PIERRE-HUGUES STEFANUTO*, JEAN-FRANÇOIS FOCANT
*Corresponding author
Organic and Biological Analytical Chemistry Group, MolSys research unit, University of Liège, Belgium

Comprehensive two-dimensional gas chromatography in industry: present situation and potential developments

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ABSTRACT

For analytical scientists, the ultimate goal is to develop and implement original methods to solve practical issues. At first, this quest of perfection has to take into account the pure analytical robustness and trueness of the approach. Nevertheless, costs and practical aspects may not be forgotten and should seriously be considered. This complex balance is even more complex for industrial analytical solutions as it also should include an 'ease of implementation' factor. Comprehensive two-dimensional gas chromatography (GC×GC) has a recognized added value in some industrial fields where complex sample characterization is required (e.g. oil and gas, fragrance, food, ...). The high separation power of the two chromatographic dimensions provides the required resolution to fingerprint most of complex samples. This analytical power made GC×GC the method of choice for untargeted screening in different industrial applications. However, the cost and complexity of GC×GC are the most limiting factors for its widespread acceptance. The development of fully integrated GC×GC solutions, including data processing, would support its development and implementation in other fields.

INTRODUCTION

Comprehensive two-dimensional gas chromatography (GC×GC) has been present in the separation science landscape for almost 30 years (1). From lab-made first proof of concept instruments to fully integrated commercial solutions, the technique has been through the classical development curve of complex hyphenated analytical techniques. In order to successfully reach industry acceptance, robust instruments and data processing softwares were required. The first challenge was the development of robust and reliable hardware equipment allowing the distribution of commercial equipment. The two main areas of development were the creation of robust modulators and the coupling to fast acquisition mass spectrometry (MS) detectors (2).

Today, method development and data handling are the ongoing challenges met by most users, on both industrial and academic sides. The development and exploitation of GC×GC workflows still require expert users. Such expertise requirement can easily dampen industry's interest for the technique. Time is money and the learning and development time required to implement such a new method has to be worth the investment and result in clear added values. For most industrial applications where complex mixtures of (semi) volatile compounds have to be considered, the relative complexity of GC×GC, coupled to MS or not, will always be rapidly counterbalanced by the quality of the information obtained after analysis.

As most of the biggest achievements and strongest developments of GC×GC in industry stay unpublished, the market share of GC×GC (over 1DGC) in industry is probably underestimated. Despite this lack of visibility, industrial laboratories that seek for solutions in separation science are heavy users. Next to the petrochemical industry, other sectors like tobacco, flavour and fragrance, food, environmental, medical, forensics… are significant users of GC×GC at the industrial level.

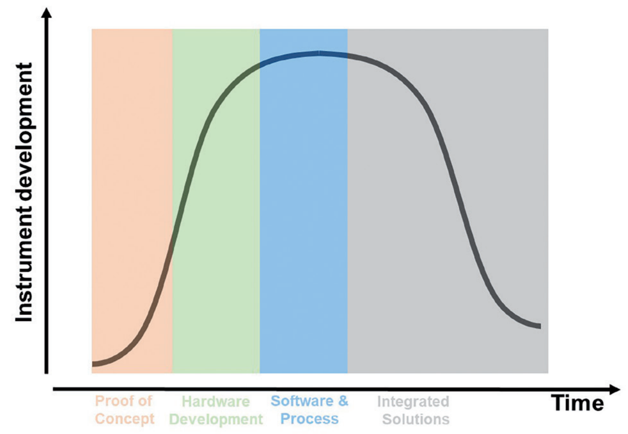

Figure 1. Development curve for complex analytical instruments.

ROBUST MODULATORS AND HIGH-RESOLUTION DETECTORS

On the modulator side, there is a range of possibilities available on the market. Next to the historical cryogenic-based solutions, there are multiple options for robust cryogenic-free thermal modulator and flow-based systems (3). The development of the liquid nitrogen-based modulator by Zoex® represents the first robust commercial modulator system. Unfortunately, even if very efficient, the large consumption of cryo-fluids has discouraged many potential industrial users. The development of flow modulators certainly permitted to compensate that and opened the door to a lower running cost GC×GC solution. This was however accompanied by more complex method development needs and limitations regarding the coupling to vacuum outlet MS systems due to the required high career gas flow of such flow modulators.

