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Without Test Tubes, 3 Win Nobel in Chemistry

By KENNETH CHANG

Chemistry, meet computer science.

This year's Nobel Prize in Chemistry was awarded to three researchers for work that did not involve test tubes or lab coats. Instead, they explored the world of molecules virtually, with computers. Such numerical simulations enable the closer study of complex reactions like photosynthesis and combustion, as well as the design of new drugs.

Martin Karplus, 83, of the University of Strasbourg in France and Harvard University; Michael Levitt, 66, of Stanford University; and Arieh Warshel, 72, of the University of Southern California, share the honor and the approximately $1.2 million that accompanies it. Their computer programs use the classical laws of motion dating from Newton to track the movement of a multitude of atoms, and quantum physics to describe the breaking and forming of chemical bonds.

All three winners are naturalized American citizens. Dr. Karplus, born in Austria, is also an Austrian citizen. Dr. Levitt, born in South Africa, also holds British and Israeli citizenships, and Dr. Warshel, born in Israel, is also an Israeli citizen.

The Royal Swedish Academy of Sciences in Stockholm, which awards the prize, cited the three "for the development of multiscale models for complex chemical systems." As a news release explained it, "Chemists used to create models of molecules using plastic balls and sticks," but "today the modeling is carried out in computers," thanks in part to work done in the 1970s by the three new laureates.

Their work has long been supported by federal science grants, said Francis S. Collins, director of the National Institutes of Health, which has had to send home most of its scientists because of the government shutdown. Noting that Monday's winners of the Nobel Prize in Physiology or Medicine were also underwritten by the N.I.H., Dr. Collins said in an e-mail to a reporter on Wednesday, "The irony continues."

For Dr. Levitt, the unexpected phone call from Stockholm came at 2:15 in the morning. "It was an enormous shock," he said, admitting that he had checked various Nobel predictions on the Internet. "You will not find my name on any of them. I'm not sure it was a good thing or a bad thing."

With committee members he knew personally informing him that he had won, Dr. Levitt realized it was not a hoax.

“One of the members I promised to send a review to maybe a couple of years ago, but I haven’t done it yet,” Dr. Levitt said. “He said, ‘We haven’t gotten your review yet, but we’re still going to give you the prize.’ ”

Dr. Levitt then called his 98-year-old mother in London and told her to turn on the computer and watch the news conference on the Web. She asked him to spell the Web site — nobelprize.org. Dr. Levitt told her, “Just Google ‘Nobel Prize,’ and it’ll be the first hit.”

In the laboratory, experimental chemists can readily tell the beginning chemical ingredients and the final products. But the actual reactions usually occur very quickly. “It’s like seeing all the actors before Hamlet,” said Sven Lidin, chairman of the Nobel selection committee, during the prize announcement webcast on Wednesday, “and all the dead bodies after, and then you wonder what happened in the middle. And actually there is some interesting action there, and this is what theoretical chemistry provides us with — the whole drama.”

But in the 1960s, when a computer filled a room, computer programs had to be crammed into small slices of memory, limiting what could be done. At the Weizmann Institute of Science in Israel, Dr. Warshel, who was then a doctoral student, and Dr. Levitt, who worked with Dr. Warshel as a computer programmer, calculated the behavior of molecules, even very large biological molecules, although that early work used Newtonian physics and not quantum effects.

Meanwhile, at Harvard, Dr. Karplus’s research group developed computer programs that simulated chemical reactions and employed the full power of quantum physics, which looks at physical reactions at the microscopic level. After completing his doctorate, Dr. Warshel joined Dr. Karplus’s laboratory as a postdoctoral researcher, and in 1972, they published a paper that combined quantum and classical physics in describing the chemical behavior of certain molecules.

Later, Dr. Warshel renewed his collaboration with Dr. Levitt, who had completed his doctorate at the University of Cambridge in England, expanding their programs to tackle enzymes, which are proteins that govern chemical reactions in living organisms. From bouncing X-rays off proteins, chemists knew the shapes of some enzymes, but less about their functions.

“It’s like seeing a watch and wondering how it actually works,” Dr. Warshel said. “So in short, what we developed is a way, which required a computer, to take the structure of a protein and then to eventually understand how exactly it does what it does.”

They found that they could not understand the behavior of the enzyme without including the effects of the surrounding molecules — water, in particular. “This was really, in my view, the conceptual breakthrough,” Dr. Warshel said. “I realized that everything you want to do with

computers could be done if you make it simple enough. We wrote in a way that did not require too much memory."

Experimental scientists were slow to accept the new work, Dr. Warshel said. "When you do something on computer, it's very easy to dismiss it and say you made it up," he said. He said the experimentalists were happy when the calculations agreed with the experiments, but not when Dr. Warshel claimed to be describing phenomena not seen in the experiments.

"The last thing people want is that you will come and explain their system," he said. "I never succeeded to convince anyone. I just made them angry."

Today, Dr. Lidin of the Nobel committee said, computer simulations have become as informative as the experiments. "You still have to do the experiment," he said. "But the predictions that theory make are becoming so much powerful these days that we can perhaps save 90 percent of the experimenting and concentrate on the 10 percent where we know that the most important results will lie."

Lawrence K. Altman contributed reporting.