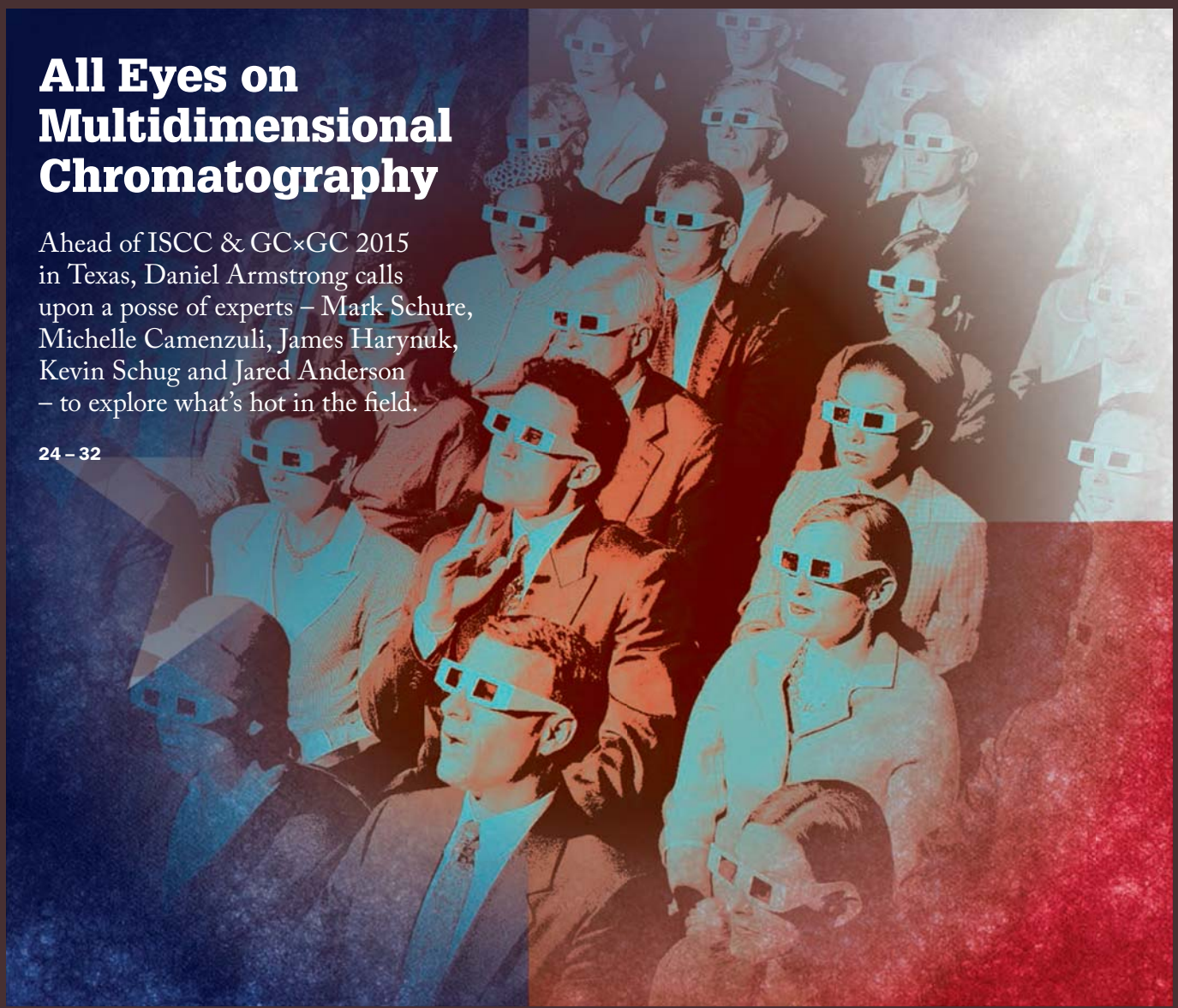
APRIL 2015 # 27

# the Analytical Scientist





## All Eyes on Multidimensional Chromatography

Ahead of ISCC & GC×GC 2015 in Texas, Daniel Armstrong calls upon a posse of experts – Mark Schure, Michelle Camenzuli, James Harynuk, Kevin Schug and Jared Anderson – to explore what's hot in the field.

