Special Series HPLC

Are we still pushing the limits of liquid chromatography? Absolutely, say our experts – who continue to surf on the edge of LC innovation – as part of our special collection of recent HPLC insights.

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What to Expect from HPLC 2025

Gert Desmet reveals how HPLC 2025 is set to tackle the major trends and challenges facing separation science today

What is the overall mission statement of the HPLC conference?

The HPLC conference series – as far back as 1974 – has always set out to be the premier venue to learn about the newest technologies and advances in liquid chromatography and related techniques. To achieve this, the conference includes lectures on the hottest scientific and technological evolutions, short courses and tutorials, an exhibition showcasing the newest instruments and columns, and a rich social program to stimulate networking. European HPLC editions usually draw a crowd of between 1200 and 1500 delegates.

How would you describe the current scope of the HPLC meetings?

The HPLC program covers all aspects of separation sciences in liquid and supercritical fluid phases, as well as hyphenation in advanced detection technologies (mass spectrometry in particular). With the 2025 program in Bruges, we'd also like to spotlight the "Related Techniques" extension in the official designation of the HPLC conference series. Furthermore, liquid chromatography is seldom the only separation technique in an analyst's toolbox, which is why we also offer dedicated sessions and tutorials for related separation sciences; such as preparative chromatography, supercritical fluid chromatography, gas chromatography, field-flow fractionation (FFF) and other particle separation techniques.

What would you say are the main developments and challenges in separation science today?

One key trend in pharma in recent years has been a move towards the analysis and characterization of evermore complex modalities, including adeno-associated viruses (AAVs) and mRNA-loaded lipid nanoparticles. Chromatographers are, therefore, being encouraged to expand their toolbox with new techniques, such as asymmetric flow-field flow fractionation (AF4). To meet this need, dedicated tutorial and topical sessions on FFF are planned for our program.

Another important trend is the implementation of AI at all possible levels of data analysis and instrument automation. To help those unfamiliar with AI and machine learning, HPLC 2025 is organizing a short, entry-level course and tutorial. For the experts (or just those with a keen interest), we'll have dedicated sessions on AI for data analysis and a session featuring AI-based instrument automation, called "The Intelligent Instrument."

Sustainability also remains a hot topic. In turn, the program will feature a dedicated oral session, as well as a tutorial by Elia Psillakis on how to best quantify the greenness/sustainability level of your methods/lab. A topical poster competition featuring an assessment of methods displaying green metrics is also planned.


Gert Desmet

Which other sessions or innovations do you expect to make up the highlights of the program?

We're expecting some buzz during the poster sessions, which for the first time will be organized as "poster & exhibitor fests," including new opportunities for interactions with the exhibitors.

We're also expecting a lot from our "bring your boss to the HPLC conference" initiative. For senior lab managers joining this program, there will be two "invitation-only" half-day sessions wherein industry leadership can share experiences and good/bad practices in lab management and organization. There will also be the opportunity to develop their views on HPLC instruments, laboratories, workflows, and the skills required by the next generation of analytical talents. The conclusions of these sessions will then be discussed with the rest of the delegates in a plenary debate session.

"We believe the future of the HPLC conference series will be an event where active chemical analysts can expand their chromatographic knowledge, discover new automation and data processing methods and, above all, learn from each other's experiences."

Could you expand a little more on the theme of industrial developments?

While advances in academic chromatography research have slowed in recent years, the total number of HPLC industry professionals nonetheless keeps growing. However, the number of active HPLC practitioners working in the industry who didn't receive their primary training in chromatography and separation science also continues to grow. Therefore, we believe the future of the HPLC conference series will be an event where active chemical analysts can expand their chromatographic knowledge, discover new automation and data processing methods and, above all, learn from each other's experiences.

A new initiative to facilitate this is our dedicated "industry stories" sessions, showcasing the most interesting examples of problem solving in industry. In addition to typical success reports, here we'll encourage presenters to reveal the mistakes they've made (if any), and any challenges or setbacks faced.

Next, we will also have dedicated oral presentation sessions on sustainability, lab and workflow automation, data processing and preparative chromatography.

Another cornerstone in the industry-oriented part of the program will be a plenary debate on the current challenges and future opportunities for HPLC analysis in industry.

Can you name some speakers to look out for?

Koen Sandra will kick off the conference with a didactic and visionary talk about the (very timely) topic of mRNA structural characterization. Our second plenary opener will be professor Kerstin Thurow – she heads the center for life science automation (CELISCA) and will be talking about current developments and future perspectives in analytical laboratory automation.

A few more notable topics include thoughts on recent innovations in mass spectrometry from Alexander Makarov, the processing and mining of chromatographic data with industry perspectives by Joachim Richter (former VP at BAS, before his recent retirement), and demonstrations from Ryan Kelly on in-depth single-cell proteome coverage in 5 minutes or less. We'll have Bob Pirok speaking on the sense (and nonsense) of AI in chromatography, numerous contributions on oligonucleotide and AAV analysis and Pascal Mieville from the EPFL Lausanne will discuss the road towards a self-driving laboratory.

Finally, why choose Bruges?

Bruges is a great city to host a conference, with all hotels, city highlights, restaurants and pubs (and there are many of these) within walking distance. Often referred to as the "Venice of the North," Bruges is famous for its well-preserved medieval architecture and culinary delights, such as Belgian chocolates, waffles, and beers. The entire city is a UNESCO World Heritage site with easy accessibility through the well-connected international airport in Brussels. Major European cities such as Amsterdam, London and Paris are within a range of maximally 300km, and all are easily connected by high-speed trains.

Tivadar Farkas: Industry's Chromatography Crusader

2025's Uwe D. Neue Award winner, Tivadar Farkas, shares his key lessons learned from a career in separation science spanning three decades

Could you give us an introduction to your background and career journey?

I began my career back in 1983 by engaging with professionals within the industry, research institutions and academia. Most of these years were spent gaining practical experience in analytical chemistry, specifically gas chromatography. In 1992, I moved to the US to pursue a PhD with the late Georges A. Guiochon at the University of Tennessee, Knoxville. During this time, I studied HPLC column heterogeneity using a variety of detection techniques.

How do you reflect on your time – close to three decades – at Phenomenex?

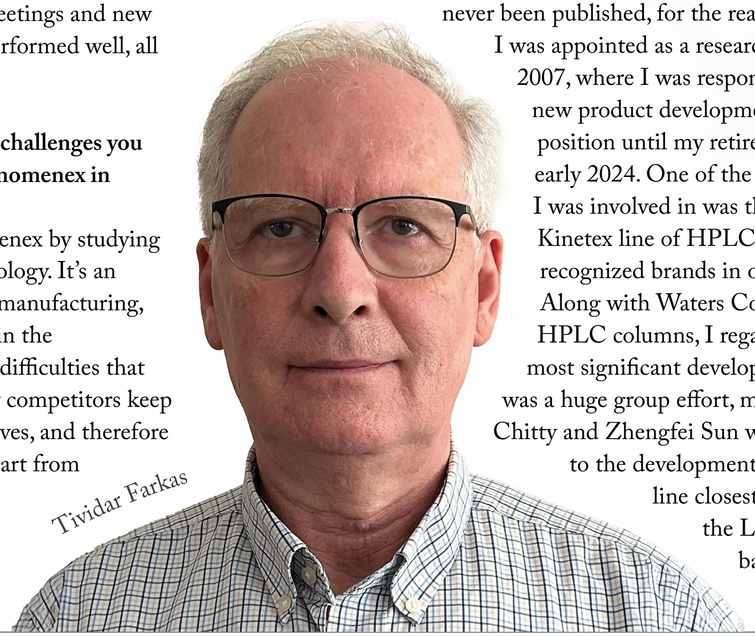
I joined Phenomenex as a senior research scientist in 1997. It was a great opportunity for me to take up a position in a young and dynamic company with a healthy work culture, a wealth of success-driven employees and minimal internal politics. The president, Fasha Mahjoor, ensured that our working atmosphere stayed conducive to success across many decades. Fasha was open to new ideas and initiatives and ready to provide funding for many. Owing to its dedication to customer support, a culture of innovation, and the hard work of many of its employees, Phenomenex quickly succeeded in asserting itself as a leading product supplier for chromatography.

