Special Series

GC×GC Detective Stories

Meet the scientists using comprehensive two-dimensional gas chromatography to uncover hidden compounds, follow chemical clues, and solve analytical mysteries



the Analytical Scientist x LECO

Not Just a Pretty Face

Mariosimone Zoccali discusses the evolution of GCxGC, which he describes as "one of the most exciting stories in separation science"

Earlier this year, the chromatography community descended on Riva del Garda for the return of the 44th International Symposium on Capillary Chromatography (ISCC) together with the 21st GC×GC Symposium – where a clear theme emerged.

"The main take-away message from Riva 2026 is that GC×GC has matured into a central, application-driven platform that is no longer limited to specialists but is increasingly used for real analytical decisions across diverse fields," says Mariosimone Zoccali, Associate Professor of Analytical Chemistry at the University of Messina (Italy), and chair of the Riva 2026 organizing committee. "The conference demonstrated that comprehensive two-dimensional GC is now valued not only for its extraordinary peak capacity, but also for its power in identification, fingerprinting, classification, and both target and non-target workflows."

Given the buzz around GCxGC at Riva 2026, we thought we'd reach out to leaders in the field as part of a new series, GCxGC Detective Stories, to understand how the technique is being used to unravel analytical mysteries in a range of application areas.

Here, Zoccali walks us through the evolution of GCxGC, which he describes as "one of the most exciting stories in separation science," and casts an eye on the technique's future potential.

How has GCxGC evolved in recent years?

From my perspective, the evolution of GC×GC has been one of the most exciting stories in separation science. In its early years, the technique stood out mainly because of the chromatograms it produced: dense, visually impressive, and almost landscape-like in their appearance. Those images had a real impact, because they showed that a complex sample could contain far more information than conventional GC was able to reveal.

What has changed over time, however, is not just the way we look at GC×GC, but the way we use it. A major part of this progress has come from the instrument itself. Modulators have become more robust, more reliable, and more affordable, which has made the technique much easier to adopt and maintain. At the same time, method-development software and data-processing tools have become much more intuitive, which has lowered the entry barrier for new users and made the whole workflow more practical for routine laboratories.

This instrumental evolution has been crucial. GC×GC is no longer seen only as a technically sophisticated option for specialists, but as a mature analytical approach that can be integrated into real workflows. That is particularly evident in petrochemistry, food analysis, fragrance and flavour



Meet Mariosimone

I am Mariosimone Zoccali, Associate Professor of Analytical Chemistry at the University of Messina (Italy), where I work in the MeIT laboratory. As a scientist, my core expertise lies in multidimensional chromatography, particularly comprehensive two-dimensional gas chromatography (GC×GC) and in sample preparation techniques. I focus on resolving highly complex mixtures and extracting chemically meaningful information, with applications in food analysis and authentication, environmental screening, and the development and validation of chromatographic methods.

As chair of the organizing committee, I was involved in the organization of the 44th International Symposium on Capillary Chromatography (44th ISCC) and the 21st GC×GC Symposium, held in Riva del Garda from May 17–22, 2026.

research, and biomedical studies, where GC×GC helps extract meaningful chemical information from highly complex matrices.

What makes the technique so compelling today is that it combines separation power with interpretative value. It does not simply generate beautiful chromatograms; it turns complexity into information that can be trusted, compared, and used.

Where does GC×GC now stand in relation to other analytical techniques?

In chemical analysis today, GC×GC stands as a central tool in comprehensive separation science, especially for complex mixtures where one-dimensional GC is insufficient. Its strength lies not only in resolving peaks, but in generating structured chemical information that can be interpreted in a robust and meaningful way. GC×GC is particularly powerful when combined with mass spectrometry, because the additional separation dimension reduces spectral overlaps, gives cleaner MS spectra, and improves identification confidence. It also supports advanced data analysis, including fingerprinting, classification, and non-target screening, which are increasingly important in fields like food safety, environmental monitoring, and biomedical research.

Another important advantage is the improvement in signal-to-noise ratio, which often leads to higher method sensitivity. By reducing co-elution and separating analytes from matrix interferences, GC×GC can make trace compounds easier to detect and quantify, especially in very complex samples. In practice, this means that GC×GC is not only a higher-resolution technique, but

Which awards were given in GC×GC ` at Riva 2026?

The award structure at the 21st GC×GC Symposium told a very clear story about the field. On one side, it honored long-term scientific leadership and the researchers who have helped define GC×GC over the years; on the other, it gave strong visibility to the next generation, whose work is already pushing the technique into new application areas. In this sense, the awards were not just ceremonial recognition, but a snapshot of where GC×GC stands today and where it is heading.

At the higher end of the spectrum, the GC×GC Lifetime Achievement Award recognized sustained and influential contributions to the field, reinforcing the idea that GC×GC has now become a mature scientific discipline with its own history and intellectual continuity. The John Phillips Award continued this tradition from another angle, honoring researchers who have already made a strong impact early in their careers and are showing the kind of leadership that will shape the future of the field. This balance between senior recognition and emerging excellence is important because it shows that GC×GC is no longer a niche technique, but a community with a solid foundation and a clear trajectory.

The young-scientist awards made that trajectory even more visible. The Genzo Shimadzu Best Oral Awards highlighted contributions on metabolomic profiling of wood, analysis of plant-based protein powders, the toxicologically relevant fraction of mineral oil, and non-target screening of house dust from several European countries. These are highly relevant topics, ranging from materials and food to environmental exposure, and they show that young researchers are already applying GC×GC to real-world analytical problems with strong scientific and societal relevance.

The poster prizes reinforced the same message. The Richard Sacks GC×GC Poster Awards recognized work on crude oil and tar characterization, VOC profiling in recycled plastics, and the rapid screening of light hydrocarbons in crude oils using advanced data analysis.

The ABC Springer Best Poster Presentation Award highlighted a study on recycled plastic as a food contact material, while the MDPI Best Oral Presentation Award was given for AI-driven volatilomics with GC×GC-HRMS. Together, these awards show that GC×GC is being advanced not only through method development, but also through applications in petrochemistry, recycled materials, food contact safety, and machine-learning-assisted data interpretation.

Seen as a whole, the award structure maps the evolution of GC×GC very effectively. It highlights excellence at the top level, but it also makes visible the contribution of young scientists who are bringing fresh ideas, new applications, and a more data-driven mindset to the field. That is perhaps the most important message: GC×GC is progressing because it now combines strong methodological foundations with a vibrant and continuously renewing scientific community.

also a more sensitive and more reliable one in many challenging analytical contexts.

In practice, GC×GC is used when: the mixture is too complex for 1D-GC, identification confidence must be maximized, fingerprinting or classification is required, and trace components must be detected in the presence of major interferents.

This makes GC×GC a key technique for modern analytical challenges where complexity, sensitivity, and reliability are critical.

Please give some example applications

In petrochemistry, GC×GC is essential for resolving highly complex hydrocarbon mixtures. It enables detailed characterization of fingerprints that would be very difficult to interpret with one-dimensional GC, supporting applications such as source identification, quality control, and process monitoring.

In food science, GC×GC supports authenticity studies, aroma profiling, and the detection of trace contaminants or markers of fraud. It can separate complex volatile and semi-volatile profiles, revealing minor components that are decisive for product quality, geographical origin, or processing history.

For flavors and fragrances, GC×GC helps disentangle very dense volatile profiles. It reveals minor components that can be critical for product identity, stability, or consumer perception, and it supports robust classification and quality control.

In healthcare, GC×GC is increasingly attractive for complex sample profiling, such as metabolomics or lipidomics, especially when linked to high-quality MS and advanced data processing. The technique can resolve overlapping compounds and improve identification confidence in highly complex biological matrices.

Who is driving progress in GCxGC?

I would like to highlight the contribution of younger scientists, who were one of the most energetic and promising voices at Riva 2026. The program gave them real visibility, not only through poster contributions but also through dedicated oral lectures, and several of those talks pointed clearly to where GC×GC is heading next. What stood out was the range of topics: PFAS screening, bioanalytical applications, food authenticity, sustainable fuels, waste characterization, and even AI-driven data interpretation. That breadth is important because it shows that the next generation is not entering GC×GC as passive users, but as active contributors who are already expanding its scope and relevance.

What was especially interesting is that many of these contributions were genuinely forward-looking applications. Some young scientists were working on PFAS discovery and prioritization, others on breast skin volatilomics, olive oil profiling, plant-based proteins, or the characterization of recycled and pyrolyzed materials. In practical terms, this means they are helping turn GC×GC into a technique that speaks to some of the most current analytical challenges of our time: environmental contamination, food authenticity, sustainability, and complex biological systems.

The message from Riva was clear: GC×GC is being carried forward by a new generation that combines chemistry, instrumentation, and data science with remarkable confidence. Their work is pushing the field into new territory, and that is exactly what gives the technique renewed momentum.

Where is GC×GC heading in the near future?

In the near future, GC×GC is likely to move further away from





being seen as a specialist technique reserved for a few experts, and more toward a routine analytical platform for solving complex problems in a practical way. Today, the real challenge is to make the technique easier to use, easier to interpret, and easier to integrate into everyday laboratory workflows. That shift is already visible in the way the community is developing more robust instruments, more intuitive software, and more accessible method-development strategies.

A major direction will certainly be the tighter coupling with mass spectrometry, especially for flow-modulation. This would make GC×GC more powerful in real applications, because the additional separation dimension helps deliver cleaner spectra, better identification confidence, and stronger performance in non-target and suspect-screening workflows. In complex matrices, where co-elutions and matrix interferences can easily obscure important signals, this combination will remain one of the main strengths of the technique.

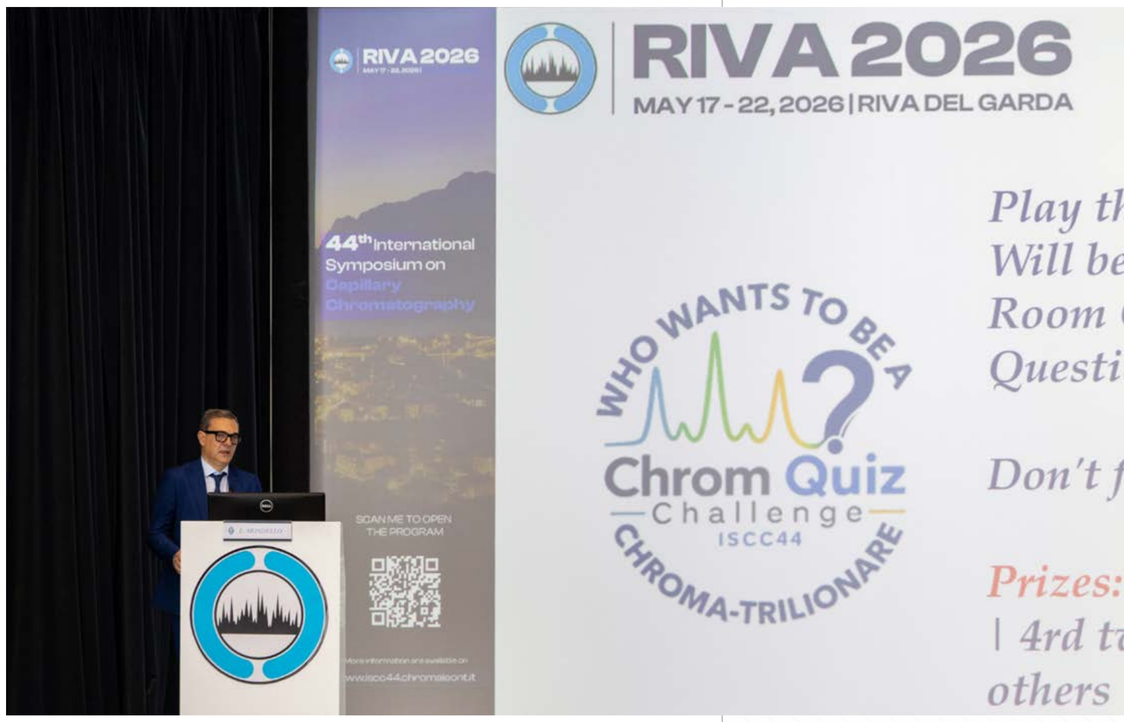
Another important trend is the growing role of data analysis. GC×GC generates a huge amount of information, and the future of the field will depend increasingly on how well that information can be processed, visualized, and interpreted. Chemometrics, machine learning, and smarter visualization tools are becoming essential because they help turn dense chromatographic data into useful chemical knowledge. This is especially important when the goal is not simply compound identification, but pattern recognition, classification, or the comparison of large sample sets.