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# The Frontier of Gas Chromatography

**When I was asked to evaluate a brand-new instrument with disruptive potential in my field, I did not spend long thinking about the answer. Here, I share a little background and my first impressions.**

*By Hans Mol, Group leader Natural Toxins and Pesticides, RIKILT Wageningen UR.*

I've been working for nine years at RIKILT-Wageningen UR in the Netherlands, predominantly working with the government on aspects of food and feed safety. For that reason, we are always interested in evaluating new instruments and techniques that can address the current – and future – challenges facing us. As such, I am very pleased to have a pre-production version of the much-anticipated GC-Orbitrap sitting on my lab bench...

Looking back, I've often been fortunate in finding myself at the cutting edge of GC.

My analytical journey really began when I did my masters project in Udo Brinkman's group at the Free University in Amsterdam – he was well-known and respected, and my interest grew. I continued onto a PhD at the Technical University in Eindhoven under professor Carel Cramers – a couple of years behind Hans-Gerd Janssen (who actually supervised my PhD). My research was very much focused on large volume injections (for residue analysis), using programmed temperature vaporizing (PTV) injectors. PTV is commonplace now, but this was in the early 1990s – and it was somewhat disruptive technology back then, competing with retention gap, on-column-type of large volume injections from other groups. We were pretty sure early on that, in routine applications for food and environmental samples, PTV would become the industry standard.

I finished my PhD in 1995 and continued on as a post-doctoral research working on GC coupled to both MS and an atomic emission detector (AED). I then worked for about 10 years for a contract research organization offering analytical services for food, (agro)chemical and pharmaceutical industry. Importantly, we did a lot of method development work on LC-MS, GC-MS – and myriad other techniques – and I gained a great deal of experience. And that brings me to RIKILT.

There have been many technological advances over the past 20 years or so. The availability of LC-MS for food and environmental analysis was a huge milestone. When I started, the field was very GC oriented. If compounds were not amenable to GC, we would use derivatization to make them amenable. LC was a last resort in some ways – until the commercialization of electrospray ionization. As the instruments became increasingly affordable (they were already in use in big pharma with its big budget) – they changed the field.

Another step change was the introduction of high-resolution MS (HRMS) techniques (time-of-flight (TOF) or Orbitrap instruments) to LC-MS; indeed, in certain applications these are now replacing triple quadrupole instruments.

But what about similar progress in GC? Much of the effort from instrument suppliers seemed to be focused on LC (remember the pharmaceutical industries big budget?) and GC – despite its utility in persistent organic pollutants and pesticides – was left behind. Until now.

I expect the new GC-Orbitrap instrument will count itself among the aforementioned milestones and redress the imbalance!

## GC-Orbitrap Technology lands

Just this very week (at the time of writing), one of the first GC-Orbitrap instruments was installed in my lab. Ahead of installation, the space we created raised a few eyebrows with certain visitors (other instruments had to be relocated). Anticipation has been high and so keeping the secret has not been easy.

Previously, we had the opportunity to see the instrument at Thermo Fisher Scientific's operations in Runcorn, UK, and it looked very promising. And while it's still early days, I have high expectations – as do my colleagues, who have formed a relatively orderly line, samples in hand! Over the next few months, we will be putting the instrument through its paces.

The main challenge in my particular field is the sheer number of pesticides of interest – around 1400. The question is relatively simple: "are there any pesticides in this sample, and if so are they above the maximum residue limit (MRL)?" For targeted analysis, you can use a triple quadrupole MS system, but you're limited in terms of scope, because you are only measuring pre-defined compounds. If you want to look for something new or different, you need to go back to your sample and re-run the analysis.

