

JILA

LIGHT & MATTER

vol. 10

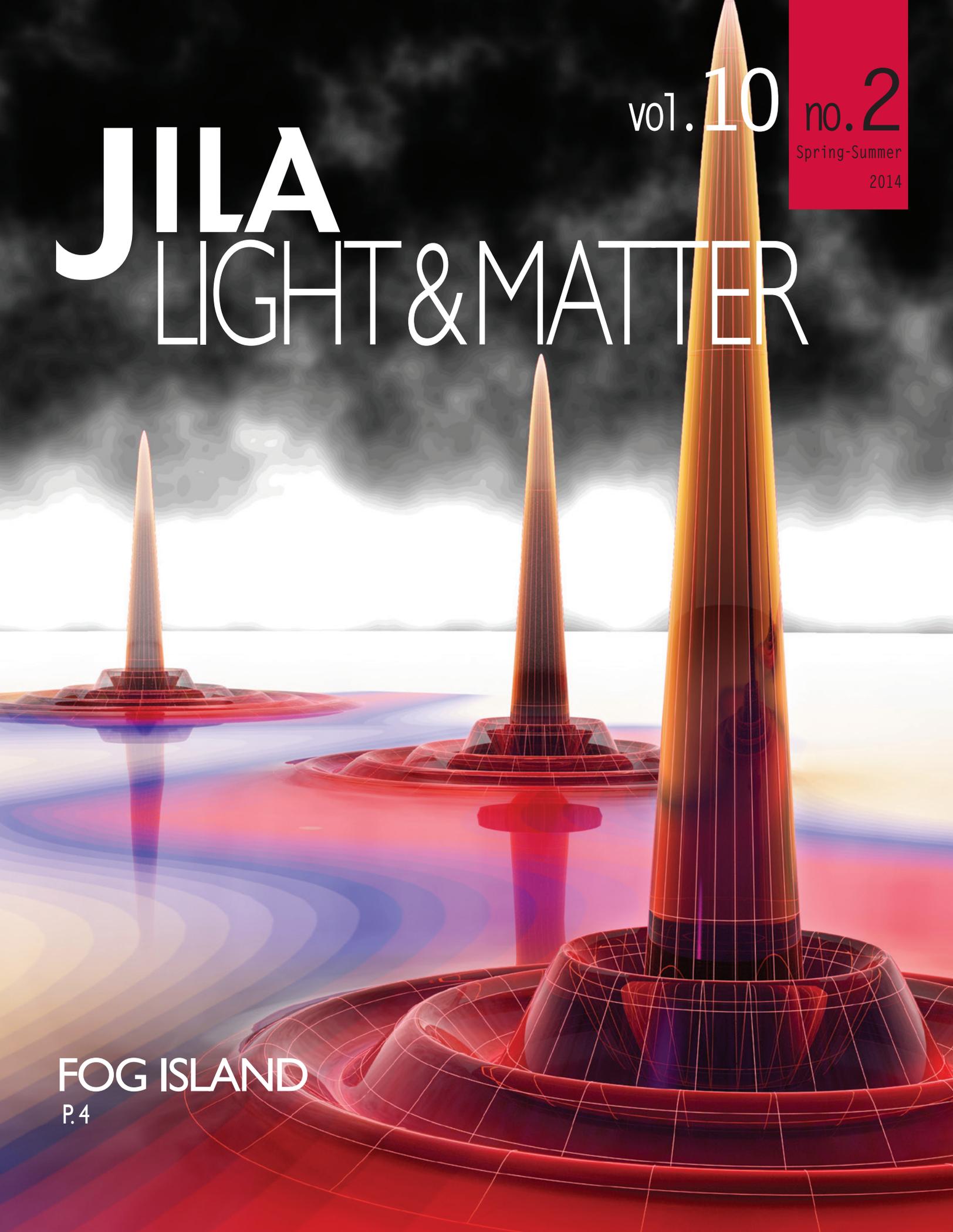
no. 2

Spring-Summer

2014

FOG ISLAND

P.4





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(Opposite) Working in the new Keck Lab.

Credit: Brad Baxley, JILA

FOG ISLAND

When Andy Hunter and his colleagues in the Cundiff group shined a laser on a sample of gallium arsenide (GaAs), the last thing they were expecting to create was a fog of liquid-like quantum droplets. The droplets are a new, stable form of matter much like an ordinary liquid—with one key difference.

Unlike normal everyday liquids, the droplets contain charged particles. The particles are negatively charged electrons and positively charged “holes.” Holes are like bubbles created when electrons in GaAs are excited by light.

When it discovered the quantum droplets, the Cundiff group was actually investigating the use of intense laser light to generate biexcitons, which are molecule-like structures in GaAs made of two excitons. Excitons are hydrogen-like quasi particles made of an electron and a hole.

“But the experiment didn’t behave at all in the way we expected,” Hunter said. “We expected to see the energy of the biexcitons increase as the laser generated more electrons and holes. But, what we saw when we did the experiment was that the energy actually *decreased!*”

The energy decrease meant that the researchers certainly were seeing something other than biexcitons. In fact, they weren’t sure what they had made. At this point, experimentalists Hunter, former research associate Hebin Li, and Fellow Steve Cundiff consulted their theorist colleagues at Philipps-University Marburg in Germany.

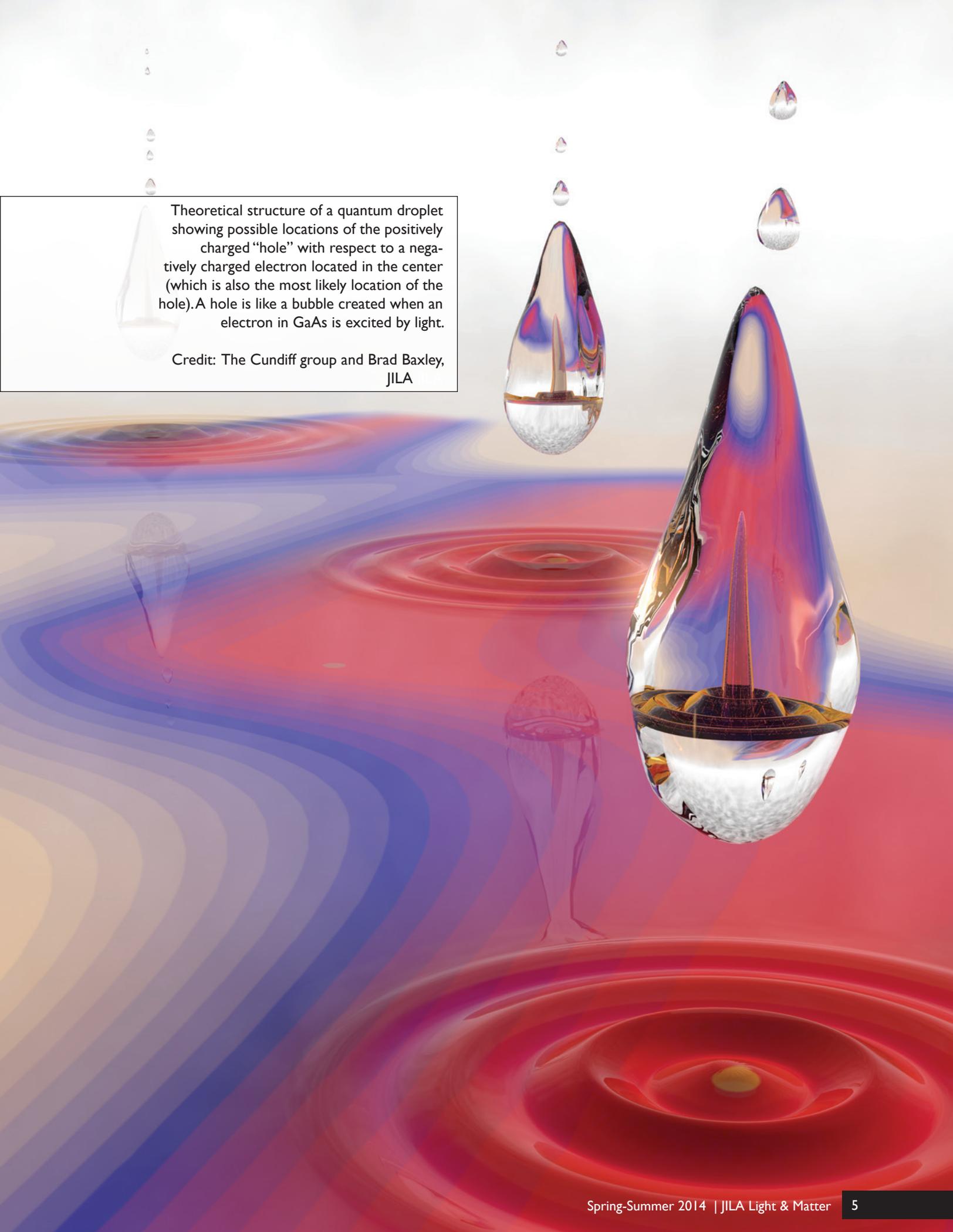
The German collaborators came up with the idea that the experimentalists had made quantum droplets. A quantum droplet is a structure containing multiple electrons and holes (for example, 4, 5, or 6 of each) that is in between the structure of a traditional atom with positively charged nucleus surrounded by negatively charged electron(s) and an older model of the atom that viewed it as a positively charged sphere with electrons embedded in it. The droplets behaved quantum mechanically because they contain only a few electrons and holes.