Sustainability will also shape the next phase of GC×GC development. There is a clear push toward greener workflows, including miniaturized systems, lower solvent consumption, reduced carrier gas use, and more efficient sample preparation. This is particularly relevant because modern analytical chemistry is increasingly expected to combine performance with environmental responsibility. GC×GC will need to keep delivering high information content while becoming lighter, cleaner, and more efficient in its overall analytical footprint.

At the application level, the technique is likely to gain even more ground in areas with clear societal impact. Environmental screening, PFAS analysis, food authenticity, food safety, biomarker discovery, and forensic or exposure-related studies are all areas where the strengths of GC×GC are especially valuable. These are fields where complexity is the rule rather than the exception, and where a technique that can separate, classify, and reveal hidden information has a clear future.

What makes this progression so promising is that GC×GC is becoming not just more powerful, but more usable. Better automation, smarter software, and more robust hardware are reducing the barrier to entry, which means the technique can spread beyond a narrow community of specialists. That combination of analytical strength, practical usability, and growing application relevance is what will define the next stage of GC×GC. In that sense, the future of the technique is greater intelligence, more accessibility leading to its continued development into a trusted tool for modern chemical analysis.





Follow Your Nose

Fulvia Trapani is developing the tools required to understand the complex process of aroma and taste perception

PhD student Fulvia Trapani walks us through her research project at Unilever to develop the analytical tools required to understand the complex process of how humans perceive aroma and taste. We also speak with "senior detectives" Chiara Cordero, Fulvia's PhD supervisor, and Hans-Gerd Janssen, who oversaw the research project.

The case of the disappearing Aroma

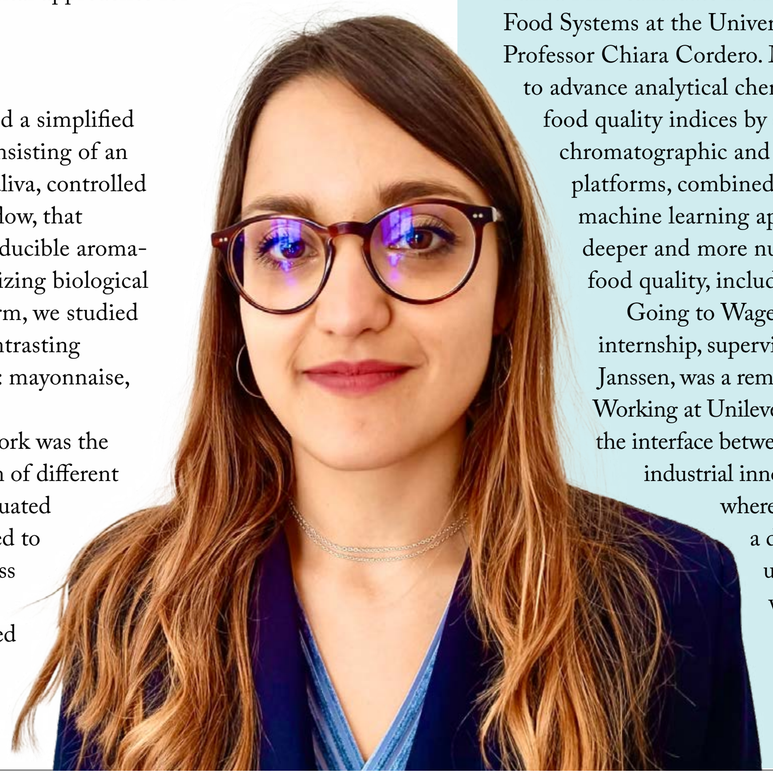
The project focused on one of the most challenging aspects of flavor and food science: understanding aroma perception as it occurs during food consumption. Flavor perception is highly dynamic. Volatile compounds are continuously released while food is being processed in the mouth, and the timing of their release can be just as important as their concentration. However, many conventional analytical approaches rely on static or endpoint measurements, which provide only a snapshot of a constantly evolving process.

The goal was therefore to develop an analytical framework capable of investigating aroma release under controlled, consumption-relevant conditions, and to systematically compare different instrumental approaches for capturing these dynamics.

A mystery in the mouth

To achieve this, we developed a simplified simulated mouth system, consisting of an aqueous phase mimicking saliva, controlled stirring, and a constant gas flow, that allowed us to generate reproducible aroma-release profiles while minimizing biological variability. Using this platform, we studied three food matrices with contrasting compositions and structures: mayonnaise, ketchup, and mustard.

A central aspect of the work was the development and comparison of different analytical platforms. We evaluated four options: SICRIT coupled to Orbitrap high-resolution mass spectrometry for real-time monitoring; GC-MS operated in selected ion monitoring mode; direct-inlet electron



Meet Fulvia

I am a PhD candidate in the National Doctorate in Food Systems at the University of Turin, supervised by Professor Chiara Cordero. My doctoral research aims to advance analytical chemistry beyond conventional food quality indices by employing advanced chromatographic and mass spectrometric platforms, combined with chemometric and machine learning approaches, to develop a deeper and more nuanced understanding of food quality, including its sensory dimension.

Going to Wageningen for my PhD internship, supervised by Prof. Hans-Gerd Janssen, was a remarkable opportunity. Working at Unilever Foods R&D placed me at the interface between academic research and industrial innovation, in an environment where the science conducted has a direct impact on products used by millions of people worldwide.

ionization mass spectrometry (EI-MS); and thermally modulated direct EI-MS, the latter incorporating principles derived from comprehensive two-dimensional gas chromatography (GC×GC-MS) (Figure1). Each platform offered different strengths in terms of temporal resolution, sensitivity, compound selectivity and analytical depth.

One of the most interesting outcomes was that all platforms revealed consistent underlying release behaviors despite their different analytical characteristics. We identified recurring release patterns across different food matrices and analytical approaches, suggesting the existence of common kinetic signatures governing aroma release.

Beyond the individual experimental findings, the project resulted in a practical decision-framework based on multi-criteria decision analysis (Figure 2). Rather than identifying a single "best" instrument, the work demonstrated that platform selection should depend on the specific analytical question. Real-time monitoring, targeted quantification, comprehensive profiling, and routine screening all require different analytical characteristics. In this sense, the project provides both scientific insights into flavor-release mechanisms and practical guidance for researchers and industry scientists selecting analytical tools for flavor studies.

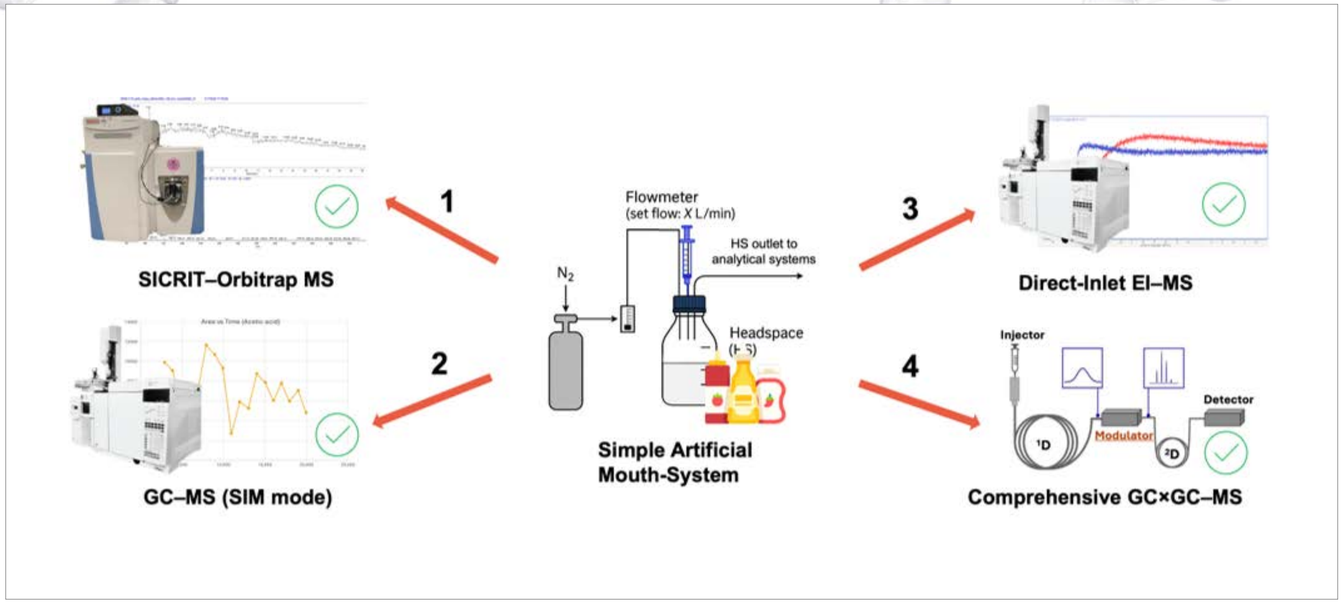


Figure 1. Schematic overview of the flow-through simulated mouth system developed in this study, showing four analytical platforms evaluated for real-time aroma release monitoring: SICRIT-Orbitrap MS, GC-MS in selected ion monitoring mode, Direct-Inlet EI-MS, and comprehensive GC×GC-MS.

Lessons from the investigation

I truly enjoyed this project because it allowed me to explore an aspect of food science I had never investigated so deeply before: the dynamic relationship between food composition and human perception. During my PhD, I have worked extensively on the characterization of complex food and biological systems, often focusing on the chemical information hidden within large, multidimensional datasets. This project shifted the perspective from "what is present" to "what is actually perceived, when, and how".

What fascinated me most was realizing that flavour is not a static property of food. We often consider composition as the main determinant of sensory characteristics, but this work highlighted how the timing of aroma release can be equally important. Two products may contain similar volatile compounds yet generate completely different sensory experiences because those compounds are released differently during consumption. Understanding this temporal dimension gave me a new appreciation for the complexity of flavour perception and for the analytical challenges involved in studying it.

Another aspect I particularly valued was the opportunity to compare different analytical platforms not only in terms of performance, but also in terms of their ability to answer specific scientific questions. The project reinforced an idea that has become

increasingly important to me during my PhD: analytical science is not about using the most advanced technology, but about choosing the most suitable strategy to generate meaningful knowledge. In this case, each platform provided a different perspective on the same phenomenon and understanding their specific answers was as important as evaluating their individual strengths.

Working at Unilever also gave me the opportunity to experience a highly multidisciplinary research environment. I enjoyed seeing how analytical chemistry, flavour science, sensory understanding, product development and industrial innovation are strongly interconnected. It was inspiring to observe how scientists with different expertise contribute to a common goal such as improving food products and ultimately enhancing the consumer experience. Beyond the technical skills I gained in mass spectrometry, chromatography and data analysis, this project surely broadened my perspective on the role of analytical science in food research, showing me how important it is for industry. But also, it reminded me that behind every analytical measurement there is always a human dimension, because understanding how people experience food is ultimately what gives meaning to most of our work.

