CHEMISTRY NOBEL GOES VIRTUAL

Pioneering theorists in computational chemistry given their due

Theoretical chemist John A. Pople was breakfasting with his family at a Houston hotel when the call came. Meanwhile, it was 5 AM in Santa Barbara, Calif., and physicist Walter Kohn's phone was also ringing.

"My initial thought was that something terrible had happened. If you get a call at 5 AM, you worry," Kohn says. "My wife picked up the phone, and when I saw the expression on her face, then I was sure that something terrible had happened. But it turned out fortunately otherwise."

The "fortunately otherwise" was that Kohn, a physicist at the University of California, Santa Barbara, and Pople, chemistry professor at Northwestern University, Evanston, Ill., had together won the 1998 Nobel Prize in Chemistry.

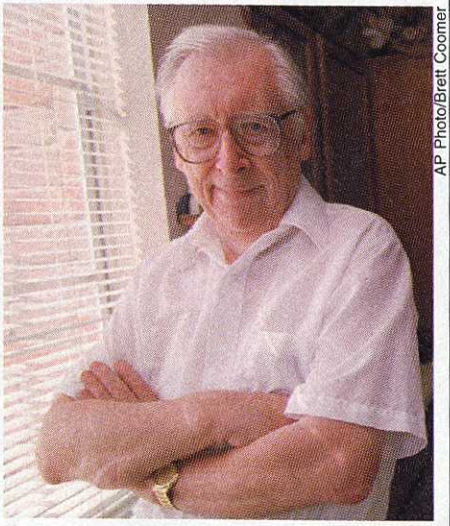
The Swedish Academy of Sciences is bestowing the world's highest scientific honor on Pople for developing much of the quantum chemical methodology used today—notably, his creation of the original and widely used Gaussian molecular modeling programs—and on Kohn for developing density functional theory—a theoretical tool that enables chemists to model complicated molecular systems.

Both winners say they have no idea yet how they'll spend nearly $1 million in prize money, which they will split.

Theoretical chemists say they're delighted to see their field get such recognition. During the past decade, the discipline has burst into the mainstream, and chemists across the board now routinely use computational chemistry to help predict and explain chemical behavior—thanks in large part to the groundwork laid by Kohn and Pople in the late 1960s and early 1970s.

"We [quantum chemists] are all very happy about this prize," says Robert G. Parr, chemistry professor emeritus at the University of North Carolina, Chapel Hill. Parr, along with Pople, is one of the developers of the well-known Pariser-Parr-Pople model of π electrons in conjugated and aromatic systems.

"Pople and Kohn are really pioneers of different aspects of theoretical chemistry," adds Gregory A. Voth, chemistry professor and director of the Henry Eyring Center for Theoretical Chemistry at the University of Utah, Salt Lake City. "They set the foundations for the way things are occurring today—they are really very deserving."


AP Photo/Brett Coomer

Pople

Kohn was born in Vienna, Austria, in 1923. After Austria was annexed by Nazi Germany in 1938, Kohn, who is Jewish, fled with his sister to England. His parents died in concentration camps. He then came to the U.S. and earned a Ph.D. in physics from Harvard University.

Pople, born in 1925 in Burnham-on-Sea in Somerset, England, is still a British citizen. He received a Ph.D. degree in mathematics at the University of Cambridge in 1951, and spent a decade in England as a researcher and lecturer.

Coincidentally, Pople and Kohn narrowly brushed shoulders during their early careers. Kohn was a professor at Carnegie Institute of Technology (now Carnegie Mellon University) in Pittsburgh from 1950 to 1960. Pople arrived there around the time Kohn was leaving. "I was in the physics department, and he was in chemistry; so we just barely knew each other," Kohn recalls.

The two pursued their separate interests for several decades. Kohn was professor of physics at the University of California, San Diego, until 1979. He then moved to Santa Barbara, and until 1984, directed the Institute of Theoretical Physics at UCSB, where he still works. Pople remained at Carnegie Mellon until 1986, when he moved to Northwestern, where he is still professor of chemistry.

In the late 1960s and early '70s, Pople harnessed the newfound power of computer technology to perform the complex mathematical operations of quantum chemistry. In 1970, he introduced Gaussian 70, a computational chemistry program that quickly became the mainstay of theoretical chemists. Now managed and marketed by Gaussian Inc., in Pittsburgh, Gaussian programs continue to evolve: The latest version, Gaussian 98, was recently released. "He took the machinery of electronic structure and put it into a form that's so advanced, any chemist can use it," Voth says.

Pople is a prolific publisher, having written more than 400 articles, some of which are among the most cited in the chemical field.

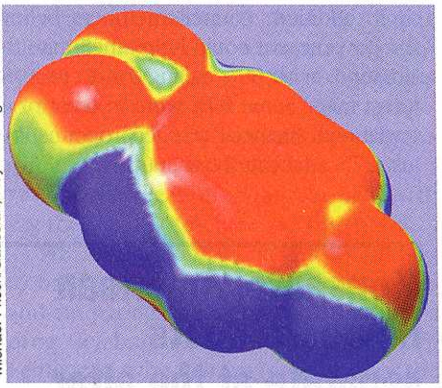
In the 1960s, Kohn and his colleagues determined that they could describe a quantum mechanical system, such as atoms or molecules, in terms of electron density rather than the motions of each individual electron. This greatly simplified what would ordinarily be horribly complicated mathematics. The theory was first applied to atomic structure. Although scientists could see it might have use in molecular systems, Kohn says, many were initially skeptical.