Quantum droplets aren’t made up of multiple excitons because the electrons and holes in them are not bound into pairs. In a quantum droplet, all of the electrons interact equally with all of holes and vice versa. In an excitonic molecule, such as a biexciton, the electrons and holes form excitons, which then form molecules. In this case, each electron primarily interacts with a single hole. It’s completely different with quantum droplets.

According to the quantum-droplet theory calculations (as represented in the figure), the electron is in the middle of the tall structure in the middle of the droplet. The hole and the electron are most likely right on top of each other. However, the hole could also be just above, just below, or even next to the electron. The next most likely location of the hole is somewhere on the first ring. The third most likely location for the hole is on the second ring. The least likely location is in the gaps between the rings. As the density of electrons and holes increases inside a droplet, so too does the number of rings, as shown in the background of the figure.

The experimental observations made by Hunter and his colleagues fit perfectly with the new theory. The researchers realized that they had inadvertently created a quantum fog of electrons and holes in close proximity to one another, but not paired. In the process, they had discovered a new particle structure as stable as an atom or a solar system. This story is featured on the cover of the February 27 online issue of *Nature*.

A. E. Hunter, H. Li, S. T. Cundiff, M. Mootz, M. Kira, and S. W. Koch, *Nature*. **506**, 471–475 (2014).



Theoretical structure of a quantum droplet showing possible locations of the positively charged “hole” with respect to a negatively charged electron located in the center (which is also the most likely location of the hole). A hole is like a bubble created when an electron in GaAs is excited by light.

Credit: The Cundiff group and Brad Baxley, JILA



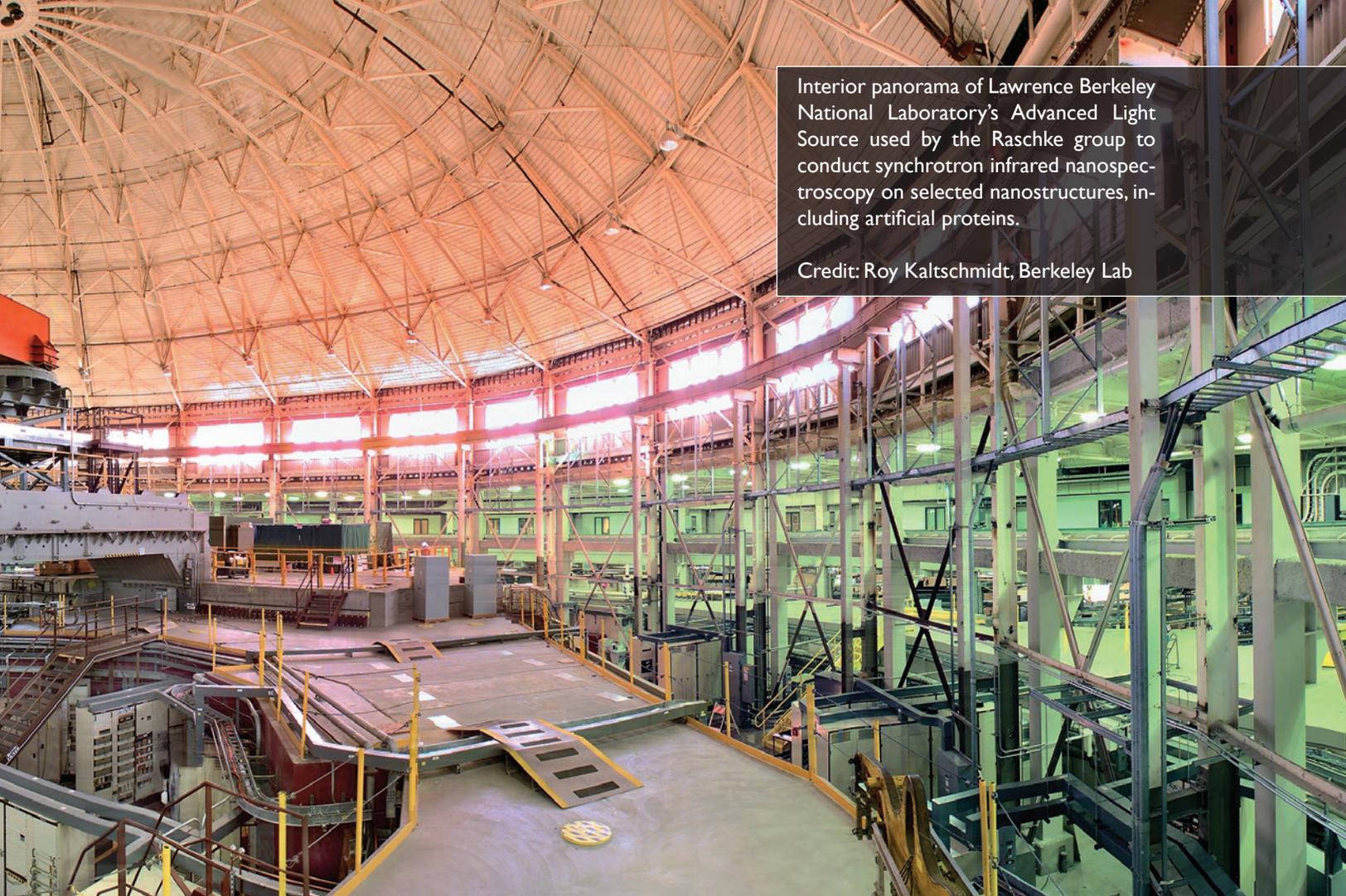
THE SINS OF MARKUS RASCHKE

The Markus Raschke group has come up with an innovative way that may one day allow it to peer inside superconductors, new materials for solar cells, or even a single cell and identify the inner workings of these complex systems. The new method is able to determine where the different chemical constituents are located and how their spatial distribution determines their function.

The new method is called synchrotron infrared (IR) nanospectroscopy, or SINS. It combines scanning probe microscopy with IR synchrotron radiation, which is intense, directional, coherent, and spans a broad range of IR wavelengths ranging from 2 to 15 μm . This range of wavelengths is critical for detecting and identifying electronic and vibrational states in semi- and superconductors, polymers, biomolecules, and other materials.

The first-ever SINS experiment was reported online in the *Proceedings of the National Academy of Sciences of the USA* on May 6, 2014. The experiment was a collaboration of the Raschke group and members of the Advanced Light Source (ALS) Division that houses the synchrotron at the Lawrence Berkeley National Laboratory. The research team included research associate Eric Muller, former graduate student Robert Olan, Fellow Adjunct Markus Raschke, and ALS Beamline Scientist Michael Martin and Senior Scientific Engineering Associate Hans Bechtel.

The innovative experiment probed the surface characteristics of a silicon-based semiconductor material, identi-



Interior panorama of Lawrence Berkeley National Laboratory's Advanced Light Source used by the Raschke group to conduct synchrotron infrared nanospectroscopy on selected nanostructures, including artificial proteins.

Credit: Roy Kaltschmidt, Berkeley Lab

fied distinct crystal structures of calcium carbonate (CaCO_3) in a seashell, and analyzed protein nanostructures attached to a surface. The researchers were able to identify spatial variations in chemical structures of just a few molecules with a resolution of just a few nanometers.

The synchrotron experiment was the culmination of nearly a decade of effort inspired by a successful test experiment in 2005 by undergraduate student Jana Puls in Raschke's lab at the Berliner Elektronenspeicherring-Gesellschaft für Synchrotronstrahlung (BESSY), a national lab in Berlin, Germany.

"When I first saw the unique properties of infrared synchrotron light back in 2005 at BESSY in Berlin, I thought right away, we have to try using it for nanospectroscopy," Raschke said.

Thanks to some modest funding from the U.S. Department of Energy in 2008, Raschke was able to begin talks with the ALS staff about the idea of using synchrotron IR radiation in nanoscience investigations. From there, the visionary idea evolved into the successful feasibility study highlighted here.

"What excites me most about this experiment is that we started with a giant machine—the synchrotron—and we were able to focus its infrared power down to the nanoscale with the help of a tiny needle that concentrated the synchrotron light into a tiny region," Raschke explained. "This process made it possible to study ultramicroscopic processes in matter."

Hans A. Bechtel, Eric A. Muller, Robert L. Olmon, Michael C. Martin, and Markus B. Raschke, *Proceedings of the National Academy of Sciences USA*, 111, 7191–7196 (2014).

