in the United States. But there are signs\(^1\) that the vaccines tend to stimulate the production of neutralizing antibodies that best recognize not Omicron, but the ancestral virus on which the first vaccines were based. A second dose of the boosters might be needed to generate high levels of Omicron-specific neutralizing antibodies, says Cao.

Fortunately, all evidence suggests that COVID-19 vaccines old and new remain highly effective at preventing severe disease, which Nuzzo argues should be the main goal of booster programmes. This means concentrating booster campaigns on those at the highest risk of severe disease, including older people and people with underlying health conditions, who will benefit the most from the added protection. “We need a laser focus on protection against severe illness,” she says.

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**PHYSICS NOBEL FOR ‘SPOOKY’ QUANTUM ENTANGLEMENT**

Award goes to three physicists whose research laid the groundwork for quantum information science.

By Davide Castelvecchi & Elizabeth Gibney

Three quantum physicists have won the 2022 Nobel Prize in Physics for their experiments with entangled photons, in which particles of light become inextricably linked. Such experiments have laid the foundations for an abundance of quantum technologies, including quantum computers and communications.

Alain Aspect, John Clauser and Anton Zeilinger will each share one-third of the 10-million-Swedish-kronor (US$915,000) prize.

“I was actually very surprised to get the call,” said Zeilinger, a physicist at the University of Vienna, at the press conference announcing the award. “This prize would not be possible without the work of more than 100 young people over the years.”

Aspect, a physicist at the University of Paris-Saclay, received the call during a committee meeting. “I happened to be sitting near Aspect this morning when he got the call,” says Serge Haroche, an experimental physicist at the Collège de France in Paris who won a share of the 2012 Nobel Prize in Physics for work in quantum physics. When he left the room, Haroche added, Aspect’s colleagues guessed correctly that it was the Royal Swedish Academy of Sciences in Stockholm calling.

The trio’s experiments proved that connections between quantum particles were not down to local ‘hidden variables’, unknown factors that invisibly tie the particles’ outcomes together. Instead, the phenomenon comes from a genuine association in which manipulating one quantum object affects another far away. German physicist Albert Einstein famously called the phenomenon ‘spooky action at a distance’ – it is now known as quantum entanglement.

All three winners are pioneers in the fields of quantum information and quantum communications, says Pan Jianwei, a physicist at the University of Oxford, UK. The modern versions of the experiments pioneered by the three winners, she says, could be central to one of the great open questions of physics today – how to reconcile quantum mechanics with Albert Einstein’s general theory of relativity.

**Particle pairs**

Because of the effects of quantum entanglement, measuring the property of one particle in an entangled pair immediately affects the results of measurements on the other. This is what enables quantum computers to function. The machines, which seek to harness quantum particles’ ability to exist in more than one state at once, carry out calculations that would be impossible on a conventional computer. Today, physicists are using entanglement to develop quantum encryption and a quantum internet that would allow for ultrasafe communications and new kinds of sensors and telescopes.

But whether particles could be fundamentally linked in this way – such that measuring one determines the properties of another, rather than just revealing a predetermined state – had been a topic of debate since physicists laid the foundations of quantum mechanics in the 1920s.

In the 1960s, physicist John Bell proposed a mathematical test known as Bell’s inequality. This said that experimental results that seemed to be correlated beyond a particular value would be possible only through quantum entanglement, rather than being due to certain kinds of hidden variable. Quantum mechanics predicts a higher degree of correlation than would be possible in classical, or pre-quantum, physics.

In 1972, Clauser – now a physicist at J.F. Clauser & Associates in Walnut Creek, California – and his colleagues developed these ideas into a practical experiment that violated the Bell inequality, supporting the theories of quantum mechanics.

David Kaiser, a quantum physicist and historian of science at the Massachusetts Institute of Technology in Cambridge, says...
that Clauser had come across Bell’s work by chance while browsing in the library at Columbia University in New York City, where he was a PhD student. Clauser was captivated, and wrote to Bell to ask him whether anyone had tried testing his inequality experimentally. Bell replied that no one had – and encouraged him to do so. The reaction from the rest of the community wasn’t so warm, however. “People would say, in writing, that this isn’t real physics – that the topic isn’t worthy,” says Kaiser.

**Loopholes and teleportation**

Despite Clauser’s success, experimental loopholes remained that left room for hidden variables to create the illusion of quantum entanglement. It was these loopholes that Aspect set out to close in the 1980s. His experiments used a changing set-up that meant that experimental decisions could not be said to be predetermining the results.

