Hamish Small: Experimenter Extraordinaire

Hamish Small spoke to André Striegel about the secrets of his success in separation science, including the development of ion chromatography, and the value of vague thoughts in scientific progress.

André M. Striegel: Many new chromatography techniques have come from the Dow Chemical Company: ion chromatography (IC), hydrodynamic chromatography (HDC), size-exclusion chromatography (SEC) (gel permeation chromatography [GPC]) and, more recently, molecular topology fractionation. Having worked for Dow for many years, what do you think it is about the culture of this company that has allowed for the development of so many new methods?

Hamish Small: My short answer is that Dow management gave strong support to research on their lesser magnitude stars and they had a mechanism in place for developing them when they showed promise

In 1955 I joined Dow in Midland (Michigan, USA) in the Physical Research Laboratory (PRL) or "The Physics Lab" as it was more commonly known. The Physics Lab had a reputation for invention and innovation in "big" chemistry; polystyrene, polyethylene, saran, polymer foams, and the extraction of magnesium from seawater were a few of the technologies that had been pioneered there.

The PRL management was happy to support smaller scale endeavours as well, and most importantly to back them up with patent protection when novelty and invention became apparent. I think this attitude prevailed throughout Dow, not just in PRL; after all, John Moore, who invented GPC, worked in Dow's Texas division and must have enjoyed much the same freedom that we did in the PRL in Midland.

Vital to the success of these second tier inventions was Dow's decision to entrust their development to entrepreneurs outside of Dow. When ion chromatography began to show promise, there were several eager managers within Dow that wanted to take on the responsibility of making a business out of it. I was relieved when this did not happen; I could not envision our small boat surviving while navigating among Dow behemoths like caustic soda, chlorine, or polystyrene. Dow management had been smart to realize that some new discoveries were orchids that needed a hothouse environment to survive and were more likely to be found outside Dow than inside. Presciently they had created a small department with the sole mission of finding licensees who would develop these new, smaller-scale technologies in a favourable environment, under the protective umbrella of the Dow patents.

Figure 1: Hamish Small in PRL ca. 1959.

This licensing approach unleashed the entrepreneurial talents of licensees such as Dionex who, working closely with users, expanded IC to a diversity of applications. The licensing of hydrodynamic chromatography (HDC) followed a similar path, and though I am less familiar with the Dow/Waters collaboration I imagine that the gel permeation chromatography (GPC) story is much the same.

Finally, there was the great freedom that we in research enjoyed. One story in particular from those times may illustrate what I mean. One year I returned from a Gordon Conference hot with the idea that I could create, on the surface of ion-exchange particles, bi-molecular lipid layers similar to those in natural cells. I pursued the idea and discovered much that was interesting (1). I recall very vividly how my lab director, Gif Jones, brought in the "big boss" of central research, Jack Chamberlain, to see what I was up to and what I had discovered. It would have been a stretch to say that what I was doing would have any impact whatsoever on Dow's "bottom line", nevertheless I felt free to follow this digression and upper management was comfortable with that.

There is a notion among some that industrial chemists do not have the freedom afforded by academia. But I found that not to be the case. If I had an inspiration I did not have to submit a research proposal for peer review to get a grant. I went ahead and pursued my idea and if the results were promising I pressed on, and if not I shelved the project. And even "failures" often generated something useful for the "mental attic", so few ventures were a total loss.

AMS: How did your experience with the Atomic Energy Research Establishment (AERE) at Harwell, England, in the early 1950s shape or influence your future research?

HS: In early 1951 I joined the physical chemistry group at Harwell. My assignment was to examine the electrochemical properties of a

Hamish Small graduated with a B.Sc. from the Queen's University of Belfast, Northern Ireland, in 1949. In that same year he was employed by the Atomic Energy Research Establishment at Harwell, England, where he worked until 1955. In 1955, Small, with his wife Beryl and infant daughter, emigrated to the United States where he began a career at the Dow Chemical Company in Midland, Michigan.

In the mid-1960s Small made the discovery that led to HDC, a new technique for determining the size of colloidal particles.

In 1971, Small and his colleagues William Bauman and Tim Stevens made the breakthrough in ion chromatography, eluent suppression, that revolutionized much of inorganic-ion-analysis and led to the formation of Dionex Corporation to commercialize the discovery.

In his career in separation science Small has been granted 52 US patents; his first patent was granted in 1960, his most recent in 2014. He has written many articles, been invited as speaker at many conferences, and has authored a book *Ion Chromatography*.

In 1994 Small and colleagues were honoured to have two papers recognized in the ACS book *Milestones in Analytical Chemistry*, their original paper on ion chromatography and their paper on indirect photometric detection.