For several decades, the R&D department at Phenomenex has been extremely productive. Numerous new products have been launched each year for HPLC, GC, SPE and preparative LC applications. Our teamwork was excellent, perhaps as we collectively considered ourselves not as geniuses, but rather soldiers – all dedicated to the common cause. Emmet Welch – a home-grown chromatographer and our R&D director at the time – kept the team aligned and focused on delivering new products.

Given the limited access that a company of our size had to online journals, scientific meetings and new instrumentation, I think we performed well, all things considered.

What were some of the major challenges you faced during your time at Phenomenex in driving new innovation?

I started my career at Phenomenex by studying HPLC column packing technology. It's an important element of column manufacturing, and anyone who's well-versed in the technology can appreciate the difficulties that are associated with it. Industry competitors keep relevant knowledge to themselves, and therefore very little of it is published (apart from sections included in patents, perhaps). This knowledge is kept as trade secret for good reason; the livelihood of these companies depends on their essential knowhow, which has to be safeguarded. On the flipside, the lack of healthy exchange on any aspects of science and technology will always be a sizable impediment to progress.


Tividar Farkas

My following role was to manage the analytical support of new product development – selecting, designing and implementing the most informative tests for the new product candidates. The historical tests – proposed mostly from chromatographic literature – may have performed well at the standards of their time, but were long overdue an update considering how far the field had come. Again, some of this work on new column characterization has never been published, for the reasons aforementioned.

I was appointed as a research managing scientist in 2007, where I was responsible for overseeing most new product development projects. I held this position until my retirement from Phenomenex in early 2024. One of the most challenging projects I was involved in was the development of the Kinetex line of HPLC columns – one of the most recognized brands in our industry, in my opinion. Along with Waters Corporation's Acquity line of HPLC columns, I regard Kinetex as one of the most significant developments in UHPLC. While it was a huge group effort, my former colleagues Michael Chitty and Zhengfei Sun were the major contributors to the development of Kinetex. The product line closest to my heart, however, is the Lux family of polysaccharide-based chiral HPLC columns.

"Scientists working in industry have to champion their own ideas. Whenever the front door is slammed shut, they should sneak in through the back."

I spent more than a decade working with my good friend Professor Bezhan Chankvetadze on its development and promotion; and following my retirement it's remained a hobby for me – I still assist my former company with Lux as a consultant.

Do industry scientists – in contrast to academics – face greater challenges when it comes to making significant scientific contributions?
Overall, I've found working in industries that serve pharmaceutical, environmental, forensic or food analysis to be quite rewarding. It's been very satisfying to know that our products contribute to the availability of essential medicines and information on our environment and food safety.

Comparing industry to academia, it's fair to say both worlds have their own share of challenges. Scientists in industry work exclusively on unmet needs, with limited bandwidth to work on "pet projects." Furthermore, we're restricted to the pursuit of specific innovations that are essential to progress or commercial success; there's no option to walk away from a project if it seems too difficult. On top of all this, limited dialogue with industry peers or academia makes industrial research quite a challenging task, as previously mentioned.

Do you feel industry scientists are sometimes overshadowed by their academic counterparts?
Yes, industrial scientists are often overshadowed by academia – and for the wrong reasons too.

I personally have experienced occasions of neglect. The most distressing of these were instances when our company developed excellent new products, which were then handed over to third parties. These parties then got to present and publish on our products, on our achievements, and receive praise as if they were theirs. Simultaneously, when presented by the inventing team the same information was often received mildly, or with reservations. I found this unfair and the reservations unjustified.

My view on the situation is this: some academic publications have disciples who may or may not confirm the published results. Compared to commercial products, only a limited number of academic publications are subject to scrutiny; most conclusions are rarely contested. No matter the claims from the inventing company, their new product will be evaluated by hundreds of analysts, who'll decide for themselves if the product is truly worthy of incorporating into their analytical workflows – now that's scrutiny! With this in mind, I wonder: why not allow the inventors to flaunt their achievements, knowing that the day of reckoning is soon to come?

During your career in industry, what are your big innovation lessons learned?
Just like academia, industrial development is limited by resources. With livelihoods at stake, companies cannot afford to waste too much on failed projects. For this reason, no matter how promising they seem, companies have to be cautious when pursuing new ideas. Any great idea needs champions within the company, otherwise leadership will not believe it's worth taking a risk on.

It's for this reason that scientists working in industry have to be the champions of their own ideas. They should look to sell them internally – whenever the front door is slammed shut, they should look to sneak in through the back. My advice to younger industrial researchers is to be evangelists in your ideas, right up to the very end when the project is completed.

Tivadar Farkas will be presented with the Uwe D. Neue Award in Separation Science – created to recognize industrial scientists that have made and continue to make significant contributions to the field of separation science – at HPLC 2025

The HALO® Effect

Tim Langlois, President of AMT, celebrates two decades of cherishing quality and driving innovation for the HPLC community

Please give us an overview of Advanced Materials Technology – and the 20-year milestone…
Advanced Materials Technology (AMT) was founded by me and Joe DeStefano back in May 2005. AMT gave both of us an opportunity to fulfill our ambitions of starting a business that used our knowledge of liquid chromatography and silica chemistry to develop products that were both innovative and commercially successful. A combination of the resulting products, a dedicated team of employees focused on quality, lifelong connections within the HPLC community, and a strong network of knowledgeable column distributors around the world have helped make AMT a 20-year success.

Can you take us back to the development of the AMT's SPP column – what inspired the innovation?
After establishing the company, we hired our friend and former colleague Dr. Jack Kirkland – an HPLC pioneer whose name will be familiar to most in the field. He worked with us on several different silica particle projects, one of which was the design of a small-particle superficially porous particle (SPP). Although SPP is more common nowadays, AMT had to overcome the task of placing nanoparticles on the surface of a non-porous micron size bead in an orderly fashion. To put that in perspective, around 75 of these non-porous beads equate to the thickness of a human hair, while around 15,000 nanoparticles add up to that same width. Under magnification our SPP looked like a halo, inspiring the brand HALO®.

One of AMT's key innovations is Fused-Core® Technology. Can you explain how it works and how it improves chromatographic performance?
Fused-Core® Technology involves a particle composed of a solid core, surrounded by a thin layer of porous silica thermally fused onto the core at high temperature. Columns packed with such particles have been chromatographically proven to provide improved separation performance over totally porous particle columns. Why? Because the distance sample molecules travel inside Fused-Core® particles is comparatively shorter than that with totally porous particles.

Superficially porous particles (SPPs) are a means of improving the ability and efficiency of packed bed HPLC columns operating at higher flow rates, which enables faster separations. A natural desire when performing analytical separations is to carry out tasks at a greater speed. However, this challenges the fundamental relationships between mobile phase flow and the transfer of sample components between the stationary phase on the particles and the moving fluid: the transfer of components of interest is fastest with shorter paths able to move fluid through the packed bed smoothly. The Fused-Core® particles are up for the task!

What key challenges do AMT's HALO columns help to address?
Over the past 20 years, our research at AMT has pursued the development of SPP for separations of larger molecules – biological macromolecules, in particular. The ability to efficiently

separate large molecules is directly enabled by use of large pore SPP column packings (for example, 400 Å or 1000 Å). The effects of pore size and shell thickness on SPP design have been explored in many publications. These studies show that manipulating material properties enables faster and more efficient reversed-phase (RP) and hydrophilic interaction liquid (HILIC) chromatographic separations of molecules up to at least 150 kDa, such as monoclonal antibody immunoglobulin (mAb IgGs). This also extends to various conjugates of such proteins – antibody-drug conjugates, for example – and synthetic nucleic acids. As has been independently assessed, wide pore SPPs are an authentic step forward for separations, as they become frontline products in protein analytical science.

Can you give us an overview of AMT's full product line?
The HALO® product line spans a diverse range of products to meet market demands, ranging from capillary (<1 mm inner diameter) to preparative columns (>10 mm inner diameter). AMT was founded for solutions of small molecule separations, which now comprise 15 chemistries, but we continue to innovate with our HALO® BIOCLASS line of columns to ensure we remain at the forefront of bioseparations. These columns offer the necessary particle and pore morphology for the analysis of proteins, peptides, oligonucleotides, and glycans. AMT's innovative 1000 Å protein column for studying intact monoclonal antibodies (as well as other large proteins) was a first-mover separations innovation to provide high resolution characterization. We also released the HALO® Oligo column to address needs in the rapidly-growing oligonucleotide therapeutic space.

