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The Chromatographic Society would like to thank everyone who has contributed to this celebratory journal.

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Dr. Chris D. Bevan

Foreword to the Golden Jubilee Book

by Dr. Chris D. Bevan, President of the Chromatographic Society

If you are reading this book you are probably a chromatographer and perhaps have a career involving separation science. If not, you will learn of a branch of science to which many industries owe a considerable debt of gratitude.

Much of our modern world relies on the action of complex mixtures of substances combined together, often in a unique way. Drugs are probably the most obvious of such formulations and the ability to separate and analyse these is essential to the pharmaceutical and fine chemical industries. Chromatography is probably the best known of the branches of separation science.

In 1954 a meeting on gas chromatography convened by A.F. Williams and W. Murray was held in Ardeer, Scotland at ICI Nobel Division. In 1956 the emergence of GC as a useful technique for the petroleum industry created a nucleus of scientists with a common interest in discovering its scope and developing it further. The first international symposium on chromatography was held in London in 1956 with the inspired support of Denis H. Desty, and his colleagues in the Hydrocarbon Research Group of the Institute of Petroleum.

The past 50 years has seen the introduction and development of gas, liquid, supercritical fluid, capillary, preparative and numerous other variants of separation techniques that have become an indispensable part of the analytical chemist's toolkit.

When a technique is born, scientists want to discuss it, test it, apply it and make money from it. In order to encourage such discourses scientists crystallise into specialist interest groups and if sufficiently popular and useful these develop further into scientific societies. The Chromatographic Society has evolved from such roots.

The Gas Chromatography Discussion Group was formed to organise, disseminate and promote interest and information exchange in this rapidly developing science. As the various methods of chromatography were discovered and developed so the Discussion Group matured into what we now know as the Chromatographic Society.

The influence of the Society as a nucleus for discourse and a source of funding to inspire and assist progression in this area shouldn't be underestimated. The committee formed to run the society has been populated by specialist innovative practitioners and commercially inspired technologists to ensure a balanced representation across the whole field of separation science. Important connections and alliances between the UK-based scientists and their European, American and former Soviet block counterparts were, and still are, promoted and realised by the activities of the Society. The Chromatographic Society's bursaries have enabled many students and scientists without sufficient means, to attend international symposia and make important contributions by presentations of their work.

The Society's Martin and Jubilee medals are awarded to recognise particularly significant contributors to separation science.

The key and significant influence of the CS must be in hosting and managing international symposia. In the past 50 years the Society has been the principal organiser of eight International Symposia on Chromatography in the UK and Ireland. In addition to these home-based symposia the committee has assisted and cooperated with their European partners to host a further eighteen, of which the current one is in August this year in Copenhagen. The number of lectures and posters given must run into thousands and the dissemination of knowledge and know-how greatly facilitated by the Society.

Nationally the Society has been even more active with selective specialised seminars, workshops and symposia all designed to assist the discussion and adoption of knowledge, techniques and instrumentation used in chromatography.

This book's object is to enlighten you in the heritage of chromatography. Chromatography is largely an instrumentally-based science. Instrumental developments have enabled the pursuance and realisation of the separations devised by the experimentalist. In the same way as one may reminisce over cars one has driven, or holiday venues one has visited, the content and intention of this book is to allow you to indulge yourself in nostalgia by revisiting and sharing your memories of equipment with others. Amateur museum collections coupled with memories of using these instruments have been commissioned for inclusion here. A trip down memory lane for the experienced and a realisation of the evolution of instrumentation for the newcomer is catered for here. Memories from the past and visions of the future serve to commemorate the pivotal position the CS has played over the past half-century.

Photos of some members of the Executive Committees over the years have been included as a tribute to their voluntary contributions to the mission of our society. If the Society had never existed many of the advances in chromatography would still have been made but due to the activities of the Society they have been more rapidly disseminated and more widely known. Opportunities to hear, meet and interact with the innovators are truly facilitated by the society and its meetings, a catalyst for the advancement of separation science.

As President of the Chromatographic Society I hope you will enjoy reading this book and that it will inspire you to share your experiences and knowledge of our science with others. ■

50 years of the Chromatographic Society,

The Pye 104 Club and the disappearing heritage of instrumental chromatography

Ian Wilson

by Ian Wilson

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Instrumental chromatography is a relatively recent innovation, and commercial instrumentation even more recent. Indeed, there are still many amongst us who can remember when HPLC was not routine, but a new and untried technique, expensive, temperamental and frankly, when compared to packed column GC, pretty low resolution with lousy sensitivity. There are a diminishing number of pioneers who can remember the era before instrumental GC, when you made your own kit out of glass and the whole concept was completely new, where every result was novel and new discoveries were being made on a daily basis. If you want to see how exciting chromatography could be, the photograph in Figure 1 shows a commercial, all glass, gas chromatograph. It was given to me by the late Dr Roly Jones, (Martin Medallist and a former Chairman of the Chromatographic Society) and was manufactured in London by a firm trading under the imaginative name of Gas Chromatography Ltd (marketing was so much easier in those days, you had a product, you knew what it did and you sold it as that!). The firm was based at Number 176 Old Brompton Rd, SW5. Roly told me (amongst other things) that their demo lab was in a cellar that backed on to a Tube line.

When trains went past they caused so much vibration that the chart recorders couldn't function properly so, as a result, demos were run according to the train timetable. Prices started from £20 according to a price list in my possession and, if you wanted extra sensitivity you could also buy a "Lovelock Ionisation Detector". The gas chromatograph in my collection is, unfortunately, slightly damaged but Roly had apparently managed to donate another to the Science Museum in London that was intact.

Fig 1. The all glass chromatograph from Gas Chromatography Ltd, circa 1960. This is very difficult to photograph because it's 1.4 meters high but only a few cm wide. The device is shown with the boiler pipe insulation that surrounded the whole thing opened up to show the l.3m long "U" shaped, fixed, glass columns contained within the outer glass tube that acted as the oven.

However, fortunately most of us never experienced this type of equipment and increasingly, in the world of pharmaceutical analysis at least, our laboratories are filled with eager young scientists whose only exposure to chromatographic analysis is via HPLC-MS-MS. This wonderful technology is accepted as a commonplace rather than the miracle of modern analytical chemistry that it is. Indeed those of us who remember the moving belt or direct liquid interfaces had thought that, if this was the best that could be done in linking LC and MS, we could forget routine LC-MS in our lifetimes (if you are too young to remember these interfaces, be grateful).

Anyway, at some point, and I cannot really remember when it was, I noticed that the instruments I had been trained on (i.e those I could still actually use!) were disappearing from the lab. If they were lucky they were going to some deserving, but under-funded university department, but often they were heading straight into the skip. That's what happens to instruments, they become obsolete or wear out, better kit comes along, and the old stuff is replaced. And no bad thing either because, despite what people may say, in general the instruments are better these days. However, it was slightly sad to think of all of this "wonderful" old instrumentation being lost forever. After all, when it went into the skip a small part of my life went with it. Also there was some kit that was so badly designed that it deserved to be remembered so that the same mistakes would NEVER be repeated. So it was with a vague feeling of regret that I realised that I would never again have the opportunity again to burn my fingers trying to change a GC column in a hurry in a Perkin Elmer F17 (Figure 2) without breaking the column (actually it wasn't possible to change a column in a hurry in this instrument, but burning your fingers was guaranteed). Worse, it was becoming impossible to do chromatography without a computer to control the pumps and detector etc.

At some point this vague feeling of regret crystallised into a conversation on a bus (at the 20th ISC in Bournemouth) with Prof. Mike Cooke that

Fig. 2 A Perkin Elmer F17 GC once owned by the late Dr Roly Jones.

concluded that "something had to be done" (there may have been beer involved, I don't remember, though it is highly likely, but no minutes or other formal record of the "meeting" were taken). One of the things we decided to do as a result of the conversation was to form the Pye 104 Club as a special interest group of the Chromatographic Society. So why the Pye 104 Club and not the National Society For The Preservation And Celebration Of Historic Chromatographs? Well "Pye 104 Club" is shorter (and less pretentious) for a start, and also we rather thought that the people who would be interested in this sort of thing would be the sort of chromatographers who knew about this iconic instrument. A photograph of a 104 from my collection, obtained from the University of Surrey courtesy of Dr Derek Stevenson, is shown in Figure 3 (next to an almost identical looking Pye 105, which was the prep version). The 104 was built in the 1960s, and was built to last (indeed there are still some in use), it weighs a ton and is practically indestructible. It was such a popular instrument in the UK that it could be found, often in large numbers, in most industrial and university analytical labs for many, many years, and generations of PhD students learnt their craft on them. It also had the benefit of a capacious oven that you could heat your pies up in so that, even if the separation didn't work, you were at least set up for lunch. A classic. Anyway the Pye 104 Club was launched in October 1994 to a huge fanfare of publicity in the widely read and ever popular Chromatographic Society's Bulletin (Number 40). Naturally it just about sank without trace but, for those of you who really need to be a member, the 104 Club is still going and anyone who wants to join can do so by a one-off payment (for lifetime membership) of the princely sum of £15 for fellowship (where ideally you should have actually USED a 104, but we are flexible….) or membership at a trifling £10. There will only ever be 104 members in each category, so membership is much more exclusive than e.g., the Royal Society.

Fig 4. A Waters HPLC system comprised of two M6000 A Pumps, the Model 660 gradient controller, a UV detector, and a U6K injector (lying on its side in front of the pumps). I'm not sure that the UV detector is quite right for this particular model, and Ive been told that the "Rolls Royce" system came in a custom built cabinet (presumably with a proper mounting for the U6K). The 660 controlled the pumps via a pair of cables of which I have one. So anyone who can help with a contemporary UV detector, cabinet or controller cable…. I'd love to hear from you. I do have an authentic Waters refractive index detector which does fit with this set up.

What you get for this is a certificate that says you're in, which thereby implies that you have more money than you need as membership has NO benefits. However, the certificates are signed by a variety of great chromatographers including for example John Knox or James Lovelock so if you're an autograph hunter….The money goes to the Chrom. Soc. and every now and again (i.e. when there is enough) is used to provide sponsorship for students to attend meetings.

Sometime after the 104 club was formed I started to acquire instruments. Some of these I sought out, because they meant something to me, and some just turned up. They still do. They included not just GCs but also HPLC systems as well. So one of my first HPLC systems was the Waters M6000A setup shown in Figure 4. A wonderful machine, it could do gradients (of various shapes) and had a good UV detector and the U6K injector, which was good compared to e.g the Spec Ac, but lost out to Rheodyne in later years. Like the 104, the M6000 series dominated the HPLC landscape for some time before nimble predators like the Constametric pumps from Milton Roy began to bite back. I have an early Milton Roy in the collection (Figure 5) which I obtained from Klaus Borner in Germany. The instrument was delivered with a manual that said "give this to the man or men who will install the instrument", not something you are likely to see on any document these days. Next to it are a

Fig 3. A pair of Pyes!. The Pye 104 GC on the right was obtained from Dr Derek Stevenson of the University of Surrey whilst the (almost identical looking to the non-enthusiast!) Pye 105 on the left (the prep. version of the 104 was found by Dr Mark Powell (at the time of donation of Liverpool John Moores University).

Fig 5. An old Milton Roy HPLC pump (on the right) from Klaus Borner together with a ex ICI/Zeneca Constametric III HPLC pump and UV detector. The upright device between the Constametric and Milton Roy pumps is a primitive a computing integrator. No peaks, just a roll of paper giving retention times and peak areas. Things HAVE got better.

Constametric III pump (with a UV detector sitting on top) and a very user-unfriendly integrator.

As well as kit I also have acquired a whole range of interesting "bits" including some old bottles of stationary phases, columns and other ephemera.

At this point I have a total of 17 GCs in the collection (with a further 2 on long term loan to Schimadzu), I also have some 12 LC pumps and a variety of detectors. In the collection I also have the odd mystery instrument, where I don't even have the name of the manufacturer. Does anyone recognise the portable GC shown in Figure 6?

Unfortunately, I have fewer manuals than instruments, and manuals are quite important. Manuals however, do become detached from systems, and worse, thanks to GLP, are often archived when the instrument is disposed of. So if anyone as a manual for a HP5890, another iconic instrument, that they don't want I would be very pleased to receive it.

Fig 6. A mystery portable GC. I know nothing about this other than that I obtained it for Dr Derek Stevenson of the University of Surrey, no manual, no idea who the manufacturer was/is. Any help much appreciated on either front

Now, by this point many of you are probably wondering how I get away with filling the house with all of this historic equipment (or junk as it has been called by less charitable souls). Well, I'm lucky in that I have a large, and reasonably dry, cellar. Not an ideal place to store equipment, but better than a skip. I also have an understanding and long suffering wife (who doesn't yet have a use for the cellar!!!). However, if I can find a museum that will take the whole collection and look after it I will gladly pass it on (well most of it, it will take a lot to get take my last 104 and the M6000 system). But that is not as easy as you might think. For a start museums are not, as many people suppose, in the business of preserving everything that you or I might think was important. There is not enough money or space in the world for that, so they have to collect and display what will appeal to the public. At any one time very little of any museum's collection can be displayed and storage space costs. At this point ask yourself how many people in the whole of Britain are that interested in chromatography and analysis? (even with the benefit of CSI Miami etc,) and would therefore actually be interested in looking at a collection of old chromatographs and you will see the problem. Well, the group possibly includes you and me (obviously), but its not going to be a large number. Also, and this is not a criticism but a fact, museums are run by professional curators, not enthusiasts (like libraries are run by librarians and not authors). Enthusiasts run steam railways and love them, curators don't. Curators are professionals with a lot to think about and if, at some point, an artefact no longer fits in with the collection they have no compunction in disposing of it. Also, in moving things from one temporary storage space to another, things get "lost". For example I know of one major museum that cannot find a particularly large 1970s mass spectrometer (a Kratos MS8) that it had in storage and now wants. Now its not easy to "lose" something of this size (think "that's a big bit of kit", and then double it) and in all probability it was "cleared out" when the space was needed by someone who did not realise what it was, but did see that it was taking up an awful lot of room. As an aside, if you want to annoy a curator at a dinner party ask him if he knows the sad story of the last stuffed Dodo in the world. A genuine curator will. This unique exhibit, which if I remember correctly was in the Ashmolean Museum in Oxford, was in a fairly decayed state and was tossed on a bonfire by a curator who probably thought it "didn't fit the collection any more". Another curator was passing by and saw it burning. He did know its value, managed to retrieve a foot and the beak, and that is all we have left. What no museum will do these days is take an instrument on loan, you have to give it to them and, if they decide that they don't want it any more, they wont give it back (they will offer it around to other museums but if none of them want it, it's disposal time again!).

