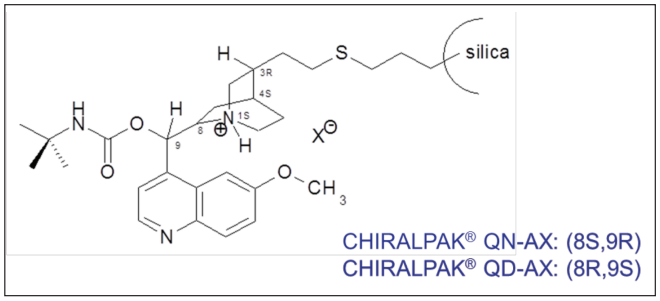
Professor Wolfgang Lindner - In Conversation with Chromatography Today

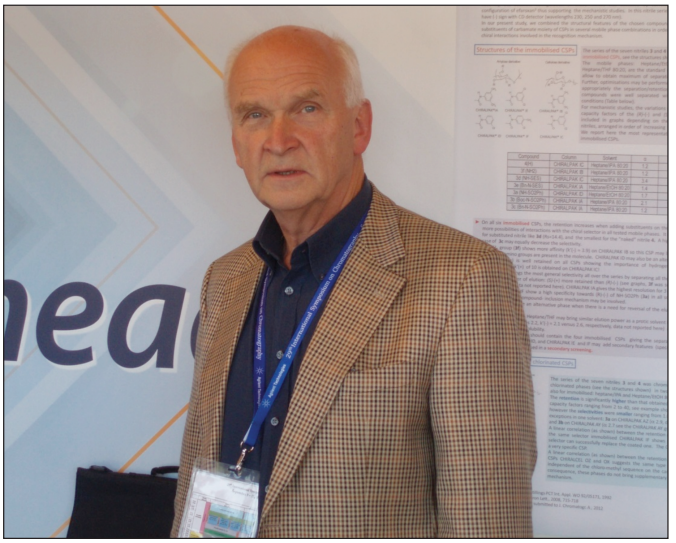
For this issue's instalment of our occasional interviews with Chromatographic Society medallists and other leaders in the field of separation science we feature not just any Chromatographic Society medallist but, up until this year at least, a unique one. When, following on from a Jubilee Medal in 1991, Wolfgang Lindner was awarded the Society's Martin Medal in 2009 he became the first person to have been awarded both medals. Strangely, the first "emerging separation scientist" to have been deemed to have actually emerged!

Of his many outstanding contributions to the field of separation science he is best known for his research work, and teaching, in the area of chiral resolution, for example products from his group having been commercialised as the ULMO, QDAX and QNAX chiral stationary phases (CSPs). He first became involved in chromatography during his PhD studies at the Karl-Franzens University of Graz looking at the gas chromatographic analysis of toxins in tobacco smoke. In 1972 he accepted an assistant professor position at the Department of Pharmaceutical Chemistry at the University of Graz, rising through the ranks to associate professor in 1982. During these years, he worked as scientist-on-leave in a number of industrial and academic laboratories -1973 and 1975 in the group of Prof. Roland Frei at Sandoz, Basel; 1978–1979 as a Max Kade post-doctoral fellow in the group of the legendary Prof. Barry Karger at Northeastern University, Boston, USA; and 1986–1987 as an invited international chemist with Dr. F. Robey at the FDA, Bethesda, USA to explore new research perspectives.



Commercialised chiral anion-exchange phases developed by Lindner: use in hydro-organic mobile phases, in polar organic mode and in SFC; give enantiomer separations for derivatised amino acids, acidic drugs and metabolites, phenols, hydroxycarboxylic acids, arylcarboxylic acids, aryloxycarboxylic acids, sulphonic acids, phosphonic acids and many other chiral organic acids

In 1996, he received and accepted the call to the prestigious chair of Analytical Chemistry at the University of Vienna, as successor of the late Prof. Josef Huber, working as part of the Christian Doppler



Wolfgang Lindner at ISC 2012 in Torun, Poland, shortly before his official retirement)

Laboratory for Molecular Recognition Materials at the Universities Department of Analytical Chemistry and Food Chemistry.