More recently, AMT has come to the market with application-specific columns to address shortcomings of environmental LC separation methods. The HALO® ENVIROCLASS line includes solutions for PFAS and PAH, joining the other small molecule chemistries for the analysis of additional environmental concerns, such as pesticides, mycotoxins, and herbicides.

How does AMT ensure that its columns continually meet high standards of quality?
Quality and customer satisfaction are paramount to the success of AMT. After all, without a satisfied customer that's willing and able to purchase the "same" column for years to come, our business ceases to be successful. AMT is an ISO 9001 company that uses quality-by-design principles. Perhaps most importantly, we create all parts in-house – from the start of the silica particle to the finished column – to ensure successful separations every time. With relentless quality, and process control from the beginning of the silica synthesis to the end column, AMT is committed to Quality (with a capital Q)!

As AMT celebrates its 20-year milestone, what's next for the company?
We've just finished a major expansion and facility upgrade to prepare ourselves for the next 10 years (and beyond) of increased business. Our new product pipeline is very healthy, with separation products addressing challenges in aforementioned "hot" areas, including oligonucleotide separations and short-chain PFAS analysis. But we are also entirely committed to the development of new columns that provide our users with greater flexibility in achieving their separation goals.

We also continue to participate in conferences – both technically and commercially – to forge new relationships with customers in the industry and build our understanding of the evolving needs of LC separations. The need for face-to-face interactions was proven when we launched our 1.5 mm ID columns: the market was demanding the sensitivity of a micro system, but with the robustness of an analytical system. Customers also had sustainability initiatives around organic solvent consumption. Our 1.5 mm ID column hardware bridged the gap between a micro-LC column and an analytical 2.1 mm ID column and, in turn, provides greater sensitivity through enhanced detector signal response while using 50 percent less solvent. All of this in a format that can be used on a commercial UHPLC system – ultimately a better solution for separations and the planet.

More recently, our developments have focused on helping separation scientists improve their chromatographic performance against basic analytes, prevalent in the pharmaceutical industry. This includes both a high pH and high temperature stable phase, as well as positively charged surface chemistry. We've also recently introduced an inert line of columns that prevent unwanted sample adsorption to stainless steel. I'm very proud to say that the team at AMT is still applying technical expertise to produce new technologies – just like we did 20 years ago! A quick browse through our latest catalog shows different particle sizes, pore sizes, including the first 1000 Å, bonded phases, and more. As we go forward, we'll continue to develop and introduce new technology to the separations community. Oh – and I should add that we are now the only SPP manufacturer who can claim 20 years of manufacturing history in sub-3 micron SPP products!

Pushing the Limits of Liquid Chromatography – Ten Years Later

In 2015, we gathered together a group of experts to ask: have we reached the limits of liquid chromatography? Our experts returned a resounding, "no!" – as they did two years later in the follow-up piece. However, ten years on – and with HPLC 2025 just around the corner – we feel the time right to revisit our provocative question: are we still pushing the limits?

With Fabrice Gritti, Principal Consulting Scientist, Waters Corporation, USA; Gert Desmet, Full Professor and Department Head, Vrije Universiteit Brussel, Belgium; and Martina Catani, Associate Professor, Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Italy

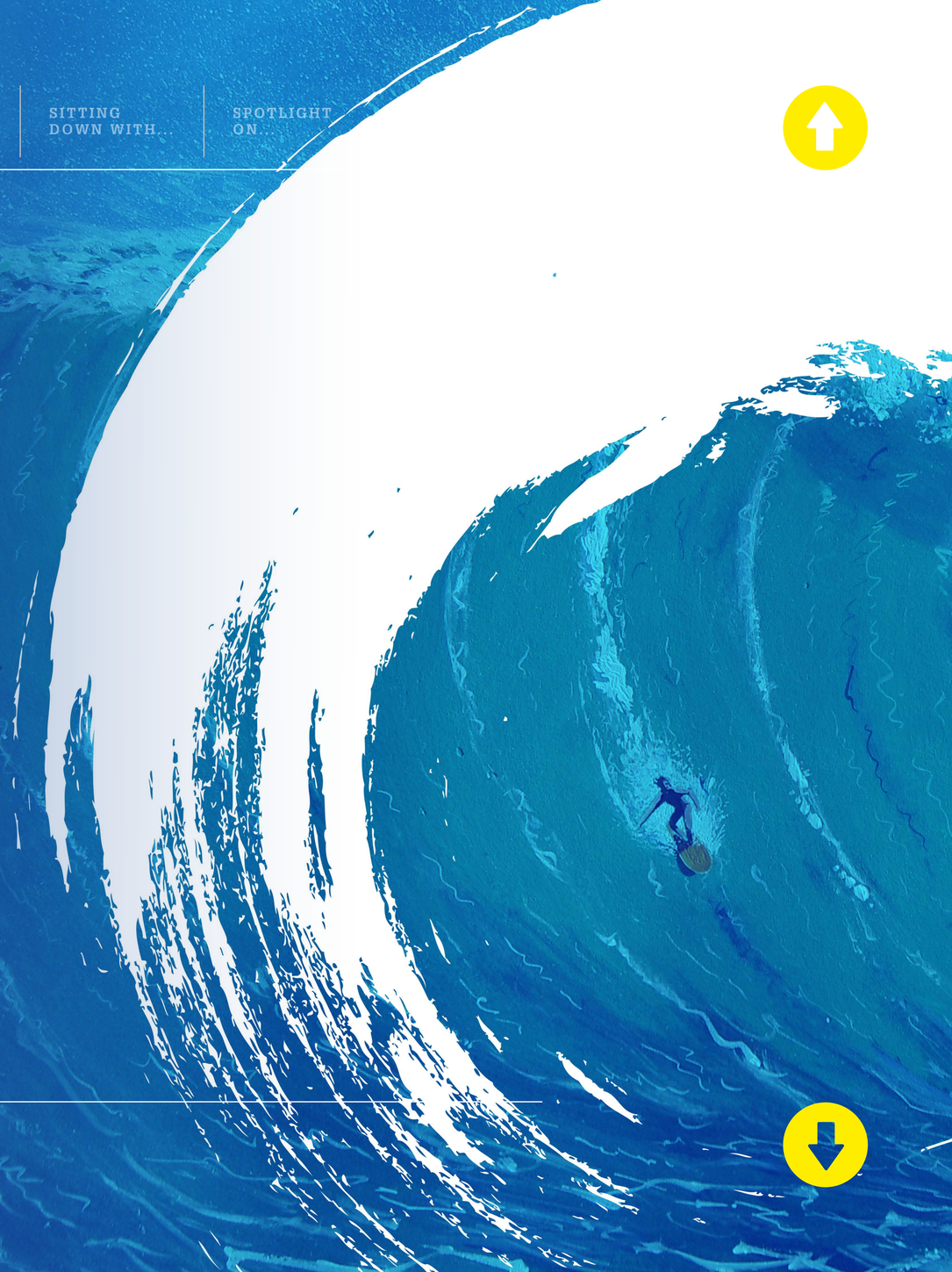
When you look back over the past 10 years, has HPLC innovation lived up to expectations?

Fabrice Gritti: Yes, I believe HPLC innovation has lived up to expectations – though not through breakthroughs in resolution, selectivity, or throughput, which have remained relatively stable (notably, UHPLC celebrated its 20th anniversary last year). Instead, the last decade has seen HPLC evolve in response to the analytical challenges posed by complex biomolecules such as monoclonal antibodies (mAbs), mRNA, adeno-associated viruses (AAVs), and lipid nanoparticles (LNPs). This growing demand has catalyzed significant advances in column and system technologies.