So whats to be done? Well the museums will conserve some of these instruments (just perhaps not the ones that you or I would have chosen) and not necessarily for ever. For example, the Science Museum in London has a very large collection but obviously, because of space constraints, most of it is not on display. Then there are a couple of positive strategies that could easily be adopted by the chromatographic community if preserving instrumentation was seen as being worthwhile. Firstly the instrument manufacturers could be asked

to keep an eye on their heritage. Many of them already do this and, as mentioned above, two of the instruments in my care are going home to Schimadzu UK in Milton Keynes on long term loan. This strikes me as one of the best options but, that said, takeovers happen, times change and companies go bust etc., (if you don't believe me try buying an analytical chromatograph from WG Pye Ltd of Cambridge). You can save the instruments yourself, if you have the space, and let the Pye 104 Club know about it (via the Chrom. Soc. or direct to me at ian.Wilson@astrazeneca.com). Perhaps in this way we can establish a extended "virtual museum" and whilst its hard to see it ever attaining the same degree of interest as you see at a steam engine rally it might still be fun. I'm not sure this is a good long term strategy (I shudder to think of the problem my heirs will have when they come to empty the cellar) but an uncertain future is better than no future at all. Then there is the option that preserves the memory but not the artefact - images on the net (not so much the ghost in the machine as the ghost of the machine!). Having just acquired a digital camera I'm in the process of photographing the instruments in my collection from all angles, and hopefully the Chrom. Soc. will put them on its web site. It would be a fitting thing to do in the Society's 50th year. Perhaps we could all do that?, its not the same as having the instrument to hand but, its better than nothing.

Finally if there is anyone out there who knows of a Pye Pan Chromatograph, a Varian Aerograph or a Perkin Elmer Model 154 Vapour Fractometer, or anything else of a historic nature that's still intact and just about to be disposed of, well I still have space in the cellar for a few more classic instruments (though at this point I need to make two important points here, 1) I save them, I don't buy them, so please don't ask me how much I will give you for an old chromatograph, and 2) please don't get in touch to say, "we had one of those until yesterday, last week, last month or last year but we chucked it away, if only we had known" I would prefer not to know). Manuals would also be of interest.

Those of you who are still in the early stages of your career probably can't see what all the fuss is about, but trust me, one day you will. ■

Patrick D. McDonald

James Waters and his Liquid Chromatography People: A Personal Perspective

by Patrick D. McDonald

James L. Waters, ca. 1965

A golden jubilee, a celebratory period provided by ancient law every 50 years — what better time to stand in the threshold of our discipline, like Janus, looking at once to both the past and the future. We are fortunate, as was Newton, to stand on the shoulders of giants whose perception, perspiration, and perseverance prompted a cycle of revolution and evolution in the practice of chromatography, leading it to its present position as a *central science* [1]. I am pleased to have this opportunity to review the role of Waters, both the man and his company [2], in some of the most fundamental developments that have determined how we practice liquid chromatography today, and that are leading the way toward solving the significant separation problems of tomorrow.

So many of the important achievements in chromatography, unlike in other scientific fields, have been accomplished by industrial scientists and engineers, not university professors. Separation science, crossing the boundaries of physics, chemistry, mathematics, and engineering, is perfectly mated to the interdisciplinary teamwork so strongly rooted in companies focused on uniting requisite resources to solve problems, create products, and partner with customers to meet their needs. Unfortunately, industrial inventors, unlike their academic colleagues, may perish if they publish, so they often labor in relative obscurity and disappear into the baseline of chromatographic history. A true entrepreneurial spirit—and a desire to make the world a better, safer place—pervades their best attempts to provide solutions that add value to, and have impact on, laboratory practice. In a sense, we in the analytical instrument industry are toolmakers. But revolutionary tools enable and challenge users to do what they were unable to do before. This activity then advances science in ways that truly improve our world.

Before Chairman Dr. Tony James [3] and Secretary Denis Desty convened, in 1956, the earliest GC practitioners and pioneers to share tips and techniques in the Gas Chromatography Discussion Group [GCDG], a young U.S. Navy veteran, armed with a degree in physics and engineering from Columbia University and his characteristic boundless determination and enthusiasm, was building instruments in the basement of his parents' modest colonial home in Framingham, Massachusetts. His mother, not wishing to have strangers in her house, decided when he hired his first employee that it was time to move his fledgling business elsewhere. In 1958, after selling his first company, James Logan Waters incorporated J.L. Waters, Inc., and moved from a spare room in a local hardware store to the basement of the former police station.

Early on, Jim developed instruments on a contract basis. But when his design for an on-line refractometer in process monitoring applications proved popular, it became a successful product for his five-man company. Engineers at Dow Chemical, Freeport, Texas, skilled at keeping current with the latest technology, spotted Jim's detector and alerted one of their polymer-chemist colleagues, Dr. John Moore. John called Jim in 1962 and asked for a custom unit with a 10x-smaller-volume flow cell. At first, Jim, unaware of what John was doing, argued that this was not necessary for process control. But, when he learned that John would pay for such a modification, Jim agreed to make it.

Several months passed. Finally, curiosity got the best of Jim. He sent his enterprising sales manager, Larry Maley, down to Texas to see how John was using his refractometer. Fortuitously, patent applications had been filed [4], so John was free to show Larry his new, homemade instrument designed to pass solvent through a column filled with controlled-porosity, cross-linked polystyrene-divinylbenzene beads and determine the molecular weight distribution of synthetic polymer samples [5]. John called his process *gel permeation chromatography* [GPC]. His concept had been inspired by the seminal work of Porath and Flodin who used dextran gels to separate biomolecules by size [6].

Larry took the decisive step on the path to the first commercial HPLC, concluding John's demonstration by boldly stating, "*Waters would like to build this for you!*" John had to convince his superiors in Midland that the best option would be to contract this dynamic, caring, but tiny, company in Massachusetts to commercialize his system, and not some giant analytical instrument concern like Beckman. In January 1963, Jim's hand trembled as he wrote a check in the daunting amount of $10,000 as a down payment on royalties for his exclusive license to GPC. He traveled to Freeport, spent three weeks learning every aspect of the process, including how to

synthesize the polymer beads, later to be sold under the mark Styragel, and returned to Framingham filled with ideas on how to construct an improved version of John's instrument. John, recalls Jim now, was a true genius who not only envisioned the mechanism, means of execution, and manifold applications for GPC but also assembled by himself all the pieces needed to practice it.

Within three months, Jim and his team had built five GPC-100 prototypes, using plywood for the cabinets to save time; three were sold to Dow, and one each to Dr. Jack Cazes at Mobil Chemical, and Dr. Dale Harmon at B.F. Goodrich. Though Jim is the first to credit the Nobel work of Professors Moore and Stein at Rockefeller University, after WWII, on systems for amino acid analysis via partition on potato starch [suggested to them by Dr. Synge], then ion exchange [7], it can be argued that these GPC-100s, delivered in March, 1963, were the first commercial HPLC systems. Professor Josef Huber in Vienna and, a bit later, Professor Csaba Horváth in New Haven, by their own admission [8], built their initial bench-top breadboard HPLC systems in 1963 and 1964, respectively. Csaba coined the name HPLC for a PittCon 1970 oral presentation [9]. And both he and Josef Huber used silica-based particles, rather than organic polymers. However, all the components of an HPLC instrument were embodied in Jim's GPC-100. In that system's manual, which Jim wrote himself, he even labeled its flow schematic *Waters Liquid Chromatography Assembly*.

It did not take long for polymer chemists to learn that a determination taking weeks could now be done in a few hours. Another brilliant move by Larry Maley was the creation of an annual GPC Symposium where successful early adopters and struggling users could learn from each other, thereby fostering best practices, not unlike the early days of the GCDG. First held in the cold of a Cleveland, Ohio, winter, 1965, it moved eventually to the warmth of Miami Beach, Florida [10], and, no doubt, like the GCDG, inspired many other user forums in our discipline — and elsewhere.

Jim's young company soon grew out of the police station and into a large building nearby which once housed the Bay State Car Company factory. In 1964, the second-generation GPC-200 debuted, and, the next year, Jim licensed some technology from Shell Development for liquid-liquid chromatography. Its implementation was unsuccessful, but two years later, in 1967, Waters introduced the **ALC**-100, a versatile system with both UV and RI detectors for executing all modes of ***A****nalytical* ***L****iquid* ***C****hromatography*. Then, in 1969, there followed the Chromatoprep™, a dedicated, open-frame, phone-booth-sized, preparative HPLC system with integral fraction collector.

Dr. Karl Bombaugh, Waters R&D Director, in the late 60s, initiated a fruitful consulting relationship with Professor István Halász, Csaba's mentor in Frankfurt [11], who guided Waters through the development of the first commercial GC and LC chemically bonded silica phases and the first pellicular silica packings for HPLC [trademarked Durapak and Corasil, respectively]. These signaled the ongoing commitment of the young instrument manufacturer to materials science, spanning both inorganic and organic substrates and surfaces, that continues to this day. However, the personal dedication Jim Waters instilled in his colleagues to make every customer successful is what carried his business to the next plateau.

Frustrated by failure on a Friday in late 1970, Dr. Helmut Hamburger, the Swiss-trained, chief postdoctoral fellow in Nobel-laureate Professor Robert Woodward's lab at Harvard, called Waters to ask for help in separating isomers of key intermediates in the total synthesis of Vitamin B^{12}. Jim had no idea who Woodward was, but when his marketing VP, Dr. James Little, told him that Woodward was perhaps one niche below Sir Robert Robinson atop the pantheon of organic synthesis gods, Jim concluded on the following Monday morning that he should tackle this problem himself. After all, he had wanted to penetrate this market ever since being told in 1968 by a Mobil colleague of Jack Cazes that every organic chemist ought to have an HPLC on his or her bench. So, he packed some columns, trundled an ALC-100 to the lab on Oxford Street in Cambridge, Massachusetts, and proceeded to solve separation problems for Helmut and his fellow postdoc, Dr. John McCall, one after another, while the master was traveling.

I was in the audience in Boston on Wednesday afternoon, July 28, 1971, when Woodward concluded an afternoon memorial symposium on Natural Product Synthesis [XXIIIrd IUPAC Congress], following such luminaries as Sir Derek Barton, Sir Alan Battersby, Professor Karl Folkers, and Professor Gilbert Stork. He began the B^{12} story at four and stopped at 7:45 p.m., pausing every 45 minutes or so to declare "*we could not have done this without liquid chromatography*." Every organic chemist of note was in the audience that had swelled to nearly 5000 after the parallel sessions ended at 5 p.m. No one left!

Woodward never mentioned who did these HPLC separations, or which company's products were used, but cognoscente spread the word like wildfire [12]. Jim Waters was not present at this seminal lecture. He was busy compiling a list of 900 names and addresses from an American Chemical Society directory of chemistry faculties. He mailed to each a package, including a glossy photo of himself with Helmut, Woodward, and, his new friend, Josef Huber [chromatography consultant to Woodward's B^{12}-race rival, Professor Albert Eschenmoser [13] at the ETH in Zürich], with the message: "*Look what we did for Woodward. We can do the same for you!*" Woodward later echoed: "*The power of these high pressure liquid chromatographic methods hardly can be imagined by the chemist who has not had experience with them; they represent relatively simple instrumentation, and I am certain that they will be indispensable in the laboratory of every organic chemist in the very near future* [14]." Following his example, a single HPLC peak soon supplanted a single TLC spot as a criterion for chemical purity in organic synthesis [15].

While following up the 100 replies to his marketing campaign catalyzed the onset of phenomenal growth for Waters, Jim, meanwhile, was supervising his last instrument design, one that inspired a succession of innovations destined to alter the HPLC landscape forever. He teamed with a brilliant engineer, Burleigh Hutchins, then VP of R&D, and an equally insightful, UK-born craftsman and machinist, Louis Abrahams, to invent the first dual-reciprocating-piston, 6000-PSI pump for HPLC, the Model 6000 [16]. Utilizing non-circular gears, a step motor, and feedback control circuitry to drive small-diameter parallel plungers sequentially for nearly pulse-less flow, this precision-volume solvent delivery device, first shown at PittCon 1972, was a true revolution — and so ruggedly reliable that many continued to be used for decades!

Competitors soon retired pressurized vessels and other primitive pumping means and sought to imitate the wildly successful M6000. Cottage industries sprang up to supply sapphire plungers, high-pressure seals, check valve assemblies, pulse dampeners, and other replacement parts. All this activity spurred rapid acceptance of HPLC in labs worldwide and accelerated the growth of the nascent HPLC industry.

