidates will join a team of nearly 400 physicists, chemists, and materials scientists from 38 nations. They will have access to state-of-the-art research infrastructure based in two cities and benefit from a powerful network made up of two universities and five distinguished research institutes of the Max Planck Society, the Helmholtz Association, and the Leibniz Association.

Applications should be submitted to **jobs.ct.qmat@listserv.dfn.de**, enclosing your CV, a list of publications, and outlining your main interests and proposed field of research. Applications arriving before January 15, 2023, will be considered preferentially; recruiting will continue until positions are filled. The positions provide comprehensive social security benefits, including health insurance.

Come and join us in Würzburg and Dresden!

Area A

- Electronic quantum materials
- Topological band structures
- Spin-orbit coupling
- Topological superconductivity

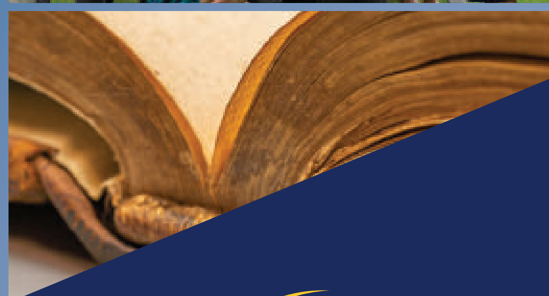
Area B

- Highly frustrated magnets
- Interacting topological systems
- Skyrmions and textures
- Intertwined electronic orders

Area C

- Photonic devices
- Topological lasers
- Chiral quantum networks
- Synthetic materials

Methods: Materials synthesis, quantum transport, spectroscopies, extreme conditions, ab-initio electronic structure, field theories, numerics



Commentary

Science and colonialism

THE HMS *BEAGLE* in the Strait of Magellan, a reproduction of the frontispiece by Robert Taylor Pritchett from the 1890 illustrated edition of Charles Darwin's *Journal of Researches* [...] (later republished as *The Voyage of the Beagle*). (Courtesy of Freshwater and Marine Image Bank, University of Washington, public domain.)

It is hard to imagine what much of modern science would have looked like without colonialism. It is equally hard to imagine what 19th- and 20th-century colonialism would have looked like minus developments in science.

To grasp the first point, one only has to think of Charles Darwin on board the *Beagle* on a five-year voyage that would take him around the world and that would provide much of the data that would drive his theory of natural selection. The young man was brought on as a naturalist and gentleman companion for the captain, Robert Fitzroy, who was tasked with a survey of the southern waters. The survey mattered for economic reasons because it could extend trade with a number of Latin American states. Fitzroy was also tasked with taking measurements that would aid imperial security and hopefully ward off French and North American interests in the same region.

Darwin himself carried an imperial sensibility with him, lauding British efforts when he arrived in Sydney, Australia, in January 1836. After walking through the town, he noted that it was "a most magnificent testimony to the power of the British nation," in the book we now know as *The Voyage of the Beagle*. "Here, in a less promising country, scores of years have done many more times more than an equal number of centuries have effected in South America," he wrote. "My first feeling was to congratulate myself that I was born an Englishman."

Imperial connections aided the physical sciences as much as the biological. Solar eclipse expeditions often involved travel to regions well outside Europe. There they relied on imperial infrastructures to help with transportation and communication, to supply skilled assistants and those able to repair complex machinery, and to access official protection when necessary. While Victorian astronomers often wrote adventurous accounts of their journeys, complete with perilous jungles and dangerous "natives", the reality was often far more staid. As the historian Alex Soojung-Kim Pang notes, eclipse expeditions were, in fact, "less like James Cook's voyages than Thomas Cook's tours."[1]

Nor, to provide a final example, were colonial structures only useful as a support for collection or observation. Imperial problems could produce quite remarkable theoretical solutions. The value of the telegraph for facilitating trade, communication, and control at vast distances was noted by a myriad of 19th-century observers. Karl Marx wrote in 1853 that India's political unity was "imposed by the British sword" and would "now be strengthened and perpetuated by the electric telegraph."[2] The attempt to lay and use transatlantic cables also led to fundamental developments in physics, not the least of which was the spread and broad acceptance of Michael Faraday's field theory in Britain in the 1850s and 1860s.

Action-at-a-distance theories struggled to explain, in simple ways that were not ad hoc, why signals traveled so much more slowly, were less crisp, and were more smeared out through undersea cables than through overhead ones. For Faraday, the answer was simple as long as one paid more attention to the material around the wire than the wire itself. Before electricity was conducted through a wire, he argued, a state of strain was induced in the surrounding dielectric, which also stored a certain amount of charge. The inductive capacity of a long cable was large, so it took some time for the charge to be stored, unlike the case of the overhead wires, where induction was close to immediate.

Faraday's explanation would soon inspire further work by William Thomson (later Lord Kelvin) and James Clerk Maxwell. According to the historian of physics Bruce Hunt, one major reason that field theory was broadly adopted in Britain by the 1860s and largely ignored in Germany until the late 1880s had to do with the difference in "technological environments."[3] Cable telegraphy was a virtual British monopoly, and cable telegraphy made field theory make sense.

As Marx's words suggest, the telegraph offers an easy example of the ways that science and technology facilitated the colonial enterprise. Communication was slow in the early 19th century, and armies require information. A story told about the sepoys who rose up against British officers in the Indian Mutiny of 1857–59 is probably apocryphal, but it is nonetheless revealing of the power that the Crown ascribed to its technology. As one rebel was led to his death, he was supposed to have noted a telegraph wire and muttered, “The accursed string that strangles us!”

Certainly, the so-called lightning wire allowed communication at speeds hitherto unimaginable. Before the age of steam, sending a letter from Britain to India and then receiving a reply could take considerably more than a year, depending on the prevailing winds. With steamships and trains, that time had been cut to two or three months by the 1850s. In the 1870s, however, a telegraph message could get from Britain to India in a number of hours, and in 1924 King George V could send himself a message that traveled the globe on all-British lines in 80 seconds.

What telegraphy made easier, medicine made possible. One set of data may serve to illustrate a larger point. According to statistics published in 1840, out of 1685 white British troops that arrived in western Africa between 1822 and 1825, 77% died between 1823 and 1827; the remaining 23% were “invalided” (that is, removed from service due to infirmity). Of the latter group, 4% died on their journey home; only 9% of the survivors were found fit for service again.[4] Quinine prophylaxis against malaria was one of the main reasons that the “scramble for Africa” became thinkable. Where death rates for Europeans in West Africa had once been on the order of 25–75% per year, by the end of the century,[5] they were closer to 5–10%.

The history of science and colonialism is, relatively speaking, a fairly new area of research. Its most fundamental claim is, however, well established: Modern colonialism and modern science could not have been what they were—and what they are—without one another.

References

1. A. S.-K. Pang, *Empire and the Sun: Victorian Solar Eclipse Expeditions*, Stanford U. Press (2002), p. 81.
2. K. Marx, *New-York Daily Tribune*, 8 August 1853, p. 5.
3. B. J. Hunt, in *History of Technology*, vol. 13, G. Hollister-Short, F. A. J. L. James, eds., Bloomsbury Academic (1991), p. 1.
4. “Statistical Society,” *Athenæum* **653**, 353 (1840).
5. D. R. Headrick, *The Tools of Empire: Technology and European Imperialism in the Nineteenth Century*, Oxford U. Press (1981), p. 70.

Suman Seth
(ss536@cornell.edu)
Cornell University
Ithaca, New York

LETTERS

Heliocentrism before Copernicus

In his interesting review of P. C. Deshmukh’s *Foundations of Classical Mechanics* (Physics Today, December 2021, page 54), Robert Scott notes “that the 14th- to 16th-century Kerala school of astronomy and mathematics developed a heliocentric model of the solar system well before the Copernican revolution.” But I believe that for historical completeness, that statement should be supplemented by a note that about 1600 years earlier, in the third century BCE, Aristarchus of Samos proposed a heliocentric model in which Earth revolved about the Sun in a circular orbit with the Sun at the center. However, the writings in which he proposed that idea have been lost, and the only reference to his work from that century is by Archimedes in a letter to King Gelon of Syracuse.[1]

Aristarchus of Samos is regrettably skipped over in many popular accounts of early astronomy—for example, in Stephen Hawking’s well-known book *A*

CONTACT PHYSICS TODAY

Letters and commentary are encouraged and should be sent by email to **ptletters@aip.org** (using your surname as the Subject line), or by standard mail to Letters, Physics Today, American Center for Physics, One Physics Ellipse, College Park, MD 20740-3842. Please include your name, work affiliation, mailing address, email address, and daytime phone number on your letter and attachments. You can also contact us online at **https://contact.physicstoday.org**. We reserve the right to edit submissions.

Brief History of Time: From the Big Bang to Black Holes (1988). Thus, years ago, when I was teaching an introductory course on the history and philosophy of science, I would ask the students whether they had heard of Copernicus, and everyone would raise their hand, but when I asked about Aristarchus of Samos, usually no hands went up. If I were still teaching, in addition to my usual covering of Aristarchus and Copernicus, I would teach about the Kerala school as well, thanks to Deshmukh's book.

Reference

1. T. Heath, *Aristarchus of Samos, the Ancient Copernicus: A History of Greek Astronomy to Aristarchus* [. . .], Clarendon Press (1913; reprint, Dover, 1981), p. 302.

Frank R. Tangherlini
(frtan96@gmail.com)
San Diego, California

Observing interstellar molecular hydrogen

Johanna Miller's Search and Discovery story "Ten billion years ago, galaxies were already running out of gas" (Physics Today, December 2021, page 20) describes evidence that some galaxies deplete their interstellar matter to fuel star formation. Particularly important are cold interstellar gas clouds, where the atomic-to-molecular transition is a key step in sustaining new star formation. The story highlights recent Atacama Large Millimeter/Submillimeter Array observations of molecular gas in carbon monoxide microwave emission and far-IR emission from dust grains.[1] But these two sentences were misleading: "Measuring the galaxies' H_2 content directly isn't an option because H_2 molecules themselves are essentially invisible. They're symmetric and lack electric dipole moments, so they don't absorb or emit radiation when they rotate and vibrate."

Rumors of H_2 invisibility have been greatly exaggerated. Although it's true that the H_2 ground electronic state has no dipole moment, two low-lying electronic states (molecular orbitals from 1*s*–2*s* and 1*s*–2*p*) do have dipole moments. Electronic absorption lines into those states lie in the far-UV and are known as the Lyman and Werner bands.[2] Widely observed in the interstellar medium by the *Copernicus* and *Far Ultraviolet Spectroscopic Explorer* (*FUSE*) satellites, they provide diagnostics of the molecular fraction, gas temperature, and UV radiation field in diffuse and translucent interstellar clouds. *FUSE* also surveyed H_2 in two external galaxies, the Large and Small Magellanic Clouds orbiting the Milky Way.[3]

UV H_2 lines have also been seen in strong quasar absorption systems redshifted into the visible band.[4] For systems in the Milky Way and local galaxies, measuring those absorption lines requires finding a bright UV background source, such as a hot star or quasar, behind the absorbing gas. That makes dark molecular clouds hard to probe in the UV. But *FUSE* observed H_2 in a number of translucent clouds[5] with one to five magnitudes of visual extinction and molecular fractions up to 75%.

Thanks to cosmological redshifting of light, H_2 has now been observed in distant intervening galaxies in spectra of background quasars. The H_2 far-UV absorption lines are shifted into portions of the UV accessible to the *Hubble Space Telescope* for galaxy redshifts $z > 0.05$ (a distance of 680 million light-years). At redshifts $z > 1.8$, the H_2 lines can be observed by optical spectrographs. The European Southern Observatory's Very Large Telescope in Chile has detected H_2 in more than 22 distant galaxies (damped Lyman-alpha absorbers) at redshifts z between 1.96 and 4.22, corresponding to cosmological distances of 10.3 to 12.2 billion light-years. The recent Decadal Survey on Astronomy and Astrophysics supported plans for a 6 m optical, UV, and IR space telescope. With greatly enhanced sensitivity in the far-UV (90–200 nm), that facility would be a powerful tool for probing the atomic and molecular gas that fuels star formation in galaxies.

References

1. K. E. Whitaker et al., *Nature* **597**, 485 (2021).
2. J. M. Shull, S. Beckwith, *Annu. Rev. Astron. Astrophys.* **20**, 163 (1982).
3. B. D. Savage et al., *Astrophys. J.* **216**, 291 (1977); J. M. Shull, C. W. Danforth, K. L. Anderson, *Astrophys. J.* **911**, 55 (2021); J. Tumlinson et al., *Astrophys. J.* **566**, 857 (2002).
4. P. Petitjean, R. Srianand, C. Ledoux, *Astron. Astrophys.* **364**, L26 (2000).
5. B. L. Rachford et al., *Astrophys. J. Suppl. Ser.* **180**, 125 (2009).

J. Michael Shull
(michael.shull@colorado.edu)
University of Colorado Boulder PT

Physics Nobel honors foundational quantum entanglement experiments

The laureates brought the conceptual features of quantum physics back to mainstream interest.

In the late 1960s, John Clauser became fascinated with a paper he stumbled on in the Columbia University library. Published a few years earlier by John Bell, it proposed a scenario in which specific predictions of quantum mechanics could be distinguished from those of a proposed rival theory.[1] Clauser was eager to conduct the described entanglement experiment. But his graduate adviser and other professors discouraged him from pursuing the topic, which they deemed to be more philosophical than physics related. If Clauser wanted a job in physics, he needed to stick with a mainstream topic, such as the ultimate subject of his thesis, radio astronomy.

Thirty years earlier many leading physicists—Niels Bohr, Albert Einstein, Werner Heisenberg, and Erwin Schrödinger, among others—devoted much of their time to grappling with the defining properties of quantum mechanics, particularly entanglement. But the pragmatic bent of physicists during World War II and the Cold War had pushed quantum mechanics interpretations from the forefront of the field to the fringes.

The three experimentalists awarded this year's Nobel Prize in Physics were pioneers who helped return the foundations of quantum mechanics to mainstream interest. In the face of discouragement and indifference from the research community, Alain Aspect, Clauser, and Anton Zeilinger pursued rigorous evidence that pinned down the properties of entanglement. And now those results and techniques lie at the foundation of quantum information science.

Hot topic, Cold War

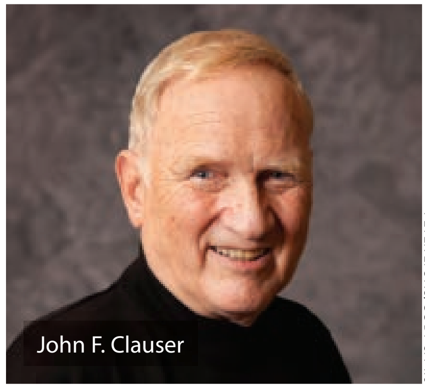
In the 1920s, physicists were still identifying and understanding the implications of quantum mechanics. Those implications, such as wave–particle duality, were in stark contrast to classical physics, and physicists started formulating different conceptions of quantum mechanics' math and measurements. Bohr and Heisenberg were among those promoting numerous ideas and attitudes that, by the 1950s, were collectively being referred to as the Copenhagen interpretation of quantum mechanics, which generally posits that rather than well-defined properties, quantum systems have only probability distributions—until the moment they're measured.

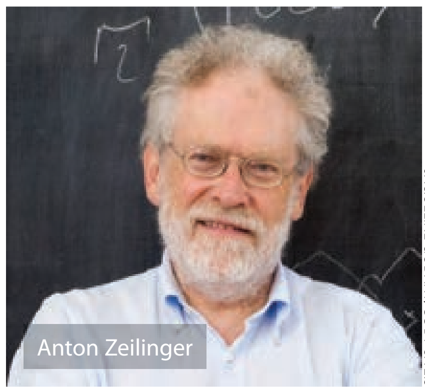
To Einstein, the Copenhagen interpretation had unsettling consequences. For example, two particles can interact such that a single wavefunction describes them both—that is, they become entangled. No matter how far apart the particles are, quantum mechanics was suggesting that the moment one is measured, the other instantaneously adopts the expected partner state. But such an observation would seem to contradict causality, as understood in the theory of relativity.

In their famous 1935 paper, Einstein, Boris Podolsky, and Nathan Rosen, known together as EPR, argued that because of such violations, quantum mechanics must not be a complete description of physical systems.[2] They suggested that a full theory should be local, in that an object is directly influenced only by its immediate surroundings, and realistic, in that nature has defined properties whether or not they're measured.

Those on the Copenhagen side argued that locality and realism might be what's wanted, not what's necessary, in a model. Einstein stuck to his convictions, and other physicists proposed the addition of hidden variables—so called because they aren't measurable—that could explain away entanglement's action at a distance. The variables would determine all a particle's measurable properties, such as position and spin, before (and regardless of) measurement, and they would have a distribution of values across particles


Alain Aspect


John F. Clauser


Anton Zeilinger

that accounts for the apparent probabilities seen in quantum experiments.

By the 1950s, however, the Copenhagen interpretation had become the standard. The decade saw some alternative quantum interpretations, notably from David Bohm and Hugh Everett. (See the Quick Study by Sean Carroll, Physics Today, July 2022, page 62.) But largely, physicists stopped thinking about quan-

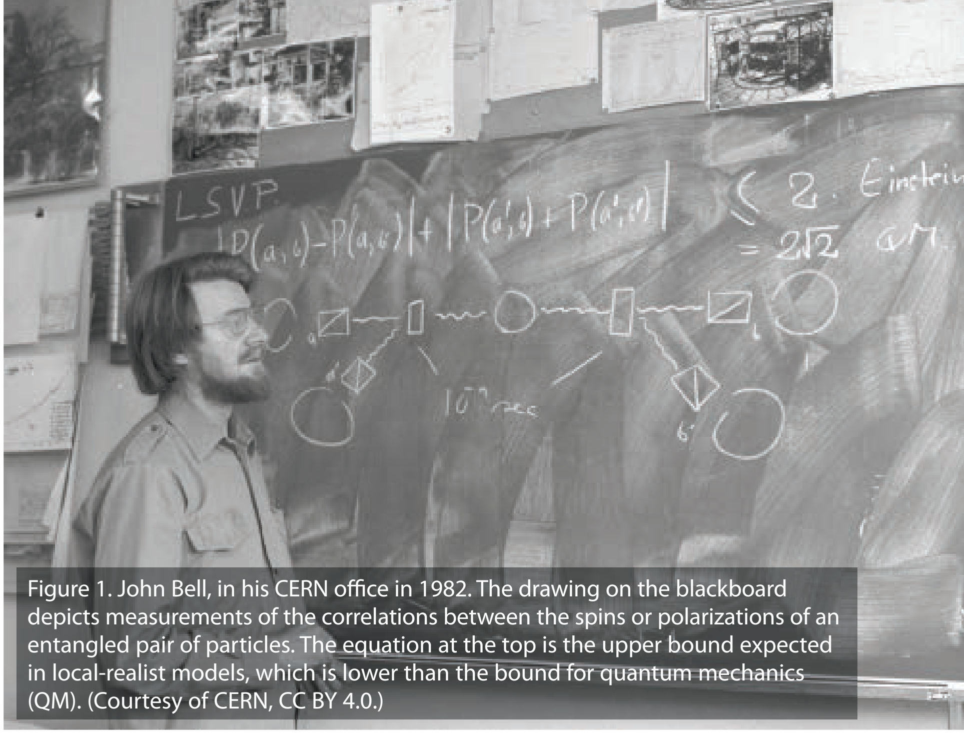


Figure 1. John Bell, in his CERN office in 1982. The drawing on the blackboard depicts measurements of the correlations between the spins or polarizations of an entangled pair of particles. The equation at the top is the upper bound expected in local-realist models, which is lower than the bound for quantum mechanics (QM). (Courtesy of CERN, CC BY 4.0.)

tum mechanics' implications. World War II and the Cold War created a physics culture centered on pragmatism rather than philosophizing. "The Copenhagen interpretation was something that folks could appeal to and say, 'Those interpretation questions seem like they were handled, and our business is elsewhere,'" says David Kaiser, a physicist and historian of physics at MIT. At universities, ballooning physics enrollment and class sizes—a reaction to massive defense projects—led professors to focus on topics, particularly calculation-based problems, amenable to a large lecture hall and rapid grading.[3]

When the physics funding bubble eventually burst in the late 1960s, job prospects dwindled, and by the end of the 1970s, physics enrollments were half of what they were at their peak near the start of the decade. With the return to smaller classes, essay and discussion questions again became part of exams and textbooks, and philosophically oriented seminars found their place on the calendars once again.[3]

EPR reevaluated

As early as his undergraduate days at Queen's University Belfast in the 1940s, Bell disliked how he'd been taught quantum mechanics. The Copenhagen interpretation distinguished quantum and classical worlds without a clear divide between the two. (See the article by Reinhold Bertlmann, Physics Today, July 2015, page 40.) While a grad student at the University of Birmingham, Bell became intrigued by Bohm's 1952 reinterpretation of quantum mechanics as deterministic and realistic through the addition of hidden variables. Bohm presented the idea in a modified version of the situation proposed in the EPR paper.

In the EPR *gedanken* experiment, two entangled particles are emitted in opposite directions, and they travel until each one has either its position or momentum measured. Bohm replaced those continuous measurements with binary measurements of spin. Bohm's hidden-variable model has a literal wave–particle duality, in that particles ride on wavefunctions, which replace quantum mechanics' probability distributions for determinism. But because measurement outcomes depend on wavefunctions, Bohm's model is still nonlocal.

After graduation, Bell went to work at CERN, alongside his wife and fellow physicist Mary Bell. But in his spare moments, Bell pondered the possibility of hidden variables that could restore locality to quantum systems. In 1964 Bell published an article about Bohm's variant of the EPR paradox.[1] He identified an experimental scenario in which Einstein's desired local-realist theory couldn't possibly replicate the results of quantum mechanics.

In the scenario, each particle of an entangled pair has its spin measured along one of two randomly and independently chosen axes, as illustrated in figure 1. For certain axes—say, parallel ones—the correlation between the pair's measured spins over many measurements will have the same upper bound for quantum and local-realist models. But for combined measurements of multiple relative angles between the axes, quantum mechanics predicts a higher upper bound on the correlation. Given the right parameters, an experiment could potentially exclude a broad class of local hidden-variable theories if the correlations are higher than the upper bound in what's now known as Bell's inequality.

California dreamin'

Despite his graduate adviser's discouragement, Clauser refused to be swayed from his desire to test Bell's inequality. He wrote to Bell to confirm that no such experiment had been done, and buoyed by Bell's confirmation and encouragement, Clauser started planning how to transform the idealized situation in Bell's paper to realistic equipment. He connected with some researchers who also were interested in Bell's inequalities: Abner Shimony and his grad student Michael Horne at Boston University and Richard Holt at Harvard University. In 1969 they published their reformulation of Bell's inequality for a realistic experimental setup.[4]

That same year Clauser started a postdoc at Lawrence Berkeley National Laboratory under Charles Townes, one of the inventors of the laser. Townes agreed to let Clauser split his time between radio astronomy and an experimental test of Bell's inequality. Over the course of two years, Clauser and Stuart Freedman, a graduate student under Eugene Commins, constructed their setup. In the experiment, calcium atoms produced entangled photons after excitation by a hydrogen arc lamp. Most excited electrons immediately returned to the ground state, but some cascaded down a series of energy levels, emitting photons along the way. The parity of the energy transitions determined the polarization state of the photons, and their shared origin entangled them.

The photons traveled in opposite directions toward a detector on each end of the setup. But first, each photon encountered a polarizer set at some angle. Some photons were blocked, and others passed through to ping the detectors. Clauser and Freedman built new, more efficient polarizers—so-called pile-of-plate polarizers—whose angles could be changed more quickly. Even so, collecting sufficient particle statistics for a range of relative polarizer angles

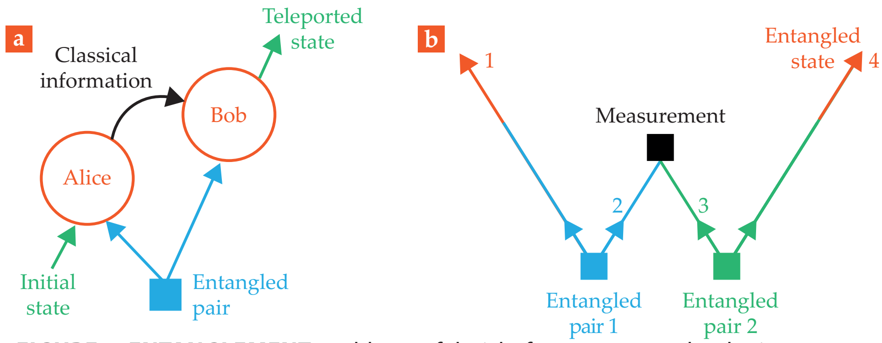


FIGURE 2. ENTANGLEMENT enables useful tricks for quantum technologies. **(a)** Quantum teleportation replicates a quantum state that starts with Alice. She and Bob each receive one particle of an entangled pair. Alice then does a joint measurement on the initial state and her entangled particle, and she sends Bob classical information about the outcome. With that information, Bob can then apply a local transformation to his particle to replicate the exact state of Alice's initial particle. **(b)** Entanglement swapping entangles particles that have never been in close proximity. Two separate entangled pairs are sent out: particle 1 to Alice, particle 4 to Bob, and particles 2 and 3 to a central location. A joint measurement on the central particles and communication of the result leaves distant particles 1 and 4 entangled. (Figure by Freddie Pagani.)

from 0° to 90° took about 200 hours.

In their paper, published in 1972, Clauser and Freedman presented the first-ever experimental Bell test. Their observations violated Bell's inequality.[5] "The result, I didn't expect," Clauser said in a 2002 oral history interview with the American Institute of Physics (publisher of Physics Today). "I hoped we would overthrow quantum mechanics." Similar experiments using mercury atoms followed from Holt, Edward Fry, Randall Thompson, and Clauser. All again matched the expectations of quantum mechanics, not local realism.

Switching it up

When Aspect started working on Bell's theorem in 1974, he had just returned from Cameroon for his graduate studies at the University of Paris–Sud. During his three years teaching in the central African country, he had read and thought about quantum theory. So when Bernard d'Espagnat recommended that he test Bell's inequality, Aspect quickly realized why the project was interesting—and experimentally tricky. But the topic was still viewed with skepticism at the time. In fact, in a discussion at CERN, Bell recommended pursuing it only if Aspect had a permanent job, which he did: a teaching job while he finished his degree. "It was possible for a young Aspect and a young Zeilinger to pursue their projects with cover from one or two influential senior colleagues," says Kaiser, "and that's what it took to get them going."

Over the course of 1981 and 1982, Aspect, Philippe Grangier, Jean Dalibard, and Gérard Roger did three tests. (See the article by David Mermin, Physics Today, April 1985, page 38.) Their experiments were similar to Clauser's—in fact, some of his equipment was shipped from California to Paris for them to use—but improved in a few crucial regards. In Aspect and his colleagues' first test, they excited the calcium atoms more efficiently, which boosted the pair production. In their second experiment, they opted for polarizing cubes, which transmit one polarization and reflect the other, rather than block it as in Clauser's pile of plates. Aspect could then measure photons with both polarizations.

The third experiment was the biggest advance. In Clauser's setup, the polarizers stayed at a given fixed angle for long periods. That design introduced what's known as the locality loophole. Information about the orientation of one polarizer traveling at or less than the speed of light would have plenty of time to reach and influence the source and the other polarizer before the entangled photons are even emitted. A local-realist model could then still explain the measured outcome, even though it seems to violate Bell's inequality. In the parlance of relativity, to close the locality loophole, each measurement should be space-like separated from the events in which the other polarizer is positioned and in which the particles are emitted. That is, ideally, the polarizers should be set during the time of flight of the two particles.

Aspect made strides in closing the locality loophole. Rotating the polarizers took too long to be done during the photons' 20 ns journey from the source to the detectors 6 m away. But with the help of acousto-optical switches that alternated between transmitting and reflecting light every 10 ns, the setup could, during the photons' flight, direct each photon to one of two possible polarizers at different fixed angles. All three of Aspect's measurements exceeded Bell's inequality. "Aspect's experiments were received more warmly than Clauser and Freedman's," says Kaiser, but largely by the small community already interested in Bell tests. "The topic was still on the margins."

Loop the loop

Aspect didn't fully close the locality loophole because the measurement settings weren't random. The two polarizers were fixed, and the switches were essentially periodic. That information is known enough in advance that one detector could still influence the other one or the particle-pair source before emission.

The locality loophole is one of three significant loopholes in Bell tests.[6] Another is what's known as fair sampling. No measurement detects every particle. If too few particles are detected, the measurement could be picking a nonrepresentative sample of the photons that artificially skews the correlations. Although nature is perhaps unlikely to play such a trick, in quantum communication technologies a hacker may well try to do so. (See Physics Today, December 2011, page 20.) Detecting more than about three-fourths of the photons takes care of that loophole.