And in 1997, Zeilinger and his colleagues at the University of Vienna used the phenomenon of entanglement to demonstrate quantum teleportation, in which a quantum state gets transmitted from one location to another. Quantum systems cannot be detected and reconstituted somewhere else, because measurement destroys their delicate quantum properties. But a state can be transferred between two particles at a distance, if each is entangled with half of a previously entangled pair.

Teleportation allows for supersecure communications, because any eavesdropping would cause particles to lose their delicate quantum states. It might also enable future quantum computers to transfer information. Since Zeilinger’s initial experiments, physicists have succeeded in teleporting electrons, as well as atoms and superconducting circuits.

In more recent experiments, Zeilinger, together with Kaiser and other collaborators, has sought to seal further loopholes in tests of Bell’s inequality by using properties of starlight emitted billions of years ago to define experimental settings.

Although the physics is now the basis of a budding industry, these kinds of experiment could continue to provide insights into fundamental physics. One hope, says Marletto, is that they will show whether two particles can become entangled through a gravitational interaction. General relativity is apparently incompatible with quantum mechanics, and such experiments could provide hints on how to develop a quantum theory of gravity to replace it. “Gravity is the elephant in the room,” says Marletto.

Zeilinger “often anticipated the strangest and most counter-intuitive phenomena” in quantum physics, says Gabriela Barreto Lemos, a physicist at the Federal University of Rio de Janeiro in Brazil, who warmly recalls her time as a postdoctoral researcher in Zeilinger’s lab. “Whenever we presented him with new ideas, he would challenge us to go further, think more outside the box, be more imaginative,” she says.

Kaiser credits the three Nobel recipients with having had the persistence and ingenuity to probe what seem like “fantastical phenomena, and to ask: ‘Can the world really work like this?’”

“At the time, it was just blue-sky research, with no applications in view,” says Haroche. “It’s a wonderful example of the connection between basic science and application,” he adds. “A demonstration of the usefulness of useless knowledge.”

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**CHEMISTS WHO INVENTED REVOLUTIONARY ‘CLICK’ REACTIONS WIN NOBEL**

Researchers honoured for game-changing chemistry, including reactions that can be run in living cells.

By Davide Castelvecchi & Heidi Ledford

Three chemists who pioneered a useful technique called click chemistry to join molecules together efficiently have won this year’s Nobel Prize in Chemistry.

Barry Sharpless at Scripps Research in La Jolla, California, and Morten Meldal at the University of Copenhagen laid the foundations for click chemistry, and both independently discovered a pivotal reaction that could link two molecules—an azide and an alkyne—with relative ease. This reaction has been used to develop a host of molecules, including plastics and potential pharmaceuticals.

The third winner, Carolyn Bertozzi at Stanford University in California, used click chemistry to map the complex sugar-based polymers called glycans found on the surface of living cells without disturbing cell function. To do this, she developed processes called bioorthogonal reactions, which are now being used to aid the development of cancer drugs.

Speaking by telephone during last week’s Stockholm press conference, Bertozzi said she had been “absolutely stunned” by the early-morning call telling her she had won.

Click chemistry has been applied to DNA-sequencing technologies and materials science, and has aided basic research into cell function and the discovery of biomolecules.

But that’s only the beginning, Bertozzi told reporters. “I think the field of click chemistry is still in its early stages,” she said during the prize announcement. “There’s probably many new reactions to be discovered.” The value of the technique is its simplicity, she added: it is highly efficient and produces relatively little waste.

“In Carolyn Bertozzi’s, Barry Sharpless’s and my groups we changed some concepts in chemistry which allow you to do things that were never possible before,” Meldal tells Nature.

This is a second Nobel prize for Sharpless, who won a share of the chemistry Nobel in 2001 for developing catalysts based on chiral molecules—those with non-superimposable mirror images. The same year, Sharpless co-wrote a review for the journal Angewandte Chemie in which he argued that chemistry needed to move towards simpler reactions, with fewer unwanted by-products. “Just a handful of good reactions are needed to assemble vast numbers of highly diverse organic molecules,” he and his co-authors wrote.

**Downhill reactions**

The authors envisioned a way to design pairs of molecules that react only with each other, and in an irreversible way. This means that they form a strong, covalent bond, in contrast to the selective but weaker lock-and-key interactions typical of many biomolecules, says Per-Ola Norrby, a computational chemist at the pharmaceutical company AstraZeneca in Gothenburg, Sweden, who worked in Sharpless’s group in the 1990s. A click reaction “is so much downhill in terms of energy, that it never goes back”, he adds. Such reactions should also occur in mild solvents, such as water, and produce only harmless by-products.

“It’s extremely difficult to do one kind of chemistry in the presence of another kind,” says Meldal. “We did something which is