two photons become indirectly linked, with one gaining the energy the other lost.

For physicist Belita Koiller at UFRJ, Jorio's research sparked an idea. She noticed the similarity between this process (in which vibrations caused by one photon affect another) and the formation of Cooper pairs in superconductivity, when distortions in an atomic lattice, caused by a speeding electron, allow the particle to attract a partner in its wake.

In superconductors, however, the vibrations are of a fleeting kind allowed by quantum mechanics, known as virtual phonons. Koiller and her team wondered whether this was true for light as well.

First, the UFRJ team showed mathematically that if photons also interact via virtual phonons, their behaviour would be an exact match for Cooper pairs in superconductors. Then the researchers at UFMG looked for evidence of such pairs by shining pulses of laser light at room temperature through water and seven other transparent liquids. They examined the emerging photons for pairs that arrived simultaneously, in which one photon had shifted towards red (losing energy) and the other towards blue (gaining energy).

The team then applied a finer filter to let through only photons with energy shifts too small to come from classically allowed vibrations, and compared the numbers they saw with both types of filter. In both cases, they saw the same rate of photon pairs, suggesting that these had to be created by the virtual process. The signal was tiny: of around 10 quadrillion photons pumped through the material per second, they saw 10 pairs (100 times the number expected by chance).

The result has both quantum-optics physicists and condensed-matter physicists wondering how far the analogy with superconductivity can be stretched. In matter, Cooper pairs are behind a wide range of intriguing effects — but so far the team has no data to hint whether the same would be true of light. "These are very important questions we're keen to answer," says Saraiva.

If the team can boost the number of photon pairs, there could also be applications. Harnessing the way the paired photons interact with matter might reveal currently invisible properties of a material. And if the particles can be shown to correlate in ways beyond their timing — to have their quantum properties intrinsically linked — room-temperature water could prove a remarkably cheap source of 'entangled' photons, which are essential for quantum cryptography and computing.

Physicists are also wondering whether the pairs might form supercurrents, behaving similarly to their electron counterparts: perhaps light would disperse less as it travels through a material, for example, leading to more efficient quantum communication. Might paired photons even make materials more transparent? At this stage, says Saraiva, we just don't know. ■

SOURCE: REF. 1

GENE EDITING

CRISPR hacks allow for pinpoint repairs

Precision tools expand the number of 'base editors' that can manipulate individual components of DNA and RNA.

BY ELIE DOLGIN

The toolbox for editing genes expanded this week, as two research groups announced techniques that enable researchers to make targeted alterations to DNA and RNA. Unlike the original CRISPR gene-editing system — a relatively unpredictable and blunt form of molecular scissors that cut sizeable sections of DNA — the new systems rewrite individual letters, or genetic bases. The ability to alter single bases means that researchers can now attempt to correct more than half of all human genetic diseases[1,2].

The tools, developed by separate teams at the Broad Institute of MIT and Harvard in Cambridge, Massachusetts, are adaptations of the CRISPR system. Whereas most past attempts to use CRISPR-based methods to fix individual bases have been crude affairs — akin to using a machete to remove a wart — the new techniques are more like "precision chemical surgery", says David Liu, a chemical biologist at the Broad Institute who led one of the studies.

Last year, his group reported[3] the first 'base editing' method for converting one target DNA letter into another without needing to cleave the genome's double helix. It has since been used around the world to correct genes in fungi, plants, fish and mice, and even in human embryos harbouring a defective gene that can cause a blood disorder. But that base editor could achieve only two kinds of chemical conversions: a cytosine (C) into a thymine (T) or a guanine (G) into an adenine (A).

The new base editor — described in a paper published on 25 October in *Nature*[1] — works in the other direction, converting T to C or A to G. It can therefore undo the most common types of 'point mutation', which involve single aberrant bases.

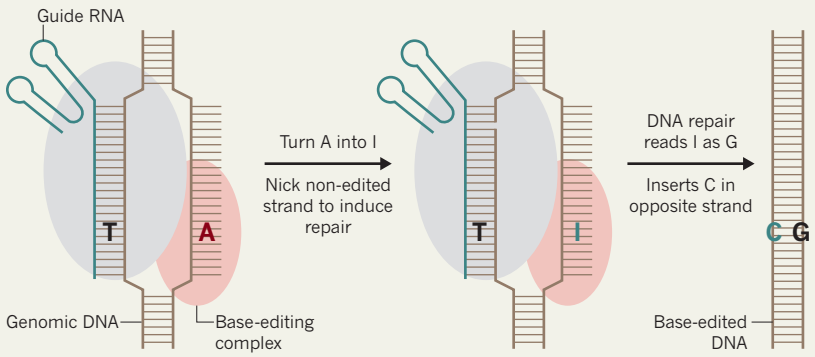
In human embryonic kidney cells and bone-cancer cells, the technique made the desired corrections with about 50% efficiency and almost no detectable by-products. By comparison, a more conventional CRISPR-based method, in which scientists insert a strand of DNA containing the desired base change, fixed the same single-base differences with less than 5% efficiency and often caused undesired insertions or deletions of large chunks of DNA.

"This is a major breakthrough in the field of genome editing," says Jin-Soo Kim, a molecular geneticist at Seoul National University.

Another method, described in a study published on 25 October in *Science*[2] and led by Broad Institute bioengineer Feng Zhang, performs a similar conversion, but for RNA instead of DNA. It turns an A into inosine (I), which is read as a G by the cell's protein-building machinery. This allows for a temporary correction of a disease-causing mutation without permanent alteration to the genome

CHANGING BASES

Researchers have devised several ways of making pinpoint changes in DNA and RNA. One technique uses a modified CRISPR–Cas9 system to edit single DNA base pairs.