Conversely, with full-scan methods, you inject your extract, measure the compounds of interest but have the option to look back into the raw data for other analytes. Moreover, the number of compounds that can be measured in a single run is much higher than a triple quadrupole. Using a dedicated triple-quad method, you can routinely target 100-150 compounds (instruments have improved here as well – shorter dwell times potentially allow a slightly higher number to be squeezed into a given method). But with full-scan analysis, you measure everything – and there are 700-800 pesticides that are amenable to GC. That's a gain we are excited about.

From a method development point of view, there are also advantages to full-scan analysis because the conditions can be quite generic. In fact, there's little optimization needed at this stage – that's addressed in the data handling. In contrast, in GC-triple quad methods, you have to set acquisition windows and if you want to add compounds you need to optimize the transitions for each of those compounds. In simple terms, it takes more time.

## Hands on – first impressions

In terms of resolution, the GC-Orbitrap is clearly a major step forward, outperforming everything on the market. And so in Runcorn, we were more interested in assessing sensitivity and selectivity. We ran a calibration curve in a more difficult matrix (a leek sample) and were impressed by the sensitivity, which was actually better than the triple quadrupole instrument in our lab. However, our instrument is previous generation, so the next question was, how does it compare with the current generation of triple quads? Fortunately, we were able to perform that experiment in Thermo's lab, which had the two set ups side by side. For the analytes tested, comparable results were obtained.

Maintaining sensitivity while adding the full-scan capability (and the advantages that come with it) is a big plus point. Selectivity is equally important but, to be honest, I think that's much more difficult judge – we need to run more samples and look at more analytes to form a fuller picture on how HRMS compares with MS/MS, which also has limitations, especially in terms of electron ionization (fragments of fragments become less and less specific after all).

Complex samples, such as food supplements, are perfect to test the true capability of GC-Orbitrap. Feed ingredients are also very complex (essentially they are manufactured from any food industry output that holds nutritional value but which cannot be used for anything else). Traditionally, such samples present real challenges in terms of detection limits, demanding more attention and time on sample preparation and method development. Broadly speaking, the GC-Orbitrap will help; we can use fewer methods because of the selectivity, and the sensitivity will allow us to reduce injection volumes (from around 5µl down to 1µl) or to use less concentrated samples. By introducing fewer co-extractants in this way, we can reduce deterioration in GC performance.

One of my colleagues works on forensic-style analysis and has expressed particular interest in the GC-Orbitrap. The samples in these 'cold cases' are 'suspect' but we don't know why – has something toxic been added at some point in the supply chain? Alternatively, there may be a dead animal and a big question mark. Different procedures apply in this field because the analysis needs to be as unbiased as possible. Samples must be screened and then cross-referenced against very large NIST libraries to find a match. Alternatively, comparative analysis against known reference products can be useful to assess which samples are deviating from 'normal' by overlaying profiles and identifying suspicious peaks. Up to now, this type of work is being done with comprehensive GC (GC×GC) with a nominal mass (low-resolution) MS system. We are very interested in the potential of doing the same analysis using one-dimensional GC coupled with high-resolution (Orbitrap) MS.

## Surveying a changing landscape

I'm not one to make sweeping predictions, but I expect that targeted methods with triple quads will be phased out as time goes on. Full scan instruments are just as capable – and even if you don't get sufficient selectivity, with Q-Orbitrap or Q-TOF you have the ability to do MS/MS as well. At a certain point, the question will become: why do I still need a triple quadrupole instrument? I can only think of one reason: its highly stable quantitative performance – and that's another area I am very interested in exploring with the Orbitrap.

Will the transition from triple quadrupole methods happen overnight – or in five years? Well, even if the instrument far exceeds all our expectations, there will be a considerable lag in wider adoption. After all, our lab is working at the cutting-edge – we're much quicker to evaluate and embrace the great and the good. In more routine analysis, extra time will be required for general acceptance – and established procedures must be challenged and changed. After all, the GC-Orbitrap is something very new and different indeed.

*Video interview with Hans Mol:*
*tas.txp.to/0415/HansMol*
*To find out more:*
*thermoscientific.com/HRAMGCMS*