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Enhancing Flame Ionization Detector Capabilities with Post-Column Reaction
Jim Luong, Yujuan Hua, Ronda Gras, Xiuhan Yang, Peilin Yang, and Guangyu Liu
The incorporation of a post-column reaction using a 3D-printed, two-stage microreactor is showing groundbreaking performance improvements for flame ionization detection in many gas chromatography applications—and delivers carbon universal response.

The Role of Microextraction Techniques in Facilitating Gas Chromatography Separation of Complex Mixtures
Emanuela Gionfriddo
Microextraction is an affordable solution for preventing “garbage in–garbage out” effects in one-dimensional (1D) and two-dimensional (2D) GC separations, by providing analyte preconcentration, interference removal, tuning of extraction coverage, and easy coupling to GC systems.

Using the Three Cs of Data Visualization as a Life Raft When You’re Drowning in Multidimensional Chromatography Peaks
Heather Bean
Correlation, clustering, and color projection techniques exploit the ability of the human brain to identify patterns from huge amounts of visual information. This process can provide a life raft for a weary chromatographer who is drowning in data.

From Recycled Plastic to Pyrolysis Oils: A Renewed Need for a Broad Range of Gas Chromatography (GC) Detector Technologies
Kevin A. Schug
Recycling plastics involves catalytically cracking polymers back into their constituent monomer mixtures, which require careful characterization for further processing. There is a resurging need for detectors that can detect and characterize heteroatom-containing species.

Gas Chromatography Meets Non-Targeted Screening
Thomas Letzel and Stefan Bieber
We take a look at the past, present, and future of applying gas chromatography–mass spectroscopy (GC–MS) techniques to non-targeted screening (NTS) in various disciplines, assessing both the opportunities and the challenges.
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Gas chromatography (GC) is one of the most well-practiced chromatographic techniques in analytical chemistry (1–3). This ubiquitous technique delivers critical analytical solutions in many areas, from targeted compound analysis for indoor pollution monitoring to characterizing toxic chemicals in forensic investigations. Some of the reasons for the popularity of GC are that it is relatively inexpensive to implement, simple to operate, easy to maintain, and has a high degree of reliability. Despite more than 50 years of existence, the role of GC has not diminished or been replaced. Instead, the use of GC increases with continual developments in hardware and techniques to tackle a steady increase in sample complexity, catalyzed by societal transformations and initiatives such as increasing recycling and sustainability efforts.

**The Flame Ionization Detector (FID)**

Unlike other analytical chemistry disciplines, GC was blessed with many detector choices (4–6). Without any doubt, one of the most important innovations in GC was the invention of the flame ionization detector (FID) that was almost simultaneously and independently reported by I. McWilliam and associates (Australia) and J. Harley and associates (South Africa) in 1957 (7–10). Since its invention, the FID has become a choice detector in GC. Justifiable reasons for the FID to be in such a dominant position are as follows: It has a respectable detection limit around 0.5 pg C/sec, which allows the detector to meet many contemporary and demanding applications, and it is relatively inexpensive to construct, operate, and service, providing one can have access to fuel gases. Also, the detector can tolerate harsh chromatographic conditions of up to nearly 500 °C and highly corrosive gases, such as hydrogen chloride or sulfur hexafluoride. However, despite its wide-spectrum application and popularity, the FID is not a panacea for all chromatographic applications. The detector has some critical constraints. For example, compounds that can not generate CHO+ ions in a hydrogen flame, such as carbon monoxide, carbon dioxide, carbonyl sulfide, and formaldehyde, can hardly be detected. Also, the FID has a reduced response for some oxygenated or functionalized species. Another important issue critical for accurate quantification is that the FID has a highly variable response throughout many organic carbon-containing compounds and, in some instances, even within the same class of compounds like short-chain aldehydes or alcohols. Reference standards must be synthesized or procured to perform the analysis. Also, it is not possible to avoid handling compounds that are highly volatile, chemically unstable, or with an elevated level of toxicity.

Several attempts to improve the performance of the FID detector for targeted compounds have been reported in the literature. For instance, the measurement of trace carbon dioxide (CO2). This application attracts attention as CO2 is a major greenhouse gas that contributes to climate change. Catalytical reduction of CO2 to methane for detection by FID was first described by Porter and Volman (11), who demonstrated that carbon oxides could be converted to methane with an appropriate catalyst, such as nickel at an elevated temperature in a hydrogen atmosphere. Analytical devices based on this approach, commercially known as the “methanizer”, have been made available for many decades as a stand-alone or integrated chromatographic tool by various instrument suppliers and manufacturers (12). Although the device functions adequately in targeting...
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carbon oxides in a relatively clean gas matrix, such as ambient air, it is susceptible to catalyst fouling because of poisoning by matrix constituents such as sulfur or halogenated compounds. Also, integrating the methanizer as an adjuvant device into the analytical system reduces the flexibility of the chromatograph while increasing the overall chromatographic void-volume of the system. The outcome of both effects is not desirable. A new reincarnation to this approach involves incorporating a more robust catalyst inside an FID jet (Jetanizer) to minimize void-volume and increase the system’s ease of service and platform flexibility (13–16). Although this approach improves chromatographic performance and robustness, the quest for carbon compound independent response capability by FID which is highly sought after by chromatography innovators, remained an elusive and moving target.