Burleigh and Jim, together with further improvements by Dr. William

Carson and John Roe [17], redefined the state-of-the-art for temperature stability and sensitivity of the differential refractometer in the benchmark Model 401 detector. To complete a nearly simultaneous triple play, Lou also invented a novel valve and fluid circuit [18] that he and Burleigh used as the core of the first 6000-PSI-capable, septum-less HPLC injector, the Model U6K. The success of these products funded the construction of, and a move in the fall of 1973 to Waters present corporate headquarters and manufacturing location in the Bear Hill woods of Milford, Massachusetts.

This M6000/U6K combination was not designed merely to meet customer needs. It was necessary to fulfill the prophecy of Dr. Martin and Dr. Synge who wrote in 1941: "the smallest H.E.T.P. should be obtainable by using very small particles and a high pressure difference across the length of the column [19]." For, in a parallel Waters R&D program, Dr. Richard Vivilecchia, with Norma Thimot and the late Richard Cotter, created the first commercial 10-micron silica columns for HPLC: µ Porasil™ silica announced in December 1972, and µBondapak® C^{18} in early 1973. Using reactions invented by John Speier at Dow Corning [20], Dick Vivilecchia synthesized octadecyldimethylchlorosilane and therewith created the first commercial monofunctionally bonded C^{18} column. Though his proprietary process for silica treatment, surface bonding, and end capping prompted a host of attempts at imitation, it remains unique to this day. Later in 1974, based upon my work in preparative LC, I suggested that Dick switch to a superior silica substrate. This improved µBondapa®k C^{18} packing produced the best-selling HPLC column in history. Waters chose not to patent the silane or disclose the process details. Five years later, when Waters subcontracted the silane synthesis on a non-exclusive basis, it became commercially available for anyone to use, and nearly everyone did!

A column's physicochemical and performance properties may ultimately lead to successful separations in the hands of experienced practitioners, but in the earliest days of HPLC, novices needed guidance and feasibility demonstrations to induce them to use this novel technique. Out of the ranks of pharmaceutical chemists, a prophet emerged to preach the gospel of reversed-phase HPLC. Charles Pidacks left his position as LC guru at Lederle Laboratories to join Waters in mid-1971 and proceeded systematically to inject every known therapeutic compound into a Corasil®/C^{18}, or later, a µBondapak™ C^{18}, column. He compiled a bible of pharmaceutical separations and, for a decade, traveled extensively to every corporate lab and industry forum to convert his former colleagues. James Clifford, an artist with a pen as well as a protocol, who personally packed more than 100,000 columns in his three-decade career at Waters, at Charlie's request, drew a cartoon showing a column flying on angel's wings. To combat the despair of those yet uninitiated in the intricacies of HPLC, Charlie used this image to show that when every good column dies, as it must, it goes to heaven, not hell. Charlie, more than any other single person, was responsible for the rapid acceptance of HPLC in the pharmaceutical arena where it rose to predominance as an analytical, and ultimately, a preparative separation tool.

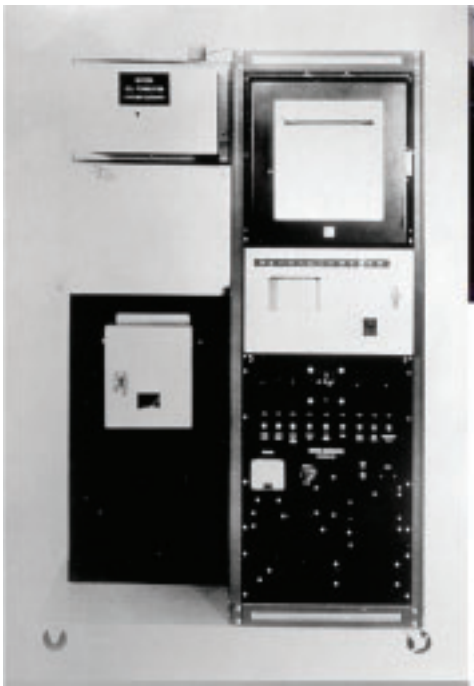
A major component outlier in the early drive by Waters to control its HPLC system destiny was the outsourced UV detector. Enter Ken Nelson, another interdisciplinary wizard, who conceived the taper cell [21] and designed the optics bench, as well as the circuitry, for the Model 440 detector, creating a benchmark for sensitivity and stability. Meanwhile, Burleigh and Lou were busy inventing another pump concept, a simpler design using only two check valves and a single motor to drive separate primary and accumulator pistons in series [22]. While the ensuing M45 product did not generate the sales of the M6000, the concepts embodied in this seminal design were used to great advantage by major competitors.

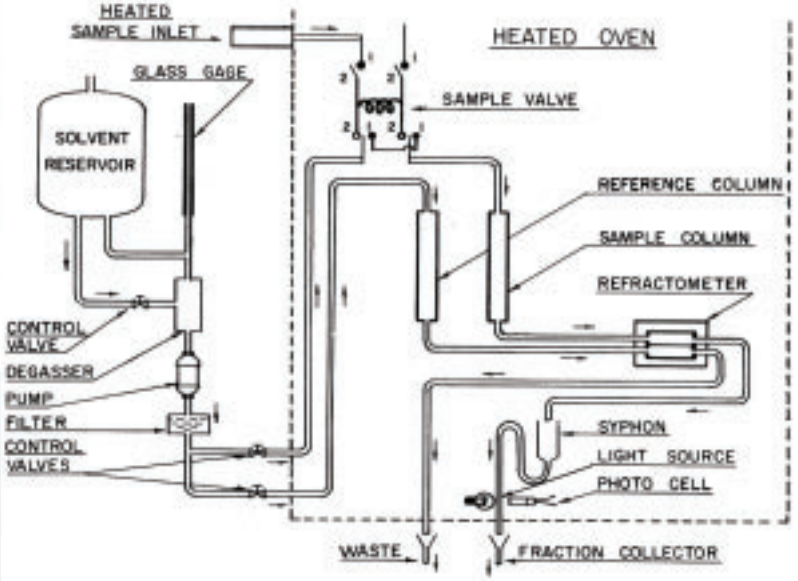
Often overlooked is the catalytic role Waters played in the emergence of LC-grade solvents for mobile phase and sample preparation. In the late 1960s, a Waters applications chemist, William Dark, asked suppliers to find a way to stabilize chloroform with something other than ethanol. Nominally 0.75%, the actual ethanol concentration varied so widely that it wreaked havoc on retention-time reproducibility in normal-phase separations on silica gel. The first to solve this problem was Mallinckrodt. They created a special grade of chloroform containing a percent of mixed amylenes, non-polar inhibitors of phosgene formation. About the same time, a young company in Michigan began to sell a range of useful, high-purity, organic solvents distilled in glass. When customers asked Waters chemists which brand of solvents they used, their recommendation was Burdick & Jackson. Word spread, and B&J's business boomed.

For a few years, before 1980, Waters forged a foray into the LC-solvent business. Specifications and analytical protocols using LC and GC that I helped to develop for our suppliers led to major improvements in the quality of methanol, acetonitrile, tetrahydrofuran, and other key mobile phase components, especially water. Even before our merger with Millipore in 1980, we taught them how to use gradient HPLC to determine trace organic levels in high-purity water. Their MILLI-Q® System, with an integral organic-removal cartridge, ultimately achieved benchmark status for water quality. When we exited the business, we shared all our test procedures and demanding requirements with the industry, thereby creating a competitive environment from which all users ultimately derived significant quality and performance benefits.

In retrospect, instrumentation expressly designed to operate new column technology, as with the GPC-100 or the M6000/U6K, has been a sure signal of separation power with the potential to alter the course of science. Waters did this a third time in March, 1976, with the introduction of the PrepLC™/System 500, incorporating a special dual-radial-compression chamber to hold dry, disposable, thin-plastic-walled column cartridges filled with nominal 75µ-silica packing. When I joined Waters in 1974, Jim Waters challenged me to prove his theory that larger particle columns, in series or via recycle, could equal the

Figure 1: Clockwise from top left: One of the first five GPC-100 Prototypes in its plywood cabinet; Parents' home in Framingham, MA, where Jim Waters began his first business; Flow schematic on page 4 of 1963 Instruction Manual for first GPC-100 [personal copy from Dr. Jack Cazes]; 1965 Waters First Gel Permeation Chromatography Symposium in Cleveland: left to right, holding model of a high-molecular-weight polymer chain: Jim Waters, Dr. John C. Moore [Dow Freeport], plenary lecturer Prof. Fred W. Billmeyer, Jr. [R.P.I.], and Waters sales manager Larry Maley; Nicky Anastis tends a Styragel® particle synthesis [reactor made from a 55-gallon metal drum] in former ladies' cell on second floor of police station; Cover of 1969 brochure for Waters Chromato-Prep preparative chromatograph [note then new 'batwings' logo]; Second generation GPC-200 [1964]. [© 2006 Waters Corporation, used with permission]





WATERS LIQUID CHROMATOGRAPHY ASSEMBLY.

separation power of small particles but with orders of magnitude higher load capacity. This I did [23] while also finding the first new way of packing columns in the then 75-year history of chromatography [24]. Operating under non-linear-adsorption isotherm conditions, flying in the face of conventional wisdom, we routinely purified ten grams of sample in ten minutes, at flow rates up to 0.5 L/min.

Our best serviceman, Richard Turner, and I installed the third PrepLC™/System 500 instrument in the chromatography lab at Harvard shared by Woodward and Professor Elias James 'EJ' Corey. That day, still on a wooden wall rack in the corner, I was excited to find the long steel columns, with tags in Jim's handwriting, that he had used in the ALC-100 there six years earlier to do the B^{12} separations. EJ, who was awarded a Nobel Prize in 1990, was so impressed with our system's performance that he later called it, in a New York Times interview: "*a revolution in liquid chromatography.*" He cited it and an Exxon catalyst as: "*good examples of the fine technological work in American industry.*" [25]

Following this success, Burleigh sought to divide the radial compression team and conquer new worlds. Carl Rausch was teamed with Dr. Yuri Tuvim, Dick Vivilecchia, and a new hire fresh from graduate school, Dr. Uwe Neue. They invented Radial-Pak™ Cartridges and the Radial Compression Separation System for analytical HPLC [26].

I, on the other hand, was commissioned to "*find new, faster, more convenient ways to do traditional sample preparation operations.*" In an internal memo, dated June 13, 1977, I proposed a project to "*solve a real analytical problem using, whenever possible, our LC technology,*" and "*get to product design and development as quickly as possible.*" Together with Dick Vivilecchia and a young chemist, David Lorenz, hired appropriately from Dr. James Thean's Florida State Department of Agriculture lab in Tallahassee, we watched the fruit of our labor ripen on October 24, 1977, the birthday of the **SEP**-PAK® Cartridge [27]. We used triaxial bed compression and hermetically sealed, individual packaging to maintain adsorbent activity, bed integrity, and performance uniformity. On January 9, 1978, we shipped the first commercial, disposable, silica-based-adsorbent LC columns for ***S****ample* ***E****nrichment and* ***P****urification* via a technique one of the myriad of competitors, J.T. Baker, years later named, in a play on acronyms, *solid phase extraction* [SPE]. Two years and eight months elapsed before a competitive product came to market. What followed was explosive growth in the application of SPE to a full spectrum of sample preparation problems in every lab around the globe. Today, nearly three decades later, SPE is still growing rapidly and stands as a predominant analytical technique.

In the 1980s, HPLC became the tool for applications in every field where a sample could be dissolved in a mobile phase. Even through this evolutionary period, there were undercurrents of invention and technology developments in many areas. At Waters, the late Dr. Herman Schultz, a brilliant polymer chemist, and his team improved all our polymer-synthesis processes while learning to tighten control of important variables such as particle diameter and pore-size distribution. He and Raymond Fisk even applied organic polymerization principles to the synthesis of an inorganic polymer [a sol-gel silica, trademarked Nova-Pak, 1982], for which they won the Grand Annual Millipore Award for Technical Innovation. This seminal groundwork led to several subsequent materials-science blockbusters, beginning with Symmetry® spherical-silica packings in 1994, synthesized by Dr. John Petersen's team in high purity directly from tetraethoxysilane. While not the very first HPLC silica made this way, it was, and remains, the most reproducible, in large measure because of Waters commitment to controlling every aspect of its synthesis.