The most impactful development of the past decade has been the emergence of fully bio-inert systems and columns, designed to overcome issues like sample loss and resolution degradation caused by metal-analyte interactions. Manufacturers have introduced metal-free hardware, new surface chemistries, and specialized columns – such as robust SEC columns with ultra-wide pores (up to 2000 Å for LNPs) and slalom chromatography columns tailored for large DNA/RNA molecules. These solutions have dramatically improved the analysis of sensitive compounds and accelerated innovation in biopharmaceutical research.

Gert Desmet: I would say the past 10 years were evolutionary rather than revolutionary, but that doesn't take away from the fact that steady improvements were made nonetheless. For example, the uniformity of commercially available particles has improved significantly, and new microfluidic techniques are being developed to improve this further still.

Martina Catani: The HPLC landscape over the past decade has been shaped by three core advancements, in my opinion. Firstly, UHPLC instrumentation evolved through innovations in plumbing, particularly with corrosion-resistant materials and metal-free flow paths that broadened biopharmaceutical applications. Concurrently, hyphenated techniques like LC coupled to high-resolution mass spectrometry, as well as comprehensive two-dimensional liquid chromatography (LC×LC), became indispensable for complex separations in proteomics and metabolomics – driven by the growing need for biomarker discovery and personalized medicine. Secondly,



automation has been improved thanks to AI-driven software integration and optimization, reducing errors and streamlining method development. Finally, sustainability emerged as a priority, marked by eco-friendly practices, such as reduced solvent consumption, novel mobile-phase formulations, and miniaturized systems like nano-LC.

So, has HPLC peaked?

Desmet: It is undeniable that research on HPLC columns and instruments is declining, especially in academia, and that most of the significant strides forward have already been made. However, nobody saw the core-shell revolution coming (and I really mean nobody, because their advantage turned out to be much bigger than can be explained based on their presumed advantage: the reduced intra-particle diffusion distances). So who's to say we won't get surprised again? Indeed, there is still room for improvement: about 50 to 60 percent of the band broadening in our columns is today still wasted to omissible eddy-dispersion.

A few years ago we were close to a new breakthrough when Agilent researchers worked on core-shell particles with radially-only oriented mesopores, showing a 33 percent decrease in plate height compared to the "normal" core-shell particles. Unfortunately, the material never made it to the production and commercialization phase. However, if someone can solve the impediments, we may just be in for another unexpected revolution in particle technology.

Gritti: Although certain aspects of HPLC, like particle size reduction and packed column performance, may have reached practical limits due to physical and chemical constraints, the technique has not peaked. About 15–20 years ago, discussions at international conferences predicted a lower limit around 1.5 µm for the particle size, due to challenges with pressure, heat dissipation, and system dispersion. Those limitations still hold today, making further gains in speed and performance from smaller particles unlikely. Similarly, major breakthroughs in column selectivity are rare, aside from some promises in mixed-mode HPLC. However, many other areas – such as bio-inert column and system design, advanced detection methods, automation, hyphenation, data handling and processing – continue to evolve rapidly.

The history of HPLC reminds us that while core principles are bound by physics, innovation often thrives in novel surface chemistry, system hyphenation and integration and application expansion.

What are some of the hottest trends in HPLC today?

Gritti: In addition to the development of improved columns and systems designed to meet the needs of application chemists working on the characterization of complex biological systems discussed above, which I would say is the hottest trend, another major trend is the rising importance of artificial intelligence in chromatography, particularly for system diagnostics and predicting compound retention based on molecular structure in untargeted metabolomics, proteomics, and lipidomics. Although still in its early stages, this approach holds significant promise due to the vast amount of data being generated in these fields.

Desmet: I agree that the evolution towards the analysis of ever larger molecules, originating from the surge in biopharmaceutical

drug development, is for sure the hottest trend. The analysis of oligonucleotides and the characterization of adeno-associated viruses (AAVs) are clear examples of this, as Fabrice mentioned. At the other end of the spectrum, I also find the quest for sensitive single-cell proteomics and robust clinical proteomics very interesting and promising.

Catani: I agree with Fabrice and Gert – the analysis of large biomolecules and proteomics/metabolomics approaches are certainly among the hottest trends. I would also add that many efforts are also given to the development of sustainable separation methods, for instance by designing novel adsorbents to be used in pure aqueous mobile phases or by exploring the possibility of replacing common organic modifiers with greener ones.

Is AI having an impact on the HPLC field today?

Desmet: Not yet – at least as much as it could have or should have. Because, with the number of HPLC practitioners without a strong separation science foundation growing bigger and bigger, it seems natural to compensate by making the instruments more intelligent. However, so far most AI and machine learning efforts are still limited to the academic groups, often focused on developing better retention time prediction models. This work has yet to led to new products for the users community.

Could machine learning be used to take control of instruments and propose new, better gradients by reviewing the results of the past gradient runs? That would certainly be interesting. Some work in that direction has been done at the University of Amsterdam, in Belgium in Brussels and Leuven too, as well as in some vendor companies, which is good news. (I happen to know some of them will report on this at the upcoming HPLC conference...)

Gritti: Agreed – currently, AI has a very limited impact on the HPLC field, as it remains primarily at the research stage rather than being a fully adopted and validated tool within the broader HPLC community or by regulatory bodies. That said, AI-supported HPLC is highly attractive and holds great promise. It has the potential to significantly accelerate method development and data handling, reduce failures in large-scale chemical processes through automated process analytical technologies, and improve the environmental footprint of preparative HPLC.

Yet, trusting AI predictions in the HPLC field is a risky business. Nevertheless, these efforts are expected to continue and expand in the coming years, especially as this area of research continues to receive strong support from grant funding agencies.

Catani: I believe that AI holds transformative potential in chromatography – to accelerate method development and enhance analytical precision, but I agree that its application is still limited to a research stage now. Recent HPLC symposia have highlighted machine learning's ability to predict optimal chromatographic conditions, such as mobile phase composition and gradient profiles, by training algorithms on minimal experimental data, leveraging molecular properties like polarity and solubility. This approach drastically reduces the time traditionally spent on trial-and-error optimization. AI-driven tools could also address complex peak deconvolution, automating integration tasks that require manual intervention, thereby improving reproducibility and throughput.

Looking ahead, I believe that AI-powered data processing could revolutionize also the field of omics sciences by extracting functional insights from large datasets, identifying patterns (e.g., compound correlations or compositional shifts in mixtures), and enabling real-time decision-making in fields like metabolomics and proteomics. This potential could position AI as a cornerstone for next-generation chromatographic innovation.

Gazing further into your crystal ball… In the decade to come, what might the next "HPLC gamechanger" look like?

Gritti: Looking into the decades ahead, I believe the next HPLC game-changer will be the integration of artificial intelligence across nearly every stage of the workflow – from sample preparation and method development to data handling and processing.

Process development for large-scale bioreactors will also benefit significantly from AI and hybrid modeling approaches (e.g., digital twins), helping to reduce both costs and carbon footprint.

Moreover, I believe that generative design – combining fundamental principles of physics and chemistry with the vast amounts of data generated today – will drive the discovery of new 3D column structures, enhancing both speed and resolution. These innovations could become accessible to HPLC users once 3D printers capable of producing at 1-micron resolution across large build volumes are widely available.

Desmet: In the area of column technology, I still expect a lot from new particle morphologies. I already mentioned the possibility of core-shell particle with radial-only oriented pores to produce columns with a reduced minimal plate height of 1; but other particle formats – such as spiky particles, for example, which would generate a drastically lower hydrodynamic resistance than conventional spherical particles – could one day emerge and surprise us all.

I also expect some important breakthroughs from the pillar-array column technology. Whereas particle packed columns have clearly reached their limit in terms of size reduction, the development of pillar array columns still only in its infancy and is far from reaching its fundamental operation limits. Nor has it already fully exhausted its potential to increase flow rate ranges.

Then there's the design of our instruments – which still have the same "hi-fi tower" design as 40 years ago and therefore generate too much extra-column band broadening compared to that created by today's state-of-the-art columns, especially when trying to meet industry's desire to work with smaller i.d. columns. Our current instruments are also not user-friendly and foolproof enough to provide a proper response to the declining degree of chromatography training of today's chemical analysts. Therefore, in the not too distant future I expect to see the emergence of radically novel instrument lay-outs, allowing columns to be installed as a simple cartridge – like we do in our printers or coffee machines – and that have enough intelligence on-board to operate fully autonomously.