The Post-Column Two-Stage Reaction and Metal Three-Dimensional (3D)-Printing Technology

The post-column two-stage reaction has the potential of being a viable solution to carbon compound independent response capability for FID. In this reaction process, organic compounds are first oxidized to CO$_2$ with a catalyst such as platinum and subsequently reduced to methane with another catalyst like nickel for detection as described in the literature (16–18). Although this strategy has merits, the extra column band broadening effect ($\sigma_{ec}$) from having two packed bed reactors between the column outlet and the detector can be quite excessive and may negatively affect the overall chromatographic performance. A typical chromatography time domain of peak width in the range of 10 to 20 s was observed, making the technique not suitable for high-resolution gas chromatography.

A novel approach to attain the same objective involves using metal 3D-printing technology for the fabrication of metal microstructure devices that are augmented with the appropriate catalysts in this microreactor embodiment (Polyarc). The assembly integrates two catalytic chambers in series where carbon-containing molecules are first converted to CO$_2$ through a combustion process immediately followed by the methanation process (19,20). Figure 1 shows the relative responses to methane of model compounds from many classes of volatile and semivolatile organic compounds with the technique described. Several key enhancements are noted. First, the employment of the post-column reaction strategy expands the capability of the FID in that critical compounds of industrial significance with low or no response by FID alone, such as carbon monoxide, carbon dioxide, carbon disulfide, and formic acid, can now be detected with excellent sensitivity in the range of 0.5 pg to 1.0 pg C/sec with a contemporary FID. Second, as shown in Figure 1, sensitivity improvements were also observed for popular oxygenated compounds and chlorinated hydrocarbons, such as formaldehyde, methanol, carbon tetrachloride, and chloroform. In formaldehyde, an improvement of sensitivity of more than ten times compared to FID alone was observed. Finally, except for acetylene, where a reduced but
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Gulf Coast Conference (GCC) encompasses everything needed for a successful, enjoyable, educational, and gratifying get together:

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Amazing Keynote speakers? Dr. Kevin Shug and Leon de Bruyn! Check, and more on that later.

GCC was started in the 1950s as a conduit for scientific innovations by a group of analytical scientists seeking to find better ways to advance the science of chemical analysis. Are you an innovator, an expert, a novice, a scientist? Then GCC is the place for you! Without hesitation, and for many years, I have recommended GCC for the analytical chemist searching for a place to find the latest technology, a place to be able to talk to experts in any analytical field, meet old friends and make new ones. And this year, even with all that has changed, that recommendation hasn’t changed.

GCC is analytical-centric. From the show floor to the hundreds of posters and presentations, everyone has a common goal: to further their education in analytical knowledge. It all starts with two amazing speakers.

Dr. Kevin Shug, Professor at University of Texas – Arlington since 2005, will be speaking about analytical advancements in chromatography on Tuesday. Dr. Shug is the Founder and Director of a K-12 science outreach program: Diversity in Science in the United States (www.discusprogram.com). He is also the institutional founder and steering committee member for CIRTL UTA, an affiliate of the nationwide Center for Integration of Research Teaching and Learning (CIRTL), preparing future faculty programs. Dr. Schug has received many prestigious awards, including the 2009 Emerging Leader in Chromatography award given by LCGC magazine, an NSF CAREER award, the 2009 Eli Lilly and Company ACACC Young Investigator Award in Analytical Chemistry, and the 2013 American Chemical Society Division of Analytical Chemistry Young Investigator in Separation Science Award. Dr. Shug brings vast knowledge of high efficiency separation and mass spectrometry for characterization of chemical compounds. As an innovator and expert, Dr. Shug will bring the essence of GCC to the keynote.

Our Wednesday Keynote Speaker is Mr. Leon De Bruyn, President and CEO of Lummus Technology where he is responsible for the strategic direction of the company and leading all aspects of Lummus’ global performance. He also serves on the board of directors of Chevron Lummus Global, a joint venture between Chevron and Lummus. With a heritage spanning more than 110 years and more than 130 technologies and 3,400 patents, Lummus Technology brings together proven, reliable solutions with the best track record for turning R&D into technology. Mr. de Bruyn joined Lummus in 1993. During his career with the company, he has built executive experience in the downstream refining and petrochemicals industry through technology development and licensing, catalyst supply and engineering, procurement, and construction activities. Mr. de Bruyn will be speaking about the State of the Affair of the Process Industry with important insight about the future of the industry.

As I am writing this article, I learned that Astronaut Michael Collins died at 90 years old. Many have called him the Forgotten Astronaut, partly because, even though he was part of the Apollo 11 mission to the moon, he did not step on it. Instead, he had the very important mission of holding down the fort (aka command module) and flew the spacecraft solo. As he spent 21.5 hours alone in orbit above his fellow astronauts, Buzz Aldrin and Neil Armstrong, when he was on the dark side of the moon, for 48 minutes at a time, Collins would have absolutely no contact with any other human being in the universe. For many of us in 2020, we may be able to sympathize with this kind of experience—a plunge into an existential crisis. But remember the rest of the mission—the safe return to Earth, or maybe simply the return to in-person conference. This brings to mind that we, human beings, are resilient. We are courageous innovators and achievers. We may have been slowed, forgotten, alone, but we are ready to meet again.

