

Commemoration

Honoring Barry L. Karger

It is with pleasure that I congratulate Barry Karger to whom this special issue of the *Journal of Chromatography A* is dedicated on the occasion of his 65th birthday. During the last four decades, Barry published more than 275 scientific papers, trained and educated more than 150 students and associates, and founded a world-famous research institute. He is one of the great figures in modern chromatography. Through his contributions to the development of the capillary zone electrophoresis (CZE) methods used for the unraveling of the human genome and for the analysis of many related and unrelated compounds, he is recognized as a towering figure in modern biochemical analysis.

Barry Karger began his scientific career at MIT in 1960 when he performed research on the foam fractionation of organic compounds under the supervision of one of the fathers of modern instrumental analysis, Professor L.B. Rogers. This work led to his first scientific publication, in *Analytical Chemistry*. Barry went on to defend his Ph.D. thesis at Cornell University in 1963. Under the direction of Professor W.D. Cooke, Barry developed time normalization, the first general and effective concept for the optimization of the experimental conditions of chromatographic analyses [1,2]. By imposing a constraint, the constant analysis time, the method allowed a precise investigation of the possible trade-offs between the various parameters of the chromatographic analysis that permit the maximization of the resolution between two compounds. In my opinion, this work is the first approach that dealt seriously with the fundamentals of the optimization of the experimental conditions under which a chromatographic separation is conducted. Although the paper was essentially experimental, hence empirical, it was apparent to me that it had great potential and I still remember how its reading was a source of inspiration. I understood rapidly that it was possible to model this work, which I did. Not surprisingly, the calculation results agreed well with Barry's experimental results, demonstrating the fundamental importance of the concept. I wrote to him about this complementary approach and, eventually, wrote a theoretical paper on this model [3].

This first interaction was followed by many others and, I am happy to say, we became friends. Interactions multiplied. Each time we attended a meeting, we visited each other. We both became close to István Halász who strongly influenced our thinking and our vision of chromatographic

and analytical problems. In 1972, Barry visited my laboratory in Paris and we wrote three papers. Two of them dealt with the modeling of interesting phenomena in chromatography, both marrying experimental results obtained in Barry's group and the results of calculations performed in mine. Not all of Barry's experiments were successful and it is noteworthy that his stay might have had far more spectacular results than our research. His use of a certain appliance caused the chemistry laboratories of a famous military establishment located in the center of Paris to be nearly set ablaze.

In the 1970s and 80s, Barry became involved in reversed-phase liquid chromatography. His first major contribution was the use of chiral reagents as ion-pairing systems, particularly in metal complexes. This led to a new mode of chiral separations. After studying hydrophobic interactions, he investigated the separation and analysis of peptides and proteins. Observing that the use of high concentrations of certain salts in the mobile phase caused the retention of proteins on resins used as packing materials for size exclusion, which defeats the purpose of a separation based on molecular size, he took a positive approach. He decided to use this phenomenon for separation purposes, prepared hydrophilic-bonded stationary phases and, using gradients of decreasing concentration of salts, demonstrated good separations with retention of the biological activity of the proteins. Hydrophobic interaction chromatography (HIC) was born. It has become widely used in protein separations, particularly for preparative purposes. Shortly after the 1986 International Symposium on Chromatography, Barry turned toward capillary electrophoresis (CE). In contrast to the conventional wisdom, that CE would compete with HPLC, he perceived that CE would compete primarily with slab gel electrophoresis. Barry made a series of major contributions to the separation of DNA fragments in gel-filled capillaries and eventually brought the method to its present level of performance: Capillary arrays can sequence over 1000 bases with high accuracy in less than one hour. Barry is a man with a goal, not one technique. His goal is the furtherance of bioanalysis. While LC and CE separate complex biological mixtures, they cannot directly identify the separated compounds. With this realization, Barry is focusing his interest on the coupling of these separation methods and mass spectrometry. In this field again, he is making major contributions.

Barry Karger had perceived early the profound importance that modern analytical techniques were going to have on the development of the biological sciences, biochemistry and molecular biology, and on their applications in the clinical and forensic areas. To promote the fruitful interactions between specialists of these remote scientific fields in 1973, he founded the Institute of Chemical Analysis, Applications, and Forensic Science which became the Barnett Institute of Chemical Analysis and Material Science in 1983. Barry became its first Director and, over the years, has patiently nursed it to the great success that it has achieved. There, specialists of chromatography, capillary zone electrophoresis, and mass spectrometry meet scientists involved in biological and material sciences and partake in fruitful exchanges. Since its inception, the Barnett Institute has been one of the few leading research centers in bioanalysis. The instinct with which Barry guided, first, the growth, now the navigation of this large vessel, with which he anticipated the changes in the orientation of the main thrust of the research in modern molecular biology is remarkable. From gas to liquid chromatography, from chromatography to CZE, from CZE to high-performance DNA separations and DNA sequencing, from DNA analyses to electrospray ionization and matrix-assisted laser desorption ionization mass spectrometric methods for proteome analyses, from genomics to proteomics and metabolomics, Barry has been involved in all the great fights of the last thirty years and nothing yet has extinguished the fire for knowledge that burns in him.

The course of Barry Karger's career and the numerous honors and awards that he received are detailed in the accompanying preface by Csaba Horváth and Andras Guttman. Barry liked particularly the 2002 Halász Medal that the Hungarian Society for Chromatography and Separation Science bestowed upon him. This medal was established in the memory of one of the most influential leaders of our generation, to whom we both owe a great debt of gratitude, as do our friends Csaba Horváth and Heinz Engelhardt. The friendships of the other great European leaders of our field, Ernst

Bayer and Josef Huber were also dear to his heart, more valuable than all honors, awards, and medals.

Barry has educated or trained more than 150 students and postdoctoral associates. Many of them have grown to become team leaders themselves. More of his coworkers have become famous and have started major groups of their own in this country and abroad than those of anybody else in our field. Directly and indirectly, he influenced two generations of separation scientists. In the long list of his coauthors it is difficult to select but a few. Nevertheless, I must recognize, besides his mentors and his friends already cited, Barry's most important associates, Roger Giese, Bill Giessen, Bill Hancock, Roy Keller, Peter Sewell, Lloyd Snyder, and Shigeru Terabe, and a few of his former coworkers, among whom Wolfgang Lindner, Nobuo Tanaka, Paul Vouros, have developed important research groups and made major contributions of their own.

In addition to his over 275 scientific papers, Barry is the coauthor of one major book and of 28 patents. Many of these patents have been commercialized. He has delivered close to two hundred invited talks, covering five continents, Africa (Egypt), America, Asia (Israel, Japan), Europe, and Oceania (Australia, Hawaii).

Having reached the pinnacle of his career, Barry shows no desire to slow down. His conversation, his talks are full of dynamism and energy. "Why stop when there is that little problem hiding behind that one that I am just overcoming" is the theme of his behavior. So, what else can I do but wish to him many more years of active and successful research?

References

- [1] B.L. Karger, W.D. Cooke, *Anal. Chem.* 36 (1964) 985.
- [2] B.L. Karger, W.D. Cooke, *Anal. Chem.* 36 (1964) 991.
- [3] G. Guiochon, *Anal. Chem.* 38 (1966) 1020.

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