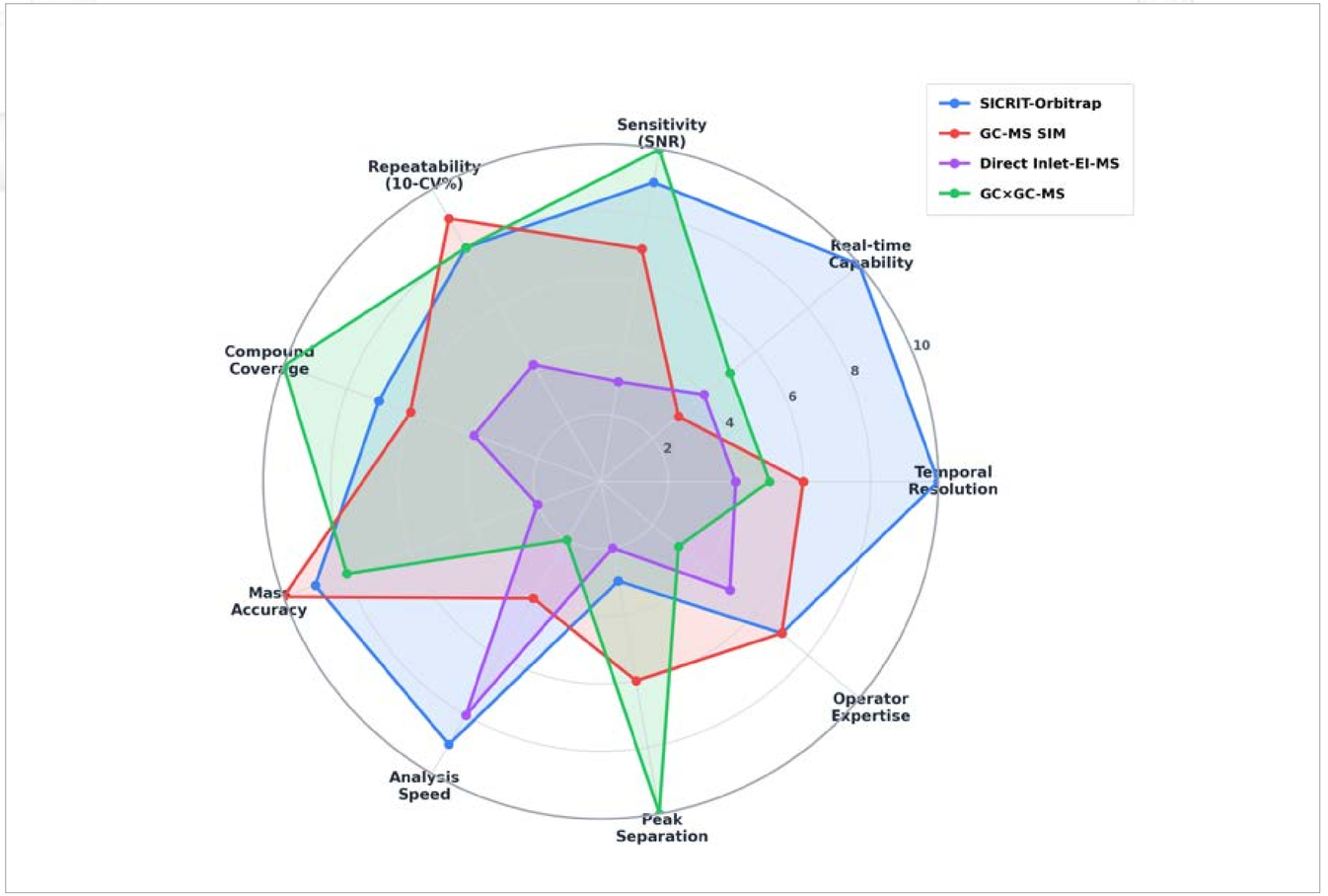


Figure 2. Multi-criteria decision analysis comparing the four analytical platforms across nine evaluation criteria. Each axis represents a performance dimension scored from 0 to 10, illustrating how the platforms differ in their strengths and trade-offs depending on the analytical objective.

The Senior Detectives' Verdict

What are the benefits of academia-industry collaborations like this?

Chiara Cordero: As a PhD supervisor, I promote these projects because they allow students to experience how excellent science is transformed into innovation. They create a unique learning environment where academia and industry work together on shared scientific challenges. In Fulvia's case, the collaboration with Hans-Gerd at Unilever provided access to industrial R&D expertise while maintaining the scientific depth expected from a doctoral project. This approach is fully aligned with our National PhD in Food Systems (https://www.dott-fstb.unito.it/do/home.pl) and with EIT Food's vision of connecting research, innovation, and societal impact (https://www.eitfood.eu/projects/global-food-venture-programme).

Hans-Gerd Janssen: Industrial research and academic studies are complementary activities in which scientific questions, conceptual innovations, and practical solutions meet. Young academics provide the "out-of-the-box thinking" needed for industry to stay up-to-date and not stick to the known. Additionally, we see that young recruits often experience a culture shock when entering their first industrial job. This program helps us to solve our problems while at the same time contributing to the development of our next generation of researchers.

What are the requirements for such a project?

Cordero: Successful projects require strong scientific foundations, a clear research objective, and close collaboration between academic and industrial supervisors. Equally important are motivated students who are willing to work across disciplines, cultures, and research environments.

Janssen: First of all, the project should be challenging and require tomorrow's technology to solve the problem at hand. It must be research at the forefront of technology, not just the rapid and superficial solution of an industrial problem. For the candidate there should be room to experiment and take risks. Moreover, both the candidate and the receiving industrial group must have the right mentality. Industry must accept that new developments take time whereas the researcher should keep the aim in mind and avoid "research for the sake of research."

How did this project contribute Fulvia's development as a scientist?

Cordero: Fulvia's PhD project focuses on the application of advanced analytical tools to move beyond conventional quality indices and develop a deeper understanding of food quality, including sensory quality. Her research stay at Unilever complemented this vision by combining scientific innovation with the pragmatism of industrial R&D, providing valuable insight into how analytical knowledge can support real-world decision-making.

Janssen: Surely Fulvia is now much better prepared to enter industry. She knows what is relevant in industrial research and understands how academic and industrial research are complementary yet different. She is now experienced with the industrial way-of-working with a very strong focus on the aim and clearer definitions of how to get there. The stay will also have deepened her understanding of how science can contribute to the development of better products. At the detail level she now understands much better how flavour is perceived by humans.

Will you continue to work on projects like this?

Cordero: Yes, for sure. For many years, our group has collaborated with companies and European consortia to translate knowledge generated through advanced analytical and omics approaches into practical measurement systems for real-world applications. Building these ecosystems requires trust, expertise, passion, and a shared vision, but the benefits are substantial for all partners involved. It is a genuine win-win strategy, and one we will continue to pursue.

Janssen: Our door is always open. Good students with the desire to learn are always welcome. As industry, we feel we have a responsibility to contribute to the education of the on-coming generation. We can offer challenging, realistic problems. We can offer excellent technical facilities, and we have motivated and experienced people who are willing to share their expertise. When such people work with motivated and talented students, great things can happen. Honestly, without students to help, our laboratory would not have the high quality and status it now has.

Chiara Cordero is a Full Professor of Food Chemistry at the University of Turin, working at the interface between analytical science, food quality research, and industrial innovation.

Hans-Gerd Janssen is a senior scientist at Unilever Foods R&D and part-time professor Analytical Chemistry at Wageningen University. His research focuses on developing tasteful and healthy consumer-preferred products based on a molecular understanding of the food.

Decoding Climate Change in Sparkling Wine

GC×GC-TOFMS reveals how origin, fermentation and accelerated aging reshape complex sparkling wine aroma profiles.



Climate change is creating a new analytical challenge for sparkling-wine producers. Rising temperatures and increasingly unpredictable weather can alter grape composition, accelerate sugar accumulation and reduce organic acids, while also influencing the metabolites that ultimately shape aroma, freshness and aging potential. For premium sparkling wines, understanding these changes is becoming increasingly important for maintaining quality and regional identity.

In this study, six sparkling-wine bases from Lombardy and Sicily were investigated using HS-SPME coupled with GC×GC-TOFMS on the Pegasus BTX 4D. Samples were produced under different secondary-fermentation conditions and compared before and after an accelerated aging treatment designed to investigate how production and storage variables influence chemical evolution.

The additional chromatographic separation provided by GC×GC exposed chemical detail that would otherwise be difficult to distinguish. Around 800 features were detected, with approximately 400 tentatively identified after filtering. Compounds with very different concentrations but similar first-dimension retention times could be separated in the second dimension, supporting clearer detection and identification of aroma-relevant species.

The investigation then moved from individual compounds to the complete sample set. ChromaTOF Tile compiled and compared the GC×GC data, combining chemical-feature information with visual tools including heat maps, bar charts and PCA. Clear trends emerged between wines from Lombardy and Sicily and between control and accelerated-aging samples. Compounds associated with freshness and fruity character could be distinguished from aging-related markers such as furfural, 2-acetyl furan and TDN.

Together, Pegasus BTX 4D, GC×GC-TOFMS and ChromaTOF Tile transform a highly complex aroma profile into actionable chemical information—supporting a more data-driven approach to precision oenology as growing conditions continue to change.

LINK



Read the Application Note

The Smell of Adventure

How a career spanning three continents prepared Meriem Gaida to bring GC×GC into fragrance safety and quality analysis



Meriem Gaida reflects on the international journey that took her from Tunis to Zurich and explains how she established a new Product Safety Science function at fragrance manufacturer LUZI. She also discusses how GC×GC-TOFMS can reveal hidden allergens and other co-eluting compounds, support investigations into off-odours and discoloration, and help address emerging regulatory and quality challenges.

Please describe your professional journey so far

I was born and raised in Tunis, Tunisia, and from a young age I was fortunate to have travel opportunities, which broadened my perspective and fostered a strong interest in international experiences. My journey so far has taken me across three continents and six countries, shaping both my personal and professional life.

My travel adventure began in high school when, for family reasons, I moved to Belgium and spent a year studying there before returning to Tunis to complete my secondary education. I then relocated back to Belgium to pursue my university studies. Throughout my academic journey, I actively sought international experiences. During the first year of my master's degree, I took part in the Erasmus exchange program in Paris, and later, in the final year of my PhD, I completed a research internship in Seattle.

After earning my PhD, I moved to the United Kingdom, where I worked in Peterborough, a city north of London. After a year there, a new professional opportunity with the fragrance manufacturer LUZI brought me to Zurich, where I have been living and working for the past two years.

What has driven you to pursue such an international path?

Curiosity has always been the main driving force behind my journey alongside the desire to keep learning, exploring, and challenging myself both professionally and personally. I have never liked staying within my comfort zone, and I am constantly looking for new challenges that push me to grow. Each move I made was an opportunity to learn, adapt, and discover something new about the world and about myself.

What have been the main challenges and highlights of living abroad?

One of the biggest challenges along the way was learning to live independently at a relatively young age. I was 19 when I

first moved abroad on my own, away from my family. Coming from a very close-knit family, the transition was not always easy. The journey had its moments of loneliness, uncertainty, and self-doubt, especially in the beginning when everything felt unfamiliar and finding a sense of belonging seemed difficult.

Another challenge of moving so often is that each new chapter required rebuilding life from scratch. It felt like every time I moved, I left pieces of my identity behind. While exciting, constantly starting over can also be emotionally draining. There is often a feeling of living between worlds, with a lot of uncertainty regarding the future and life always feeling temporary.

Another important motivation has been the opportunity to experience different cultures and meet people from a wide range of backgrounds. I enjoy being in diverse environments where perspectives, experiences, and ways of thinking differ from my own. These encounters have broadened my understanding of the world, challenged my assumptions, fostered empathy, and stimulated my creativity and imagination.

And although expatriate life can sometimes feel isolating, it offers a unique opportunity for personal growth and self-discovery. I learned how to adapt to unfamiliar situations, embrace discomfort, and navigate periods of uncertainty. Living abroad has made me more resilient, independent, and appreciative of the people and opportunities in my life. It has also helped me better understand who I am, what I value, and what I want from both my personal and professional life.

How have these experiences shaped the way you work and communicate?

The most valuable lesson I have learned is that effective communication is not about speaking the same language or sharing the same culture, but about making the effort to understand one another. In many ways, I see science as a universal language that can bring people together across borders and backgrounds. This is one of the reasons I am passionate about making science more accessible and relatable to a broader audience. I have always believed that true expertise is not demonstrated by making simple things sound complicated, but by making complex ideas understandable and more accessible. Bridging that gap between complexity and accessibility is something I find both challenging and deeply rewarding.

Can you introduce your current role at LUZI, and explain what you were brought into the company to achieve?

I was hired to establish and lead a new Product Safety Science unit within the company, with a focus on ensuring consumer safety and compliance with EU regulations related to fragrance allergens. As part of this initiative, the company had invested in two GC×GC-TOFMS instruments and wanted to leverage this technology to support regulatory compliance and product safety assessments. They were looking for a specialist who could manage the analytical platform, develop and validate methods, and define a clear strategic vision for the new function, including its role, capabilities, and long-term objectives within the organization.

How did you approach the challenge?