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A reproducible response was noted, a universal carbon response was achieved. It was postulated that the reduced response of acetylene was caused by selective irreversible adsorption of the molecule by the catalysts. The universal carbon response resulted from the catalytic conversion of a carbon-containing molecule to methane, combined with the inherent wide linear range of the flame ionization detector for a compound such as methane affords compound independent calibration with a high degree of accuracy within ±5%. This new and convenient analytical capability has the potential of eliminating the need for an analyst to handle highly toxic compounds and thereby improving industrial hygiene and laboratory safety. The technique reduces or eliminates the need for multicomponent and multilevel calibration as well as enables the measurement of analytes with no known commercially available reference materials (19,20).

The suitability of the strategy with chromatographic techniques having the most stringent requirements on band broadening, such as high-resolution gas chromatography with columns having an internal diameter of less than 150 μm and GC×GC was demonstrated (19,20). Figure 2 shows a color plot of the separation of a Canadian winter diesel by GC×GC-FID with the microreactor incorporated. An average peak width at half-height (PW½) of 200 ms was achieved. As described earlier, with the added benefit of the analytical system’s universal carbon response, the sample constituents can be expediently quantified using a single compound standard.

Apart from the reduced response of acetylene, constraints associated with this technique include chromatographic peak tailing for silicon-containing compounds. This is because of the formation of active silica in the catalyst chambers. Although the peak tailing does not negatively impact equimolar response for carbon, the technique is contraindicated if trace analysis is required for said class compounds.

The strategy of employing post-column reaction to enhance FID performance is effective and reliable. The technique was successfully implemented for routine analysis in a quality control laboratory environment. Depending on the matrix involved, when properly maintained, the catalysts can last up to two years.

Overall, the approach is an impactful and relevant innovation in advancing GC.

Acknowledgments

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References

Since the first developments in the 1940s, gas chromatography (GC) has transformed separation science, providing robust and efficient separation platforms extensively used worldwide. Improvements, particularly in column geometries and stationary phase chemistry, have progressively facilitated the analysis of a variety of matrices. Furthermore, the development of multidimensional GC techniques has provided an ideal solution for the analysis of complex mixtures by expanding the chromatographic space available for separation and enabling peak focusing, especially via thermal modulation that permits analyte enrichment (1). Extraction and sample introduction methodologies for GC, however, did not follow the same evolution path, and for decades, these important aspects of the analytical workflow have been overlooked and underdeveloped. Headspace (HS) sampling, for example, has been the technique of choice for introducing volatiles into the gas chromatograph, preventing nonvolatile contaminants from entering the GC inlet. Often, however, the technique does not provide enough analyte preconcentration with low recoveries for semivolatiles, and requires a more sophisticated instrumental setup. Solvent injection in GC after liquid–liquid extraction, sorbent-based extraction techniques such as solid-phase extraction (SPE), or even sample dilute-and-shoot overcomes some of the shortcomings of HS sampling and provides a better option for analyzing semivolatiles. However, solvent injection is more prone to instrument contamination, especially when complex samples are analyzed. The invention of solid-phase microextraction (SPME) in the early 1990s provided a convenient solution for extraction and sample introduction into GC, considering its syringe-like geometry (more commonly known as fiber SPME) (2). SPME offered the ability for simultaneous extraction and preconcentration of the analytes of interest in a single and solvent-free step. The combination of HS sampling and SPME subsequently provided the perfect fit with one-dimensional (1D) and two-dimensional (2D) GC and expanded the analytical tools available for untargeted screening or quantitative target analysis. As a result, HS-SPME has been widely employed in the past three decades. This chapter of “microextraction history” is already well known and acknowledged by the scientific community. More recent developments in the configuration and chemistry of microextraction devices have significantly improved the role of this technique in facilitating GC separation, as described below.

Thin-Film SPME: An Alternative SPME Geometry for GC

Thin-film SPME (TF-SPME) is a microextraction device that allows for depositing more extraction phases, thus having enhanced capacity compared to fiber SPME (3). The surface-area-to-volume ratio also allows for fast extraction kinetics, making TF-SPME devices ideal for ultratrace analysis. When hyphenated to GC, these devices must be desorbed in thermal desorption units (TDU) that are able to accommodate their size more conveniently compared to the conventional split–splitless injectors used to desorb SPME fibers. An advantage of using TDU units for the desorption of TF-SPME devices is the opportunity for cryofocusing the desorbed molecules when a programmable temperature vaporized injector is hyphenated. This dual-stage desorption and injection enables (Figure 1a) trapping and focusing of all the extracted analytes on the column head, greatly improving the efficiency of the separation.
The characterization of produced water shown with its application to the analysis of complex mixtures has been a technique to facilitate GC separation and the sensitivity of the method. TF-SPME devices for GC analysis are available in various formats and chemistries (polydimethylsiloxane (PDMS), divinylbenzene/polydimethylsiloxane (DVB/PDMS), carboxen/polydimethylsiloxane (CAR/PDMS), and hydrophilic-lipophilic balanced/polydimethylsiloxane (HLB/PDMS)) for multiple headspace applications and direct immersion extraction of complex samples. Compared to conventional extraction techniques and fiber SPME, TF-SPME has shown enhanced extraction kinetics and has enabled the achievement of lower limits of quantitation for analysis of pollutants in environmental samples (4,5). The potential of this technique to facilitate GC separation of complex mixtures has been shown with its application to the characterization of produced water samples, a byproduct of fracking methods used for extraction of oil and natural gas (6). Produced water is an extremely complex matrix that includes dissolved solids, high salinity, and emulsion with petroleum products. The extraction of soluble organics via TF-SPME was performed via both headspace and direct immersion mode, guaranteeing comprehensive untargeted characterization (6). Moreover, it has been demonstrated that this approach can avoid the need for any sample pretreatment such as filtration (always needed for other extraction approaches to prevent contamination of the GC injector and column saturation by nonvolatile constituents), which enables recovery of a broader range of soluble organics than what can be achieved with other methods proposed in the literature (Figure 1b).