Overall, are you optimistic about the future of HPLC?

Desmet: Sure, as long as the ion-suppression problem of MS detection does not get fundamentally solved, chromatography will remain the key technology to analyze and quantify complex samples. And given that the fundamental performance limits of the technology in terms of speed and efficiency have not been reached yet – by far – I am quite confident we will continue to witness new breakthroughs in the future.

Gritti: Absolutely. HPLC will always remain a force to be reckoned with. It is one of the most sensitive analytical techniques available, capable of detecting subtle differences in free energy, approximately 25 J/mol using recycling chromatography (for selectivity $\alpha = 1.01$), while the weakest dispersive intermolecular interactions in nature are around 50 J/mol.

That said, HPLC and multi-dimensional HPLC are not a panacea for sample characterization. Rather, they will continue to play a vital role by complementing and being hyphenated with other analytical techniques. In a world where both the amount and complexity of chemical systems to be analyzed are constantly increasing, HPLC will remain an essential tool for the success of analytical scientists.

Catani: Yes, certainly. I believe HPLC will still be considered the gold standard separation method. And given the continuous development in terms of instrumentation and column formats, I could envisage an advancement in the design of portable and miniaturized instruments for in-field analysis. This could also significantly reduce challenges in sample preparation and storage.

Looking Back, Moving Forward

Deirdre Cabooter discusses the current and future trends affecting analytical science; addressing topics such as AI, personalized medicine and the resurgence of green chemistry

What would you say has been the biggest accomplishment in the field of analytical science as a whole over the past decade or so?
I couldn't narrow it down to just one! One major advancement that has had a huge impact on society as a whole, as well as analytical sciences more generally, is the introduction and integration of machine learning and artificial intelligence. Now a part of our daily lives, it's been exciting to see how these technologies have been used in analytical science for quite some time now. They are instrumental in data analysis, for instance, as mass spectrometers become more advanced and data more abundant. Machine learning algorithms assist with data interpretation and can even make predictions, such as forecasting compound properties based on their structure. Retention time predictions also rely on these approaches. Additionally, AI helps automate tedious tasks like peak identification, integration, and tracking, to assist method development. I believe the integration of AI in decision-making will continue to grow and shape the future of the field.

Another significant accomplishment is the development and increased accessibility of affordable, user-friendly, high-resolution mass spectrometers. These instruments have become more common in laboratories, which is fantastic because it means more people have access to high-resolution techniques and their improved sensitivities. One application I've found to be particularly fascinating is their use in real-time measurements, such as in operating rooms, where they're used to make on-the-spot decisions on whether tissue is cancerous or healthy.

Lastly, something I personally appreciate as a daily user is the commercialization of two-dimensional liquid chromatography (2D-LC). In the past, this was primarily a technique used in academic labs with systems built in-house. Commercial availability has made 2D-LC more accessible, and it's now being adopted more and more in industrial settings. This represents a significant step forward in tackling the complexity of modern samples and meeting future analytical challenges.

What about trends over the past year? Are they a continuation of the ones you mentioned earlier, or did anything new emerge?
Something that stood out to me at conferences in 2024 were the numerous talks on oligonucleotides. These therapeutics are drawing a lot of attention due to the challenges they present in analysis, so it makes sense that many groups are focusing on them.

Another trend I've noticed, although not exactly new, has been a renewed interest in green chemistry. It's been around for quite a while, but possibly due to the global emphasis on Sustainable Development Goals, it seems to be regaining momentum. What's particularly interesting is that it's not just about using greener, renewable, or less toxic solvents anymore. There's also a push to make analysis more efficient; by streamlining workflows, reducing solvent consumption, and embracing automation. I think automation using machine learning and artificial intelligence is

playing a big role here, allowing us to move away from the endless "trial-and-error" approaches in favour of more efficient method development. Miniaturization and maximizing the number of analyses performed in a single run are also contributing to reducing environmental impact.

Finally, as I mentioned earlier the increased adoption of machine learning in research has been noticeable – not just in publications but also in conference presentations. It's exciting to see how this technology is being embraced by so many groups and applied in innovative ways.

Looking to the future, what would you say are the biggest challenges facing the field? Are there any in particular you'd highlight?
One area I often discuss is complex samples, which I think represent significant challenges across various fields. In health and clinical settings, we deal with biological samples and drug development, which are inherently complex. Similarly in environmental sciences, there's a lot of focus on detecting, identifying, and treating contaminants in the environment, with these efforts also involving highly complex samples.

To truly understand what's happening in these areas and drive progress, we need to be able to analyze these samples efficiently and quickly. This requires the development of better methods – high-resolution techniques that can deliver results in shorter time frames. At present, method development is still taking too much time, so we need to find ways to streamline and optimize this process. Improving the speed and efficiency of analysis will be a major focus moving forward, as faster, more robust methods will enable us to perform better and more frequent analyses, which is crucial in order to effectively tackle these challenges.

Are there any societal trends you see impacting analytical science?
Absolutely. Although analytical sciences are applied in so many fields, I think two major trends stand out. First, the environmental focus is critical – addressing contamination, monitoring pollutants, and understanding their impact is a significant driver. Second, health and the treatment of diseases are equally crucial. There's a growing demand for techniques that enable earlier, quicker, and more accurate disease detection, as well as more personalized approaches to treatment. This push toward precision medicine is shaping the field.

Both of these areas are driving the need for better, more sensitive, and higher-resolution techniques. What excites me is how these challenges force us to think creatively, to innovate, and to develop new methods that not only meet these demands but also provide broad societal benefits.

How do you feel analytical science is currently perceived by the wider scientific community?
Sometimes, I feel like we're treated as just a "tool," with people coming to us saying, "Can you quickly analyze this sample for me?" But I believe we, as analytical scientists, need to take more pride in what we do. Our techniques and methods form the foundation of understanding across disciplines.

If you want to solve a problem or make informed decisions, you first need to know what's there, what's causing an effect. This makes separation, identification, and quantification so important in making decisions and reaching conclusions. Analytical science isn't just an add-on; it's central to the entire process. I believe it will continue to play a crucial role in solving these major challenges and advancing our understanding in the years to come.

In order to shift this perception of analytical scientists as being "mere tools," what are the main areas to focus on? Could interdisciplinary collaboration help here?
Interdisciplinary projects and collaborations are happening more and more. I see it in my own work, and in the types of projects we apply for. On one hand, funding agencies are increasingly encouraging interdisciplinary approaches, often creating special funding schemes for such projects. This makes sense, as addressing big challenges like health, sustainability, and environmental issues require interdisciplinary approaches.

That being said, I think it's equally important to maintain a strong focus on the basics and ensure there's still funding for fundamental research. Funding priorities vary by country, but I always try to emphasize the importance of fundamental research in my interdisciplinary projects; I often include a dedicated work package focused on foundational developments, for example. It's essential to demonstrate that while we're capable of addressing applied problems, we can achieve even more with time and resources for investigating fundamental aspects, such as hardware improvements or new methodologies.

I think another area we need to focus on is education. It's not exactly about "adding new tools to the toolbox," but rather ensuring we train people properly in analytical sciences. Sometimes I feel that students are content with simply pressing the "start" button on an instrument and generating data, without fully understanding how the system works. In our group, we emphasize the importance of understanding the instruments – how they work, how to troubleshoot when they break, and the fundamentals behind their operation. I'm fortunate that my students are enthusiastic about

"On the chromatographic side there's still room for innovation. For example, we already use 2D-LC, but we need to integrate and optimize it further. Smarter, more efficient combinations of chromatographic techniques could help us extract even more information from complex samples."

diving into these details, but this focus needs to start early, even at the bachelor's level. We need to ensure that students grasp the instrumentation, the core concepts and the working mechanisms, as this foundational knowledge equips them to excel in their future careers and adapt to the evolving challenges in the field.

Is there anything else you think needs to happen to make that progress over the next five to ten years?

From my perspective, it's important that we focus on high-resolution techniques. I work primarily with chromatography, so my expertise isn't in mass spectrometry, but on the chromatographic side there's still room for innovation. For example, we already use 2D-LC, but we need to integrate and optimize it further. Smarter, more efficient combinations of chromatographic techniques could help us extract even more information from complex samples.

