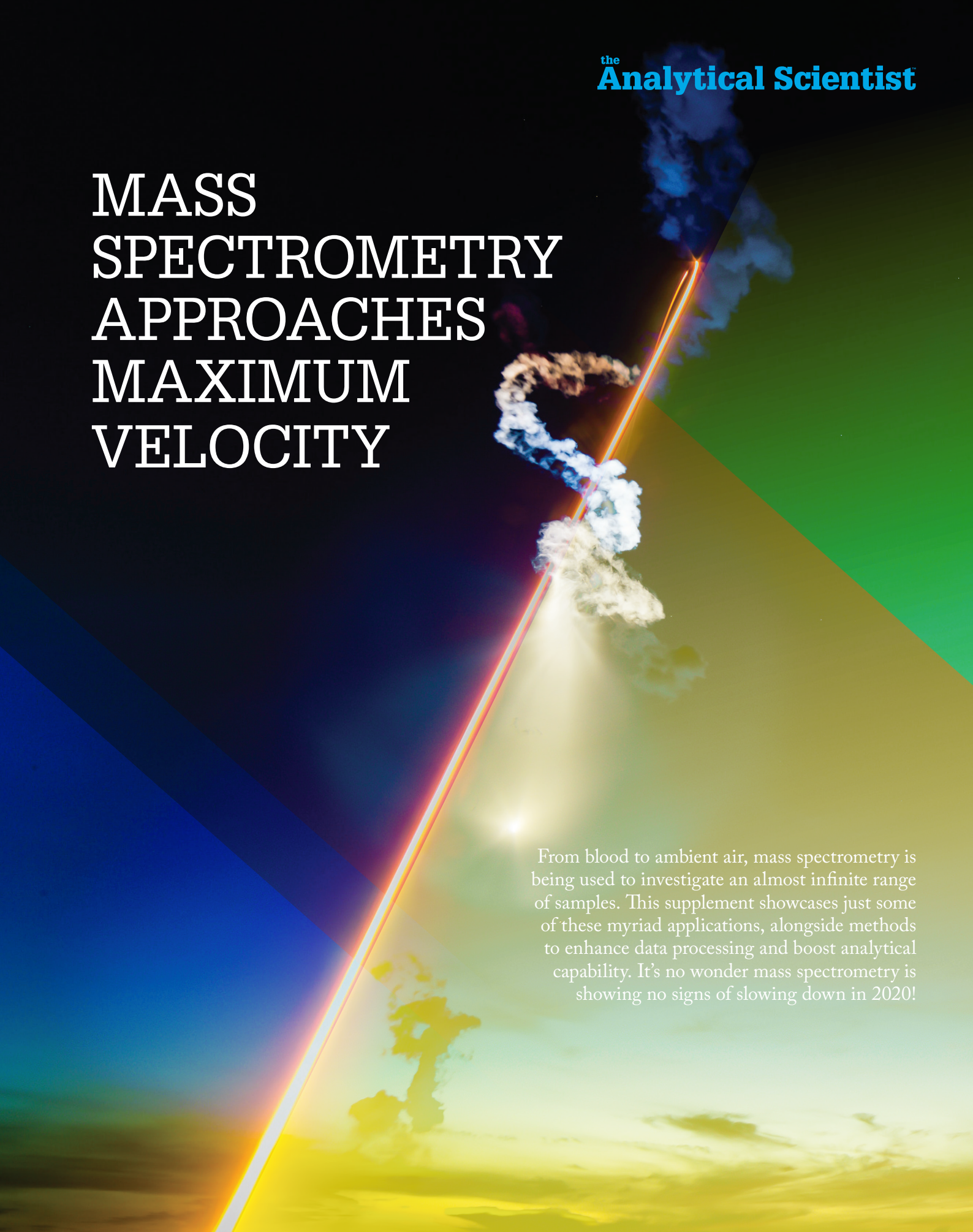
the Analytical Scientist

MASS SPECTROMETRY APPROACHES MAXIMUM VELOCITY



From blood to ambient air, mass spectrometry is being used to investigate an almost infinite range of samples. This supplement showcases just some of these myriad applications, alongside methods to enhance data processing and boost analytical capability. It's no wonder mass spectrometry is showing no signs of slowing down in 2020!

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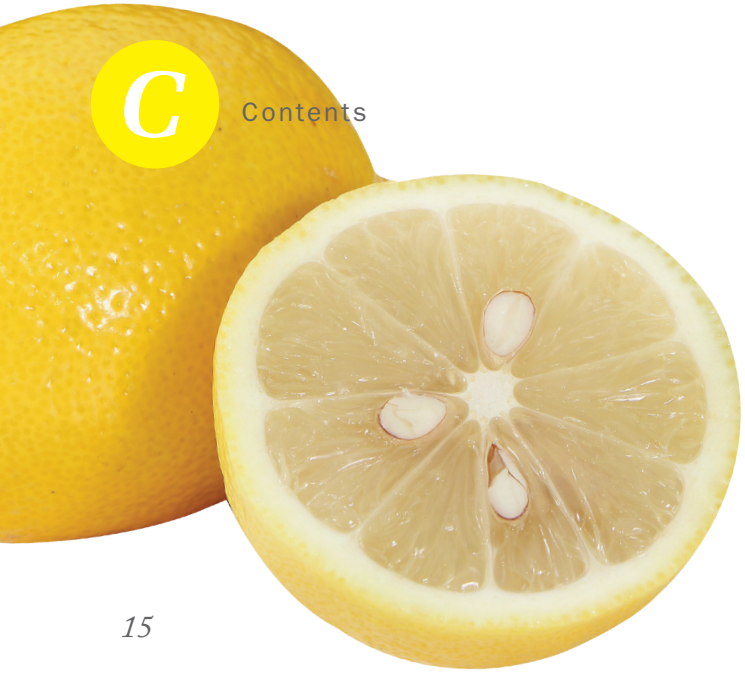

