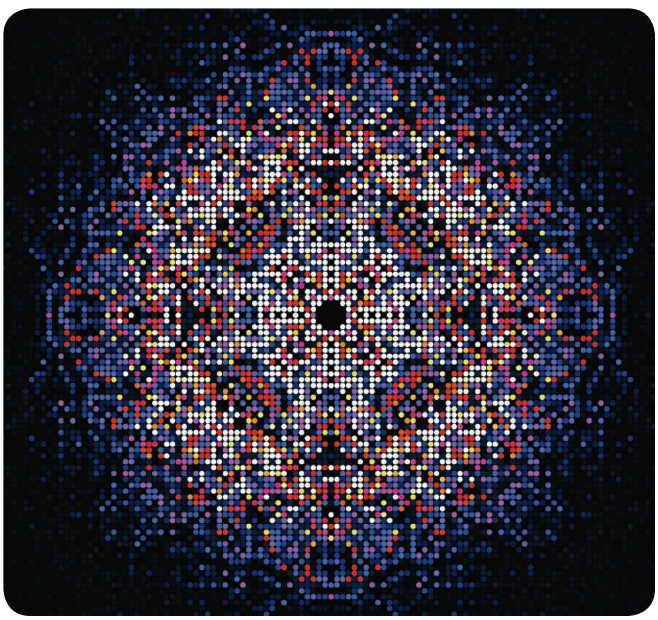
FIRST PROTEIN STRUCTURE FROM AN X-RAY LASER

One hundred years ago, physicists showed how x-rays ricocheting through a crystal could reveal the crystal's atomic-scale structure. This year, scientists pushed such "x-ray diffraction" nearly to its ultimate limit when, for the first time, they used an x-ray laser to determine the structure of a protein. The advance shows the potential of x-ray lasers to decipher proteins that conventional x-ray sources cannot.



In sum. Researchers used 178,875 individual laser pulses to generate this diffraction pattern and decipher the structure.

X-ray diffraction has long been the mainstay of structural biology. When many copies of a molecule are arranged in an orderly array called a crystal lattice, they scatter the x-rays from an incoming beam in concert. The pattern of scattering reveals the structure of the crystal, including that of the molecule. Using circular particle accelerators called synchrotrons to generate x-rays, biologists have determined tens of thousands of protein structures.

Some proteins, such as those found in cell membranes, do not readily form crystals big enough to be studied with synchrotrons, however. So, scientists hope they can probe those tough cases with new x-ray lasers, which are powered by straight-shot linear accelerators and shine a billion times brighter than synchrotron sources. In November, researchers unveiled the first protein structure revealed with such a laser.

RUNNER-UP

Working with the Linac Coherent Light Source (LCLS) at SLAC National Accelerator Laboratory in Menlo Park, California, researchers from Germany and the United States determined the structure of the inactive "precursor" form of an enzyme that's key for the survival of the single-celled parasite that causes African sleeping sickness, *Trypanosoma brucei*. To produce micrometer-sized crystals of the enzyme, they overexpressed it in cultured cells. They dropped the crystals through the beam of the LCLS, which turned on in 2009. A pulse of x-rays would obliterate a crystal even as it produced a diffraction pattern. Adding up 178,875 individual patterns, researchers determined the precursor's structure, which includes a kind of molecular safety cap that deactivates it. That information could help scientists find a drug to tie up the active form of the enzyme.

With just one new structure in the bag, it's not yet clear that x-ray free-electron lasers (XFELs) will compete with synchrotrons in structural biology. For one thing, researchers were not able to determine the structure of the enzyme de novo from the diffraction data alone, but had to use the known structure of the active enzyme as a starting point. For another, an XFEL serves far fewer users than a synchrotron does. Still, the "diffraction before destruction" approach takes a qualitative step past what synchrotrons can do. Earlier this year, researchers in Japan turned on their own XFEL, and researchers in Europe are building one that should power up in 2015.

The grand goal is to push x-ray diffraction to its ultimate limit and use an x-ray laser to decipher a protein structure by zapping individual molecules. It's not certain that can be done, but some researchers say the new result suggests that objective may not be too far out of reach.