Dealing with Loss

There's exciting news from JILA's ultracold molecule collaboration. The Jin, Ye, Holland, and Rey groups have come up with new theory (verified by experiment) that explains the suppression of chemical reactions between potassium-rubidium (KRb) molecules in the KRb quantum simulator. The main reason the molecules do not collide and react is continuous measurement of molecule loss from the simulator. That it works this way is a consequence of the quantum Zeno effect, also known as the *watched-pot* effect, as in the proverb "A watched pot never boils."

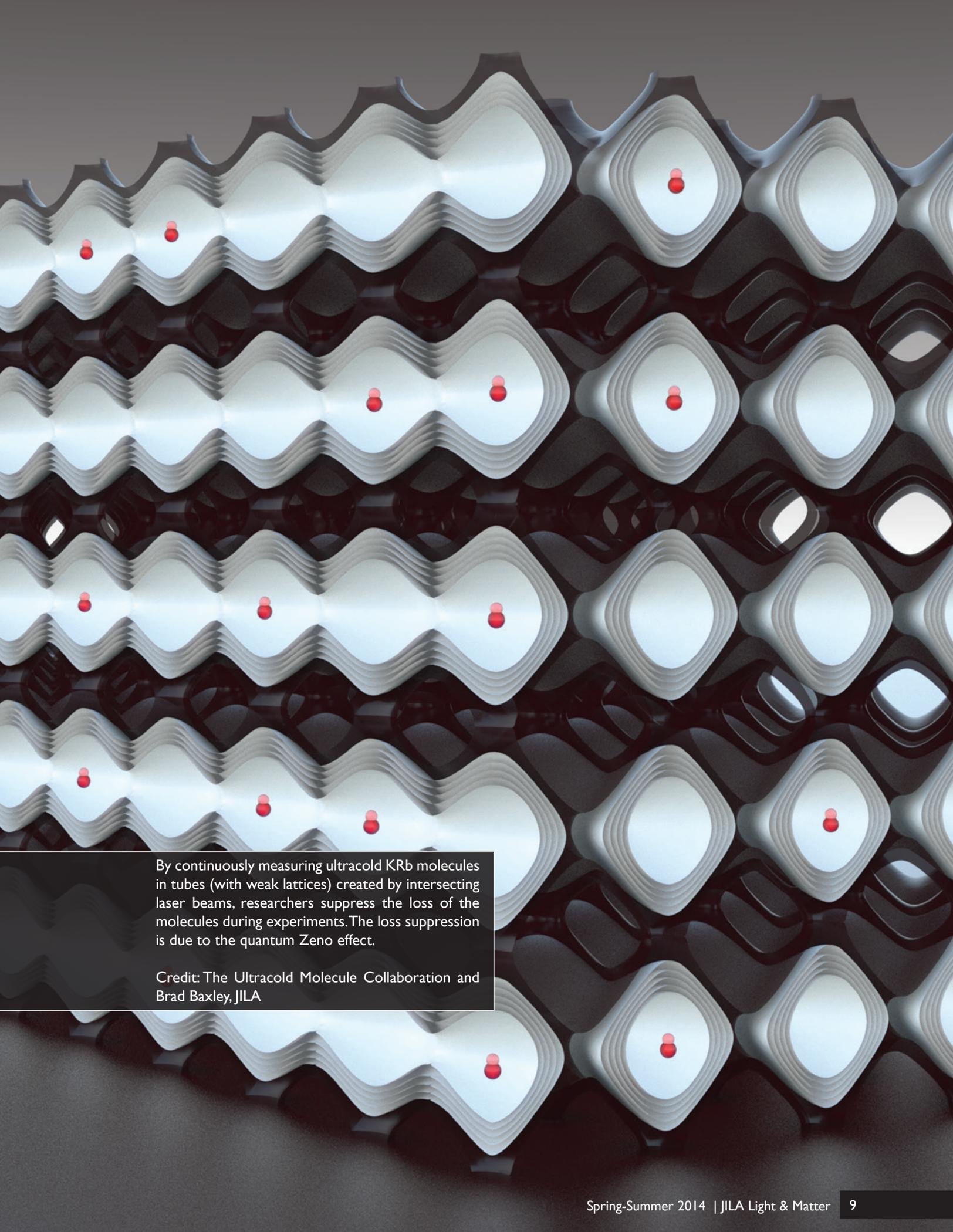
In essence, if researchers investigate a quantum system by continuously measuring it, things stop changing altogether. The strange laws of quantum mechanics are responsible for this odd behavior. These laws dictate that the act of measurement itself forces the KRb molecules into a particular quantum state. And, if measurements occur continuously, the molecules will stay in that state because the measurements themselves are collectively preventing any change in the quantum states of the molecules. The idea that continuous measurements prevent a quantum system from evolving is the essence of the quantum Zeno effect, named for the Greek philosopher Zeno of Elea.

Thus, if you adjust a quantum simulator so that (according to the laws of classical physics) the molecules inside it get lost faster and faster because of colliding and reacting, then the laws of quantum mechanics will actually make the molecules react slower and slower until they eventually just sit there forever and never get lost. It's almost as if two KRb molecules "know" from the continuous measurements not to hop into the same place in the simulator because they would react and disappear if they did. New theory by the Holland and Rey groups shows explicitly how this works. It not only verifies the quantum Zeno effect, but also demonstrates that older theories that attempted to explain this kind of quantum behavior incorrectly predicted loss to happen five times faster.

In practical terms, the previous and less accurate theories suggested that the number of KRb molecules in the simulator would be about one molecule per two lattice sites (which are energy wells created by intersecting laser beams). In practice, however, that calculation predicted too many molecules. Right now, the number of KRb molecules in the simulator is fewer, typically one per every 10 lattice sites. And, this just happens to match the amount of lattice filling predicted by the new theory. Clearly, increasing the lattice filling is going to be a lot harder than researchers originally expected it to be.

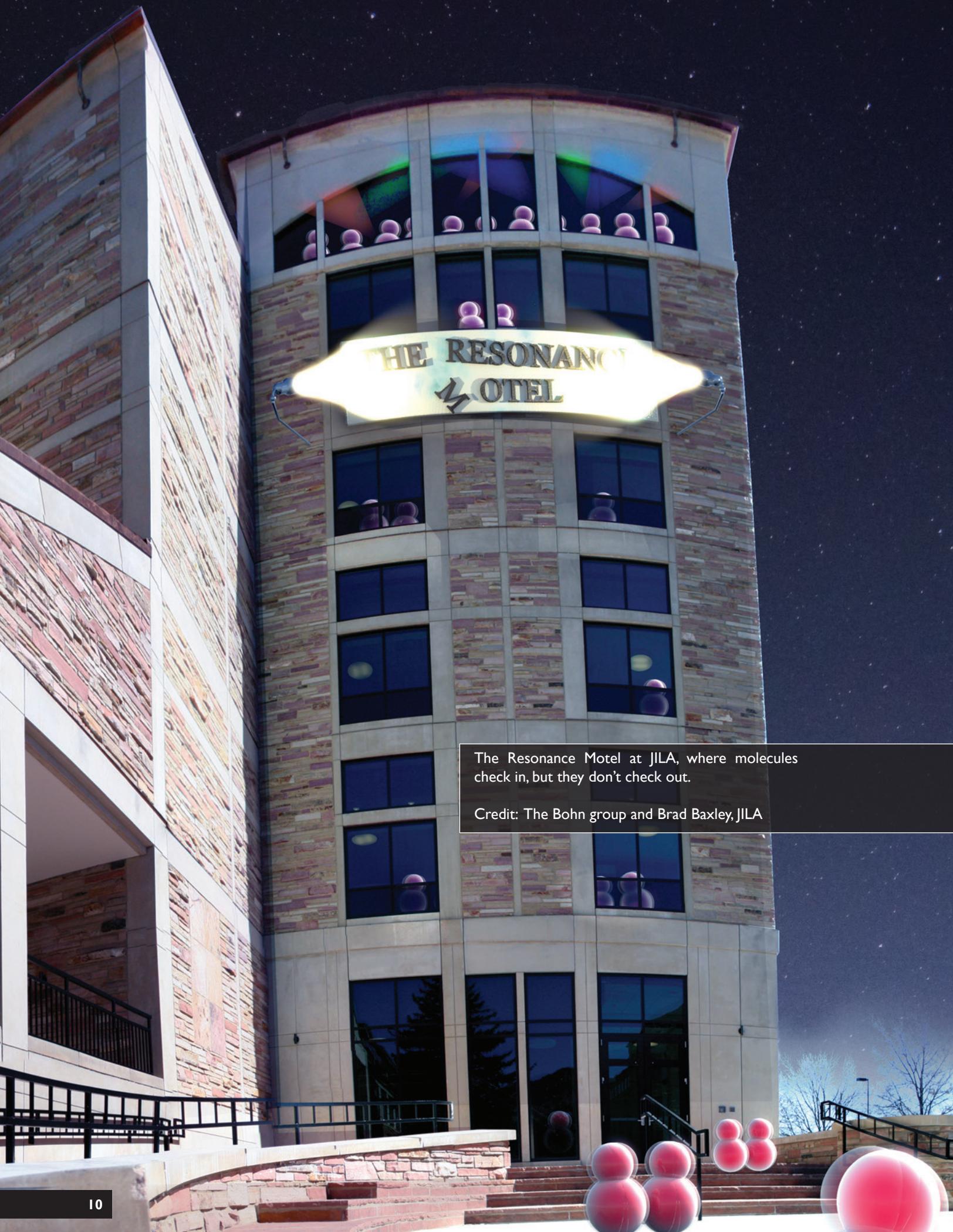
Untangling this complicated quantum behavior required the brainpower and dedication of 13 JILA researchers. The theory team comprised graduate student Bihui Zhu, recently minted Ph.D. Michael Foss-Feig, research associates Johannes Schachenmayer and Michael Wall, senior research associate Kaden Hazzard as well as Fellows Murray Holland and Ana Maria Rey. The experimental team included research associates Bryce Gadway and Bo Yan, graduate students Steven Moses and Jacob Covey, and Fellows Debbie Jin and Jun Ye.