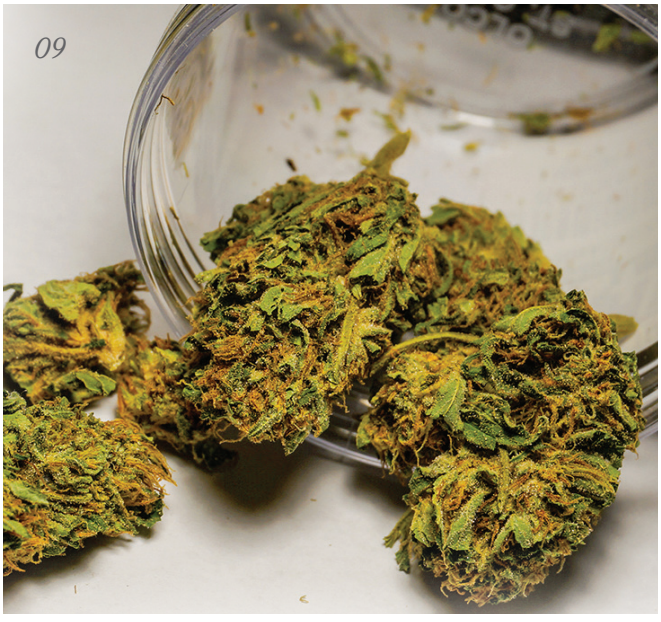

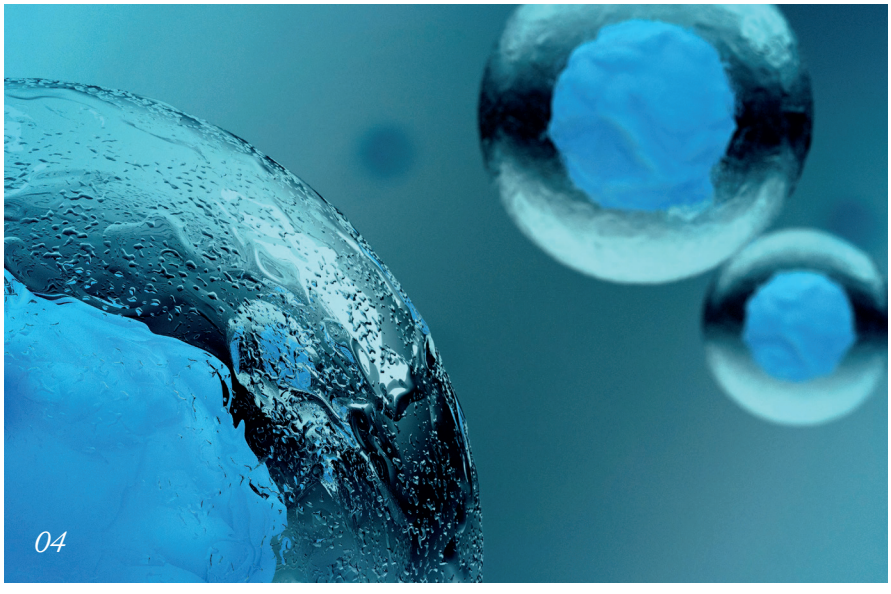

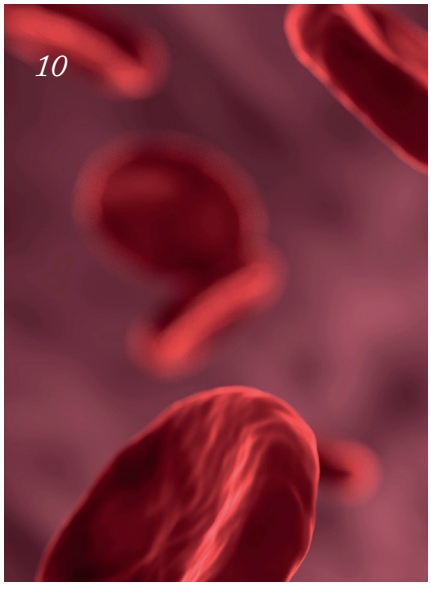

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MOVING MASS SPECTROMETRY OUT OF THE LAB AND INTO THE REAL WORLD

Real-time mobile monitoring of air with the Vocus chemical ionization TOF mass spectrometer

By Abigail Koss

The Vocus chemical ionization time-of-flight mass spectrometer (Vocus CI-TOF) is a robust, low-power, mobile instrument that measures VOCs in air in real time, addressing environmental and industrial problems not accessible by traditional mass spectrometry. In this application note, patterns of VOC emissions from a Vocus CI-TOF mobile laboratory are shown around an industrial facility and inside a manufacturing facility.

Ambient air contains a dynamic, complex mixture of volatile organic hydrocarbons (VOCs). These diverse gas-phase species are a crucial aspect of human interaction with the environment. Some VOCs harm human health or sensitive industrial processes, while the abundance and composition of other VOCs can be used as a chemical "fingerprint" to understand pollution sources, human exposure, and industrial quality control.

The Vocus chemical ionization time-of-flight mass spectrometer (Vocus CI-TOF) is a robust, low-power, mobile instrument that measures VOCs in air in real time, addressing environmental and industrial problems not accessible by traditional mass spectrometry. Ambient air flows continuously into the instrument, where one of several soft CI techniques ionizes VOCs while excluding the main components of air. The Vocus ionization reactor uses radiofrequency ion guides to achieve extremely high sensitivity (sub-ppt LOD), and the TOF analyzer acquires complete mass spectra with resolving power up to 15,000 (m/dm, FWHM). Data are typically reported with 100 millisecond to 1 minute time resolution.

In Figure 1, a Vocus CI-TOF using proton-transfer-reaction chemical ionization was installed in a mobile laboratory and driven in a search pattern around an industrial facility in eastern China. Patterns of VOC emissions over a scale of several kilometers can be used to pinpoint the sources of various industrial solvents and byproducts.

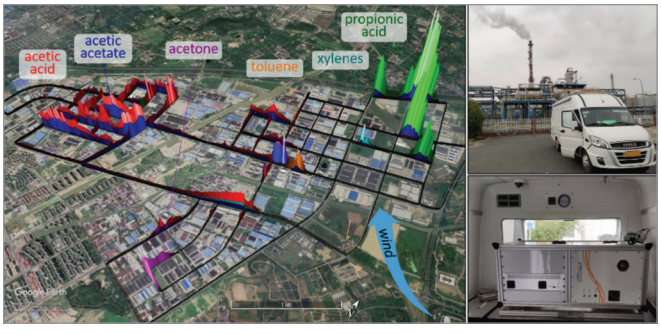

Figure 1. Mobile monitoring of pollutant emissions in China using a Vocus CI-TOF installed in a vehicle.

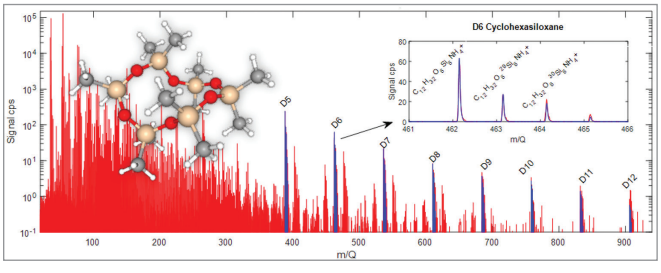

Figure 2. A mobile Vocus CI-TOF measured thousands of VOCs in the indoor air of a manufacturing facility, including the highlighted siloxanes.

In Figure 2, a Vocus CI-TOF using ammonium-adduct chemical ionization was adapted to a mobile platform with a battery pack to measure indoor air quality in a manufacturing facility. The mobile platform allowed easy movement between different rooms. A wide variety of VOCs was detected, including a significant concentration of cyclic siloxanes from personal care products and machine lubricants.

HIGH THROUGHPUT 4D-PROTEOMICS – APPLICATION OF DIA-PASEF® AND THE EVOSEP ONE FOR SHORT GRADIENTS

The timsTOF Pro offers a combination of two unique technologies, namely a 4th dimension provided by Trapped Ion Mobility Spectrometry (TIMS) to enhance ion separation and sensitivity and Parallel Accumulation Serial Fragmentation (PASEF (1)) to improve ion utilization efficiency and data acquisition speed.

Authors: Stephanie Kaspar-Schoenefeld [1], Thomas Kosinski [1], Markus Lubeck [1], Oliver Rather [1], Gary Kruppa [1], Nicolai Bache [2], Dorte B. Bekker-Jensen [2], 1 Bruker Daltonik GmbH, Bremen, Germany; 2 Evosep Biosystems, Odense, Denmark.

Abstract

In this application note, we demonstrate the benefits of dia-PASEF technology on the timsTOF Pro platform coupled to an Evosep One for high-throughput indepth proteome analysis of up to 300 samples per day (SPD). We quantify about 5200 protein groups in only 21-minutes run time. In 4.8-minutes ultra-high throughput runs (300 SPD) we are still able to quantify more than 2000 protein groups and 8500 peptides.

Introduction

Data-independent acquisition (DIA) facilitates reproducible and accurate protein identification and quantification across large sample cohorts. This is achieved by using isolation of wide quadrupole windows, rather than selecting individual precursors, to ensure that all precursor ions are fragmented in every sample. Ion mobility provides an additional dimension of separation for complex samples, which can also be used for aligning precursor and fragment ions. By making use of reproducible mobility values from the timsTOF Pro, we extend the PASEF principleto DIA resulting in a new acquisition mode, called dia-PASEF (2). This approach benefits from the sensitivity of PASEF and improves efficiency of ion usage for MS/MS with up to 100% of the ion population being fragmented for MS/MS analysis.