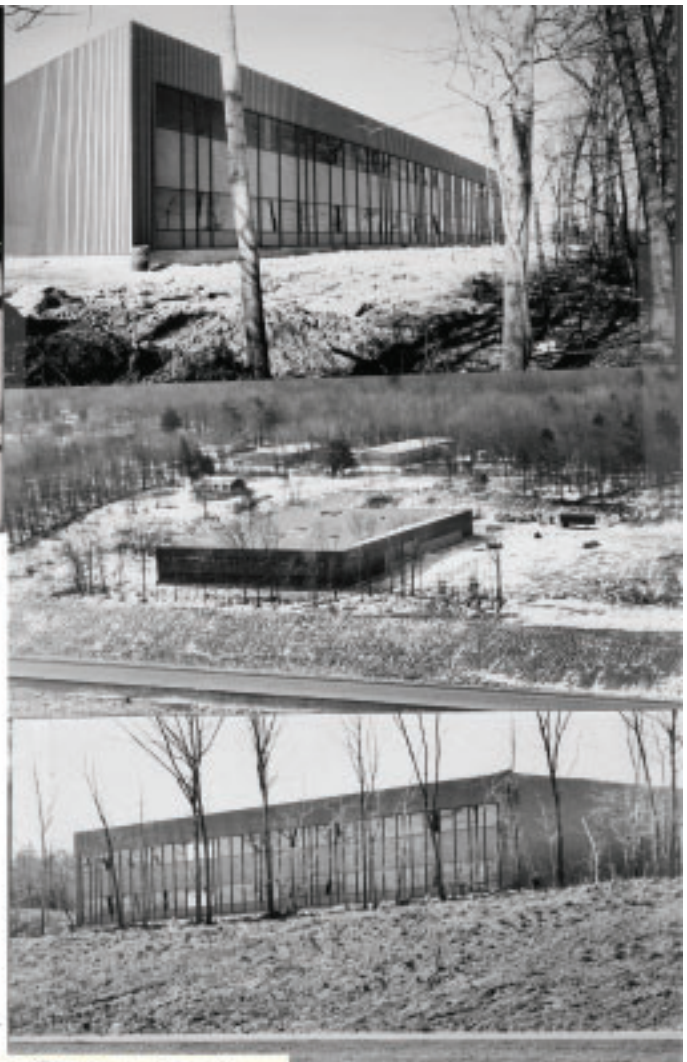
Commercially available bonded-phase functionalities [C18, C8, C4, phenyl, etc.] became generic in name, if not necessarily in quality or performance. Dr. Uwe Neue and John directed a young Ph.D. candidate, Carsten Niederländer to synthesize a new, long-chain alkyl silane containing an embedded-polar carbamate group. With this reagent, they made, in a single step, a packing material exhibiting superior peak shape for basic compounds [28]. This shield chemistry, so called because of its apparent ability to mitigate the effect of surface silanols, was used first to make SymmetryShield™ RP18 columns. Later it was applied with even greater success to silica-hybrid substrates [see later] to achieve the best peak symmetry ever seen for basic compounds, as predicted by a radically new theory about how reversed-phase separations function [29]. Shield phases serve as a unique, and, in some cases [*e.g.*, phenols], a dramatic [30], alternative to the traditional selectivity of strictly hydrophobic reversed phases. To share his vast experience and insight, Uwe, the 2005 Halász Medalist [31], literally, wrote the book on HPLC columns [32].

What Symmetry® columns did for retention times, Waters Alliance® HPLC Systems, introduced in 1996, did for flow rate and mobile phase composition, reproducibility and system reliability. Two fundamental changes in pumping practice were developed at Waters in the late 80s. First, Theodore Dourdeville and David Trumper devised, for the 600 system, a means to use a microprocessor for real-time modulation of motor speed to enhance the stability of short-term flow rate [33]. Tad then designed a pump, first used for capillary LC, with a one-motor-per-piston, linear drive and with one pressure transducer for each cylinder, to provide independence between, and precise control over, the intake and delivery strokes [34]. This concept was refined into a two-motor, two-piston, serial-flow format for the Alliance® 2690 Separations Module.

Accuracy in its low-pressure solvent-proportioning feature was thereby greatly enhanced. An overlay of ten gradient chromatograms appeared as a single trace [35]! SDI termed this new yardstick by which HPLC performance was measured "*one of the most successful products in the history of analytical instruments*" and "*an important influence in fundamentally transforming the industry.*" [36]

That same year, Waters morphed from a minor player to a major leader in mass spectrometry by acquiring Micromass® Ltd., Manchester, England. And, further validating that year's slogan, "*It's All Important,*" we introduced the next revolution in SPE at ISC '96 in Stuttgart: Waters

Figure 2: Clockwise from top left: Publicity photo for organic synthesis marketing program: left to right, postdoctoral fellow Dr. Helmut Hamburger, Prof. Josef F.K. Huber [Vienna], Jim Waters, and Prof. Robert B. Woodward [Harvard], taken in Woodward's chromatography lab [ALC-100 at right]; Three views of new 50,000-sq.-ft. Waters Milford facility under construction in early 1973 [spring snow on the ground]; Charles Pidacks, holding new brochure for Waters PIC™ Reagents [about 1977]; First issue of Waters Chromatography Notes, January 1970 [headline: The Renaissance in Liquid Chromatography]; Cover of first brochure for Model 6000 Solvent Delivery System [1973]; Waters ALC-200 series cabinet fitted with R400 Refractive Index Detector, M6000 pump, and Model U6K injector [1973]; Separation of Vitamin B^{12} synthesis intermediate cobyrinate isomers, differing only in conformation at position 13, on five 2' x 1/8" I.D. Corasil II silica columns in series, using recycle; Cover of Abstract Book from 1971 IUPAC Congress, Boston, where Woodward described this work; Cover and illustration from brochure for ALC-100 [1967]. [© 2006 Waters Corporation, used with permission]




Functional Systems . . .
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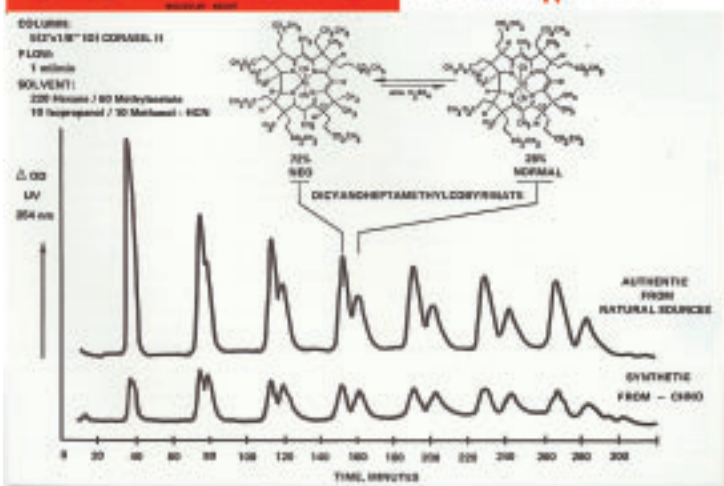
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ABSTRACTS of PAPERS
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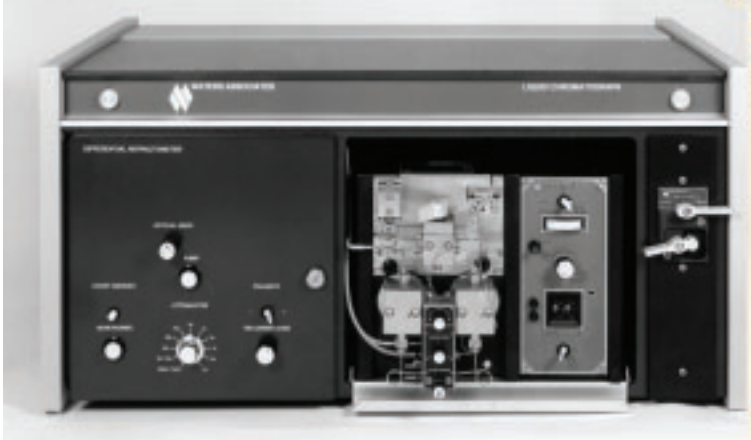


MODEL
6000
SOLVENT DELIVERY SYSTEM


Chromatography Notes

Oasis® HLB sample extraction products [37]. In the past decade, this growing family of devices, containing adsorbents based upon a patented polymer unique in its ability to remain wetted in aqueous phases, while retaining analytes by hydrophobic or mixed-mode interactions [38], has risen to a position of performance and market leadership, unmatched in the industry.

At HPLC '99 in Granada, Spain, Waters announced its next materials-science breakthrough: *hybrid-particle technology* [39]. Dr. Zhiping Jiang and his colleagues blended two co-monomers, tetraethoxysilane and triethoxymethylsilane, to create a porous spherical particle with organic functionality distributed throughout its backbone, reducing by one-third the residual population of surface silanol groups. Proprietary bonding protocols using traditional silanes generated packings with a familiar range of selectivity, improved peak symmetry, and an order-of-magnitude increase in high pH stability. Sales of XTerra® columns sky-rocketed, making them, by far, the fastest selling HPLC columns in history—until even this steep trajectory was surpassed in 2005 by that of XBridge™ columns containing second-generation hybrid technology. Now successfully armed with an ability to design and synthesize tailored particle surfaces and backbones, even deep within micropores, we may consider experiments that can challenge or confirm novel notions of how chromatographic separations occur [29].

Continuing our hybrid research program, Dr. Kevin Wyndham and his co–workers made two exciting discoveries after preparing particles made by incorporating an ethylene bridge into a silane co-monomer. Resistance to hydrolysis at high pH was improved by another order of magnitude beyond that of the first generation methyl hybrid. Even more important, their 1.7 µm-diameter particles were highly pressure-resistant [40].

This encouraged our engineers to design the ACQUITY Ultra Performance LC™ System, capable of operating at 15,000 PSI. For the fourth time, Waters created new instrumentation to accommodate novel column technology [41]. Introduced at PittCon 2004 with ACQUITY UPLC™ BEH Columns, this holistically designed system further refined the 2690 pump concept into a two-motor, two-piston serial-flow device for high-pressure gradient formation. The linear drive, as well as brilliantly designed check valves, seals, transport tubing, and software algorithms, are key for uniform delivery of compressible liquids at very high pressure.

Using 1.7 µm particles at 15,000 PSI is something about which Martin and Synge could only dream [19]. A key to minimizing band dispersion for highest efficiency, while maximizing sensitivity, in this UPLC™ system is detector flow cell design. In 1989, Dr. Anthony Gilby had transformed Ken Nelson's legacy by tapering the light beam, rather than the cell, used in Waters optical detectors in the early 90s [42]. Two years later, he and Bill Carson conceived a high-efficiency, light-guiding flow cell approach ideal for reduced-volume separations. Ongoing refinement by Tony, Tad, and Dennis DellaRovere [43] led to the cell types used in capillary-scale LC and, eventually, in the UPLC system.

UPLC performance continues to be extraordinary [44] and award winning [45]. Even more amazing is the effort of more than six dozen inventors [nearly 40 new patents filed to date] and principal contributors from Waters R&D organization, supported by a team of more than 400 who brought it to the marketplace. Unfortunately, memory and space do not permit naming here the myriad of contributors to the successful development and launch of all the Waters innovations in the last five decades.

On November 16, 2005, Jim Waters and his bride of 58 years, Faith, visited Milford to celebrate his 80th birthday [October 7th] with about thirty folks he had hired and hundreds he has inspired. He told us how proud he was that we had used his simple formula for success—*innovation, a good attitude, and hard work*—to usher in the dawn of a new era in separation science. I am humbled and honored by the opportunity to document in this golden jubilee volume, for the first time, the tale of Jim, his liquid chromatography people, and their enormous impact on the practice of liquid chromatography.

Acknowledgments:

I wish to thank Jim Waters for selling me an ALC-100 during my postdoctoral days in 1971, and Dick Vivilecchia [now at Novartis] and Burleigh Hutchins for hiring me in 1974. They introduced me to HPLC, taught me how to invent, and enabled my career. Special thanks to Jim also for his extended conversations with me in recent years, as well as several long-time Waters employees, whether retired, or still active, who have supplied many details, documents and images for this historical record. Thanks to Jim and to my talented colleagues Brian J. Murphy, Dawn Maheu, Tad Dourdeville, Uwe Neue, Tom Walter, and Mark Baynham for their critical review of this manuscript and assistance in its preparation.

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*Note: Where indicated below, use search term following * to access PDF document in Waters Library at http://www.waters.com*

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Figure 3: Clockwise from top left: Dr. Herman S. Schultz [1984]; William A. Dark [1984]; Norma Thimot [1984]; PrepLC™/System 500 with dual Prep-PAK™ Cartridge compression chamber at right–chemist pointing at retained sample debris on used cartridge [1976]; Sep-Pak® Silica Cartridges and original sealed foil pouches [Feb. 1978]; David R. Lorenz, left, and Dr. James Thean in Talahassee laboratory [1977]; Radial Compression Separation System and Radial-Pak™ Cartridges [1978]; Alliance® HPLC System [2005]; ACQUITY UPLC™ System and its principal inventors and developers, holding 2005 R&D 100 Award plaque; Synthesis scheme for second-generation hybrid particles [2004]; R&D 100 Award winners for hybrid-particle technology: left to right: front: Dr. Zhiping Jiang, Pamela C. Iraneta, Raymond P. Fisk, rear: Dr. John E. O'Gara, Christopher C. Benevides, Dr. Thomas H. Walter [2000]; left to right: Dr. William Carson, Theodore 'Tad' Dourdeville, and Dr. Richard M. King [1985]. [© 2006 Waters Corporation, used with permission]


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Ted Adlard

The Gas Chromatography Discussion Group

by Ted Adlard

In 1950, A.T. James was working with A.J.P. Martin at the National Institute for Medical Research at Mill Hill on the outskirts of London. This was a remarkable institution where scientists were given a considerable degree of freedom in their investigations so that a research project which departed from its original goal was not uncommon. An account of this remarkable institution can be found in Jim Lovelock's autobiography "Homage to Gaia."

Tony James was trying to develop an automated method for fractional crystallisation (which later became zone melting) and when he became discouraged at his lack of progress, Martin suggested that he should try gas-liquid partition chromatography (because, according to James, he, Martin, *knew that it would work*). The possibility of gas-liquid partition chromatography had been clearly stated by Martin and Synge in their seminal paper on partition chromatography in 1941 but no one had followed up the suggestion in the intervening nine years although several groups in Europe and the USA had developed gas-solid chromatography with limited success.

After trying over 30 columns, James and Martin were sufficiently successful to describe their work to small meetings of the Biochemical Society in the next two years. As biochemists, they were interested in the separation of fatty acids and amines which had the advantage that these compounds could be detected and measured by manual titration of the column effluent. However they realised that the technique should have wider general applicability and they decided to try to separate hydrocarbon mixtures. Martin contacted the Anglo-Iranian (now BP) Research Centre at Sunbury-on-Thames with a request for some sample hydrocarbons and D.H. (Denis) Desty was sent from the Research Centre to find out exactly what was required. Desty immediately realised that significance of James and Martin's work and persuaded his management that the method should be investigated at Sunbury. Somewhat earlier, an ICI research worker, N.H. Ray, had visited Mill Hill and had initiated work on gas chromatography at ICI. Ray had also suggested to Martin that a thermal conductivity device might be used as a detector. For some reason, Martin did not favour the idea and so, when he and James started to separate hydrocarbons which were not amenable to titration, Martin went on to develop the elegant, but ultimately doomed, gas density balance. Ray went on to develop the now ubiquitous method of sample injection through a rubber septum and ICI suggested to Shell that gas-liquid chromatography would be a suitable method for the analysis of commercial xylene mixtures.