The third, the freedom-of-choice loophole, arises when the measurement settings may not be free or random but could instead depend on the entangled pairs' local hidden variables because of the shared history of the detector and particle source. Taken to an extreme, the loophole can suggest that every event in all spacetime was determined by the initial conditions at the Big Bang, an idea called superdeterminism. Such a universe would obey local realism, but at the cost of free will, among other things. But even not taken to such an extreme, "it actually takes very little statistical correlation for Einstein-like models to yield all the predictions of quantum mechanics," explains Kaiser.

The loopholes at first were tackled one by one. Zeilinger's group closed the locality loophole in the 1990s in a measurement done by detectors 400 m apart whose polarizer settings were determined by an electro-optical modulator hooked up to a random-number generator. David Wineland and his colleagues closed the fair-sampling loophole in 2001 for measurements on entangled trapped ions.[7]

A real test of Bell's inequality, however, requires simultaneously closing all three loopholes. That is easier said than done, particularly because the locality and fair-sampling loopholes are at odds. The more distance between the source and the detectors, the more photons the experiment stands to lose. Nevertheless, in 2015, three groups managed loophole-free Bell tests, the first by Ronald Hanson's group at Delft University of Technology. (See Physics Today, January 2016, page 14.)

Zeilinger and his then-grad student Marissa Giustina performed their measurements in the Hofburg, a former imperial palace in Vienna. Zeilinger's group has a history of performing experiments in unusual locations, including the Canary Islands and a utility tunnel under the Danube. For the loophole-free Bell test, "it was a challenge to find a good location," says Giustina. "We pulled up a Google Maps satellite view of Vienna and looked for a spot that would be willing to let us take over for an unknown period of time and shine lasers around, with a 60-meter line of sight, stable temperatures, three-phase power, and water-chiller support for our cryostats." The dusty basement of the Hofburg was one of the few options.

Using random-number generators and high-efficiency detectors set far apart, Giustina and Zeilinger demonstrated once again that nature violated Bell's inequality. Sae Woo Nam and Krister Shalm of NIST, who likewise used photons for their loophole-free test, got similar results. And Hanson and his collaborators also saw higher correlations than in Bell's inequality, but in their case in the spin states of two diamond nitrogen–vacancy centers entangled through a trick known as entanglement swapping, which is explained below.

The freedom-of-choice loophole, however, is never fully closed. One approach to narrow it is picking detector settings based on phenomena that shrink the shared history of the settings and the entangled pairs. Zeilinger and researchers from several institutions, including MIT, Harvey Mudd College, and NASA's Jet Propulsion Laboratory, conducted a pair of experiments in 2016 and 2018 in which they set the polarizers based on the observed fluctuating properties of light from distant astronomical objects. (See "Cosmic experiment is closing another Bell test loophole," Physics Today online, 1 December 2016.) Such so-called cosmic Bell tests have pushed the most recent shared history between the experiment and the light used to derive the random settings to 8 billion years ago.

More particles

Zeilinger says that his interest was never specifically in tackling loopholes. Rather, he says, "I am interested in what conceptual features quantum physics must have." In collaboration with Daniel Greenberger and Michael Horne, "Zeilinger made the step from two entangled particles to multiple entangled particles and all you can do with that," says Hanson. Two notable examples, depicted in figure 2, are quantum teleportation and entanglement swapping, both proposed by Charles Bennett and his colleagues in 1993.

According to the no-cloning theorem, a quantum state can't be copied while keeping the original. But copying is possible if you destroy the original state. In 1997 two groups—one headed by Zeilinger, while at the University of Innsbruck, and the other by Francesco De Martini—managed to do it through quantum teleportation. (See Physics Today, February 1998, page 18.) In the scheme, a fictional character Alice teleports a quantum state to Bob with the help of an entangled pair shared between them. Alice does a joint measurement on the teleporting particle and her half of the entangled pair. She then sends Bob classical information about what measurement he should perform to put his particle into the initial particle's state.

A similar trick, known as entanglement swapping, can entangle two particles that have never directly interacted. Take two entangled pairs: particles 1 and 2 and particles 3 and 4. While particles 1 and 4 head off to their final destinations—say, distant Alice and Bob—particles 2 and 3 are both sent to Charlie. He then performs a joint measurement on those two particles that, after classical information is shared, leaves 1 and 4 entangled. The phenomenon was demonstrated in 1998 by Zeilinger and his collaborators.[8]

"Starting in the early 1990s, people began to realize that Bell's inequality and quantum entanglement could become a real-world resource for things like quantum encryption," says Kaiser. That realization is part of why the quantum information field boomed, but unlike during the Cold War, the physics community was no longer dismissive of foundational work. Entanglement, as described and understood by quantum mechanics, is now at the core of numerous current and proposed future technologies, most notably quantum computers and quantum encryption. (See the article by Charles Bennett, Physics Today, October 1995, page 24.)

Giustina, who now works at Google, explains that quantum error correction, which is an essential component of quantum computing, "stands on the foundation of Bell inequality violations and the confidence that nature consistently tends to violate Bell's inequality." (See the article by Anne Matsuura, Sonika Johri, and Justin Hogaboam, Physics Today, March 2019, page 40.) Quantum key distribution also relies on Bell tests to securely send messages and check that they haven't been hacked. (See the article by Marcos Curty, Koji Azuma, and Hoi-Kwong Lo, Physics Today, March 2021, page 36.)

But the future of quantum mechanics is more than applications. "The most important issue for future research lies in questions about the foundations of quantum mechanics," says Zeilinger. Now that Bell tests have excluded local hidden-variable theories, "we can focus on questions that have not been answered by the experiments, such as, 'Is there a deeper theory than quantum mechanics?' "

Heather M. Hill

References

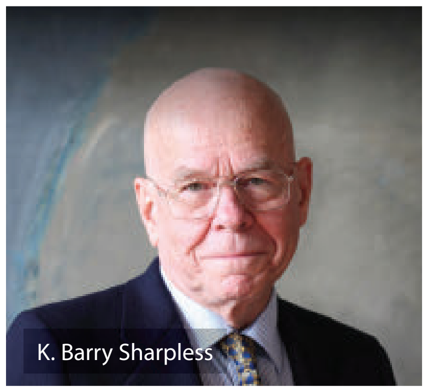
1. J. S. Bell, *Physics* **1**, 195 (1964).
2. A. Einstein, B. Podolsky, N. Rosen, *Phys. Rev.* **47**, 777 (1935).
3. D. Kaiser, *How the Hippies Saved Physics: Science, Counterculture, and the Quantum Revival*, W. W. Norton (2011).
4. J. F. Clauser, M. A. Horne, A. Shimony, R. A. Holt, *Phys. Rev. Lett.* **23**, 880 (1969).
5. S. J. Freedman, J. F. Clauser, *Phys. Rev. Lett.* **28**, 938 (1972).
6. D. Kaiser, in *The Oxford Handbook of the History of Quantum Interpretations*, O. Freire Jr et al., eds., Oxford U. Press (2022), chap. 13.
7. M. A. Rowe et al., *Nature* **409**, 791 (2001).
8. J.-W. Pan, D. Bouwmeester, H. Weinfurter, A. Zeilinger, *Phys. Rev. Lett.* **80**, 3891 (1998).

Chemistry Nobelists developed reactions that are "compatible with almost everything"

Most chemical reactions require stringent conditions and can interfere with other molecules in their environment. But a few do not—and they've proved tremendously useful.


Carolyn Bertozzi
DO PHAM/STANFORD UNIVERSITY


Morten Meldal
LARS KRABBE


K. Barry Sharpless
IKE SHARPLESS

Molecules aren't Tinkertoys. Chemists can't just pluck atoms out of a box and connect them however they want. Rather, they rely on an inventory of reactions, accumulated over generations of research, for manipulating molecular structures. Building a new molecule means solving an intricate puzzle of which reactions to perform in which order.

Those reactions can be temperamental. They can depend sensitively on solvents, temperatures, and other parameters. The reactants don't always find each other, and they don't always react as planned. In a complex environment, they often react with the wrong thing entirely to form unwanted by-products. In a multistep synthesis of a complicated molecule, the inefficiencies quickly compound, and chemists often need an enormous amount of starting material to make even a tiny amount of product.

A few special reactions buck the trend. Their reactants seek out and react only with each other, with nearly 100% efficiency, regardless of what other molecules might be around. This year's Nobel Prize in Chemistry recognizes three researchers who made key contributions to developing and harnessing the power of those ultraefficient reactions: Carolyn Bertozzi of Stanford University, Morten Meldal of the University of Copenhagen, and K. Barry Sharpless of Scripps Research.

Sharpless coined the term "click chemistry" to describe the reactions, likening the joining of molecules to the satisfying "click" of a push-buckle tab inserted into its socket. Bertozzi introduced the term "bioorthogonal chemistry" to emphasize how the reactions can be so indifferent to their surroundings that they can be carried out in living cells, or even living animals, with no ill effects.

The distinction between the two terms is largely in the application; the reaction properties they refer to are very similar. "We talk about reactions that are compatible with biology," says UCLA's Ellen Sletten, who earned her PhD under Bertozzi in 2011. "But really we design these reactions to be compatible with almost everything."

Beyond its use in chemistry, biology, and related fields such as materials and polymer science, click chemistry has been a great benefit to scientists in many other disciplines, including physics, by making the tools of chemistry accessible to researchers who aren't trained as chemists. "The main selling point is that it's really easy to do," says Katie Bratlie of the National Academies of Sciences, Engineering, and Medicine, "so it's really beneficial for lots of applications."

Seeing sneaky sugars

The story's molecular protagonist is the azide, a group of three nitrogen atoms bound together as part of a compound or larger molecule. When made into a sodium salt, azide has been used as the active ingredient in car airbags. Sodium azide is a stable solid until it's heated, when it rapidly decomposes to release nitrogen gas. For azides in organic molecules, the chemical details differ, but the effect is similar: The azide is nearly inert, but it carries a lot of pent-up potential energy. So when it finds the right reaction partner, it's ready to react vigorously.

But there aren't a lot of azide reaction partners. It's what's known as a soft reactant: Its charge density is spread out, and it's highly polarizable. Chemistry—and especially biology—doesn't have many other soft reactants; most reactants are hard, with concentrated, relatively unmovable charge distributions. Because hard reacts with hard and soft with soft, azides don't react with much.

In the late 1990s, Bertozzi started to recognize azides' potential. She was interested in glycans, the complex sugars that coat the outsides of cell membranes, about which little was known. To study the behavior of a new biomolecule in a cell, a good first step is typically to label the molecule with a fluorescent tag and then directly observe where it is and what it's doing. For proteins, the labeling could be done through genetic engineering (see PHYSICS TODAY, December 2008, page 20), but that was no help for glycans. New tools were needed to label those.

The key is that cells are lazy in constructing their glycans. They don't build the complex sugars atom by atom. Rather, they take the simple sugars that they ingest, such as glucose and galactose, and assemble the glycans directly from those building blocks. Bertozzi discovered that if she fed a cell a sugar molecule bound to a chemical group that's not supposed to be there, the cell still inserted the sugar, unchanged, into one of its glycans—as long as the unnatural group was sufficiently small and unreactive. Azides fit the bill, and she started tricking the cells into making their own azide-tagged glycans.

Azides by themselves aren't fluorescent. To complete the fluorescence labeling, Bertozzi needed to flood the cell with a fluorescent dye bound to something that reacts with the azide. In those early years, she used a reaction called the Staudinger ligation, in which the azide reacts with a phosphorus atom bound to a benzene ring.[1] But although the Staudinger ligation was bioorthogonal—it could harmlessly label glycans in cells and even in live mice—it wasn't especially fast: Labeling a glycan took the better part of a day, and the benzene–phosphorus molecule was degrading and getting eaten by cells almost as fast as it was reacting with the azides. Clearly, a different azide reaction partner would be better, if one could be found.

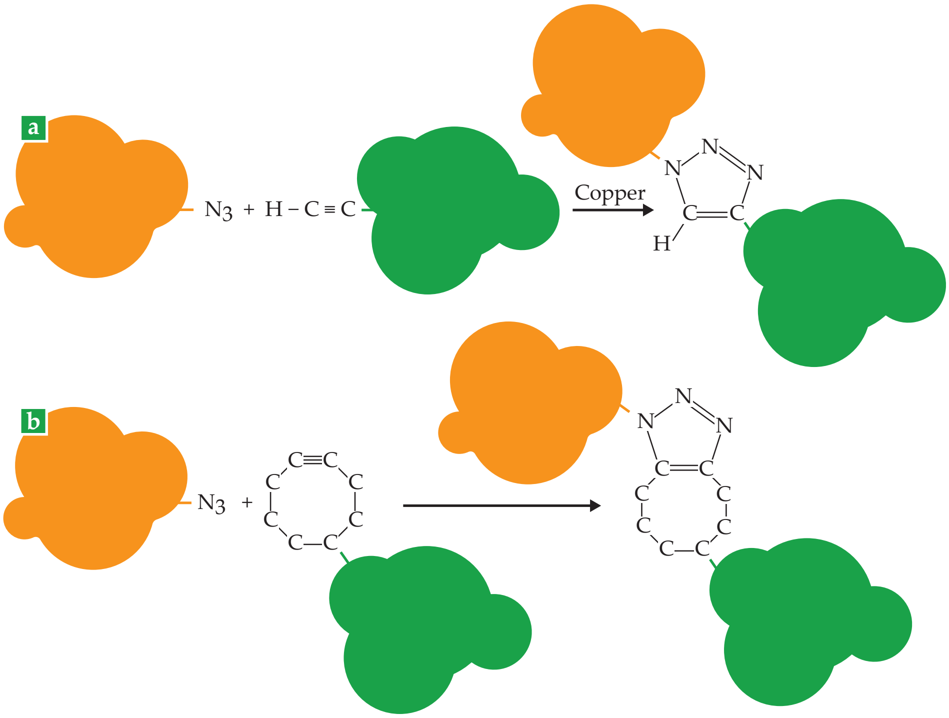


FIGURE 1. CLICK REACTIONS efficiently connect almost anything to anything else: The orange and green blobs can represent molecules, solid surfaces or particles, or even living cells. **(a)** The classic click reaction, discovered independently by the groups of Morten Meldal and K. Barry Sharpless, joins an azide (N_3) with an alkyne (a carbon–carbon triple bond), catalyzed by copper. **(b)** Instead of a simple alkyne, Carolyn Bertozzi used an alkyne in a strained octagonal ring. Because it requires no toxic copper catalyst, the cyclooctyne reaction can be performed in living cells. (Figure by Freddie Pagani.)

Function over structure

Meanwhile, Sharpless was formulating a bold vision of what he hoped would be a new way for chemists to think about organic synthesis. In the conventional approach, chemists begin with the end in mind: If they want to create, say, a new pharmaceutical, they first identify the precise molecular structure they want to make, and then they figure out how to make it. The drawback of that strategy is that even if they succeed in making the target molecule—which may take years—the synthesis could be highly inefficient. If the ultimate goal is to manufacture the new substance on a commercial scale, they may be dooming themselves to an extremely expensive end product.

Sharpless's idea, which he articulated in the 2001 paper that introduced the term "click chemistry," was to change the focus from structure to function.[2] The space of possible molecular structures is indescribably vast; it stands to reason that for any desired function, there ought to be many different molecules that are fit for the job. Moreover, those molecules probably aren't all equally difficult to make. Sharpless argued that chemists stood a greater chance of discovering valuable new substances by focusing on the molecules that are easiest to synthesize and taking the functions as they come.

That's where the click reactions came in. Molecules are easy to synthesize if they can be assembled through reactions that are efficient and simple to carry out. For a reaction to retain its efficiency in the context of many different molecular assemblies, it needs to be highly specific: Its reactants should react only with each other, not with anything else that might be present.

Sharpless went on to list several candidate click reactions, although most of them fell short of the ideal of perfect efficiency and selectivity. "But the paper challenged chemists around the world to look for even more efficient reactions," says Jeremiah Johnson of MIT. "And seeding that idea has led to transformative advances."

Copper-catalyzed click

The quintessential click reaction, shown in figure 1a, came on the scene a year later, discovered independently by Sharpless's own group and by Meldal's.[3] Although Meldal wasn't motivated directly by Sharpless's ideas, he recalls that the push for more efficient reactions was in the air. In Meldal's case, he was looking for reactions he could use to make new classes of protein-inspired molecules. "We weren't looking for a whole new way of doing chemistry," he says, "but we hoped to be able to synthesize a lot of things that were not possible before."

The reaction the groups discovered joins an azide with an alkyne—two carbon atoms joined by a triple bond—in the presence of a copper catalyst, to make a pentagonal carbon–nitrogen ring. The bare reaction, without the catalyst, had been well studied by generations of chemists, and Sharpless mentioned it briefly in his 2001 paper. But it was slow and required high temperatures and pressures.

The catalyst increases the reaction rate by a factor of 10 million. Although the reasons for the speedup are now understood—the electrons in the copper ions couple with uncanny precision to those of both reactants—they weren't at the time. "We discovered the catalysis by serendipity," says Meldal, "which I think is how most big discoveries happen. If something was easy to foresee, someone else would have foreseen it a long time ago."

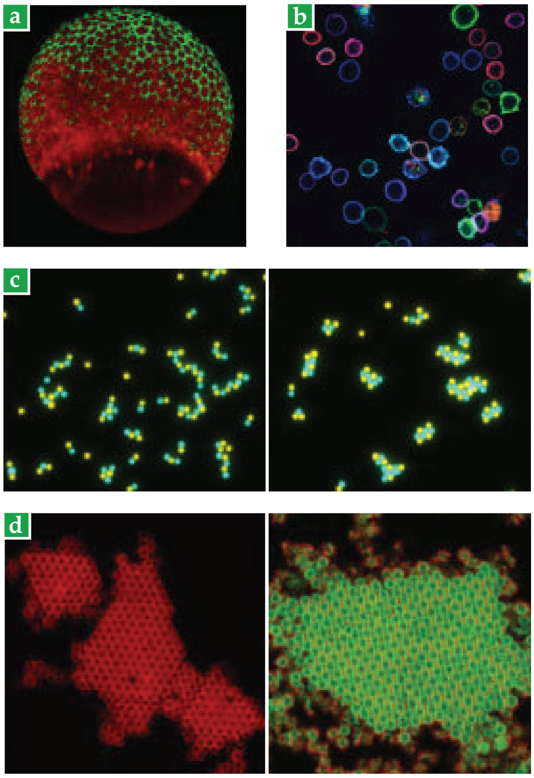


FIGURE 2. BIOLOGY AND PHYSICS applications of click chemistry. **(a)** Glycans in a living zebrafish embryo are tagged with a green fluorophore. (Adapted from J. M. Baskin et al., *Proc. Natl. Acad. Sci. USA* **107**, 10360, 2010.) **(b)** A bone marrow sample contains different types of cells, including nascent white blood cells and their marrow precursors. Tagging living cells with different colored fluorophores helps distinguish their type. (Adapted from J. Ko et al., *Nat. Biotechnol.*, 2022, doi:10.1038/s41587-022-01339-6.) **(c)** Liquid droplets functionalized with biomolecules self-assemble into complex structures. (Adapted from A. McMullen et al., *Nature* **610**, 502, 2022.) **(d)** Solid colloidal particles coated in DNA form crystalline arrays. (Adapted from Y. Wang et al., *Nat. Commun.* **6**, 7253, 2015.)

Both Sharpless and Meldal repeated the reaction with the azide and alkyne bound to many different molecules, including some that in any other context would be extremely reactive. None of them could distract the azide and alkyne from finding each other and reacting. The robust reaction could attach almost anything to anything else.

A milestone in the adoption of click chemistry came in 2004, when Craig Hawker, of IBM Almaden Research Center in California, and colleagues used the azide–alkyne reaction to synthesize a dendrimer, a tree-like branched polymer that had been extremely difficult to make.[4] "I knew click chemistry would be a big deal when the materials scientists started to use it," says Georgia Tech's M. G. Finn, a coauthor of Sharpless's 2001 paper, "because they're focused on function, and click chemistry is all about function." Use of the reaction spread rapidly through the materials and polymer communities: for functionalizing electrodes, formulating new adhesives and self-healing materials, and more.

Among organic chemists, Sharpless's idea of searching for function among easy-to-make molecules coexists with the traditional structure-focused philosophy of molecular discovery. Most molecules can't be assembled purely by click chemistry, and there's still a lot of interest in the ones that can't. "The beauty and challenge of synthesizing complex structures remains, and it remains hugely valuable," says Finn. "That hasn't gone away, and it shouldn't go away."

Bioorthogonal explosion

Bertozzi, who was still on the lookout for an azide reaction that could improve on the Staudinger ligation, was also thinking about ways to speed up the azide–alkyne kinetics. "The copper-catalyzed reaction was useful for a lot of things, but it wasn't useful for us," she says, because the copper catalyst was toxic to living cells. Independently of Sharpless and Meldal, she came up with a different solution.

Digging into the literature, she found a 1961 paper published in German that described a version of the reaction shown in figure 1b, between an azide and a cyclooctyne—that is, an alkyne in an octagonal ring.[5] Nobody in her group was proficient enough in German to read the paper thoroughly, but they realized they may have found the reaction they were looking for when they saw it described as "explosionsartig."

It was no mystery why azides would react more explosively with cyclooctynes than with simple alkynes. An alkyne's preferred structure is linear: The two triply bonded carbon atoms and the two atoms on either side of them all lie in a straight line. When that linear structure is forcibly bent into half an octagon, it endows the molecule with additional pent-up energy that's ready to be released in a reaction.

Even so, the reaction is explosive only when the reactants are mixed in their pure form. When diluted in a biological system, they react as slowly as in the Staudinger ligation. Fortunately, cyclooctyne offered plenty of room for improvement. By decorating the edges of the octagon with other chemical groups, Bertozzi managed to speed up the reaction by a few orders of magnitude—enough to fluorescently label an azide-tagged glycan in a minute or two.[6] With no toxic copper required, the reaction could be performed harmlessly in living animals, such as the zebrafish embryo in figure 2a.

Finally equipped with the chemical tools to image glycans *in vivo* and in real time, Bertozzi and her group have gone on to gain extraordinary insights into the formerly elusive biomolecules, including their roles in animal development, immune activity, cancer, and other diseases. To translate her research into useful technologies and treatments, she's launched nine startup companies, including OliLux Biosciences, which she cofounded with her former student Mireille Kamariza. OliLux is working to develop a test for tuberculosis—a leading cause of death in Kamariza's home nation of Burundi—based on a molecule that's part sugar, part fluorescent dye. The tuberculosis bacteria recognize the sugar and eat it, and the dye's fluorescence changes once it's in the low-dielectric-constant environment of the cell. "Unlike other tests, this detects only living bacteria," says Bertozzi, "so you can tell if the drugs you're using are working."

Chemistry for all

In the 20 years since Sharpless and Meldal discovered the azide–alkyne click reaction, more reactions have joined the click-chemistry portfolio. "But they're mostly not as robust," says Wolfgang Binder of Martin Luther University of Halle-Wittenberg in Germany. "So when you look at the literature, there are orders of magnitude more citations for the azide–alkyne reaction than for all of the others combined." The lone exception is the reaction between tetrazine and transcyclooctene, which does rival the azide–alkyne reaction in speed and selectivity; it's been used in many recent fluorescence-labeling studies, including the one shown in figure 2b.

Vibrant research continues into many variations on the click-chemistry theme, including photoclick chemistry, in which click reactions are triggered by light; fluorogenic click chemistry, in which the reactants are not fluorescent but the product is; and a concept Johnson calls "clip chemistry," which seeks to sever chemical bonds with the same specificity and efficiency as click chemistry forms them.[7]

And the range of click chemistry's potential uses is near limitless, because its pool of potential users is near limitless. "The reactions are very easy, even for physicists like me," says Susumu Takahashi of the University of Southern California. Takahashi uses click chemistry to tether biomolecules to diamond surfaces so he can probe the molecules with nitrogen–vacancy centers embedded in the diamond. "Many physicists worry about working with wet labs and chemicals. Click chemistry makes everything much more accessible—and the reactions are really fun!"

"Before click chemistry, it was a nightmare," says Jasna Brujic, a soft-matter physicist at New York University (NYU). She and her group program liquid droplets to self-assemble into larger structures, such as those shown in figure 2c, by attaching DNA and other molecules to the droplets' surfaces. "If the attachment was too inefficient, we got all these nonspecific by-products and imperfections," she says, "which completely messed up the large-scale structure."

Beyond click chemistry's efficiency and ease of use, another benefit is that its reactants are small, explains David Pine, also at NYU. He studies the crystallization of DNA-functionalized colloidal particles, shown in figure 2d. To attach the DNA to the colloids, he explains, "we used to follow the biologists' protocol of biotin–streptavidin binding: We'd put biotin on the colloids and streptavidin on the DNA, then attach them together." But streptavidin is a protein, and its bulkiness meant that the DNA coatings were sparse and nonuniform. "With the click reaction, we increased the DNA areal density by an order of magnitude," he says.

"Maybe click chemistry will help break down the barriers between chemistry and everything else," says Bertozzi. "It's really democratized chemistry." Meldal agrees: "A very good principle is to keep it simple," he says, "to make your work useful to a lot of people. If it's too complicated, then nobody's going to pay attention."

Johanna Miller

References

1. E. Saxon, C. R. Bertozzi, *Science* **287**, 2007 (2000).
2. H. C. Kolb, M. G. Finn, K. B. Sharpless, *Angew. Chem. Int. Ed.* **40**, 2004 (2001).
3. V. V. Rostovtsev et al., *Angew. Chem. Int. Ed.* **41**, 2596 (2002); C. W. Tornøe, C. Christensen, M. Meldal, *J. Org. Chem.* **67**, 3057 (2002).
4. P. Wu et al., *Angew. Chem. Int. Ed.* **43**, 3928 (2004).
5. G. Wittig, A. Krebs, *Chem. Ber.* **94**, 3260 (1961).
6. E. M. Sletten, C. R. Bertozzi, *Acc. Chem. Res.* **44**, 666 (2011).
7. P. Shieh et al., *Chem. Rev.* **121**, 7059 (2021).

Giant telescopes take small but significant steps toward realization

Can closer communication with Native Hawaiians turn the tide for the Thirty Meter Telescope?

"A year ago, I would have been pessimistic about building the Thirty Meter Telescope on Mauna Kea," says John O'Meara, deputy director and chief scientist for the W. M. Keck Observatory, one of 13 observatories on Mauna Kea, the Northern Hemisphere's premier site for optical and IR astronomy. Opposition to the Thirty Meter Telescope (TMT) has long been strong, and in 2019, hundreds of Native Hawaiians and others blocked the road to prevent its construction on the mountain. (See "Thirty Meter Telescope faces continued opposition in Hawaii," Physics Today online, 5 August 2019.)

But changes in the TMT leadership and in its approach to interactions with Native Hawaiians, as well as a new governance structure for Mauna Kea, may open the door to more fruitful dialog. O'Meara, who is not involved in the TMT, says recent developments make him "optimistic about astronomy on Mauna Kea, whether or not TMT is part of it." And Robert Kirshner, who in May took the job of TMT executive director, says the TMT's "new community-based model" gives him hope that the TMT can be built "through mutual stewardship of Mauna Kea."

DAMIEN JEMISON, GIANT MAGELLAN TELESCOPE—GMTO CORPORATION

CHUNKS OF LOW-EXPANSION GLASS are placed in a mold for casting one of seven segments, each 8.4 meters across, that will form the primary mirror of the Giant Magellan Telescope in Chile. This work is being done at the University of Arizona.

The perceived potential for rapprochement lines up timewise with steps NSF is taking with the US Extremely Large Telescope (ELT) Program. The agency is evaluating the environmental and cultural impacts of building the TMT on Mauna Kea and will soon review the designs of the TMT and the 25.4-meter-diameter Giant Magellan Telescope (GMT), the other US-led ELT project, which has a site in northern Chile.

The 2020 decadal survey by the US astronomy community named NSF investment in the TMT and GMT as its highest priority for ground-based projects. Known as Astro2020, the survey recommends that NSF get a 25% share in each of those international facilities in order to give access to US-based users who are not affiliated with TMT and GMT member institutions. If only one of the telescopes is built, NSF should go for a 50% share for the broader US community, says Astro2020. (See "Astro2020 proposes new approaches to realizing projects," Physics Today online, 18 November 2021.)

Meanwhile, construction on the European Southern Observatory's 39-meter Extremely Large Telescope is well underway on Cerro Armazones in Chile, some 700 kilometers north of the GMT site. The European telescope is on schedule for completion by the end of the decade, well ahead of the others.

The sky access that would be gained by building the GMT in the Southern Hemisphere and the TMT in the Northern Hemisphere would give the US a scientific edge. If neither US ELT is built, astronomy in the US would suffer; the access policy for the European Southern Observatory ELT for astronomers from nonmember countries has yet to be defined. Even with only one of the two, says O'Meara, it would be hard to remain at

ʻOHANA KILO HŌKŪ/KEITH UEHARA

STARGAZING EVENTS such as this one from 27 August at Moʻokini Heiau, a National Historic Landmark on the island of Hawaii, are among the activities that the Thirty Meter Telescope outreach team is collaborating on with Native Hawaiians in efforts to build positive long-term relationships.

the top of the field. "US leadership in astronomy needs big glass."