This method, which is able to identify ~200 soluble organics present in produced water by 1D-GC, can be improved by using 2D-GC coupled to TF-SPME extraction to provide a better separation platform for the characterization of these complex samples. TF-SPME also has been hyphenated to portable GC–mass spectrometry (GC–MS) systems, providing a convenient solution for on-site sampling and guaranteeing enough preconcentration to allow detection of environmental pollutants at low parts per billion levels (7).

### Biocompatible Extraction Phases for Direct Immersion Extraction of Complex Samples

The development of biocompatible extraction phases for fiber SPME represented a turning point in the analysis of complex samples by SPME-GC. Although HS-SPME has been broadly applied over the years, limitations of the technique arose when analysis of organic molecules with a low Henry’s law constant (which do not partition efficiently into the sample headspace), was needed at parts per billion (ppb) or parts per trillion (ppt) levels. Although conventional extraction phases could be used for both HS or direct immersion SPME, the issues in the latter case consisted of the short lifetime of the extraction device because of fouling and introduction of contaminants or production of artifacts into the GC system. To overcome these limitations, a new extraction phase, PDMS/DVB/PDMS, was developed (8) and tested for a variety of food, environmental, and biological samples (9). These biocompatible extraction phases were found to be an excellent solution to prevent the production of artifacts (such as those generated in the GC injector at high temperatures) and thus, demonstrated their usefulness both for 1D- and 2D-GC separations (Figure 2) (10,11). For the analysis of fruits, Maillard

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**FIGURE 1:** (a) Schematics of the two-stage thermal desorption unit for thin-film solid-phase microextraction (TF-SPME) (photo courtesy of Gerstel Inc.). CIS: cooled injection system; TDU: thermal desorption unit; GC: gas chromatography. Reproduced with permission from the literature (3). (b) Representative chromatograms obtained by TF-SPME-GC–MS analysis of untreated and filtered produced water samples.

**FIGURE 2:** Elution windows of GC×GC extracted ion chromatograms of furfural, a Maillard reaction byproduct, from in vivo metabolic profiles obtained by (a) DVB/CAR/PDMS and (b) PDMS-overcoated DVB/CAR/PDMS, a biocompatible extraction phase.
Conclusions

The role of microextraction in facilitating separation of complex samples via GC is obvious and has facilitated the development of important applications. Although technical developments in GC—such as sophisticated multidimensional GC systems and their hyphenation to high-resolution MS—that simplify the analysis of complex mixtures are also on the rise, their availability may not be widespread. For this reason, microextraction provides an affordable solution for preventing “garbage in–garbage out” effects in 1D- and 2D-GC separation. The ability of microextraction approaches to provide analyte preconcentration, interference removal, tuning of extraction coverage, an easy coupling to GC systems, and an opportunity for automation constitute the “most powerful analytical alliance” (14) with gas chromatography for targeted and untargeted analysis of complex samples.

References

The untargeted chemical analysis of samples with complex matrices, such as those commonly encountered in metabolomics, petroleomics, foodomics, or environmental analysis, can be an exciting exploration of uncharted waters. The goals of untargeted analyses are to explain the complete chemical profile of a sample or a system (represented by many samples), and along the way discover many true unknown compounds—or compounds that were previously undetected and unknown to exist in the system. Comprehensive two-dimensional gas chromatography (GC×GC) is an ideal analytical tool for the task because the added dimension of separation enables the detection of the true unknowns by separating them from the coeluted compounds that otherwise obscure these hidden chemical treasures (1). Pairing a GC×GC system with mass spectrometry (GC×GC–MS) or with high resolution mass spectrometry (GC×GC–HRMS) also enables the identification of the separated compounds, which is a siren song that entices curious chromatographers to wade into deep waters of chemical information. However, the delight of swimming in such rich data can quickly turn to dread. Because samples with complex matrices typically contain several hundred to several thousand detectable chemical features, the size of the data matrices that are generated from more than a few GC×GC–MS samples—or just a single sample analyzed by GC×GC–HRMS—can drown even skilled chromatographic explorers. Fortunately, data visualization methods serve as life rafts that can rescue weary scientists and save chemical expeditions.

**Visualizing Untargeted Metabolomics Data: Beyond Principal Components Analysis**

Untargeted GC×GC metabolomics analysis of volatile metabolites has enabled the rapid expansion of volatile metabolite catalogs for microbes, plants, animals, and humans (2). The ability to detect hundreds to thousands of volatile metabolites in a single sample also makes GC×GC a powerful tool for the volatile biomarker discovery through the comparative analysis of sample groups (such as for disease and control). However, the goal of turning the chromatographic data into biological information is rarely straightforward because issues, such as missing data, sparse matrices, high sample group variance, and too few samples relative to the number of chemical features, can confound statistical approaches for biomarker identification. Applying correlation, clustering, and color to exploit the ability of the brain to identify patterns from huge amounts of visual information can provide a life raft for a weary chromatographer who went from swimming in data to drowning in it.