By 1952 James and Martin's work was becoming more widely known and Courtenay Phillips at Oxford who had been investigating gas-solid chromatography switched to gas–liquid chromatography with considerable success. The real breakthrough occurred at a meeting of the Society for Analytical Chemistry held in Oxford in September of that year, attended by some 400 people from industry. Martin and James presented a paper which, among other things, described an elegant automatic titration detector which they had designed and built. The enormous leap forward that their equipment represented can be best appreciated by comparing it to the apparatus described by Claesson in his work published in 1945. Phillips also gave a paper that included the first example of column temperature programming. The excitement generated by these presentations was intense and many industrial organisations, particularly Shell, BP, ICI and Distillers instituted major development programmes, Advances followed rapidly and Desty persuaded his immediate supervisor, Dr S.F. Birch, to obtain the backing of the Hydrocarbon Research Group to sponsor a symposium which was held in London in May/June 1956. (The Hydrocarbon Research Group had been established during the war by a number of major UK companies to sponsor research on the synthesis of pure hydrocarbons required for the IR analysis of enemy fuels). This meeting was an outstanding success and it was agreed that a discussion group should be formed to disseminate the wealth of ideas that were being generated by the new technique on an almost daily basis. Again Denis Desty was the instigator and champion of the idea and so the Gas Chromatography Discussion Group was formed. The second international symposium took place in Amsterdam in 1958 and in retrospect it is clear that this meeting was almost the most important in the history of chromatography since Ian McWilliam described the flame ionisation detector and Marcel Golay described capillary columns. Perhaps the only comparable advances were the development of HPLC in the early 1970s and of silica capillary columns in 1979. Golay worked for Perkin Elmer in the USA and it is somewhat ironic that whereas capillary columns were eagerly seized upon in Europe (especially in the petroleum industry) it was not until the development of silica capillaries that such columns were much used in the USA.

From 1957 the Gas Chromatography Discussion Group held 3-4 meetings a year where people such as Ray Scott, Howard Purnell, Ervin Kováts and Jim Lovelock gave papers on their work. It was at one of these meetings that Lovelock first described the argon ionisation detector, the forerunner of the electron capture detector. From 1957 until 1972 the Gas Chromatography Discussion Group was run under the auspices of the UK Institute of Petroleum which provided secretarial help and a venue for committee meetings. This was a mutually advantageous arrangement, bearing in mind the very large part in the development of GC played by the petroleum companies but by 1972 this arrangement had outlived its

usefulness and the Group became an independent organisation based at Nottingham Trent Polytechnic. This came about through Ralph Stock, a member of the Group for many years and the head of the Science Department at Trent Polytechnic. At this time liquid chromatography was beginning to appropriate the instrumental developments of GC and became HPLC, so it was decided to change the name to the Chromatography Discussion Group. In 1984 the name was finally changed to the Chromatographic Society, the Chairman became President and the secretariat moved to offices in the centre of Nottingham. C.E.R.(Roly) Jones was the first President under this new title.

The Gas Chromatography Discussion Group was the model for similar organisations in a number of European countries such as France, Germany and Denmark and for similar bodies in the USA. By the late 1970s the membership was well over 1000 but gradually declined from this number as GC and HPLC became "mature" techniques.. The strength of chromatography was greatly enhanced when first GC and then HPLC were successfully combined with mass spectrometry (a combination predicted by Howard Purnell in the late 1950s). GC-MS instruments were first manufactured in the early 1960s but it was not until the advent of the quadrupole mass spectrometer and computer data handling that the combination was anything but a research tool. We have now reached the stage of HPLC-UV-MS-MS-NMR and who knows what the future holds. The next advances are likely to be in the realm of microtechnology so elegantly predicted by Martin in 1962. It is hard to imagine what the analyst would do if chromatographic methods did not exist and no doubt Tswett and Martin would be amazed to see how their infant ideas have grown to the overwhelming importance they have today. ■

A Century of Separation Science. Celebrating the Past: Predicting the Future

On 1st and 2nd April 2004, the Chromatography and Electrophoresis (C & E) Group of the UK Royal Society of Chemistry held a meeting on the above topic in York, to mark the 100 years that have passed since Michael Tswett's first publication on chromatography. Twenty-two papers were presented covering practically the whole range of separation science from its earliest beginnings to possible future prospects. The meeting was attended by 130 delegates from a number of countries and also hosted an exhibition by the major instrument and supply companies.

The Chromatographic Society, one of the sponsors of the meeting, invited a number of it past Chairmen/Presidents and the group photograph of all those who attended shows a line up of a number of "old timers" who thoroughly enjoyed the reunion. Sadly Dr C.E.R. (Roly) Jones, shown fifth right on the front row, died the following week. Tom Lynch, the Chairman of the C & E Group, is slightly to the left in the middle ground, immediately behind Professors John Knox and Keith Bartle.

Dr Greg Saunders

A Historical Overview of Size Exclusion Chromatography

by Greg Saunders, Polymer Laboratories

Introduction

The development of polymers has had a profound effect on the modern world. These versatile materials are used in an almost limitless array of products, ranging from drinks bottles and compact discs to shampoo additives and prosthetic hip joints. The first modern truly synthetic polymer was 'Bakelite', developed by Baekeland in 1907 from the condensation of phenol and formaldehyde. During the 1950s, advances in polymer science led to the development of many of the now common synthetic polymers, such as polystyrene and poly(vinyl chloride). Engineering polymers such as polyethylene, polypropylene and polyurethane followed in the 1950-60s, and have become extremely important commodities. Recent developments have been in the area of speciality high technology materials, such as polymers displaying high thermal and chemical stabilities like the polyaryletherketones, polyimides and polytetrafluoroethylenes. Over the years, many thousands of different classes of polymer have been developed from a range of different chemistries, making plastics the most versatile of materials.

The increase in the popularity of plastics has necessitated the need to develop methods to fully characterise these materials. There are many parameters that affect the performance of the polymer, including melt viscosity, toughness and glass transition temperature. However, one property that strongly influences many other physical parameters is the molecular weight distribution or the distribution of chain lengths in the sample. This article discusses the development of size exclusion chromatography (SEC) as a technique for analysing polymer molecular weight distributions. (Note: The term gel permeation chromatography (GPC) is also a widely used term to describe this separation.) The development of hardware will be considered but the discussion of columns shall be restricted to polymeric SEC gels, not the silica materials that often are used for the separation of proteins and other biological macromolecules. The development of SEC methodologies for the rapid determination of molecular weight employed in high throughput experiments are also outside the scope of this article.

Column Technologies for SEC

Generally speaking, there has been a significant advancement in the columns used for SEC. With improvements in the manufacturing processes used for the preparation of SEC media, higher column efficiencies are now achievable compared to the materials originally employed for separations. Consequently, the number and length of columns used in a typical analysis have decreased significantly, with a concurrent reduction in typical analysis times. Whereas early SEC experiments may have taken several hours, analysis times of less than thirty minutes are now commonplace and much faster chromatography is achievable for specialist applications.

Chromatographic techniques for separating polymeric materials on the basis of size in solution were first developed in the late 1950s and early 1960s using polydextran and polyacrylamide 'soft gel' materials. The technique was named 'gel filtration chromatography (GFC)' and was used to separate water soluble polymers. These soft gels had a 'microporous' structure, in which a low degree of crosslinking (typically under 10%) yielded a non-rigid material with the pore structure introduced by swelling in a solvent. Unfortunately, the low mechanical stability of these materials restricted their use to applications involving low flow rates and long analysis times and they were also intolerant of extremes of pH and organic solvents. These materials are still employed for the analysis of proteins and polyacrylamide, agarose and polystyrene/divinyl benzene softgels are readily available. However, it was the limitations inherent in these materials that led to the development of highly crosslinked macroporous materials.

Macroporous semi-rigid particles for SEC were first developed by Moore. Synthesised by suspension polymerisation, these materials had far higher crosslinking than the microporous gels, resulting in rigid structure with limited swelling. The pore structure was introduced by the use of porogens during synthesis and was well defined compared to the soft gels. As a result, these semi-rigid particles were mechanically strong and could be used at higher flow rates. The pore structure could also be tailored during synthesis to generate materials with a range of pore sizes. Figure 1 compares and contrasts micro and macroporous materials.

As a result of the controlled pore sizes and mechanical stability of macroporous materials they are far more widely used for size separations than microporous gels. They are available in a wide variety of chemistries from (relatively) polar to non-polar, the most popular being copolymers of styrene and divinyl benzene. Early suspension polymerisations produced macroporous gels with a narrow pore size distribution and a fairly narrow particle size distribution. A range of manufacturers commercially produces these 'individual pore size' gels.

SEC columns packed with individual pore size materials are quite versatile in application, being robust enough for use with a wide variety of organic solvents. The limitation of individual pore size materials is that they only give resolution over a short range of molecular weight. Therefore, to increase the resolving range of the separation, several columns of different pore size must be combined together in series, for example, a column set

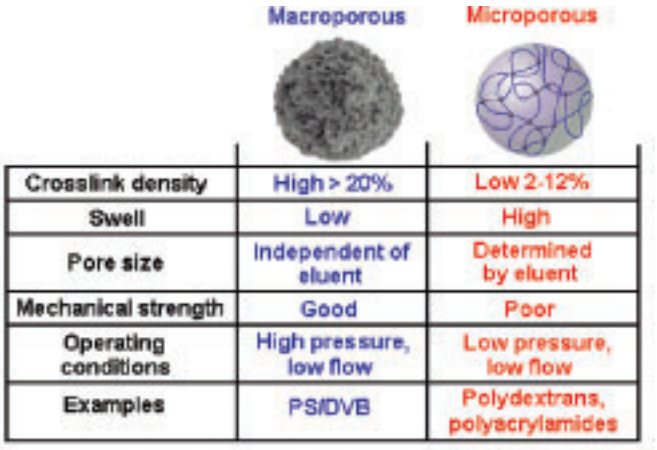


Figure 1. Comparison of micro and macroporous materials for size exclusion separations.

comprising a PLgel 5µm 106Å, 104Å and 500Å resolves from over 10,000,000 g/mol down to 500 g/mol (polystyrene equivalent in THF).

A further limitation of individual pore size materials is the artefacts that can occur when combining columns together due to the overlap of the resolving range of the columns. Mismatches in pore volume in these regions can cause shoulders on chromatograms known as 'dislocations'. To combat this effect, a new column type was introduced in the early 1980s, the 'linear' or 'mixed bed' column. In these columns, a homogenised mixture of individual pore size gels is introduced to cover the desired resolving range, with the proportion of each gel carefully selected to ensure that the resulting calibration curve is linear and that no dislocations occur. The majority of SEC applications are now performed on columns of this type.

Recently there has been a new development in organic SEC with the introduction of 'multipore' gels. These materials are composed of a single gel type (like individual pore size materials) but each polymeric particle contains a wide range of pore sizes. Consequently, 'multipore' columns packed with a single type of material have very wide resolving ranges, removing the possibility of dislocations and the necessity to blend materials (as in mixed bed or linear columns). A further advantage of the methods used to manufacture these gels is that the pore volume is very high, leading to an increase in resolution compared to traditional SEC materials. These 'multipore' materials represent the cutting edge in SEC column technology.

Aqueous SEC columns have been developed in parallel with the products for organic solvents, but the range of columns available is much smaller due to the limited market for water soluble polymers. Of the three column types discussed above, aqueous columns based on 'individual pore size' and 'mixed bed' gels are available, but there are no currently available 'multipore materials. For SEC columns to work successfully in water, the hydrophillicity of the packing material must be increased significantly. Polymeric-based gels are typically highly non-polar and so some modification of the gel must be performed, either in terms of secondary treatment of the surface or alteration at the synthesis stage to utilise different monomers. However, for many aqueous separations silica based materials are still popular.

Table 1 shows examples of the three classes of columns available from various manufacturers. Figure 2 shows an overlay of calibration curves for typical individual pore size, mixed bed and multipore columns (Polymer Laboratories' PLgel 5µm 500Å, PLgel 5µm MIXED-C and PolyPore columns).

Column type	Column Range	Organic or Aqueous	Manufacturer
MultiPore	PlusPore		Polymer Laboratories
	TSK-GEL HXL	Organic	TosoBiosep
	Shodex K-series		Showa Denko
Mixed / Individual	PLgel	Organic	Polymer Laboratories
	PL aquagel-OH	Aqueous	
	TSK-GEL HXL	Organic	TosoBiosep
	TSK-GEL PW	Aqueous	
	Shodex K-series	Organic	Showa Denko
	Shodex OH pak	Aqueous	
	Styragel	Organic	Waters Corp.
	Ultrastyragel	Aqueous	

Table 1. Examples of column ranges from various manufacturers (the list should be in no way considered exhaustive).