The ELTs will be able to detect more-distant and fainter objects than is possible with existing 8- to 10-meter-class optical–IR telescopes. One area of anticipated discovery is exoplanets. "We'll be able to see planets by reflected light. They don't have to be hot. They could have habitable temperatures," says Kirshner. "Looking at the atmospheres of other planets will be very powerful." In the long run, he says, "it's not kooky to talk about learning biology with the ELTs."

Observations may also provide clues to the nature of dark energy, dark matter, and the origin and expansion of the universe, and they will test general relativity in the strong fields of black holes. The ELTs will be trained on objects spotted by the *James Webb Space Telescope* and the Vera C. Rubin Observatory. "We'll also follow up on gravitational-wave observations by LIGO [the Laser Interferometer Gravitational-Wave Observatory]," says Kirshner.

Two telescopes, one priority

In recommending that NSF treat the TMT and GMT as a single priority, Astro2020 reset the tone between the projects; the astronomy rivalry between two of their lead institutions—Carnegie Institution for Science for the GMT and Caltech for the TMT—goes back decades before either telescope was proposed.

Good relations between some of the astronomers on the projects have always existed, of course, and there is crossover among the leadership; Kirshner, for example, was on the GMT board for 12 years before taking the TMT reins. But ties are better now because of their being a joint priority. Wendy Freedman, former GMT board chair and a professor at the University of Chicago, says that relations between the projects are as good as they've ever been, but that "when there is concern that only one will be built, everyone gets nervous."

Worldwide, 16 telescopes in the 8- to 10-meter class exist, Freedman notes. "There is so much exciting science to do. It would be so nice to have all three ELTs. It would be a tragedy to have any fail."

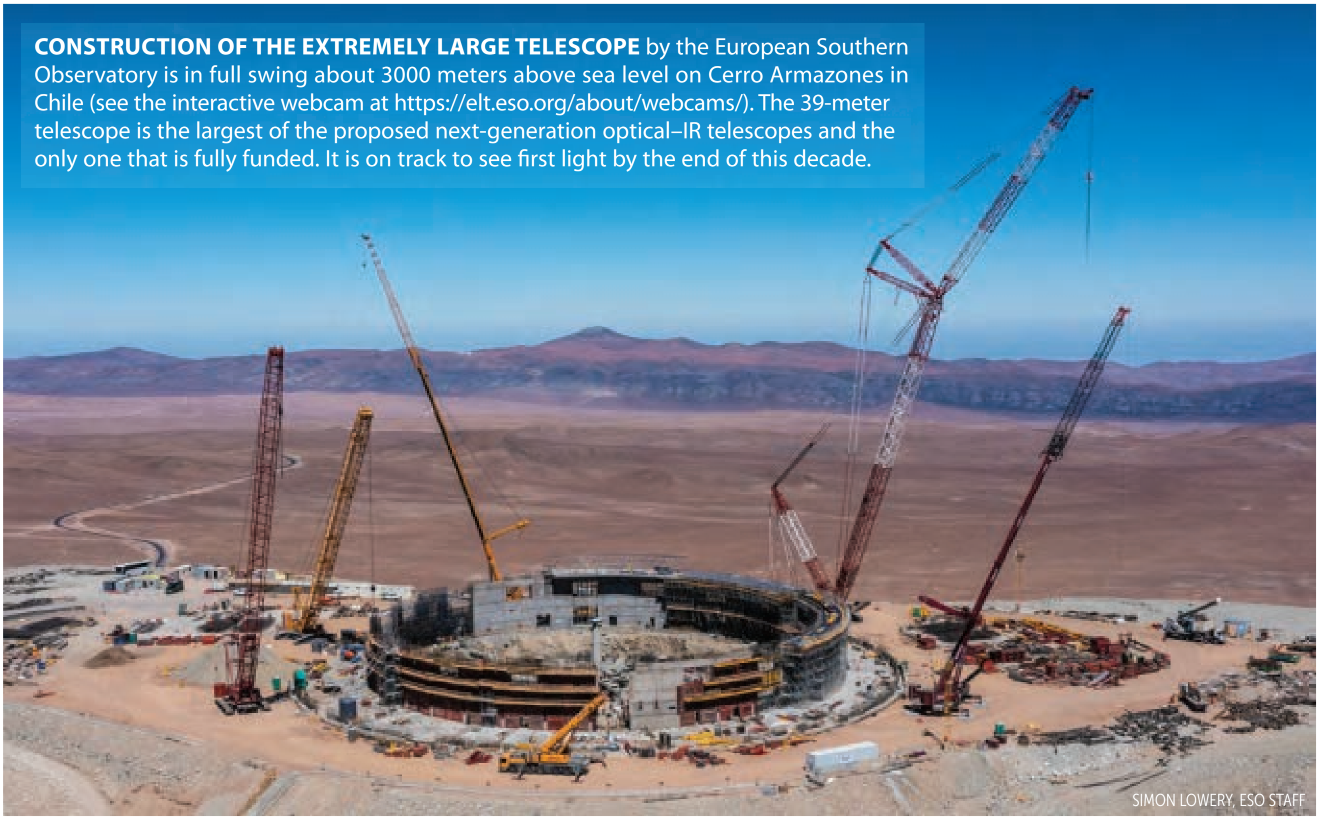
Both US-led projects have ready designs, US and international partners, and partial financial and in-kind commitments, and both have begun manufacturing mirrors and other parts. Their technologies differ, as will their astronomical instruments, but their science goals and capabilities are similar.

The GMT primary mirror is to be formed from seven 8.4-meter mirrors. Six of those have been cast, and three are fully polished. Site excavation was completed in 2019. The next large items are the telescope mount and the enclosure, says the board chair, Walter Massey. So far, the collaboration has amassed commitments totaling about $800 million. Project partners include more than a dozen institutions in the US, Australia, Brazil, and South Korea. The newest partner, the Weizmann Institute of Science in Israel, came on board in fall 2021.

The TMT mirror will be made from 492 1.4-meter segments, using the same technology as both the Keck telescopes and the European ELT. Some 50 of them are in the roundel stage, waiting to be formed into the hexagons needed for tiling. Cash commitments to date total roughly $400 million—with half coming from the Gordon and Betty Moore Foundation. Partners have also made in-kind commitments of comparable value for the enclosure, mount, and mirror supports. The TMT partners are Caltech and the University of California in the US, and government departments and institutions in Canada, China, India, and Japan.

The Astro2020 cost estimates for construction are $2 billion for the GMT and $2.4 billion for the TMT; those tabs will likely rise due to time delays, inflation, and supply issues. For comparison—rough, given differences in costing methods—the European ELT price tag is on budget at €1.4 billion (about $1.4 billion).

The NSF plans to decide about funding the US ELT by late 2024. That's the ideal timeline to enter full construction-phase funding, says Richard Green, interim director of the US ELT Program at NOIRLab, NSF's National Optical–Infrared



CONSTRUCTION OF THE EXTREMELY LARGE TELESCOPE by the European Southern Observatory is in full swing about 3000 meters above sea level on Cerro Armazones in Chile (see the interactive webcam at https://elt.eso.org/about/webcams/). The 39-meter telescope is the largest of the proposed next-generation optical–IR telescopes and the only one that is fully funded. It is on track to see first light by the end of this decade.

Astronomy Research Laboratory, which would manage time allocation, data, and other user interfaces for the projects. "But a lot has to happen for that to happen." A green light could mean first light in 2035 for the TMT and at the end of this decade for the GMT. The US ELT would be NSF's largest research-facility investment ever.

Funding and other challenges

For the GMT, the big challenge is funding, says Massey. "I'm convinced that we have demonstrated that we know how to build the telescope."

The TMT, too, is technologically ready, but it faces a web of challenges involving money, international politics, and access—both legally in terms of locating on Mauna Kea and socially as far as addressing Native Hawaiian opposition. The TMT's backup site, on the Spanish Canary Island of La Palma, comes with other political hurdles. And for either location, the deterioration in US–China relations could cloud China's continued participation.

Earlier this year, the state of Hawaii established a new governance body for Mauna Kea lands. The 11-member Mauna Kea Stewardship and Oversight Authority will have representatives from the Native Hawaiian community, for which the mountain holds sacred and cultural significance. It will also include stakeholders with expertise in land resource management, public education, and business, as well as representatives from the University of Hawaii and the state's Board of Land and Natural Resources. Nominees by the state's governor—including one representing the observatories, Rich Matsuda—still must be confirmed by the state senate. The new body will take over management of—and have extended jurisdiction over—the lands currently managed by the University of Hawaii under the supervision of the Board of Land and Natural Resources.

For astronomy, the most important decisions facing the authority concern access to the land. The current 65-year lease held by the University of Hawaii for 11 000 acres centered on the summit of Mauna Kea—where all of the observatories are located—expires in 2033, as do subleases for each observatory on the mountain. Absent new land authorization, the observatories will need to be decommissioned and the land restored, which could take years. And to go ahead with new projects requires confidence in long-term access. "NSF is unlikely to authorize expenditures for the TMT without a land commitment," notes Douglas Simons, director of the Institute for Astronomy at the University of Hawaii at Manoa, and a longtime Hawaii-based astronomer. With the new authority having "unprecedented power" and being more representative, he adds, the hope is that "there will be more harmony going forward."

The new authority's decisions for land use are needed by 2028—when the transition from the University of Hawaii to the authority is completed. "That's as late as you can push it," says Simons. "I have a healthy dose of concern about how much has to be done in the short time available."

Listening to Native Hawaiians

Meanwhile, in parallel with legal and other planning activities, the TMT team is working to improve relations with the Native Hawaiian community. Fengchuan Liu is the new TMT project manager. Liu is a physicist who had been the TMT deputy project manager and before that had worked on several space missions at NASA's Jet Propulsion Laboratory. In June 2021, he moved from California to Hawaii and went out to talk to Native Hawaiians, including TMT opponents.

In the past, says Liu, the TMT was successful in connecting with Native Hawaiian families whose kids had access to college education and were interested in science, but not with those who lacked such opportunities or who preferred career paths that would allow them to stay near their land. Like everyone else, Liu says, Native Hawaiian families want their children to have opportunities. "We are learning from the communities and working with the communities."

The TMT outreach and education team tutors in schools and hosts evenings of storytelling and stargazing. It is collaborating with a community college to provide scholarships, training, and placement in internships and jobs in local businesses, including observatories, with the aim of improving job prospects across many fields. The team is also planning a program through which Native Hawaiian high school students can visit their Indigenous counterparts in TMT partner countries. "All of these programs came through listening and community requests," says Leinani Lozi, a Native Hawaiian and TMT community outreach specialist.

Rather than asking what it would take to convince the Native Hawaiian community to support TMT construction, Liu says, "we are asking, 'What can we do for the community? What are the right things to do to build long-term relationships?'" That approach goes beyond the TMT, he says. "It is about the future of astronomy and about how science communities relate to Indigenous people, culture, and lands."

Kealoha Pisciotta is a Native Hawaiian cultural practitioner who for years worked as a telescope technician on Mauna Kea (see the interview with Pisciotta, Physics Today online, 23 October 2019). "I have no qualms about them wanting to help the community," she says, "but it can't be transactional." She is skeptical that such activities will lead to acceptance of the TMT and worries that, unless it works by consensus, the new stewardship authority will steamroll Native Hawaiian voices. "People are fed up with the continual 'We are going to do better.' It's kind of obnoxious," she says.

Astronomy in Hawaii contributed \$221 million to the economy in 2019 and was responsible for more than 1300 jobs, according to a January 2022 report by the University of Hawaii Economic Research Organization. The local economy would take a hit if astronomy were to leave Mauna Kea, Pisciotta admits, "but I think people are more interested in protecting the land." Native Hawaiians are not against astronomy, she emphasizes, but, noting that the community has "had to sue to get the telescopes to follow the law," she says that astronomers and other users of Mauna Kea "have acted in bad faith for too long."

The Office of Hawaiian Affairs (OHA), a quasi-autonomous state body that advocates for Native Hawaiians, wrote NSF on 17 September in response to public hearings held this past summer. The office recommends that the agency delay its environmental review of Mauna Kea. "OHA does not advise gambling on overly optimistic and presumptuous lease expectations," the letter says. Given the change in authority over the mountain, it says, delaying the review would be the rational approach and would also be "respectful of the new authority's position and prerogative."

Still, with NSF's involvement making the federal government a player, more opportunities for negotiating are possible, says Simons. He points to the 2011 deal for the solar telescope on Maui, which included \$20 million over a decade to train Native Hawaiians in science, technology, engineering, and math fields at the University of Hawaii Maui College. A similar arrangement may be possible for the TMT, he says, "but with more money, plus other creative solutions, and involvement of community voices in important decisions."

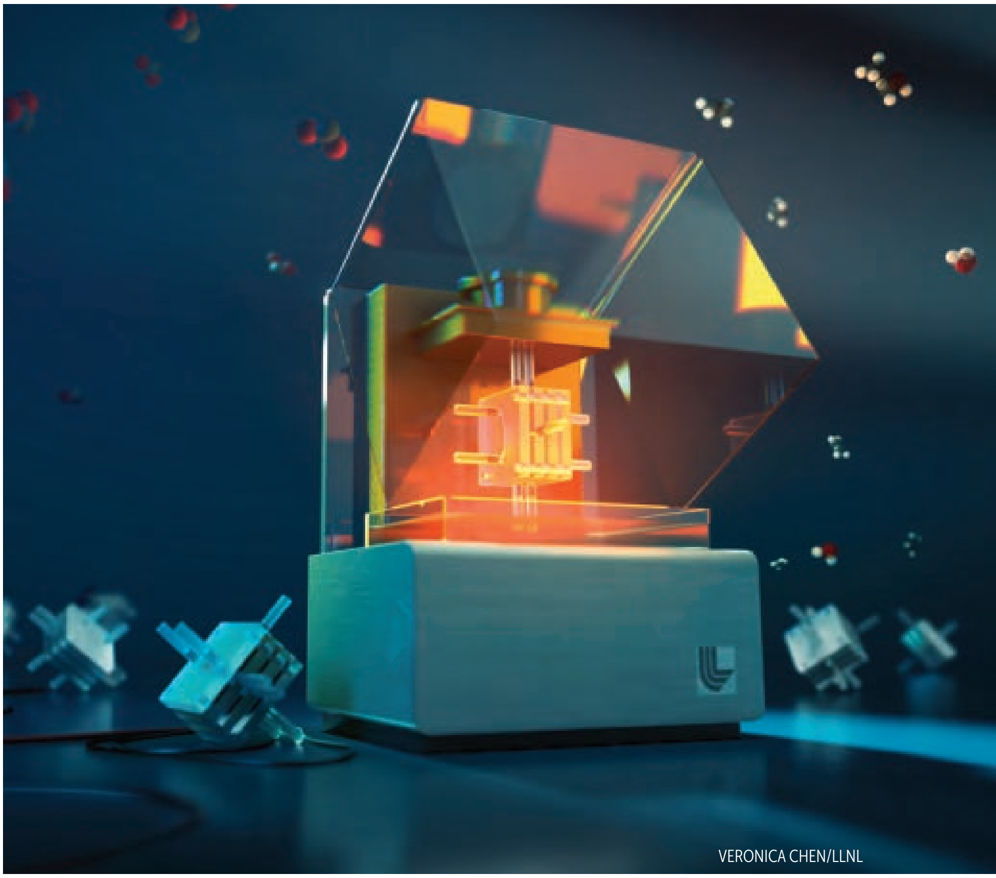
Other areas for negotiation include capping the number of telescopes on the mountain, hiring more Native Hawaiians at the observatories, taking measures to help endangered species, and paying more rent—under the current lease, the observatories pay \$1 per year to the state and grant the state's astronomy program at the University of Hawaii 10–15% of telescope time. "Sometime, many decades in the future," says O'Meara, "there should be no more telescopes on the mountain. That's part of the commitment we should make."

If Mauna Kea doesn't pan out for the TMT, plan B is to build it on La Palma. That site would allow most of the science, but it comes with different twists. Many astronomers worry that NSF won't invest in the TMT if it's not on US soil; it's different for the GMT because the US has no territory in the Southern Hemisphere and has a long history of astronomy investments in Chile.

Toni Feder

The quest is on to remove petro- from petrochemicals

R&D on making petroleum-free petrochemicals is making strides. But the scale-up may come too late to meet urgent climate change goals.



VERONICA CHEN/LLNL

THREE-DIMENSIONAL PRINTING can shorten the time it takes to make improved versions of devices to electrochemically convert carbon dioxide to chemicals. Shown here is a rendition of a 3D printer with a palm-sized reactor housing being printed. Assembled reactors are on the table. The research is a collaboration between Stanford University, the oil and gas company Total American Services, and Lawrence Livermore National Laboratory.

Experts agree that industry and long-distance transport will be the most difficult sectors of the economy to decarbonize. But the petrochemical industry is doubly challenged: Not only are enormous quantities of carbon dioxide released during the manufacture of chemicals and plastics, but the products themselves embed carbon taken from the geosphere, most often natural gas or petroleum.

The manufacture of petrochemicals—the building blocks of plastics, solvents, detergents, lubricants, synthetic fibers, and many other products—is responsible for up to 5% of global CO_2 emissions, according to the United Nations Environment Programme. In the US, chemical plants contribute around one-fifth of industrial CO_2 emissions. That doesn't count the carbon that reenters the atmosphere when the chemicals or plastic products eventually decompose.

Big reductions in CO_2 emissions from petrochemical production can be had by decarbonizing the fossil-fueled high-temperature heat and power that's needed for the steam crackers that thermally break down long-chain hydrocarbons into smaller molecules. But achieving true decarbonization of the industry will require removing the "petro" prefix.

Universities, government labs, and chemical companies are devoting considerable R&D efforts to achieving that end. Electrochemical- and biological-based processes can synthesize chemical building blocks from sources of concentrated CO_2, such as waste gases from steelmaking, or from future air-capture plants, in combination with hydrogen produced with renewable energy.

A few companies have begun making chemicals directly from captured CO_2 and water. The Stanford University spin-off Twelve, for example, is working with industrial partners to apply its electrochemical process to the production of sustainable fuels, plastic car parts, and detergents. In July, it announced an agreement with Alaska Airlines and Microsoft to commercialize its sustainable aviation fuels made from industrial waste gases. The company says it will build a commercial-scale production plant next year at an unannounced site. It's also supplied material for sunglasses made by Pangaia.

In October, LanzaTech, based in Skokie, Illinois, reported that it had made ethylene, the most widely used petrochemical, directly from CO_2 using engineered microbes. Since 2018, the company has made ethylene, a precursor to polyethylene and other plastics, from ethanol that's fermented from CO_2 in industrial waste gases. Its products include packaging, polyester fabrics, and detergents. A LanzaTech spinoff, LanzaJet, converts ethylene to the longer double- and single-bonded hydrocarbons that are used in aviation fuel.

Earlier this year, LanzaTech reported it had manufactured acetone, a solvent that can be used to make acrylic glass, and isopropanol, an antiseptic and precursor chemical, using engineered microbes feeding on industrial waste gases. Michael Köpke, the company's vice president for synthetic biology, says that process is carbon negative. "Typically, per kilogram of acetone, you emit two and a half kilograms of CO_2," he says. "We can avoid those emissions but also lock in 1.8 kilograms of CO_2 per kilogram of acetone."

In October the Department of Energy awarded a team from Northwestern University, LanzaTech, Yale University, and the National Renewable Energy Laboratory \$18.5 million for R&D aimed at accelerating biosystems design for carbon-negative biomanufacturing. Michael Jewett, director of Northwestern's Center for Synthetic Biology and the project's principal investigator, says the goal is to reduce to two days the amount of time needed to engineer a carbon-hungry microbe to make different bioproducts, biofuels, and biomaterials; the process currently can take up to a year.

"We need to advance and apply our capacity to partner with biology to make what is needed, where and when it is needed, on a sustainable and renewable basis," Jewett says. "This project will allow us to grow US-based manufacturing through fundamental research insights."

Improving on photosynthesis

One potential method for transforming CO_2 into useful compounds is artificial photosynthesis, where sunlight, CO_2, and water are transformed directly into useful chemical compounds. Tobias Erb is one researcher working on enzymatic pathways to solar-driven chemical synthesis. Erb, director of the department of biochemistry and synthetic metabolism at the Max Planck Institute for Terrestrial Microbiology in Marburg, Germany, and colleagues have found or engineered multiple enzymes that improve on the efficiency of RubisCO, the enzyme used by plants to fix CO_2 into their biomass. One of their early carbon-fixing cycles required 17 enzymes from nine organisms, including three that were synthesized or had their active sites altered to react with more substrates. Compounds they have made include terpenes, a class of 5-carbon compounds, and a soon-to-be-published paper will describe the synthesis of a 15-carbon compound that serves as the backbone of erythromycin, a commonly used antibiotic.

The artificial photosynthetic approach can accomplish simultaneously in a continuous process cycle reactions that might require 10 or more steps in chemistry, each one requiring new solvents and energy to purify the product for the next step, says Erb. He's developed a microfluidic platform that spits out tiny droplets of artificial chloroplasts, and he is working to move them into the cells of living organisms such as *Escherichia coli*. He stresses that the work is still in the basic research stage.

Genetically engineered microbes have the capacity to produce a wide array of diverse, high-value chemicals and compounds, and R&D has advanced rapidly in the last decade, says a September report from the Engineering Biology Research Consortium. But the document, *Engineering Biology for Climate and Sustainability*, says those processes still must be engineered to capture and recycle all of the CO_2 that is emitted by the organisms as they digest and transform it into useful compounds.

Electrochemical pathways

As cheap renewable energy makes electrochemistry more affordable, the technique is finding new applications, including decarbonizing petrochemicals, says Adam Weber, a senior scientist at Lawrence Berkeley National Laboratory. "We like to say that electrochemistry is the thermal chemistry of the 21st century," he says.

One of the costliest petrochemical processing steps is the post-cracking separation of ethylene from ethane that remains in the mix. Weber works to optimize an alternative: the electrochemical reduction of CO_2 to carbon monoxide. The CO is combined with electrolytically produced hydrogen to make syngas, which can further be converted to ethylene.

Berkeley Lab is a partner in the Caltech-led Liquid Sunlight Alliance (a successor of the Joint Center for Artificial Photosynthesis), which has long worked on electrochemical CO_2 reduction using photons to produce sustainable fuels. "What we see is if you want to be industrially relevant, you need to go to higher fluxes. And in any photosynthetic or artificial photosynthetic process, if you are tied to the flux of light coming in, you won't get to high fluxes," Weber says. Higher reaction rates can be achieved with the use of electricity and catalysis. "That's where we see industry wanting to go when we talk to them about electrochemistry, electrochemical refining, and CO_2 production."

Researchers at Lawrence Livermore National Laboratory have demonstrated that three-dimensional printing can be used to rapidly enhance vapor-fed electrochemical reactors designed for CO_2 conversion, increasing their efficiency while broadening the fundamental understanding of the reactions. "Mass transport is key," says the principal investigator, Jeremy Feaster. "We can have the best catalysts in the world, but if we can't get the reactants to the catalyst surface, then it doesn't matter." The team has been repurposing electrolyzer designs used in water splitting that can take weeks to make and cost thousands of dollars each. He estimates that his team has built around 150 palm-sized reactors in varying geometries, printing them in a few hours for about \$10 apiece. They are now scaling them up in size, using much larger printers.

A team effort

The most efficient production process for petroleum-free chemicals could team electrochemistry with biology. Electrochemically generated CO or formic acid, for example, might be fed to microbes that are genetically engineered to spit out more-complex hydrocarbons, such as polyhydroxyalkanoates, a class of polymers that is compostable.

The cleverly titled Bio-Optimized Technologies to Keep Thermoplastics out of Landfills and the Environment (BOTTLE) consortium, headed by the National Renewable Energy Laboratory, published a paper in *Science* in October in which the researchers described a process that would allow recyclers to skip sorting plastic by type. In their approach, first the different polymers were broken down to their building blocks through a catalyzed oxidation process that accomplished in minutes the degradation that naturally takes place over years or decades.

The researchers next fed the mixture of chemical compounds—including benzoic acid, terephthalic acid, and dicarboxylic acids—to a genetically engineered soil microbe, *Pseudomonas putida*, for conversion to either polyhydroxyalkanoates or beta-ketoadipate, the latter of which can be used to make new performance-advantaged nylon materials. An experiment selected to fly aboard the International Space Station next year will test whether microgravity conditions can improve the bacterial conversion rate.

Energy inputs

Despite their promise, however, technologies to displace fossil carbon in the

STEAM CRACKERS, such as the ones in this BASF facility in Ludwigshafen am Rhein, Germany, require a significant amount of fossil energy to break down long-chain hydrocarbons into smaller, more usable products. The reactions are typically conducted at about 850 °C. Crackers are one of the largest sources of CO_2 emissions in the manufacture of petrochemicals.

raw-materials feedstock are still in their nascent stages, and bringing them to industrial scales is likely to take decades, says Julia Attwood, the principal author of a May analysis by the consulting firm BloombergNEF, *Decarbonizing Petrochemicals: A Net Zero Pathway*, that explored the industry's route to net-zero emissions by 2050. The R&D thus might do little to help the chemical sector achieve net zero in 28 years. The industry is likely to focus mainly on removing fossil energy inputs to the chemical manufacturing process, says the study.

The report estimates that the chemical industry can achieve near-net-zero status in the 2050 time frame for a cost of $759 billion. The largest reduction, 40% from current levels, would come from adding carbon capture and storage systems to the crackers and to the combined heat and power plants at the manufacturing sites. The introduction of electrified steam crackers, which are still in development, could cut emissions by 35% more.

The study does foresee industry's having to turn to renewable methanol, very little of which is produced today, to provide the feedstock for around 20% of its output. Most aromatics—benzene, toluene, and xylene—essential for some plastics are a by-product of oil refineries, Attwood explains, and that supply will likely plunge as refineries either close or sharply curtail their output of gasoline and diesel fuels because of vehicle electrification.

Methanol is the most likely option for replacing the lost aromatics, but nearly all methanol is derived from gas and coal today. Green ethanol will triple the cost of the petrochemical products that are made from aromatics, says BloombergNEF. Not surprisingly, dozens of renewable methanol projects are in development globally, the largest number of them in Europe, according to the Methanol Institute.

A study by George Mason University and other contributors released in September said that 80–90% of CO_2 emissions from polyvinyl chloride production could be eliminated by 2050 through a combination of carbon capture and storage and replacing fossil fuels with hydrogen to provide heat and power. PVC is the third-most-produced plastic by volume, behind polyethylene and polypropylene. The researchers said their recommendations would add 5–15% to PVC prices. Stringent regulatory policies or breakthroughs that reduce the capital costs of carbon capture and storage would drive substantial abatement more rapidly.

Those estimates, however, assume an existing infrastructure is available to transport green hydrogen from its source and to move CO_2 to where it will be injected underground for permanent storage. Last year's bipartisan infrastructure law included $8 billion for hydrogen production and infrastructure (see PHYSICS TODAY, August 2022, page 22). The high concentration of refineries, petrochemical plants, hydrogen-production facilities, and associated pipelines along the Gulf Coast could be adapted for those purposes, notes Brett Perlman, CEO of the nonprofit Center for Houston's Future. The organization is preparing a bid to become one of 6–10 regional hydrogen hubs the Department of Energy is planning to support.

The authors of the PVC study said that petroleum-free processes won't likely be ready in time to meet the urgency of the CO_2 emissions challenge. Adoption of electric crackers will be dependent on more affordable electricity from a decarbonized grid.

David Kramer PT

ISTOCK.COM/ELENAMICHAYLOVA

Peter Fischer heads the Institute of Food, Nutrition, and Health at ETH Zürich in Switzerland. His research focuses on rheology and structure of complex fluids.

Sand and mucus: A toolbox for animal survival

Peter Fischer

Studying animals' use and manipulation of complex fluids from materials-science and rheological points of view can help to understand animal behavior and provide new insights for mimicking biomaterials.

Animals are under constant pressure to survive in their surrounding environment, and they have evolved countless strategies to adapt, colonize, and reproduce successfully in their habitats.[1] Almost acting as materials scientists, animals may directly manipulate complex fluids around them or secrete complex fluids themselves to fulfill a specific task. Mucus, for example, demonstrates a wide range of rheological properties depending on its physiological purpose—locomotion, sexual reproduction, protection against predators, or one of countless other uses. And when conditioned properly, sand present in the habitat can be used for movement or for predation.

Rheologically active materials—those with unusual or nonlinear responses to an applied force (stress) or deformation (strain)—often have clearly defined action windows, so matching the material properties with an animal's desired outcome is essential. To exploit the rheological properties for the specific task, the animal therefore must sense and, if needed, manipulate the rheology of the surrounding complex fluids. Rheology and materials science provide a valuable approach to study materials originating from the habitat or secreted by an animal, with implications for biomimetic materials design and ethology.