Nevertheless, the combination of the flow modulation technology with FIDs or other elemental detectors has been and still is a popular option for the oil and gas industry (4). The continuous development since the first flow-based system has conducted to highly efficient valve-based modulators (e.g. reverse fill/flush flow modulator, Insight™ modulator) systems that further pushed GC×GC at the industrial level. Nowadays, cryogenic-free thermal modulators as well as solid-state modulators are completing the commercial offer and allow the use of MS detection without the need of diverting part of the eluents prior detection. Irrespective on modulation modes, most recent modulators can easily be installed on existing 1DGC systems to upgrade capabilities at the GC×GC level in routine laboratories. This offers unique possibilities to industrials to access GC×GC while minimizing the needs for major modifications of running accredited 1DGC methods. The major remaining limiting factor has become the price of such upgrade that is still ranging from 20 to 40 kEUR for commercial solutions.

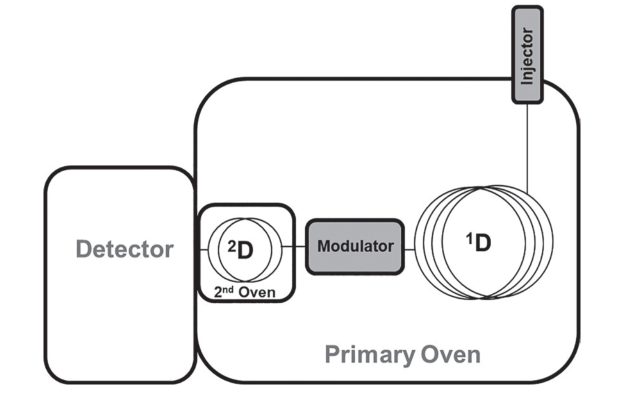

Figure 2. Scheme of a GC×GC system.

For the detector, a wide choice of regular 1DGC elemental detectors and non-specific detector (e.g. FID) have been used since the beginning of the technique. The first big development on the detector side was the implementation of fast acquisition time-of-flight mass spectrometers (TOFMS) making the MS dimension compatible with the GC×GC resolution. In the following years, the development of fast scanning quadrupole systems offered a cheaper alternative than TOFMS when signal deconvolution was not important. The implementation of MS detector compatible with GC×GC system has represented a significant development for the identification of complex mixture components. Moreover, the smart use of the mass spectral information through library searching and MS scripting offers a powerful third dimension (5). More recently, the development of high-speed high-resolution (HR) TOFMS opened the door for new applications where accurate compound identification is mandatory. This development of HRMS detector further generates a growing enthusiasm for soft ionization techniques (e.g. photoionization) allowing the preservation of parent ion signals necessary for identification based on accurate mass measurements. Ultimately, such high accuracy spectral data can be used for Kendrick mass defect (KMD) calculations and classifications, adding up an extra dimension to the set of data (6,7). Nowadays, GC×GC is mostly present in applications requiring high adaptability to the sample and high needs for untargeted measurements. For the petroleum industry, GC×GC went from global group type analysis to more advanced complex sample characterization, including high temperature applications. Recently, Giri and colleagues have developed a soft ionization GC×GC-HRMS approach to characterize different base oil samples. The unsupervised screening conducted to the identification of correlations between the chemical composition and macroscopic properties of the oils (8,9). These examples illustrate the future potential for industrial R&D analyses. Indeed, the constant development in untargeted analytical methods and data science make possible the development of intelligent models for assisted product development.

