

Obituary

Csaba Horváth (1930–2004)

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The news of the death of Professor Csaba Horváth, Roberto C. Goizueta Professor of Chemical Engineering at Yale University (13 April 2004, in New Haven, CT, USA) reverberated quickly and sadly across the worldwide chromatographic community. All chromatographers knew Csaba for his great scientific achievements, the luminous clarity of his presentations, and his urbanity. Everywhere in the world, analysts use HPLC and RPLC methods that arose from concepts pioneered by Csaba. He was the most

influential of the few founding fathers of high-performance liquid chromatography (HPLC). He made reversed-phase HPLC the most widely used analytical method of separation. He pioneered bioengineering and bioanalytical chromatography. In so doing, he had a profound impact on the evolution of the modern biotechnologies.

Born on 25 January 1930, in Szolnok, Hungary, Csaba Horváth graduated as a chemical engineer from the Technical University in Budapest in 1952. Although he had literary

and artistic inclinations, he soon realized that, under the political system ruling Hungary at that time, a scientific career was safer and he joined the Department of Organic Chemical Technology as a faculty member. When the Hungarian Revolution was crushed by the Soviet army in 1956, he escaped with many of the scientific elite of that country. For the following 4 years, Csaba worked at Farbwerke Hoechst AG in Frankfurt am Main, first in a pilot plant, then doing research and development work on the surface chemistry of organic pigment dyes. The knowledge gained from this experience was helpful when he left the Hoechst company in 1961 to join the group of Professor István Halász under whose supervision Csaba did doctoral research on open-tubular columns (OTCs) for gas chromatography at the John Wolfgang Goethe University. Together they invented and developed the porous-layer OTCs which offer several remarkable advantages over the wall-coated OTCs, a higher loadability and the ability to take advantage of all the retention mechanisms afforded by adsorption, including adsorption on dye pigments. They also prepared surface-treated beads, an approach that was used later in the context of HPLC. Csaba kept a fond memory of this time spent in István's group. He had a profound respect for the achievements and the integrity of this great scientist who taught him the importance of clear and logical thinking, of honesty in science, and of common sense in the interpretation of results, and with whom he remained a close friend. Having received a Ph.D. (*magna cum laude*) in 1963, Csaba moved to the USA where, as a post-doctoral fellow under the direction of Professor S.R. Lipsky in the School of Medicine of Yale University, he began working on the development of analytical methodologies for lunar samples, searching for trace compounds which could show the presence of life on the moon in a distant past.

The need to work with very small samples and to look for life indicating compounds led him to turn toward liquid chromatography, inspired him to apply to LC the same principles as he had used earlier in GC, and to build the first instrument for high-pressure liquid chromatography. He understood very early the potential of this new separation method which was going to revolutionize biochemistry and molecular biology. However, Csaba realized that his first task was to make it work and to demonstrate its power and potential. From the beginning, he had to overcome the four fears of the biochemists which he, later, came to name barophobia, lithophobia, siderophobia, and adiaphanophobia: the fears of pressure, of silica, of steel, and of all devices that are not transparent. He worked with a company called Picker-Nuclear, and developed the first commercial instrument for HPLC. I still vividly remember the shock that I experienced when he showed it to me for the first time, and the thrill of his words, and my thoughts. That was fascinating. Rapidly Csaba converted most of those who were still doing active research in GC to HPLC. First, his former mentor, István Halász, then Jack Kirkland and his colleagues at DuPont, myself and others. Lloyd Snyder, already an authority in classical LC, had no difficulties in understanding

the extraordinary advantages of HPLC and so did the specialists of size-exclusion chromatography. Among the early authorities in HPLC, the late Professors Josef Huber, then from Amsterdam, later Vienna, and J. Calvin Giddings had already started working in this area independently. Those were the three founding fathers of HPLC and, because of his vision and his mastery of the chemical interactions involved, Csaba, I believe, was the *Primus inter Pares*. Because, from the beginning, he focused his interests on the separation of samples of biological origin, Csaba is the pioneer of modern bioanalytical chemistry. However, if the new chromatographic method was a rapid success among scientists, it was slower to gain acceptance among analysts. Difficulties related to the reproducibility and the stability of the packing materials used as stationary phases, the reproducibility, the precision and the accuracy of the analytical data would require considerable research to overcome. It took more than 10 years for HPLC to reach the community of analytical chemists and nearly 20 to turn it into the ubiquitous separation method that it has become.

Although he always was most successful in his research, Csaba encountered serious travails at the beginning of his career. Ivy league Colleges were more closely knit societies than they are now; they were difficult to penetrate. He was neither a physician nor a biochemist but a chemist working in a School of Medicine. He was not a traditional chemical engineer either. The golden years of analytical chemistry were beginning but the powers-that-were did not know that yet. It would take a long time to convince academics that HPLC was an invention of profound importance. The beginning of his career was slow and difficult. The life of the bright, promising chemists was not as easy in the 1960s as it has become now that we have been recognized to be important potential rainmakers. After being a research associate at the School of Medicine of Yale University (1964–1970), Csaba became a lecturer and finally an Associate Professor of Physical sciences at this School (1967–1975). He eventually became an associate professor of engineering and then of chemical engineering (1972–1979), before he became fully acknowledged as a scientist and a scholar. He was promoted as professor of chemical engineering (1979–1985), selected as Acting Chairman then Chairman of that department (1985–1993, 1994–1995), as the Llewellyn West Jones Professor (1993–1998) and, finally, the Roberto C. Goizueta professor of chemical engineering (1998–2004).