We previously showed the applicability of dia-PASEF for different gradient lengths, with about 6400 protein groups identified in single 30-minute runs from human cell lines (3).

For true clinical proteomics, robust analysis of several hundreds of samples per day is highly desirable which in turn requires fast and robust instrumentation. The Evosep One is a conceptionally new HPLC that dramatically increases robustness and sample throughput while maintaining sensitivity inherent to nanoflowLC (4). The timsTOF Pro with very high sensitivity and speed and the Evosep One turn out to be a perfect combination that could meet these requirements for analysis of clinical samples in a high-throughput robust manner.

In this application note, we demonstrate the performance of dia-PASEF on the timsTOF Pro mass spectrometer (Bruker Daltonics) in combination with the Evosep One HPLC system (Evosep) using ultra-short gradients for analysis of up to 300 samples per day.

Methods

Sample preparation

Whole HeLa cell pellets were purchased from CIL Biotech (Mons, Belgium). Cell lysis was performed using trifluoroethanol (TFE) according to (5). Briefly, the suspension was kept 10 minutes on ice and then incubated at 56°C for 20 min. 200 mM dithiothreitol (DTT) was used to reduce the cysteine residues at 90°C for 20 min and 200 mM iodoacetamide (IAA) for alkylation of reduced cysteine residues (90 min at room temperature). Proteins were enzymatically cleaved overnight by adding trypsin in a 1:100 (wt/wt) enzyme:protein ratio. De-salting and purification were performed using a solid phase extraction cartridge (SepPak C18, Waters, USA) by diluting and washing protein digest with 0.1% formic acid (ACN) and subsequent elution with 50% (w/w) ACN in 0.1% FA. Purified and dried peptides were reconstituted in 0.1% FA.

We created a resource-specific library generated from 24 high-pH reversed phase peptide fractions. Samples were fractionated according to (6). Briefly, 100 µg of peptides from the in-house HeLa digest was fractionated at pH 10 on a reversed phase column (Waters Acquity CSH C18 1.7 µm 1 x 150 mm) on a Dionex Ultimate 3000 system (Thermo Fisher Scientific). The fractions were freeze-dried and reconstituted in 0.1% FA.

The samples were loaded onto EvoTips according to the manufacturer's instructions and analyzed on the Evosep One

system (Evosep Biosystems, details see Table 1). The resource-specific library was generated using Evosep's 60 samples per day (SPD) method and dia-PASEF data has been acquired with the new and improved 60, 100, 200, and 300 SPD methods and associated new column recommendations.

Eluting peptides (200 ng) were analyzed on the timsTOF Pro mass spectrometer (Bruker Daltonics). The timsTOF platform is uniquely equipped with state-of-the-art dual-TIMS funnel ion optics that sorts and time-focuses ions before they enter the quadrupole-time-of-flight (Q-TOF) mass analyzer, enabling 4D-Proteomics.

For dia-PASEF, the instrument firmware was adapted to perform data-independent isolation of multiple precursor windows within a single TIMS frame. An optimized dia-PASEF scheme for the short gradient methods was applied, targeting +2 and +3 ions in a three-window method (per 100 ms). Eight of these scans (resulting in 24 windows, each using 25 Da window size) covered an *m/z* range from 400 to 1000. Each dia-PASEF cycle includes 1 MS frame (100 ms) resulting in a total cycle time of 900 ms per dia-PASEF cycle.

For targeted data extraction, we used the resource-specific library generated form 24 high-pH reverse-phase fractions acquired with PASEF using a default proteomics method (see (3) for details). PASEF synchronizes MS/MS precursor selection with TIMS separation. This allows fragmentation of more than one precursor per TIMS scan and increases the sequencing speed several-fold without loss of sensitivity. The precursor selection engine dynamically selects precursors on intensity, *m/z*, and ion mobility.

Data processing

The four-dimensional dia-PASEF data was processed using Spectronaut (version 14, Biognosys, Figure 1). The ion mobility enhanced libraries were generated using Spectronaut's Pulsar database search engine with 1% FDR control at PSM, peptide and protein level. We generated a resource-specific library using the 60 SPD LC-method on fractionated samples, which was directly used for targeted data extraction from the 60 SPD dia-PASEF data. For the shorter gradients (100, 200, 300 SPD) project-specific libraries were created by processing the dia-PASEF runs using the directDIA approach available in Spectronaut. By combining the resource- and project-specific libraries into hybrid libraries (7), retention-time precision can be preserved for the different gradients while still achieving completeness from the indepth resource-specific library. For targeted analysis of dia-PASEF data we set a 1% FDR at the peptide and protein level.

Results and discussion

dia-PASEF combines the PASEF method with DIA which allows multiplexing of DIA windows in a single 100 ms ion mobility separation frame. Here we applied the dia-PASEF method for the analysis of human cell lines using very short gradients on the Evosep One system (Figure 2).

We used an optimized dia-PASEF method with 3 windows in each 100 ms dia-PASEF scan. Eight of these scans (resulting in 24 windows) covered the diagonal scan line in the *m/z*–ion mobility pane to ensure coverage of doubly and triply charged species with narrow 25 *m/z* isolation windows (Figure 3). Each dia-PASEF cycle contains a MS1 survey frame followed by 8 dia-PASEF frames (see Figure 3). This setup results in a total cycle time of 900 ms (1x 100 ms MS1 survey frame, 8x 100 ms dia-PASEF frames), which allowed us to obtain sufficient data points over the

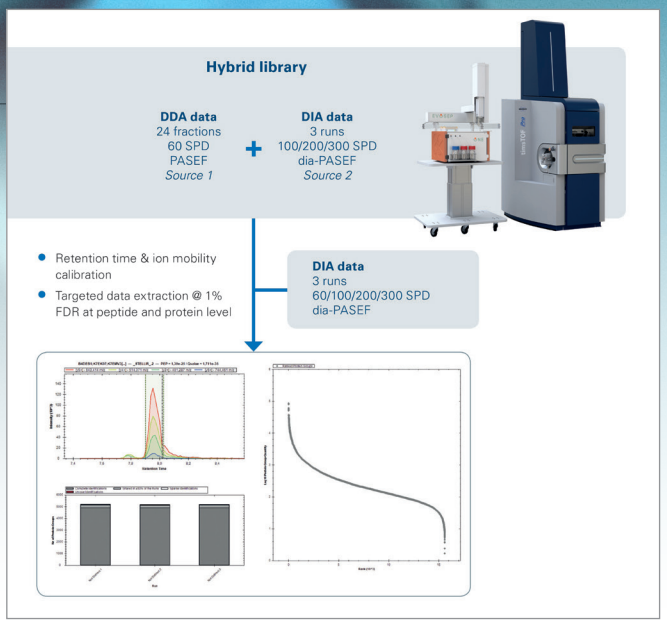

Figure 1. dia-PASEF data processing workflow using Spectronaut (v14). A resource-specific library was created from 24 fractions acquired using the 60 SPD Evosep method in combination with PASEF technology. Additionally, project-specific libraries were created for the 100, 200 and 300 SPD methods using dia-PASEF data to allow for source-specific retention time alignment. Both libraries have been combined into "Hybrid Libraries" used for targeted data extraction from the dia-PASEF data.