B. Zhu, B. Gadway, M. Foss-Feig, J. Schachenmayer, M. L. Wall, K. R. A. Hazzard, B. Yan, S. A. Moses, J. P. Covey, D. S. Jin, J. Ye, M. Holland, and A. M. Rey, *Physical Review Letters*, **112**, 070404 (2014).



By continuously measuring ultracold KRb molecules in tubes (with weak lattices) created by intersecting laser beams, researchers suppress the loss of the molecules during experiments. The loss suppression is due to the quantum Zeno effect.

Credit: The Ultracold Molecule Collaboration and Brad Baxley, JILA



The Resonance Motel at JILA, where molecules check in, but they don't check out.

Credit: The Bohn group and Brad Baxley, JILA

THE RESONANCE MOTEL

WHERE MOLECULES CHECK IN, BUT THEY DON'T CHECK OUT

Quantum chaos just showed up in an ultracold gas of erbium atoms, and the Bohn theory group knows why. Theorists expect quantum chaos to appear when quantum mechanical objects get sufficiently complicated. But until now, scientists hadn't realized that something as simple as a pair of colliding atoms could be complicated enough for quantum chaos to appear. For instance, the Bohn group has spent several years investigating the theoretical spectra of ultracold molecules, which contain a plethora of densely packed, randomly spaced Fano-Feshbach resonances. The researchers speculate that the spread of these resonances will be similar to patterns explained by quantum Chaos Theory.

It turns out that complicated atoms like erbium also have a boatload of resonances, as reported by Bohn and his experimental collaborators in *Nature*. Nearly 200 resonances showed up in a relatively narrow magnetic-field scan that would have captured only two or three Feshbach resonances in rubidium or other "simple" alkali atoms studied at JILA and all around the world. There are so many resonances in ultracold erbium that it may not be possible to investigate them individually. The best possible route to understanding them may be to ask what the resonances are like when taken together.

Luckily, the well-known physicist Freeman Dyson came up with a theory in the 1960s to describe all sorts of bumping and shaking going on inside the nuclei of atoms. Dyson's statistical analyses of atomic nuclei not only revealed that resonances tend to be spread out relatively evenly, but also that resonances seemed to follow the patterns explained by classical Chaos Theory. The Bohn group decided to look at classical Chaos Theory as a way to begin to understand chaos in the ultracold quantum world.

The group realized a while ago that a chaotic spread of resonances might not be good news for experimentalists planning to investigate ultracold molecules. That's because molecules are attracted to the "Resonance Motel." They like to check in. Ordinarily, if the molecules bump into each other at sufficiently low temperature, there isn't usually enough energy to cause a chemical reaction, and they eventually bounce harmlessly off one another. However, in a resonance, the molecules exploit their energy of attraction to get them rotating and vibrating, so there would be lots of jiggling and bumping around.

But the trouble is, when the molecules move into this resonant mode, it takes a long time before one of the molecules randomly acquires enough energy to escape rather than to just jiggle. In fact, most of the time, escape would take longer than an ultracold experiment lasts. This is a problem for scientists because when molecules are living in a resonance motel, they disappear from view in the experiment. No wonder on a recent occasion at a conference, researchers who investigate ultracold molecules referred to Bohn as the "Angel of Death!"

Bohn's Innsbruck collaborators also approached him at a conference to ask if he thought they'd be able to see a slew of resonances in erbium since it was a complicated atom. Bohn told them it would be worth a look. They looked and found 190 resonances in one isotope and 189 of them in another isotope. (Isotopes have the same number of protons in their nuclei, but different numbers of neutrons.)

Thanks to the Innsbruck team, the world has seen the first experimental verification of chaotic behavior in

the interactions between ultracold atoms—a stunning result that promises to entirely change the landscape of ultracold atomic and molecular physics.

In developing a theory of ultracold resonant behavior, Bohn worked with research associate James Croft, graduate student Brandon Ruzic, former research associate Michael Mayle, and former senior research associate Goulven Quémener. His experimentalist colleagues included Albert Frisch, Michael Mark, Kiyotaka Aikawa, and Francesca Ferlaino of the Universität Innsbruck. Constantinos Makrides, Alexander Petrov, and Svetlana Kotochigova of Temple University contributed to the theoretical analysis of quantum chaos in ultracold collisions of erbium.

Albert Frisch, Michael Mark, Kiyotaka Aikawa, Francesca Ferlaino, John L. Bohn, Constantinos Makrides, Alexander Petrov, and Svetlana Kotochigova, *Nature*, **507**, 475–479 (2014).

CLUES

ACROSS

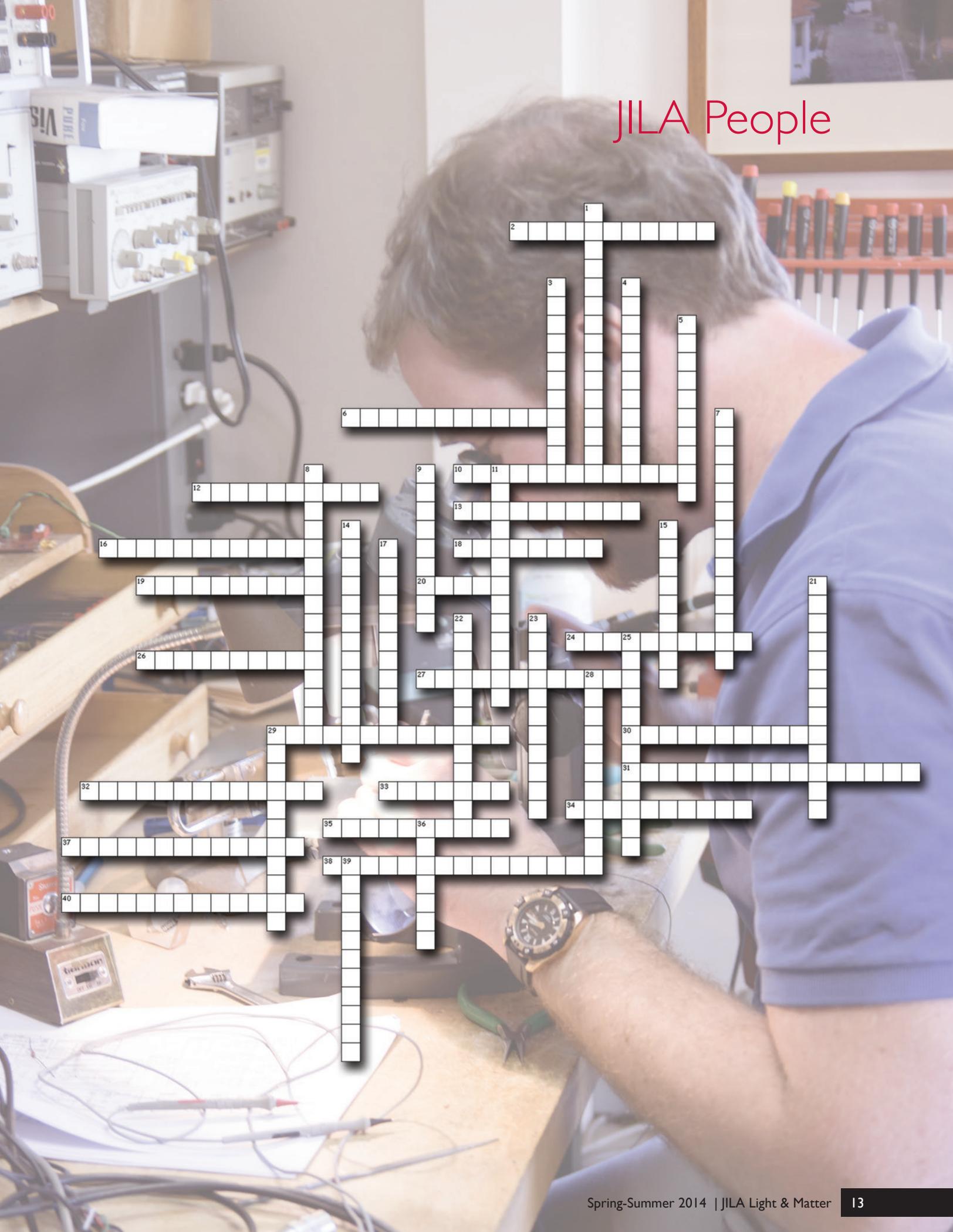
2. Glass blowing guru
6. Exploder of nano particles
10. Chair supporter
12. QPD fearless leader
13. Loves LISA
16. Senior K/M dude
18. Physics of baseball guy
19. Electric leader
20. Celine's dad
24. PFC supporter
26. On the clock team
27. Awesome nature photographer
29. The great entangler
30. eEDM gal
31. Senior Toomre dude
32. Grew up in Sante Fe, NM
33. MAC/PC guy
34. PISEC principal
35. Transitioned to blonde
37. Superradiant fellow
38. Number One volunteer
40. Dick Thomas awardee last