The project was particularly rewarding because it involved establishing a new structure within the company. So, it was important to take a holistic approach, focusing first on understanding the broader business needs before moving into the technical implementation. My priority was to identify how this new structure could create value for the company, engage with key stakeholders, and determine how the data generated could support product quality, consumer safety, and regulatory compliance. With this foundation in place, I worked closely with cross-functional teams to define analytical requirements and ensure alignment with business objectives. I then focused on developing and optimizing analytical methods using the GC×GC-TOFMS platform. My key goal was to establish a robust method capable of resolving co-eluting compounds while maintaining a runtime suitable for routine industrial applications.

What added value has GC×GC brought to LUZI?

GC×GC delivered significant added value to the company, both technically and strategically. The technology was very well received

across the company, particularly because most teams were only familiar with conventional one-dimensional GC data. The enhanced separation power and two-dimensional chromatographic visualizations made it easier to communicate complex analytical findings and demonstrated the capabilities of product safety science.

From an analytical perspective, GC×GC enabled us to overcome limitations associated with conventional GC, particularly in cases where co-eluting compounds could hide regulated substances. The improved resolution allowed us to detect, identify, and quantify compounds that would otherwise have remained hidden, providing greater confidence in our safety and compliance assessments.

In addition, combining GC×GC data with chemometric approaches proved to be a powerful tool for discovery-based analyses. As a result, we were able to address complex product issues such as off-odours and discoloration more efficiently and with a higher degree of scientific confidence. The technology not only strengthened our regulatory compliance capabilities but also became an important resource for product quality troubleshooting.

Could GC×GC become the gold standard for fragrance analysis?
For many years, GC×GC use was largely limited to academic research due to the complexity of the instrumentation, data processing, and method development. However, as the technology has matured, it is increasingly being adopted in industrial environments and implemented as a routine analytical tool.

Despite its advantages in terms of higher resolution, increased sensitivity, and better compound characterization compared to conventional one-dimensional GC methods, introducing GC×GC into a routine industrial workflow presents several challenges. One of the main hurdles is the limited availability of trained personnel with hands-on experience in GC×GC method development and data interpretation. The technique involves a complex interplay of parameters that requires a deeper level of expertise than traditional GC methods. Troubleshooting can also be more demanding, as issues may arise from multiple components of the system and their interactions. In addition, the large volume of data generated by GC×GC requires appropriate software tools and a structured approach to data management and interpretation.

From an implementation perspective, companies should view GC×GC as a medium- to long-term investment. While basic operations can be learned relatively quickly, developing robust routine methods, building internal expertise, and fully integrating the technology into business processes often takes several months to a few years. Success depends not only on acquiring the instrumentation but also on investing in training, method standardization, and demonstrating clear business value through practical applications.

How has your work with GC×GC been received across LUZI?
The work was received very positively. The outcome was highly appreciated, and the team recognized the value of GC×GC in supporting the continuous improvement of our product quality. The technique also generated considerable interest across the company, with many colleagues expressing a desire to visit the laboratory to learn more about the technology, understand how it works, and see the instruments in operation.

What are the next steps for GC×GC at LUZI?
Now that the method has been successfully established and is delivering positive results, we are looking to expand its application to address new regulatory challenges and broaden the scope of its use. The implementation of the technique has also helped us build a strong collaboration with the QC department. Together, we are using the method to evaluate the quality of raw materials and to assess the reliability and consistency of the data provided by our suppliers. This partnership is creating additional opportunities to leverage GC×GC as a valuable tool for quality assurance and continuous improvement.

The Case of the Disappearing Diesel

How GC×GC helped to reopen the "Silent Fall" oil-spill investigation and reveal what happened to diesel buried beneath Cape Cod's salt marsh

By Christopher M. Reddy, Chemical oceanographer, Marine Chemistry & Geochemistry, Woods Hole Oceanographic Institution (WHOI), USA



If you're going to tell a detective story about comprehensive two-dimensional gas chromatography (GC×GC), it helps to start with a system where conventional tools had already hit their limits.

For me, that system was a salt marsh in Cape Cod, Massachusetts, contaminated by the grounding of the barge Florida in September 1969. The spill released about 189,000 gallons of diesel fuel into a biologically productive marsh. The impacts were immediate and devastating for marine life and birds. The event became known locally as "Silent Fall" – a reference both to the season and to Rachel Carson's Silent Spring, underscoring the ecological severity of the incident.

At the time, industry representatives claimed the oil would persist for only about two weeks. One of the world's premier analytical chemists at my institution, the Woods Hole Oceanographic Institution (WHOI), Max Blumer, treated that claim as an empirical question. Long before GC×GC was available, this site became a test bed for what analytical chemistry could tell us about the fate of petroleum hydrocarbons in the environment – laying the groundwork for oil-spill science.

The first phase: 1D GC and the emergence of UCM

Blumer and colleagues – including Howard Sanders, John Teal, and Kathy Burns (all at WHOI) – followed the Florida spill from 1969 to about 1975. They characterized the initial diesel composition and its evolution using one-dimensional gas chromatography (GC). In the early years, their chromatograms displayed numerous well-resolved peaks, corresponding to individual n-alkanes, isoprenoids, and other identifiable petroleum hydrocarbons. As the system aged, evaporation, dissolution, and especially microbial degradation progressively altered the composition.

By the mid-1970s, the chromatograms were dominated by an unresolved complex mixture (UCM) – a broad hump indicating that the residue was now a highly complex assemblage of partially degraded compounds and transformation products that a single GC column could not separate into discrete components. The UCM was most likely dominated by hydrocarbons from the

original spill that had become preferentially enriched as other components were lost.

This work was foundational in environmental chemistry. It demonstrated that spilled oil undergoes substantial weathering and biodegradation, and it helped define conceptual models of oil fate in coastal systems. But from an analytical point of view, the case was stuck: the UCM signaled complexity, yet traditional GC could no longer provide detailed compositional resolution.

After the Exxon Valdez spill in 1989, colleagues revisited the Cape Cod marsh to assess whether any of the Florida oil remained. Two decades after the spill, they still found measurable residues in some sites, challenging the original notion of rapid disappearance.

By the time I returned to the marsh in 1999, the key questions were:

- What is the chemical nature of this decades-old residue?
- Which processes – evaporation, dissolution, biodegradation, burial – have dominated its long-term evolution?

Traditional GC had already taken us as far as it could. We needed an analytical approach with greater peak capacity and orthogonal selectivity.

Introducing GC×GC: orthogonal separation for a "solved" case

Around the early 2000s, I met Rick Gaines and Glenn Frysinger at the U.S. Coast Guard Academy, who were among the pioneers applying GC×GC to complex environmental mixtures. We sent an extract from the 1999 Florida residues to Rick and Glenn for GC×GC analysis. That decision fundamentally changed our understanding of this system.

The GC×GC chromatograms that came back showed far more resolved peaks and organized patterns than we would ever have inferred from the old 1D chromatograms. Two main insights emerged.

1. Biodegradation intensity and termination

By examining compound distributions and homologous series across the GC×GC plane, we could infer that biodegradation had been vigorous in the initial years after the spill but appeared to decline substantially by the mid-1970s. Patterns such as preferential loss of n-alkanes relative to more recalcitrant biomarkers, changes in isoprenoid-to-n-alkane ratio, and altered distributions within specific hydrocarbon classes all pointed to an early period of active microbial metabolism followed by a plateau.

We interpreted that this was because of changing redox conditions in the marsh sediments (transition to more anoxic conditions with burial) and/or a shift in microbial community substrate preference toward other organic matter. GC×GC allowed us to link detailed compositional fingerprints to plausible biodegradation kinetics and environmental controls, which 1D GC could no longer resolve once the system had evolved into UCM.

2. Preferential loss of aromatic hydrocarbons: evidence for solubilization

When we compared GC×GC chromatograms of the weathered residues to those of fresh diesel fuel, we found that, for compounds with similar first-dimension retention times (and thus broadly similar volatility), the more polar and aromatic hydrocarbons were selectively depleted.

This systematic depletion is consistent with aqueous solubilization: repeated tidal inundation and flushing can preferentially remove more soluble, often aromatic components from the oil matrix. Because GC×GC separates compounds according to both volatility and polarity/aromaticity, these trends became visually and quantitatively apparent across the 2D chromatogram.

That observation, made around 2002, initiated a long-term effort in my lab to use GC×GC for mass-balance-style assessments of weathering processes – disentangling the relative contributions of evaporation vs. dissolution and, where possible, biodegradation. We began to think in terms of analyzing the chromatogram almost on a pixel-by-pixel basis, quantifying how different regions (representing different compound classes) were affected by environmental processes.

From historical case study to operational tool

While the Florida barge work is, in one sense, a retrospective, research-driven case, the approaches developed there have been applied

"GC×GC has allowed us to move from simple metrics such as total petroleum hydrocarbons or limited biomarker ratios to a more high-dimensional description of composition and transformation, directly tied to environmental processes."



in multiple operational spill contexts, including Bouchard 120 (Buzzards Bay, MA; 2003), Cosco Busan (San Francisco Bay, CA; 2007), Deepwater Horizon (2010; Gulf of Mexico), and oil residues that had traveled over 8,000 km on plastic bottles before arriving in Florida. In all these systems, GC×GC has allowed us to move from simple metrics such as total petroleum hydrocarbons or limited biomarker ratios to a more high-dimensional description of composition and transformation, directly tied to environmental processes.

Implications for the future of GC×GC in environmental chemistry

The Florida barge case – 189,000 gallons of diesel, severe ecological damage, and a residue that persisted long after "Silent Fall" – illustrates several general points about the future role of GC×GC. Where 1D GC yields an unresolved complex mixture and effectively reaches an analytical endpoint, GC×GC recovers substantial structural and compositional information, reopening questions that previously seemed intractable. Because GC×GC organizes compounds in a way that reflects both volatility and chemical functionality, it becomes a tool for diagnosing processes – biodegradation timing, redox constraints, selective solubilization – rather than just cataloging components. It can extract new information from archived samples and also operate in real time during modern spill responses, providing continuity of methodology across decades. And the techniques and interpretive frameworks developed in this "cold case" now directly inform industry, regulatory, and response questions about persistence, toxicity, and remediation strategies in coastal and offshore environments.

For my lab, that first GC×GC analysis of the Florida residues transformed a well-known, seemingly exhausted case study into a cornerstone of nearly two decades of work. It showed that adopting GC×GC is not simply about denser and "prettier" chromatograms – it is about recovering mechanistic, decision-relevant insight from mixtures that once looked analytically opaque.



Tracking Persistent Pollutants Through Complex Sediments

SPE-GC×GC-TOFMS resolves OCPs and PCBs at ultra-trace levels in challenging environmental matrices.

Persistent organic pollutants can leave a chemical record in the environment long after their original use. Organochlorine pesticides (OCPs) and polychlorinated biphenyls (PCBs) are of particular concern because of their toxicity, persistence and tendency to bioaccumulate. Sediments can therefore provide valuable evidence of contamination—but their chemical complexity also makes ultra-trace analysis challenging.

This application note demonstrates an environmental workflow combining solid-phase extraction (SPE) with GC×GC-TOFMS on the Pegasus BTX 4D. SPE provides cleanup and enrichment of the sediment extracts before analysis, while comprehensive two-dimensional gas chromatography adds the separation capacity needed to distinguish target compounds from a complex matrix. TOFMS then provides sensitive full-spectrum detection for the simultaneous investigation of multiple OCPs and PCBs.

The result is a workflow designed around one of the central challenges in environmental analysis: finding important target compounds when they are present at very low levels and surrounded by far more abundant matrix components.

By spreading those components across two chromatographic dimensions, GC×GC reduces coelution and provides a more structured view of the sample. Coupled with the fast acquisition of the Pegasus BTX 4D, the approach provides the resolution and sensitivity required for rigorous assessment of complex sediment extracts and supports analytical requirements associated with environmental monitoring and regulatory criteria.

For laboratories investigating persistent contamination, the workflow demonstrates how enhanced separation can turn a difficult sediment extract into clearer analytical evidence—helping analysts determine what is present with greater confidence.

LINK



Read the Application Note

Biomarkers, Biofuels, and Shape-Shifting Molecules

Philip Marriott – together with Renée Webster and Konstantinos Kouremenos – explores three cases in which comprehensive two-dimensional gas chromatography revealed chemical information hidden by conventional separations.