BRAIN-MACHINE INTERFACES START TO GET A GRIP

This week researchers in Pennsylvania reported that a 53-year-old woman paralyzed from the neck down by a genetic neurodegenerative condition had learned to manipulate a robotic arm with her thoughts. Surgeons had implanted two 4×4-millimeter grids of hair-thin electrodes in her brain to capture signals from an area involved in planning hand movements. A computer translated those signals into commands to move the robotic arm, which was engineered to have nearly all the same movement capabilities as the real thing. In videos, the woman uses the arm to grasp and move various objects, removing plastic cones stacked on a base and restacking them one by one on another base, for example. The demonstrations represent the most complex movements yet performed by a paralyzed human patient using a brain-machine interface (BMI), as such sophisticated prosthetics are often called.

RUNNER-UP

By demonstrating more fluid and natural movements, this case study improves on another impressive report earlier this year. In that study—the first published demonstration that paralyzed human patients can use a BMI to execute complex movements in three dimensions—a 58-year-old woman who had been unable to speak or move her limbs for 15 years manipulated a robotic arm with her thoughts, reaching out to grasp a bottle and take a sip of coffee. A tetraplegic man, 66, also learned to touch and grasp objects.

All of this work builds on more than a decade of research with monkeys and other animals. And that work continues to advance. In 2011, researchers described a prosthetic system that provides tactile feedback by stimulating the somatosensory cortex, the brain region responsible for the perception of touch. And in April of this year, a team used signals from electrodes implanted in the motor cortex of the brain to stimulate muscles in the temporarily paralyzed arms of two monkeys, enabling the animals to pick up rubber balls and place them in a chute. Such

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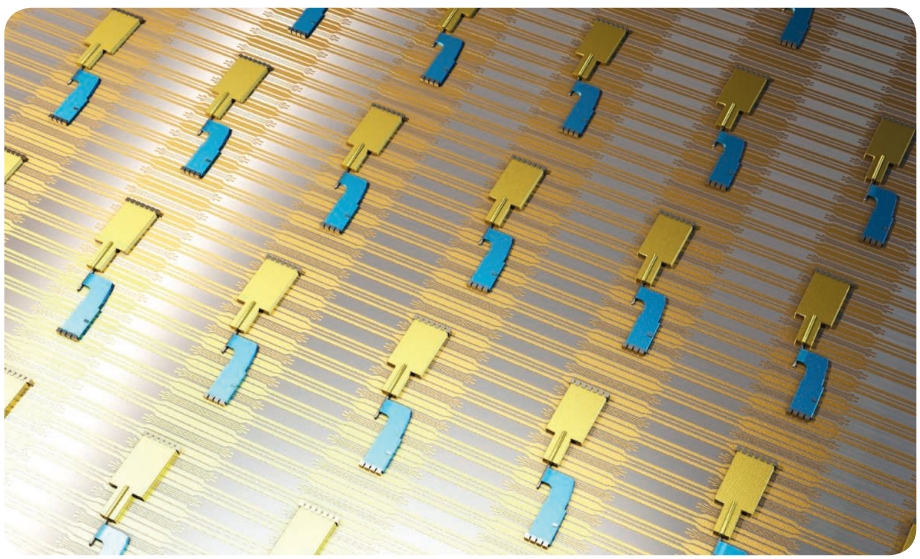
MAJORANA FERMIONS, QUASI-HERE AT LAST

Nanoscience is more than just a fashionable buzzword. It's already paid off in billions of dollars worth of products including better batteries and baseball bats. This year, researchers in the field delivered a different type of value: their first-ever likely particle discovery, known as Majorana fermions.



Particle detectors. At the heart of each device in this array is an indium antimonide nanowire, one end is gold-coated and the other is a superconductor (blue). Majorana fermions are produced at the ends of the nanowires.

Speculation about the existence of Majorana particles dates back more than 7 decades, when a young Italian physicist named Ettore Majorana crunched some equations in the emerging field of quantum mechanics. His mathematics united the quantum understanding of fermions, particles such as electrons that show a type of angular momentum known as spin, with Albert Einstein's equations of relativity that impact particles traveling near the speed of light. Majorana's insights implied the existence of a new type of fermion that could act as their own antimatter and annihilate themselves.