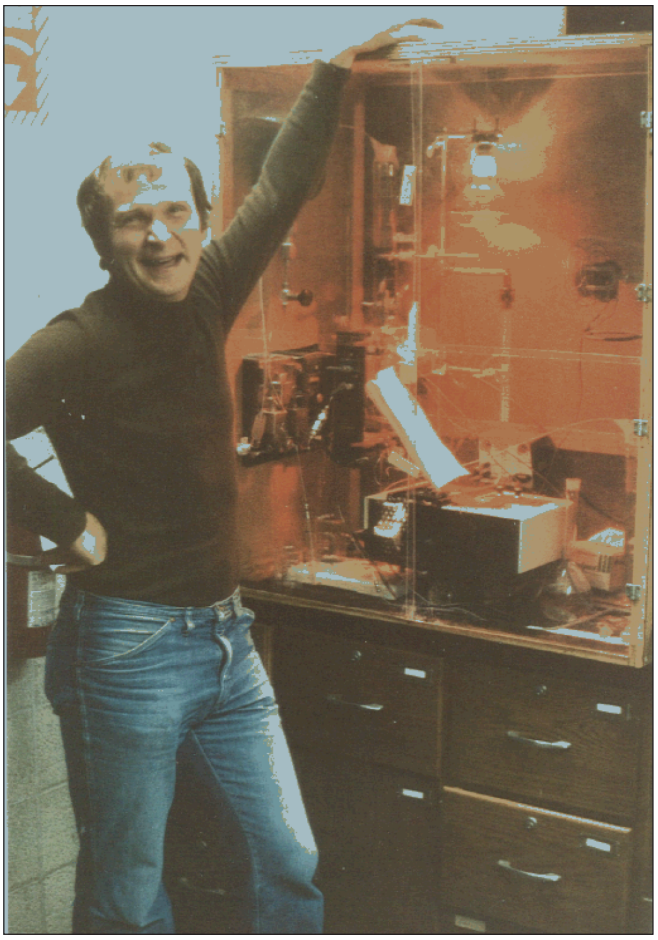
Having officially retired at the tail-end of 2012, Lindner has seemed to manage to still keep himself very busy, amongst other things being heavily involved, as Honorary Chair, in the organisation of ISC 2014 which will take place in Salzburg between September 14th and 17th this year. Happily he did find time though to chat to Chromatography Today not only to reflect on his distinguished career but also to muse on the current status of separation science.

Many of the early chromatographers started off as physical chemists and, later, many got into it via applications. You started off in chromatography doing GC of toxins in tobacco at Graz. Was Graz your local university? Did you start off as a chemist? Were you an aspiring chromatographer who happened to work

on tobacco or a tobacco specialist who drifted into separation science? To cut a clumsy, multi-question short, what triggered off your interest in chromatography?

Graz became my local university after I have moved from Vienna to Graz in 1965, mainly for personal reasons. I finished my PhD in June 1972. At that time Doris and I were children of the so-called '68 generation'. Politically, socially and economically a very dynamic period of time and being raised in a rather small and not very rich country, like Austria was at that time, most of my student colleagues and friends dreamed from going abroad after having finished the studies. However, on 27th August 1968, 6 days after the 'Prague Spring' where the Russian tanks stood at the long East-European border. I got married to Doris and in 1969 our first son Fritz was born. As a student couple and family the dreams came back to earth, we worked hard to earn our daily life but enjoyed that time very much.

After finishing my PhD in Chemistry I had to search rather quickly for a job as our second son Philipp was born in June 1972. After the PhD it was an eminent question for me which way to follow, do I go to industry or should I enter an academic life. Finally it was a gut decision in deciding for academia although the salaries were much less than in industry. Doris was and has been fully understanding; we never regretted this decision. I moved from the Organic Chemistry Department of the University of Graz to the Pharmaceutical Chemistry Department where I could quickly establish a laboratory specialising in GC, and soon LC, methodologies applied to pharmaceutical analysis. During my PhD at the Organic Chemistry Department I was able to bridge organic chemistry with modern GC and GC-MS



Early career Wolfgang Lindner, looking every inch '68 generation'

Wolfgang Lindner with mentors the late Roland Frei (centre) and the late Joseph Huber (right)

technology (already in the 70s my supervisors Dr. Binder and Prof. Zigeuner had access to this instrumentation). I worked on the analysis of tobacco smoke and analysed highly reactive compounds (ketenes, carbonsuboxide, etc.) generated via pyrolytic reactions in the Glüh-zone of the cigarette. I established pyrolysis GC in simulating these processes. As a student I smoked heavily but in 1972 I finally quit and never smoked again. The early work with GC fascinated me and I was intrigued by the enormous power separation science has in the course of the analysis of organic species. Already in 1973 I was able to purchase a superb Hupe-Busch HPLC instrument (this company was bought up 1974 by Hewlett-Packard) and from there on I worked in the fields of GC and HPLC whereby the HPLC technology inspired me particularly due to the enormous potential. Already at that time I had realised for myself that my professional love is research and teaching, so I had been fully satisfied with the decision I had had to make in 1972.

