How does Stanford's Nobel winner illuminate dark cells, revealing life and death?

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Molecules are busy actors on the cellular stage, gathering and dancing to create life and trigger death. But they had been too tiny to see in action, a frustrating scientific impasse - until three scientists, including Stanford University's William E. Moerner, found techniques to peer deeply into cells, inventions that on Wednesday were honored with the Nobel Prize in Chemistry.

The trio shared the $1.1 million prize for getting molecules to glow on demand, illuminating the inner workings of a cell with a light source far brighter than ever before.

It is the third year in a row that a Stanford University researcher has been awarded the Nobel Prize in Chemistry, science's highest honor. Michael Levitt won in 2013, and Brian Kobilka won in 2012.

"It's like using little beacons of flashlights," Moerner said in a telephone news conference from a meeting on the coast of Brazil. He shares the prize with Eric Betzig of Virginia and Stephen Hell of Germany.

"We can now more deeply understand what is going on in cells, whether they're live or sick," the Stanford chemistry professor said.

The techniques they invented make it possible, for instance, to view the toxic protein accumulations in brain cells of patients with deadly Alzheimer's and Huntington's diseases. They can also study how biomolecules - such as DNA and enzymes - work in cells to carry out the processes that are critical to life.

Before the three men threw new light onto minute cellular activity, scientists thought it impossible to view a single living molecule. Experiments had to use ensembles of millions, even billions, of molecules.

Other tools, such as electron microscopes, can see deeply inside a cell, but individual molecules are tough to discern. And the electron beam kills cells, so living interactions can't be observed.

Moerner first detected a single molecule inside a cell in the 1980s while working at IBM Almaden Research Center in San Jose. Techniques improved as he worked with different teams at different labs - so more insights could be gleaned about the tiny but mighty clusters of atoms.

"It was a new surprise: Molecules were jumping around and moving away from observable light!" he said. "We also saw blinking and molecules switching on and off."

The history of science, noted Stanford provost John Etchemendy, progresses through "increasing ability to see and detect things at smaller and smaller sizes" under microscopes "or further and further distance from humans" via telescopes. He credited Moerner with making major contributions to enable researchers to examine molecules "at the smallest scale."

"We could not be more proud to have him on our faculty," Etchemendy said.

Moerner heard the news of his prize while stepping out of the shower in Recife, Brazil, via a 7 a.m. phone call from his wife.

"My heart was racing - can this be true? - that feeling when you're surprised by something truly wonderful," Moerner said later in the morning.

Moerner, 61, whose name rhymes with "Werner," was born in Pleasanton's Parks Air Force Base, now Camp Parks. From birth, his family called him by his initials W.E. to distinguish him from his father and grandfather, also named William. He grew up in Texas and now lives in Los Altos with his wife Sharon, a teacher, and his son Daniel, a student at Yale University. He is a ham radio enthusiast and sings in a campus group.

He fondly recalled his early days at San Jose's IBM "when you could be famous for both your science and your technology." So while he worked on specific optical storage schemes, he was also free to study the fundamental science that underlies molecular behavior.

The multidisciplinary approach drew him to Stanford, he said. "We have electrical engineers, biophysicists and chemists all in one group," he said, clustered in labs near the School of Medicine.

Moerner worked on his discovery independently of the other winners: Betzig works at Howard Hughes Medical Institute in Ashburn, Va., and Hell is director of the Max Planck Institute for Biophysical Chemistry in Germany.

In its award to the three men, the Nobel award recognized two separate but related approaches. One enables stimulated emission depletion microscopy, developed by Hell in 2000. It uses two laser beams, one to stimulate fluorescent molecules to glow, another to cancel out all fluorescence except for that in a nanometer-size volume. Scanning over the sample, nanometer by nanometer, yields a high-resolution image.

Betzig and Moerner laid the foundation for the second method, single-molecule microscopy. They attach a fluorescent green protein to the cell, which "labels" it and illuminates the individual molecules. Scientists image the same area repeatedly, letting just a few molecules glow each time. Superimposing these images yields a dense super-image with nanolevel resolution.

Together, these techniques launched the field known as nanoscopy, allowing scientists to visualize the pathways of single molecules inside living cells. That has scientists optimistic about the potential to accelerate research into some of our most confounding diseases.

"It is too early to make a lot of claims about specific diseases," said Moerner. "But we are extracting as much information as possible from each single molecule."

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