DOWN

1. Resident genius 1
3. X-Wing liaison
4. The Time Lord
5. Staff chief
7. HR pro
8. Married to Huanqian Loh
9. Resident genius 2
11. Black holes on his mind
14. Super Drupal girl
15. Winter crossword puzzle winner
17. Apps volunteer
21. RNA pseudoknot prober
22. Terrific tenor
23. Single neutral atom guy
25. 1982 Appalachian Trail walker
28. Resident genius 3
29. Spectroscopy champ
36. Rey & Holland grad student
39. Junta Jefe

First Person to turn in a correct puzzle to SCO wins a \$25 Starbucks gift card

JILA People

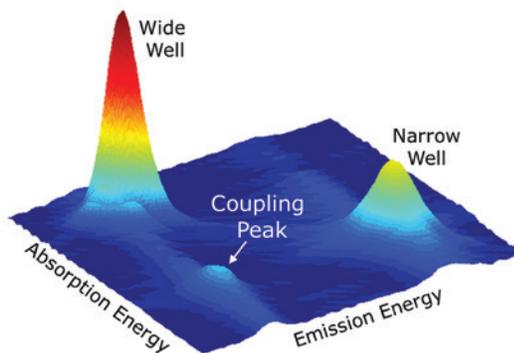


ADVENTURES IN COUPLING

Real-world quantum mechanics may not always work exactly like the simple picture presented in textbooks, according to observations made by research associate Gaël Nardin and his colleagues in the Cundiff group.

In an experiment (described in *Physical Review Letters*), the group found evidence of coupling between particles in semiconductor quantum wells that hadn't been predicted by simple textbook calculations. Semiconductors are materials whose electrical conductivity increases when light shines on them, and quantum wells are extremely thin layers of semiconductor materials. They are so thin that particles in them exist as waves, and their behavior is dominated by quantum mechanics. Thus quantum wells are ideal for studying quantum physics, including some unexpected particle couplings.

The coupled particles studied by Nardin and his colleagues were excitons, which consist of negatively charged electrons bound to positively charged "holes" in semiconductors. Holes are like bubbles created when electrons are excited by light. Excited electrons and holes then pair together to form excitons when laser light interacts with quantum wells.



Experimental results of the Cundiff group's "real-world" coupling experiment. This 2D spectrum shows a coupling peak due to the interactions of many particles in adjacent quantum wells. Credit: Gaël Nardin (Cundiff group), JILA

The researchers created excitons in two adjacent quantum wells, one wide and the other narrow. Then

they probed the interactions of the excitons with a precision optical instrument called the JILA MONSTR (Multidimensional Optical Nonlinear SpecTRometer). The research team included Nardin, newly minted Ph.D. Galan Moody, graduate students Rohan Singh and Travis Autry, former research associate Hebin Li, Fellow Steve Cundiff, and François Morier-Genoud of Switzerland's École Polytechnique Fédérale de Lausanne.

The researchers expected to see what the textbooks predicted: coupling between the two quantum wells due to the wave-like nature of the electrons and holes in the wells. Because they are waves, the electrons and holes can tunnel through the barrier between the wells; in contrast, if they were governed by classical physics they would have had to jump over it.

At first, the experiment confirmed the presence of coupling between the narrow and the wide quantum wells. A coupling peak appears in the two-dimensional measurement produced by the JILA MONSTR, shown in the figure. However, a careful analysis of the experimental results revealed that the coupling had not originated from textbook quantum coupling, but rather from the collective interaction of multiple excitons in both quantum wells. This finding implies that scientists should include interactions of many particles to reproduce what Mother Nature is actually doing in the quantum world.

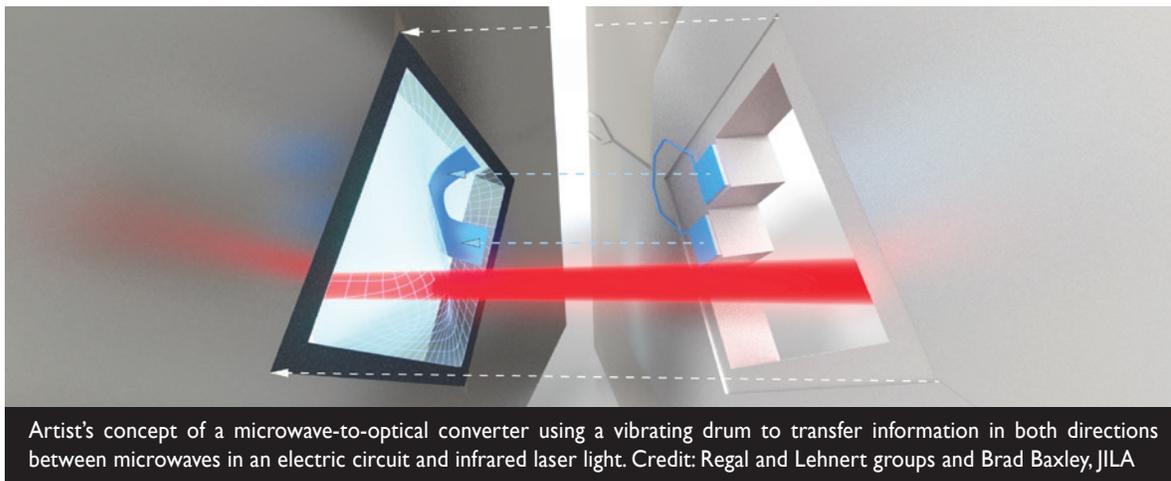
The new picture of coupling between quantum wells may help scientists better understand light harvesting in plants and bacteria. In light harvesting, energy is transferred between pigments that can be modeled as quantum wells because electrons can hop from one pigment to another. This behavior is similar to what Nardin observed with excitons in his experiment.

The Cundiff group's research into real-world quantum coupling of many particles promises to facilitate applied research on quantum cascade lasers, which employ multiple adjacent quantum wells to produce lasing.

Gaël Nardin, Galan Moody, Rohan Singh, Travis M. Autry, Hebin Li, François Morier-Genoud, and Steven T. Cundiff, *Physical Review Letters* **112**, 046402 (2014).

GOOD VIBRATIONS: THE EXPERIMENT

The Regal-Lehnert collaboration has just taken a step towards the goal of building a quantum information network. Large-scale fiber-optic networks capable of preserving fragile quantum states (which encode information) will be necessary to realize the benefits of superfast quantum computing. Such networks will require new technology to reversibly convert microwave light (i.e., electrical signals) to infrared or visible light, without losing any information. This JILA collaboration has just made important progress toward developing a device that will be able to accomplish this conversion.



The two JILA groups partnered with researchers at NIST to build a converter that not only links the low-frequency microwave and high-frequency optical portions of the electromagnetic spectrum, but also preserves classical information encoded in the light. The converter works equally well in both directions and faithfully and efficiently transfers the information. The researchers responsible for this accomplishment were graduate students Reed Andrews and Robert Peterson, research associate Tom Purdy, Fellows Cindy Regal and Konrad Lehnert, and NIST scientists Katarina Cicak and Ray Simmonds.

The light-conversion experiment was reported in *Nature Physics*. In the experiment, researchers transferred classical signals between microwave and optical light with conversion efficiencies of $\sim 10\%$. The experiment worked so well that the researchers have calculated that if the device were cooled from its current operating temperature of 4 K to below 40 mK, it would be able to coherently transfer quantum states.

The heart of the device is a silicon nitride drum that can “talk” to both microwave and optical light, which cannot otherwise communicate with each other. Infrared laser light passes through the drum near, but not touching, a tiny electronic circuit. Microwaves in the circuit cause the drum to vibrate, altering the phase or amplitude of the laser light. Changes in the phase or amplitude of the laser light cause the drum to vibrate, producing a signal that encodes the information in microwave light.

The converter is actually quite small. The vibrating drum measures a millimeter on each side, while the top blue electrical piece is 250 μm long, and the bottom blue square electrical pieces measure 170 μm on a side. When the device is closed and operational, the two halves are separated by about half the width of a bacterium, or < 500 nm.