Defining terms

Selective pressure on animals originates from the entire set of environmental factors acting on them. Those factors can be classified as biotic or abiotic. Biotic factors include all other organisms in an individual's environment, the animal itself, and the resulting consequences, such as competition for food, space, or shelter. Abiotic factors include the chemical or physical nature of the surroundings, such as temperature, humidity, nutrients, and materials' mechanical properties.

Animal–material interactions can be further distinguished by the material's origin, whether endogenous (produced by the animal itself) or exogenous (provided by the habitat).[2] For example, endogenous abiotic material, such as the "net" of air bubbles a humpback whale blows to trap fish, originates from an animal but is not formed by a biological process. Exogenous biotic material is formed by a living organism but not by the animal that uses it later on: Cow dung, for instance, provides shelter and nutrients for insects and their larvae. Endogenous biotic material originates from the animal that also utilizes it; examples include saliva and mucus for digestion and lubrication.

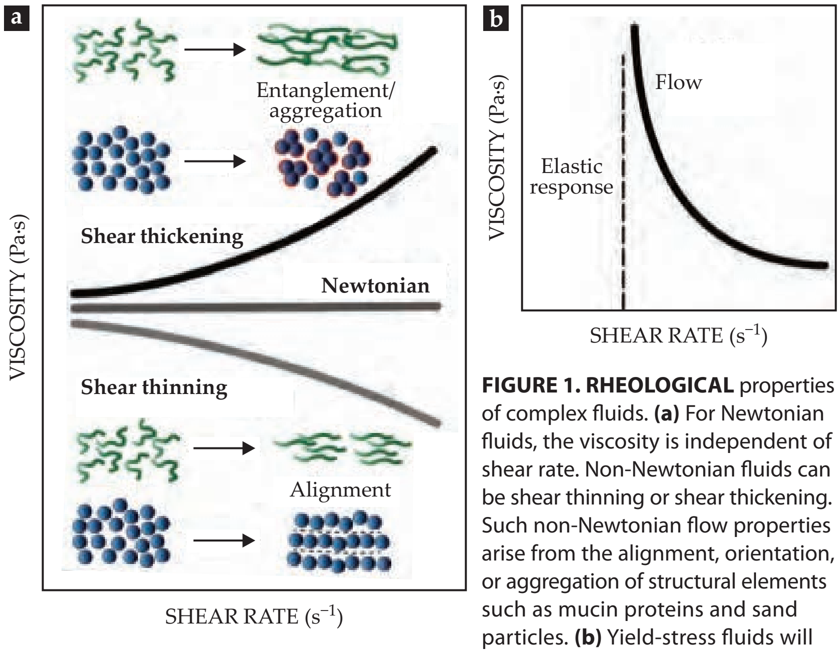


FIGURE 1. RHEOLOGICAL properties of complex fluids. **(a)** For Newtonian fluids, the viscosity is independent of shear rate. Non-Newtonian fluids can be shear thinning or shear thickening. Such non-Newtonian flow properties arise from the alignment, orientation, or aggregation of structural elements such as mucin proteins and sand particles. **(b)** Yield-stress fluids will only begin to flow—with Newtonian or non-Newtonian behavior—once a minimum deformation or stress is applied. (Adapted from ref. 3.)

Animal–material interactions also depend on a whether a material is hard or soft, as determined by its mechanical and rheological properties. Hard exogenous materials generally do not change much over time or as a function of applied mechanical stress, and thus they offer little physical response for animals to exploit. Fluids, on the other hand, do respond to external forces and often have fascinating material properties as a function of applied stress or strain as well as time and temperature.

The simplest and most convenient way to describe the mechanical properties of fluid is by its viscosity, which expresses the internal friction during flow and deformation. For Newtonian or linear fluids, the viscosity is a constant, independent of the acting forces, as shown in figure 1a. Complex fluids—macromolecular or multiphase systems consisting of molecular, colloidal, and noncolloidal components in liquid, solid, or gaseous states—exhibit more complex, non-Newtonian flow behavior. The viscosity of a non-Newtonian fluid, also called a nonlinear fluid, might increase (shear thickening) or decrease (shear thinning) under applied mechanical deformation.

Shear-thickening and shear-thinning behaviors arise from the flow-induced orientation and alignment of the structural elements of the fluid, such as mucin proteins in mucus or suspended sand particles, as shown in figure 1a. Without flow, those structural elements could arrange in solid-like structures and require a certain deformation or stress to yield before Newtonian or non-Newtonian flow properties are observed (see figure 1b). Last but certainly not least, complex fluids also may exhibit elastic properties (solid-like energy storage) and viscous properties (liquid-like energy dissipation) at the same time and are thus defined as viscoelastic materials; they also exhibit linear and nonlinear responses. The broad spectrum of rheological properties of soft materials provides the playground for exploitation by animals under different environmental cues.[3]

This article focuses on two very different complex fluids: sand, an exogenous abiotic material, and mucus, an endogenous biotic material. Both exhibit strain- and time-dependent flow behavior, which animals sense, manipulate, and use in their survival strategies. The mechanical and rheological properties of granular materials such as sand are mainly determined by the moisture content and the particle size distribution, shape, and roughness. The governing equations to describe the flow properties extend from frictional rheology, describing the interplay between inertial and viscous forces, to more classical suspension rheology.

Mucus is a collective term for substances with similar composition and properties; it appeared early in the evolution of multicellular animals and probably evolved multiple times independently.[4] It is composed of water, proteins, lipids, salts, and cellular debris and is constantly renewed by the secreting goblet cells of mucosal membranes. The main component, mucins, are proteins densely covered with covalently bound oligosaccharides (carbohydrates). Mucus is used for various well-targeted physiological applications, such as cell protection and food and gas uptake, and also for locomotion, defense, and predation, as discussed below. Mucus can fulfill those different tasks because of an almost endless combination of proteins and oligosaccharides, which determine the viscoelastic or gel-like properties of the physically cross-linked material.[5]

Locomotion

Terrestrial gastropods, such as snails and slugs, use their entire body as a single foot to crawl by so-called adhesive locomotion. The propulsion is powered by muscular waves that propagate from tail to head along the ventral side of the foot. The periodic contraction–relaxation waves (see figure 2a) are transmitted to the ground by a thin, sticky layer of viscoelastic mucus constantly secreted by the animal.[6] The nonlinear rheology of the mucus enables the gastropods to propel by partly detaching from the ground via a stick-and-release mechanism.

The mucus's rheological properties must be threefold: a solid-like elasticity at low stresses (including at rest); a high, sharp yield point with a transition to a highly viscous, shear-thinning liquid; and a fast recovery of network structure after stress release. A movement cycle, as visualized in figure 2b, starts with elastic, solid-like mucus anchoring the resting part of the foot. The approaching muscular wave shears the mucus, increasing the stress until, at the yield point, the mucus structure breaks and liquefies. During the interwave, there's no shear, and the mucus network recovers its elastic, solid-like properties that anchor the foot for the next cycle. The movement cycle generates an asymmetric shear force under the foot that allows the animal to crawl forward.[7]

Although adhesive locomotion is the most energy-intensive form of movement, the largest energy expense is mucus production, not muscle activity. Within the stick–slip cycle of resting and sliding, the transient rheological properties represent a fine-tuned interaction between the animal and its environment. The secreted mucus layer also provides adhesion, which allows the animal to climb walls and trees and crawl across ceilings and overhangs, and it enables a spectacular mating performance, as discussed below. But locomotion is significantly slowed down on rough surfaces or granular matter—not because of the surface properties per se but because of the increased amount of mucus required to lubricate the ground.

Some snakes and lizards that are native to semiarid or arid areas exhibit an exceptional way of locomotion: swimming-like movement. (See the Quick Study by Yang Ding, Chen Li, and Daniel Goldman, Physics Today, November 2013, page 68.) Under certain conditions, a granular material like sand can flow like a liquid, enabling that unique way of locomotion. Animals living in such surroundings can locally fluidize the granular material around them by changing the packing fraction—the fraction of space occupied by the particles. Digging has proved to be a favorable escape strategy for animals such as the sandfish skink (*Scincus scincus*, seen in figure 2c); burying eggs in the sand to protect them from predators is commonly seen too.[8,9]

In addition to their dependence on the packing fraction, the mechanical properties of granular media also change dramatically between dry and water-saturated conditions. As a consequence, rain in the desert renders the dry sand into a compact suspension that is much harder to shear, thereby temporarily stopping underground locomotion until the sand has dried up again. Granular flow is classically described by frictional rheology: In dry conditions, the macroscopic friction is characterized by the dimensionless inertial number (relating the inertia forces to the imposed shear forces), while in wet conditions, it is replaced with the dimensionless viscous number (relating shear forces to normal forces). Both dimensionless numbers are a function of the local solid packing fraction.

To "swim," the sandfish locally fluidizes dry sand using undulating stresses (see figure 2d). Locomotion in granular media can be divided into different regimes depending on the relative digger size compared with the grain size and on the inertial number; sandfish belong to the class of large and fast digging animals.[9] Analogous to an aqueous swimmer at low Reynolds number (the ratio of inertial to viscous forces), the sandfish achieves a net forward displacement by undulating motion. Interestingly, the scallop theorem claims that at low Reynolds numbers, a simple symmetrical back-and-forth motion is not sufficient for locomotion. But if the swimmer is immersed in a non-Newtonian liquid, such back-and-forth movement can cause a net forward displacement. For the sandfish, the packing density and thus the friction in the front and rear parts of the animal differ, which enables the forward movement.

Catching prey

Velvet worms (phylum Onychophora) use an endogenous complex fluid that is strain hardening and adhesive to immobilize their prey.[10] The worms, which inhabit humid regions of the

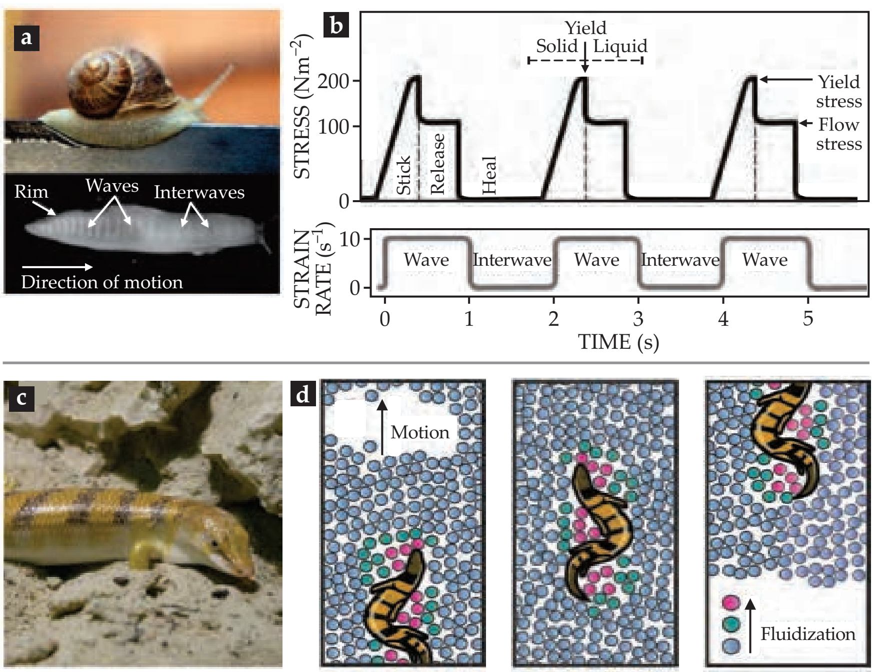


FIGURE 2. LOCOMOTION exploiting mucus and sand. **(a)** Slugs and snails move via traveling waves along their body that rely on the yield-stress and shear-thinning behavior of the viscoelastic mucus that the animals excrete. **(b)** The transient rheological properties of the pedal mucus of the Pacific banana slug (*Ariolimax columbianus*) during locomotion.[6] As the body wave passes, the mucus yields and begins to flow; between waves, it recovers its solid-like elastic behavior. **(c)** The sandfish skink (*Scincus scincus*) lives in arid and semiarid climates. **(d)** The sandfish swims through sand using undulatory motion that fluidizes the sand particles surrounding it. (Adapted from ref. 3.)

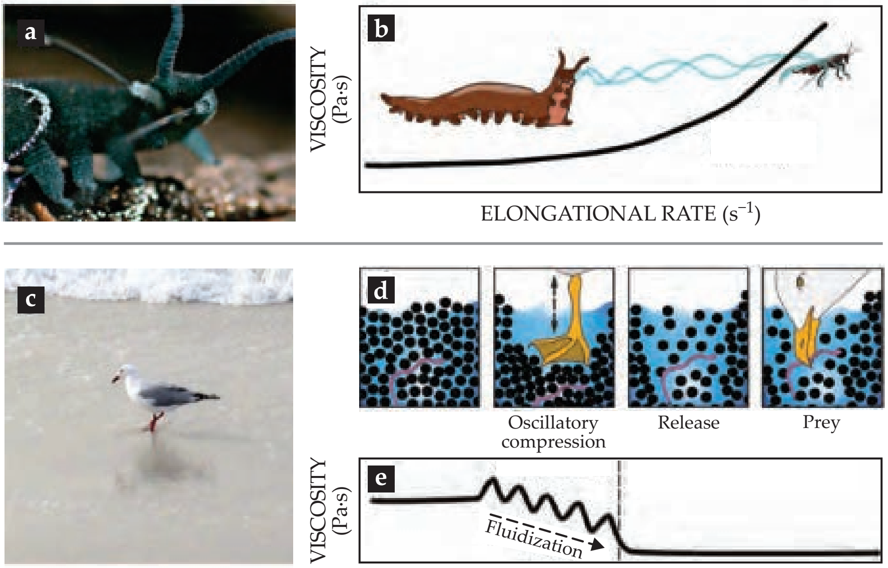


FIGURE 3. CATCHING PREY with the help of complex fluids. **(a)** Slime ejection from the slime papillae of a *Euperipatoides rowelli* velvet worm.[10] **(b)** Hypothesized viscosity change of velvet-worm slime during ejection. As the initially fluidlike slime gets extruded, it thickens into a viscoelastic fiber. **(c)** A seagull feeding on worms by pedaling its feet to fluidize a sandy beach. **(d–e)** Proposed rheological behavior of wet sand under a seagull's oscillatory compression. When the compression is released, the surrounding water refills the void and dilutes the sand; the eased flow makes it easier to extract prey. (Adapted from ref. 3.)

tropical and temperate zones and have lengths of 0.5–20 cm, crawl up on their prey and eject a sticky slime from two papillae flanking their mouth, as shown in figure 3a. The slime ejection produces an uncontrolled papillae oscillation at 30–60 Hz, which causes the threads to cross in midair, leading to an entangled slime net that traps the prey. The worm then injects the prey with hydrolytic, enzyme-containing saliva that kills it and induces liquefaction for later ingestion.

In contrast to other secreted adhesive fibers like spider or silkworm silk, which are solid upon excretion, velvet-worm slime is a remarkable showcase of a biological complex fluid with fine-tuned transient properties. Fluidlike in the slime glands and papillae, it develops cohesiveness and mechanical strength during the elongational flow upon ejection. The functional components of the aqueous slime (90% water by weight) are protein–lipid nanoglobules, which are about 50% protein and 1% lipid and exemplify the important role of additives in biological and biomimetic composite materials. The nanoglobules are approximately 150 nm in diameter and have a narrow size distribution. They are probably formed by the complex electrostatic aggregation of oppositely charged protein moieties.[11] Although the exact amino-acid sequence and the folding of the proteins is unknown, the proteins have a high molecular weight, high charge density, and some portion of β-sheet structures, which all favor intra- and intermolecular electrostatic interactions.

The transition from fluidlike slime to viscoelastic fibers upon extrusion outside the animal's body suggests that elongational strain thickening is crucial for the slime's functionality. That untested hypothesis is depicted in figure 3b. In elongational flow, the protein–lipid nanoglobules rearrange into stretched protein fibers. The fibers have a coating layer with a higher lipid content compared with the protein-rich core. The protein fibers are probably responsible for the toughness of the final slime. The role of the lipids is not fully clear yet; they may act as interfacial stabilizers of the nanoglobules and control their assembly prior to and during elongation.

The final slime filament consists of thin, elastic threads with several adhesive globules distributed along their length. Dried threads undergo a glass transition and reach a stiffness of about 4 GPa. Interestingly, the initial protein–lipid nanoglobules can be re-formed upon rehydration of the dried slime, and new fibers can be drawn from the regenerated slime. That behavior supports the current model, which says that noncovalent electrostatic interactions are responsible for slime formation and that the liquid–liquid phase separation into dispersed protein–lipid nanoglobules returns the slime to its equilibrium state.

Seagulls (family Laridae) and numerous plovers (family Charadriidae) in tidal zones use a two-footed pedaling technique (see figure 3c) to exploit granular material properties: The pedaling loosens and liquefies the structure of the wet sand and eases the extraction of worms. Granular rheology suggests the following mechanism: The glossy sand in tidal zones is a randomly close-packed and completely wetted material. Upon impact or pedaling—whether by humans, gulls, or other animals—the sand is spatially rearranged and the water table is lowered temporarily, making the sand's surface appear matte. Immediately after the structural rearrangement, the surrounding water refills the void and dilutes the sand, which then can flow with far less resistance because of its lower solid volume fraction (see figure 3d). A preying animal such as a seagull is thus able to pick its prey from a diluted suspension rather than from densely packed sand with its high resistance to digging and deformation.

The pedaling, a form of oscillatory compression (see figure 3e), results in a more dilute sand structure, an effect known as positive dilatancy. A similar phenomenon is the Brazil nut effect, even though no diluting secondary fluid is involved. When something is lost in granular matter, just shake the container; depending on the density difference, the object can be collected at the bottom or top of the container.

Reproduction

One of the most spectacular examples of using endogenous complex fluids is the mating ritual of leopard slugs (*Limax maximus*). Slug twosomes use a thread of gel- or rubber-like mucus to suspend themselves in midair to perform their circus-like sexual act (see figure 4).

Like other gastropods, leopard slugs usually use mucus for adhesive locomotion. But once a twosome reaches a desirable location, preferably the bottom side of a tree branch or even a wall, the slugs start to intertwine and stimulate the formation of a thick mucus layer around themselves. The mucus secretion and rubbing continue for up to an hour until the mucus achieves a gel- to rubber-like consistency. The slugs then dive headfirst from the supporting branch or wall, dangling by the mucus thread. The midair position allows full extension of male genitalia, a feat difficult to perform without being suspended.

Slugs and snails are known to produce mucus with different composition and rheological properties depending on its use. But for mating leopard slugs, the time-dependent change of the rheological properties is crucial. The yield stress and viscosity of salivary, nose, and slug mucus generally increase upon drying. And mucus viscosity scales as the cube of mucin concentration. But the transition from a viscoelastic fluid to a gel-like thread cannot be explained only by a higher concentration of mucin or other mucus components. The applied shear stresses induced by the constant intertwining could promote mucus elasticity through the formation of intermolecular bridges. That possibility is supported by the observation that shear forces cause mucin molecules to aggregate into larger network-like structures.

Before performing their slow-motion headfirst dive together, the slugs must somehow sense when the drying and intertwining have achieved the ideal gel-like mucus properties: Go too early and the thread will not hold the weight, and the slugs will crash-land in the bushes. Wait too long and the dried-out mucus will lose its gel-like properties and become solid, and again the slugs will not be able to exploit the viscoelasticity to safely lower themselves. As sketched in figure 4d, both the storage modulus (a measure of the elastic response) and loss modulus (a measure of the viscous response) increase during the prelude until a gel-like consistency supporting the headfirst dive is reached. The mucus thread experiences a strong extensional force as it holds two fully grown leopard slugs, which weigh up to 8 g each. That gravitational force has to be balanced by the network structure of the mucus thread.

Defense

Hagfish (including *Myxine glutinosa* and *Eptatretus stoutii*) present a particularly striking example of an animal defense mechanism that uses complex viscoelastic fluids. The eellike animals play an important role in aquatic ecosystems: By burrowing and feeding on carcasses that sink to the seabed, they contribute significantly to substrate turnover and ocean cleanup. When hagfish are disturbed in their daily duty and attacked by predators, such as sharks or suction-feeding fish, they form huge amounts of slime in less than a few hundred milliseconds (see figure 5a).

That remarkably fast slime formation is triggered by the release of a protein-based exudate from ventral glands into the surrounding seawater. Once in contact with seawater, the exudate rapidly forms a fibrous hydrogel that clogs a predator's mouth and gills.[12,13] The exudate itself is composed of keratin-like protein threads, which are coiled up into microscopic balls called skeins, and mucin vesicles. In contact with seawater, the skeins unravel into long threads with lengths of up to 15 cm and form a wide-ranging network structure. The mucin vesicles, meanwhile, swell and eventually burst, releasing the water-absorbing mucin molecules into the network.[14]

Hagfish slime thus can be considered a double network structure formed by the skein and mucin components. The long skein threads are crucial for the slime's cohesion and viscoelasticity, whereas the mucins facilitate water entrapment. Both have their own mechanical and structural properties, such as elasticity and pore size. Together they form a soft yet elastic hydrogel with a water content higher than any other known biological hydrogel.

The rheology of hagfish slime is fine-tuned for its defense functionality. In extensional flow, such as the suction flow of suction-feeding fish, the mucin's extensional viscosity increases by two orders of magnitude in just a second, making it harder for the predator to swallow and additionally clogging its gills (see figure 5b). On the other hand, the slime is shear thinning, and the hagfish can easily wipe the slime off itself by forming a knot that moves down its body; that feature allows the hagfish to escape its own trap after successfully deterring the predator (see figure 5c). As a viscoelastic material, the slime

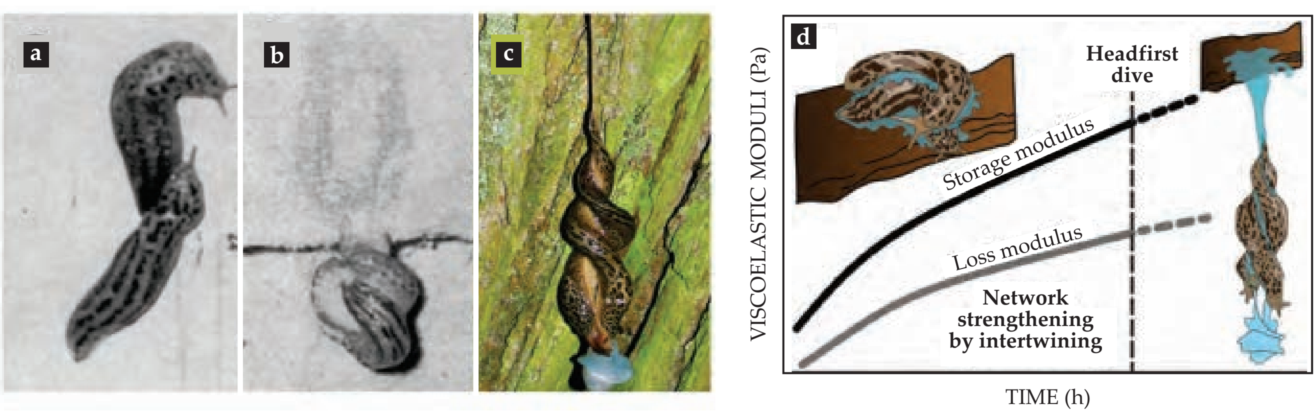


FIGURE 4. VISCOELASTICITY IN COURTSHIP. (a–c) After a leopard slug (*Limax maximus*) meets its mating partner, they intertwine and secrete mucus, which thickens to support a headfirst dive that allows hanging intercourse. **(d)** Hypothesized change in viscoelasticity as expressed by the storage modulus (elasticity) and loss modulus (viscosity) of leopard slug mucin over time during courtship and mating. (Adapted from ref. 3.)

shows gel-like behavior at small deformation and fluidlike behavior at larger deformation above the yield point. Besides its fast deployment, hagfish slime is also unique in that its formation requires very little exudate—the final slime is about 0.02% solids by weight—and no additional energy input (gelatin, for example, requires heating to gel). The slime is an economical yet efficient defense mechanism, and it might serve as a template for future gelling agents.

The notorious hagfish is not the only creature that uses slime to deter predators. When disturbed, the slime star (*Pteraster tesselatus*) presses water through mucus-lined channels to rapidly produce large quantities of mucus-based slime that engulfs it.[15] No rheological data are currently available on the slime, but it shows viscoelastic and transient rheological properties similar to those of hagfish slime. And the parrotfish (*Chlorurus sordidus*) secretes mucus during the night to form a gelatinous sleeping bag around its body to protect itself from parasites. In contrast to the instantly formed but short-lived slimes of hagfish and slime stars, parrotfish mucus is produced within one hour, and its protective function remains for up to five hours.[16] Although no rheological characterization of parrotfish mucus has been reported, it is described as gel-like or even solid-like, suggesting a higher solid content than other slimes.

Sand-dwelling crabs (genus *Dotilla*) use sand-based structures—either vertical burrows or igloo-like structures[17] (see figures 5d and 5e)—for protection. As discussed above, dry sand acts like a fluid whose behavior can be described just by the friction between the individual particles. With increasing water content, the sand's cohesiveness increases because of rising suction forces. Eventually, at elevated water content, the resulting sand–water suspension regains a more fluidlike character. The crabs adapt their construction designs depending on the sand's water content. When the water content in the sand is low, the crabs create vertical burrows. Under unstable, semifluid conditions, they change their behavior and build igloo-like structures. Semifluid sand doesn't allow for a vertical burrow—it would immediately collapse. The crabs instead exploit the water-induced suction forces to produce self-standing architectures. Figure 5f depicts the proposed link between the burrow's design and the cohesiveness of sand.

A versatile toolbox

Animals have generally little to no influence on the ambient conditions at which they exploit complex flow phenomena. As a consequence, some of the presented survival strategies are seen only in specific habitats. For example, the "swimming" locomotion in sand is only possible in arid or semiarid regions where sand can be locally fluidized with relatively small effort. On the other hand, the construction of complex sand formations is only possible in tidal zones where the water content makes sand cohesive—a strategy we humans also intuitively exploit when building sandcastles. Some animals, like the sand crabs, adapt their behavior depending on the surrounding material properties.

For endogenous complex fluids like those used by the velvet worm, the leopard slug, and the hagfish, ambient conditions such as temperature and humidity are not that critical for the initial performance. Instead, the imposed flow field—shear, elongation, or a combination thereof—triggers the fluid to fulfill its physiological task. An example is hagfish slime, which through a combination of shear- and ion-sensitive mucin vesicles and protein skeins manages to gel vast amounts of water instantly despite being expelled in a vast body of cold ocean water. After successfully deterring the predator, the slime eventually becomes diluted and dissolves in seawater—an important after-use behavior. The behaviors of both hagfish and velvet-worm slime are determined not by environmental cues but by the close relationship between the endogenous material's chemical composition and the exerted flow profile that the material experiences during its employment.[18]

The time scales on which complex fluids need to alter or retain their properties range from milliseconds to days. Many animals have developed materials during their evolution that allow for rapid change in fluid structure and properties. Hagfish slime is short-lived and dissolves rapidly in seawater after use, which helps the hagfish to escape from the slimy trap. On the other hand, the mucus-based cocoons of parrotfish remain stable for several hours in seawater to prevent parasite infestation

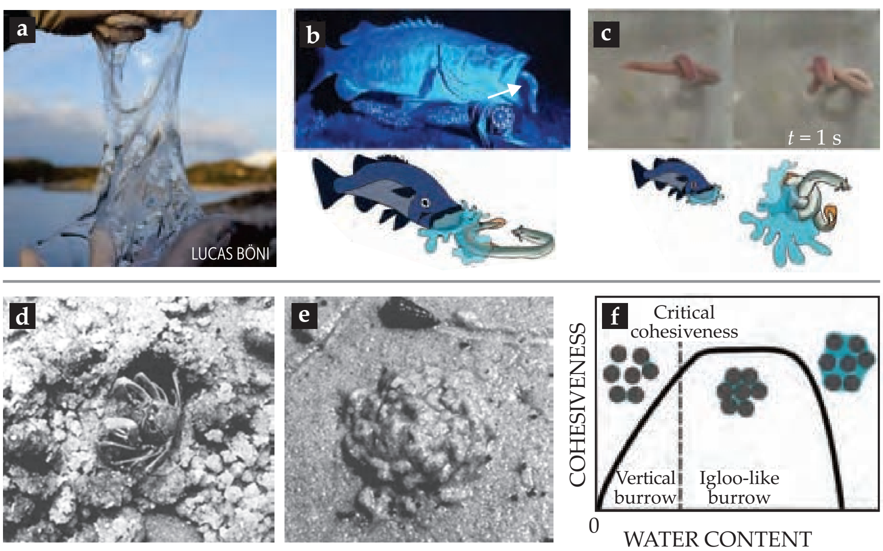


FIGURE 5. DEFENSE AND PROTECTION using complex materials. **(a)** Eellike hagfish (family Myxinidae) can form huge amounts of slime in a few hundred milliseconds. **(b)** The excreted slime clogs the mouth and gills of would-be predators.[12] **(c)** By forming a knot that propagates rapidly down its body, the hagfish can shear off its slime and escape.[13] **(d–e)** Sand crabs (genus *Dotilla*) build a vertical burrow or igloo, depending on the water content in the sand.[17] **(f)** Proposed link between the burrow's design and the cohesiveness of sand as a function of increasing water content. (Adapted from ref. 3.)

during sleep. And the mating ritual of leopard slugs illustrates the importance of proper timing as material properties change.