**Using the Three Cs of Data Visualization as a Life Raft When You’re Drowning in Multidimensional Chromatography Peaks**

Heather Bean
The goal of data visualization in multisample analyses is to capture all the data in a single graphic. This enables our brain to process that information and identify the relationships between the samples and their chemical features. There are several visualization approaches for leveraging HRMS data, such as the Kendrick mass defect and the van Krevelen plots, that have been developed and applied to great effect in geochemistry and petroleomics (3). However, the majority of untargeted GC×GC metabolomics studies are collected with unit mass resolution, and therefore are more reliant on chromatographic data, such as group-type analysis based on retention time patterns. The downside of this approach is that it requires a lot of time and expertise to assign the chemical classifications for the group analysis, and therefore visualization approaches that utilize group-type analysis are not our first choice.

Principal components analysis (PCA) is often the first method we apply, especially to evaluate the overall structure of our data (2). PCA is broadly used to reduce high-dimensionality GC×GC data to two or three dimensions for display. However, because our preprocessed and aligned metabolomics data matrices often contain hundreds of variables, we typically find that a two-dimensional (2D) or three-dimensional (3D) PCA is capturing less than 20% of the total variance in the system. Although this limitation can be addressed by additional supervised or unsupervised data reduction methods before PCA analysis, such as chemical group binning (4,5), such methods are time consuming. Therefore, PCA often does not get us to our data visualization goal of displaying all of the data in a single graphic, and we have begun supplementing PCA with analyses that utilize correlation and clustering, enhanced by color: the three Cs.

**The Three Cs of Data Visualization**

The three Cs of data visualization are correlation, clustering, and color.

**Correlation**

Correlation analyses provide a measure of similarity between two samples based on their chemical features, or between two features based on their measurements over multiple samples. The Pearson correlation and Euclidian distance are two commonly used measures of similarity or dissimilarity, but there are others to try, such as Spearman correlation, Manhattan distance, and Mahalanobis distance, that may be better suited to your data. As an example, in a study to investigate the relationship of metabolism to immune response, we calculated the Pearson correlations within metabolites (M), within immune markers (I), and
between the two variable types, using measurements of each of the variables across 16 samples (Figure 1). We identified 23 metabolites that were significantly correlated—positively or negatively—to 26 immune markers, and displayed the degree of correlation using color.

Clustering
Clustering is where the magic happens, and clustering methods build off of correlation data. When you use clustering—linking samples based on their correlation—broader patterns of relatedness within your system emerge. In Figure 1a, no clustering has been applied to the metabolites and immune marker correlations (the variables are ordered in the graphic as they were listed in the data matrix). Though it is possible to evaluate the pair-wise correlations between two variables in this format, once clustering is applied (Figure 1b) systemic correlations are visible. There are a lot of clustering options to try, but I recommend starting with agglomerative hierarchical clustering analysis (HCA) using the default settings in your data analysis program of preference.

Once you are ready to explore, you can try altering the linkages, using options such as complete, minimum, or average. In Figure 2, you can see examples of how modifying combinations of correlation and linkage alter the clustering in interesting ways. In this data set, we are performing cluster analysis of both the samples, depicted in rows, and the volatile metabolites, depicted in columns. In Figure 2a, we have used the default R `pheatmap` clustering method and in Figures 2b or 2c we have applied alternative similarity measures or linkage methods, or both. In Figure 2c, you can see how the combination of similarity and linkage methods generated nice clustering of the replicate sample types in the rows. Additionally, combining the sample clustering with the volatile metabolites clustering and heatmap data enables the identification of sets of volatile metabolites that distinguish sample classes.

Color
Color matters. This fact seems self-evident, but the default colors of a data analysis or data graphing program are often not the optimal choices for the clustering patterns that your specific data are generating. After you have settled on the best clustering option, try alternate color combinations to enable the viewer to interpret the data at a glance, and be open to going back to grayscale, which sometimes is the best option. Finally, check your colored graphics for color-blindness readability and make sure that all of the key pieces of information that the colors are conveying are broadly accessible (6).

Selecting the Best Life Raft for Your Chemical Expedition Occurs by Trial and Error
In the descriptions above, I referred to data analysis and visualization options that we commonly explore using R packages, such as `pheatmap`, `factoextra`, `Hmisc`, and `corrplot`, among others, but similar options will exist in Matlab, SASS, and other programs. The key message is that once you get the hang of using the default settings for correlation, clustering, and color, you can start exploring the other options built into the program; don’t expect that one-size-fits-all of your data.

*Continued on Page 21*
From Recycled Plastic to Pyrolysis Oils: A Renewed Need for a Broad Range of Gas Chromatography (GC) Detector Technologies

Kevin A. Schug

The global plastics recycling market is currently $50 billion dollars and growing rapidly. Although thermal processing is still part of the procedure, much effort has gone into developing new technologies for catalytically cracking polymers back into constituent monomers. These constituent monomers can then serve as feedstocks for fuels and other chemical products. There are several challenges in characterizing these monomer mixtures. They vary in content with the variability of input material and cracking conditions. The resultant monomer mixtures, or pyrolysis oils, are complex and require careful characterization for further processing. They are high in olefin content, and it is desirable to know their aromatic content as you would for a traditional refined hydrocarbon stream, but there is also a large need to characterize heteroatom-containing species in the mixture. Excessive heteroatom content can further compromise processing the pyrolysis oils if not appropriately accounted. Gas chromatography (GC) is an indispensable tool, but the traditional pantheon of detectors do not provide satisfactory performance to accomplish the task. There is a resurging need for detectors that can detect and characterize heteroatom-containing species. Many were developed long ago and exist in textbooks but are unfamiliar to those who work in analytical laboratories. It is time to revisit these detection technologies and involve them more in analysis to help advance the growing plastics recycling market. Some of these detector types are sulfur chemiluminescence, flame photometric, nitrogen-phosphorous, and vacuum ultraviolet (VUV) detectors.