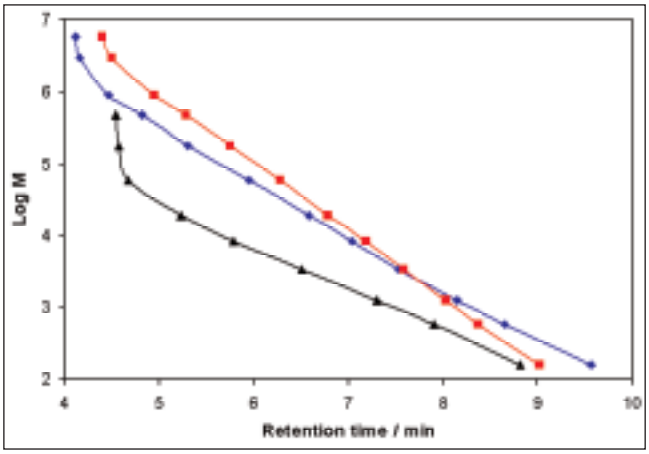


Figure 2. Overlaid calibration curves of typical individual, mixed-bed and multipore SEC columns (Polymer Laboratories' PLgel 5µm 500Å, PLgel 5µm MIXED-C and PolyPore columns).

Hardware Technologies for SEC

Like other high performance liquid chromatography (HPLC) systems of the time, the first SEC systems were home-made instruments. These systems were followed by 'modular' SEC equipment comprised of separate pump, injection and detector modules, with various ancillary devices such as autosamplers and column ovens. The advantage of these modular systems was that components could be mixed and matched between manufacturers, however, there was no communication between instruments and the user had to learn to control the interface of each device. For this reason, the use of modular systems required skilled operators who were familiar with each component.

The emergence of integrated systems specifically designed for SEC has been the trend over the last ten years. These instruments contain all the components required for the analysis (pump, injection system, column compartment, detectors and ancillary devices) within a single unit. The benefit of such devices is that the positioning of the components can be optimised, various safety features can be introduced and custom computer software can be developed to control all parts of the system. Such instruments are therefore easier to use (requiring less training) than modular systems, and contain considerably more safety features. They can also be tailored to suit particular analyses, such as high temperature work, much more easily

Figure 3. The PL-GPC 50

than modular systems. An example of an integrated system expressly designed for SEC is the PL-GPC 50 shown in Figure 3. This instrument can be operated from ambient to 50°C and is designed to accommodate a range of detector options.

SEC employing a single concentration detector is often termed conventional SEC. In this analysis, molecular weight averages are calculated relative to a series of standard polymers of known molecular weight. The disadvantage of this method is that the SEC column separates on the basis of size not molecular weight, which leads to discrepancies if the standards used for calibration are a different chemistry (and therefore size in solution) to the sample. Of increasing interest over the last ten years has been so-called 'multi detector' SEC, employing one or more detectors that respond to molecular properties other than concentration. Light scattering detectors and viscometers are the most common detectors used in these applications, with the use of both devices (along with the required concentration detector) termed 'triple detection'. These devices further aid the analytical scientist in that they reveal other parameters relating to the behaviour of polymer molecules in solution. Light scattering detectors can be used to estimate the size of molecules in solution (in terms of Rg, the radius of gyration), and viscometers give an indication of the molecular density of polymer molecules (a property related to the intrinsic viscosity). These parameters can then be exploited to investigate the morphology of polymer molecules, an important property for many industrial applications.

Static light scattering detectors respond directly to molecular weight and so do not rely on a column calibration, and can also give information regarding the size of the polymer molecules in solution. The development of light scattering theory is well established, but the first commercial instrument was only available from the 1960s. Since then, many instruments have been developed specifically for coupling to SEC systems, covering the range of designs and prices. As a consequence, light scattering has grown from a niche area of academic interest to a very popular technique. The relatively high cost of light scattering instrumentation and the expertise required for operation can, however, prove prohibitive.

Viscometry detectors can be employed to improve the accuracy of SEC molecular weight calculations by removing the dependence of the calculated molecular weights on the chemistry of the standards and sample. This is achieved using the Mark-Houwink relationship and the Universal Calibration. Viscometry gives the intrinsic viscosity of the sample under investigation, a property that can be related to the molecular density of the polymer molecules. Flow through (i.e. compatible with liquid chromatography) viscometry detectors were developed in the 1960s, and although many types exist, those which employ liquid flow-through capillaries are by far the most common. The advantage of viscometry is that the technique can greatly improve the accuracy of a nSEC analysis compared to a conventional experiment, and the instruments tend to be robust and reliable, although, historically the cost of such devices had limited their appeal. Recently, new and more cost effective designs have become available and viscometry is becoming increasingly common in the SEC laboratory.

The growing popularity of SEC and the development of integrated instrumentation have led to increased software requirements. Data collection in early SEC systems was through chart recorders, with data handling either by hand or through custom programming. These early systems were slow and difficult to use, and the calculations performed on the data were cumbersome, greatly hindering the versatility of SEC and making these methods clearly not suitable for widespread use. However, as SEC grew in popularity, specialised data collection hardware and handling software was developed. Many companies with an interest in SEC have released software that is modern, powerful and versatile, and software now represents a major component of the modern SEC system. The majority of these SEC software packages are intuitive to use and Windows (TM) based, with some companies offering to fill compliance and regulatory requirements where necessary.

Table 2 shows a brief summary of some of the commercially available integrated systems, light scattering and viscometry detectors and software developed specifically for gel permeation chromatography.

Product type	Name	Application	Manufacturer
Instrument	PL-GPC 50, 120, 220	Integrated SEC systems	Polymer Laboratories
	PL-BV 400, PL-ELS 1000	SEC detectors	
	TDA	Integrated SEC system	Viscotek
	LALS, Viscometer	SEC detectors	
	Alliance	Integrated SEC systems	Waters Corp.
	DAWN EOS, ViscoStar	SEC detectors	Wyatt
Software	Cirrus	SEC and Multidetector	Polymer Laboratories
	OmniSEC	SEC and Multidetector	Viscotek
	Millenium	SEC and Multidetector	Waters Corp.

Table 2. Examples of commercially available integrated systems, light scattering and viscometry detectors and software developed specifically for gel permeation chromatography (the list should be in no way considered exhaustive).

Conclusions

Initially introduced for the separation of water soluble polymers by size in aqueous solution, the technique of gel permeation chromatography has been greatly developed to allow the analysis of a huge variety of synthetic and natural polymers. Early microporous soft gels have been replaced in the majority of applications with more robust semi-rigid macroporous polymeric materials that allow analysis in a wide range of solvents. The development of mixed bed or linear columns and now multiporous high pore volume materials has greatly increased the versatility of SEC. Progress in the design and technology of SEC instruments has occurred to match this growth in interest. Integrated instruments specifically designed for SEC have superseded the early modular systems, and several companies now produce light scattering and viscometry detectors, instruments once only available in dedicated research laboratories. Specialised SEC software is available that greatly enhances the ease-of-use of SEC.

Since its inception, SEC has grown steadily in popularity to become a mainstay of the analytical laboratory. The growing number of new developments in SEC demonstrates the popularity and versatility of the technique, and bodes well for those looking to separate macromolecules on the basis of size in solution. ■

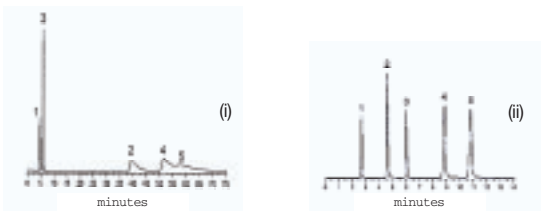
The Evolution of HPLC Column Packings

Nicola Vosloo, Stuart McKay, Hichrom Limited, Reading, UK

Since the introduction of liquid chromatography by Tswett in 1903, the field of separation science has expanded to encompass all branches of chromatography.
The packing materials for HPLC columns, primarily silica based, have evolved from pellicular and irregular porous bead types of support in the early 1970s to the spherical, chemically bonded ultra high purity phases used today.

The materials used in the early commercially available HPLC columns, now commonly referred to as conventional or type A silicas, were recognised as having limitations for the chromatography of basic analytes (figure 1 (i)). Breakthrough spherical materials of that era, whilst offering improved chromatography over the irregular materials, still exhibited variations in batch to batch reproducibility and the addition of an ion-pair reagent was commonplace to improve the chromatography of basic analytes.

Figure 1: Chromatography of basic analytes on (i) conventional silica, (ii) ultra high purity silica.

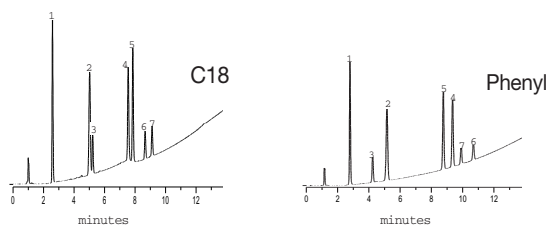


1) Norephedrine 2) Nortriptyline 3) Toluene 4) Imipramine 5) Amitriptyline, 22°C, 215nm
Mobile Phase: 80:20 MeOH/25mM KH_2PO_4 pH6.0, 250 x 4.6mm, 1.0ml/min

The purity and the bonding technology of the silica phases improved, with pioneers such as Jack Kirkland at the forefront of phase development. Column selectivity and peak shape are influenced by the characteristics of the underlying silica. Thus the resulting ultra high purity phases, also referred to as type B silicas, give excellent chromatography of not only neutral and acidic compounds, but also basic compounds (figure 1 (ii)). These ultra pure silica materials have a low metal ion content, a uniform silica surface and very low silanol activity, which in turn offer enhanced stability at low pH[1] and also at elevated pH[2].

Silica based alkyl bonded phases have shown to be the workhorse for many pharmaceutical separations. Alternative chemistries developed, (e.g. CN, Ph and PFP) bonded to ultra high purity silica bases, now offer alternative selectivity[3], (figure 2) whilst maintaining excellent batch to batch reproducibility and exhibiting improved column lifetime compared to their conventional counterparts.

Figure 2: Separation of vitamins: changing selectivity with C18 and phenyl bonded phases.



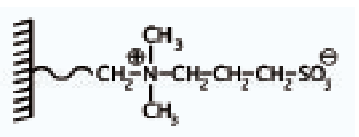
Column: 150 x 4.6mm 5µm ultra high purity silica Mobile phase: MeOH/20mM KH_2PO_4 (pH2.9), linear gradient, 5 to 95% MeOH in 20 mins Flow: 1.50ml/min
Components; 1: Pyridoxine, 2: Pantothenic acid, 3: p-Aminobenzoic acid, 4: Cyanocobalamine, 5: Folic acid, 6: d-Biotin, 7: Riboflavin, i: impurity

The growth in LC/MS analysis has driven down the column dimensions used in some application areas, but more traditional columns sizes (e.g. 250x4.6mm), are still ubiquitous. There has also been a trend towards smaller particle sizes, from 10µm in the 1970s to 5µm, established as the analytical standard, and down to 3µm in the 1990s. The recent emergence of sub-2µm particles, whilst offering a slight increase in efficiency, requires investment into new instrumentation and the higher packing pressures involved may effect column bed stability.

The nature of samples analysed today is changing, resulting in an increased demand for the analysis of more polar, more hydrophilic and ionisable compounds. Using standard reversed-phase columns, such samples are often poorly retained, eluting close to the void volume. Chromatographers can consider an AQ or polar embedded column (with an amide functionality for example within the alkyl chain) which allow 100% aqueous mobile phases to be used without any drop in retention. However such phases often suffer from increased column bleed, and for very polar compounds retention is still unacceptable.

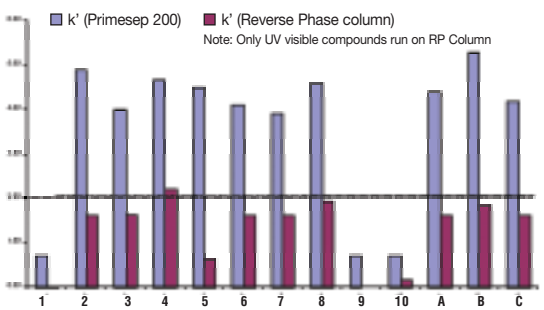
Moving to an alternative column, such as HILIC[4] or mixed mode phase, can solve the problem of poor retention of polar compounds.
Unique HILIC columns, such as the ZIC-HILIC phase, figure 3, employ a hydrophilic zwitterion as the functional group, which offers complementary selectivity to reversed-phase and the added benefit of improved MS sensitivity.

Figure 3: Structure of the ZIC-HILIC phase.



A novel range of mixed mode phases, Primesep, has emerged which combines both ion-exchange and hydrophobic interactions. The Primesep columns have an embedded ion-exchange group within the alkyl chain and by controlling the pH of the mobile phase, the extent of ionisation of the embedded group can be altered to tune the separation resulting in the desired retention. Now the retention of polar compounds can be readily achieved, and as figure 4 illustrates, the Primesep 200 column offers superior retention of a range of polar pharmaceutical entities.

Figure 4: Comparison of Pseudo k' figures: Primesep 200 vs. 'Reversed-Phase polar column', data courtesy of GSK.



Polar test compounds: A=Procainamide B=Cephaloridine C=4-Guanidinobenzoic acid, Compounds 1-10, GSK polar compounds. 100x2.1mm column Mobile Phase A: 0.05% TFA in Water Mobile Phase B: 0.20% TFA in MeCN Flow = 0.4ml/min direct into MS. Gradient 0 to 100%B in 6 mins, hold for 3mins, back to 0% in 0.5 mins.

Despite the development of novel phases, the preferred starting point for method development for many remains the tried and tested C18 column chemistry, at low pH, which offers longevity of column lifetime coupled with excellent column and batch reproducibility.