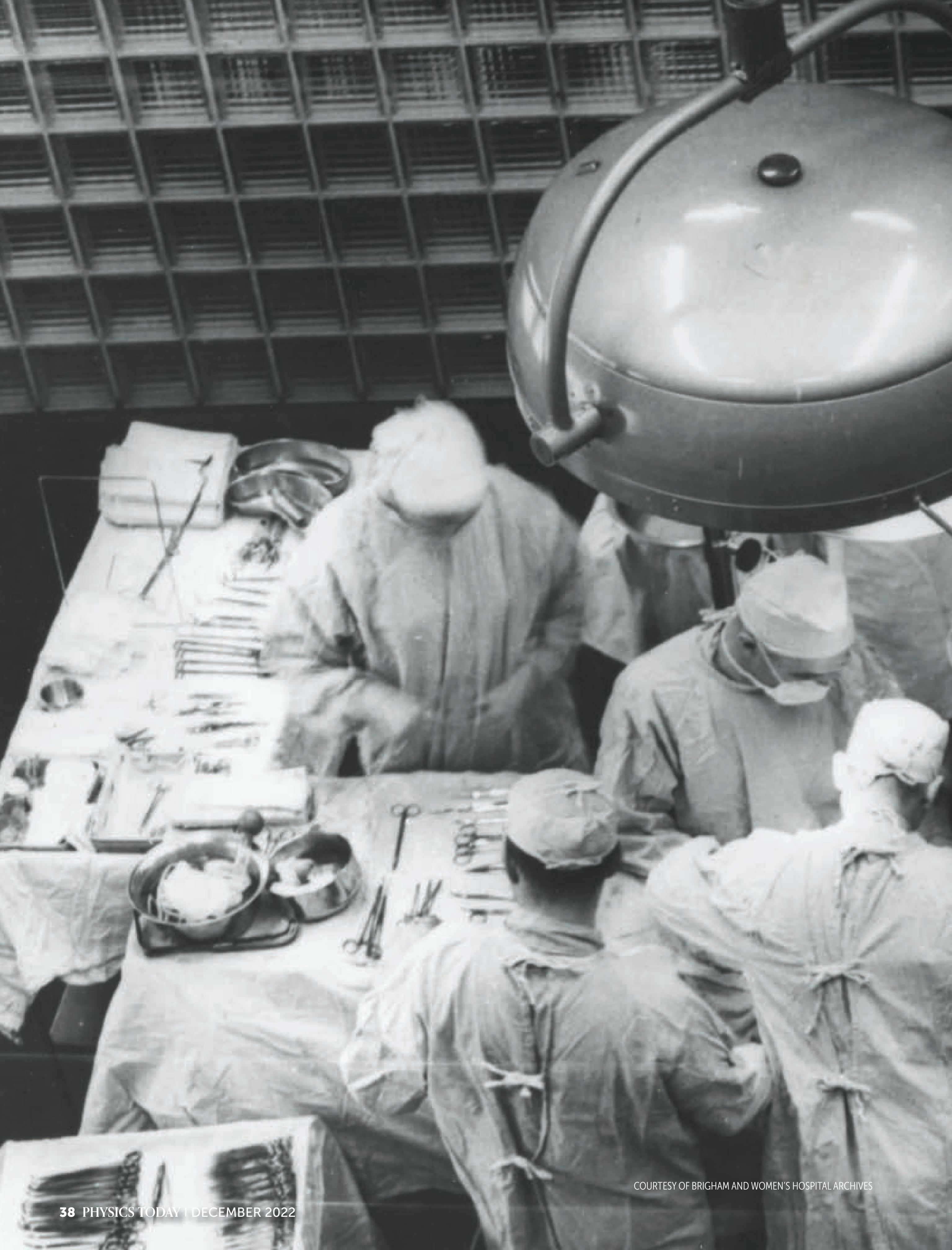
Except for the velvet-worm nanoglobule extrudate, hagfish slime, and granular media, the rheological and structural properties of endogenous and exogenous complex materials under physiological conditions and usage by animals are relatively unknown. Differences in mucin composition are only well studied for humans and pigs, for example; for most other animals, such information is largely missing. How the choice and ratio of protein and oligosaccharide moieties and the overall solid content influence the rheological properties and stickiness of mucus remains to be studied for some of the examples discussed here. Furthermore, the motion of slugs shows that endogenous biotic material can rapidly cycle between a breaking state and a healing process. The rapid adaptation of those materials to the environmental condition suggests that phase transitions or concentration fluctuations govern the materials' structural changes and resulting performance.

During evolution, animals found ways to use the rheology and structure of complex fluids to gain advantage and increase their Darwinian fitness. Studying the interactions from soft-matter, materials-science, and rheological points of view can help in understanding animal behavior, yield new insights for mimicking biomaterials, and provide a quantitative approach to ethology.

This article is a shortened adaption of "Complex fluids in animal survival strategies," by Patrick A. Rühs, Jotam Bergfreund, Pascal Bertsch, Stefan J. Gstöhl, and Peter Fischer,[3] Soft Matter ***17**, 3022 (2021), doi:10.1039/d1sm00142f.*

REFERENCES

1. J. M. Smith, *The Theory of Evolution*, Canto ed., Cambridge U. Press (1993).
2. R. A. Campbell, M. N. Dean, *Integr. Comp. Biol.* **59**, 1629 (2019).
3. P. A. Rühs, J. Bergfreund, P. Bertsch, S. J. Gstöhl, P. Fischer, *Soft Matter* **17**, 3022 (2021).
4. T. Lang, G. C. Hansson, T. Samuelsson, *Proc. Natl. Acad. Sci. USA* **104**, 16209 (2007).
5. P. Fischer, in *Recent Advances in Rheology: Theory, Biorheology, Suspension, and Interfacial Rheology*, D. De Kee, A. Ramachandran, eds., AIP Publishing (2022), chap. 3.
6. M. Denny, *Nature* **285**, 160 (1980).
7. J. H. Lai, J. C. del Alamo, J. Rodríguez-Rodríguez, J. C. Lasheras, *J. Exp. Biol.* **213**, 3920 (2010).
8. A. E. Hosoi, D. I. Goldman, *Annu. Rev. Fluid Mech.* **47**, 431 (2015).
9. R. D. Maladen, Y. Ding, C. Li, D. I. Goldman, *Science* **325**, 314 (2009).
10. A. Baer, S. Schmidt, S. Haensch, M. Eder, G. Mayer, M. J. Harrington, *Nat. Commun.* **8**, 974 (2017).
11. A. Baer, S. Hänsch, G. Mayer, M. J. Harrington, S. Schmidt, *Biomacromolecules* **19**, 4034 (2018).
12. V. Zintzen, C. D. Roberts, M. J. Anderson, A. L. Stewart, C. D. Struthers, E. S. Harvey, *Sci. Rep.* **1**, 131 (2011).
13. L. Böni, P. Fischer, L. Böcker, S. Kuster, P. A. Rühs, *Sci. Rep.* **6**, 30371 (2016).
14. J. E. Herr, T. M. Winegard, M. J. O'Donnell, P. H. Yancey, D. S. Fudge, *J. Exp. Biol.* **213**, 1092 (2010).
15. J. M. Nance, L. F. Braithwaite, *J. Exp. Mar. Biol. Ecol.* **40**, 259 (1979).
16. A. S. Grutter, J. G. Rumney, T. Sinclair-Taylor, P. Waldie, C. E. Franklin, *Biol. Lett.* **7**, 292 (2011).
17. S. Takeda, M. Matsumasa, H.-S. Yong, M. Murai, *J. Exp. Mar. Biol. Ecol.* **198**, 237 (1996).
18. M. A. Meyers, P.-Y. Chen, M. I. Lopez, Y. Seki, A. Y. M. Lin, *J. Mech. Behav. Biomed. Mater.* **4**, 626 (2011).



COURTESY OF BRIGHAM AND WOMEN'S HOSPITAL ARCHIVES

Ashkan Shafiee is a researcher in clinical physics in the department of radiation oncology, Wake Forest School of Medicine, and **Elham Ghadiri** is an assistant professor of chemistry, both at Wake Forest University in Winston-Salem, North Carolina. **Robert Langer** is an Institute Professor at MIT in Cambridge, Massachusetts.

FABRICATING HUMAN TISSUES: HOW PHYSICS CAN HELP

Ashkan Shafiee, Elham Ghadiri, and Robert Langer

By understanding and applying the physics of cellular self-assembly, scientists aim to predict tissue behaviors and accelerate the regeneration of human tissues and organs.

On 23 December 1954, the first successful organ transplantation was accomplished by a team of scientists and clinicians, including Joseph Murray, who was awarded the 1990 Nobel Prize in Physiology or Medicine for that breakthrough procedure.[1] It was performed at the Peter Bent Brigham Hospital in Boston. The surgery, captured in the photograph on the opposite page, involved transferring a kidney from Ronald Herrick to his identical twin, Richard. Having both donor and recipient genetically identical reduced the risk of adverse immune reactions and eliminated the chance of organ rejection.

In subsequent years, immune suppressive medicines enabled organ transplantation from genetically unrelated donors. In 1968 a Harvard University ad hoc committee on brain death (a neurological criterion for organ donation) recommended that individuals who have irreversible loss of brain function can be considered deceased.[2] The same year, the Uniform Law Commission drafted the Uniform Anatomical Gift Act, a regulatory framework for organ donation. Ever since, numerous types of organs—including heart, lung, liver, and pancreas—have been transplanted.

Despite remarkable advances in organ transplantation, the shortage of organ donors and the large number of patients who need a replacement have produced long waiting lists, which puts patients' lives at risk. The shortage inspired one of us (Langer) and Joseph Vacanti to introduce tissue engineering in the 1980s and early 1990s, wherein physical sciences, cell biology, and chemical engineering would be used to regenerate human tissues and eventually organs.[3] To that end, new hope has dawned for patients with end-stage organ failure.

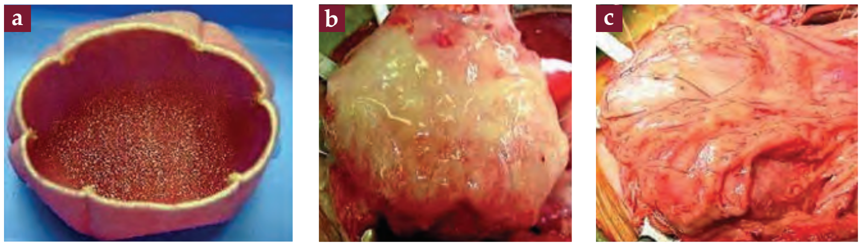


FIGURE 1. TISSUE-ENGINEERED human organs are transplanted into a patient. **(a)** A scaffold is shaped like a bladder and seeded with the patient's own cells. **(b)** The engineered bladder is then sutured to the patient's bladder. **(c)** A surgical material known as fibrin glue covers the scaffold's exterior. (Adapted with permission from ref. 4.)

Biofabrication

Engineered tissues can be made from cells from a patient's own body, another individual's body, or another species—referred to as autografts, allografts, and xenografts, respectively. Among them, the most promising are autografts because they largely eliminate the chance of rejection and require little, if any, immunosuppressive medication.

In 2006 Anthony Atala (Wake Forest University School of Medicine) and coworkers reported the biofabrication and transplantation of human bladders created from the patients' own cells[4] (see figure 1). The same group later reported the fabrication and transplantation of other organs, such as urethras and vaginas.

Autologous organ and tissue fabrication involves several steps, including cell biopsy and culturing, biofabrication of three-dimensional biological constructs, tissue maturation, and transplantation. The time needed to create a new organ, however, may be much longer than a patient can afford to wait, particularly when they urgently require transplantation.

From the point of view of a physicist, human organ fabrication is a 4D project because time is a tremendously important factor when considering the big picture of tissue and organ regeneration. Physicists are trying to understand the behavior of multicellular systems and the dynamics of cellular self-assembly in an effort to improve their ability to accelerate tissue and organ fabrication. Although cells are the building blocks of tissues and organs and are investigated largely in terms of their genetic and biological attributes, it is physical laws that they must ultimately follow, irrespective of the underlying biological processes.[5] Therefore, understanding and applying the physical principles of the dynamics of multicellular systems may help control the tissue regeneration procedure. Consequently, the physics of tissue engineering has gained more attention recently.

One can envision four types of organs: flat, such as skin; hollow and tubular, such as the urethra and vagina; hollow and nontubular, such as the bladder; and solid, such as the heart, liver, and kidneys. The challenge when fabricating solid organs is to vascularize the tissues to make thicker structures while maintaining their viability and function. Although scientists have fabricated some organs, the procedure is still not widely available. The goal is to eventually manufacture all the organs that patients need.

Biofabrication can be scaffold based or scaffold free. In scaffold-based tissue engineering, different natural or synthesized materials—polymers, mostly—can be used to mold the cells into appropriate structures during fabrication and after transplantation. The scaffolds are chiefly made of materials that degrade over time, thereby allowing tissue and organ integration into the body. As such, familiarity with the physics of how the cells interact with the scaffolds may help improve the biofabrication process.

Scaffold-free tissue engineering, on the other hand, uses cellular structures; no template biomaterials are required. Therefore, cellular self-assembly and the dynamics of multicellular systems play an important role in helping the fabricated tissue reach the maturation phase and to be ready for the next steps.

Bioprinting

There are a number of biofabrication techniques used for tissue engineering. Bioprinting is one promising technology for tissue and organ fabrication—and, ultimately, organ manufacturing—given that it is a reliable and precise technique for making 3D biological structures. (To learn about different bioprinting approaches, see reference 6.)

Organ and tissue printing is a term used in the tissue engineering, bioengineering, and biomaterials communities. It refers to a series of activities performed to biofabricate human organs using computer-controllable 3D printers. Although bioprinting shares many concepts with the ordinary 3D printing of objects, a key difference is that in normal 3D printing, the object is ready immediately after printing, whereas in bioprinting, the postbioprinting process is essential for achieving a reliable biological structure.

Immediately after the bioprinting, there are only 3D biological structures composed of cells and supporting materials that must undergo cellular self-assembly to become the tissue construct ready for the following steps. Cellular self-assembly—including but not limited to cell migration to physiologically appropriate locations and tissue fusions that provide mechanical integrity for the bioprinted tissue—occurs postbioprinting. Here again, understanding and applying the physics of the multicellular system can help engineers bioprint tissues and organs.

Physics of multicellular systems

Scientists looked toward the developing embryo, which is the quintessential tissue and organ engineering process, to understand the physics behind organogenesis. Their work relied on Malcolm Steinberg's pioneering model of tissue liquidity, a loose analogy that allowed scientists to use the known properties of liquids to assess tissue behavior.[5,7] That analogy was based on the many similarities between tissues and liquids. For example, tissues try to minimize their surface energy and form a sphere out of cylindrical or cubical shapes. Spheroids made from the same type of tissue fuse together to create larger tis-

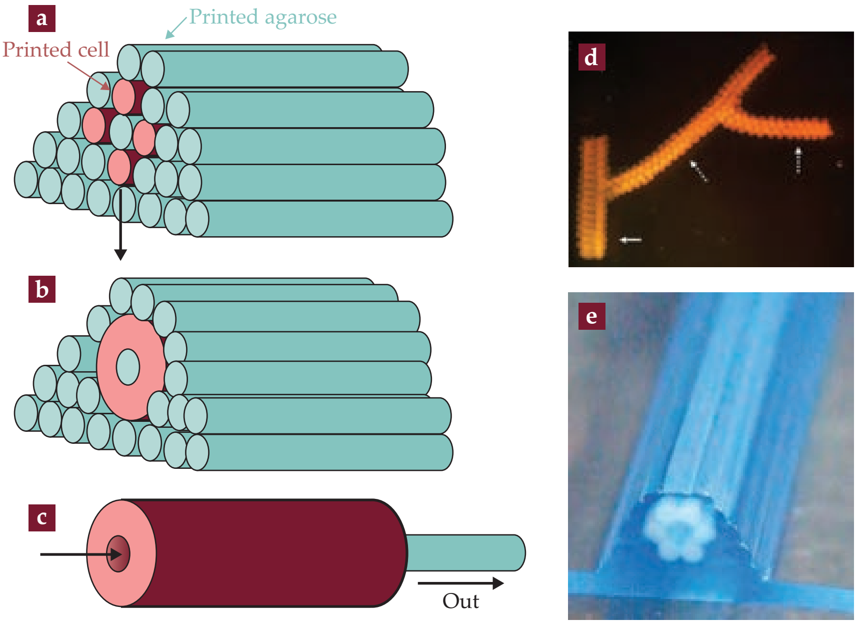


FIGURE 2. BIOPRINTING BLOOD VESSELS, scaffold free. **(a)** In this schematic, red rods depict cellular bioinks, each composed of millions of cells, and green ones depict agarose, a printable hydrogel that serves as a structural support layer. **(b)** After fusion is complete and cellular self-assembly occurs, the bioprinted structure is ready for the next steps. The time that elapses for the construct to change from the structure in panel a to that in panel b is critical for the final regenerated tissue. **(c)** The supportive layers of agarose can then be removed, leaving a hollow tube. (Panels a–c adapted from ref. 10.) **(d)** This bioprinted branched tubular structure has different inner diameters: 1.2 mm (solid arrow) and 0.9 mm (dashed arrows). **(e)** This image shows a bioprinted blood vessel just after the printing process. Blue rods are agarose cylinders and white rods are bioinks composed of cells. (Panels d–e adapted with permission from ref. 9.)

sue, as would, for example, two droplets of water. Moreover, different tissue types separate, based on their viscoelastic properties, much like droplets of immiscible liquids, such as oil and water.

In what's known as the differential adhesion hypothesis, Steinberg stated in 1963 that cells in different tissues adhere to each other with different strengths.[7] That property was subsequently shown to be a feature of 3D cellular structures, not 2D monolayers. Different tissue-fabrication techniques from the same cell source could provide different strengths.[8]

Gabor Forgacs of the University of Missouri and his collaborators, including Steinberg, quantified the biophysical parameters of many tissue-related properties, such as the apparent tissue surface tension. A measure of how cells adhere in a tissue, surface tension can help scientists predict the interaction pattern of different tissues. For example, tissues with higher surface tensions are engulfed by those with lower surface tensions, similar to how oil engulfs water.

That prediction of the interaction patterns of two tissues is helpful when calculating the self-assembly of a mixture of different cell types postbioprinting, given that bioprinted structures such as blood vessels and nerves undergo cellular self-assembly to become sturdy biological structures with physiologically appropriate cell localization.[9] Cyrille Norotte (then at the University of Missouri) and collaborators used the prediction of tissue interaction to print human blood vessels, in which microtissues comprising smooth muscle cells had a higher surface tension than did those comprising fibroblasts. The postbioprinting cellular self-assembly mimicked the exact pattern observed in human blood vessels.[9]

A bioprinter can deposit bioinks on supportive layers, which are mostly hydrogels, such as agarose. Bioinks are either spherical or cylindrical paste-like materials composed of millions of cells that are loaded into a bioprinter's cartridge to be 3D printed. Figure 2 demonstrates the concept of cellular self-assembly, postbioprinting.

Models for cellular behavior

Most primary works to understand the physics of cellular self-assembly and the dynamics of multicellular systems investigated embryonic morphogenesis. To that end, cell sorting, movement of cell collections, and early morphogenesis have all attracted the attention of researchers.[5]

More recent works have concentrated on tissue-engineering applications and the physics of tissue regeneration, with the ultimate goal of predicting and controlling the time it takes tissue to mature.[10] Most models successfully predicted the behavior of tissue with a limited number of cells, and one of the challenges that remained was addressing tissue behavior for multicellular systems with millions of cells.

Garrett Odell and coworkers from the University of California, Berkeley, performed investigations on multicellular systems more than 40 years ago when they sought to understand cellular behavior in sea urchin embryos.[11] They hypothesized that a decrease in the apical circumference of the epithelial layers of a blastula—a multicellular aggregate—occurs because of the contractile activity of actin filaments. In a developing embryo, the process of cleavage of the single-cell-stage zygote results in the formation of the blastula and is considered an example of early morphogenesis.[5]

Eirikur Palsson of the City University of New York and Hans Othmer of the University of Minnesota introduced a model for cell movement in a slime mold, in which they considered cells to be deformable viscoelastic ellipsoids, and integrated signal transduction and cell–cell signaling into their model.[12] The subcellular-element method, which was able to describe the dynamics of larger numbers of interacting cells, was introduced by Thea Newman, then at Arizona State University.[13] She considered the subcellular elements as fundamental dynamical variables and used the inter- and intracellular potentials to understand the dynamics of multicellular systems.

The ultimate goal of understanding the physics of cellular self-assembly is to predict and control tissue behavior. Controlling self-assembly can be used to either decelerate tissue migration in oncology or accelerate tissue maturation in tissue engineering. Most of the models presented so far, however, failed to describe the behavior of cells beyond a certain number. Therefore, physicists have been working hard to predict the

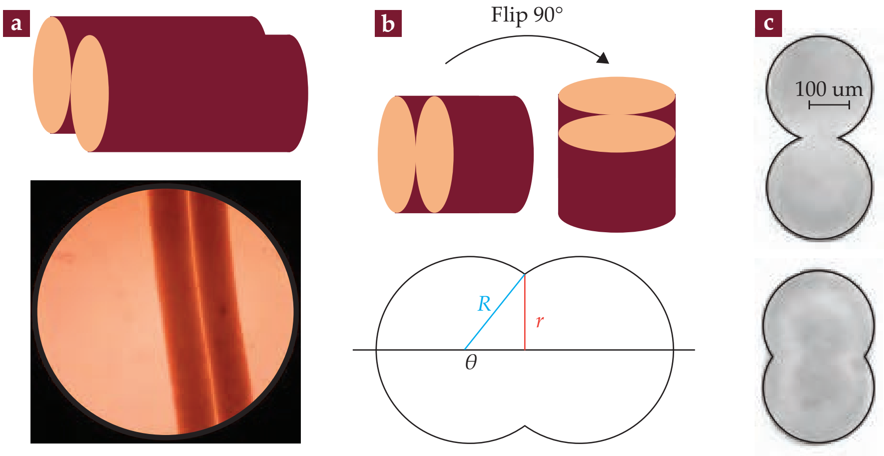


FIGURE 3. BIOINK FUSION. (a) Shown schematically, two cylindrical bioinks sit next to each other, immediately after being bioprinted. **(b)** A few hours later, they have evolved into fused pieces and can be cut into smaller sections. By flipping the fused bioinks by 90° and recording their cross-sectional geometric parameters *r*, *R*, and *θ*, at different times during that evolution, researchers can obtain the characteristic fusion time—a quantitative measure of the cellular self-assembly procedure. **(c)** Twenty hours of evolution separate the top and bottom light-microscopy images of fused cylindrical bioinks. (Adapted from ref. 10.)

time of tissue relocation, postbiofabrication, across the scales to address tissue sizes and greater cell numbers.

That time of tissue relocation is essential in the process of tissue regeneration. In figure 2, for example, if the biological construct is removed from the container in which it was bioprinted before it gains its mechanical integrity during cellular self-assembly, the structure may fall apart. On the other hand, if the structure is given more time than it requires to mature, it may develop some necrotic cores with dead cells that may impact the functionality of the structure after transplantation.

To predict the optimum time, Ioan Kosztin of the University of Missouri and collaborators, including Forgacs, introduced cellular particle dynamics (CPD).[14] It provides a theoretical, computational, and experimental framework to address the tissue dynamics and time of tissue fusion, postbioprinting.[15,16] CPD involves examining the fusion of two spherical and cylindrical bioinks or microtissues that are used to 3D print biological structures. After the bioprinting is complete, tissue fusion allows the biofabricated tissue to adopt the mechanical properties required for its function and is one of the most important steps in tissue maturation. Figure 3 shows the fusion of two cylindrical bioinks and the experimental procedure to measure the fusion time.

The CPD formalism coarse-grains each cell into a finite number of equal regions and considers them cellular particles (CPs). The interactions among those CPs are introduced using short-range contact forces, and their dynamics are explained by an overdamped Langevin equation.[14] The ultimate goal of that formalism is to predict the time evolution of a multicellular system, specifically the change in the biological structure's shape.

In 2014 Matthew McCune, then at the University of Missouri, and collaborators accomplished that goal by computing and recording the simulated trajectories of all CPs. Using the formalism, they were able to predict the fusion of same- and different-sized spherical bioinks as well as cylindrical bioinks. Their framework consists of a comprehensive experimental component to evaluate the theoretical part and calibrate the simulation.

Controlling time with zipper CAMs

Although CPD was able to predict the fusion time of different structures with different cell types and geometries, it was not capable of controlling the time.[15,16] To the best of our knowledge, the only model that provides different biophysical parameters to control and fine-tune the behavior of multicellular systems is the zipper cell adhesion molecules (CAMs) model introduced by two of us (Shafiee and Ghadiri) and our collaborators.[8,10,17]

CAMs are cell surface proteins by which cells bind either to each other or to the extracellular matrix—a network of proteins and molecules essential for tissue integrity. The dynamics of those molecules play an important role in the zipper CAM framework, in which the analysis of experimental data for tissue fusion considers how the cell surface adhesion molecules are involved in tissue dynamics.

Forgacs and colleagues previously showed the relationship between the number and strength of CAMs on the surface of the cells and their respective surface tensions; the researchers found that a higher number of CAMs causes a higher tissue surface tension. On the other hand, using the zipper CAMs model, Shafiee, Norotte, and Ghadiri showed that cellular bioinks with higher surface tension have faster fusion and tissue maturation rates.[8] The finding implies that a higher number of CAMs or stronger ones may help accelerate tissue fusion.

In that framework, cells are imagined to lie on ribbons, or lines, atop spherical and cylindrical bioinks. The fusion of two bioinks starts when they are located in close vicinity to each other. The outermost cells of two close bioinks detect each other on their surfaces via their CAMs and develop new bonds. After the CAMs of all cells positioned on the first imaginary line bond, their proximity will force the next line of cells to approach each other. Based on the adhesion molecules' chemistry, their length when they form bonds is shorter than that of their free state. Figure 4 demonstrates the basics of the zipper CAMs model for fusing cylindrical bioinks.

It is essential to understand that in the model, cells attach to each other one by one, and the imaginary lines are mentioned only to demonstrate the location of a group of cells involved in each step. The cellular attachment resembles a zipper. In a zipper, the slider passes through teeth that engage each other and close one by one. Likewise, in the zipper CAMs model, the cells use their CAMs to attach to each other when they develop their bonds.

With that analogy, therefore, statistical mechanics was used for the zipper CAMs model, with energy equal to zero for the (unbonded) ground state and ε for a (bonded) excited state. The researchers used the appropriate partition function to establish a mathematical technique to identify the energy and force in-

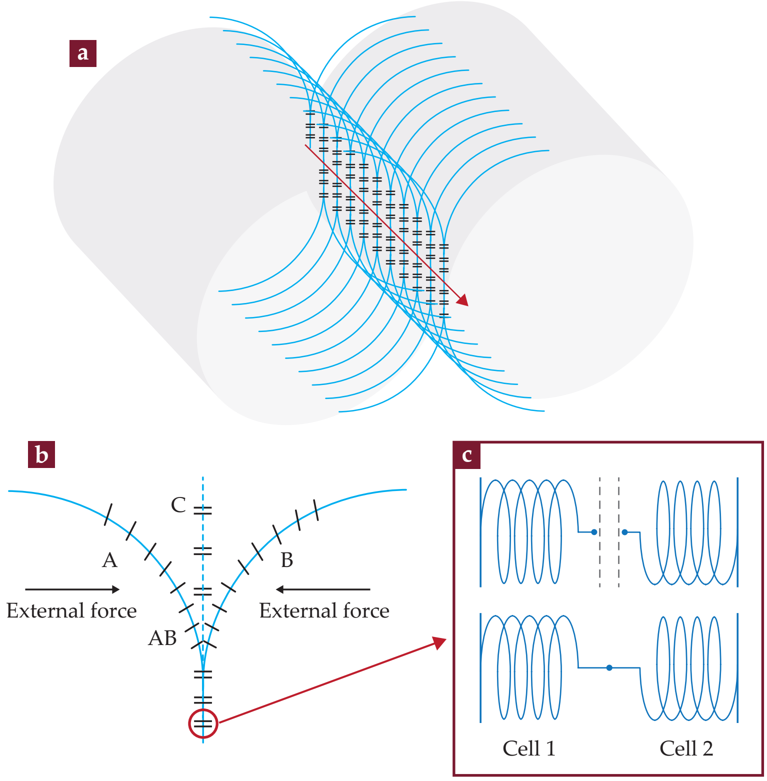


FIGURE 4. ZIPPER CAM. The zipper cell adhesion molecules (CAMs) model describes how to use different biophysical parameters to accelerate tissue formation. **(a)** In the case of cylindrical bioinks, the cellular attachment is considered as two series of closing zippers (above and below the contact line, shown in red). **(b)** The solid curves show the original site of adhesion molecules on the surface of each bioink. The dashed line represents the final location of cells after attachment when fusion is complete. Cell adhesion molecules of outermost cells on each bioink are shown as A and B in the unbonded, ground state; C represents the developed bond, the excited state. **(c)** The adhesion molecules can also be studied as springs, wherein a deviation bond length and applied external force help the bond develop faster. (Adapted from ref. 10.)

volved in tissue fusion—and hence cellular self-assembly. The identification of energy and force in cellular self-assembly was not previously possible.