Beyond separation, we need to focus on hyphenated techniques – integrating separation with detection and identification. The goal is to not only separate as much as possible but also to detect and identify everything we can within a sample. However, as these techniques improve and generate more data, we'll face the challenge of managing and interpreting all of it. Generating efficient algorithms will be essential to make sense of the abundance of data these methods will inevitably produce.

Could you talk about the role of chromatography in achieving these big goals and ambitions?

Questions about whether you still need chromatography if you have high-performing mass spectrometers come up often. But I absolutely think chromatography remains crucial, as it addresses limitations that mass spectrometers alone cannot solve. For example, mass spectrometry struggles to differentiate between compounds with identical masses. In these instances, chromatographic separation is essential for resolving these issues.

Chromatography also mitigates problems like matrix effects in mass spectrometry. A better separation leads to cleaner sample introduction, which is especially important when dealing with unknown compounds. This, in turn, strengthens and simplifies identification. I see chromatography and mass spectrometry as complementary tools, with neither replacing the other. Together, they provide the best possible outcomes for analyzing complex samples.

What's your overall perspective on the future of the field?

I'm very positive about the future. I still wake up inspired by the challenges and opportunities ahead – whether it's improving hardware, advancing software, or tackling exciting new applications. Every day brings new possibilities, whether in clinical analysis, food safety, or environmental monitoring.

I don't see the field as fully mature or nearing its limits. There's so much more to explore and innovate. I'm particularly excited about interdisciplinary projects, where we collaborate with people from other fields to brainstorm, solve problems, and develop new techniques and solutions for societal challenges. These opportunities keep the work fresh and meaningful.

Ask me again in five or ten years, but for now, I remain extremely excited and optimistic about what's to come!

HALO® Elevate: Universal Column for Small Molecule Method Development

Many chromatographers are familiar with the difficulties of separating basic compounds on silica-based columns due to the increased peak broadening and tailing that may occur, however, it is important to note that silica-based columns are preferred due to faster equilibration times, along with much higher-pressure stability. (compared to polymer-based columns)

There are several ways to improve the peak shape of basic compounds such as increasing the ionic strength of the mobile phase (adding a salt/buffer), use of an ion pair agent, elevating the pH of the mobile phase, using a non-silica-based column, or even using an alternative stationary phase such as a charged surface material.

The main objective during HALO® Elevate development was to make a material that is stable under alkaline conditions to improve the peak shape and retention for basic analytes. In order to achieve this goal, an organic/ inorganic surface modification was introduced protecting the silica from harsh alkaline conditions. This modification allows users to run in alkaline conditions for extended periods of time. Figure 1 demonstrates both the benefits and the reproducibility of this modification; a separation of amitriptyline (peak 3/base) and acenaphthene (peak 2/neutral) over the course of 500 injections run at pH 10, 60 °C.

HALO® Elevate incorporates a wide pH compatibility from 2 to 12 which allows not only chromatographic separations to be performed under high pH conditions, but low pH conditions are also possible. This versatility allows for easier method development along with achieving selectivity differences that may benefit the separation.

Whether you are separating acids, bases, or neutrals, HALO® Elevate allows you to achieve excellent peak shape and column stability under a wide pH range due to its alkaline resistant properties. Adjusting the pH of your mobile phases is an excellent way to modify retention, improve peak shape, and achieve improved selectivity for your chromatographic separations.

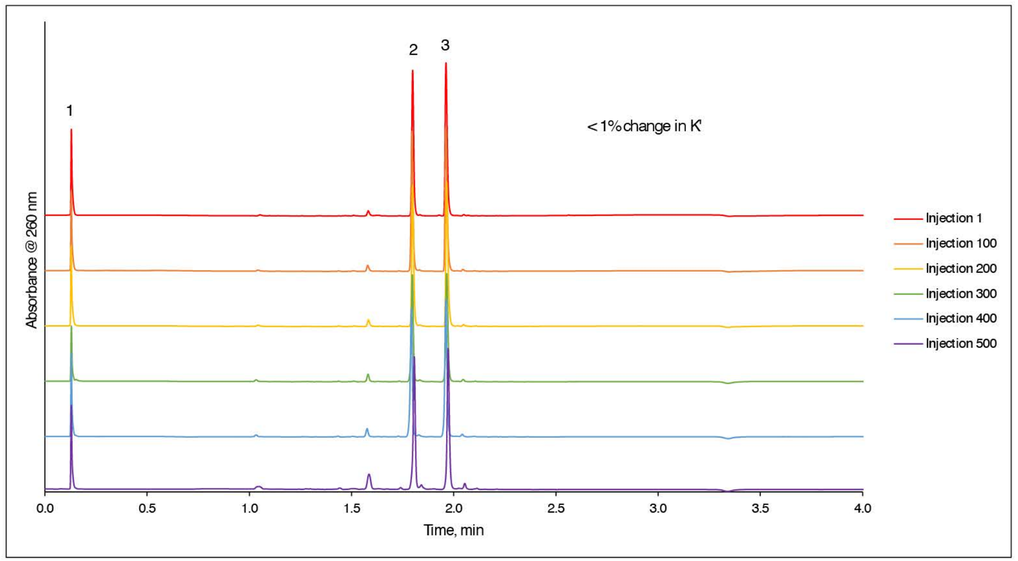


Figure 1: A stability run of a common tricyclic antidepressant (amitriptyline, 3) is achieved using a HALO® Elevate C18 column run at 60 °C, pH 10. Less than a 1% change in retention is achieved over 20,000 column volumes.

LINK


HALO® Elevate: Universal Column for Small Molecule Method Development

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Enter the Vortex

How can we overcome the hard limits to column miniaturization and tackle previously intractable separations?

Chromatography has undoubtedly reached a level of maturity, offering excellent performance for routine separations – and that's why it has been widely adopted across various industries, such as pharmaceuticals, chemicals, environmental monitoring, and the food sector. However, there remains room for improvement in separating highly complex mixtures.

One fundamental challenge associated with chromatography stems from the intrinsic behavior of liquid flow within channels, where the liquid does not flow at a uniform velocity along the channel width. I've been thinking about this problem for quite some time – over a decade at this point. I spent my PhD and post-doc fellowship working on pillar array columns – attempting to reduce the pillar dimensions. Eventually, I realized that, when downscaling, defects and imperfections (even at the nanoscale level) put a limit on decreasing structure sizes much further.

So, I started thinking about some more exotic ways to enhance mass transport, so that large channels would behave as small channels, suffering less from the aforementioned fabrication and pressure drop limitations. After an extensive study of possible ways of achieving lateral mixing (including magnetic, acoustic, and electroosmotic principles) I landed on a potential solution: vortex chromatography. With some first considerations regarding feasibility, I submitted a Starting Grant at the European Research Council, which was accepted in 2015. This was the start of my exciting vortex chromatography journey.

The solution developed by myself and colleagues at the µFlow group of the Vrije Universiteit Brussel (VUB) relies on the creation of microvortices within the channel, which ensure that all molecules move (roughly) at the same axial velocity through the column. By generating exclusively laterally oriented vortices in micron-sized channels, we were able to show a reduction in plate height at high velocities by a factor of 3–5.

The how – and why

Why use a vortex for chromatographic separations? Well, in vortex LC you create a chemical system that behaves as if it has an increase in molecular diffusion coefficient, but then only in the direction that is useful to suppress velocity field induced dispersion (so called C-term or related Taylor-Aris dispersion).

There are two important aspects to vortex chromatography. First, higher performance can be obtained in the presence of vortices. Second, it is possible to achieve decent separation performance in channels of a few µm, which, when combined with vortex flows, behave chromatographically as sub-micron channels. With pressures of just a few bars and a low voltage battery to induce lateral flows, we can achieve chromatographic performance that is normally gained using a high-pressure pump in an expert lab environment.