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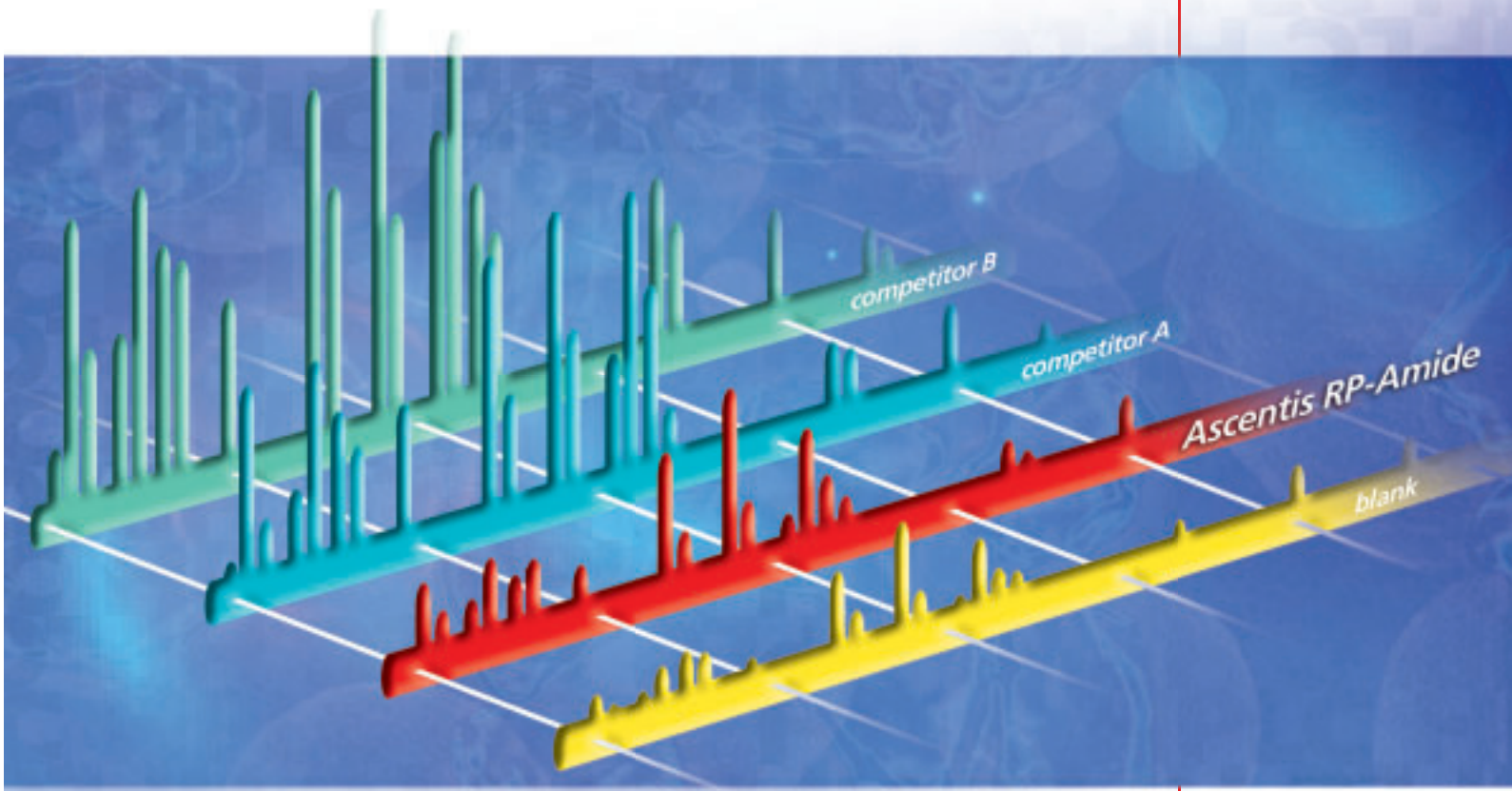


NOTE: Fewer and lower intensity responses on Ascentis RP-Amide than on competitive embedded polar phase HPLC columns.

Separation of Anesthetics

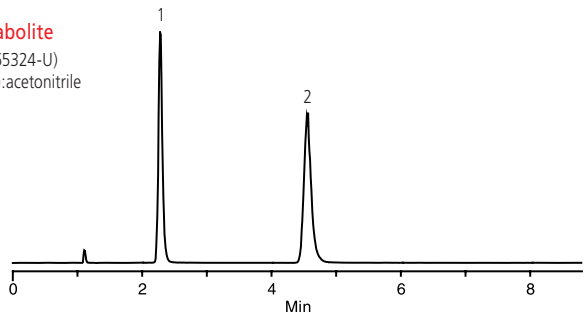
The Ascentis RP-Amide HPLC column is the first amide-based embedded polar phase to exhibit ultra-low bleed for LC-MS. This virtually eliminates background mass response that can interfere with analyte identification and quantification.

This application demonstrates the suitability of Ascentis RP-Amide for the efficient separation of the anesthetics phencyclidine and 4-hydroxyphencyclidine by LC-MS.

LC-MS Analysis of Anesthetic Phencyclidine and Hydroxy Metabolite

column: Ascentis RP-Amide, 15 cm x 4.6 mm I.D., 5 µm particles (565324-U)
mobile phase: 70:30, 10 mM ammonium acetate (pH 4.5 with acetic acid):acetonitrile
flow rate: 1 mL/min.
temp.: 35 °C
det.: ESI (+)
injection: 10 µL
sample: 1 µg/mL each in mobile phase

1. 4-hydroxyphencyclidine (m/z 260)
2. Phencyclidine (m/z 244)



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The Future of Chromatography

by Peter Myers

My great friend and mentor Denis Desty told me that when you are thinking of and writing about the future, be bold. Establish your thoughts from a sound basis and develop them in all directions. Don't let conventional thinking restrain you. Denis practiced this in his work, being very bold in his experimental work, but even bolder in applying his thoughts to the future. Therefore, I have taken this as my start in writing this short paper on my personal views of the future. Denis got some things very wrong,, mainly on time scales, but in concept, he got many things correct. I hope I can come close to some of his visions.

The basis from where I start is the latest developments we have seen in liquid chromatography in the last five years. In this time we have seen the introduction of monolithic columns offering a lower back pressure for the same plate count as a classical particle-packed column. And opposing this we have seen the introduction of sub-two micron particles offering higher plate counts but at the expense of far higher back pressures. Are either of these the future of chromatography, well let me make my first bold statement and say no. My reasoning behind this comes from the strong basic work that has recently (2005) been reported by Gert Desmit from the University of Gent who has shown how the classical van Deemter plot has real limiations and maybe can even confuse us when we are looking at the efficiencies of the small particle columns and comparing them to classical 3 micron and above columns and to monoliths.

In the kinetic plot approach, H and E are plotted as a function of the pressure drop-limited plate number (N). Such kinetic plots are as easy to establish as a normal van Deemter plot and offer the advantage that the performance of differently shaped and sized LC supports can be directly compared. The kinetic plots can also be used to show areas of improvement for LC columns as shown in fig 1.

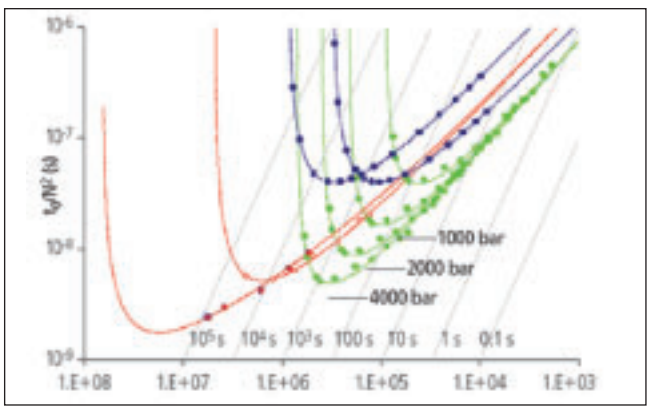


Fig 1 Kinetic Plot as described by Desmit

The area to the right of the graph has been termed the forbidden area. To develop chromatography further in terms of column efficiency and reduced separation time we need to develop supports and packings that will take us into this area. From these plots it is clear that this can be done by increasing the order of the packing and decreasing the skeleton size of a monolith or the particle size.

Is all this possible?

Yes it is; today we have 1.5µm porous particles and instruments that will take us to 1500 bar, but I really don't see this as the way forward. If I look at the past and all developments in technology, everything that has moved forward has been made smaller and simplified. Look at the development in television; from the 60's we have seen a change in electric valve technology, high voltage CRT tubes and large boxes, to today's slimline, low voltage LCD TV's. Another example is in the revolution we have seen in mobile telephone technology. In the late 80's I remember using a portable telephone that had a separate battery pack weighing over 2Kg. Today most of us use a portable that is much smaller and uses far less power so that it can operate for days on a 3.7V Li-ion battery. In these comparisons I am comparing power requirements to pressure. Although we can achieve the high pressures required for the present systems there are problems in total system requirements. The alternative and what I think is the way forward into the future is the approach that was started by Fred Reginer and now continued by many including the work shown in Fig 2 by Peter Schoenmakers

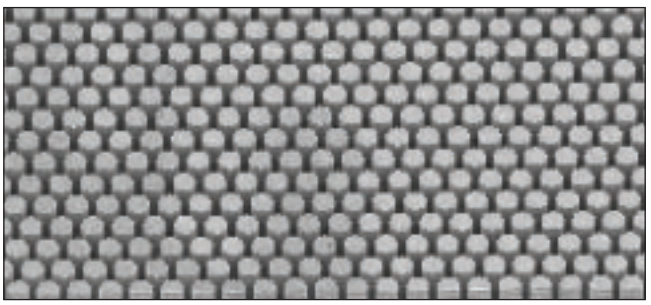


Fig 2 Ordered pillared structures from the Schoenmakers group

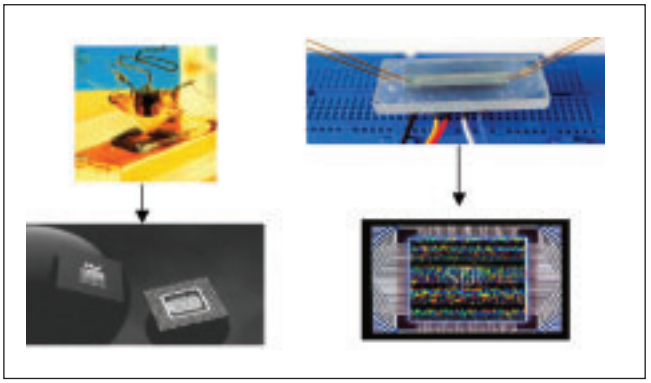
Such structures give an increase in the order of the packing and by controlling the interstitial spacing of the columns also give the required porosity. But the format of these new columns will also be very different. Today we have not moved on in column design since the first LC columns with compression end fittings. It still takes skill to fit these columns into an instrument. After many years of trying I today can just about connect a 4.6mm id 25cm column onto an instrument. My bad fitting that introduces 2 microlitres of dead volume can be accommodated. But I cannot connect a 150micron id column that still uses compression fittings as, in connecting, the column moves back and so introduces that dead volume and on such small id capillary columns destroys the separation. So new column connectors, maybe totally integrated column systems must be

developed. The way forward must be to build the injectors and detectors into the column. Work on detectors using the total column has been started by David Goodall.

But let's go further forward. I do think that the column is the heart of any separation system, so in the future the columns used in chromatography will also be the centre of the system. They will carry a smart chip not only to identify the column but a chip that will carry the method, such that no longer will we purchase a C18 column but a column for PAH analysis or a column for basic drugs. The column will be placed inside the instrument and it will be the column that will set up the system parameters, perform QC procedures and calibrations and finally decide when it requires replacing.

But this is only the first stage; there is no reason why using modern micro and nano fabrication, techniques cannot be further developed for columns such that a whole range of functions can be integrated into a single column format. Such that at the front of a totally integrated column there will be a solid phase extraction column, followed by a pre and then main column with a post column reactor before the analytes are placed onto a Maldi target. Like in the previous device, the separation chip will control the instrument and as it will have its own unique IP address, it will be able to reorder new reagents and then another column to replace itself when or before it fails its internal QC.

But let me move forward into the real future and I hope this is only about ten years ahead, I believe we could see the end of the chromatography column for analytical separations. One possibility is the new developments we are seeing in dynamic field gradient focusing. In this, separation is achieved by setting a constant hydrodynamic flow velocity against step changes in electrophoretic velocity. Where these two velocities are balanced for a given analyte, the analyte focuses at that point because it is driven to it from all points within the separation channel. The position of the focused analyte can be change dynamically through changing the electric field gradient. By dynamically changing the position of the focused bands they can be taken off the device or passed to another dynamic field gradient device for further separation. Hence, individual devices can be linked together to form a separation array. I liken this to the way the first transistors were used in the manufacture of complex circuits, these small DFGF devices could likewise be linked together. ■



In fig 3 the transition from the first transistor into the integrated circuit is shown on the left. On the right the first experimental DFGF chips that could be miniaturised and made into a DFGF separation array. To achieve such a device a great deal of work needs to be done in the measurement and computer control, but I did say this was ten years ahead.

Fifty years of The Chromatographic Society:

Past and present Chairmen/Presidents of the Society

Dr A.T.James FRS (1957-1960)

A.T. (Tony) James and A.J.P.Martin were the first people to develop gas-liquid chromatography in the early 1950s and Tony became the first Chairman of the Gas Chromatography Discussion Group. He went on to occupy a senior position at Unilever Research Centre at Colworth House, Bedford. After retirement from Unilever, Dr James became a director of the Wellcome Foundation.

C.S.G. Phillips (1961-1965)

Courtenay Phillips was a Fellow of Merton College, Oxford. He started research on GC in 1947 and was the first person to publish the use of temperature programming in 1952.