The framework then predicted that by applying an external force—by pushing the bioinks toward each other—the cellular attachment could be further expedited.[10] Shafiee and collaborators therefore investigated the effect of external force on tissue dynamics and confirmed that tissue fusion was indeed faster. They developed a mechanotransduction-based bioprinter to evaluate the prediction and used an external force to push the bioinks toward each other immediately after bioprinting.

The external force had to be limited, however, to prevent any damage to cells and tissues. The mechanotransduction-based bioprinter deposits bioinks inside the grooves of agarose so that the two bioinks experience the force from the walls of the grooves pushing them toward each other. That configuration could help the fusion procedure by providing cells with a limited external force to facilitate their migration. A normal bioprinter deposits bioinks on a flat surface, and the tissue fusion occurs only by using the energy and force involved in self-assembly, fueled only by the biochemistry of CAMs.

Comparing different bioprinted structures from a mechanotransduction-based bioprinter and normal bioprinters demonstrates that the fusion occurs almost three times as fast for the products of the mechanotransduction bioprinter.[10] The comparison attests to the use of CAMs as a building block of tissue movement and to the versatility of the zipper CAMs model in terms of controlling or accelerating tissue maturation.

Future directions

The physics of tissue engineering in general and of bioprinting in particular is a relatively new field that could provide numerous opportunities for tissue and organ fabrication and regeneration. Increasing the number of physicists who can investigate the different aspects of tissue dynamics could help the field move forward and introduce more complex structures and additional materials.

It appears that the amount of computational and theoretical work aimed at predicting tissue behavior far exceeds the number of experimental studies.[18] On one hand, it is good to have a number of different computational approaches that save money and time, but the fruits of those endeavors have not significantly reached the tissue-engineering community.

It would be helpful to have more physicists working together with biologists and bioengineers to optimize the physics of every single step of tissue fabrication. As stronger experimental approaches to the physics of tissue engineering are developed, computational investigations can help advance our abilities to tackle more complex problems in the field. Physics can identify different biophysical parameters with which to fine-tune tissue behavior and introduce innovative techniques and technologies to adjust those parameters to achieve the desired tissue behavior.

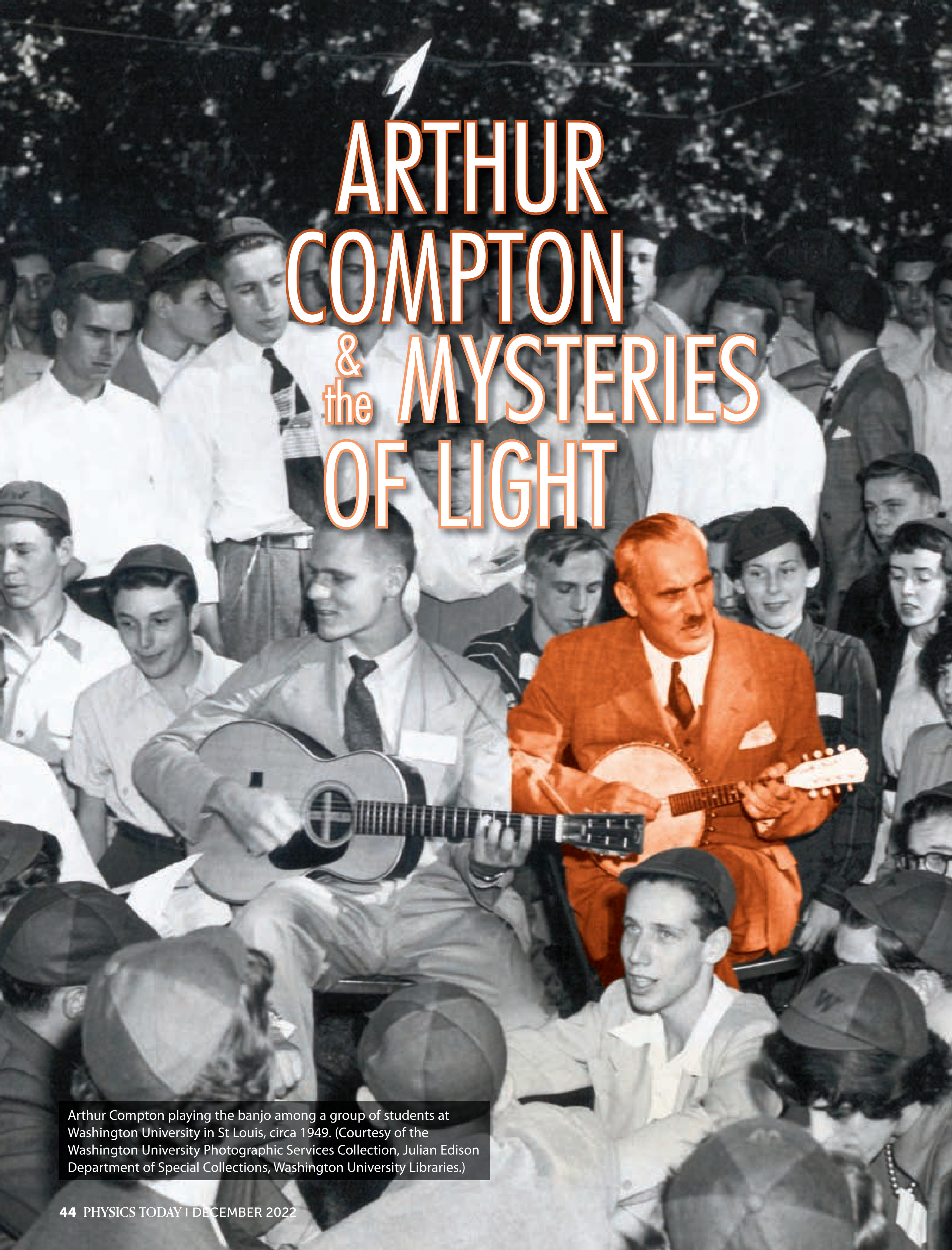
Ashkan Shafiee would like to thank Jareer Kassis for fruitful discussions and comments on the manuscript.

REFERENCES

1. J. M. Barry, J. E. Murray, *J. Urol.* **176**, 888 (2006).
2. C. F. Barker, J. F. Markmann, *Cold Spring Harb. Perspect. Med.* **3**, a014977 (2013).
3. R. Langer, J. P. Vacanti, *Science* **260**, 920 (1993).
4. A. Atala et al., *Lancet* **367**, 1241 (2006).
5. G. Forgacs, S. A. Newman, *Biological Physics of the Developing Embryo*, Cambridge U. Press (2005).
6. A. Shafiee et al., *Appl. Phys. Rev.* **6**, 021315 (2019).
7. R. A. Foty, M. S. Steinberg, *Dev. Biol.* **278**, 255 (2005).
8. A. Shafiee, C. Norotte, E. Ghadiri, *Bioprinting* **8**, 13 (2017).
9. C. Norotte et al., *Biomaterials* **30**, 5910 (2009).
10. A. Shafiee et al., *Phys. Rev. Res.* **3**, 013008 (2021).
11. G. M. Odell et al., *Dev. Biol.* **85**, 446 (1981).
12. E. Palsson, H. G. Othmer, *Proc. Natl. Acad. Sci. USA* **97**, 10448 (2000).
13. T. J. Newman, *Math. Biosci. Eng.* **2**, 613 (2005).
14. I. Kosztin, G. Vunjak-Novakovic, G. Forgacs, *Rev. Mod. Phys.* **84**, 1791 (2012).
15. M. McCune et al., *Soft Matter* **10**, 1790 (2014).
16. A. Shafiee et al., *Biofabrication* **7**, 045005 (2015).
17. A. Shafiee et al., *Bioprinting* **14**, e00047 (2019).
18. S. Arjoca et al., *Acta Biomater.* (2022), doi:10.1016/j.actbio.2022.07.024.

PT

ARTHUR COMPTON & the MYSTERIES OF LIGHT



Arthur Compton playing the banjo among a group of students at Washington University in St Louis, circa 1949. (Courtesy of the Washington University Photographic Services Collection, Julian Edison Department of Special Collections, Washington University Libraries.)

Erik Henriksen is an associate professor of physics at Washington University in St Louis in Missouri. His research focuses on fundamental electronic structures and emergent quantum phenomena of low-dimensional materials.

Erik Henriksen

For nearly 20 years, Einstein's quantum theory of light was disputed on the basis that light was a wave. In 1922 Compton's x-ray scattering experiment proved light's dual nature.

In November 1922 Arthur Holly Compton sketched a diagram for his students at Washington University in St Louis, Missouri. From the left, a photon, or "incident quantum," collides with a stationary electron, which causes the pair to recoil and conserve momentum and energy. That was the first time Compton shared his breakthrough formulation of x-ray scattering from electrons.[1] A month later he delivered the same message to the American Physical Society; shortly thereafter his paper "A quantum theory of the scattering of x-rays by light elements" appeared in the *Physical Review*.[2]

Writing in 1929, Werner Heisenberg cited Compton's discovery as the key finding that "opened up" the path toward the subsequent rapid development of quantum theory[1,3] in the mid 1920s. Similarly abbreviated stories appear in myriad introductory texts alongside Compton's famous result for the change in wavelength of an x ray upon scattering from an electron,

$$\lambda' - \lambda = \frac{h}{m_e c}\,(1 - \cos\theta)\,,$$

in which λ is the initial wavelength, λ' is the wavelength after scattering, h is Planck's constant, m_e is the electron mass, c is the speed of light, and θ is the scattering angle (see figure 1). But those versions of the story pass over the fascinating history of how the corpuscular nature of light was experimentally established.

Compton's scattering results resolved long-standing controversies regarding the nature of free radiation and rescued Albert Einstein's long-neglected *Lichtquant*—"light quantum," or photon—from the radical fringe of physics. For the discovery, Compton was awarded the Nobel Prize in Physics in 1927, which he shared with Charles Wilson, the inventor of the cloud chamber. After scientists spent nearly three decades struggling to understand x rays, Compton's clear and compelling data led to a swift and broad adoption of the new quantum picture. His results arrived at a timely moment: In the aftermath of World War I, a small but growing number of European researchers had begun reconsidering the quantum theory of light. The news from the US landed like a spark on dry tinder.

The path to recognizing the quantum nature of x rays was hardly straightforward: Like many episodes in the history of science, it was replete with successes and failures, human errors, fruitless investigations, confounding claims that later proved to be hogwash, and slow, painstaking advances earned by piecemeal improvements in experimental apparatuses.[4] Because Compton's quantum theory of x-ray scattering is of central relevance to the foundational notion of wave–particle duality, the path to his discovery is worth recalling as we approach the centennial anniversary of the development of modern quantum mechanics.

X-ray research before World War I

The mysterious rays discovered by Wilhelm Röntgen in 1895 were a puzzle from the start. Their ontological status was continually under discussion.[5] The mechanism used to produce them—bombarding an anode with an electron beam—was highly suggestive of bremsstrahlung emission, so x rays were viewed as an unusual cousin of visible light. The rays propagated in straight lines, were not deflected by electric and magnetic fields, and could expose photographic plates: clear visual evidence of familiar light-like behavior. But emission from charged-particle collisions should occur in short pulses, so a picture of x rays as innumerable, aperiodic spherically propagating impulses held sway in the prewar years. That view gained credence when J. J. Thomson calculated the distribution of energy in such pulses and found that it was in accord with early x-ray experiments.

But for a decade following the discovery of x rays, further evidence of well-known wave phenomena was hard to come by: X rays did not obviously diffract or interfere and were only first seen to be polarizable in 1905 by Charles Barkla.[6] Their seemingly contradictory properties led to some intriguing alternative ideas: William Henry Bragg, for example, argued for years that the rays were actually electrons paired with a putative positive charge.[7] But by 1912 Bragg's position had evolved, and he began searching for an x-ray theory that included the characteristics of both a particle and a wave.[5]

That hypothesis was driven in part by a growing recognition that x-ray scattering in gases posed a serious challenge to classical electromagnetism. If x rays emanate from decelerating charges, the expanding sphere of influence will rapidly attain a size far exceeding the distances between atoms in a rarefied gas. Yet the electrical currents through ionized gases pointed to a very small ionization rate, on the order of one in 10^{12} atoms.[8] Why should so few atoms be affected by a wave passing equally over all? Moreover, the released electrons contained a significant part of the incident energy, as if the expanding pulse suddenly concentrated all its energy on a vanishingly tiny portion of its surface.

Despite their best efforts, researchers failed to resolve those anomalies in the first two decades of the 20th century. Arnold Sommerfeld suggested that a focused relativistic beam of "needle radiation" might explain the phenomenon, but the beam would still illuminate broad regions of the gas. A version of the same problem arose in the photoelectric effect: Even at vanishingly small light intensities, electrons were emitted the instant a metal surface was illuminated. That meant it was impossible for energy to slowly accumulate from successive spherical disturbances. Worse, as those experiments pushed into the x-ray regime, the seemingly problematic behavior of x rays began to infect visible light, which had heretofore been safely in classical territory.

More x-ray troubles

Still, evidence that x rays were simply unusual electromagnetic impulses began to pile up. In the spring of 1912, at the suggestion of Max Laue—whose name would not carry the aristocratic *von* until his family was ennobled the next year—Paul Knipping and Walter Friedrich demonstrated that diffraction patterns arose from x rays passing through copper sulfate crystals en route to a photographic plate. Although those patterns evince periodic wave behavior, many prominent individuals who supported the wave picture of x rays, including Barkla and Sommerfeld, were either highly resistant to that interpretation or skeptical that such behavior could be observed.[9]

At any rate, Hendrik Lorentz soon demonstrated how short impulses—namely, finite trains of oscillating waves representing x rays—could show interference just like monochromatic waves. And within a year, the father–son team of William Henry Bragg and William Lawrence Bragg, who were already comfortable with a more corpuscular picture of x-ray motion, also derived the equation governing coherent reflection from successive separated crystalline layers. In a prescient letter to Ernest Rutherford that anticipated the eventual discovery of wave–particle duality, William Henry noted that "the ray travels from point to point like a corpuscule [yet] the disposition of the lines of travel is governed by a wave theory. Seems pretty hard to explain, but that surely is how it stands at present" (reference 5, page 210; brackets in the original).

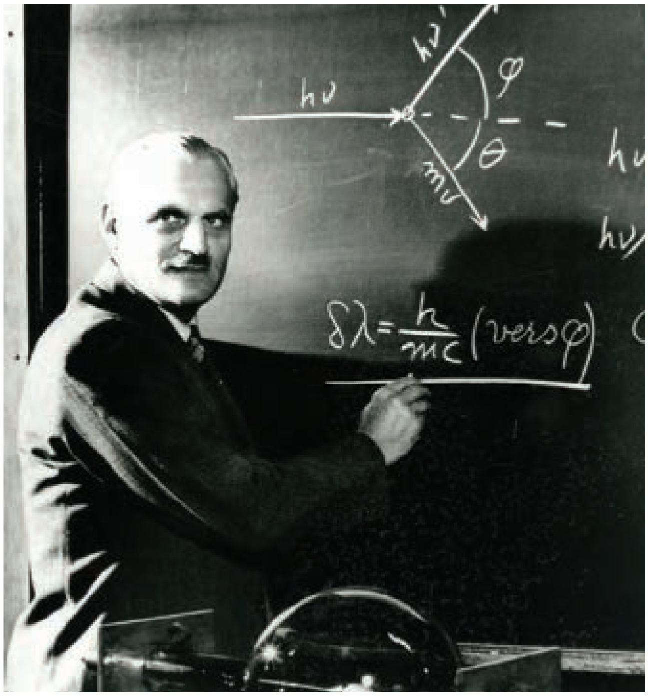


FIGURE 1. ARTHUR COMPTON pictured at a blackboard with the central result of his quantum scattering theory, as written in archaic versine notation. (Courtesy of the Washington University Photographic Services Collection, Julian Edison Department of Special Collections, Washington University Libraries.)

Researchers also discovered that scattered x rays displayed a phenomenon akin to fluorescence. In the classical theory, electrons accelerated by passing radiation can reradiate only at the incident frequency, so the observed wavelength increase was ascribed either to inhomogeneous secondary bremsstrahlung emission from electrons liberated by the primary beam or to a material-specific homogeneous emission. In many pre–World War I experiments, the inhomogeneity of primary x-ray beams made the resolution of secondary emission sources difficult. But even after switching to use the more homogeneous characteristic rays as a source, researchers continued to detect a mysterious spectrum of scattered rays at lower energies than the incident beam.

The advent of crystal diffraction delivered even more superior beams, sourced from Bragg spectrometers, that were bright, monochromatic, and tunable. But the roaring success of Niels Bohr's atomic model, which he presented in 1913, proved to be

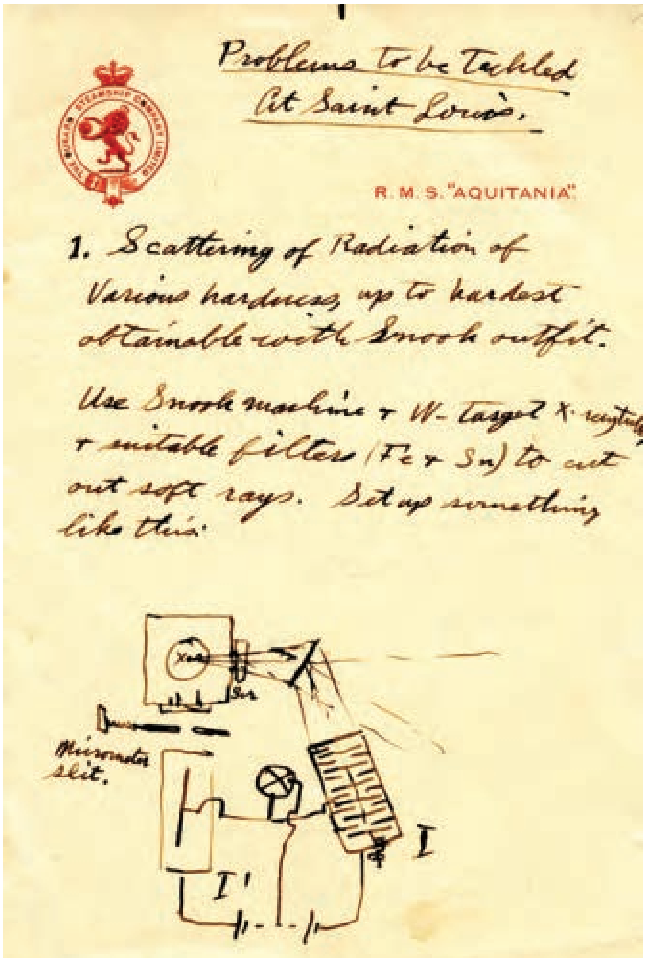


FIGURE 2. THE FIRST PAGE of Compton's handwritten list "Problems to be Tackled At Saint Louis," which he composed while returning from the UK in 1920 on the RMS *Aquitania*. (Courtesy of the Arthur Holly Compton Personal Papers, Washington University Photographic Services Collection, Julian Edison Department of Special Collections, Washington University Libraries.)

far more attractive for experiments than the muddle of contradictory facts surrounding free radiation. For several years afterward, x-ray spectroscopy was almost exclusively applied to exploring atomic energy levels. With the onset of World War I, researchers shelved interest in the fundamental nature of x rays.

With hindsight, Einstein's quantum theory of light would resolve those difficulties, but for years the idea was radioactive. Modern textbooks list the photon among the revolutionary ideas in Einstein's 1905 *annus mirabilis*, but at the time virtually no one aside from Einstein felt the idea had credence. Johannes Stark argued as early as 1909 that light quanta would scatter from electrons in a particle-like fashion, and he highlighted momentum conservation even before Einstein. But Stark's enthusiastic support was not widely shared. In 1907 Wilhelm Wien employed Planck's quantum theory to relate the kinetic energy of an electron to the width of an x-ray impulse, but he avoided any interpretation in terms of a spatially localized quantum like Einstein's *Lichtquant*.

The idea of a localized quantum of light was not unknown, but it was just a leap too far. Even William Henry Bragg's theory that x rays were a corpuscular neutral pair was applied only to high-energy rays and carried no notion of a connection to visible light. Although the 1921 Nobel Prize in Physics awarded to Einstein lauded "his discovery of the law of the photoelectric effect," the actual linchpin of his argument—that light is composed of quantized packets—was not widely accepted.

In his own Nobel lecture a year later, Bohr sardonically punned away the quantum theory as a model of merely "heuristic value" that was "not able to throw light on the nature of radiation." In 1916 Robert Millikan, whose own precision measurements left no doubt as to the total validity of Einstein's photoelectric equation, dismissed the quantum theory of light as "so untenable that Einstein himself, I believe, no longer holds to it."[10] Even Stark, the quantum theory's early and outspoken supporter, gave up on the *Lichtquant* following the discovery of x-ray diffraction. As for Compton, he was firmly on the side of classical electromagnetism.

An American's x-ray initiation

Born in 1892 Compton showed an aptitude for experimental science from an early age. He built a camera that attached to a telescope so that he could photograph Halley's comet in 1910. He reproduced the Wright brothers' flight experiments by building his own triplane glider and flying it an exhilarating distance of 185 feet. But at the alarmed urging of his parents, he abandoned further flying and gave his craft a bonfire send-off. At 21 he published a method for measuring Earth's rotation based on the momentum of water flowing in a circular tube.[11]

Compton and his brother Karl first encountered x rays in the physics laboratory at the College of Wooster, where their father was a professor, and continued investigating them during their graduate studies at Princeton University. After Karl became an assistant professor at the Ivy League institution, the brothers collaborated on several projects, such as improving electrometer precision. Their model was the most precise electrometer of its day: It was able to resolve currents of 10 fA in a minute.[12] Those experiences informed Compton's lifelong preference for building his own apparatus. An accomplished glassblower, he fabricated his own x-ray tubes, and he greatly improved the precision of x-ray spectroscopy by using his own electrometer in place of a traditional electroscope to measure the x-ray-induced ionization charge.

After finishing his PhD and teaching at the University of Minnesota for a year, Compton worked at the Westinghouse Lamp Company for two years. Although he was promised resources for his experimental x-ray research, the needs of the company quickly took precedence: He was tasked with improving light bulbs. So he began pursuing theoretical work on x rays in his spare time, and he started analyzing two discrepancies between recent experimental work and the classical picture of x-ray scattering from point-like electrons. The first of those anomalies had to do with the radiation from electrons excited by transverse fields. Although Thomson's classical theory predicted it should be symmetric along the incident axis, gamma-ray-scattering experiments clearly showed an excess of scattering in the forward direction. The second discrepancy came from x-ray absorption coefficients, which Barkla and others had reported to be unexpectedly low for beams of increasingly shorter wavelength.

Both observations violated Thomson's scattering theory of radiation. Compton pursued those issues to surprising ends. Regarding the first anomaly, he showed complete confidence in classical electrodynamics by proposing that x rays must not only reradiate but also diffract from electrons in materials. Because diffraction occurs for light scattering from objects whose size is of the order of the wavelength, Compton sought to determine the shape and size required to generate the observed scattering distribution. For nearly three years, he would argue for a ring-shaped electron with an enormous radius of approximately 2 pm that reproduced the excess forward scattering.[13]

To pursue the second issue of anomalously low absorption, Compton left Westinghouse in 1919 to spend his National Research Council fellowship with Rutherford at Cambridge University's Cavendish Laboratory. In the UK, he absorbed the latest gamma-ray experiments and saw his ring-electron theory publicly rebuffed by Rutherford. Introducing him before a talk, the famous physicist once pronounced, "This is Dr. Compton. . . . I hope you will listen to him attentively. But you don't have to believe him!" (reference 14, page 29).

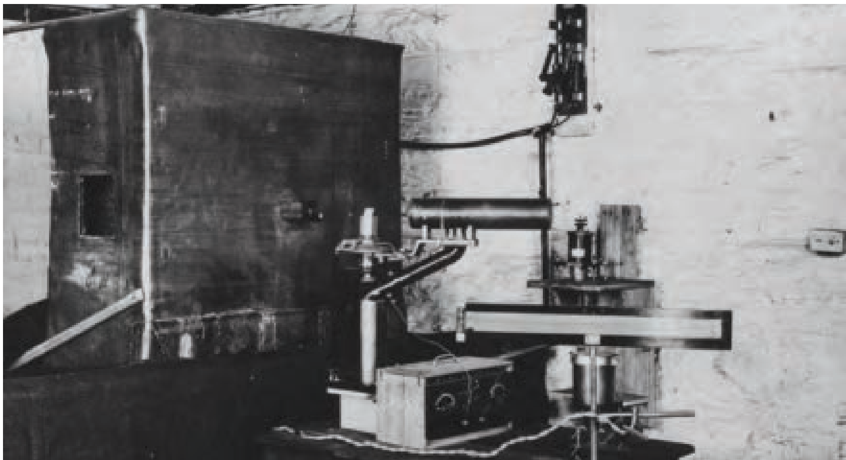


Figure 3. The x-ray apparatus used by Compton in his experiments. At left is a large lead box, which housed the x-ray source and graphite block. After exiting the lead box, the beam glanced off the calcite crystal (visible at center) and was detected by an ionization tube connected to a four-quadrant electrometer. (Courtesy of the Washington University Department of Physics.)

Replacing Rutherford's venerable gold-leaf electroscope with his own four-quadrant design, Compton proceeded to study gamma-ray scattering. He soon found that the energy of secondary rays decreased unexpectedly when scattered to higher angles. Compton deemed that effect a new type of fluorescence: Guided by a strong classical intuition, he had begun to delineate the secondary rays into "truly scattered" and fluorescent radiation. As required by classical electromagnetism, truly scattered rays had the same wavelength as the primary beam. In contrast, Compton ascribed the longer-wavelength fluorescent radiation to Doppler-shifted emission from high-velocity electrons set in motion by the primary beam. Interestingly, Compton still relied on diffraction to account for the angular distribution, although his results forced him to abandon the ring-shaped electron in favor of a solid, spherical model.[4] But with a 5 pm radius, his proposed spherical electron was still enormous!

"Problems to be tackled at Saint Louis"

Buoyed by those experiences, Compton returned to the US to take up a position at Washington University in St Louis. It may be surprising that he chose a university that at the time, in his own words, "was a small kind of place," but Compton was intentionally seeking to avoid the centers of x-ray science, where he worried he might be "led away by the thinking of the time" (reference 14, page 31). En route to his post, he penned on ocean-liner stationery a plan of attack several pages long that he labeled "Problems to be Tackled At Saint Louis," shown in figure 2. Intriguingly, that plan shows he was aware of the quantum relation, $E = h\nu$, and the implication of such an interaction with single electrons. It also contains a sketch of a direct beam from an x-ray tube, which Compton ultimately abandoned. Instead, from the outset he used a Bragg spectrometer as a wavelength selector to deliver precise monoenergetic beams (see figure 3). He was soon making rapid progress.

Now Compton was able to show for certain that, contrary to two other contemporaneous findings,[4] the longer wavelength fluorescent radiation he had first seen in gamma rays persisted in x-ray scattering. Then, in collaboration with Charles Hagenow, Compton found that the fluorescent radiation was completely polarized: a result that could be naturally explained as scattered light. But truly scattered light should not change its energy. Perhaps, he hypothesized, the polarization could be maintained if the secondary emission were to occur at the same instant an electron scattered the primary emission. That was the first time Compton considered the possibility of simultaneous scattering and emission events. Around the same time, he was tasked with writing a review on the status of secondary radiation for the National Research Council, which obligated him to revisit older literature and confront the possibility of a quantum nature of light. He tacked a note to that effect at the review's end that signaled his first willingness to break with total adherence to classical electromagnetism.