As a child, I was fascinated by recycling plastic. I learned to connect the numbers on plastic bottles and containers with different chemical names, even if I did not understand what the names meant. I remember that, initially, some plastics were acceptable to put in the recycling bin, whereas others were not. Where I grew up, that approach changed over time to one where they at least collected all plastics, even if maybe they did not process them all. I remember visiting different places and noticing that the recycling instructions and capabilities often varied considerably with location.

Plastics production has increased almost 10% every year since 1950. Today, the global production of plastics is around 300 metric tons (MT) annually. Plastics can have variable life spans, but roughly 40% is estimated to have a usage life of less than one month. More than three-quarters of the plastics produced are recyclable thermoplastics. These thermoplastics include polyolefins, such as polyethylene, polypropylene, polystyrene, and polyvinylchloride, among others. Once waste plastics are collected, they are initially separated based on density, before they are subjected to a cracking process to depolymerize the material for refining and reusing. There are three predominant cracking processes used, namely hydrocracking, thermal cracking, and catalytic cracking. The latter is currently an area of intense research and development.

As the name connotes, catalytic cracking involves the use of a suitable catalyst to carry out the depolymerization process. The use of catalysts reduces both the time and temperature needed for cracking. The resulting products, often termed pyrolysis oils, are characterized by a narrower distribution of carbon atom number, centered more around lighter carbon chain lengths, and are attained at much lower temperatures compared to the products of other cracking processes. Once plastics are cracked and characterized, the resulting pyrolysis oils can be further refined into fuels and feedstocks for chemical production. Anecdotally, I have heard that diesel fuel could be obtained from refined pyrolysis oils that is cleaner than that generated from a traditional petroleum stream. Catalysts and their application conditions are constantly under development. Clearly, this development must be aided by capable analytical measurements to characterize the pyrolysis oils produced.

Currently, there appears to be an almost limitless feedstock for recycled plastics. On the one hand, the global plastics demand is expected
to continue to increase over the next 30 years. On the other hand, by 2050, more than half of plastic production could be based on plastic reuse and recycling. The share of reused plastics from recovered monomer or recovered feedstock from catalytic cracking is expected to increase by more than 15% annually in the same time frame. Environmental and social corporate governance (ESG) considerations will continue to drive the use of recycled products and feed stocks over virgin sources (1).

The large variability in the plastics feedstocks, catalytic processing, and the resulting pyrolysis oils presents a number of significant challenges to the analytical chemist. Generated pyrolysis oils can be characterized in much the same way as hydrocarbon streams, but their content is markedly different. For example, it is not uncommon for pyrolysis oils to have as much as 50% or more olefin content. Further, heteroatom content (such as sulfur, nitrogen, and oxygen) can be highly variable and much higher than in hydrocarbon streams. These contents need to be well known and understood for pyrolysis oils to be further refined. For example, excessive sulfur content can poison many catalysts, if not appropriately accounted for or removed.

Homing in on the heteroatom content in a mixture of hydrocarbons ranging from approximately C6 to C40 requires more than just the standard gas chromatography (GC) detectors. This field of hydrocarbon analysis is the first place where I have seen a clear application for many GC detection systems that were only known to me previously as an acronym. The comprehensive analysis of pyrolysis oils will require the use of multiple separation and detection systems.

Without ultrahigh resolution, mass spectrometry (MS) will get quickly bogged down in the extreme number of isomers and mixed class species, as the carbon number increases. Ultrahigh-resolution MS is a powerful, but expensive, tool that has been applied to the characterization of pyrolysis oils from a wide range of feedstocks (2). One can often delineate heteroatom content as part of generated elemental formulae, but it can still be difficult to completely define to what chemical compound these heteroatoms are connected, without the aid of other tools, including some selective separations. A recent publication from Focant and coworkers demonstrated the power of on-line comprehensive two-dimensional GC (GCxGC), in combination with photoionization–time-of-flight (TOF) MS, for characterizing commercial dodecene (primarily, C12 olefin) mixtures (3). This complexity already provides a significant challenge for one of the highest resolution analytical approaches we have available.

Vacuum ultraviolet (VUV) spectroscopic detection offers considerable power for overall classification of species as paraffins, isoparaffins, olefins, napthenes, or aromatics (PIONA) (4). Chemical classification based on gas phase absorption detection from 120 to 430 nm has been shown to be highly complementary to MS measurements, especially delineating isomeric species, but its application to high carbon number species still needs further development. Although VUV may have significant ability to delineate mixed class species (such as a chemical compound that possesses both olefin and aromatic character), its ability to delineate heteroatom attachment to that species is generally lacking. A recent publication by Dunkle and coworkers is a good example of the state-of-the-art in the application of GC-VUV for the characterization of pyrolysis oils in comparison with standard hydrocarbon streams (5).

Inevitably, the conversation around characterizing heteroatom content in pyrolysis oils turns to some acronyms that you have probably heard when first learning about GC detection but never had a chance to use. Flame ionization detection (FID) is quite ubiquitous in GC, but its usefulness in the current application is minimal, given its response to any carbon-containing molecule and its inability to provide any further qualitative information. The same could be said for thermal conductivity detection (TCD).