You seem to have had three 'sabbatical' periods during your career. Were these a great influence and of importance to you? Did you take different things from each? Is it a matter of regret that such opportunities are rarely afforded to today's academic separation scientists?

The University of Graz was a good starting point and provided an environment to develop a career as a researcher. The 70s were booming years all over Europe, everywhere new institutes were built and the feeling for the future was very optimistic. Nevertheless, I realised that sooner than later I had to go abroad to move on in my academic career, albeit this was not so easy as we were already a family of four with children starting with the school. In 1977 I attended the first time an HPLC symposium in Salzburg presenting a poster together with a mentor of mine, the late Professor Roland Frei. We became friends during two stays at Sandoz-Basel (now Novartis-Basel) in the years 1973 and 1974. There I got exposed to top pharmaceutical analysis laboratories. At that I got also to know Fritz Erni being in friendship since then. My plan was to approach in Salzburg Professor Barry Karger who was already a big figure (guru) in the HPLC scene and to ask him for a post-doc stay. He agreed spontaneously although I was not so young anymore. From the Max Kade Foundation I got a stipend which enabled me and my family to go to Boston where we had one of our best years as a family.

It was 1978/1979. Soon I realised that our Austrian education in chemistry provided an excellent basis for the advancement in new fields. At Barry Karger's labs I started to work in the field of enantiomer separations, a hot topic at that time. Via my background in organic and pharmaceutical chemistry and bridging it with up-to-date separation technologies lead us quickly to a level where I earned some recognition worldwide. This was the start of becoming a 'chiral technology' specialist working in various areas of chirality driven research niches. It accompanied my scientific and academic life thereafter. To date I am still fascinated by chirality and what can be discovered along that line.

Returning from Boston to Graz I finished the Habilitation in Pharmaceutial and Analytical Chemistry in 1982. Then I was offered good working opportunities in Graz, so I decided to stay there. In the mid-80s I patented together with a colleague from the Organic Chemistry Department, Georg Uray, a methodology to prepare, on a large scale, enantiomerically pure betablocker type drugs. This technology could be licensed to companies in the pharmaceutical industry and we also sold the products to Aldrich etc. It was the start of my entrepreneurship which was chequered with several other, more or less successful, patent applications.

Based on my steadily growing standing as separation scientist with particular know-how in enantiomer separation I was then invited to the FDA in Washington DC by Irving Wainer to take up a position as a Visiting Scientist (1986/1987). However, due to re-arrangements within the FDA, I ended up in Bethesda working on peptides and antibodies. For me it was an entirely new field, but at the end it was very fruitful as I could expand my know-how substantially.

Was working in the USA very different from Europe?

In the years 1978 and before we in Austria at the universities were still a bit behind the level of modern instrumentation compared to Switzerland and Germany where I had already been working previously (e.g. Sandoz-Basel). At Barry Karger's labs in 1978/79 the instrumentation was not much better than here in Austria; they had just a bit more instruments installed. Nevertheless there was a clear difference in the availability of consumables, chemicals etc. due to a much better funding. In Boston I learnt that if you want to be competitive in science and to be fast in publishing just order the consumables you need via a phone call and do the experiments you have envisioned. Do not waste time since outside there is competition! One wants to be the first and this in turn is necessary for successful grant applications.

Nowadays we have adopted a similar attitude at least in my labs, but 20 years later. However, one has to confess that this attitude is really wasteful and a lot of not so fruitful experiments get made and discarded. However one needs also to make a number of 'wasteful looking experiments' in order to find new routes. It is the concept of serendipity if we learn from all these type of 'negative' but also 'surprising' looking results. To summarise, yes, in Boston I learnt to accept competitiveness in science, the run for being the first in publishing results and the run for project money via the writing of research proposals, creating cooperations with industry which in the USA has a much better attitude to supporting research.

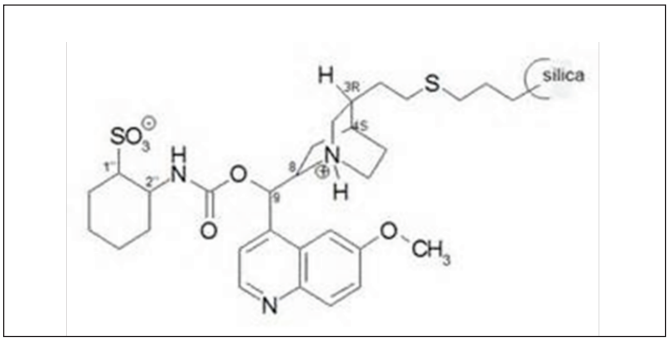
I also learnt in the USA that you as a person gets credit upfront; you may fulfil the expectations or you may fail. However if you have failed you get a second chance which was (is) a bit different to our culture.