After becoming professor in the chemical engineering department of Yale University, Csaba devoted all his attention to the development of the theory and the applications of reversed-phase liquid chromatography. Not only is he credited with designing and building the first HPLC chromatograph and the first microbore HPLC columns (for ion-exchange separations of biological compounds), he later pioneered the use of reversed-phase HPLC (or RPLC), the most widely applied chromatographic method of analysis, the use of displacement chromatography for preparative HPLC, and innumerable applications of HPLC

to the separation of samples of biological origin. He developed the solvophobic theory of retention in RPLC, the use of entropy–enthalpy compensation in the study of retention mechanisms, and the fundamentals of electrochromatography. The importance of his pioneering HPLC, RPLC, and their applications in the life sciences, fields in which these new methods are permitting countless breakthroughs, is such that his contributions will remain among the major scientific achievements of the 20th Century.

Csaba is the author or coauthor of 300 publications, with 10% cited more than 100 times since their publication (ISI Web of Knowledge, late April 2004). His landmark paper, “Solvophobic interactions in liquid-chromatography with nonpolar stationary phases” [Cs. Horváth, W. Melander, I. Molnár, *J. Chromatogr.* 125 (1976) 129], has a considerable impact, within and beyond the chromatographic community. It was cited 985 times (ISI). Half-a-dozen of the follow-up papers have been cited between 300 and 500 times which, for analytical chemistry publications is an extremely large number, far exceeding the scores of any one else in our field. Many more of his publications have influenced the work of an immense number of analysts. Csaba has presented hundreds of lectures at meetings or seminars held all

over the world. These lectures attracted huge crowds. They were often delivered to standing room only audiences. He had a unique ability to combine a profound understanding of the fundamentals of retention mechanisms, clear explanations of his thoughts, with brilliant presentations, artistic and inventive slides, and witty comments. He was deeply interested in philology and forged numerous words, some (isocratic, multimodal) have become so common that their origin is lost, others which still delight his friends (e.g., the four ailments of analytical biologists, see earlier).

Among the numerous honors bestowed upon Csaba are the Stephen Dal Nogare Award of the Forum of the Delaware Valley (1978), the Anniversary Tswett Medal of the USSR Academy of Sciences (1979) and the Tswett Chromatography Award (1980), the Humboldt Award for Senior American Scientists (1982), the Chromatography Awards of the American Chemical Society (1983) and of Eastern Analytical Symposium (1986), the Merit Award of N.I.H. (1993), the A.J.P. Martin Gold Medal of the Chromatographic Society (1994), the I. Halász Medal Award of the Hungarian Separation Science Society (1997), the Golay Award (1999), the Michael Widmer Award of the Swiss Chemical Society (2000), the Austrian “Goldene Verdienstkreuz für Wissenschaft und Kunst der Republik Österreich Ehrenkreuz” for Arts and Sciences, first class (2002), the Torbern Bergman Medal of the Swedish Chemical Society (2003) and the Eureka Medal of the Hungarian Chemical Society (2003). The Halász Award was particularly dear to his heart as was the Honorary Doctorate received earlier from his alma mater, the Technical University of Budapest (1986). Csaba was the 24th W.N. Lacey Lecturer in chemical engineering at Caltech. In 1984, Csaba organized the Eighth International Symposium on Column Liquid Chromatography, which he named HPLC’84 and which was the first immensely successful symposium on HPLC. He was an external member of the Hungarian Academy of Sciences (1990), a member of the Connecticut Academy of Sciences and Engineering (1992), a Founding Fellow of the American Institute for Medical and Biomedical Engineering (1992), a Fellow of the American Institute of Chemical Engineers (1994) and of the California Separation Sciences Society (1998). In January 2004, Csaba was elected a member of the US National Academy of Engineering. The Csaba Horváth Institute of Bioseparation Science of the University of Innsbruck has been funded by the Ministry of Education, Science and Culture of Austria. It will open in October 2004, under the direction of Professor Dr. Günther Bonn.

Csaba married Valeria Scioscioli in Rome and by 1964 had a daughter who needed special care. Lingering uncertainties on the future of HPLC in the mid-1960s to mid-1970s, difficulties at Yale, and health care costs made life hard for Csaba during this period of his life. He had to concentrate on his development of the first ever HPLC instrument. Work constraints limited his publications during the 1960s and early 1970s. Consequently, Csaba’s critical role in the conception and birth of HPLC has been over-



looked and is only now coming to light. This is probably why he never got the phone call from Stockholm that he deserved.

While Csaba's work has had a profound influence on the development of analytical biochemistry, forwarding the progress of the life sciences for the last 30 years, his influence on an immense number of scientists was greater. He strongly influenced the thrust of the research of his mentor, Professor István Halász. He confirmed my inclinations to study preparative chromatography when I moved to the USA in 1984, counsel for which I am most grateful. He had a strong influence on the orientation of the research work of Barry Karger toward more and more biochemical applications. Directly and indirectly, Csaba influenced the research work of all the chromatographers of his generation. To his graduate students, Csaba's mentoring was demanding and rewarding. He educated nearly 70 students and guided them through their Ph.D. degree in chemical engineering. It is a

tribute to his human qualities as a teacher that they have formed a close community, the "Csabaites," with their own private web site and that they recently organized events celebrating him. Many of them have reached highly responsible positions in the American industry or achieved fame in the academic community. The grief of the "Csabaites" community is heartbreaking and we share it. Csaba was the most charming companion for a dinner, a party or an outing. He was a wonderful, sweet, loyal friend, a most understanding, sensitive person.

To his family, Csaba's present and former coworkers, his friends, we offer our sympathy. Csaba Horváth's memory will live forever in all of us.

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