

Method for controlling brain cells with light wins Nobel

Karl Deisseroth, Peter Hegemann, and Georg Nagel honored for developing optogenetics

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The winners of this year’s Nobel Prize in Physiology or Medicine are announced at a press conference this morning. JONATHAN NACKSTRAND/AFP VIA GETTY IMAGES

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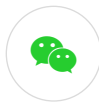
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The creators of a powerful way to control key brain cells with light, which has clarified nerve circuits in healthy and diseased brains, have been honored with this year’s Nobel Prize in Physiology or Medicine. The method, known as optogenetics, has recently been adapted to help a few blind people regain modest sensitivity to light and is also [being tested as a treatment for epilepsy, pain](#), and



more.

Karl Deisseroth of the Howard Hughes Medical Institute and Stanford University, Peter Hegemann of the Humboldt University of Berlin, and Georg Nagel of the Julius Maximilian University of Würzburg received the award “for their discoveries concerning light-gated ion channels and optogenetics,” the Nobel Assembly at Karolinska Institute [said in a press release](#) this morning.

“This is amazing news,” says Michael Häusser, a neuroscientist at University College London. “I think it’s a fantastic recognition of a transformative discovery that has changed the way we do neuroscience and also promises to change the way we treat diseases in the brain.”

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In an interview with *Science*, Deisseroth said he had just gone to bed when he got the news—he had to call the Nobel Committee back. “I was in a dreamlike state and I heard the buzzing but I couldn’t connect in time,” he says. He says he’s spent the day emailing colleagues, including Hegemann and Nagel, with whom he has collaborated. “I really look forward to a more relaxed discussion with them and maybe having a beer together.”

Before the development of optogenetics, scientists studying the brain’s circuitry largely relied on observational studies in which they linked particular patterns of neuronal activity to an animal’s behavior or destroyed brain areas and documented the fallout. But to properly establish cause and effect, “neuroscientists dreamed of a neuronal switch, a tool to turn specific neurons on or off with great precision,” neuroscientist Abdel El Manira, a member of the Nobel Committee, explained at the press conference today.

Hegemann and Nagel paved the way for the creation of such a switch. In the 2000s, the pair discovered that a [protein on the single-celled alga *Chlamydomonas responds to light*](#). Under a blue light, a channel on the protein opens, allowing charged ions into the cells. They called the protein channelrhodopsin. Optogenetics “emerged from this obscure corner of biology,” Häusser says. “I think it’s a beautiful story, because it illustrates that really fundamental science can provide the keys for new approaches that can be used to treat disease.”

Deisseroth subsequently introduced the gene for channelrhodopsin into cultured rat neurons, and then later in living mice, creating a light-activated switch that produces a nerve signal. “When they illuminated the neurons with light, the result was remarkable: The neurons reacted on command, instantaneously, with millisecond precision,” El Manira said. “Those papers were absolutely mind blowing,” says Doris Tsao, an optogenetics researcher who recently joined the nonprofit research foundation Astera as its chief scientist for “neuro.” “It was just unbelievable, the level of control.”

Optogenetics has allowed researchers to activate specific types of neurons in living animals and trace out brain circuits involved in forming memories, producing pain, responding to rewards, and many other aspects of cognition and behavior. In addition to engineering mice that produce the channelrhodopsin protein in specific types of brain cells, researchers can also make cells light



responsive by directly injecting the rhodopsin gene or delivering it via viruses that only infect certain cell types. Optical fibers embedded in the brain transmit light to specific neurons or brain regions.

Previous neuron-activating techniques that relied on electrical stimulation are often described as “playing a piano with a mallet,” says neuroscientist Andrew Jackson of Newcastle University. “You got what you wanted, but you hit the surrounding notes as well.” Optogenetics “has completely revolutionized how we probe neural circuits in neuroscience,” Häusser says.

Desseroth considers the most exciting thing that has come out of the technology to be the ability to deconstruct brain states such as emotions or behaviors into their basic building blocks: cells and the processes that connect them.