In October 1921 Compton made the crucial choice to explore the spectrum—rather than just the intensity—of the secondary radiation. Employing his Bragg spectrometer for its original purpose, he measured the spectrum of a molybdenum K-alpha line scattered to 90 degrees from a block of graphite and produced the data seen in figure 4a. But in his early analyses, Compton apparently referred only to tables of data rather than plots and so mistook the small peaks at right as the Doppler-shifted emission from rapidly recoiling secondary electrons that absorbed all the energy of the strong peak in the primary beam.

In the ensuing months he realized the error and understood that the wavelength shift was far smaller. Now believing the second tall peak—the solid line in figure 4a—to be the Doppler-shifted K-alpha line, he erred again when determining, by solely conserving momentum, the velocity of the recoiling electron. Just weeks later he got it right: Drawing on the same data, he entirely abandoned the Doppler shift in favor of a pure scattering picture and drew the diagram reproduced in figure 4b. From that he immediately derived his quantum theory of scattering by conserving both energy and momentum.

Further measurements of the intensity of scattered radiation and the absorption coefficient agreed with the quantum theory and explained the low absorption that had set Compton on that path. As he noted, there was now "little doubt that the scattering of X-rays is a quantum phenomenon" (reference 2, page 501). He presented those results outside his classroom for the first time at an American Physical Society meeting in Chicago in early December 1922, a little over a week before Bohr delivered his Nobel lecture in which he expressed skepticism of Einstein's *Lichtquant*. Compton submitted his paper to the *Physical Review* on 13 December, just two days after Bohr's lecture. Interestingly,

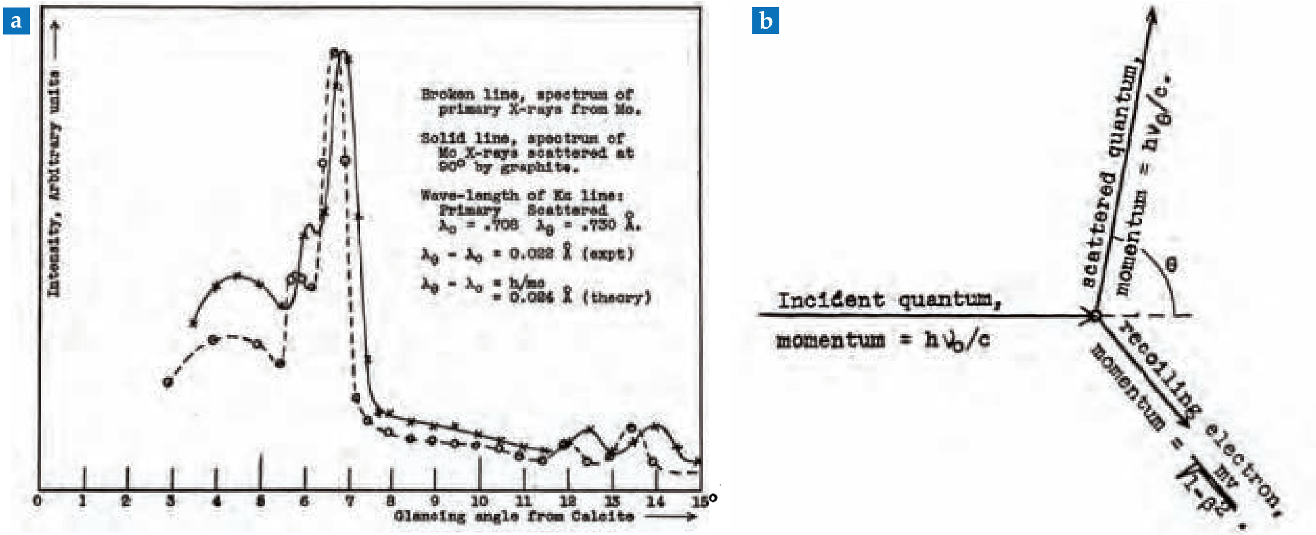


FIGURE 4. TWO DIAGRAMS from Compton's 1923 paper in the *Physical Review* that announced his x-ray scattering results. **(a)** This plot shows the wavelength-shifted spectrum of molybdenum x rays scattered to an angle θ of 90 degrees from a graphite block. As the "glancing angle" increases, so does the wavelength that the Bragg spectrometer is sensitive to. **(b)** This diagram illustrates conservation of momentum and energy for an x ray scattering from an electron. (Reproduced from ref. 2.)

his paper does not cite Einstein. Instead, it begins by discussing the failure of Thomson's scattering theory, as Compton bid goodbye to a purely classical world. By the end of 1923, Charles Wilson had observed the recoiling electrons in his cloud chamber,[15] as depicted in figure 5.

Waves and particles

Of course, apart from his x-ray tubes, Compton was not working in a vacuum. The speed at which his discovery was accepted—indeed, the seeming about-face regarding the reality of photons that was quickly performed by most physicists—was possible because those ideas had been in the air. With World War I over, European scientists had returned to their labs, where old ideas, including the paradoxes of x rays, were being reconsidered.

Notably, the French noble brothers de Broglie—Maurice, an accomplished amateur x-ray scientist, and Louis, a budding theorist—were intrigued by the quantum theory from early on. Maurice took advantage of the developing field of beta-ray spectroscopy to explore the transfer of energy during x-ray absorption in the photoelectric effect. He soon became convinced that electrons were emerging with the entire energy of the incident x rays and argued that it "must be corpuscular, or, if it is undulatory, its energy must be concentrated in points" (reference 5, page xi). Hendrik Kramers, too, had apparently sketched the basic picture of the quantum scattering result in 1921 but had been harried by Bohr into not publishing it.[16]

Motivated by the same issue of low absorption that had spurred Compton's investigations, Peter Debye derived a more general scattering theory than Compton and prodded his colleague Paul Scherrer to pursue experiments on the secondary rays. Unfortunately for Debye, Scherrer did not take up that invitation. Although Debye submitted his article after Compton, it appeared in print two months earlier. But he always acknowledged Compton's priority. In any case, that the same ideas were being discussed simultaneously on two continents by established but independent researchers no doubt hastened their acceptance.

In 1922–23 Sommerfeld was a visiting professor at the University of Wisconsin, and while in the US, he closely followed Compton's advances. Upon his return to Europe, Sommerfeld became a key proselytizer of the new paradigm. Writing to Compton in October 1923, he reported on how the discovery "keeps the scientific world in Germany extremely busy" (reference 4, page 247), and he noted that he was already including a section on the *Comptoneffekt* in the next edition of his textbook *Atombau und Spektrallinien* (*Atomic Structure and Spectral Lines*). With some hyperbole, he claimed it "sounded the death knell" of the wave theory.

On the contrary, Compton's discovery forced the physics community to reckon with the persistence of obvious wavelike aspects of light. Light was not suddenly and only a particle. It couldn't be, given the established observations of polarization and diffraction. Compton himself made that point in a remarkable way: A mere four days before submitting his quantum scattering results, he submitted a separate paper announcing the discovery of total reflection of x rays,[17] a wavelike effect if ever there was one. There could be no objection on the basis

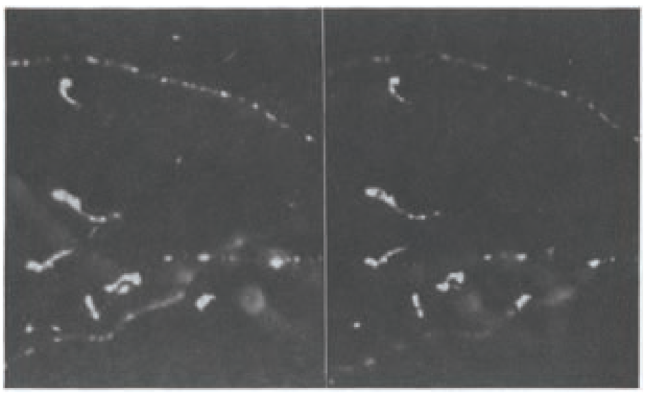


FIGURE 5. SO-CALLED FISH TRACKS, or spherical clouds with small tails, photographed by Charles Wilson in his cloud chamber and published in his 1923 paper. Wilson suggested in that article that the tracks were left by recoiling electrons from Compton scattering. (Reproduced from ref. 15.)

that light was either a particle or a wave; physicists would now have to contend with the fact that it was both.

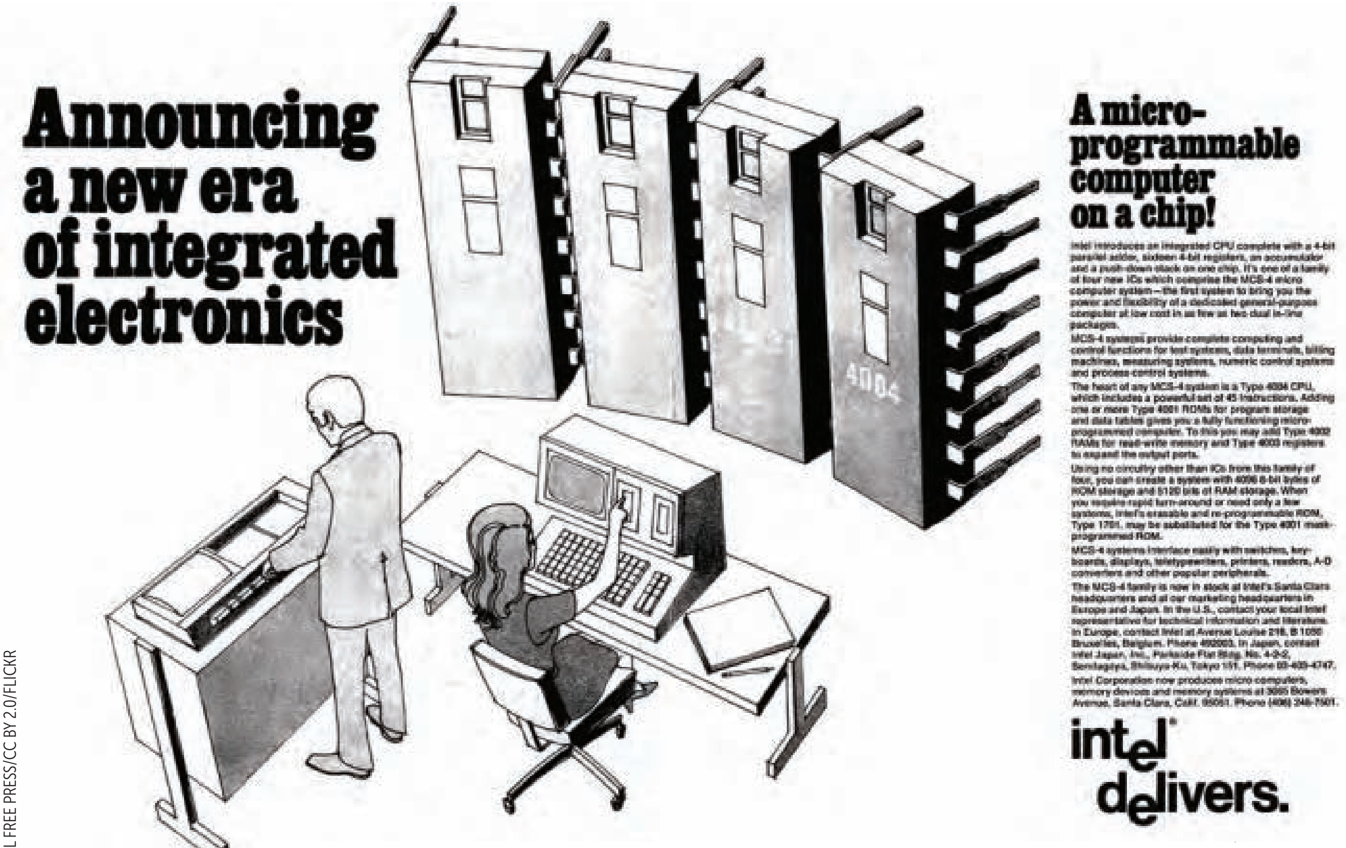
Not everyone was on board. For some time Bohr remained incapable of relinquishing his devotion to a purely wave-based conception of the nature of light. The depth of his opposition was sufficient to motivate him to jettison an absolute notion of the conservation of energy and momenta in favor of a weaker statistical conservation. Working with Kramers—who himself was now fighting a rearguard action against a theory he had previously argued for—Bohr adapted John Slater's idea of a virtual radiation field and developed a theory that had discontinuous quantum jumps between atomic states in a classical electromagnetic field.[18] But the nature of those novel virtual oscillators was far from clear.

For a paper with only a single equation, the Bohr-Kramers-Slater article, as it became known, is notable for proposing a probabilistic formulation of conservation laws in a manner robust enough to be disproved. Indeed, Walther Bothe and Hans Geiger soon demonstrated that the arrival times of recoiling electrons and scattered x rays were sufficiently close to rule out a statistical interpretation. Compton weighed in with similar findings. Thus, as a direct consequence of the quantum picture of scattering, an experimental basis for the event-wise conservation of energy and momentum was also found.

Compton's repeated and sometimes outlandish efforts to couch the outcomes of x- and gamma-ray-scattering experiments in the language of classical electrodynamics vividly illustrate how he had not initially set out to spark the shift in viewpoint from a wave–particle dichotomy to a wave–particle duality. But once he accepted the new quantum scattering paradigm revealed by his experiment, he elegantly argued in the October 1925 issue of *Scientific American* that "most physicists look forward" to a solution that would be found in "some combination of the wave and quantum theories," just as William Henry Bragg had anticipated in 1912.

REFERENCES

1. R. H. Stuewer, *Ann. Phys. (Berlin)* **512**, 975 (2000).
2. A. H. Compton, *Phys. Rev.* **21**, 483 (1923).
3. J. G. Perillán, *Science Between Myth and History: The Quest for Common Ground and Its Importance for Scientific Practice*, Oxford U. Press (2021).
4. R. H. Stuewer, *The Compton Effect: Turning Point in Physics*, Science History (1975).
5. B. R. Wheaton, *The Tiger and the Shark: Empirical Roots of Wave–Particle Dualism*, Cambridge U. Press (1983).
6. C. G. Barkla, *Philos. Trans. R. Soc. London, Ser. A* **204**, 467 (1905).
7. W. H. Bragg, *London, Edinburgh, Dublin Philos. Mag. J. Sci., Ser. 6* **14**, 429 (1907).
8. J. J. Thomson, E. Rutherford, *London, Edinburgh, Dublin Philos. Mag. J. Sci., Ser. 5* **42**, 392 (1896).
9. P. Forman, *Arch. Hist. Exact Sci.* **6**, 38 (1969).
10. R. A. Millikan, *Phys. Rev.* **7**, 355 (1916), p. 384.
11. A. H. Compton, *Science* **37**, 803 (1913).
12. A. H. Compton, K. T. Compton, *Phys. Rev.* **14**, 85 (1919).
13. A. H. Compton, *Phys. Rev.* **14**, 20 (1919).
14. M. Johnston, ed., *The Cosmos of Arthur Holly Compton*, Knopf (1967).
15. C. T. R. Wilson, *Proc. R. Soc. London A* **104**, 1 (1923).
16. M. Dresden, *H. A. Kramers: Between Tradition and Revolution*, Springer (1987).
17. A. H. Compton, *London, Edinburgh, Dublin Philos. Mag. J. Sci., Ser. 6* **45**, 1121 (1923).
18. N. Bohr, H. A. Kramers, J. C. Slater, *London, Edinburgh, Dublin Philos. Mag. J. Sci., Ser. 6* **47**, 785 (1924). PT

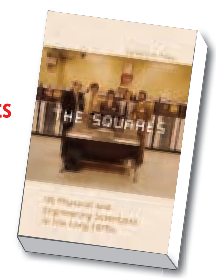


An ad for the Intel 4004 microprocessor that first appeared in the 15 November 1971 issue of *Electronic News*.

The world is square

The Squares
US Physical and Engineering Scientists in the Long 1970s

Cyrus C. M. Mody
MIT Press, 2022. Open access ($65.00 paper)



Everybody likes shiny things, including historians of science. When researching the history of physicists and engineers in the "long 1970s"—which the historian Cyrus C. M. Mody defines as the era spanning from around 1966 (the peak of military science funding) to roughly 1983 (the reprise of Cold War tensions early in Ronald Reagan's first term)—the historian's eye is naturally drawn to the protesters, commune builders, thermonuclear utopians, and curmudgeons. They leap off the archival pages and demand that their stories be told. The catch, as Mody rightly notes, is that the overwhelming majority of physical and engineering scientists of that era were neither Edward Teller fanboys nor especially "groovy." As he puts it, they were "politically ambivalent or reticent." They were squares.

The squares have waited a long time to be featured as the stars, rather than the straight men, and they are fortunate that a person of Mody's talents has taken them up. (The gendered language in this review is deliberate, as essentially everyone discussed in this book, especially the major characters, is male, an overwhelming demographic asymmetry well reflected in the data on the profession Mody cites.) *The Squares: US Physical and Engineering Scientists in the Long 1970s* adopts two approaches to its subject. The first sees Mody in an oracular mode, as he analyzes sociological trends and looks for patterns in the social evolution of the square scientist as a type. Those revelations cast the 1970s as not simply a transitional caesura but as an era with its own character and importance.

The second approach is the historian's fondness for case studies. Mody dives deep into the weeds and sometimes even the gaps between the weeds. His characters come to life in those pages: globalizers at the Silicon Valley stalwart Signetics ("the squarest [case] in this book"), proponents of automated agriculture, and the increasingly obsolescent NASA engineer—whose raison d'être, reaching the Moon, was a fabulous success but catastrophically annihilated the rationale for governmental budgetary largesse. But, as with all composites of case studies, one wonders: Are those examples cherry-picked?

Mody's refreshingly frank answer is yes and no. Case studies are hard work and demand access to archives, and Mody concentrated on those that were most proximate to his academic career: Santa Barbara for a nanotechnology and society working group at the University of California that he collaborated with, Houston because he taught at Rice University, a smattering of Dutch sources because of his current position at the University of Maastricht, and so on. His choices of scientists and engineers to highlight "are meant to be illuminating rather than representative"; they are illustrative individuals, not Platonic squares.

Even if his subjects are not statistically representative, the middle, non-oracular chapters of the book make for fascinating reading. My favorite is on Jack Kilby, widely credited as one of the inventors of the integrated circuit, for which he was awarded the Nobel Prize in Physics in 2000. That work was done at Texas Instruments. Mody starts there and follows Kilby's path into a kind of corporate-subsidized independent scholar.

He zeroes in on one proposal by Kilby to develop solar power for the suburban home, which was not a response to the groovy vibe for green technology but an affordable solution to the energy crisis. Kilby's system ended up in limbo, in part because, as Mody persuasively argues, he refused to build alliances with environmentalists and other longhairs: "In Kilby's future America, no credit for the country's energy transformation would go to leftie environmentalists." When the economic rationale for his kind of middle-class solar energy dissipated in the go-go 1980s, so did Kilby's Texas Instruments Solar Energy System.

When examining the other cases, one cannot help but question how "square" they really are. (Not Kilby: He's spot on.) Indeed, the first square Mody follows closely is David Phillips, an industrial consultant and part-time physics instructor at the University of California, Santa Barbara, who dedicated his research to . . . parapsychology. I am the last person to argue that research on extrasensory perception should be exiled from the history of science, but it hardly seems the best example to introduce us to the notion of squareness. Mody maintains that Phillips was "square relative to some of [his] peers and flamboyantly countercultural relative to other colleagues." Even so, there remains a risk of bending a very useful category out of its analytical precision.

In the end, the oracular voice provides the punch of the book for nonspecialists, and that punch is worth the price of admission. One of Mody's main aims in the conclusion is to give an account of how social responsibility in science—or what today is often termed responsible research and innovation—has come in and out of vogue over time. Mody's contextualization of that cyclical trajectory from the long 1970s to today offers much food for thought. Even the squares of that era got on board with developing science for a sustainable future—at least for a time. Will today's scientists do the same, and for how long?

Michael D. Gordin
Princeton University
Princeton, New Jersey

MICHAEL D. DUNCAN/AIP ESVA

A 2007 portrait of Mildred Dresselhaus.

Thoroughly modern Millie

Carbon Queen
The Remarkable Life of Nanoscience Pioneer Mildred Dresselhaus
Maia Weinstock
MIT Press, 2022. $24.95

For the first time, in 2023 the annual awards ceremony at the APS March Meeting will include the Mildred Dresselhaus Prize in Nanoscience or Nanomaterials. Born in 1930, Dresselhaus spent 57 years at MIT. After seven years as a researcher at the university-operated Lincoln Laboratory and one year as a visiting professor in an appointment designated for women, she broke tradition in 1968 when she became the first female tenured full professor in the department of electrical engineering. In 1983 she received a joint appointment in the MIT physics department.

Dresselhaus's research had many practical applications for semiconductors, conductors, and superconductors, but she most enthusiastically studied the fundamental electrical and thermal properties of materials. When investigating alkali metals such as potassium or sodium, for example, she sought to determine whether they could be inserted (or intercalated) between graphite layers of carbon atoms to make a superconducting system. Her evolving specialties were graphite, carbon fibers, large carbon clusters such as fullerenes, and by the 1990s, tubular fullerenes—now known as carbon nanotubes.

Two coauthored 1992 papers on nanotubes, for example, showed that they conduct differently depending on their diameter and the orientation of their carbon hexagons around the tube or cylinder. By the early 2000s, Dresselhaus had been nicknamed the "queen of carbon science," as indicated in the title of this engaging and inspirational new biography by Maia Weinstock.

A writer and lecturer on the history of women in science, Weinstock met Dresselhaus only once, in 2014, a few days before Dresselhaus received the Presidential Medal of Freedom from Barack Obama: one of many awards, prizes, honorary degrees, and elected professional offices that she received before her death in 2017. Weinstock's biography nonetheless skillfully makes use of interviews, oral histories, and published materials. The fast-moving chronological narrative offers a clear account of Dresselhaus's scientific research and valuable insights into the building of her successful career as a woman scientist.

The child of a financially struggling Polish Jewish immigrant family, Mildred "Millie" Dresselhaus (née Spiewak) spent her early years in inadequate and gang-ridden public schools in Brooklyn and the Bronx. With determination, hard work, and a keen intellect, Millie was accepted into Hunter College High School, which at that time was an all-girls institution, from which she continued to Hunter College. A Fulbright Fellowship took her to the University of Cambridge for a year before she began graduate studies at Radcliffe College. She finished her PhD at the University of Chicago, where she found less prejudice against women than in Harvard Yard.

Teachers helped shape the curious and unflappable Dresselhaus. Her mentor at Hunter College was Rosalyn Yalow, who would later be awarded a share of the 1977 Nobel Prize in Physiology or Medicine. Yalow told Millie that she was perfectly capable of graduate work in math and science and did not have to settle for a "female" trajectory of high school teaching or nursing school. At Chicago she boarded for a year with another future Nobel winner, Maria Goeppert Mayer, and came to know as teacher and mentor a third Nobelist, Enrico Fermi, whose habits of hosting student dinners and giving out handwritten notes before lectures she later adopted.

Most important was Gene Dresselhaus, a young theoretical physicist who made his first mark while in graduate school at the University of California, Berkeley, by discovering that electron spin can affect the range of energies of an electron in a solid material. Millie and Gene met at Chicago and married in 1958. They then moved to Cornell University, where he had a faculty job and she took an NSF postdoc. After Cornell's faculty made it clear that they would not hire her or even let her teach without pay, the Dresselhauses left for MIT's federally funded Lincoln Laboratory. Gene stayed at Lincoln until 1976, but Millie left after she was told to stop bringing their young children to the lab.

Because of her experiences, Dresselhaus saw one of her roles at MIT as being a voice for the university's few women students and faculty. She worked steadfastly with the food scientist Emily Wick, the aeronautics engineer Sheila Widnall, and others to further opportunities for women and to advocate for their equal treatment at MIT. Dresselhaus and Widnall also created an undergraduate course titled What Is Engineering to help students, especially women, learn how to make progress and to find engineering jobs. She continued such efforts throughout her career.

By the time of her death, Dresselhaus had published some 1700 research articles and eight books. Most of those were coauthored with a large array of coworkers, students, colleagues, and her husband, whose MIT position was in her research group. In their research together, he was the theoretician, she the experimentalist, she the writer, and he the editor. They became known as the materials-science power couple.

Although *Carbon Queen: The Remarkable Life of Nanoscience Pioneer Mildred Dresselhaus* ranges from the 1930s to the 2010s, little attention is given to how the political and social events of those decades (such as 1960s equal-opportunity legislation and the 1972 prohibition on sex-based discrimination in education) influenced Dresselhaus's life and career. Nevertheless, Weinstock's biography will appeal to a wide audience in science, engineering, gender studies, social studies of science, and sociology of science. Considerable attention, both scholarly and popular, has been paid to the dilemmas faced by women in the sciences. *Carbon Queen* provides an inspiring story of one very capable woman's response.

Mary Jo Nye
Oregon State University
Corvallis

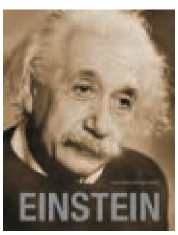
NEW BOOKS & MEDIA

A Traveler's Guide to the Stars

Les Johnson
Princeton U. Press, 2022. $27.95

Although people have been dreaming of space exploration for decades, visiting and settling other worlds is still the stuff of science fiction. Nevertheless, in *A Traveler's Guide to the Stars*, the physicist Les Johnson, a long-time proponent of interstellar travel, discusses what it will take to reach for the stars. After first providing a brief history of spaceflight and pondering potential destinations, Johnson launches into the core of the book: the technology challenges that will need to be met, which include revolutionary advancements in spacecraft propulsion, communications, navigation, and life-support systems. Rather than discourage, however, Johnson aims to encourage readers from all disciplines, not just science and engineering, to "think big." —CC

Einstein



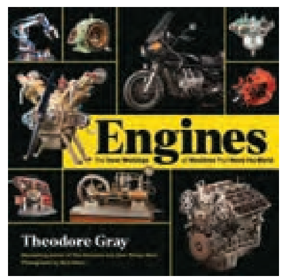
The Man and His Mind

Gary S. Berger and Michael DiRuggiero
Damiani, 2022. $70.00

Nearing 70 years after Albert Einstein's death, the mystique surrounding the physicist shows no signs of abating. Probably the first celebrity scientist, his name alone is synonymous with genius. This new coffee-table book published by the Italian art press Damiani reproduces over a hundred Einstein-related items—including photographs, letters, and offprints of his scientific articles—from the private collection of Gary Berger. It distinguishes itself from the realm of kitschy Einsteiniana in how the documents illustrate the physicist's human side: The letters and the inscriptions on the photos show how even after decades in the US, Einstein's social circles remained dominated by Germanophone émigrés such as the photographer Lotte Jacobi. —RD

Engines

The Inner Workings of Machines That Move the World



Theodore Gray; photographs by Nick Mann
Black Dog & Leventhal, 2022. $32.00

This new large-format book by Theodore Gray, an author and chemistry enthusiast, is a tinkerer's dream. Featuring images, cross sections, and diagrams of engines and motors of all varieties, *Engines* delves into how those ubiquitous devices function. A particular highlight is Gray's deep dive into the diesel-powered hydraulic motors used by the Amish, who generally eschew electricity but still need to produce furniture on an industrial scale: They retrofit commercial electric devices to use compressed-air motors. The book mainly focuses on steam engines, internal-combustion engines, and electric motors, and a final chapter examines a grab bag of devices such as linear motors and sewing machines. —RD PT

NEW PRODUCTS

Focus on cryogenics, vacuum equipment, materials, and semiconductors

The descriptions of the new products listed in this section are based on information supplied to us by the manufacturers. PHYSICS TODAY can assume no responsibility for their accuracy. For more information about a particular product, visit the website at the end of its description. Please send all new product submissions to ptpub@aip.org.