— a potentially safer option when it comes to gene-fixing therapeutics, although the treatment would need to be administered repeatedly. It would also mean that researchers could alter a treatment as they gain a better understanding of the disease. "If you use RNA therapy," Zhang says, "you can upgrade."

His team's RNA editor is based on a naturally occurring enzyme that rearranges the atoms in A to resemble I instead. The researchers fused the enzyme to a disabled version of the CRISPR system — one involving an RNA-targeted enzyme called Cas13, instead of the usual DNA-binding Cas9. With the help of a sequence-specific guide RNA molecule, they successfully corrected disease-causing mutations 23–35% of the time, with low incidences of off-target activity.

In the base-editing method pioneered by Liu's team last year, the researchers engineered a naturally occurring enzyme and tethered it to a dud Cas9, which allowed them to convert C to T. But there is no equivalent enzyme found in nature for the opposite conversion in DNA. So the researchers started with an RNA-editing enzyme similar to the one Zhang's group used.

The team guided the evolution of bacterial cells through seven generations, and used some protein engineering in the lab, to produce an enzyme that would recognize and manipulate DNA. The enzyme was able to rearrange atoms in adenine to change it into an inosine, which the cell reads as a guanine. The system then tricked the cell into inserting a cytosine into the unmodified DNA strand (see 'Changing bases').

COVERING THE BASES

"It represents a heroic effort," says Dana Carroll, a genome-engineering researcher at the University of Utah in Salt Lake City, noting that the directed-evolution approach was something of a shot in the dark. "I wouldn't have had the guts to try what they did," Carroll says. "My hat's off to David Liu."

The ability to make four types of single-base conversion — A to G, G to A, C to T and T to C — "will be extremely valuable for precise therapeutic and agronomic editing", says Caixia Gao, a plant geneticist at the Chinese Academy of Sciences' Institute of Genetics and Developmental Biology in Beijing.

It could also prove useful in drug discovery and for DNA-based data storage (see *Nature* **537,** 22–24; 2016), says Marcello Maresca, a gene-editing researcher at AstraZeneca in Gothenburg, Sweden.

The development of any other base editors will require enzymes that do not occur in nature, even for conversions in RNA. But that kind of obstacle has not stopped Liu before. "We'll keep trying until the community has developed all possible base editors," he says. ■

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2. Cox, D. B. T. *et al. Science* http://dx.doi.org/10.1126/science.aaq0180 (2017).
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SPACE EXPLORATION

India gears up for second Moon mission

The Chandrayaan-2 orbiter, lander and rover signal India's lunar ambitions.

BY T. V. PADMA

In a large shed near the headquarters of the Indian Space Research Organisation (ISRO) in Bangalore, a six-wheeled rover rumbles over dark grey rubble in a landscape designed to mimic the Moon's rocky surface. This test and others scheduled for the next few weeks are crucial steps in India's quest to launch a second mission to the Moon next March.

The country's much-anticipated Chandrayaan-2 comes almost a decade after India began its first journey to the Moon, in 2008. "It is logically an extension of the Chandrayaan-1 mission," says Mylswamy Annadurai, director of the project at ISRO. The spacecraft comprises an orbiter that will travel around the Moon, a lander that will touch down in an as-yet undecided location near the Moon's south pole, and a rover.

India's maiden Moon trip was a significant achievement for its space programme, but ended prematurely when ISRO lost contact with the orbiter ten months into the planned two-year mission. However, an instrument on a probe that reached the Moon's surface did gather enough data for scientists to confirm the presence of traces of water.

Chandrayaan-2 will attempt more ambitious technical manoeuvres. For the first time, ISRO will try to steer a lunar craft to a controlled, or soft, landing. The agency has had to develop advanced systems that can guide the lander to a touchdown and successfully deploy the rover.

Lunar missions are also being planned by China, Japan and other countries. Like those efforts, India's explorations are designed to improve understanding of the Moon's environment, which would help if governments or private entities decide to establish a human settlement there. One poorly studied phenomenon is floating lunar dust. Without an atmosphere like Earth's, the surface of the Moon is buffeted by solar wind and ultraviolet radiation, creating a layer of charged ions called a plasma sheath in which dust particles can levitate.

If humans colonize the Moon, this dust will be a big challenge, says planetary scientist Penny King of the Australian National University (ANU) in Canberra. It gets into everything, from astronauts' suits to machinery and equipment, where it causes damage, she says. "Understanding how it moves around is pretty critical." ISRO says the Chandrayaan-2 orbiter and lander will carry a first-of-its-kind instrument, called the Radio Anatomy of Moon Bound Hypersensitive ionosphere and Atmosphere (RAMBHA), to measure the density of the plasma and how it changes over time.

The spacecraft's other instruments will help scientists to study other aspects of the Moon's environment and how it has evolved. Chandrayaan-2's lander will take the first thermal measurements of the lunar surface near a polar region, says Annadurai, who is also director of ISRO's Satellite Centre in Bangalore. In three to four weeks, ISRO will begin final tests to integrate all of the mission's components.

> ***"A nice part of the Indian space programme is that they manage to do things so cheaply."***

The budget for the mission is just 6.03 billion rupees (US$93 million), including the rocket and launch. Chandrayaan-2 will be carried into space on one of the agency's three-stage rockets, a Geosynchronous Satellite Launch Vehicle Mark II, taking off from a spaceport on the island of Sriharikota in the Bay of Bengal. "A nice part of the Indian space programme is that they manage to do things so cheaply," says ANU astrobiologist Charles Lineweaver. "If it succeeds, maybe everyone else will see that their mission didn't really need that extra bell or whistle." ■

Additional reporting by Nicky Phillips.