“Identifying how those components can be broken apart and put back together was pretty exciting,” he says. “To have the parts be exchangeable and fungible is actually a fundamental way in which species can adapt and individuals can adapt to their environment.”

Deisseroth, who is a psychiatrist and performs clinical research, says he is especially excited about the indirect applications of optogenetics, such as identifying the cells underlying the symptoms of disorders and designing medications based on these precise pathways.

Although optogenetics has mostly been used to conduct basic brain research, “the field is very slowly starting to live up to its promises in medicine,” says Ulrich Schwarz, a biophysicist at Heidelberg University. In 2021, for instance, the technique was used to [restore some vision](#) to a blind man who, because of a condition called retinitis pigmentosa, had lost the cells in his retina that transform light into electrical signals. To compensate for his absence of photoreceptor cells, researchers introduced a gene into his eye that caused the ganglion cells—which normally transmit visual information from the photoreceptors to the brain—to produce a channelrhodopsin protein.

With the help of the newly light-responsive cells and light-amplifying goggles, he was able to make out objects. There are now five or six companies developing optogenetic therapies for retinitis pigmentosa, notes Toshihide Kurihara, an ophthalmologist and cell biologist at Keio University who is leading a clinical trial on one approach. He predicts that treatments might reach the clinic “very soon, in less than 5 years.”

Optogenetic studies of lab animals have also helped researchers [understand the brain circuits stimulated by deep-brain stimulation](#) (DBS) implants used to treat Parkinson’s disease. “What people now think about a lot is how we can refine or reinvent DBS with all the knowledge we have” from that work, says Christian Lüscher, a neurobiologist at Geneva University. The same could be true for understanding and treating circuits that drive conditions such as obsessive-compulsive disorder or addiction.

The ability to manipulate neural circuits via optogenetics at least partly drove the advancement of other neuroscience technologies, such as viruses that can deliver genes to certain types of cells but not others. “It caused people to really think about other ways to express useful molecules within neurons,” Jackson says. “There are fields now of chemogenetics where instead of expressing light-activated proteins, you express receptors that are activated by designer drugs, or sonogenetics, where people are working on trying to develop ion channels that



will be activated by ultrasound,” he says. Either approach may be more practical for human use than delivering light deep within the brain.

As is often the case with Nobel Prizes, several researchers who made important contributions to optogenetics were left out of today’s awards, including Edward Boyden of the Massachusetts Institute of Technology, who as a Ph.D student was first author on a key paper with Deisseroth and did further pioneering work. The prize can only be awarded to three people at once, and can only be given to living scientists. Dieter Oesterhelt, Hegemann’s Ph.D. supervisor who died in 2022, and Gero Miesenböck, a neuroscientist from the University of Oxford, also could have been honored, some in the field say. In 2005, 2 years before Deisseroth published his work in mice, Miesenböck’s team showed it could [control fruit fly behavior](#) with light after adding a different kind of ion channel to its neurons.

In 2013, Miesenböck shared [the Brain Prize](#) with the three new Nobel laureates, Boyden and another scientist for contributions to optogenetics. Miesenböck says “it was hard” to learn this morning he had not been included in the Nobel Prize. The committee took “the narrowest possible view of optogenetics,” he says. “The intellectual history does not begin with rhodopsin.” Nevertheless, Miesenböck says he extends “heartfelt congratulations” to today’s winners.

With reporting from [Kai Kupferschmidt](#), [Ailie McWhinnie](#), and [Dennis Normile](#). Updated at 4:40 p.m.

Correction, 5 October, 7:15 p.m.: Due to an editing mistake, this story originally said Dieter Oesterhelt had shared in the Brain Prize.

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ABOUT THE AUTHOR



Matthew Warren [✕](#)

Editor

Matthew Warren is the international news editor of *Science*.



Gretchen Vogel [✉](#) [✕](#)

Author

Gretchen Vogel is a contributing correspondent for *Science* magazine based in Berlin, Germany.



Sara Reardon [✉](#)

Author

Sara Reardon is a staff writer based in Boston, where she covers biomedical research and policy. She can be found on Signal at [sara_reardon.59](#)

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