Parameter	Settings
LC-System	Evosep One (Evosep Biosystems) Plugin version RC.Net driver 1.3
Separation Columns	Reversed-phase C18, 8 cm x 150 µm i.d., 1.5 µm, Evosep (for 100 and 60 SPD) Reversed-phase C18, 4 cm x 150 µm i.d., 1.9 µm, Evosep (for 200 and 300 SPD)
Mobile Phases	A: 0.1% formic acid (FA) in water B: 0.1% FA in Acetonitrile
Gradient	60 SPD 100 SPD 200 SPD 300 SPD
Column Temperature	50°C

Table 1. LC conditions.

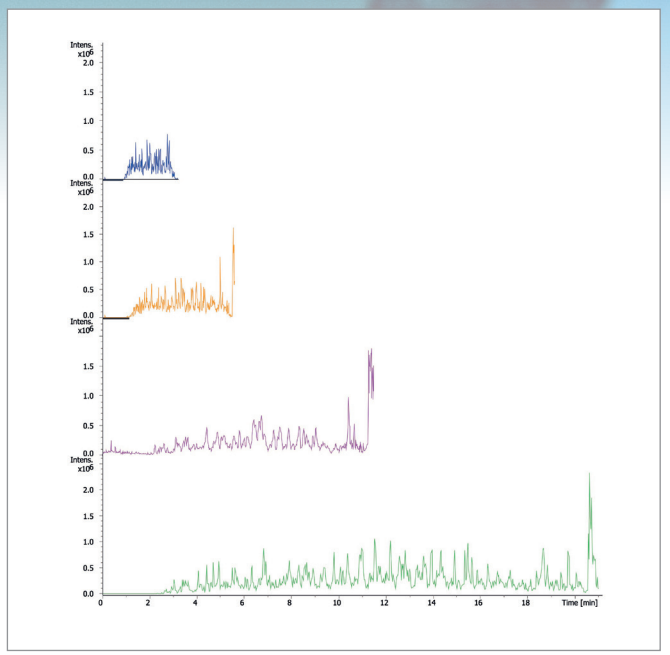

Figure 2. Example base peak chromatogram traces for the different Evosep One gradients for high throughput proteomics (300, 200, 100, 60 SPD).

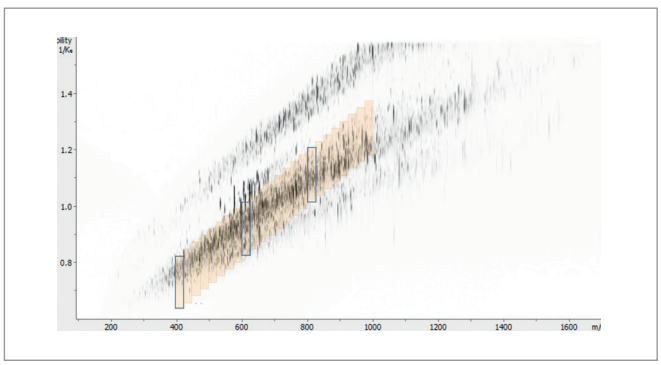

Figure 3. 4D-Proteomics method scheme for dia-PASEF. The applied method consists of three windows in each 100 ms dia-PASEF scan. Eight of these scans cover the diagonal scan line for doubly and triply charged peptides in the *m/z* – ion mobility pane with narrow 25 *m/z* precursor windows.

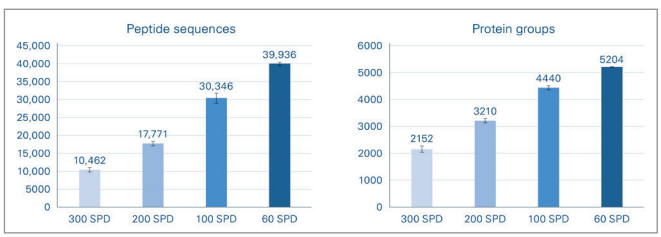

Figure 4. Average number of identified peptide sequences and protein groups (@ 1% peptide and protein FDR) from triplicate injections of 200 ng HeLa sample.

chromatographic peak while maintaining maximum coverage of +2 and +3 precursors.

Currently DIA workflows mainly rely on spectral libraries for correlating extracted fragment ion spectra with the available peptide spectrum. The resource-specific library data were acquired using DDA PASEF and processed in Spectronaut which resulted in a library of 8381 protein groups and 93,301 peptide sequences. Data acquisition time for library generation was just ~10 hours using the 60 SPD method. Targeted 4-dimensional extraction from the 60 SPD dia-PASEF data using this comprehensive resource-specific library resulted in the identification and quantification of on average 5204 protein groups and 39,936 peptide sequences at a 1% FDR (Figure 4). This translates into an identification rate of up to nearly 4000 peptides per minute of gradient time (Figure 5), underlining the exceptional sensitivity of the timsTOF Pro at high acquisition speed. The identified proteins cover a dynamic range of nearly 5 orders of magnitude. The median coefficient of variation was 8.2% at the peptide level and 5.9% at the protein group level for triplicate injections.

We further shortened the run time to increase sample throughput using the 100, 200, and 300 SPD methods on the Evosep One system.

When analyzing the HeLa sample using 4-D data extraction and the the highest throughput method (300 SPD), we identified more than 2100 protein groups and 10,462 peptide sequences on average in just 3-minutes gradient time (4.8-minutes total run time, Figure 4).

For large scale proteomic studies it is not only important to increase the proteome coverage in single runs, but also to reproducibly identify and quantify proteins and peptides to mitigate the missing value problem. DIA-based approaches benefit from sampling all the precursors present in the selected mass ranges rather than being dependent on precursor selection algorithms leading to very reproducible peptide and protein identification. The timsTOF Pro provides accurate and highly reproducible collisional cross section (CCS) values that adds a 4th dimension for feature matching and alignment during data processing, thereby further improving data completeness. When evaluating the triplicate injections of the 60 SPD method, we detected only a slight cumulative increase of 102 protein groups (Figure 6). More than 94% of the protein groups (4915 out of 5213) were identified in all three runs (Figure 7). This underlines the outstanding reproducibility of identified proteins using dia-PASEF.

In addition to excellent data completeness in dia-PASEF, quantitative accuracy strongly benefits from the 4th mobility dimension. Analyzing the reproducibility of protein intensities between the technical replicates revealed that 81% of the 5315 identified proteins could be reproducibly quantified with a CV

below 20% and 65% with a CV below 10% (Figure 7).

In summary, these results highlight that the combination of the Evosep One with dia-PASEF and 4D-Proteomics is ideally suited for high-throughput proteomic profiling of hundreds of samples per day.

Conclusion

timsTOF Pro using dia-PASEF and 4D-Proteomics in combination with the Evosep One system is ideally suited for very high-throughput proteomics akin to clinical settings:

- On average 5200 protein groups can be identified and quantified in single-shot analysis using a short LC gradient (60 samples per day)
- Using a 300 SPD method (4.8-minutes total run time) dia-PASEF identifies and quantifies more than 2000 protein groups per run.
- dia-PASEF delivers extremely reproducible identification and quantitation information making the approach perfectly suited for the challenges of quantitative proteomics.

More information: www.bruker.com/timstofpro

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Bruker Daltonik GmbH
Bremen · Germany
Phone +49 (0)421-2205-0

Bruker Scientific LLC
Billerica, MA · USA
Phone +1 (978) 663-3660
ms.sales.bdal@bruker.com – www.bruker.com

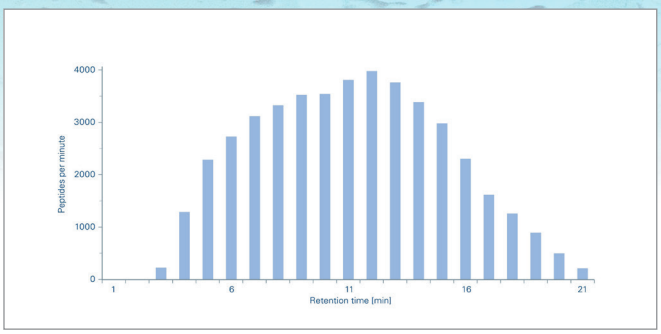


Figure 5. Numbers of peptides identified by 4-D data extraction across the 60 SPD method (21 min run time) for dia-PASEF using 200 ng sample load.

