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OBITUARY

Robert J. Cotter (1943–2012)

Robert J. Cotter, a mass spectrometrist and educator who was best known for developing time-of-flight mass spectrometers for biological structural analysis, died on November 12, 2012 of heart failure at his home in Baltimore at the age of 69. At the Johns Hopkins University since 1978, Bob was Professor of Pharmacology and Molecular Sciences, Professor of Biophysics and Biophysical Chemistry, and a member of the Applied Physics Laboratory. He co-founded the Middle Atlantic Mass Spectrometry Laboratory with Catherine Fenselau at The Johns Hopkins University School of Medicine in 1979 and had served as its director since 1987. Bob was an active participant in many local, national, and international scientific organizations and had served as an officer of the US Human Proteome Organization (USHUPO) and the American Society for Mass Spectrometry (ASMS). In particular, Bob was President of ASMS from 1998 to 2000. Born in Washington, DC and raised in Massachusetts, Bob received his B.S. in chemistry from the College of the Holy Cross, and then continued his studies in physical chemistry in the laboratory of Walter S. Koski at the Johns Hopkins University, where he received his M.S. and Ph.D. in 1971 and 1972, respectively. After graduating from Johns Hopkins University, Bob pursued his love of teaching in the Chemistry Department at Gettysburg College. However, he ultimately returned to Johns Hopkins in 1978, where he could more intensively pursue his passion for mass spectrometry research while also lecturing and mentoring graduate students.

An author of over 350 research papers, inventor of 14 patents, and sole author of a widely-read book on time-of-flight (ToF) mass spectrometry (Cotter RJ. *Time-of-Flight Mass Spectrometry: Instrumentation and Applications in Biological Research*, American Chemical Society, Washington DC, 1997), Bob Cotter was recognized in 2011 by the American Chemical Society with the Frank H. Field and Joe L. Franklin Award for Outstanding Achievement in Mass Spectrometry (Figure 1) and by ASMS with the 2011 Distinguished Contribution in Mass Spectrometry Award. He was also given the Award in Chemical Instrumentation by the American Chemical Society Analytical Division. Always innovative, Bob contributed substantially to the development of mass spectrometry technology as well as to its applications. His contributions to instrumentation included development of desorption chemical ionization, elucidating mechanisms of desorption ionization, and development and miniaturization of ion trap and time-of-flight mass spectrometers.

In addition to designing and building innovative mass spectrometers, Bob also became known for elegant applications of these instruments to biomedical and defense research and even space exploration. He miniaturized ToF instruments to become portable detectors for biological agents, environmental monitoring, and clinical diagnostics. His miniature ion trap mass spectrometers were designed for extraterrestrial exploration. His last miniature ion trap mass spectrometer, optimized for analysis of biomolecules on Mars, is scheduled for launch to the Red Planet in 2018. Bob's many biomedical applications of mass spectrometry included studies of microorganisms, immune system function, and proteomics. His paper reporting the identification of β-amyloid (1-42) as a major constituent of Alzheimer's disease plaques has been cited over 500 times. However, Bob became best known to the mass spectrometry community for his innovations in ToF mass spectrometry.

Figure 1. Bob Cotter with his wife Catherine Fenselau in 2011 after receiving the Frank H. Field and Joe L. Franklin Award from the American Chemical Society (photograph taken by Bob's son, Bruce Cotter)

When Bob Cotter began his research on ToF mass spectrometry in the late 1970s, biomedical applications of this instrument were rare, and commercial production had virtually

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Figure 2. Bob Cotter introducing his "Time-of-Flight" song during the International Mass Spectrometry Conference in Kyoto, Japan, September 2012 (photograph courtesy of Scott A. Kuzdzal)

ceased. At that time, most believed that laser desorption was limited to the evaporation of neutral molecules and that a separate gas-phase ionization step would be required to produce ions suitable for mass spectrometric analysis. Bob challenged this notion and proved that both desorption and ionization may be accomplished together using a single laser pulse. Furthermore, he showed that a pulsed laser was ideal when paired with a ToF mass spectrometer that analyzes packets of ions in a similar pulsed manner. Many of his fundamental papers on laser desorption mass spectrometry have been cited more than 100 times each (some more than 200 times) and continue to be cited today. To put Bob's scientific contributions to ToF mass spectrometry in perspective, laser desorption mass spectrometry is the direct precursor to matrix-assisted laser desorption ionization (MALDI) ToF mass spectrometry, for which Koichi Tanaka shared the Nobel Prize in Chemistry in 2002.

The explosive growth in the capabilities and applications of mass spectrometry for proteomics and the analysis of other large molecules such as oligonucleotides may be traced in large part to Bob's lifetime work in the development and application of ToF mass spectrometry and laser desorption ToF mass spectrometry. Bob recognized the potential for biomedical applications of ToF mass spectrometry and began by constructing in 1980 a ToF mass spectrometer with IR laser desorption and delayed extraction. This work made possible the development of MALDI-ToF mass spectrometry. Next, Bob developed MS-MS capabilities for this mass analyzer, and in 1993 developed a tandem time-of-flight (ToF/ToF) mass spectrometer that anticipated the commercial ToF-ToF mass spectrometers for proteomics that are available today.

Another significant contribution Bob made to ToF mass spectrometry was the invention of a nonlinear field reflectron known as the curved-field reflectron. The curved-field reflectron eliminates the need for stepping of the reflectron voltage to obtain product ion mass spectra and focuses the entire product ion mass range simultaneously. For tandem instruments, the curved-field reflectron eliminates the need for decelerating precursor ions before collision, reaccelerating or "lifting" product ion energies, or using second sources and, instead, permits the use of high (20 keV) collision energies for optimum structural information. To illustrate the impact of Professor Cotter's innovative ToF and ToF/ToF mass spectrometers incorporating his innovations such as curved-field reflectron, delayed extraction, and high energy CID, hundreds of these instruments have been manufactured and sold by Kratos and then Shimadzu. The potential benefits of high energy (20 keV) collisions are just now being appreciated, with perhaps the most exciting being the possibility of carrying out "top-down" or "middle-down" analyses on a MALDI ToF/ToF mass spectrometer and of implementing charge-remote fragmentation for structure determination in lipidomics and related areas.

During his career, Bob mentored more than 70 graduate students, medical students, visiting scholars, and postdoctoral fellows, who then pursued careers in academia, industry, or government. All who studied with Bob (I was a postdoctoral fellow with Bob in the early 1980s) or collaborated with him are continuing his legacy of excellence in scientific research and education. When giving lectures and teaching class, I always imagine how Bob would have made the presentation and then try to express his level of enthusiasm for science.

In addition to scientific research, Bob loved jazz and could be heard playing piano at hospitality suites during mass spectrometry conferences and other events (Figure 2). As recently as September 2012, he played piano and led a group of several hundred mass spectrometrists in the singing of his "Time-of-Flight" song during the International Mass Spectrometry Conference in Kyoto, Japan. Unquestionably, the mention of ToF mass spectrometry will nearly always bring the name of Robert J. Cotter to mind. His legacy is the breadth of his outstanding contributions to mass spectrometry, especially ToF instruments, their applications to proteomics, and other biopolymers made over many years, as well as his mentorship of others in this important analytical field.

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