The next step for the Regal-Lehnert collaboration is quantum state transfer between microwave and optical light. The challenge will be figuring out how to get all the pieces perfectly aligned and cooled down to near absolute zero.

R.W.Andrews, R.W.Peterson, T.P.Purdy, K. Cicak, R.W.Simmonds, C.A.Regal, and K.W.Lehnert, *Nature Physics* **10**, 321–326 (2014).

THE FLIP SIDE

Fellows Mitch Begelman and Phil Armitage have solved the 40-year old mystery of what causes the gas of stellar debris surrounding black holes in binaries to flip back and forth between a spherical cloud and a luminous disk.

When stellar-sized black holes orbit around another star, the black holes feed themselves by pulling material off their companion stars, funneling it in close. Once near a black hole, the stellar debris exists either as (1) an extremely hot spherical cloud that isn't very bright or (2) a thin and opaque disk of hot gas that is very luminous. Curiously, these black holes don't stay in the same state for more than a few weeks to a few months. Rather, they flip back and forth between the two states in a systematic, but somewhat unpredictable fashion.

The strangest aspect of the switch is what happens to the luminosity. The gas will switch from being a disk to a spherical envelope around the black hole only when the luminosity is very low. With time, the luminosity increases as more and more matter from the neighboring star arrives near the black hole. However, the gas near the black hole remains in a very hot spherical state until extremely high luminosities occur. Then the gas suddenly flips into a very luminous, thin disk. Over time, the thin disk gets less and less luminous, but it doesn't flip back to a hot sphere until it gets to a very low luminosity. The actual transition between states is quite rapid.

Through the years, many scientists have scratched their heads over this puzzling cycle, but no more, thanks to Armitage and Begelman. They suggest that the culprit is a systematic, but random, ebb and flow of magnetic fields in the gas surrounding the black hole. The hot spherical structure favors the accumulation and growth of magnetic fields. Matter flowing toward the black hole drags magnetic fields generated near the outside of the cloud close to the black hole. Once that happens, the magnetic field cannot escape. The strong magnetic field helps the gas cloud remain hot and spherical for much longer than it would otherwise be able to do.

Then, for reasons that are still not yet well understood, the cloud suddenly flips into a disk. Once this happens, the magnetic field leaks away fairly quickly. Without a strong magnetic field, the disk state is more persistent, and doesn't flip back to a hot cloud until the luminosity becomes very low.

So why does the magnetic field eventually return? Out beyond the disk of hot gas (and the sphere of hot gas as well), there's always a cold disk of stellar matter that doesn't change state. Both the hot disk and the cold disk randomly generate small magnetic fields with north and south poles that quickly cancel themselves out. However, at the border between the hot and cold disks, it's possible for the magnetic poles to get separated and uncorrelated. And, when there are many random, uncorrelated events, there's always some chance that something big will happen.

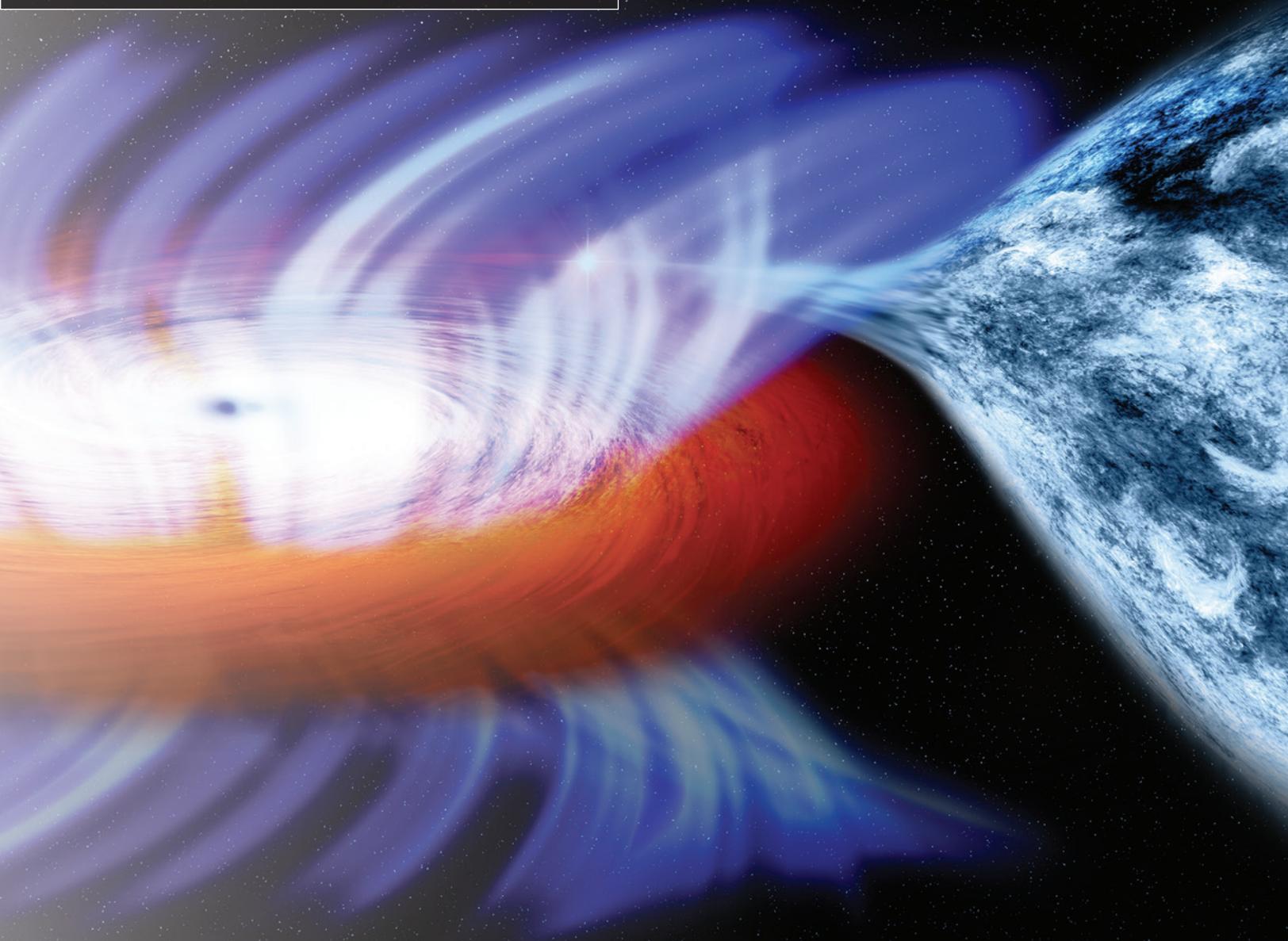
It turns out that if magnetic fields come and go across the border between the hot and cold disks for several months, there's a good chance that a strong magnetic field will build up near the black hole. When this happens, the hot cloud once again becomes more robust, and the cycle repeats. Armitage and Begelman don't yet know the details of how the hot cloud collapses to a thin disk or how the thin disk becomes a sphere. But, they now know what causes the transitions.