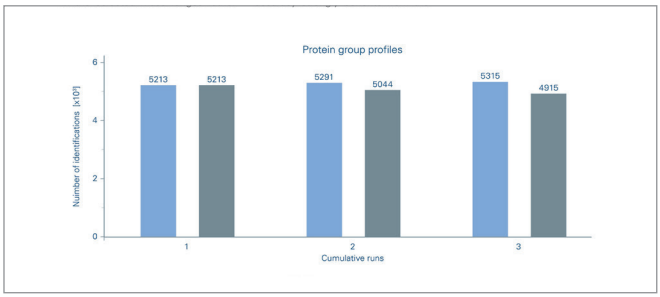


Figure 6. Overview cumulative protein groups profiles for the triplicate injections using the 60 SPD method. Sparse profiles are shown in blue and full profiles are shown in grey.

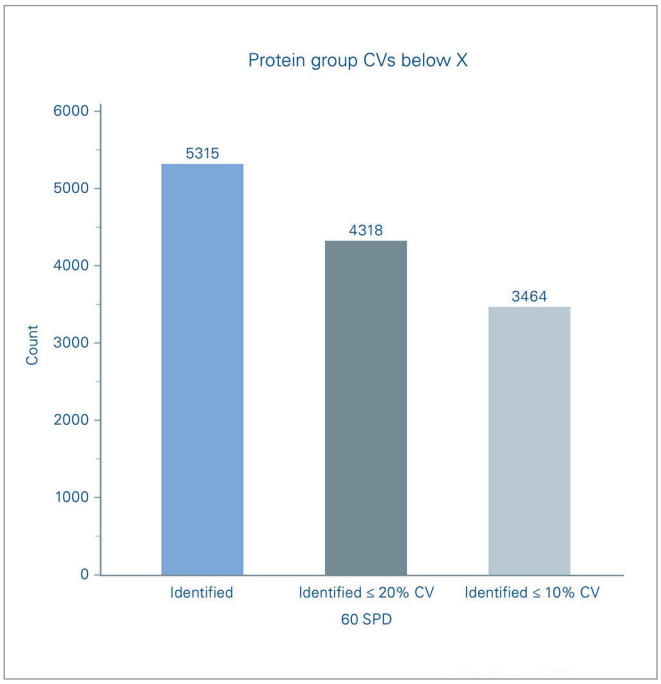


Figure 7. Number of all protein identifications (blue), proteins with CV < 20% (gray) and < 10% (light grey) for triplicate injections using the 60 SPD.

PROCESS AND REPROCESS HIGH-THROUGHPUT DATA IN MINUTES

High-throughput LC/MS data adds up quickly, but with the right data-management system, scientists can process and make decisions in minutes

By Richard Lee and Charis Lam

Processing and reprocessing high-throughput LC/UV and LC/UV/MS data is computationally intensive. Through software-architecture redesign, ACD/Labs will help you cut HT analytical-data processing time twenty-fold.

Medium-to-large pharmaceutical companies generate gargantuan volumes of high-throughput (HT) data. By one estimate, chromatography alone produces at minimum 2 TB/year. To turn this data into decisions, scientists manually draw connections between each data set and its corresponding reaction.

This tedious task gets automated with Katalyst D2D™ software. Designed for HT experiments, Katalyst supports every step from experiment design to data reprocessing and review. All information is available in one interface, where LC/MS data is linked with the originating reaction. Scientists see all the information they need to make a data-driven decision.

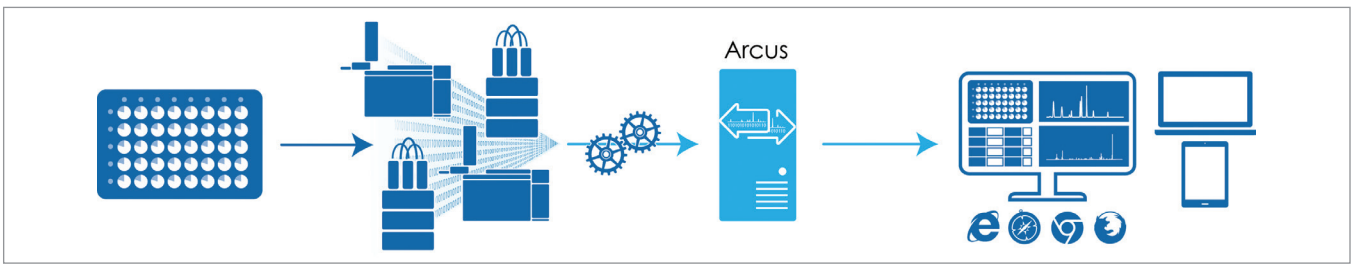
In the HT workflow, a common bottleneck is analytical-data processing. Automation has helped somewhat, but automatically processed LC data uses standard settings that are not optimized for each experiment. Typically, 20–80 percent of the data must be reanalyzed.

So, even with automation, reprocessing remains tedious – and time-consuming. Much computational time is required to handle the hours of data that come from a 96-well plate. Katalyst also solves this problem. It cuts processing time 20-fold with a new data-management sub-system (the Arcus server) which provides fast data exchange. A 96-well plate that once took 60 minutes to reprocess now takes 3 minutes.

The interface compares the original and reprocessed analyses.

Scientists trigger reprocessing from a web interface, which compares the old and new results. It also shows data linked to the design that produced it. From designing an experiment to cleaning up the results and deciding what they mean, Katalyst helps scientists move projects forward.

For more information, see www.acdlabs.com/data-container.



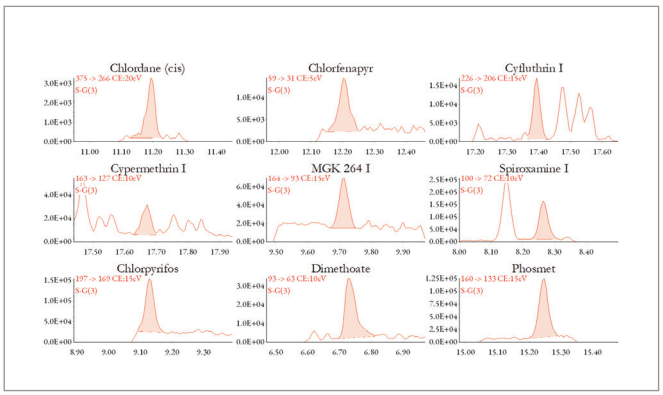
Data is automatically retrieved from instruments and stored in Arcus, which supplies it quickly for reprocessing. The scientist sees the data linked to reaction wells.

ANALYSIS OF PESTICIDES IN CANNABIS SATIVA MATRIX

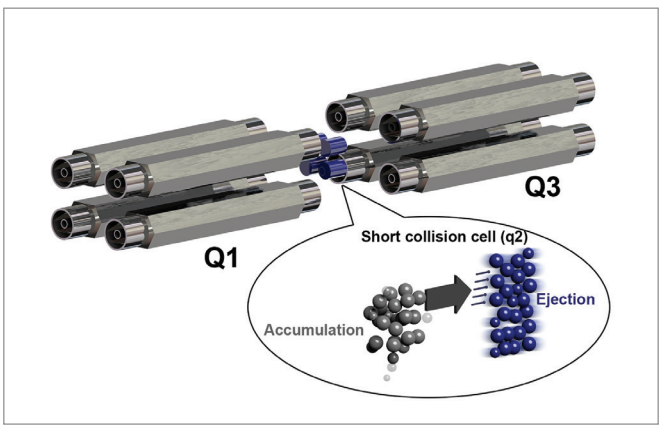
Pesticides in *Cannabis sativa* matrix were analyzed using the SRM capabilities of the JEOL JMS-TQ4000GC gas chromatograph triple-quadrupole mass spectrometer. At concentrations of 1 ppb or less, 41 pesticides were detected with good linearity and very little matrix interference.