Instead, in this instance, more selective approaches, based on technologies like sulfur chemiluminescence detection (SCD), nitrogen-phosphorous detection (NPD), flame photometric detection (FPD), and flame thermionic detection (FTD) come to mind. As the name connotes, SCD is a highly selective and quite sensitive (low picogram detection limits) detector for sulfur. A notable advantage of SCD is its ability to respond uniformly to sulfur-containing compounds; in other words, a calibration curve prepared for one sulfur-containing compound is often sufficient for the analysis of another if both compounds contain the same number of sulfur atoms. In the detector, sulfur species are first oxidized under extremely high temperature (around 1000 °C). They are then made to react with ozone, where excited-state sulfur species will chemiluminesce, releasing light that can be detected. The SCD is generally considered to be a more complex GC detector to operate.

Another detector with obvious applications is the NPD. It provides selective detection for nitrogen- and phosphorous-containing compounds. Nitrogen-containing compounds can be enriched in pyrolysis oils generated from plastics containing dye molecules. The NPD is a type of FTD that relies on heating the effluent in the absence of a significant hydrogen:air ratio. This approach minimizes hydrocarbon ionization, but facilitates ionization of the nitrogen- and phosphorous-containing compounds, the signal for which is collected by an electrometer. Because of its excellent sensitivity (low picogram detection limits), high purity gases for operating the detector is a must.

The FTD also responds selec-
to different detectors, but this is not necessarily ideal in terms of maximizing sensitivity. Some detectors offer the potential to flow through, such as the case for VUV, so that a second detector could be placed in series. However, this approach has not been well developed, to date. Of course, linking data acquired from two different systems with different detectors would be possible, but aligning the data also presents its own challenge.

In the end, there is room to innovate to create more powerful analytical configurations that are applicable for use in a market that is growing by leaps and bounds. Rarely a day goes by that you cannot find the announcement of another initiative or partnership that expands plastics recycling and processing worldwide. Just as the use of multiple detectors can offer significant benefit to delineating heteroatom content in addition to classification of molecules in the mixture, so will increasing use of multidimensional separations. Given the ultimate complexity of compounds desired to be speciated in pyrolysis oils, analysis of recycled hydrocarbons is a rich area for the further development of multifaceted GC technology, including advanced data treatment algorithms.

Disclaimer
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References

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You may find that Euclidian distance and average linkage provide beautiful hierarchical clustering for one study, but for another (ostensibly similar) data set those methods look like a mess, while Pearson correlation and complete linkage generates meaningful results. It takes some trial and error to find the right combination of the three Cs for each study. Whatever you settle on, make sure you report the correlation and clustering methods when you publish your data (7)!

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WWW.CHROMATOGRAPHYONLINE.COM

JUNE 2021 HOT TOPICS IN GAS CHROMATOGRAPHY 21
Gas Chromatography Meets Non-Targeted Screening

Thomas Letzel and Stefan Bieber

We take a look at the past, present, and future of applying gas chromatography–mass spectrometry (GC–MS) techniques to non-targeted screening (NTS) in various disciplines, assessing both the opportunities and the challenges.

The application of gas chromatography (GC) to non-targeted screening (NTS) has a short (but already fine) history. For instance, a recent search for the term gas chromatography–mass spectrometry (GC–MS) in article titles, abstracts, and keywords in the literature database Scopus, linked with keywords such as untargeted screening, non-targeted screening, or untargeted analysis, led to 53, 80, and 395 scientific reference hits, respectively. Initial research studies on this topic were published in the late 1990s; however, most publications have been released in the last decade.

In practical laboratory environments, many scientists feel that GC–MS has already been quite well implemented for NTS applications. This assessment mostly reflects a misunderstanding of real NTS. A typical GC–electron impact (EI)–MS run, in which the ionization is performed by “hard” EI, followed by a National Institute of Standards and Technology (NIST) database search, is really more of a suspects screening approach (for “known unknowns”) than a classical NTS.

This year, however, GC–MS vendors and several users came together for the first time to present and discuss their experience with “real” NTS by GC–MS, and to explore the options for such studies. This workshop, which took place online in February 2021, was consequently called “GC meets NTS.” In this meeting, participants discussed, clarified, and accentuated the power and excellent usability of GC–MS in NTS, and decided to form a nonaffiliated expert group. A 20-minute video that summarizes the two days of presentations and platform discussions is available online at https://afin-ts.de/gc-mets-nts/.

Topics like analytical instrumentation and data analysis strategies in NTS were the focus of that workshop, and they also represent the tasks that have to be addressed for GC–MS to have a successful future in NTS. Some of these challenges are discussed in this article.

Instrumental Needs for NTS with GC–MS

Comprehensive NTS requires a broad analytical view of (mainly) organic molecules—a smart combination of analytical techniques in sample preparation, extraction, and injection, as well as GC separation coupled to highly accurate and high-resolution MS (HRMS) systems. One key aspect of GC–MS and NTS is the use of soft ionization (SI) sources in addition to the classical EI interfaces. Soft ionization sources, such as chemical ionization (CI), mainly form molecular ions and fewer “in-source” fragments (as observed in EI). Recent developments of various soft ionization sources open the door to perform GC–MS analysis within a new context. Several options for coupling analytical instruments and performing NTS workflows on instrumental level are shown in Figure 1. In addition to low pressure ionization techniques, such as CI, nowadays many atmospheric pressure ionization sources can be used in GC–MS. Examples are atmospheric-pressure chemical ionization (APCI), atmospheric-pressure photoionization (APPI), atmospheric-pressure laser ionization (APLI), and dielectric barrier discharge ionization (DBDI). Finally, a combination of GC–EI–MS and GC–SI–MS might be the perfect solution for enabling comprehensive analysis in NTS. The value of such a combination is underscored by a rumor that the first GC–CI&EI-time of flight (TOF)–MS system may soon be available on the market.