In the context of specific industrial applications, recently available vacuum ultra-violet (VUV) detector also offer great potential. The selectivity and specificity of such spectroscopic dimension allows to selectively detect target compounds or group of compounds, such as aromatic compounds, oxygenates…

ONGOING CHALLENGES: CHROMATOGRAPHIC BIG DATA

During the recent Multidimensional Chromatography Workshop (http://www.multidimensionalchromatography.com/), a focus group was dedicated to the implementation of GC×GC in industry and the ongoing related challenges. According to the industry scientists who were present, the biggest challenge encountered for GC×GC is the development of fully integrated solutions. The hardware is robust and commercially available but the method development and data handling are still too complex and require expert users. These limitations are still slowing down the widespread industry acceptance of the technique.

Indeed, the lack of fully integrated solutions is preventing the development of routine industrial applications. There is currently a strong effort from the research community to fill that gap. Optimization tools based on design of experiment, models based on thermodynamic calculation or sample descriptors are currently under development (10,11). In addition, the elaboration of optimized processing tools, including in-depth statistical treatments, is going to contribute to the development of fully automated solutions (5).

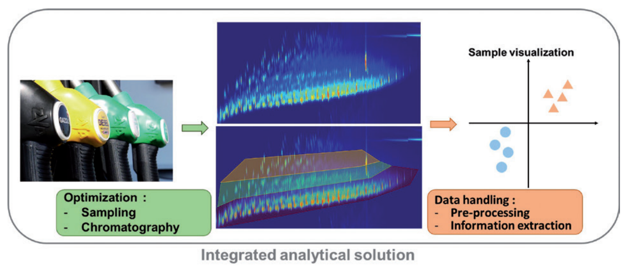

Figure 3. Complete analytical workflow for GC×GC.

RISK AND CHALLENGES OF IMPLEMENTING NEW APPROACHES

Another aspect that may slow down the implementation of GC×GC in the industry where target analyses are performed in line with legislative compliance efforts, is the high resolving power of the technique, especially when hyphenated to mass spectrometers. The detection of new compounds that are currently not seen (regulated) could be more of a problem than a solution. Indeed, the screening of hazardous substance is generally performed by target 1DGC-MS methods. Those methods are only monitoring a defined list of dangerous compounds. With GC×GC, the complete sample composition is available in a single analysis, which can generate question regarding unknown compound toxicology. On the other hand, such a capacity for untargeted screening of potential toxic compounds also makes GC×GC the method of choice for new regulated compounds screening.

The technique will for example have a card to play in the emerging field of mineral oil contamination in food and feed (12). In any case, having access to a better and more accurate description of any types of complex samples should be seen as a clear added value.

CONCLUSION

In conclusion, GC×GC is still in a growing phase regarding industrial applications. The high cost and complexity of the techniques, compared to 1DGC, have most probably slowed down its industrial implementation. Nevertheless, the constant developments of cryo-free low-cost modulators and HR detectors are making GC×GC more and more appealing for routine applications. Current efforts in the development of computer-assisted tools for method optimization and data processing are going to make fully integrated GC×GC solutions available. User-friendly GC×GC is going to speed up its development in industry, where untargeted screening tools are more and more required. Finally, evolving from 1DGC towards GC×GC should not be seen as exiting the comfort zone but seen as expending the comfort zone. It is not because you upgrade to GC×GC that 1DGC is not available anymore… it all depends on the needs.

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ABOUT THE AUTHORS

*Dr. **Pierre-Hugues Stefanuto** is a research scientist and lecturer at Liège University in Belgium. His main research interest is the development of analytical solutions based on chromatography and mass spectrometry technology. He is interested in the development of statistical models for method optimization and data handling. He is working on the development on multimodal solutions of untargeted screening of small molecules.*

*Professor **Jean-François (Jef) Focant** is the Head of the Chemistry Department of the University of Liège in Belgium. He is leading the Organic and Biological Analytical Chemistry group. Main research interests are coupling of sample preparation procedures, development of new chromatography strategies in separation science, hyphenation to various types of mass spectrometric detectors through multidimensional systems, and implementation of emerging strategies under QA/QC requirements for biological applications.*