With the recent surge in legalization of *Cannabis sativa* for recreational use, there is a need for reliable analytical tools to meet the regulatory requirements for pesticide testing. Action limits for each pesticide vary between jurisdictions, but can be as low as 10 ppb. The JEOL JMS-TQ4000GC triple-quadrupole GC-MS/MS system offers high speed and high sensitivity for quantitation of trace pesticides. The TQ4000 combines a unique short collision cell with JEOL's patented ion accumulation and timed detection technology to provide high sensitivity and selectivity, as well as the fastest selected reaction monitoring (SRM) switching speed available (up to 1000 SRMs/s). In this application note, we describe a sensitive method for analyzing pesticides in extracted *Cannabis sativa* matrix by using the SRM capabilities of our triple quadrupole system.

Cannabis sativa flower buds were extracted by sonication, diluted 10X, and cleaned up by dispersive solid-phase extraction (dSPE). The extracted matrix was spiked with pesticide standards and measured on the JMS-TQ4000GC using SRM measurement in the high-sensitivity mode. The SRM database was created using JEOL's built-in SRM tools to choose optimal SRM transitions for each pesticide. Of the 46 pesticides measured, 41 pesticides were detected at 1 ppb or less, which translates to 10 ppb on the plant. Excellent linearity was calculated for all detected compounds. Chlorinated pesticides that are typically difficult for LC-MS, such as cypermethrin, cyfluthrin, and chlordane, were detected at 1 ppb without issue. Although some matrix effects were observed for some pesticides, system performance was generally good with very few pesticides affected by matrix interference.



Short collision cell of JEOL triple-quad GC-MS/MS.



Select SRM chromatograms for pesticides at 1 ppb in *Cannabis sativa* matrix.

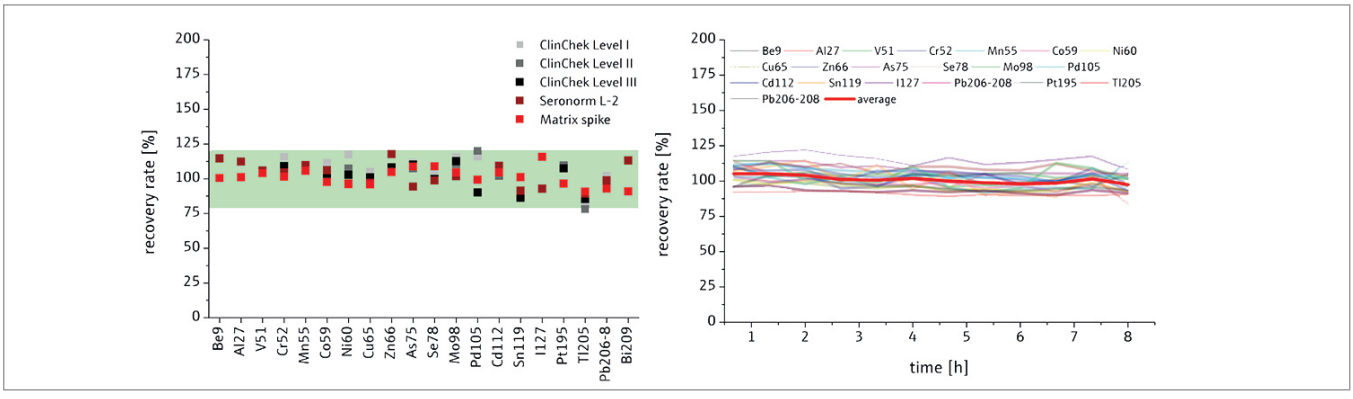
BOOSTING LIMITS OF DETECTION FOR CHROMIUM AND OTHER TRACE ELEMENTS IN BLOOD

BOOST technology in the PlasmaQuant MS Q enables accurate measurement of lowest quantities of chromium and other elements in blood.

Accurate quantification of the metallic profile in whole blood with a robust method ensuring lowest LODs for elements that are typically affected by strong interferences. The BOOST technology of the PlasmaQuant MS Q enables the accurate measurement of lowest quantities of chromium and other elements in whole blood.

The blood circulatory system is a transport system which continuously supplies the body with the oxygen, vitamins, fatty acids and nutrients it needs. With iron being the most prominent example, many elements are dissolved in blood or embedded in proteins that are required for the proper functioning of the organism. The presence of too high or too low concentrations of these elements can be an indication of a deficiency or an intoxication potentially leading to severe diseases. For this reason, the metallic profile of biological samples such as blood, serum, plasma and urine is routinely analyzed. In recent years, inductively coupled plasma mass spectrometry (ICP-MS) has become the method of choice for analyzing these sample types because of its speed and low detection limits. Whole blood is a complex sample matrix with solid and liquid components and a relatively high carbon content deriving from the proteins and lipids in the blood. In some cases, it is sufficient to determine the elemental concentration in the serum. However, some elements are partially located in the non-soluble blood fraction, the hematocrit, making the analysis of whole blood necessary. Due to its solid and liquid components the sample preparation of whole blood samples is difficult, as solid components must not precipitate. For this reason, different procedures for sample preparation have been developed. Here, we present a robust method for obtaining a metallic profile of whole blood with concentrations ranging from ppt to ppm level using alkali dilution for easy and fast sample preparation. With the patented BOOST technology, elements such as As, Se, Cr and V, which are typically difficult to measure in whole blood with ICP-MS, can be analyzed correctly with method limits of detection in the ng/l range. The accurate quantification of all elements during a long-term measurement of 8 hours proved the applicability of the method for the routine analysis of whole blood.

Read full article: https://www.analytik-jena.us/fileadmin/content/applications/ICP-S/AppNote_ICPMS_0024_en_01.pdf



Recovery rates of the certified reference materials (CRMs) and matrix spikes as a function of the element analyzed (left) and as a function of time (right). The measured concentrations of the CRMs and the matrix spike were within the specified uncertainty (80–120%, highlighted in green). The matrix spike was accurately measured over 8 hours proving the robustness of the method and the instrument.

STREAMLINE METABOLITE IDENTIFICATION WITH A SINGLE SOFTWARE PLATFORM

One metabolite-identification platform replaces a tangle of data files and programs for more efficiency and a smoother workflow

By Charis Lam and Richard Lee

Simplify your metabolite-identification workflow without losing result quality or analytical power. Move from a tangle of proprietary data formats, programs, and files to one purpose-built platform that supports your entire metabolite-analysis project.