However, as Parr notes, "There was obvious beauty in what he had done, and obvious applicability to chemistry."

During the past decade, density functional theory finally became popular with chemists. With traditional methods, describing a system of more than 10 atoms


AP Photo/Phil Klein

Kohn


Michael Frisch/Gaussian, Roy Dennington/Semichem

A theoretical electron density surface of p-nitroaniline shows the difference between predictions calculated with Kohn's density functional theory (DFT) and the earlier Hartree-Fock method. Blue indicates the DFT-calculated electron density is higher than Hartree-Fock, while red indicates DFT produced lower electron density. The graphic was generated with Gaussian 98 and GaussView—the latest versions of computational software originally developed by Pople.

can be prohibitively difficult and expensive, but density functional theory can aid chemists' study of large complex systems, such as proteins. In the early 1990s, Pople was able to include Kohn's density functional theory in his methodologies.

The power of Kohn's and Pople's work has, of course, been fueled by the enormous progress in computer technology, theorists say.

"The speed with which computers developed astonished me," Pople tells C&EN. "Much more is possible than I imagined 20 years ago."

Elizabeth Wilson

Nobel Prize in Medicine goes for research on NO

Three U.S. researchers whose work helped identify nitric oxide as a key biological signaling molecule will receive this year's Nobel Prize in Physiology or Medicine.

The award will be shared by Robert F. Furchgott, 82, distinguished professor emeritus at the State University of New York in Brooklyn; Ferid Murad, 62, professor and chairman of the department of integrative biology, pharmacology, and physiology at the University of Texas Medical School at Houston; and Louis J. Ignarro, 57, professor of pharmacology at the University of California, Los Angeles, School of Medicine.

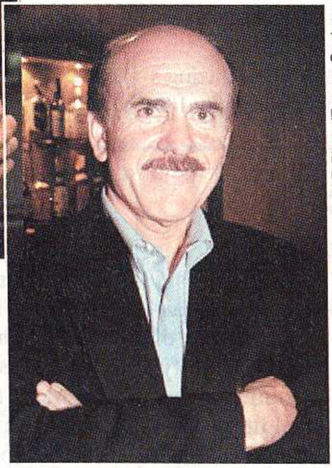
The three researchers, working independently, made key discoveries that helped reveal that this gaseous free radical passes from one cell to another to regulate the dilation of blood vessels. "Signal transmission by a gas that is produced by one cell, penetrates through membranes, and regulates the function of another cell represents an entirely new principle for signaling in biological systems," the Karolinska Institute noted in announcing this year's prize.

The prize is being awarded specifically for work on NO's role in the cardiovascular system, but NO's role within the body is now known to be much broader than that. Nerve cells use it to help regulate the signals that pass between them, and it may play a role in memory. Macrophages produce NO to kill bacteria and other infectious agents and to fight cancer. NO initiates erection in the penis by dilating blood vessels, helps regulate blood clotting, and is involved in recognizing smells.


AP Photo/Pat Sullivan


AP Photo/Adam Nadel

Nobel winners (clockwise from above) Murad, Ignarro, and Furchgott.


AP Photo/Franco Castano

In 1977, Murad, then at the University of Virginia, and his colleagues showed that drugs such as nitroglycerin—which had been in use for more than a century to dilate blood vessels and treat angina—work by releasing NO.

In 1980, Furchgott found that the drug acetylcholine could cause blood vessels to relax only if the cells that line the blood vessel walls—the endothelium—were healthy and the lining intact. He proposed that the endothelial cells were being stimulated to release a relaxing factor that diffused into neighboring smooth-muscle cells.

In the early 1980s, Ignarro and his colleagues were also investigating the metabolism of nitroglycerin. In 1986, he and Furchgott independently proposed that the NO produced from nitroglycerin and the relaxing factor released from endothelial cells in blood vessels were one and the same.

Researchers who work on NO were delighted by the award selection. "This is very exciting," says Larry K. Keefer, who as chief of the chemistry section of the Laboratory of Comparative Carcinogenesis at the National Cancer Institute, Frederick, Md., is working to develop better NO-releasing drugs. "I'm ecstatic not only because it's good for the field, but because of the individuals. I know these gentlemen, and I'm very pleased for them. The award is well deserved."

Michael A. Marletta, a Howard Hughes Medical Institute investigator and professor of medicinal and biological chemistry at the University of Michigan, Ann Arbor, says, "I'm delighted that the Nobel Committee has recognized research on the biological effects of nitric oxide. It's an important area, evidenced probably best by the fact that it's already had significant influence on human health and disease." In the 1980s, Marletta was one of the first researchers to uncover the presence and function of NO in macrophages.

"The people recognized have all made important early contributions to the field," Marletta notes. "It's too bad that the Nobel Prize can only honor three people, since there are a number of investigators—Salvador Moncada and others, for example—who have also made critical contributions to the early discoveries and our current understanding of the role of NO in biology." In 1987, Moncada, then with Wellcome Research Laboratories, Beckenham, England, used chemiluminescence methods to show that endothelial cells release NO at levels high enough for it to be the relaxing factor.

Rebecca Rawls