When did you first start making your own chiral stationary phases (CSPs)?

As I have already intimated, I started to make my own CSPs in the early 80s after I returned from Barry Karger's labs. These phases dealt with chiral ligand exchange chromatography. In parallel we developed π - π selective phases as in the 80s I was already working extensively on column switching and multidimensional LC-LC systems. To understand and to improve chromatographic selectivity was always a major focus. None of the early phases have been commercialised but it changed when we developed the ULMO phase together with G. Uray and N. M. Maier. These CSPs attracted interest from the Regis company in the USA who scaled up the synthesis and launched the product onto the market.

In parallel I developed the idea of generating chiral ion exchangers. As it was unique at that time we patented the concept and the material of QN-AX and QD-AX columns in the hope that chromatographic column producers would get interested in the concept and launch the columns. The dream worked and after the Bischoff company the world market leader in chiral columns, Chiral Technologies Europe (CTE) licensed the patent exclusively. The columns have now been on the market for about 20 years.

Following this concept we subsequently developed and then patented chiral cation exchangers and chiral zwitterionic ion exchangers. The latter CSPs are now sold by CTE as ZWIX(+) and ZWIX(-) columns. As you know they work nicely for the resolution of ampholytes. Chiral ion exchanger type CSPs and columns relate to a niche type application area in comparison to the polysaccharide type CSPs. However they offer the opportunity to deal also with very polar compounds which can only be dissolved in water or water-based media. This is a clear advantage. All the CSPs we developed are offered in analytical column formats but also in preparative scale. In summary, the chiral ion exchanger materials as such stand out from the many other chiral materials available from various companies. From the molecular interaction mechanism they represent clearly unique materials.



Lindner's zwitterionic chiral stationary phase launched by Daicel in 2012 as CHIRALPAK® ZWIX™

What do you regards as your main chromatographic achievements outside of your work on chiral separations?

As I said before, the tuning and understanding of 'selectivity' as the key parameter in chromatography was always in focus of my work. What can be learnt from 'enantioselectivity' is valid in a broader sense. Therefore in the past ten years we have also developed various HILIC type phases and columns in order to understand better the HILIC type selectivity space. We have also developed affinity type stationary phases to mimic bioaffinity type selectivity and property profiles for antibody purification.

In summary, over the many years of my engagement in chromatography I have been working with (a) normal phase chromatography using silica, (b) extensively with reversed phase

(a)

(b)

Lindner on the conference stage (a) at the podium in determined spirit (b) with wife Doris being honoured at HPLC 2013, Amsterdam with friends and co-workers including Barry Karger (3rd from left)

Lindner (right) at HPLC 2013, Hobart, Tasmania with other Chairpersons: (l to r) Hopfgartner (HPLC 2015, Geneva), Buchberger and Laemmerhofer (ISC 2014, Salzburg) and (back to camera in true Chromatographic Society photograph fashion) Haddad (HPLC 2013, Hobart)

chromatography, (c) with ion exchange chromatography, (d) with affinity chromatography, (e) with HILIC, (f) with p-p type chromatography, (g) with chiral chromatography, etc. In all of these modes the role of the mobile phase was studied more explicitly in context with the troica (as I call it) in defining the physico-chemical properties of the Analyte-Stationary Phase-Mobile Phase.

You certainly seem to be managing to keep yourself reasonably busy during the early stages of your retirement. Part of this, of course, is your involvement with the 30th International Symposium on Chromatography (ISC 2014) in Salzburg. How is this going? What can we expect in Austria in September?

As you will be aware, the International Symposium on Chromatography (ISC) represents a well-established congress series of major European Chemical Societies. It was first organised in 1956 in London and since then held biannually in various major European cities. The ISC 2014 being held in Salzburg and organised under the auspices of the Austrian Society of Analytical Chemistry (ASAC) will be the 30th event of this symposium series. (Austria has already hosted a very successful ISC in Vienna in 1988 chaired by the late Professor J. F. K. Huber). For ISC 2014 in Salzburg we hope to develop the themes of the series but hope to be distinctive in developing some particular themes.