The investigation begins with the search for a biomarker associated with a rare newborn metabolic disorder, where a diagnostically important compound was concealed beneath a much larger chromatographic peak. It then moves to aviation fuel, where trace oxidation products had to be distinguished from an overwhelmingly complex hydrocarbon matrix. The final case concerns "shape-shifting" molecules that interconvert during chromatographic separation, producing a mysterious plateau whose composition could not be resolved using one-dimensional GC.

Marriott and colleagues take us through the three investigations and explain what the additional separation dimension allowed the researchers to discover.

Story 1: The Biomarker Hidden in Plain Sight

Newborn babies are routinely screened for various genetic disorders. Most people will be familiar with the heel-prick sampling performed soon after birth. There is now an incredible library of blood spot samples stored in hospitals.

Analytical procedures are fundamental to assessing these disorders and may draw on a broad range of techniques, depending on the markers associated with the particular condition. These markers can range from large molecules, such as proteins, to small molecules, such as short-chain acids. The appropriate technique will depend on the molecule, but identifying the marker to target is no easy task.

Considerable research may be needed to identify the disease, determine whether specific markers can connect a disease or symptom with the endpoint of a metabolic pathway, and establish how best to isolate and measure those markers. The analyst must consider the sample matrix, extraction procedures, and the sensitivity required for the measurement.

Here, we outline a discovery strategy using GC×GC to search for new small-molecule markers of aciduria – an inborn error of metabolism (IEM).

Inborn errors of metabolism are mostly monogenic disorders caused by defects in enzymes or transporters that disrupt a step in an intermediary pathway. When flux through the normal route stalls, the substrate and its proximal precursors accumulate and are shunted into secondary reactions, including β-oxidation,

ω-oxidation, transamination, glycine or carnitine conjugation, and glucuronidation.

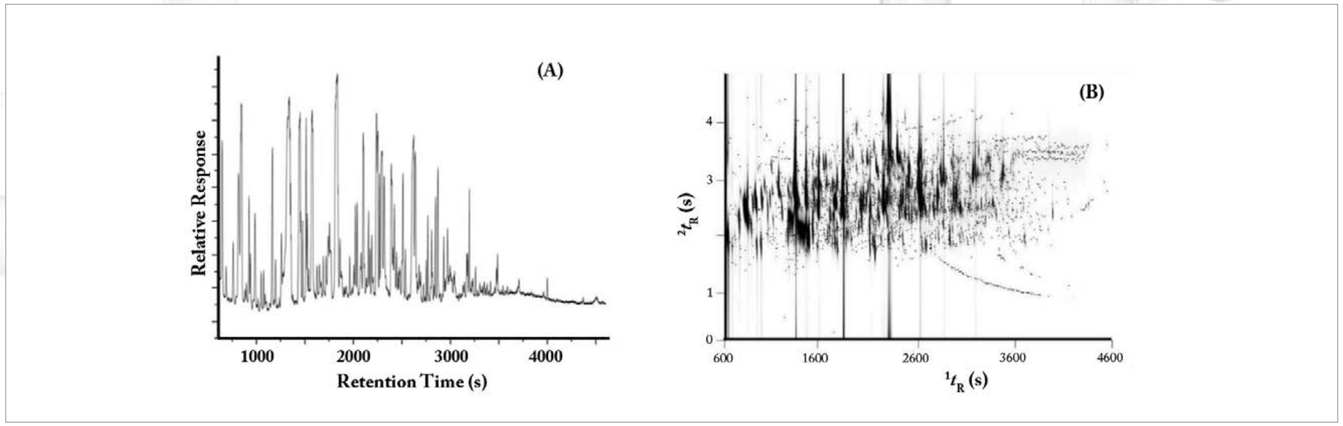
Many of the resulting metabolites are carboxylic acids that exceed renal reabsorption thresholds and spill into urine. Diagnosis rests on detecting the direct substrate of the enzyme or a downstream by-product. Examples of species monitored in IEMs include methylmalonic acid; 3-hydroxyisovaleric acid; glutaric and 3-hydroxyglutaric acids; ethylmalonic, adipic, and suberic acids; orotic acid; succinylacetone; and N-acetylaspartate.

Choosing the right analytical approach

Methodologies have generally evolved in the following order:

1. Colorimetric or spot tests, including DNPH, cyanide-nitroprusside, and Benedict's tests
2. Paper and thin-layer chromatography
3. GC-MS of derivatized urinary organic acids
4. FIA-MS/MS of acylcarnitines and amino acids in dried blood spots, which forms the basis of expanded newborn screening
5. LC-MS/MS for the same analytes and for more polar or labile species

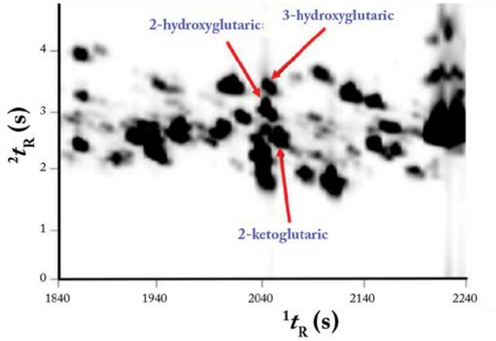
GC-MS remains the reference technique for urinary organic acid analysis because organic acids are small, chemically diverse, and amenable to derivatization to increase their thermal stability and volatility. The GC-MS workflow includes:



Graphic 1. The chemical complexity of the human urinary metabolome. More than 3,000 endogenous metabolites create substantial and unavoidable peak coelution under conventional one-dimensional GC conditions. This is illustrated by a comparison of (A) a representative one-dimensional GC–MS separation and (B) the corresponding GC×GC–TOFMS separation of the same sample.

- Forming oxime derivatives of keto acids using hydroxylamine
- Acidifying the sample, saturating it with NaCl, and extracting into ethyl acetate or diethyl ether
- Silylating hydroxy and carboxy groups with BSTFA or MSTFA to yield TMS ethers and esters

LC-MS/MS can also be used for this task. It avoids derivatization, and many analytes are not suited to GC. However, it also has some limitations relative to GC. Universal spectral libraries comparable to those available for electron ionization do not exist for LC-MS, so identification largely depends on accurate mass, MS/MS, and reference standards. Matrix effects, including ion suppression, can be substantial in urine. Very small, highly polar acids, such as lactate, glycolate, and oxalate, may also elute near the void on reversed-phase columns. Most metabolic



Graphic 2. The 3-hydroxyglutaric acid example. In glutaric aciduria type I (GCDH deficiency), 3-hydroxyglutaric acid is separated in the second dimension from 2-hydroxyglutaric acid and 2-ketoglutaric acid.

laboratories therefore employ GC-MS and LC-MS/MS in parallel to cover complementary chemical space.

Revealing the hidden biomarker

Using GC×GC-TOFMS, we identified crotonylglycine as a novel urinary biomarker of 3-hydroxy-3-methylglutaryl-CoA synthase 2 (HMGCS2) deficiency. The analyte had eluded detection by conventional one-dimensional GC-MS because it coeluted with a substantially more abundant adipic acid peak. Separation in the second dimension resolved the two components, exposing the underlying diagnostic signal.

Elevated crotonylglycine was subsequently confirmed in further patients with proven HMGCS2 deficiency. However, the urinary organic acid profile can be transient and is most clearly manifested during episodes of metabolic decompensation, making the deficiency difficult to identify at other times.

A later, expanded patient study further evaluated crotonylglycine as a more persistent and diagnostically informative urinary marker of HMGCS2 deficiency. Its susceptibility to false-negative results when samples are collected during periods of metabolic stability underscores the importance of sampling during, or shortly after, an acute presentation.

This case illustrates a wider paradigm in which advances in chromatographic resolution have expanded the biomarker repertoire available for diagnosing IEMs. The HMGCS2/crotonylglycine example is one of several instances in which a clinically relevant marker is obscured in one-dimensional GC-MS. Other examples include:

- Methylmalonic and succinic acids, which are notoriously difficult to resolve fully using single-column systems. Misintegration can affect quantification when concentrations are elevated, whereas further separation on a polar second-dimension column resolves the pair.
- Ethylmalonic and methylsuccinic acids in short-chain acyl-CoA dehydrogenase deficiency, ethylmalonic encephalopathy, and multiple acyl-CoA dehydrogenase deficiency.

Story 2: Following the Biofuel Oxidation Trail

High-performance fuels, such as those used in military fighter jets, are specialized products that must conform to tight tolerances and performance criteria. When the fuel powering a precision aircraft degrades, the consequences can be catastrophic.

This was borne out in a little-known incident in 1976, when US Navy pilot Commander P. W. Ogle was forced to eject from his A-7E Corsair after engine failure during a flight from the aircraft carrier USS Ranger. The subsequent investigation attributed the failure to oxidized jet fuel. Although the incident occurred 50 years ago, oxidative degradation remains an important challenge for modern high-performance aviation fuels, for which chemical stability is essential to reliable operation.

During routine transportation, storage, and use, modern military and specialty jet fuels are exposed to air and temperature fluctuations that can induce oxidation reactions. The resulting products can form gums and deposits, attack fuel-system components, and ultimately compromise engine performance.

Aviation fuel is a highly complex material that may contain hundreds of thousands of different chemical species. Against this background, the oxidation products capable of producing such dramatic downstream effects are present only at trace concentrations and are difficult to resolve from the dominant hydrocarbon matrix. As new bio-based and other alternative fuels enter the market, they too will be subject to similar oxidative stress.

Finding trace products in a complex matrix

Assessing trace oxidation products requires either extracting them from the fuel or developing a method for analyzing them in situ, followed by an instrumental method capable of identifying the products. Although this might sound like a straightforward matter of applying an effective extraction strategy – for example, solvent extraction (SE), solid-phase extraction (SPE), or solid-phase microextraction (SPME) – the biofuel matrix makes effective removal of the matrix while retaining the oxidation products difficult. In some cases, a range of extraction and instrumental methods has failed to isolate and accurately identify the oxidation products in alternative fuel samples.

The target products are likely to include acids, alcohols, ketones, aldehydes, and compounds such as furanones. It is also important to measure these compounds at trace levels so that the early stages of degradation can be detected and mitigated. Measuring antioxidants added to a sample – even one as complex as a mineral

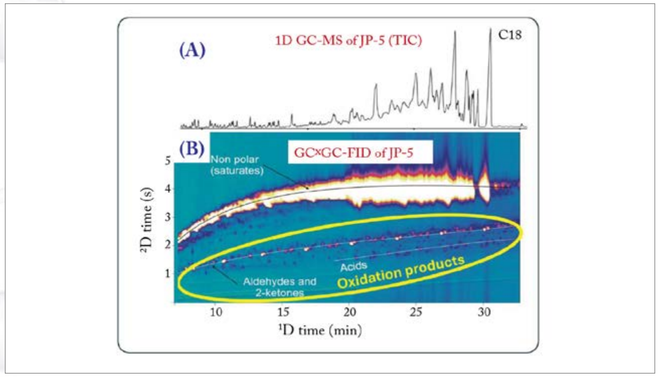
fuel or biofuel – is relatively straightforward using targeted analysis and an MS/MS strategy. This can indicate when an added antioxidant is approaching depletion, but it does not address the presence of oxidation by-products, which remain a primary target of the analysis.

A separation strategy for oxidation products

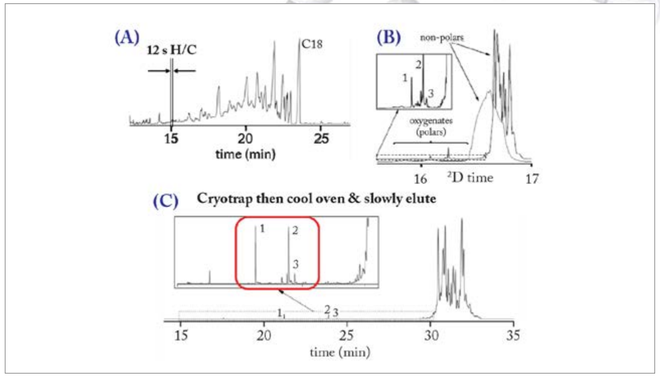
Our research group offered an industry workshop on advanced multidimensional gas chromatography (MDGC) and comprehensive two-dimensional gas chromatography (GC×GC). Participants were invited to bring samples – or, ideally, send them to us before the workshop – so that we could develop an analytical strategy tailored to the sample and the aims of the analysis.