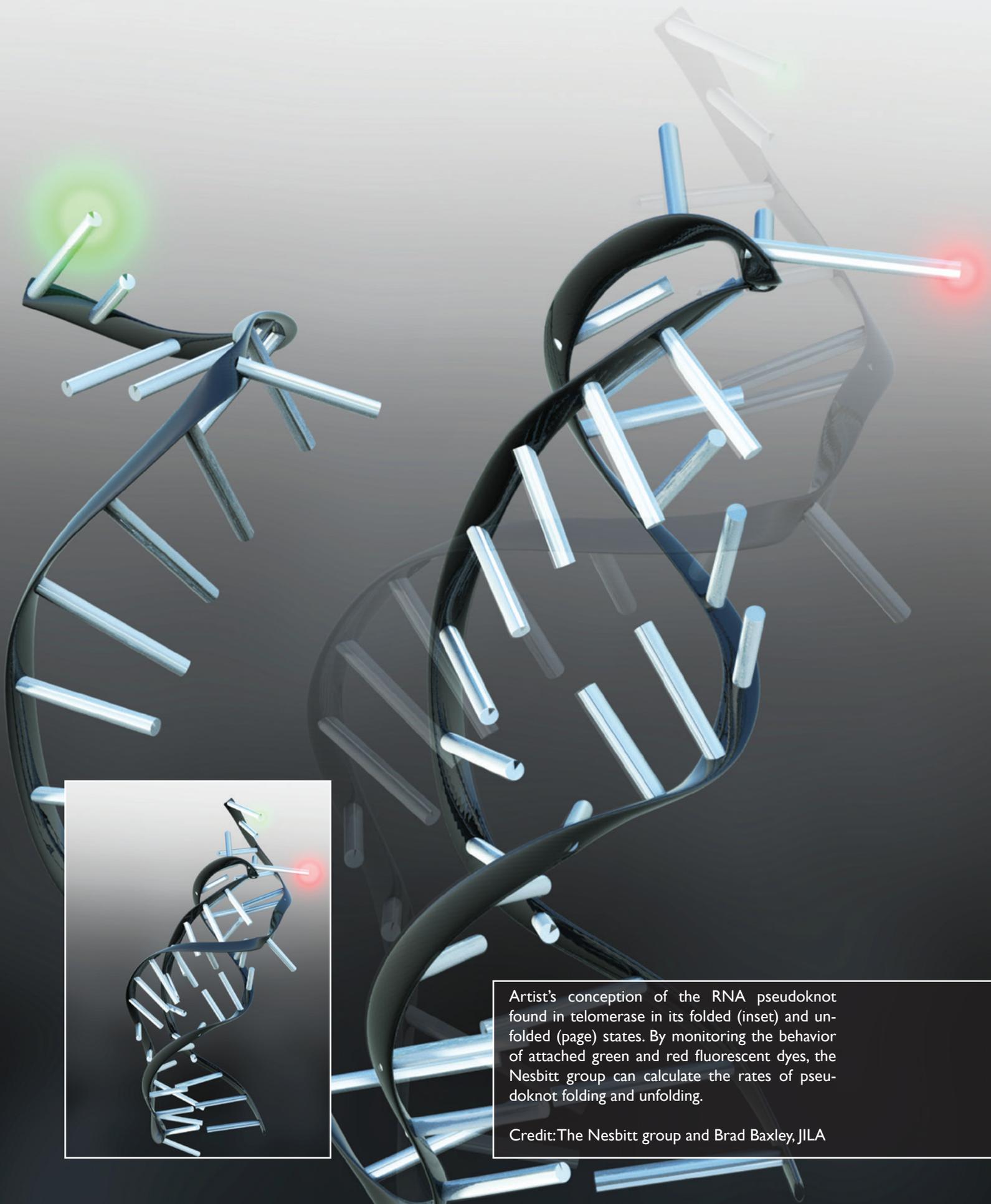
For decades, astronomers have observed black holes in binary systems flipping back and forth over and over again. And, now astronomers know why the observed cycles don't repeat exactly. It's because of the random nature of the regeneration of a magnetic field in the disk.

Mitchell C. Begelman and Philip J. Armitage, *The Astrophysical Journal Letters* 782, L18 (2014).

Binary black hole feeding off its companion star. In binaries like this, the stellar debris around the black hole systematically, but randomly, cycles between a low-luminosity sphere of hot gas and a luminous thin disk.

Credit: NASA/CXC/M.Weiss





Artist's conception of the RNA pseudoknot found in telomerase in its folded (inset) and unfolded (page) states. By monitoring the behavior of attached green and red fluorescent dyes, the Nesbitt group can calculate the rates of pseudoknot folding and unfolding.

Credit: The Nesbitt group and Brad Baxley, JILA

THE UNFOLDING STORY OF TELOMERASE

Graduate student Erik Holmstrom and Fellow David Nesbitt have applied their laboratory research on the rates of RNA folding and unfolding to the medically important enzyme telomerase. Telomerase employs both protein and RNA components to lengthen chromosomes, which are shortened every time they are copied.

If one short piece of the RNA in telomerase is folded into an organized structure called a pseudoknot, then the enzyme works properly. The enzyme repeatedly adds short pieces of DNA to the chromosomes within the cells of people and many other organisms. Because it counteracts the natural shortening of chromosomes, telomerase is vital for keeping cells alive and healthy through multiple cell divisions.

If, however, the pseudoknot contains mutations that interfere with folding, the result can be the serious genetic disorder dyskeratosis congenita, which causes a variety of skin and blood diseases. New work by Holmstrom has revealed why mutations in the pseudoknot are so harmful.

When the pseudoknot unfolds, telomerase stops working. In normal people telomerase works efficiently because the pseudoknot is folded about 99.9% of the time. But, in people who suffer from dyskeratosis congenita, this enzyme does not work properly because it is only folded half the time. Holmstrom discovered why: In the laboratory, a mutated pseudoknot folds 400 times more slowly than a normal pseudoknot and unfolds five times faster.

Holmstrom was able to determine the rates of folding and unfolding using a technique known as single-molecule fluorescence resonance energy transfer (smFRET). He attached dyes that fluoresce green and red to a small piece of RNA consisting of just the pseudoknot. Then Holmstrom shined laser light on the pseudoknots, causing the green dye to fluoresce green. When the RNA folds, the two dye molecules are brought close together, which allows the green dye to transfer energy to the nearby red dye, causing it to fluoresce red. By carefully monitoring the patterns of red and green dots in a microscope, Holstrom could “watch” the pseudoknots fold and unfold, which provides information about the rates at which these processes were occurring.

The new understanding of the role of the pseudoknot in regulating telomerase activity may one day lead to improvements in two important areas of medicine: tissue regeneration and cancer treatment. For successful tissue regeneration from stem cells, medical researchers will benefit from being able to turn on and maintain telomerase activity until a new liver or pancreas is built up cell by cell. On the other hand, oncologists want to develop new drug therapies to turn off active telomerase, which is present in 85–90% of all cancerous tumors. If telomerase were disabled by drugs, cancer cells would stop dividing as soon as their chromosomes lost enough DNA to irreversibly damage their genetic code.

This work is a good example of how basic research in biophysics may lead to future medical advances.

Erik D. Holmstrom and David J. Nesbitt, *Journal of Physical Chemistry B* 118, 4053–4260 (2014).

THE MEASURE OF SMALL THINGS

Fellow Tom Perkins' group is significantly closer to realizing its long-standing dream of using atomic force microscopy (AFM) to study how membrane proteins fold and unfold. Historically, scientists have used AFM to measure the mechanical forces needed to unfold individual proteins and watch the resulting increase in their lengths. However, the limitations of AFM itself have prevented researchers from watching the unfolding process in detail.

For AFM to resolve protein unfolding in detail, three things must happen: (1) AFM must respond rapidly enough to shifts in protein conformation to detect short-lived folding-related changes, (2) its force measurements must be precise, and (3) the force measurements must be stable over time. Unfortunately, with commercial AFM cantilevers (the delicate diving-board-like structures to which the measurement tip is attached), researchers could only get one or two of these things to happen at the same time, but never all three.

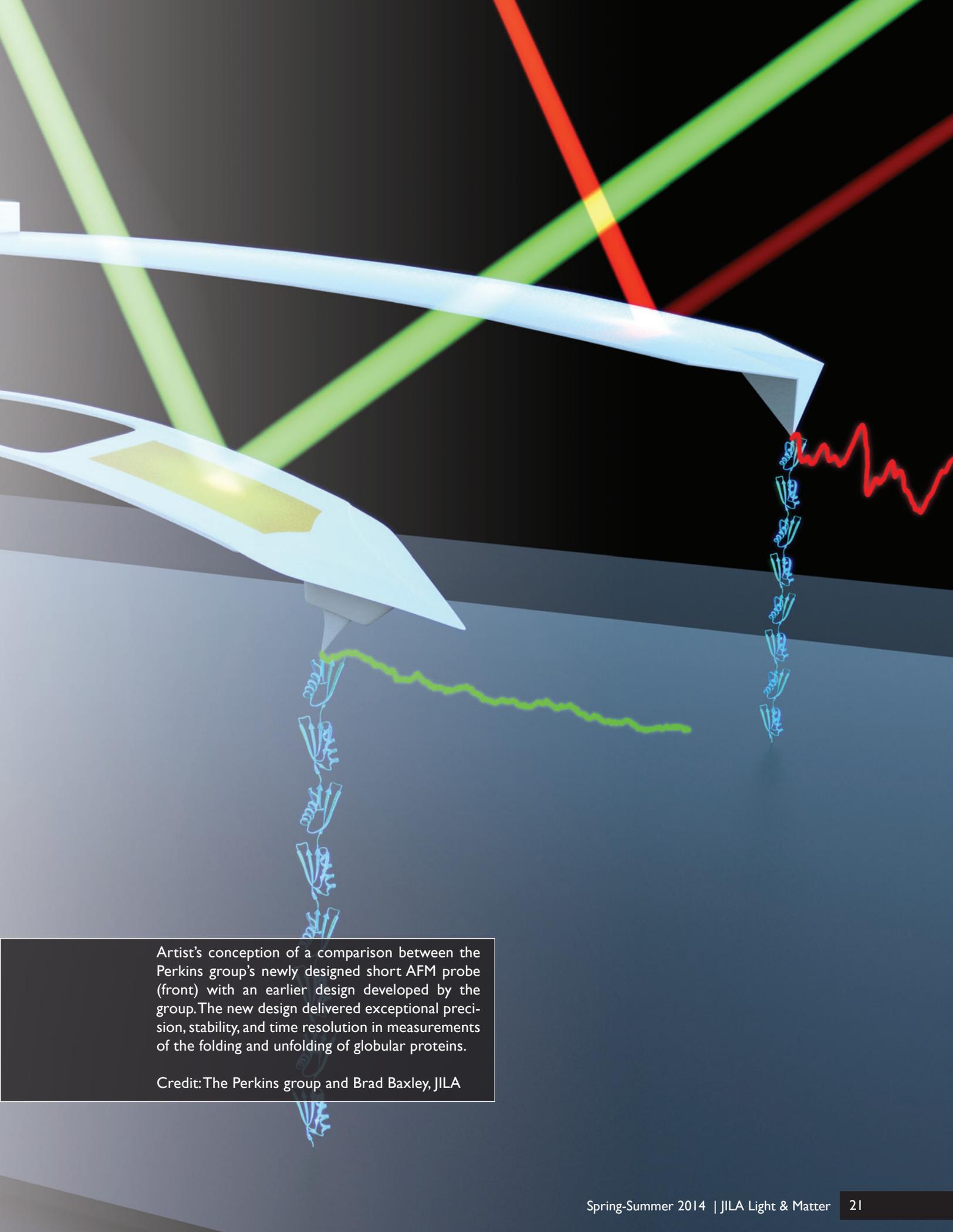
That's why the Perkins group has just spent more than five years improving AFM cantilevers and tips, which are actually attached to the protein under study. Most recently, the researchers modified a short AFM cantilever to be much less noisy and much more stable. These two changes allowed them to resolve the motion of single proteins! This long-sought capability was made possible by the merger of nanofabrication and biophysics. It was reported in *ACS Nano*.