D.H.Desty (1966-1968)

Denis Desty was almost the first person outside the biochemistry field to appreciate the enormous importance of gas-liquid chromatography. Denis worked tirelessly to advance the technique and to ensure that information on developments should be available to all. To this end he was the instigator and prime mover of the Gas Chromatography Discussion Group. Denis spent his entire career at BP's research centre at Sunbury-on-Thames.

C.L..A.Harbourne (1968-1970)

"Happy" Harbourne was a colleague of Denis Desty at B.P.s research centre at Sunbury–on-Thames for many years. He eventually left industry and took up a teaching career.

Ted Adlard (1970-1973 & 1979-1982)

Ted was for many years a Senior Scientist at Shell Research Ltds, Thornton Research Centre near Chester. He was one of the first dozen people in the world to make and use a GC. He was a pioneer of the coupling of GC to mass spectrometry but in the early 1960s the equipment was so unreliable that no work on the topic was ever published!

R.Stock (1974-1976)

Ralph Stock was one of the very early workers on gas-liquid chromatography and a member of the Gas Chromatography Discussion Group from its inception. In 1972 when the Group decided to part company with the Institute of Petroleum and become an independent body, Ralph was instrumental in finding a new home for the Group at Trent Polytechnic (now Nottingham Trent University). He was also responsible for finding the first two permanent secretaries, both of whom gave sterling service to the Group over many years.

G.A.P.Tuey (1976-1978)

Like Ralph Stock, Peter Tuey was a founder member of the Gas Chromatography Discussion Group and played a key role when the Group decided to become an independent body. The Rules of the Society, to this day, are essentially the same as the ones written by Peter in the 1970s. Peter worked at May and Baker for most of his career.

C.E.R.Jones (1982 - 1985)

C.R.R. (Roly) Jones was widely known as a unique, larger-than-life "character". Roly was a pioneer of pyrolysis GC for the analysis of polymeric materials and did much to standardise this technique. In his latter years Roly was a Visiting Professor in the archaeology department of a local university and in addition to his scientific achievements, was an accomplished organist and musician.

Dr John Dolphin (1985-1988)

John was an early pioneer of HPLC. Until his recent retirement he worked in close collaboration with Prof J.H.Knox on the production of specialist column packings for liquid chromatography.

I.D.Wilson (1988-1990 & 2000-2001)

Ian Wilson works for what used to be ICI, Pharmaceuticals Divn. but is now AstraZeneca at their research establishment at Alderley Park, Cheshire. Ian has won a number of awards including both the Silver and Gold medals of the Analytical Division of the Royal Society of Chemistry. He is, perhaps, best known today as the exponent of the "big black boxes", HPLC-UV-NMR-MS-MS and their application in drug research.

M. B Evans (1990-1992)

After starting work in the chemical industry, Prof M.B.Evans was in turn a Lecturer, Senior Lecturer and Professor at Hatfield Technical College, now Hatfield University. He supervised many Ph D students from industry in various applications of HPLC.

Tony Fell (1992-1994)

Tony Fell came to Bradford University from the Herriot-Watt College, Edinburgh. At Bradford he is a Professor of Pharmaceutical Chemistry and is now in charge of the Graduate School of the University. Tony is best known for his pioneering work on the use of photodiode array detection in HPLC. He has close connections with scientists world-wide, in particular those from Eastern Europe.

Prof M.C.Cooke (1994-1996)

After some time in industry Mike Cooke was a Professor at Sheffield Hallam University and then at the Royal Holloway College, University of London. Has now retired to country life.

D.Stevenson (1996-1998)

Derek Stevenson started his career in industry and then entered the academic field. For the last ten years he has been largely responsible for the very successful Bioanalytical Forum meetings held at the University of Surrey, Guildford. He also initiated the first two meetings on chiral separations run by the Society. Derek is currently a Senior Lecturer in Analytical Chemistry at the University of Surrey, specialising in environmental and biological problems.

Prof K.D. Bartle (1998-2000)

Keith Bartle was Professor of Chemistry at Leeds University until his recent retirement. Until becoming an academic Keith served his apprenticeship to chromatography under Dr David Grant. Keith has carried out research on many aspects of chromatography including SFC, Comprehensive 2-D GC and Universal chromatography. Nowadays he can be found at Headingly or Trent Bridge if it's not raining.

Dr. Chris D. Bevan (2001-2006)

Chris Bevan has been President of the CS for the last 5 years which has been a particularly difficult time for the Society. Chris works at the GSK Medicinals Research Centre at Stevenage. He has organised three outstandingly successful meetings at the Stevenage/Harlow sites of GSK on the applications of large scale chromatography. This is now a major technique for the preparation and purification of pharmaceutical compounds. Currently he is organising three meetings during the year to celebrate the 50th anniversary of the Gas Chromatography Discussion Group/Chromatography Discussion Group/ Chromatographic Society.

M.S.Tswett
"The man who started it all", Warsaw 1906

R.L.M.Synge
Joint Nobel Prize Winner with A.J.P.Martin for their 1941 paper on partition chromatography

Martin with Synge in the background receiving their Nobel Prizes from the King of Sweden,1952.

Archer John Porter Martin 1910-2002 With his colleague, R.L.M.Synge they can be considered to be the founders of the modern chromatography era.

Front row 2nd L, Dr R.P.W.Scott, Centre Prof. Phyllis Brown, 1st R Prof. Georges Guiochon, 2nd R Dr J. J.(Jack) Kirkland, ca. 1965. Ray Scott was one of the pioneers of GC in the 1950s. Jack Kirkland was a pioneer in the production of HPLC packing materials and the co-author of a well-known textbook. As a member of GAMS, Georges Guiochon was a close collaborator with the Society in the 1970s and 1980s.

Dr J.Janak,Dr R.P.W.Scott and Prof.Howard Purnell. Edinburgh 1960 Dr Janak was an early pioneer of GC and inventor of a method of gas analysis using CO_2 as the carrier gas. Howard Purnell was the author of the definitive book on the theory of chromatography for many years.

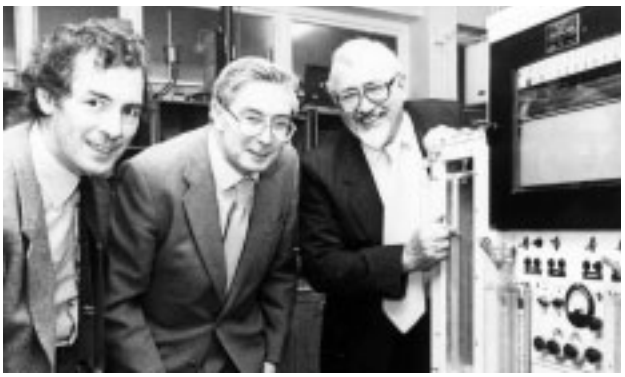
Dr S.Lipsky and Dr J.Janak
Sandy Lipsky of Yale University was an early exponent of capillary columns in the USA and collaborated with Jim Lovelock on ionisation detectors.

Denis Desty, Martin and Victor Pretorius in South Africa ca. 1975

Ted Adlard receiving the Martin Medal from A.J.P.Martin 1982.

Professor L.S.Ettre, Martin Medallist, 1982. Well known for his many original contributions and for his work on the history of chromatography

Dr G.A.P. Tuey , A.J.P. Martin, Dr R. Stock, E.R. Adlard, Dr C.E.R. Jones and D.H. Desty at the Science Museum, London, 3May 1984.



E.Rees, E.R.Adlard and C.E.R.Jones with a Griffin and George GC presented to the Science Museum, London 1987.

Back row: Dr J. Dolphin and Prof M.B. Evans. 2nd row: Dr G.A.P. Tuey, Mr I.W. Davis and Mr M. Cooke. 3rd row: Dr P.A. Sewell, Mrs J.A. Challis and Mr M. Perry. Front row: Mr N.G.McTaggart, Dr C.E.R. Jones, Mr E.R. Adlard at the Science Museum, 3 May 1984. These were the members of the CS Committee at the time.

Dr John Dolphin, Dr Henri Colin, Prof J.H.Knox and Prof E.Sz Kováts. Prof. Ervin Kováts was the inventor of the relative retention system that bears his name.

Prof. John Knox receiving his Martin Medal from Dr John Dolphin.

Professor J.E.Lovelock and Mrs D.Desty at the Royal Institution, London, 2001. Jim Lovelock is holding a miner's lamp presented to him by the Chromatographic Society.

Prof. M.B.Evans, Mrs J.A.Challis and Dr C.E.R.Jones on the occasion of Mrs Challis' retirement. Jennifer Challis was the Secretary of the CS for 15 years. She now lives in Devon with her husband Prof Laurie Challis, former Professor of Physics and Pro Vice-chancellor of Nottingham University.

Dr Michel Martin.
Dr Martin was a member of GAMS (the French society that organised symposia on chromatography) for many years and collaborated with the CS on a number of meetings. He did research at the Ecole Polytechnique, Paris under Prof Georges Guiochon. *(See group photo on page 34).*

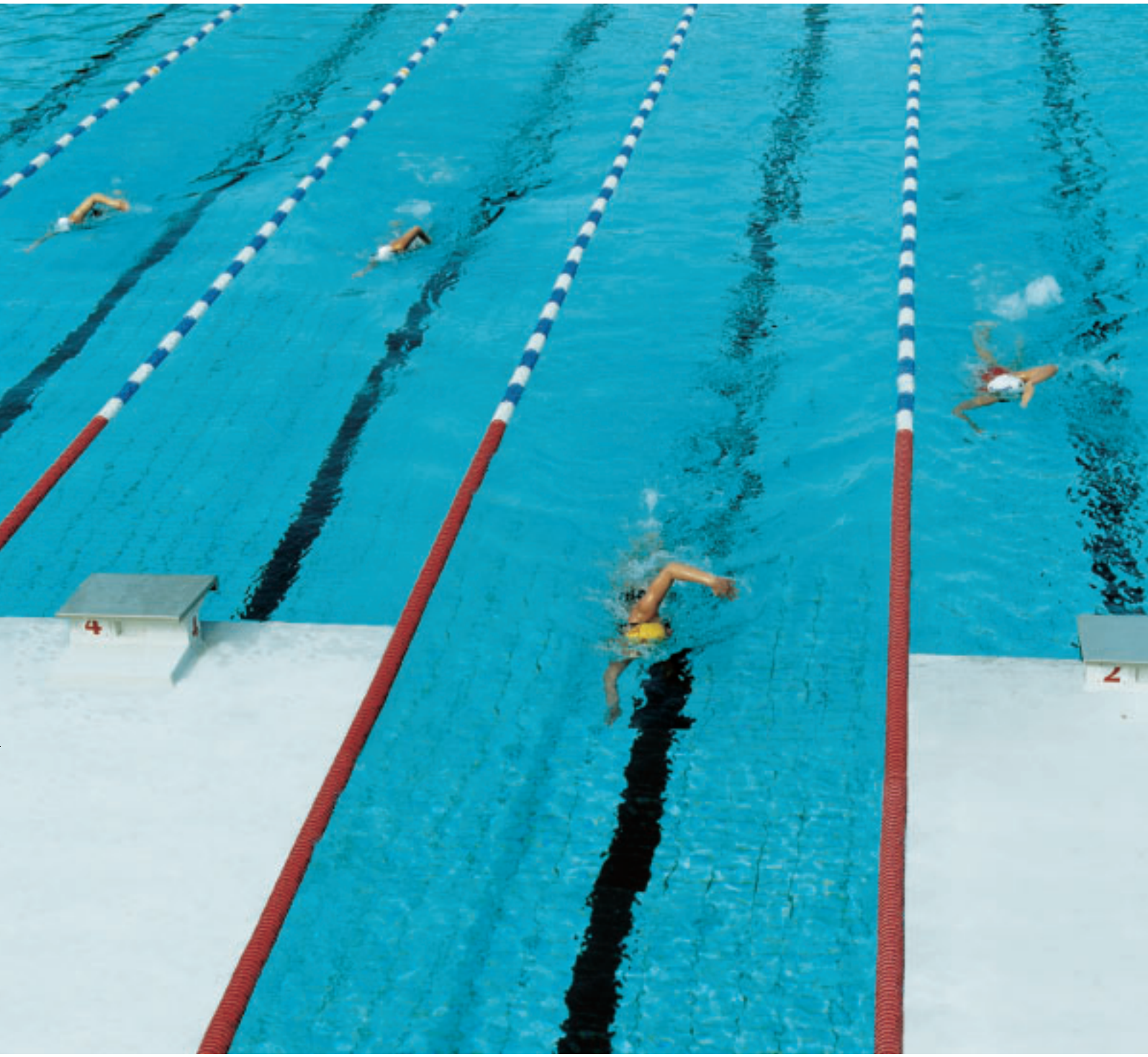
Dr John Dolphin, Prof Ernst Bayer and Dr C.E.R.Jones. Prof Bayer, formerly Professor of Organic Chemisrty at Tubingen University, died in 2002. Prof Bayer did his PhD under Prof Kuhn and can therefore be said to be a direct link, through Willstätter, to Michael Tswett. Prof Bayer was one of the earliest workers on chromatography in Germany.

Prof. Walt Jennings, ca 2002, US pioneer of capillary GC. Until his recent retirement Walt Jennings was known world-wide for his dynamic lecture courses on GC.

Alan Handley, current Vice-president of the CS. Alan formerly worked for ICI but now works for LGC at the Heath in Runcorn. His chromatography credentials go back many years.

Professor Peter Myers, former Vice-president of the CS, at a Royal Society of Chemistry meeting in York in 2004 demonstrating particle packing with the aid of a packet of M&Ms™.

Dr Ken Jones. Ken Jones was the Hon Treasurer of the CS for a number of years. Among many other claims to fame, Ken was one of the founding directors of Phase Separations Ltd.



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