Of the many awards that he has won, Small is most proud of The Herbert H. Dow Gold Medal, Dow Chemical Company's highest award to its scientists, and the American Chemical Society Award in Chromatography, particularly as he is one of the few industrial scientists to win this prestigious award.

In 1983 Small retired from Dow to continue in research and invention; in this phase of his career he collaborated with and had the support of Dionex Corporation.

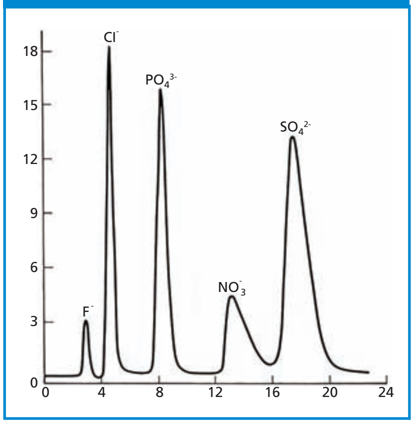
In 2010 Dionex honoured Small by endowing a chair in his name at the University of Texas at Arlington. It will be known as "The Hamish Small Chair in Ion Analysis".

In 2013 Small "officially" retired and continues to delight in the company of Beryl and family, and their four wonderful grandchildren.

relatively new material, a synthetic cation-exchange resin. The ion exchange process captured my interest immediately; the elegance of its "mechano-chemistry", as I like to call it, evoked in me a rapture that is still with me today. I would spend the next two years on this assignment, years that would establish and cement my love of research and determine the course of my future career. And ion exchange would be at the heart of much of what I was to do.

AMS: Which scientist or mentor had the biggest influence on you, and why?
HS: My immediate supervisor in the Harwell group was Geoffrey C. Barker, the first scientist that I would work with closely. He would go on to become one of the leaders in modern electrochemistry, notably as the inventor of square-wave polarography. Barker was already a senior scientist when I joined him but he was unusual in the British scientific culture. Where senior scientists generally used assistants to experiment and gather data, Barker was very much a hands-on investigator; he designed and built his own electronic equipment, did his own glass blowing, and made measurements himself. So for two years we worked side by side, Barker working on polarography while I explored the electrical conducting properties of my ion exchanger. Closely observing this remarkable man made the next two years probably the most influential in shaping my career. Barker helped set the mold; from then on I would be very much an "at-the-bench" researcher.

Figure 2: Anion chromatogram PRL ca 1974.



AMS: What was the biggest difference you experienced in doing research in Europe versus the US? Do you think this difference still exists today?
HS: I have spent a much larger part of my career in the US so I hesitate to make a comparison but I will venture the opinion that in the US I found a much bolder approach to all manner of things, less reluctance to disturb the *status quo* for example, and I found that very appealing. Do I think this attitude still exists? I surely hope so!

AMS: IC and HDC are fairly different separation methods and apply to quite different analytes, the former to generally small species, the latter to ultrahigh molar mass macromolecules and colloids or particles. What part(s) of your background allowed you to develop both these methods?
HS: IC had its origin in my ion-exchange background and my drive to develop a new technique for ion analysis (2). It was on a detour from ion exchange that I discovered HDC.

In the mid-1960s, with only one consumer product, its famous Saran, Dow decided to expand its consumer products. Its first venture, a household oven cleaner, was giving its developers fits because they had no reliable way of evaluating and comparing the efficacy of their formulations. So they appealed to research for help and I latched on to their problem.

It was a challenging project but I achieved success, which made me a sort of hero to consumer products, so they plied me with more problems.

André Striegel received his Ph.D. in analytical chemistry in 1996 and his BS in chemistry in 1991, both from the University of New Orleans, USA. From 1996 to 1998 he performed postdoctoral research for the U.S. Department of Agriculture, at the National Center for Agricultural Utilization Research. For the next six years he worked for Solutia (now Eastman Chemical), at their Springfield, Massachusetts R&D center, first in the Physical and Analytical Sciences Center and then in Films R&D, achieving the rank of research specialist. From 2004 to 2011 he was assistant professor of both analytical and materials chemistry in the Department of Chemistry and Biochemistry at Florida State University (FSU). In September 2011 he joined the National Institute of Standards and Technology (NIST), where he is a research chemist in the Chemical Sciences Division of the Material Measurement Laboratory.

His research interests lie in the area of polymer characterization, in particular applying separation science to determine structure—property relations of complex macromolecules, and in the fundamental aspects of separation and detection methods.

He has received the Eli Lilly Analytical Chemistry Grantee Award, the inaugural ACS-DAC Award for Young Investigators in Separation Science, and an FSU First Year Assistant Professor Award. He has also received a Solutia Technical Achievement Award for his research in private industry, and served as inaugural Professor in Residence for Preservation Research and Testing at the U.S. Library of Congress.