Andreas Mandelis

Software for cryogenic probe stations

Lake Shore Cryotronics now ships its cryogenic probe stations with a Windows PC workstation preloaded with the company's MeasureLINK software. The versatile, intuitive software lets users easily control sample temperature—and on certain models, magnetic field—for on-wafer probing measurements. By setting up discrete or continuously varying measurements, users can watch how temperature stabilizes as it approaches a set control. A process view window in MeasureLINK displays the system's internal status at various points, including the temperature at the sample stage and on the probe arm. The collection of electrical measurements can be controlled as a function of temperature or magnetic field using Lake Shore's MeasureReady and some third-party instruments. That eliminates the need to write custom code so that different instruments can communicate with one another. ***Lake Shore Cryotronics Inc***, *575 McCorkle Blvd, Westerville, OH 43082, www.lakeshore.com*

Durable vacuum transducers

According to Thyracont, the new generation of its Smartline vacuum transducers—the cold-cathode VSI and Pirani/cold-cathode VSM models—ensure a longer sensor lifetime by systematically reducing the high voltage of their cold cathodes in high-pressure ranges. Because of the physical characteristics of cold-cathode gauges, at pressures higher than 1×10^{-4} mbar, their inherent sputter effect causes increased abrasion. Endurance tests at 1×10^{-3} mbar demonstrated that the new sensors are three times as durable as other gauges. The devices now also feature a readout of the sensors' deterioration and an operating-hours counter for predictive maintenance. The Smartline vacuum transducers are used in coating, analytics, medical engineering, and vacuum-furnace applications. ***Thyracont Vacuum Instruments GmbH***, *Max-Emanuel-Str 10, 94036 Passau, Germany, https://thyracont-vacuum.com*

Vacuum-pump controller

In one place, the EJGO and EJGO MC controllers from Edwards provide the information and metrics needed to intelligently manage, direct, and regulate the operation of the company's vacuum-pump systems. Users can easily pull up relevant data on a touch human–machine interface or a web browser on a laptop, tablet, or mobile phone. They can configure data and parameters relevant to their process and observe their pump's performance on the go. The EJGO can generate trends maps that allow comparison of multiple metrics across pump cycles and at various times. Available in standard and premium options, the EJGO MC offers advanced central control over vacuum pumps—up to 20—and processes to ensure the best combination for optimum power consumption. The EJGO and EJGO MC automatically update to the latest cybersecurity protocols so that users' networks are secure when connected to the internet of things. ***Edwards Ltd**, Innovation Dr, Burgess Hill, West Sussex, RH15 9TW, UK, www.edwardsvacuum.com*

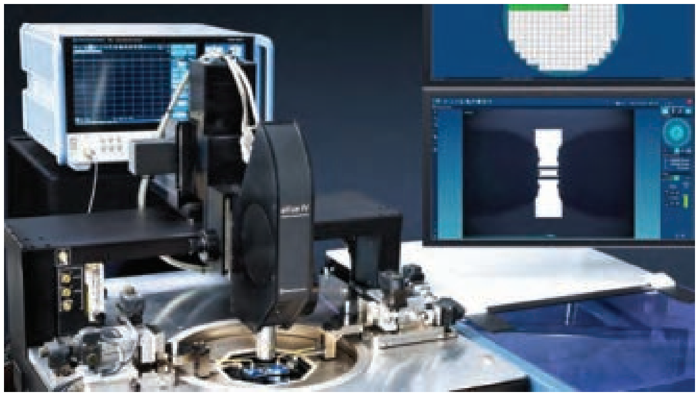
Silicone elastomer

Master Bond MasterSil 323AO-LO, a two-component silicone elastomer with a self-priming feature, is designed for bonding, sealing, and gap-filling applications. The electrically insulating and thermally conductive compound meets NASA's low-outgassing specifications and can be used in the aerospace, electronic, optoelectronic, and specialty OEM industries. It has a thermal conductivity of 1.15–1.30 W/(m·K). It is highly flexible with a low tensile modulus of 500–700 psi, an elongation of 50–60%, and a hardness of 70–75 Shore A. Those properties enable it to withstand aggressive thermal cycling and mechanical shock. MasterSil 323AO-LO bonds well to various substrates, including metals, composites, glass, ceramics, plastics, and other silicones, without imparting residual stress when heat cured. It is serviceable from −54 °C to 204 °C. Its paste-like consistency allows it to be used as a gap-filling material where minimum flow after application is desired. ***Master Bond Inc**, 154 Hobart St, Hackensack, NJ 07601-3922, www.masterbond.com*

Vacuum and prevacuum pump

With an ultimate vacuum of up to 1.5 mbar absolute at a flow rate of up to 36 L/min, KNF's N 952 diaphragm pump series is a suitable support for advanced analytical instrument applications. Other areas of application include scanning electron microscopy, mass spectrometry, and gas chromatography and analysis. The N 952 pump is powerful, chemically resistant, and oil-free. Its ability to retain a high pumping speed even close to ultimate vacuum makes it appropriate as a prevacuum pump for turbomolecular pumps in research and industry. Supported by new brushless DC motors developed in-house, speed-controlled vacuum performance provides the required vacuum profile and low-vibration operation in drying chambers or heating ovens. Particularly vibration-sensitive systems can be provided for by a stand-alone N 952 version with a separate power switch. ***KNF Neuberger Inc***, *2 Black Forest Rd, Trenton, NJ 08691-1810, https://knf.com*

On-wafer device characterization



Rohde & Schwarz (R&S) now offers semiconductor manufacturers a test solution for on-wafer characterization of the RF design of devices under test early in the development phase and during production. To ensure proper RF capabilities for frequency coverage and output power while optimizing energy efficiency, the test setup combines the company's R&S ZNA vector network analyzer with engineering probe systems from FormFactor. The vector network analyzer characterizes all RF qualification parameters at coaxial and waveguide levels, and frequency extenders for application ranges above 67 GHz. FormFactor examines the wafer contact with manual, semiautomated, and fully automated probe systems including high-frequency probes, probe positioners, and thermal control and calibration tools. FormFactor WinCal XE software calibrates the complete test system, including the R&S ZNA. ***Rohde & Schwarz GmbH & Co KG***, *Mühldorfstraβe 15, 81671 Munich, Germany, www.rohde-schwarz.com*

Explosion-proof Roots pumps

Pfeiffer Vacuum has expanded its OktaLine ATEX series of Roots pumps, which are designed for use in potentially explosive environments or for evacuating explosive gases. ATEX certified for low- and medium-vacuum applications, the pumps meet the highest explosion-protection requirements. They are appropriate for chemical, biotechnological, pharmaceutical, and industrial applications, such as in vacuum furnaces and heat treatment. Pumping speeds now range from 280 m^3/h to 8100 m^3/h. Variable differential pressure and flexible rotational speed make the pumps suitable for universal use; they can all be employed at ambient temperatures ranging from −20 °C to 40 °C. Because of their magnetic coupling, OktaLine pumps are hermetically sealed and achieve the very low leak rates of 10^{-6} Pa m^3/s. They are resistant to pressure surges of up to 1600 kPa, and there is no risk of zone entrainment. The integrated temperature sensor protects against thermal overload and monitors the gas temperature in the outlet area. ***Pfeiffer Vacuum Inc****, 24 Trafalgar Sq, Nashua, NH 03063, www.pfeiffer-vacuum.com*

EBSD analysis system

Edax, a unit of the materials analysis division of Ametek, has added the Clarity Super to its electron backscatter diffraction (EBSD) product line. According to Edax, the Clarity sensors provide single-electron detection sensitivity, a superior signal-to-noise ratio, and high dynamic range. Optimized for high performance across a broad range of voltages with an emphasis on efficient data collection, the sensors are suitable for analysis of ceramics and semiconductor materials where lower beam currents are needed, or for applications such as high-resolution EBSD that require superior EBSD pattern quality. The existing Clarity Plus offers electron collection sensitivity down to approximately 7 kV; the new Clarity Super extends that range to 3 kV. It can therefore be used to analyze beam-sensitive samples such as perovskite organic–inorganic solar cells and fine-grained materials where improved spatial resolution is needed. ***Edax Inc****, 91 McKee Dr, Mahwah, NJ 07430, www.edax.com* PT

Robert Floyd Curl Jr

Robert Floyd Curl Jr, a codiscoverer of the hollow-cage carbon compounds called fullerenes, passed away on 3 July 2022 in Houston, Texas, at age 88.

Bob was born on 23 August 1933 in Alice, Texas, a small town that has produced two Nobel laureates, James Allison and Bob. His parents gave him a chemistry set to spur his childhood interest in science. Although Bob's experiments nearly destroyed his mother's stove, it inspired him to be a chemist. The family moved frequently before settling in San Antonio, where Bob attended high school. When his chemistry teacher recognized Bob's talent and encouraged him to build a Cottrell precipitator as a special project, it hooked him on science.

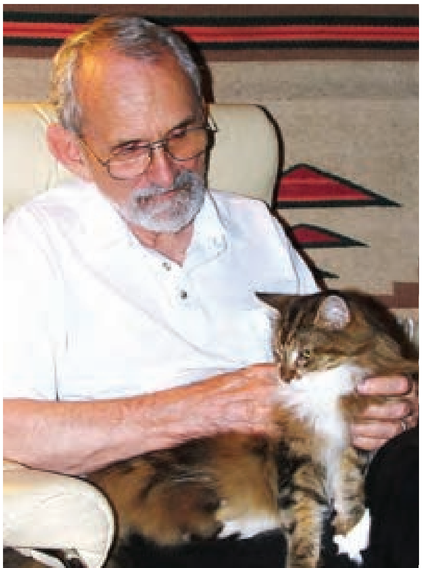
Bob attended Rice University (then Rice Institute), a school known for its science and engineering focus and free (!) tuition. At Rice, Bob developed a lifelong interest in molecular structure by taking Natural Products, a course taught by Richard Turner, an innovator in determining heats of hydrogenation. Turner emphasized how rotation about single bonds could interchange conformations in steroids and produce large physiological effects.

After earning his BA from Rice in 1954 as one of the top two students in his class, Bob moved to the University of California, Berkeley, for graduate study with Kenneth Pitzer, a physical chemist and pioneer in molecular conformational studies. Pitzer apparently considered conformations a solved problem and advised Bob to extend the law of corresponding states to predict thermodynamic properties. The resulting Curl–Pitzer method gave entropies of vaporization that were accurate to within about 0.5%, which proved so useful for chemical-plant design that the Institution of Mechanical Engineers in London awarded the two men a James Clayton Fund Prize for a paper they wrote while Bob was still a graduate student. To satisfy Berkeley's expectation that PhD students must conduct experiments, Bob measured matrix-isolation spectra of samples cooled to 20 K by liquid hydrogen and determined that the silicon-oxygen-silicon bond of disiloxane was bent. He gave credit to Dolphus Milligan for helping to avert disaster during his hydrogen transfers.

Bob received his PhD in chemistry from Berkeley in 1957 and moved to Harvard University for postdoctoral research on molecular conformations with E. Bright Wilson Jr. His stay at Harvard was cut short when George Bird, a former Wilson student, left the Rice faculty and Bob was recruited to take his place. He thus returned to Rice as an assistant professor of chemistry in 1958, just four years after leaving with his bachelor's degree. Bob inherited not only Bird's microwave spectrometer but also a brilliant graduate student, James Kinsey, who later became chair of the MIT chemistry department before returning to Rice as dean of natural sciences. On the occasion of Bob's retirement in 2008, Kinsey said, "He's scary smart, but he is also an extraordinarily decent human being, a sweet person."

At Rice, Bob published 63 papers on microwave spectra of various free radicals. As lasers advanced in the 1970s, he expanded his studies into gas-phase IR spectroscopy; chemical kinetics, with Graham Glass; laser development, with Frank Tittel; and reaction transition states, with one of us (Brooks). In the mid 1970s, Bob was instrumental in recruiting a brilliant young colleague, Richard Smalley, who accepted largely because of Bob's presence. Their first joint publication was a photoionization study of semiconductor clusters produced in Smalley's cooled molecular-beam apparatus.

Bob had long been intrigued by the origin of the diffuse interstellar bands. Upon learning of Harold Kroto's studies on carbon molecules thought to be formed near red giants, he invited Kroto to Rice to study carbon clusters and then convinced Smalley to participate. Their initial experiments with graduate students James Heath, Sean O'Brien, and Yuan Liu showed a mass spectrum peak indicating 60 carbon atoms. Within days they deduced that C_{60} had a cage structure



Robert Floyd Curl Jr

resembling a soccer ball. They named it buckminsterfullerene in reference to the architect Buckminster Fuller, who popularized the geodesic dome. Their discovery launched the new field of fullerene chemistry, leading to the publication of more than 100 000 papers and the award of the 1996 Nobel Prize in Chemistry to Bob, Smalley, and Kroto.

Bob contributed enormously to Rice during his 64 years as an active and emeritus professor. He and his wife, Jonel, were the first magisters (resident supervisors) of the Lovett residential college, from 1968 to 1972, and provided guidance, especially during student unrest of that period. He served as chair of the chemistry department, lent his wisdom to countless university and national committees, and lobbied the Texas legislature on behalf of science. Bob was famously humble as well. One former student commented, "He listened. He really listened." After the Nobel award, Rice's president asked Bob if the university could do "anything" to make him happy. He modestly replied that it would be nice to have a bicycle rack installed near his building.

Bob's many friends, students, and colleagues deeply miss this exceptionally brilliant and decent man.

R. Bruce Weisman
Philip R. Brooks
Rice University
Houston, Texas

Nick Holonyak Jr

Known as the father of the LED and semiconductor visible laser, Nick Holonyak Jr, the John Bardeen Endowed Chair Emeritus in Electrical and Computer Engineering and Physics at the University of Illinois at Urbana-Champaign, died in Urbana on 18 September 2022 at the age of 93.

Holonyak was born on 3 November 1928 in the southern-Illinois coal-mining town of Zeigler. He attended the University of Illinois and earned his BS in 1950, MS in 1951, and PhD in 1954, all in electrical engineering. During his PhD, he worked for John Bardeen—two-time Nobel laureate in physics—as his first graduate student and set up germanium semiconductor research.

After getting his PhD, Holonyak went to work at Bell Labs in Murray Hill, New Jersey. Under John Moll, he developed diffused p–n junction technology for silicon transistors. Holonyak was drafted into the US Army in 1955 and assigned to the Signal Corps at Fort Monmouth in New Jersey and then to Yokohama, Japan. During his duty in Japan, he often participated in informal technical seminars on germanium and silicon device technology with Japanese scientists and engineers.

After his discharge, Holonyak joined General Electric in Syracuse, New York, and began an investigation of the closed-ampoule vapor-phase transport growth of $GaAs_{1-x}P_x$ alloy semiconductors. He used his apparatus to make a small single-crystal sample and produce a diffused p–n junction for his studies of tunneling in III–V semiconductors. Many of the GaAsP alloys covered a region of compositions where the energy bandgap was direct. Holonyak developed the first visible red LEDs. He also identified the direct–indirect transition composition in those alloys.

In October 1962 Holonyak demonstrated the first alloy semiconductor laser diode, a $GaAs_{1-x}P_x$ diffused p–n junction emitting in the red spectral region at around 710 nm at 77 K. Those results established definitively that semiconductor alloys were not simple physical mixtures but had a defined bandgap energy—the first bandgap engineering. Today, III–V heterojunction devices with at least one ternary alloy layer are widely employed for several generations of novel devices that could not otherwise be realized.

Nick Holonyak Jr

Holonyak was invited by Bardeen in 1963 to join the faculty at the University of Illinois. He was appointed a full professor in the departments of electrical and computer engineering and physics and established a small research laboratory to study III–V compound semiconductor materials and devices. He set it up in the Electrical Engineering Annex, one of the early buildings on campus. His group developed liquid-phase epitaxy and grew bulk crystals using the closed-ampoule approach to study various III–V alloys. In 1970 Holonyak and his students developed the first quaternary-alloy semiconductor, $Al_xGa_{1-x}As_{1-y}P_y$; such quaternaries are now widely used in many devices. Seven years later Holonyak demonstrated the first quantum-well laser diodes, composed of multiple thin layers about 50 nm thick of $In_{1-x}Ga_xP_{1-z}As_z$ quantum wells. Today every semiconductor LED and laser diode incorporates similar quantum wells.

From 1980 to 1990, Holonyak investigated various postgrowth processes that included impurity-induced layer disordering and the controlled oxidation of aluminum-bearing III–V alloys to selectively form stable native-oxide insulating regions inside a device structure. Today those innovative methods are used for the commercial manufacture of advanced laser diodes, including oxide-defined aperture for vertical-cavity surface-emitting lasers, which are used for energy-efficient high-speed optical data links in mega data centers, 3D sensing in smartphones, and new applications in autonomous vehicles and cryogenic computing.

Holonyak, with one of us (Feng), realized in 2003 that the photon energy from direct-bandgap transistor-base electron–hole recombination (spontaneous and stimulated) could be a new signal optical output in addition to the transistor collector current output. With quantum wells embedded in the base of heterojunction bipolar transistors, they demonstrated the first laser operation in a transistor in 2004. The transistor-laser-based integrated photonics technology could open a new front of inter- and intrachip optical data links and all-optical logic processors to alleviate the latency and overhead associated with massive data movement by today's network fabrics.

Holonyak's many pioneering semiconductor materials and device innovations underpin much of the technology supporting high-efficiency lighting, high-speed communications and information processing, and advanced solar-power systems used in space, laser processing systems, and lidar systems for autonomous vehicles. In his 50-year career at Illinois, Holonyak published more than 600 refereed technical articles and directed 60 PhD students, many of whom have made important contributions of their own to the field. The world is a brighter and safer place because of Holonyak's engineering contributions. He is missed by his students and many of his colleagues who knew or collaborated with him.

Russell D. Dupuis
Georgia Institute of Technology
Atlanta

Milton Feng
University of Illinois at Urbana-Champaign PT

RECENTLY POSTED NOTICES AT
www.physicstoday.org/obituaries

David Arthur Shirley
30 March 1934 – 29 March 2021

Joseph W. Motz
11 November 1917 – 26 April 2020

Lydia Mäthger is a biologist at the Marine Biological Laboratory in Woods Hole, Massachusetts.

How the blue-ringed octopus flashes its rings

Lydia Mäthger

The animals flex and relax fast-acting muscles to expose light reflectors hidden in specialized skin pouches.

Shown in figure 1, the blue-ringed octopus may be small—the size of a golf ball, typically—yet equipped with a highly potent neurotoxin it can be deadly. As their name suggests, the octopuses feature around 60 highly conspicuous blue rings and (in some species) lines along their bodies and arms. The blue rings and lines exhibit iridescence—that is, they change color with the angle of observation and angle of illumination—an optical phenomenon caused by the differential refraction and reflectance of light waves on the animal.

Cephalopods, who spend much of their time hidden, are well known for their instant camouflage. Yet within the blink of an eye, the animals can change their appearance to be stunningly bright and colorful. Blue-ringed octopuses are no exception. When threatened, they quickly expose their blue rings in a series of bright flashes. Those flashes are an example of aposematism, a warning intended to deter predators. But unlike other aposematic animals, such as poison dart frogs, which permanently display their bright colors, blue-ringed octopuses hide their rings most of the time and only show them when necessary.

Skin reflectors

Optical physicists and materials scientists, particularly those working in the field of biomimetics, are interested in those displays for a number of reasons. One is that no energy is required to illuminate the animals' rings; the process of making the rings visible is entirely passive. Indeed, all cephalopods reflect parts of the ambient electromagnetic spectrum from specialized structures in their skin. That reflectivity spans not only the visible part of the spectrum, but also near-UV and near-IR light. Another reason is that the displays are not always static. Some cephalopods have the additional ability to fine-tune the spectrum of their skin colors and change the reflected wavelength in a matter of seconds.

The skin of cephalopods is equipped with thousands—and in some species millions—of neurally controlled pigmented chromatophores. They are considered organs, each containing a sac filled with either dark brown, black, red, or yellow pigments. Attached to the pigment sac are several radial muscle fibers that are directly innervated by the brain. Contracting those muscles expands the sac and exposes the pigment. Relaxing them has the opposite effect: It causes the sac to retract into a tiny round ball. To appreciate how a chromatophore changes color, think of a partially inflated party balloon. Flattening the balloon with a glass plate would be analogous to muscle contraction, which exposes the pigment sac by pulling it into a thin disk; lifting the glass plate would relax the muscle and prompt the sac to retract and take on its normal round shape.

In addition to chromatophores, cephalopods generally have two types of structural reflectors. Leucophores are broadband reflectors responsible for creating white spots and lines in cuttlefish, octopuses, and some squid. By contrast, iridophores are cells made up of multilayered stacks of reflector plates consisting of a protein interspersed by spaces of cytoplasm—each plate differing in refractive index. The scattering of light in those stacks produces constructive interference.

Constructive interference

The iridophores inside the rings of the blue-ringed octopus contain a large number—as many as 30 in some cells—of those densely packed plates. All plates have roughly the same thick-

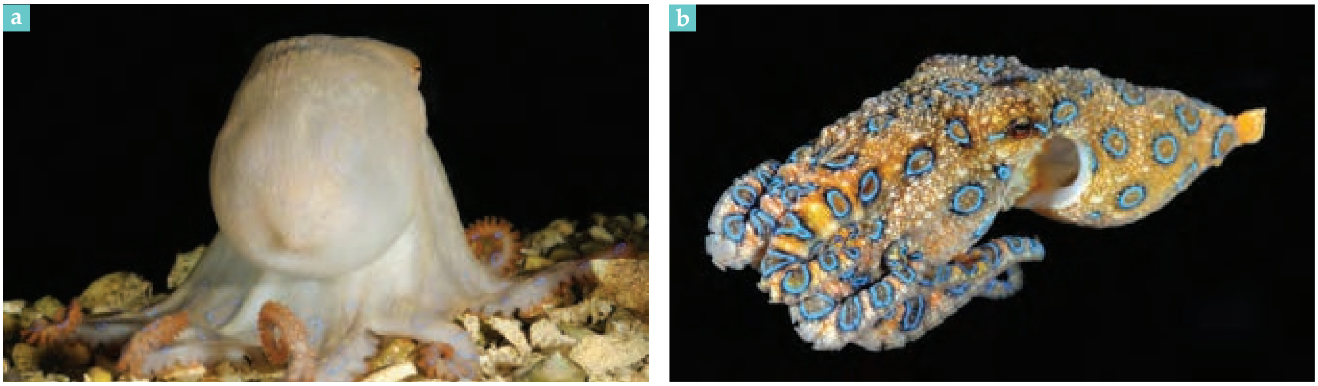


FIGURE 1. A BLUE-RINGED OCTOPUS, roughly 6 cm in length, is shown **(a)** camouflaged and **(b)** flashing its rings. (Courtesy of Roy Caldwell, University of California, Berkeley.)

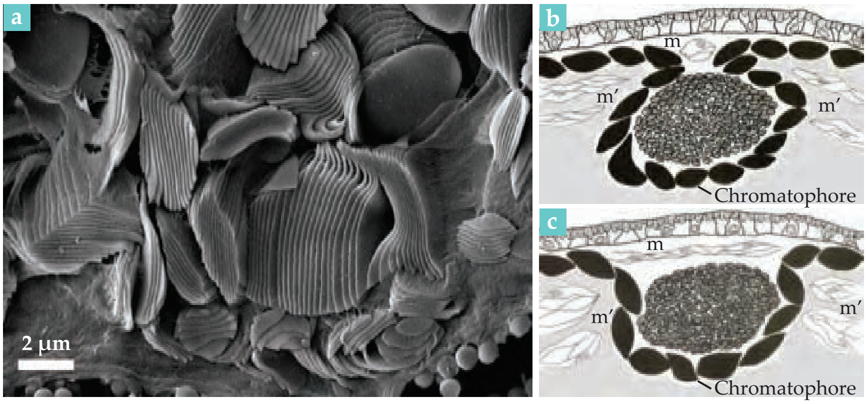


FIGURE 2. BLUE-RING IRIDOPHORES are shown **(a)** as a parallel arrangement of plates in this scanning electron micrograph. **(b)** In a closed ring, contraction of transverse muscles (m), located above the iridophores (central round structure), covers iridescence. **(c)** Relaxation of those muscles, combined with contraction of muscles around the perimeter (m′), exposes iridescence. The sketches in panels b and c illustrate the rings' flashing mechanism. (Adapted from L. M. Mäthger et al., *J. Exp. Biol.* **215**, 3752, 2012.)

ness (around 62 nm, as shown in figure 2a), which allows them to act as an ideal quarter-wave stack.

The wavelength that they most strongly reflect equals $4nd$, where n is the refractive index of the plate and d is its thickness. Assuming a refractive index of 1.59 and 20% tissue shrinkage—introduced by the processing required for electron microscopy—plates would reflect at 499 nm.

Because individual stacks are arranged at multiple angles in the skin, the iridescence is visible from a wide range of viewing angles. The arrangement is important because once the animal is threatened, the flashing rings need to be visible all around it.

How does the blue-ringed octopus show its blue rings when needed? It turns out that the rings contain physiologically inert iridophore cells, arranged to reflect blue-green light in a broad viewing direction. Dark pigmented chromatophores are located beneath and around each ring to enhance visual contrast. There are no pigmented chromatophores above the ring. That's an unusual feature for cephalopods, which typically use chromatophores to cover or spectrally modify iridescence. But their absence holds the key to how the rings are flashed.

Surrounding the iridescent rings are muscle fibers that, as shown in figure 2b, hide the reflectors by pulling the overlying skin together—somewhat like two sliding doors closing over a pouch of reflector cells. When those muscles relax and the muscles on the outside of the ring contract, as shown in figure 2c, the iridescence becomes visible. Moreover, because the skin is so flexible, the iridophores are brought closer to the skin surface for maximum visibility. All those muscles are under direct neural control, which makes the flashes happen quickly, within 0.3–0.5 seconds.

Lessons from cephalopod color change

Every cephalopod species is different, and not every color change method is found in every species. All cephalopods have pigmented chromatophores, and most species have many thousands in their skin. The structural reflectors, which are usually located in a layer beneath the chromatophores, can be tuned in some species—in many squids, for example—via specialized neurotransmitter receptors. They can also be tuned by the action of the chromatophores themselves, which indirectly block or spectrally filter the iridescence.

Although tuning the iridescence physiologically takes seconds to minutes, presumably because of changes to the physical state required to enable the optical changes, spectral change via chromatophores is much faster because the surrounding muscles are under direct neural control and muscle contraction is almost instant.

But cephalopod chromatophore pigments generally reflect longer-wavelength colors, such as reds, oranges, and yellows, which alone are insufficient to create high-contrast patterns. Those longer-wavelength colors are comparatively ineffective for underwater communication—at least at greater depths—where long-wavelength photons are quickly absorbed. Adding greens and blues to the signaling repertoire is paramount to creating a conspicuous visual signal, and using specialized reflector cells, cephalopods have mastered the challenge beautifully.

Of course, camouflage is still the most important survival strategy for cephalopods, so the brightly iridescent signals need to be obscured most of the time. While some species physiologically turn their iridescence off, which takes time, the blue-ringed octopus has found a way for its conspicuous warning signal to be available almost instantly, by contracting a specific set of muscles and moving the skin folds that hide the rings out of the way. When the danger is gone, those muscles relax, and another set of muscles contracts, pulling the iridescent rings back into their specialized skin pouches.

The color-changing mechanism described here, whereby highly reflective iridophores are hidden inside specialized skin folds, has not been found in any other cephalopod—or in any other animal for that matter. The uniqueness is mysterious, but it is a reminder that the natural world is highly complex and there is still much to learn. Octopus skin is extremely elastic and muscular, lending the animal the ability to give its skin three-dimensional texture, which is particularly useful for camouflaging on visually diverse underwater backgrounds. Given the dense network of muscles and nerves in their skin, it is perhaps not too difficult to imagine how the conspicuous flashing may have evolved in blue-ringed octopuses.

Additional resources

- ► R. T. Hanlon, J. B. Messenger, *Cephalopod Behaviour*, 2nd ed., Cambridge U. Press (2018).
- ► R. M. Kramer, W. J. Crookes-Goodson, R. R. Naik, "The self-organizing properties of squid reflectin protein," *Nat. Mater.* **6**, 533 (2007).
- ► L. M. Mäthger et al., "Mechanisms and behavioural functions of structural coloration in cephalopods," *J. R. Soc. Interface* **6**, S149 (2009).
- ► L. M. Mäthger et al., "How does the blue-ringed octopus (*Hapalochlaena lunulata*) flash its blue rings?," *J. Exp. Biol.* **215**, 3752 (2012).
- ► L. M. Mäthger et al., "Bright white scattering from protein spheres in color changing, flexible cuttlefish skin," *Adv. Funct. Mater.* **23**, 3980 (2013). PT

Pre-satellite weather balloons

John Brown and Emmett Pybus are shown here conducting upper-atmospheric water-vapor studies in Antarctica. Brown and Pybus were meteorologists working for the US Army's Ballistic Research Laboratories, Aberdeen Proving Ground, Maryland, in the 1960s. Their studies involved flying balloons equipped with dew-point hygrometers to measure the water-vapor profiles at different layers of the atmosphere. Before the late 1960s, few satellites were collecting meteorological data, so the hygrometers provided a majority of information about the upper atmosphere. This balloon would ultimately travel more than 32 kilometers aboveground.

Although meteorological studies are conducted all over the world, Antarctica is a unique environment. The upper atmosphere at the poles differs from that in the middle latitudes because of magnetic field differences. Also, the angle at which solar radiation hits the surface affects the amount of water that evaporates into the atmosphere. The Arctic Ocean has seasonal sea ice, but Antarctica is covered by a year-round solid shelf of ice, making it a more permanent location from which the atmosphere can be measured from the ground. This photo and additional ones of Antarctic researchers can be found at the Emilio Segrè Visual Archives of the American Institute of Physics (publisher of Physics Today). A 2015 oral history with Pybus is available in the Oklahoma State University Library digital collection as part of its oral history research program (https://dc.library.okstate.edu/digital/collection/ostate/id/8934). —KJ

TO SUBMIT CANDIDATE IMAGES FOR BACK SCATTER VISIT https://contact.physicstoday.org.