For a biofuel sample supplied by one participant, we wanted to measure the full range of oxidation products. GC×GC appeared ideally suited to resolving polar compounds within a non-polar matrix. The reverse problem – resolving non-polar compounds in a polar matrix – would also be well suited to GC×GC. Our experience with petrochemical analysis, and with the chemical-class speciation it provides for alkanes, saturated cyclic compounds such as cyclohexanes and cyclopentanes, olefins, and aromatic compounds, suggested several possible strategies.

Of the two broadly classified GC×GC column-set options – non-polar/polar (NP/P) or polar/non-polar (P/NP) – the most obvious choice was P/NP. With this configuration, alkanes are the most strongly retained analytes on the second-dimension column. The biofuel matrix consisted primarily of non-polar compounds,



Graphic 1. (A) GC-MS analysis of JP-5 jet fuel. The mass spectrum is dominated by m/z 57, 71, and 85 ions, characteristic of hydrocarbons, making oxidation products difficult to analyze. (B) GC×GC-FID analysis of the whole biofuel sample. Saturated non-polar compounds elute last from the second-dimension non-polar column, while a rich series of polar oxidation products elute earlier. The oxidation products are completely resolved from the saturated compounds, clearly displaying the complex mixture of acids, alcohols, aldehydes, and ketones.



Graphic 2. (A) The JP-5 sample from Graphic 1(A) was analyzed using successive 12 s fractions, with each cut shifted by 12 s. A 12 s fraction collected at 15 min is shown. (B) The fraction from (A) is transferred directly to the 2D column at the sampling time; the oxygenated compounds are shown in the inset. (C) Repeating the process with cryogenic trapping and oven cooling before elution of the trapped fraction provides considerably greater resolution of the oxygenated species.

particularly alkanes. We therefore established conditions under which the alkanes eluted within an acceptable second-dimension retention time (^{2}tR), as determined by the modulation period (PM). The polar, oxygenated compounds then eluted earlier. This is advantageous because the high concentrations of alkanes do not interfere with the earlier-eluting polar compounds. By contrast, with an NP/P column set, very polar compounds may exceed the PM setting and undergo wrap-around, while earlier-eluting, highly abundant alkanes may tail and cause interference.

During the workshop, a single GC×GC analysis revealed the full complexity of the oxygenated products. At a given first-dimension retention time (^{1}tR), the retention order was acids < alcohols < aldehydes ≈ ketones. The sheer number of compounds was astounding.

No extraction procedure – which might have selectively extracted or lost different oxygenated species – was required. GC×GC was exceptionally well suited to this analytical problem. Its speed, selectivity for oxygenated species, sensitivity, and ease of interpretation through the 2D separation space elution patterns made it a powerful approach. The method could be used to investigate changes over time or under different experimental and environmental conditions, including variations in storage, oxygen exposure, temperature, and humidity, without requiring extensive and costly extraction procedures.

We also developed a novel sampling, trapping, oven-cooling, and temperature-programming approach to achieve still greater resolution when needed. This involved heartcutting a very narrow, 12 s portion of the biofuel elution from the first column, cryogenically trapping the fraction at the head of the

second-dimension column, cooling the oven, and then separating the fraction on the second-dimension column using a second temperature-programmed analysis.

The resulting strategy brought together the principal features of a successful analytical study, with GC×GC firmly at its center.

Story 3: The Curious Case of Shape-Shifting GC Molecules

In 1984 at the National University of Singapore (NUS), Professor Lai Yee Hing and author (PM) supervised an honors student, Ms Tan. As part of her project, she synthesized 9,10-bis(2-methylphenyl)phenanthrene.

The GC spirit in me suggested that we should study the GC analysis of one of her intermediates, which we expected to be semivolatile. That first product and analysis, at about 300 °C, produced a remarkable and fascinating phenomenon.

With packed-column GC, we observed a shoulder on the main peak – an unusual result. Seeking better separation, we moved to capillary GC. The "pure" compound now produced two well-resolved peaks. More remarkably, the peaks appeared to be joined by a raised plateau, or bridge.

Discussing the phenomenon with Professor Lai, we presumed that the two discrete peaks corresponded to E and Z isomers associated with the positions of the 2-methylphenyl substituents at the 9- and 10-positions of the phenanthrene. The peaks had different abundances, suggesting differences in the energetics of forming the E and Z isomers. The plateau appeared to arise from an on-column, sterically hindered rotational isomerization that converted E to Z and Z to E. At the high oven temperature, the energy supplied during GC analysis must have been sufficient to promote this isomerization.

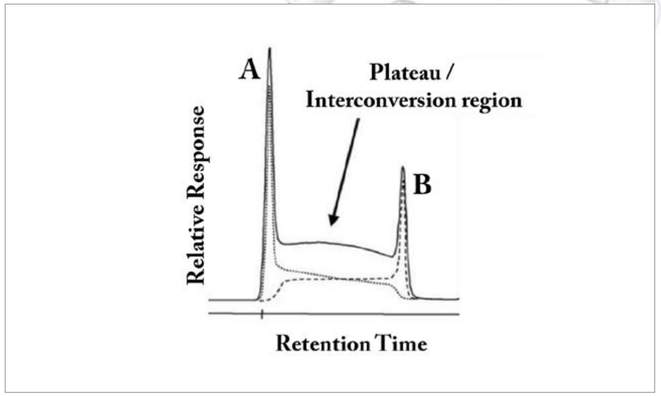
Changing the oven temperature and flow rate altered the plateau in the way expected for a kinetic process. We then synthesized an anthracene analogue with 2-methylphenyl substituents at the 1- and 2-positions. In this case, the E and Z isomers had very similar abundances, giving the overall peak-and-plateau profile an almost symmetrical shape.

Similar observations were made for 2-methylnaphthalene with $Cr(CO)_3$ π-bonded to one ring. The chromium group can migrate between the rings, giving two resolvable terminal peaks connected by a plateau. We also observed the phenomenon for chromium tris(trifluoroacetylacetonate), which has Δ and Λ forms and again produced a plateau.

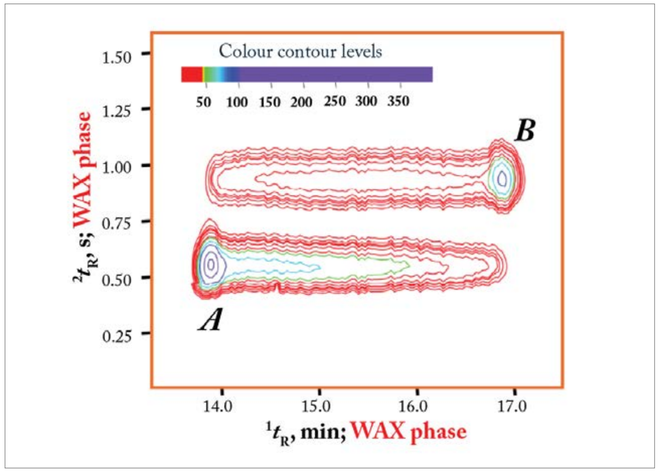
Much later, we became aware of other on-column structural rearrangements, including Cope rearrangements and the different plateau shapes observed in myrrh oil. Another example is the conversion of pyrethrum to isopyrethrum in chrysanthemum extracts, involving on-column conjugated double-bond shifts during GC analysis. Much of our work, however, has focused on E/Z isomerism in oxime compounds, R-C(H)NOH. Their lower elution temperatures are accompanied by correspondingly lower energy requirements for isomerization.

The problem of the plateau

We had observed the plateau, but still lacked a satisfactory explanation of how the separation process produced it.



Graphic 1. An example of shape-shifting molecules during GC analysis, in which both A → B and B → A transformations occur on the column. The plateau contains both A and B.



Graphic 2. GC×GC provides complete resolution of compounds first separated on the ^{1}D column and then, of the species present within the plateau, or bridge, region on the ^{2}D column. The result was obtained under isothermal conditions. Compound B transforms on-column to produce the A tail, while compound A transforms to produce the B tail.

The plateau between the two terminal peaks also presents a particular identification problem. In most cases, the two compounds are isomers – usually E/Z isomers – making it impossible to use strategies such as GC-MS to quantify the individual species within the plateau. The ^{1}D separation is intriguing, but the composition of the plateau cannot be quantified.

By this time, however, we had developed cryogenic modulation for GC×GC. It therefore seemed logical to apply GC×GC to this shape-shifting process.

Revealing the hidden profiles

GC×GC makes it possible to measure the actual amounts of the two isomers at any point over the plateau. It can also address more complex cases, including the enantioselective separation of chiral oximes.

Provided the individual compounds – in this case, oxime isomers – can be separated on the ^{2}D column, the complete profile can be resolved within the ^{2}D separation space. There should be no difficulty in achieving this because GC×GC is designed to do exactly that.

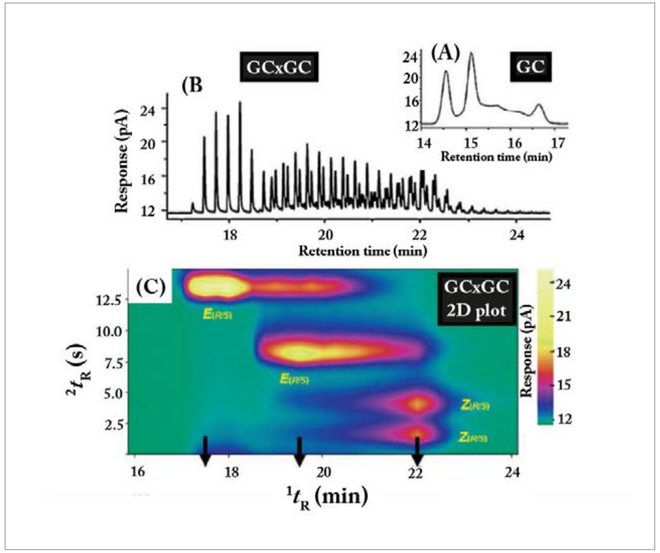
Importantly, the same stationary phase can be used for both the ^{1}D and ^{2}D columns. The reasoning is straightforward: if compounds A and B can be resolved using a particular phase on the ^{1}D column, they should remain resolvable using the same phase when they coexist throughout the plateau region. This is subject to a sufficient difference in retention factor on the short ^{2}D column, while the very narrow input band entering that column should further promote separation.

Using the same stationary phase for the ^{1}D and ^{2}D columns still constitutes GC×GC. Provided that the ^{2}D column resolves species that remain unresolved on the ^{1}D column, the method meets the requirements of an effective GC×GC separation.

The hidden profiles of the individual species can then be clearly revealed. We have reported the analysis of a racemic mixture of oximes, with enantiomer separation on the ^{1}D column, as well as the unprecedented separation of the enantiomers on both the ^{1}D and ^{2}D columns. This is shown in Graphic 3; the corresponding ^{1}D GC result in panel A is difficult to interpret.

The curious case of on-column interconversion therefore provides a clear example of how multidimensional separation can reveal information that is inaccessible using ^{1}D GC.

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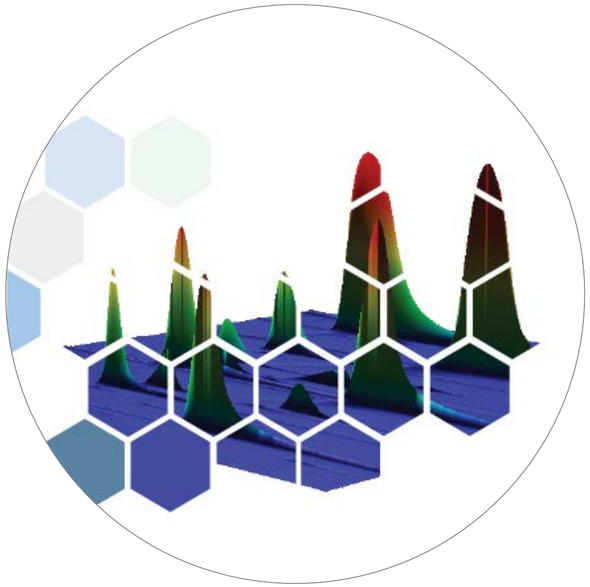
Graphic 3. The result for a racemic mixture of oximes with four species: E(R), E(S), Z(R), and Z(S). Panel A shows the ^{1}D separation, which is difficult to interpret. Panels B (direct detector response) and C (GC×GC 2D plot) show the GC×GC separation using different chiral columns. The 1D phase both separates and gives interconversion of the enantiomers, while the 2D phase separates all the R and S and E and Z isomers. The result reveals the individual profiles concealed within the ^{1}D plateau.