He is the author of nearly 70 peer-reviewed publications, lead co-author of the second edition of *Modern Size-Exclusion Liquid Chromatography* and editor of the book *Multiple Detection in Size-Exclusion Chromatography*. He was, until recently, associate editor of the *Encyclopedia of Analytical Chemistry*, and is a member of the editorial board of various polymer science and analytical chemistry journals. He recently became co-editor of *Chromatographia*.

I became quite adept at finding novel solutions so it was natural for my laboratory director to point me towards a department that needed a rapid means of measuring the size distribution in a plastisol resin, an aqueous suspension of 1-μm particles. I had hardly got my feet wet on the project when, as so often happens in industry, the plastisol product was terminated and with it that department's interest in particle size analysis. But the hook was set and since Dow had a big latex business, I decided I would find a new means of particle-size analysis that would be faster than any of the available methods.

From my acquired knowledge of colloid chemistry, I was aware that, all other conditions being the same, large colloid particles were more inclined to coagulate than smaller ones, so I posed the question: could chromatography be extended to particulate materials where coagulation/de-coagulation would be analogous to sorption/desorption in the chromatography of molecular-sized species?

To test this we would "elute" an injection of two different size latex particles through a packed bed of ion exchange particles and see what happened. The first attempt in late 1967 was disappointing and puzzling; disappointing because the separation was so poor, and puzzling because it seemed that larger particles were exiting the column ahead of smaller particles. I had expected that the larger particles would show a greater tendency to "coagulate" with the packing and exit last. But in early 1968, after taking some obvious steps to improve resolution, I confirmed the order of particle elution and began to understand its hydrodynamic origin. We applied for a patent on the discovery and HDC (my name) was on its way. HDC added such a benefit to the latex business that I was refused permission to talk about it outside the company and it was not until 1974, after I had appealed to management at a fairly high level, that I was able to publish our first paper (3) and give the first public report of the discovery, in Austin (Texas, USA) in June of that year.

Allow yourself to think vaguely; don't feel all the steps you take must be well grounded in established science.

AMS: Are there still improvements to be made in IC and HDC, besides just introducing more robust instrumentation?

HS: In IC, ion reflux (4), or some variant, is the key to true reagent-free IC and Kyle Elkin and John Riviello have been making significant progress in that direction (5) .

Figure 3: Left to right: Bauman, Small, and Stevens win the Sperry award for IC in 1979.

In the early days we tried to do IC with water as eluent but were stymied by not having a suitable stationary phase. Water is the ideal eluent for sensitive conductometric detection but sorption of analytes from water does not, as yet, offer the flexibility of an ion exchange process. However, the outstanding conveniences afforded by a water eluent cannot be ignored; no eluent need be prepared, electrochemically or otherwise, and no suppressor is required. This may sound like heresy coming from one of the inventors of eluent suppression but surely there must be many niche applications where the great advantages of water-elution beg to be exploited.

And if I had the resources, freedom, and energy that I once had, I would "take a flyer" at super-heated steam as an eluent.

In HDC much could be done to improve on the resolving power of packed beds. Tijssen's group in the Netherlands has done notable work on single capillary HDC (6); how about amplifying the capillary mode by operating in the annular gap between a solid fibre and a capillary that encapsulates it?

I have done work (unpublished) on additives to the eluent that enhance the HDC effect, and there is much more that could be done in this area.

AMS: The introduction of on-line light scattering detection, especially when used in a multi-detector set-up, has provided a step-change for many macromolecular separation methods such as SEC and field-flow fractionation (FFF). Do you think it can make a similar difference in HDC?

HS: Absolutely! My first detector in HDC was a homemade light scattering device. We abandoned it when UV absorption instruments were found to be adequate. They had the advantages of being widely available and had a much smaller detecting volume than my homemade instrument. Light scattering has two major advantages over absorbance measurements; it is fundamentally more sensitive and the multi-angle-scattering from particles can provide more information than an absorbance measurement.

AMS: Any advice for young separation scientists?

HS: Yes, but for young investigators in general.

You may be exhorted by some to set goals, and indeed goals and meeting deadlines are essential for the success of many enterprises. In research, try not to be too goal-obsessed. Drill some holes in your blinkers, and sometimes an idea will emerge right out of the blue; indirect photometric detection (7) came at me in that way.

Allow yourself to think vaguely; don't feel all the steps you take must be well grounded in established science. My initial attempt to separate particles chromatographically was motivated by some vague thinking.

Try to identify and avoid the "abominable no-men" who disparage your dreams, who say "it won't work" or "who needs it?" Cultivate associates who will absorb your thought or idea and return it with "spin".

I have read that it was Nicholas Schoorl (1872–1942), Izaak Kolthoff's advisor at Utrecht, who said "theory guides, experiment decides", so, experiment, experiment, experiment. Trust Mother Nature; she will keep you on the straight and narrow.

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