The conference is committed to the promotion of research and knowledge in separation science, considering the whole variety of modern chromatographic and electrophoretic techniques. It puts its focus on separation methodologies in all scales from nano /micro-scale to preparative scale, on fundamental and applied science, and on application fields comprising (bio)pharmaceutical, bioanalytical, environmental, clinical/ toxicological, and food analysis research and many more.

As can be seen from the list of technologies and application areas, ISC 2014 Salzburg covers both LC and GC but also CE and is thus one of the rare opportunities to connect with experts of these major analysis technologies at the same conference. This way we want to bridge fields and bring together the colleagues in providing a platform for mutual interaction and discussion.

A strong focus of the conference will also be related to the hyphenation of separation technologies with mass spectrometry, as systems like GC-MS, LC-MS and CE-MS represent the gold standards and modern analytical settings for unquestionable identification of analytes. Besides the high level of qualitative information it is of utmost importance that all these methodologies provide also quantitative data with adequate precision and reliability.

A conference dedicated to pure and applied separation science must constantly widen its scope and horizon in order to keep up with the progress of the techniques and the challenges in analytical sciences.

A conference like the ISC 2014 Salzburg may help to bring disciplines together that were traditionally maybe less close than they should have been. Besides lectures and poster presentations dealing with the most recent scientific achievements in separation science, the program will also include Tutorials and Short Courses that provide a more didactic approach to various relevant topics. It is true that the Internet has become a source of an immense amount of useful information, unfortunately often less well structured. It is also true that nowadays webinars are offered to complement the traditional form of seminars. Nevertheless, a conference like the ISC 2014 Salzburg may serve as a possibility for 'one-stop shopping' where one can get all the information one has been looking for, and also the option for immediate discussion with experts (so one always can immediately get a 'second opinion' on a certain problem). The personal contacts are most important, and it is always an advantage to know the face behind the name of an author of a scientific publication.

In Salzburg we will try to provide a well-balanced conference programme and thus a mix of technological, methodological and application oriented aspects.

We want to bring together separation scientists from different areas. We also want to bring together theory and practice. And we want to bring together academia and industry by inviting plenary and keynote speakers from university and industrial labs. We have to learn from each other in order to speed up progress in our field. ISC has been established as a conference series that is always held in Europe, but it is certainly not restricted to Europe but presents a truly global conference. We have speakers from Europe, Japan, China, Australia, Russia, South America, USA etc. On the other hand, ISC 2014 is certainly one of the nearest locations for Europeans to present their results to an international audience and to get 'the whole picture' of modern separation science within the frame of Analytical Sciences.

As chairpersons we will have the opportunity to give the conference a particular flavour. We have decided to put a strong focus on mass spectrometric detection and its hyphenation with separation techniques. Another very up-to-date focus is multidimensional chromatography and biopharmaceuticals analysis. Mass spectrometry and hyphenation with chromatography is challenged inter alia in the -omics field (metabolomics, proteomics, lipodomics, glycomics, you name it). To shed a proper spotlight on these topics we have invited internationally most renowned plenary speakers.

Jeremy Nicholson will outline a few visions on how this powerful technique could be used in the near future in clinical analysis.

Hans Maurer will present the feasibility and needs of high-resolution MS in forensic toxicological analysis.

Gerard Hopfgartner will introduce us to the realms of ion-mobility mass spectrometry as another dimension in metabolomics and metabolism studies.

Pat Sandra and Govert Somsen will discuss challenges and advances in biopharmaceutical analysis, including CE MS.

Dan Armstrong will give an overview of what can be achieved with ionic liquids in separation sciences in particular GC. Just to name a few highlights.

The tutorials and Short Courses will have a strong focus on separation technologies and sample preparation. Besides UHPLC (Gert Desmet), SFC (Caroline West), HILIC (David McCalley), Separation Techniques in Bioanalysis (Christian G. Huber) ISC 2014 will feature tutorials on LCxLC (Peter Schoenmakers) and GCxGX (Luigi Mondello) as well as specific topics in MS (Quantitative MS by Kevin Schug and CE-MS by Markus Himmelbach).

Karl-Siegfried Boos will highlight the use of LC-MS/MS technology in the clinical labs.

This will be complemented by many keynote lectures of academic and industrial opinion leaders in separation science, mass spectrometry and certain application areas.

In summing up we think that the ISC 2014 Salzburg offers an excellent platform to our colleagues from all over the world to present and to discuss their newest results. Salzburg is a most charming city of very high cultural and scientific level. We look forward to welcoming a large audience at Salzburg Congress in September 2014 and to share an exciting time.

That's certainly an ambitious agenda. We wish you all the best for Salzburg and beyond that in what seems likely to be an active "retirement".