Spotlight On...



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ChromaTOF Sync 2D: Turn Complex Data into Clear Answers

Process, align and compare GC×GC-MS datasets across multiple samples to uncover meaningful chemical differences, trends and patterns faster.

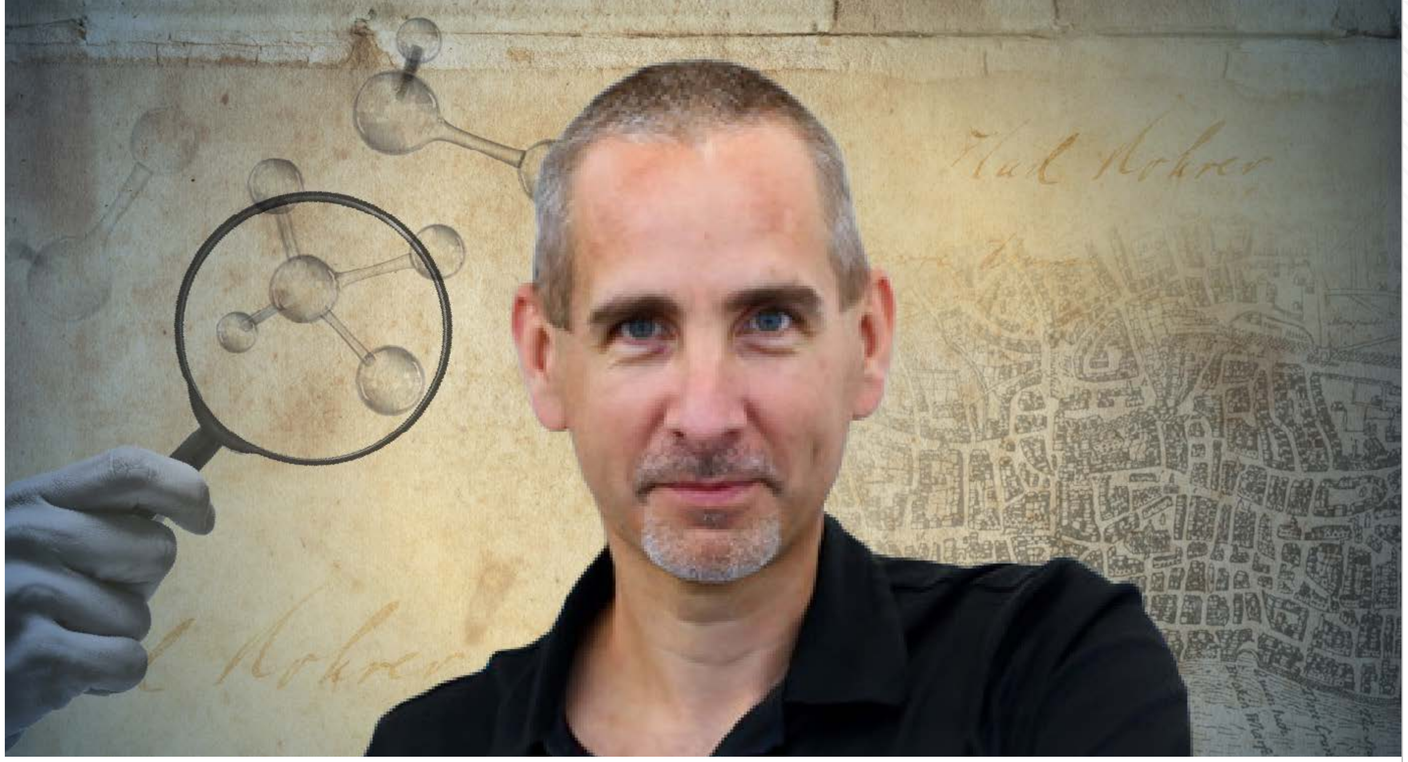


Pegasus GC-HRT+ 4D: Add Confidence to Complex Discoveries

Combine GC×GC separation, high-resolution accurate mass and multiple ionization modes to investigate complex samples with greater identification confidence.

Another Piece of the Precision Medicine Puzzle

Jean-François Focant explores how GC×GC could help piece together a more detailed picture of patient health – and what it will take to bring those insights into hospitals



How did you first become interested in GC×GC?

I started my PhD in 1998, working on dioxins and PCBs. When you measure dioxins and PCBs, you must work at the parts-per-trillion level, which creates a lot of sample preparation challenges because you have to concentrate the sample to access such low levels of dioxins and PCBs. I was working mainly with one-dimensional GC and mass spectrometry, using sector instruments in selected ion monitoring mode. But when I was doing my literature review at the beginning of my PhD, I came across some of the first publications on GC×GC. At that time, it was being presented as a possible alternative to simplify the cleanup procedure when working with very complex matrices.

The idea was that, because of the two dimensions, you could reduce the time spent getting rid of matrix effects, because the matrix components would be separated from the compounds of interest in the two-dimensional chromatographic plane. That's what interested me at the time.

Back in June 1999, as Belgium was hit by the Dioxin crisis, I was visiting Don Patterson Jr. at the dioxin lab at CDC to learn about automation of sample preparation to increase our lab capacities for better crisis management. I also knew that Don had been doing some early GC×GC work on dioxins and that John Dimandja, a former student of John Phillips, the inventor of GC×GC, was also at CDC by then. I met John there and he irrevocably contaminated me with his enthusiasm for the technique.

I asked whether I could spend some time at the CDC with him to explore the technology. He said yes, so I went there for three months. I was super excited, but we only managed to produce one chromatogram in that time because the coupling and modulation were so poor. But I went back for three more summers to better learn the technique. Then I finished my PhD and went back to CDC for a two-year postdoc with Don Patterson, using GC×GC for multi-POPs human biomonitoring .

So, to answer the question, I first heard about GC×GC as a tool to simplify the cleanup procedure, which wasn't really what it could do. If you inject dirt into your GC system, the liner is still a liner, and when it gets dirty, it gets dirty.

The real discovery for me was the ability to use the chromatographic space to look at dioxins, PCBs, pesticides, and flame

retardants all in a single injection. That's really where the added value was for me.

Since then, I've been using GC×GC in the lab. And nowadays, we only do GC×GC – we don't use one-dimensional GC anymore – to investigate our Separation Science challenges.

How has GC×GC evolved over the past 25 years?

When I first went to the CDC, I was using the sweeper – that was the name of the modulator at the time. It was a moving-part modulator, which probably worked 10 percent of the time. The other 90 percent, you were trying to fix issues with it. Today, any modulator will do the job on a routine basis.

But the most important changes have probably been on the software side. Today, you can do data processing, data reduction, and alignment using commercial software from LECO, GC Image, or ChromSpace, for example.

In short, you can be up to speed immediately on a modern GC×GC system. It's not just a research tool anymore; it can really be used routinely – and that wasn't the case 15 years ago.

How does GC×GC compare with other analytical techniques today?

I think the evolution of GC×GC was probably slower than some other techniques. One of the main reasons was competition between the people who were there at the beginning, where there was a lot of reluctance to share information and new advances. As a young scientist, I was surprised by that because – and perhaps I'm naïve – when I do something, I want to share it with everyone because I think that's what science is about. I think that slowed down the evolution and development of the technique, and it's one of the reasons why GC×GC was seen as an exotic technology for a long time.

Thankfully, that's no longer the case. You can now find GC×GC-MS in routine industrial laboratories.

Has GC×GC reached a turning point in recent years?

There's definitely been a change. In previous years, when you went to a GC×GC meeting or listened to a GC×GC presentation at ISCC or elsewhere, people would talk about the new modulator or software they'd developed, or that they'd been trying GC×GC to solve this problem.

We're now in a new era, which is even more exciting because we see GC×GC being used, for example, as a real metabolomics tool – not an exotic trial from an exotic lab somewhere. Some metabolomics labs really use GC×GC daily now. Indeed, we do a lot of medical applications in our lab that wouldn't be possible without GC×GC.

But it's not that we've reached a plateau now that the hardware is quite stable and we can use it routinely. A lot of know-how and manual input are still needed to process data. It's easy to generate a chromatogram, a peak table, or an image. But if you're looking for biomarkers of exposure, for example, from the more than 1,000 features you get, you need to isolate the important molecules.

People know how to do that now, but everyone has their own recipe. If I take a dataset and give it to you, as an expert GC×GC user, you'll process it with your own methodology and end up with a set of biomarkers. If I process the same data with my methodology, I'll isolate another set of biomarkers. And in every lab, it will most probably be another set.

I'm not saying it doesn't work, but there isn't enough harmonization and compatibility between what's done in one place versus another. The Metabolomics Standards Initiative and the mQACC goe in that direction, not only for GC×GC. But if we want to convince a clinician to use the technology, we have to be able to say that the data we produce and the outcomes of the research will be reproducible in any hospital – and that's not yet the case today.

That's where we are, and it still requires a lot of work.

Is this challenge unique to GC×GC?

I don't think it's unique to GC×GC, but I think the problem is even more significant for GC×GC because the quantity of data you're generating is huge. If you think about GC×GC coupled with high-resolution TOF-MS in particular, the number of data points you're collecting, and the size of the data matrices you have to process, are tremendously bigger than with one-dimensional GC, for example, or even LC.

The larger your data matrix, the more difficult it is to harmonize the way you're going to treat those data. The more data you have, the more options you have when applying statistics and everything else. That's where the challenge lies.

What are the main research priorities in your lab today?

We're more focused now on volatile compounds. Medical applications probably account for 75 percent of what we do, but we'll tackle any analytical challenge involving VOCs.

Sometimes we're contacted by industry – the food industry, the fragrance industry, or the petroleum industry. With the energy

transition, for example, we have to characterize pyrolysis oils, which are very complex and very different from crude oils. We've also been working in archaeology, for example, to characterize very old pieces of hafting equipment. We still do some more theoretical modeling and model development to predict the use of chromatographic space. But breathomics, volatilomics, and lipidomics are the keywords in the lab right now.

The good thing is that everything we develop in one niche of application can be used in another. So an advance we make in data processing for the petroleum industry can be applied in the medical domain quite quickly afterward. That's really a good return on the investment in research.

What impact could GC×GC have in clinical medicine?

We're trying to improve our understanding of the chemical composition of patient samples. We know we can collect blood, urine, feces, or exhaled breath samples from patients. That's not new. But we're trying to get a more precise and exhaustive chemical description of what's in those samples to help identify a pathology – to distinguish between a cancer patient and a non-cancer patient, for example.

This is just one extra piece of the big puzzle that medical doctors have to solve. They already use genomics, proteomics, and a lot of clinical testing. Looking at VOCs and other volatile compounds provides an extra piece of information they can integrate into their assessment of the patient's overall condition. That's how I see our contribution.

There's also another opportunity at the screening level. The more patients you screen, the better your chances of identifying a pathology at an early stage.

We're working on ways to visually differentiate between the two-dimensional chromatogram of a patient and that of a control. How do those two images compare? Could we use that comparison for rapid screening and perhaps highlight some biomarkers?

But if you want to move this into hospitals, taking a GC×GC high-resolution TOF-MS system and putting it in a hospital isn't the way to go. It's still too complex. At this stage, the best approach is still to sample patients (exhaled air, micro-volumes of blood, and so on) inside the hospital infrastructure under strict procedures and then transfer samples to the analytical lab for analyses.

Instead, we can also use GC×GC in non-target screening mode to identify a few biomarkers and then transfer those findings to target techniques (e.g. 1D-GC-MS using specific sample preparation) if enough specificity can be ensured towards the targets.

Another option is to use proton-transfer-reaction mass spectrometry (PTR-MS) or selected-ion flow-tube mass spectrometry (SIFT-MS), in non-target mode, using multiple chemical precursors and specific ion channels. These are simpler, direct-inlet mass spectrometry techniques, which are much more suitable for hospitals. A SIFT-MS system is about the size of a dishwasher, and the patient can simply blow directly into it. That's what we're trying to do now. We've been duplicating studies using GC×GC-TOF-MS and SIFT-MS, and we're seeing very good correlations between the two.