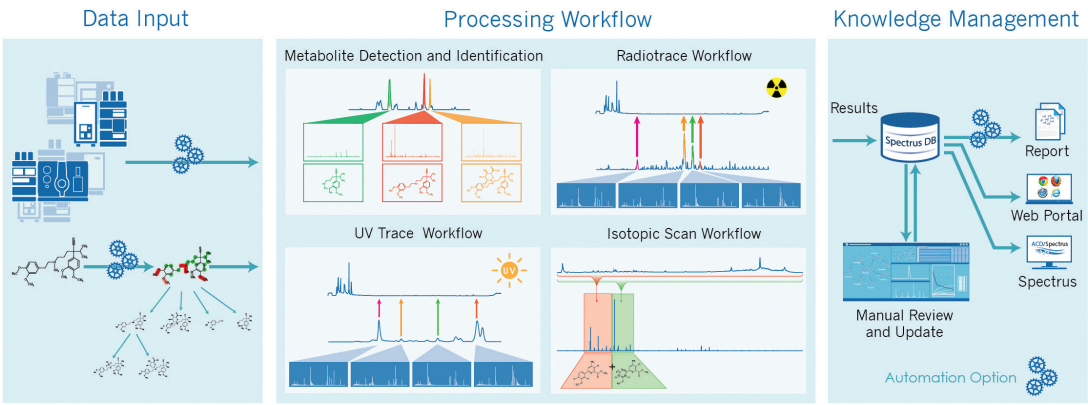
To identify metabolites, scientists must synthesize several streams of information: structural information, biotransformation rules, and analytical data. Complicating matters further, most laboratories use several vendor instruments, each with their own software and file formats. These disparate files must also be amalgamated to survey the entire experiment.

Connecting these information streams can be tedious, confusing, and time-consuming, but it needn't be. ACD/Labs' MetaSense® software supports metabolite analysis by providing a single platform for a scientist's entire workflow. MetaSense handles all necessary information and evidence: taking data from most major analytical-instrument vendors, locating reactive sites, predicting biotransformations, processing data, linking MS features to structures, and producing biotransformation maps and kinetic plots. It offers four workflows to handle most metabolic experiments – LC/MS/MS, radiotrace, UV trace, and isotopic scan. It even accepts third-party metabolite-prediction lists from Lhasa Ltd. Meteor Nexus and Molecular Discovery MetaSite. All metabolite-identification (MetID) data and analyses are gathered in one place for easy processing, review, and search.

Purpose-built for MetID, the software uses its own chemical intelligence and accommodates expert review. First, it predicts the full metabolic tree. For every potential metabolic site in a compound, a statistical model estimates the reaction likelihood. The software then matches the predicted metabolites to extracted-ion-chromatogram peaks by mass and isotopic pattern. To distinguish isomeric metabolites, biotransformation sites are identified using MS/MS fragments and physiochemical-property prediction. MetaSense also detects unpredicted metabolites by control-sample comparison and fractional mass difference, and it displays all metabolites in a biotransformation map and kinetic plot. Each step can be performed automatically or manually. Users may review and edit, adjusting processing and analysis routines and adding missed metabolites.

The software combines several streams of evidence to help the scientist build a final interpretation. By seeing information from different experiment types (LC/MS, LC/UV, etc.) and from all stages – raw data to final interpretation – users can review the entire experiment at once. With a single automated platform, MetID experts can spend less time wrangling multiple files and programs and devote more attention to applying their expertise.

For more information, see www.acdlabs.com/complete-metid.



The MetaSense workflow supports all metabolite-analysis steps.

THE MASSBOX MASS SPECTROMETER SIMPLIFIES SOLID SAMPLE ANALYSIS FOR TRACE-LEVEL QUANTITATION

A Laser Ablation Laser Ionization Time of Flight Mass Spectrometer (LALI-TOF-MS) for applications requiring low detection levels

By Ellen Williams, Jon Putman, Jeff Williams

The Massbox is the first commercial Laser Ablation Laser Ionization Time of Flight Mass Spectrometer (LALI-TOF-MS). It combines high detection capabilities with low-cost, uncomplicated operations. Thus, it simplifies solid sample analysis for any application requiring trace-level quantitation

Many commercial techniques exist for solid sample analysis. Compared to tools for simple bulk analysis, instruments with high detection capabilities are typically more expensive to maintain, involve more complicated sample preparation, and require a highly skilled, trained operator. Recent advancements in solid-state lasers, computing power, and software user interfaces have contributed to a new instrument – the Massbox. Combining improved technical capabilities with reduced operational challenges, the Massbox is the first Laser Ablation Laser Ionization Time of Flight Mass Spectrometer (LALI-TOF-MS).

The LALI method uses two lasers to first ablate (or desorb, in the case of organics) material from the solid sample's surface and then ionize that material in a second step. By analyzing solid samples directly, LALI eliminates intricate dissolution/digestion sample preparation procedures that complicate other techniques. The initial ablation (or desorption) process creates both a temporal plasma and a neutral particle cloud, and the second laser ionizes the neutrals. Compared to other plasma-ionizing techniques, targeting neutral particles greatly reduces the matrix effects.

Figure 1 shows color-contoured periodic tables comparing detection limits of LALI-TOF-MS to those of other common methods for solid sample analysis: 1) Laser Ablation Inductively Coupled Plasma Mass Spectrometry (LA-ICP-MS), 2) X-ray Fluorescence (XRF), and 3) Laser Induced Breakdown Spectroscopy (LIBS). In this graph, the color gradient denotes detection limits with the darker colors representing the lowest levels.

As shown in Figure 1, detection limits for LA-ICP-MS are most comparable to those of the new LALI-TOF-MS – ranging from ~1 to 100 parts per billion. Estimating the total cost of the ICP-MS instrument and the additional ablation chamber for LA-ICP-MS are beyond the scope of this application note. Thus, the authors present the following cost comparison of techniques, which builds upon a previously-published evaluation of ICP-MS, ICP-OES (Inductively Coupled Plasma-Optical Emission Spectrometry) and two other systems (1). Because LALI-TOF-MS requires little calibration/training, a technician can operate it. Contrarily, the more complicated operation of ICP-MS involves a Doctor of Philosophy (PhD). Figure 2 compares total yearly operating costs among the three methods. Compared to ICP-OES and ICP-MS, LALI has 35-60 percent lower operating costs, and its cost per sample is approximately 10 times lower. With the intuitive operations of its all-in-one system, the Massbox is the ideal instrument for commercial applications requiring trace-level quantitation.

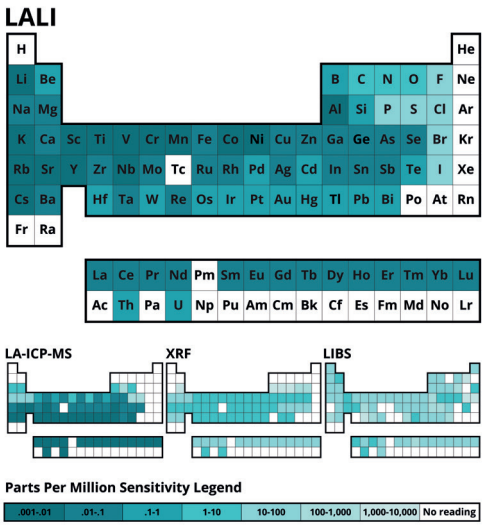


Figure 1. Detection limits for LALI-TOF-MS, LA-ICP-MS, XRF, and LIBS. Each element is colored by its respective limit of detection. Darker colors represent lower detection limits.

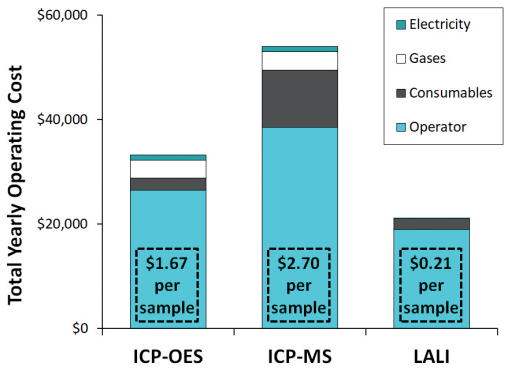


Figure 2. Yearly operating costs for ICP-OES, ICP-MS, and LALI-TOF-MS, assuming instruments run 1,000 hours per year (1).