Physicists have long suspected that neutrinos are Majorana fermions. Thus far, they've been unable to nail down the case. And prospects for finding other Majorana fermions long seemed remote. But a few years ago, theorists suggested that the collective motion of electrons in nanoscale wires adjacent to a superconductor may form "quasiparticles" that for all intents and purposes behave as if they were a fundamental Majorana particle themselves. The race was on. This year, a team of physicists and chemists in the Netherlands crossed the line showing compelling evidence that the Majorana quasiparticles exist.

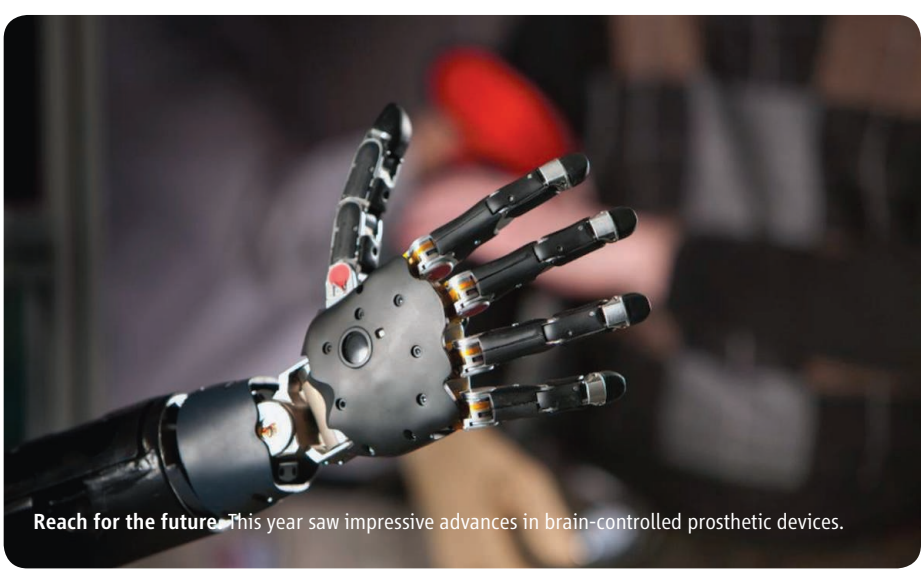
RUNNER-UP

The discovery has already prompted efforts to use the new particles to build a stable quantum computer. Such computers operate on quantum bits, or qubits. Unlike regular bits of digital information represented as 0s and 1s in calculations, qubits can be virtually any combination of a 0 and 1—say, 57% 0 and 43% 1, or 12% 0 and 88% 1. As a result, quantum computers have the potential to store and process information in ways that conventional digital machines can't hope to match. For some types of calculations, crunching just 300 qubits could generate an answer that today's best supercomputers would struggle to solve.

However, current qubit technology is far too fussy for practical computing. The slightest bump in temperature or other outside influence typically wipes out the information stored in a standard qubit. Theoretical calculations show that Majorana fermions should be able to "remember" their quantum state even when buffeted by outside forces. So now the Dutch team and others are hot on the trail to see whether that is the case. If it is, nanoscience may soon be able to add to its bragging rights.

findings hint at the tantalizing possibility that it may one day be possible to reanimate paralyzed limbs in people.

As hopeful as these developments are, it will be years before large numbers of people can benefit from BMIs. The robotic arms are experimental and extraordinarily expensive, and patients use them only in the lab, aided by a team of technicians. And the movements enabled by BMIs aren't nearly as fast and graceful as the movements made by uninjured individuals. Advances in the algorithms that decode neural signals and convert them into commands a computer or prosthetic limb can understand should help with that. Progress in that area continues apace, but for hundreds of thousands of patients paralyzed by strokes, spinal injuries, and other conditions, it can't come quickly enough.



Reach for the future. This year saw impressive advances in brain-controlled prosthetic devices.

CREDITS (TOP TO BOTTOM): TU DELFT 2012; THE JOHNS HOPKINS UNIVERSITY APPLIED PHYSICS LABORATORY (JHU/APL)

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