To gain the most comprehensive perspective on samples in NTS, it is important to detect as many molecules as possible. Therefore, sample preparation, extraction, and injection are very important not only in terms of their efficiency, repeatability, and robustness, but also in ensuring that all techniques used allow the
recovery of as many molecules as possible. As a result, one has to take sample preparation into account and to document the processes (such as whether chemical derivatization or other such techniques were used) in a detailed and meaningful way. Various effective sample preparation–injection systems are available for GC, but all affect samples differently, and because some are highly orthogonal, they can and should be used thoughtfully. The documentation of all applied steps of the analytical procedure is key to ensuring the comparability of NTS results. Sample preparation and injection strategies should not complicate the data analysis that will be performed later; rather, they can contribute to better understanding of the analytical results.

GC–MS allows the use of multiple dimensions (in separation and detection), and more dimensions might come in the future. Independent of the analytical strategy applied, GC, GCxGC, and GCxGC–MS—including GCxGC–MS using soft ionization, using ion-mobility MS, and using ion-mobility tandem MS, all have the high repeatability, robustness, and quality that are of critical importance in GC analyses. Laboratories conducting routine analysis tend to focus more on stability and reproducibility, whereas research laboratories favor the flexibility. Both reproducibility and flexibility can be handled in NTS today, and for the long term requirements, it should be possible to combine both aspects effectively. Just as in many other aspects of our lives, a good approach is to keep things as simple as possible and combine only as much components as is truly needed.

**Applying NTS Strategies Across Analytical Techniques**

NTS is used in different analytical fields, and developments in one analytical technique can often be applied to others. Some NTS developments and solutions are specific to modern GC–MS/MS systems. However, some strategies and workflows from liquid chromatography–MS/MS (LC–MS/MS) analysis can and should be included wherever possible in GC NTS strategies, and vice versa. Of course, LC–MS also can provide solutions that complement those of GC–MS. A Scopus database search related to NTS, like the one described previously, but with substituting “LC–MS” for “GC–MS” led to 57, 111, and 796 scientific references, respectively (most of them from the last 20 years). Of course, GC and LC are highly orthogonal techniques with very different application areas because of the different classes of compounds they can separate. However, in NTS we aim to assess samples in a highly comprehensive way. As a consequence, the combination of LC–MS, GC–MS, and GC–EI–MS will bring enormous benefits.

**Data Analysis for NTS**

Taking data evaluation strategies from one discipline and applying them to another will strengthen our analytical concepts. Of course, there are some specialties for data evaluation in one technique or another, but in the end, they all rely on the same basic steps. The idea is always to use all available data and information about a sample and thus find an answer to the analytical question. This approach will be helpful for identifying molecules as well as for specifying statistical solutions. Characteristic workflow schemes are presented in Figure 2.

The range of NTS applications of GC–MS spans qualitative needs (such as authenticity and identification) and quantitative specifications (such as pesticides in foods). For such qualitative and quantitative applications of complex molecular information, an automated and digitalized data handling process are needed. Careful documentation and
harmonization of parameters such as polarity, boiling point, empirical formula, molecular fragments, and signal intensities, are needed, along with correct statistical handling of these data.

**Analytical Fields in Which GC–MS Is Being Applied to NTS**

Currently, the majority of applications of NTS are focused on identifying unknown organic molecules, but improved implementation of robust NTS strategies opens the door to other (statistically-based) solutions, potentially yielding more detailed molecular analysis. This opens up the possibility of answering questions that have not yet been asked. GC NTS techniques may find their way into applications and fields such as biological screening, metabolomics, biomarker screening, brand piracy (to ensure authenticity of origin as well as for safety concerns about impurities in counterfeit products), environmental analysis (air and water), food fraud (in products like olive oil, vanilla, herbs, and additives), food safety and stability (for fingerprinting, batch tests, and aroma stability), leachables and extractables (for pharmaceuticals or consumer products), and monitoring of production processes (like chemical synthesis).

**What Will Come Next in “GC Goes NTS”**?

At this point, all of us in the analytical science community have to keep in mind that NTS is a complex analytical strategy, and that we should all aim for the highest standards in robustness, comparability of results, and validity. Bringing together highly complex analytics, advanced data evaluation, and powerful statistical methods in NTS is a huge challenge. Next, each laboratory has to decide if data handling solutions should be centralized or decentralized, on site or in the cloud, and whether vendor-driven or open-source solutions should be used. Finally, data handling must be professional and sustainable; and care must be taken to determine whether real retrospective analysis of NTS data can be done in the future, or whether claims of retrospective analysis capabilities will just become a publicity ploy.

Let’s come together to take advantage of the current momentum for NTS using GC–MS to create something global and sustainable. If you want to participate, don’t hesitate to join the group! You can also present your projects and thoughts at the International Conference on Non-Target Screening (ICNTS 21), which will be held October 4–7, 2021, in Erding, Germany, and online (https://afin-ts.de/icnts-21).

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