How do we induce vortices? By applying an oscillating electrical potential (below 10 V) across the channel boundaries. This results in a sustained vortex flow, which has as an effect that all species in a chromatographic species band have an average axial velocity with a much narrower velocity distribution. This results in narrower bands, faster separations, and a higher resolution. I have been lucky to be surrounded by many different groups over the years that have opened my eyes to potential solutions – and applications. For example, during my PhD I spent most of my time at the Mesa+ Institute in The Netherlands – an institute that is built around many technology groups where researchers from totally different disciplines are continuously exposed to one another. This has trained me to think and feel comfortable in domains centered around different physics. I have been fortunate to work in several cleanrooms, where I learned the craft of microfabrication, allowing me to propose very detailed process flows for devices that we wanted to conceive – an important skill given the large cost of such devices; you typically only have a single shot because of budget limitations!

Now at VUB, I am again surrounded by top-notch groups active in biotechnology, microbiology, fertility, optics, chemical engineering, diabetes – all areas wherein

Credit: Thierry Geenen

"Our vortex chromatography approach can be applied in plastic substrates that can be potentially mass-produced at very low cost. And because the columns will operate at low pressure and detection will be integrated in the column, we also expect the instrument size and cost to be reduced in the future."

after intensive discussions we were able to identify a critical hurdle that could be overcome with microfabrication.

Our vortex chromatography approach can be applied in plastic substrates that can be potentially mass-produced at very low cost. And because the columns will operate at low pressure and detection will be integrated in the column, we also expect the instrument size and cost to be reduced in the future. As a first high impact application we will focus on the quantification of glycosylated hemoglobin in human blood for diabetes monitoring. We are currently also pursuing acoustic actuation to conduct vortex chromatography, as an alternative to electroosmotic mixing. It seems that whatever I do, it always ends with a chromatographic application!

Overall, I've found joy in the exercise of finding technological solutions to problems, such as the limitations of flow-related methods; and I'm excited to see where we – and others – can take vortex chromatography!

A clean start

The group of collaborators, enthusiastic researchers, and developers at my university and professional circle that can benefit from microfabrication is now so large that we have constructed a new cleanroom (MICROLAB core facility) with a focus on ultra-high aspect ratio patterning of glass and silicon devices, mainly for microfluidics. We will develop applications wherein extreme control of structures is essential to enable novel separations. One such potential application is the continuous (production scale) separation of small molecules.

Another area is acoustofluidics, with which we are separating particles, including motile particles like sperm cells. This is another example where the channel dimension after etching should remain within a few percent of the target dimension. As the channel is deeper, the attainable throughput can also be increased, making the method relevant for production environments in the pharma environment, for example.

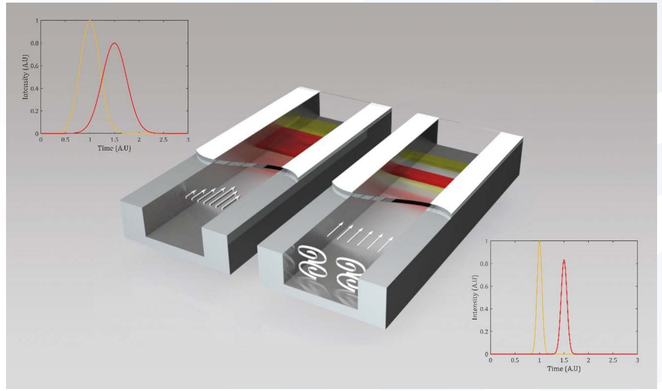

Figure 1 - Credit: Wim de Malsche

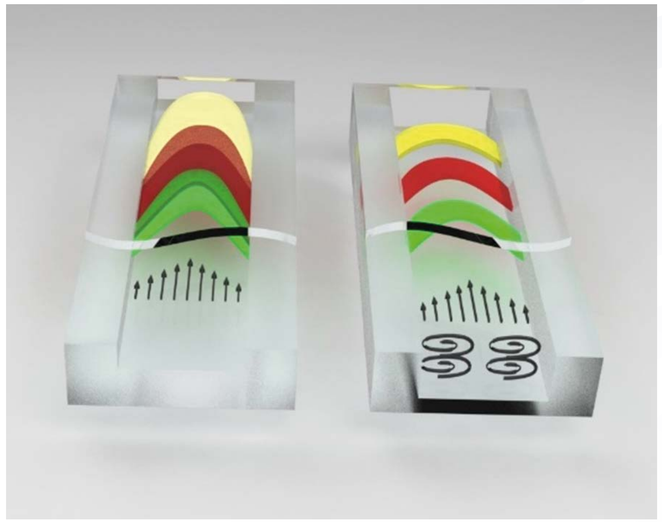

Figure 2 - Credit: Wim de Malsche

Super Charging LC and LC-MS Separations

How using a charged surface chemistry HPLC column improves peak shape of basic compounds

One of the easiest ways to improve the peak shape of basic analytes while using low ionic strength mobile phases such as formic acid is to alter the stationary phase of the HPLC packing material. This includes a positively charged surface material from Advanced Materials Technology. The HALO® positively charged surface (PCS) column offers improved performance of basic compounds under acidic conditions. With these HALO® PCS columns, built on Fused-Core® technology, chromatographers can rely on fast and efficient separations of basic compounds for both small molecule and biological separations. The HALO® PCS small molecule chemistries are offered in C18 and Phenyl-Hexyl allowing selectivity options for method developers. The HALO® PCS C18 Peptide is engineered with a 160 Å pore size ideal for peptide analysis. Peptides have acidic and basic sites (amphiprotic) and can be difficult to analyze especially when trying to run a separation using MS detection. Formic acid conditions for peptides may lead to high tailing factors while using a more traditional C18 stationary phase.

HALO® PCS can be run with most standard mobile phases, but does rely on acidic conditions to make use of the charged surface interaction. By running under low pH conditions, the basic compounds gain a proton becoming positively charged and repel from the positively charged surface of PCS. With the reduced retention of the basic compounds, tailing is reduced, but the strength of the organic mobile phase may need to be reduced to have adequate retention. It should be noted that this is true for any positively charged surface stationary phase. Operation at neutral to high pH conditions will negate the benefits contributed by a positive charge from the stationary phase.

It is widely recognized that ionizable analytes such as basic drugs have much lower sample loading capacities compared to low polarity neutral compounds. The HALO® PCS stationary phase allows for higher sample loads on column due to the increased performance (maintaining peak shape) for basic analytes. This is demonstrated in figure 1 which shows a mixture of tetracyclines at different sample loads (10-50 ng on the column). Sharp, symmetrical peaks with ~50% smaller peak widths are observed on the HALO® PCS Phenyl-Hexyl column (ex. Tetracycline: 0.036 vs. 0.073 PW@50% at 25 ng).

HALO® PCS stationary phases provide chromatographers with a surface chemistry that can improve separations of basic analytes for small molecules and peptides. Having multiple bonded phase choices enhances selectivity and increases the chances for method development success. The positive charge surface allows for higher sample loading, enabling easier detection of impurities within a sample. With all of the benefits for basic compound analyses, chromatographers should consider a positively charged surface modification in their method screening.

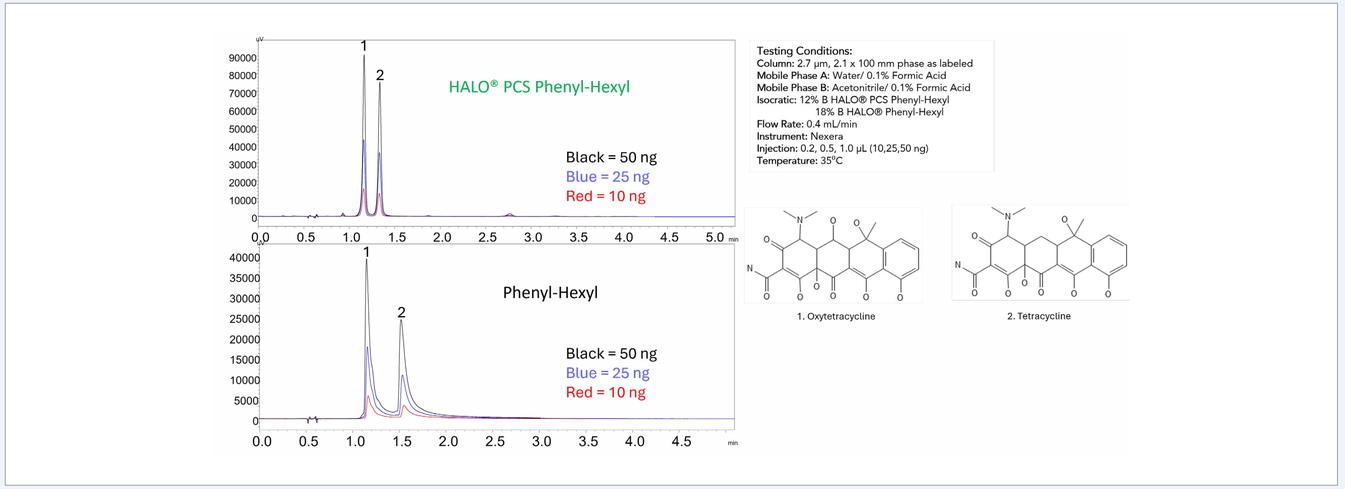

Figure 1: Separation of tetracyclines on HALO® PCS Phenyl-Hexyl vs. Phenyl-Hexyl. Improvement in peak shape over increasing sample load is observed with the positive charge surface material.