CU undergraduate Matt Bull (now a graduate student at Stanford University) led the research effort. The goal was to make flexible, but short, cantilevers. However, like a shorter diving board, shorter cantilevers are inherently stiffer. Bull used (and improved upon) a popular nanofabrication technique to come up with a soft and short cantilever capable of making precise force measurements. And, he did this without sacrificing long-term stability or the ability to detect changes in real time.

The three key modifications of the short AFM cantilever were (1) the use of a focused-ion beam to carefully cut out a large rectangular hole at the base of the cantilever, increasing its sensitivity and responsiveness; (2) the addition of a transparent protective patch over the cantilever's gold coating, preserving the cantilever's high reflectivity; and (3) the removal of the remaining-unprotected gold coating from cantilever and the probe tip, enhancing stability. These improvements resulted in dramatically improved cantilever performance.

To show that the new cantilevers worked with real proteins, Bull and his colleagues mechanically unfolded, then studied a collection of proteins connected head to toe. The new enhanced cantilevers performed well, as shown by the green signal in the picture. The relatively noisy red signal came from the group's previous favorite cantilever. The new cantilevers were 50 times better at detecting protein motions in real time, with no loss of stability. The enhanced stability was even preserved when the researchers pulled on a protein anchored to a surface.

After years of effort, the Perkins group has an AFM setup that leads the world in force precision and force stability. It is poised to watch individual proteins fold and unfold in minutes, a feat that is a 25-fold improvement over what was possible before.



Artist's conception of a comparison between the Perkins group's newly designed short AFM probe (front) with an earlier design developed by the group. The new design delivered exceptional precision, stability, and time resolution in measurements of the folding and unfolding of globular proteins.

Credit: The Perkins group and Brad Baxley, JILA

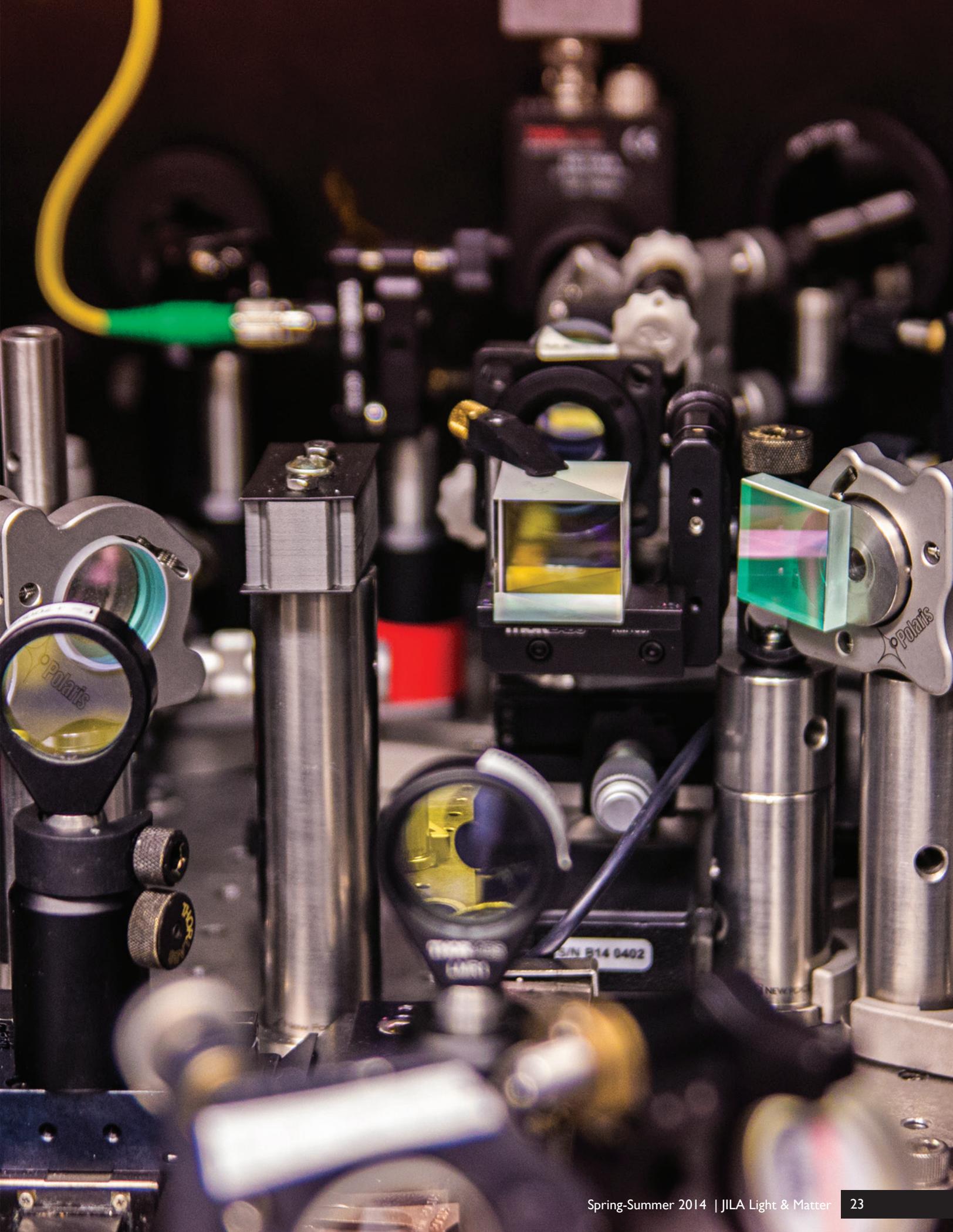
What's more, the new cantilevers are easy to make, easy to use, and relatively inexpensive. Some group members have already begun investigations of the folding and unfolding of membrane proteins with the new "home-made" AFM cantilevers. They're focusing on membrane proteins because these proteins are the targets for 50% of all drugs, making them of great interest to medical science.

Other group members continue to work on improving AFM technology to make it an even better tool for research on single biomolecules. Better instruments that can track folding and unfolding over seconds rather than minutes will allow researchers to probe deeper into the complex behavior of the molecules that make up living organisms.

Matthew S. Bull, Ruby May A. Sullan, Hongbin Li, and Thomas T. Perkins, *ACS Nano* **8**, 49844995 (2014).

Using a combination of mirrors and lenses, the Ye group shapes a pulsed near-infrared laser beam before converting it to the extreme ultraviolet (XUV) via high-order harmonic generation. The group plans to use the XUV light to study processes at attosecond timescales and probe quantum matter.

Credit: Steven Burrows, JILA



KUDOS TO...

Dana Anderson, chief technology officer and co-founder of ColdQuanta, for having ColdQuanta named as Boulder Company of the Year by the University of Colorado Technology Transfer Office.

Henry C. Kapteyn and **Margaret Murnane** for being named Inventors of the Year, CU-Boulder for their work on ultrafast lasers by the University of Colorado Technology Transfer Office.

Tom Perkins for being awarded a 2013 Arthur S. Flemming Award. This award honors outstanding Federal employees in their first 15 years of Federal service.

Cindy Regal for receiving a 2014 Cottrell Scholars Award from the Research Corporation for Science and Advancement. The Cottrell Scholar Awards are given to early career faculty members who excel at both research and teaching.

Greg Salvesen for being given the 2014 R. N. Thomas Award. The award, given to a top young scientist studying astrophysics, includes \$500.00 and a copy of the book, *Richard Nelson Thomas: nonequilibrium thermodynamical astrophysicist*, about the life of the JILA co-founder.

JILA Light & Matter is published quarterly by the Scientific Communications Office at JILA, a joint institute of the University of Colorado and the National Institute of Standards and Technology.

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