Reference:

1. *R Thomas, "Money to burn: do you know what it costs to run your atomic spectroscopy instrumentation?", Mass Spectrometry & Spectroscopy, 18–19 (2016).*

ACHIEVING LOWEST DETECTION LIMITS IN ICP-MS TO CALIBRATE AT PPQ LEVELS

In the determination of trace and ultra-trace concentrations, instrument performance, laboratory environment and correct sample handling are crucial factors.

Achieving lowest detection limits to accurately and precisely calibrate an ICP-MS at parts per quadrillion (ppq) concentration levels is possible with the PlasmaQuant MS Elite S due to market leading sensitivity and efficient interference removal using the patented integrated collision reaction cell (iCRC) for accurate quantification of lowest concentrations.

ICP-MS, mass spectrometry with inductively coupled plasma, is a powerful multi-element technique to quantify elements at lowest concentrations. ICP-MS is capable of analyzing almost the entire periodic table of elements in various matrices. In the determination of trace and ultra-trace concentrations, not only the instrument performance but also the laboratory environment and correct sample handling are crucial factors. This application note highlights the capabilities of the PlasmaQuant MS Elite family in the accurate and precise determination of lowest quantities of analytes.

For typically low abundant elements, such as rare earth elements, instrument sensitivity is key for achieving lowest limits of detection. The superior sensitivity of the PlasmaQuant MS Elite S leads to outstanding limits of detection of down to a few pg/L. The robust design allows to accurately calibrate the instrument even at low parts per quadrillion (ppq) concentrations close to the limit of quantification making the PlasmaQuant MS series the ideal solution for the robust and correct quantification of smallest amounts of elements.

Read full article: https://www.analytik-jena.us/fileadmin/content/applications/ICP-MS/AppNote_ICPMS_0029_en.pdf

IONICON PTR-TOF INSTRUMENTS DEPLOYED FOR COVID-19 DETECTION IN BREATH

By Jens Herbig and Lukas Märk

There is a high probability that COVID-19 can be detected in the exhaled breath. Moreover, monitoring the impact of treatment or medication is highly relevant. IONICON PTR-TOF systems have become the de-facto standard for real-time breath analysis and a quick, non-invasive SARS-CoV-2 test to identify an infection would be a tremendous step forward.

Advantages of direct and real-time breath gas analysis

Breath gas analysis of volatile organic compounds (VOCs) has progressed in recent years. Researchers are trying to detect volatile biomarkers in exhaled breath that are indicative for a disease or for the response to pharmacological treatments. Several hundred volatile compounds have so far been identified in exhaled breath and their concentrations, typically in the parts-per-billion (ppb) range, are a challenge to most modern analyzers.

IONICON PTR-TOF systems are particularly well suited for breath gas analysis: their detection limits are in the ppt range (1 ppt = 0.001 ppb) and the high mass resolving power allows to separate isobaric compounds. Moreover, in addition to offline analysis where breath is collected in a container and then analyzed, the high sensitivity and fast response time of these systems allows to analyze breath directly and in real-time. This provides immediate results and avoids complications often arising from sample collection and storage. With IONICON PTR-TOF analyzers, several hundred compounds can be measured simultaneously from a single exhalation.

A critical add-on is our specialized breath sampling inlet (BET) which employs clinically certified, disposable, non-rebreathing mouthpieces to minimize the risk of contagion between patients.

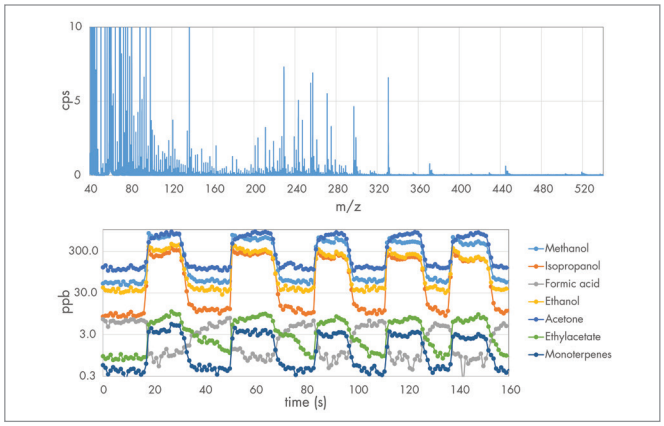


Figure 1. Breath gas spectrum collected by IONICON PTR-TOFMS and extracted real-time concentrations of selected VOCs.

Applied COVID-19 breath VOC pattern research and medication monitoring

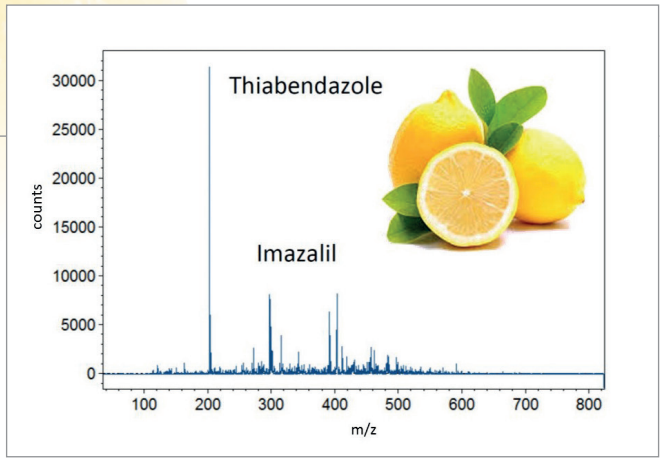
Looking at the pathophysiology of COVID-19, there are several indicators that a SARS-CoV-2 infection is detectable in the breath VOC pattern. The disease has been reported to cause a multitude of symptoms and can affect several organs. This supports the assumption that the metabolism is affected in more than one way and that the volatile metabolite distribution is altered.

The rapid detection of COVID-19-specific breath VOCs would be a great step forward for diagnostic purposes and a spectrum of VOCs could be used for monitoring disease progression or response to conventional or investigational drugs. Moreover, since therapies for COVID-19 are experimental at this stage, directly monitoring the effect of a therapeutic drug speeds up the development of an efficient treatment for COVID-19.

Thanks to breath researchers like Dr Stanislas Grassin Delyle from the Hôpital Foch in Suresnes, France and University Paris-Saclay (UVSQ), our PTR-TOF solutions are currently deployed directly at the forefront of international scientific efforts.

"We use an IONICON PTR-TOF system to monitor breath VOCs in ventilated patients with COVID-19. The direct and fast measurement of so many breath VOCs at the same time allows us to study the progression of the disease and the response to therapeutic strategies." reports Dr Grassin Delyle. We wish him and all other customers who try gaining insights in SARS-CoV-2 all the best!

DETECTION OF RESIDUAL PESTICIDES ON FRUITS AND VEGETABLES USING PORTABILITY™ MINIATURE MASS SPECTROMETER



Mass spectrometry can now be deployed for on-site pesticide screening in real time

A case study for residual pesticide screening on fruits and vegetables is reported. All produce was purchased from a local market in San Jose, California and immediately analyzed by TD-ESI coupled to the Portability™ mass spectrometer without any sample preparation. The portable analyzer was able to detect ppm levels of pesticides such as thiabendazole, imazalil, flutolanil, and permethrin. Featuring light weight and compact size, BaySpec's novel mass analyzers based on linear ion trap technology are the most sensitive portable devices available on the market with parts-per-trillion detection sensitivity. These extremely compact instruments are simple to operate and maintain, and they are ideal for a variety of bulk or trace on-site detection in real time. Learn how you can bring the lab to the sample with portable analytical tools from BaySpec by reading our educational application note for pesticide screening of produce.

Read the full app note: http://tas.txp.to/1018/ANBaySpec