LINK

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LC Sommelier

Sitting Down With… André de Villiers, Professor of Chemistry and Polymer Science, Stellenbosch University, Stellenbosch, South Africa

Did you always want to be a scientist?
To be frank, I was never sure about what direction I wanted to take. In fact, I planned on becoming a veterinarian after university. However, after a rather momentous discussion with Pat Sandra and Henk Lauer in my fourth year, I decided to take separation science as a postgraduate. And I've never looked back.

What sparked your interest in chromatography?
As I delved into separation science, I became particularly interested in wine chemistry. After discussions with wine researchers at Stellenbosch, the importance of analytical chemistry in this area was evident. I was very fortunate to complete both my MSc and PhD degrees under the supervision of Pat Sandra, who introduced me to experts across the chromatography field. To this day, I continue to work with these scientists, focusing my research on wine phenolic chemistry, improved separation, and characterization of tannins. The complexity of wine tannins make it an ideal application for testing the performance of the liquid chromatography (LC) and 2D-LC-MS methods my research group develops.

What's the most significant change or development in separation science that you have seen during your career?
One noteworthy development that precedes my introduction to the field is capillary electrophoresis (CE), which became the focus of my MSc degree. Despite this, there are two developments in particular that stand out: ultra high pressure liquid chromatography (UHPLC) and multidimensional LC. I was fortunate enough to be involved in HPLC research as a postdoc fellow at Pfizer Analytical Research Centre (PARC) just as commercial UHPLC instrumentation was introduced. Today, this technology is commonly used, and I think the paradigm-shift we've seen in performance as a result isn't appreciated enough – neither are some of the lessons learned surrounding extra-column dispersion and frictional heating. Even today, many of our LC-MS methods don't optimally exploit the available chromatographic performance due to instrumental constraints.

Additionally, despite being developed many years ago, multidimensional LC has rapidly developed over the past 20 years – specifically in terms of fundamental concepts, instrumentation, methodologies, and applications. I was also first introduced to multidimensional LC during my time at PARC – and, since 2006, 2D-LC has been a main focus of my research groups activities.

I must also mention the rapid advancements in MS technology and hyphenated chromatography-MS methods. These standout developments have provided us with more robust, flexible, faster, sensitive, and higher-resolving MS detection systems for high-resolution chromatography – allowing us to investigate compositions of complex samples in much more detail. Moreover, ion mobility spectrometry (IMS) has added additional value to LC-MS workflows. With data analysis becoming even more essential and progressively more complex within the chromatographic protocol, these advancements have been crucial in allowing us to extract relevant information.

What is the biggest challenge facing the field today?
The training of suitably qualified chromatographers. Though chromatography is used extensively in research and industrial environments, it's often in the context of an "analytical tool" and so relatively few users of advanced chromatography and mass spec systems are experts. Much of this can be overcome by on-the-job training, but the increasing complexity of our technology requires genuine expertise to extract optimal performance. I believe that too few highly experienced PhD and postdoc fellows are trained in chromatography. Maybe because the field isn't considered "sexy enough" compared with other avenues.

In 2019, you spoke about multidimensional 2D-LC stepping into the spotlight – were your predictions correct in the short term?
Fortunately, yes! This is evidenced by the number of 2D-LC contributions at the HPLC conference series over the past few years. It's also gratifying to see that the quality of experimental results and the application scope have noticeably increased over this period.

We can see further evidence of the growing use of 2D-LC in literature; indeed, a recent review article (1) highlights the growing application of multi-dimensional liquid chromatography (MD-LC) in industry (1) – an important development indicative of the maturation of 2D-LC.

I see this trend continuing in the near future, primarily in terms of growing numbers of applications. At present, good quality commercial instrumentation is available with capabilities of a range of different operational modes. Additionally, much of the fundamental groundwork has been laid, making it easier for new users to enter the field. The complexity of instrumentation, method development, and data analysis are hindrances to more widespread use of this technique – and that's something a number of groups are currently focusing their research on.

In 2020, you predicted that HPLC instrumentation 20 years from now will have moved on from the current modular design to accommodate more efficient column formats. How are we progressing?
Whether instrument design fundamentally changes in the foreseeable future remains to be seen. However, the concerns regarding extra-column dispersion have arguably become more relevant today. As Gert Desmet and Ken Broeckhoven stated in 2019 (2): "The current state-of-the-art chromatographic columns have become too good compared to the quality of most instruments," and "It is also very difficult to eliminate the effect of extra-column band broadening from our instruments without sacrificing in S/N-ratio or make a radical change to the current modular 'hi-fi tower' design adopted by all instrument manufacturers." Ultimately, this limits development of further high-performance column formats.

Extra-column dispersion also represents an important constraint on the performance of comprehensive 2D-LC separations – especially when hyphenated to MS. It is currently common practice to use high flow rates in the second dimension to reduce cycle times. However, these flows require splitting prior to MS detection, which has a drastic detrimental impact on peak profiles (3). It is no surprise that LCxLC-UV contour plots are almost exclusively reported in literature; too much separation performance is sacrificed with MS detection, albeit that MS is the most important detector for LCxLC separations.

What are you currently working on?
Our work currently focuses on the use of MS – particularly with cyclic IMS (cIMS) – in combination with one and two-dimensional LC for complex natural product analysis. The emphasis in MD-LC is on developing tools for improved method development and data analysis. All of this is tied to particular applications, such as analysis of tannins, cannabis, and South African plants.

What are your hopes for the future?
I'd like our field to receive more recognition as an independent research area. Often chromatography in particular is taught at undergraduate level primarily from the aspect of an analytical tool, which doesn't reflect the exciting research and career opportunities within the field.

What advice do you have for the next generation of analytical scientists?
Pay attention to your data – not just from the perspective of the planned publication, but also for what can be learnt from the data. Often, "failed" experiments are the most interesting and can lead to further exciting research avenues. They can certainly contribute to our understanding of the tools we use. Apart from this, be curious, work hard, and make the best of the opportunities that come your way.

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Spotlight On...

HALO® Elevate – Taking Separations to a Higher Level

HALO® Elevate C18 incorporates surface modified organo-silane technology for alkaline resistance. With a wide operational use range of pH 2-12, HALO® Elevate allows for robust method development and improved separations for basic compounds that may present problems at lower pH (poor peak shapes, inadequate retention, or limited load tolerance).

Find out more

HALO® OLIGO – Solutions for Reverse Phase Oligonucleotide Separations

HALO® OLIGO columns are designed with Fused-Core® technology for high efficiency, high speed separations and optimized for oligonucleotide separations. This incorporates surface modified organo-silane technology for alkaline resistance, resulting in excellent stability under elevated pH operating conditions. The inert column hardware also addresses absorptivity concerns so the highest recoveries can be achieved.

Find out more

HALO® PCS – Positive Charge Surface Material for Improvement in Basic Analytes

HALO® PCS columns are a positively charged surface chemistry designed to deliver improved peak shape and loading capacity for basic compounds under low ionic strength mobile phases conditions. Available in either 90 Å or 160 Å pore size for small molecule and peptide analysis.

Find out more