Could GC×GC contribute to more personalized approaches to medicine?

For sure. The idea is to get a quick picture of an individual patient's condition. We're also doing more studies where we follow patients after treatment. For example, if a patient is diagnosed with cancer, we can monitor them over time. Are they responding to the treatment? Can we see differences in their volatolome that might help us better understand their response?

There's also growing interest in virtual biobanking where my colleague Pierre-Hugues Stefanuto is exploring how GC×GC data sets could contribute to creating high resolution chemical descriptors of exhaled air samples rather than long term delicate storage of raw samples.

In general, when genomics, proteomics, and metabolomics are used in the framework of personalized medicine, we think that GC×GC-TOF-MS can contribute to that. It's something we'll be working on in the near future.

What other developments in GC×GC do you find particularly promising?

One important area of development is miniaturization, which could enable online measurements in chemical processes or the pharmaceutical industry.

We're seeing more valve modulators coming back now, with more robust designs that could allow us to make them smaller and smaller while maintaining good modulation efficiency for specific applications.

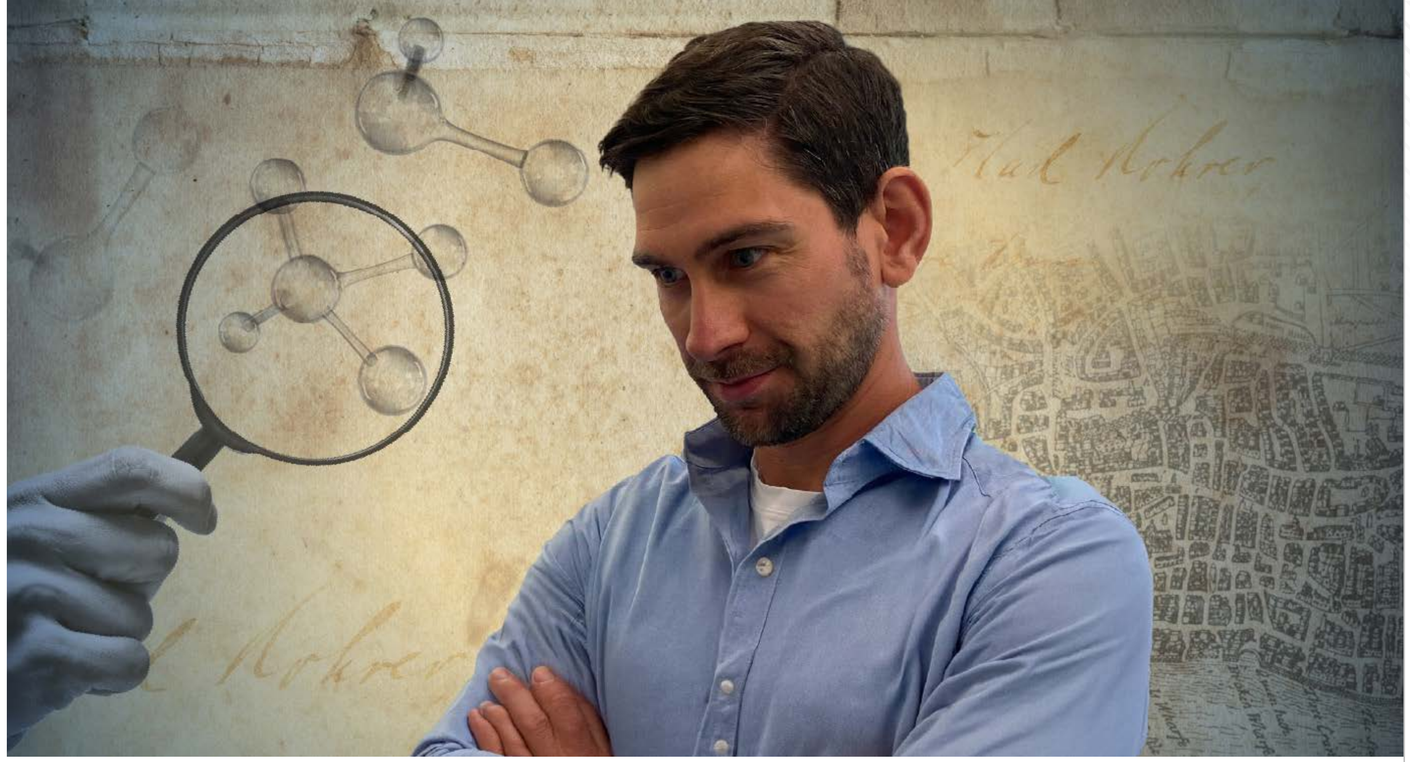
I think it's now possible to imagine miniaturized, robust GC×GC systems designed for particular applications. That's probably the next big thing – smaller systems that can be used continuously to monitor things like air quality for exposomics, for example, where we need more separation power than one-dimensional GC can provide.

Another important development will be the increasing integration of machine learning and artificial intelligence into data processing. This is typically a field where AI could help with data reduction, for example.

Closing the Case

Pierre-Hugues Stefanuto on the achievements, bottlenecks and open questions in modern GC×GC

By Pierre-Hugues Stefanuto, Lead Scientist and Lecturer, University of Liège, Belgium



This year has been rich in separation science conferences, and multidimensional chromatography has been one of the big hits. From the Multidimensional Chromatography Workshop to the International Symposium on Chromatography, including the highly successful return of Riva, multidimensional chromatography, and especially GC×GC, has shown its maturity and attractiveness in many fields.

Over the past three months, The Analytical Scientist's GC×GC Detective Stories have portrayed the status of multidimensional gas chromatography. They show that, building on a rich history of impactful research, the global quest for separation resolution has turned the technique into a "must have" in many analytical laboratories.

Every good detective story ends with the investigator gathering everyone in one room and laying out the evidence. It is time to do the same for GC×GC: to review what the series has established, to name the bottlenecks that remain, and to ask the questions that remain open. In short, it is time to close the case by presenting the final arguments.

A technique going across fields and across generations

The GC×GC Detective Stories brought together the vision of different generations of leaders in the field.

The first generation built the instrument itself. Their stories are about hardware development: modulators that could reliably trap and reinject narrow fractions of the first-dimension effluent, column combinations offering complementary selectivity, and detectors fast enough to capture peaks only a few hundred milliseconds wide. Just as important were the essential proof-of-concept studies that demonstrated the exceptional capabilities of the technique. Ordered patterns of chemical families in the separation space, the resolution of thousands of compounds in a single run, and the detection of trace constituents previously buried under matrix peaks convinced a cautious community that comprehensive two-dimensional separation was more than an academic curiosity.

The next generation took these tools out of the specialist laboratory. Petroleum and fuels, where sample complexity made GC×GC almost indispensable, were followed by environmental monitoring, food, flavor and fragrance, forensics and, more recently, metabolomics, exposomics and breath analysis. With each new field came new questions, and the technique adapted: flow modulation broadened access by removing the need for cryogens, fast-acquisition mass spectrometry became routine, and software

began to turn raw data into chemically meaningful information.

The youngest generation, finally, is growing up with GC×GC as a standard tool rather than an exotic one. For them, the question is **no** longer whether the technique works, but how best to use it: how to design studies, how to process large data sets, and how to translate chemical fingerprints into answers that matter outside the analytical community. Read as a whole, what stands out in the series is the continuity between these generations. The same curiosity that drove the first modulator designs now drives the search for robust data-processing workflows, and each wave of practitioners has inherited, and extended, the tools of the one before.

A technique that all detectives want on their side

If one theme runs through every case in the series, it is GC×GC's ability to reveal what one-dimensional separations miss. Whether the investigation concerned a contaminated food product, a disease signature in exhaled breath or the origin of a petroleum sample, the critical evidence was often a minor compound co-eluting with something far more abundant – invisible until a second dimension pulled the two apart.

From pictures to decisions

GC×GC's 2D plot is iconic for good reason: structured patterns of homologous series and chemical classes make complex samples readable at a glance. But the plot matters less for its beauty than for the interpretation it enables. For example, in process monitoring, it shows how a feedstock is transformed or how a product degrades over time; in clinical research, it supports the search for diagnostic patterns of volatile compounds; and in regulatory settings, it provides the evidence needed to demonstrate compliance or to flag a non-conforming sample. In each case, the value lies in the decision that follows the picture.

The bottleneck has moved

In the early days of GC×GC, the limiting factor was the instrument. Today, commercial systems are robust, and modulators and detectors are no longer the main obstacle. The bottleneck has moved to operator training, data handling, and standardization. Operating a GC×GC system well, choosing the right column set and modulation conditions, and then making sense of files containing thousands of features requires skills that are not yet part of most analytical curricula. Data processing in particular remains time-consuming and operator-dependent, and the lack of common formats and procedures makes it difficult to compare results across laboratories or software packages. This is where investment is likely to have the largest impact in the coming years.

The good news is that these are problems the community knows how to address. Hands-on courses, shared tutorials and open data sets lower the entry barrier for new users, while vendor-independent processing tools and agreed file formats would make results easier to share and reproduce. Detectives rarely work alone, and neither should GC×GC users: the most convincing cases in the series were built by teams combining instrumental expertise, chemometrics and deep knowledge of the application.

A technique that is still aiming for its full potential

The series also helps define what GC×GC is, and what it is not.

The core value is unmasking co-elution

Every case in the series could be summarized the same way: the answer was hidden under a bigger peak. This is the fundamental strength of comprehensive two-dimensional separation, and the reason it keeps finding new applications. Whenever a sample is complex enough that co-elution compromises identification or quantitation, the second dimension offers a way out.

Fit-for-purpose thinking

A second dimension of separation isn't always required. Many routine analyses are perfectly served by a well-optimized one-dimensional method, and choosing the more powerful technique by default adds cost, complexity and data burden without adding information. The most successful users start from the analytical question, not from the instrument. That discipline will be essential if the technique is to be adopted beyond its current strongholds.

In practice, this means asking early whether the problem really requires a second dimension, which compounds or classes must be resolved, and how the data will be interpreted once acquired. Answering these questions before the first injection saves time, keeps

"On the evidence presented, the verdict is clear: GC×GC has proven its value. It has grown from a laboratory curiosity into a mature technique used across fields and generations, and it has repeatedly uncovered evidence that would otherwise have remained hidden."

data sets manageable and makes the added value of GC×GC easier to demonstrate to colleagues, managers and reviewers.

Read critically, the stories also reveal several gaps, and these point to the questions that remain open.

Quantitation and harmonization

The series said little about quantitation, validation or harmonization between laboratories. Yet these are precisely what regulators, clinicians and industrial quality managers need before they can rely on a method. Interlaboratory studies, reference materials and agreed reporting practices for GC×GC are still rare, and closing this gap would do more for the credibility of the technique than any new modulator.

Artificial intelligence

AI is mentioned as an aspiration, with no demonstrated results. Machine learning is clearly well suited to the rich, structured data that GC×GC produces, and expectations are high. But the series offered no case in which AI had already changed the outcome of an investigation. Demonstrating one, with transparent methods and validation on independent samples, remains an open challenge for the community.

Looking forward

Most success stories look back at past cases. This is natural for a series built around stories, but it leaves the future less clearly drawn. Which questions will GC×GC answer in five or ten years? Which fields are still waiting for it? A more forward-looking agenda would help newcomers see where their contribution could make a difference.

A broader industrial voice

The industrial perspective came only from food and fragrance companies. These sectors are important early adopters, but they are not the only ones. The experience of petrochemical, pharmaceutical, chemical and environmental testing laboratories, where GC×GC is also used, would give a fuller picture of how the technique performs under routine constraints such as throughput, cost and regulatory scrutiny.

Closing the case

So, can the case be closed? On the evidence presented, the verdict is clear: GC×GC has proven its value. It has grown from a laboratory curiosity into a mature technique used across fields and generations, and it has repeatedly uncovered evidence that would otherwise have remained hidden. The remaining challenges are no longer about whether the technique works, but about how it is taught, how its data are processed and shared, and how its results are validated and trusted.

In the best detective tradition, closing one case often opens the next. For GC×GC, the next investigation will be less about separation power and more about people, data and standards. That may well prove to be the most interesting story yet.

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