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OBITUARY

John Bennett Fenn, 1917–2010

On December 10th of last year, John B. Fenn passed away at the age of 93 years. Through the development of electrospray mass spectrometry, now the basis of most of proteomics and of a billion-dollar mass spectrometric industry, John has had an unparalleled influence on biological mass spectrometry. He was a unique character, with his own views on everything, and he will remain irreplaceable for all of us who knew him. John's general biography is available from others and from himself [1–6]. Here I will mainly focus on his unique story and contribution to the field of modern mass spectrometry and proteomics as I experienced them as his graduate student in the 1980s.

John Fenn's father was first an engineer in industry and later taught at Berea, a combined high school and college in the impoverished Appalachian region of the American South. This provided John with an opportunity to complete undergraduate courses in less than the time it normally takes to finish high school alone. While only in 10th grade, he resolved to marry Margaret (Magee) Wilson, a secretary at the college. Although Magee was 10 years his senior, she eventually succumbed to his persistence, and the two of them had a close and happy marriage until her death in a traffic accident in 1992.

After college, John wanted to work for a company, but this being depression times, he could not easily find a job and chose to do graduate work in chemistry at Yale University instead. Here he did, by his own account, 'very boring work'—nothing like the science fiction stories of molecular rays that had attracted him to science in the first place. After receiving his Ph.D. from Yale after only 3 years in 1940, John did spend a number of years at several chemical companies, including a small company (Experiment, Inc.) that encouraged research and let him publish papers. John enjoyed his years in industry—in fact they rekindled his interest in scientific research. He then went to Princeton, at first to direct a large project financed by the Navy involving jet propulsion. He was soon itching to do his own research in this area, namely in 'molecular beams', which are supersonic beams of gas formed at a small hole into a vacuum system. Supersonic free-jet beams sport exotic features such as colossal temperature drops in microseconds. Crossed molecular beams were for a while seen as the ultimate way to do chemistry under controlled conditions. The molecular beam field was John's main scientific

John Fenn, ASMS Conference, 1997

home throughout his career, and he contributed ground work that assisted several Nobel-Prize winners such as his friends Dudley Herschbach, Yuan T. Lee, and John C. Polanyi, who won the Chemistry prize in 1986. To get the best molecular beams, the pumps had to be as big as possible. John's lab—first at Princeton University and starting in 1967 at Yale—featured enormous stainless steel manifolds and oil-diffusion pumps that could be cleaned by a small lab member who was suspended inside them.

Upon moving to Yale, John was asked by colleagues at the Medical School about Malcolm Dole's recently published work on electrosprayed macromolecules that apparently ended up in a desolvated and ionized form in the gas phase of a vacuum. Given his knowledge of the free-jet expansion in molecular beams, John realized that Dole could not in fact have observed free, ionized macromolecules. Nevertheless, the idea intrigued him, and in the 1970s, he began to investigate electrospray ion sources in an attempt to improve on Dole's work. (One of John's dictums was that 'a good experimentalist will try everything at least once'). These experiments did not yield the hoped-for beams of macromolecules, but resulted in the idea of a counter-current gas flow. John knew that complete desolvation of the ions is crucial to obtaining mass spectra, and he thought that this

Correspondence to: Matthias Mann; *e-mail:* mmann@biochem.mpg.de

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was his most crucial contribution to making electrospray work. Several years later, after receiving a new low molecular weight quadrupole (up to a *m/z* of 400), and with a brilliant visiting scientist, Gado Yamashita, John tried again. This time it worked beautifully and resulted in the electrospray "apparatus" patents and several publications. (It should give pause for thought to milestone-obsessed granting agencies that these crucial experiments were performed by Gado, whose real project had been to investigate electrospray as a potential means of rocket propulsion!). As John had predicted, the fact that only thermal energies were involved in electrospray meant that not only very labile and polar molecules such as vitamins became amenable to mass spectrometry but also that those fragile samples could be introduced directly from solution. In this respect, electrospray was different from the other ionization methods of that time, which all used high energies to desorb and ionize high molecular weight molecules.

Lab members subjected other biomolecules to electrospray and made the intriguing observation that peptides of about 1000 Da (considered large biomolecules at the time), sometimes had another signal at half the expected *m/z* value. John had the idea to investigate this 'multiple charging' phenomenon on a polymer mixture of defined mass, namely polyethylene glycol. PEGs of higher and higher mass could carry more and more charges as revealed by the fact that the 44 Da monomer mass difference became smaller and smaller on the *m/z* scale. John's work on electrospray had not attracted much attention, but at least upon publication of this finding, the mass spectrometric world began to take note. Fortunately for our lab, the notice was not widespread. It was only when we showed the same results with proteins that everybody got excited. (Ironically, we only went back to proteins because the PEG spectra were becoming too complicated.) Our results were then quickly replicated by others, who had much better laboratory equipment and funding. The rest, including John's Nobel Prize in 2002, is history.

John was a strong-willed and brilliant scientist, who would not let himself be taken off the track that he intuitively felt was correct, and he never followed the crowd. He was an outsider in the world of mass spectrometry and his 'crazy ideas' were often turned down for funding by the granting agencies and by his peers. Sadly, even after this breakthrough, obtaining funding remained difficult—this time on the grounds that others were in a better position to pursue what he had initiated. Likewise, Yale University, much beloved by John, played a less than noble role in John's achievements. First the university tried to force him out at the then mandatory retirement age of 70. John resourcefully and persistently fought those attempts. Interestingly, electrospray owes its development to John's intransigence because most of the work was done after he reached the normal retirement age of 65.

As he did with his previous apparatus patents, John reported the crucial invention of "deconvolution of multiply charged spectra" to Yale, his only obligation under the Yale Patent Policy. When the Yale patent office did nothing in spite of several reminders, John filed a patent application on his own a week before a statutory deadline. While John's side of the story has yet to be told, suffice it to say even though he saved a valuable patent for Yale and was well within his rights, his "reward" was a bitter decade-long legal battle with Yale.

After his first wife's death and since he no longer felt welcome at Yale, John moved his laboratory to Virginia Commonwealth University in Richmond where he married Frederica Mullen. John was blessed to have had two wonderful marriages, and Freda cared admirably for John in his last years.

John Fenn was an entirely original and refreshing personality and humble to a fault—they don't make them any more like that (another expression of his). He was a wonderful 'southern gentleman', always charming and a great story teller. He was well-versed in American classics, on occasion even quoting poetry, and an excellent writer himself. As an adviser, he was unbelievably generous both of his time and his help in all matters of graduate student life, even picking up students' pay checks by himself when the grants ran out (we only found out much later). Despite consistently swimming against the tide and despite his shoestring funding, he was extremely successful in the end, probably because of his combination of scientific brilliance with a good portion of stubbornness in the service of doing the right thing.

Matthias Mann
Max Planck Institute of Biochemistry,
Department of Proteomics and Signal Transduction
Am Klopferspitz 18, 82152 Martinsried, Germany

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