timsMetabo™

Discover MoRE with Mobility Range Enhanced 4D-Metabolomics™

Innovation with Integrity

Introducing the **timsMetabo** for enhanced 4D-Metabolomics and 4D-Lipidomics at speed, depth and scale

A peak-performance research engine

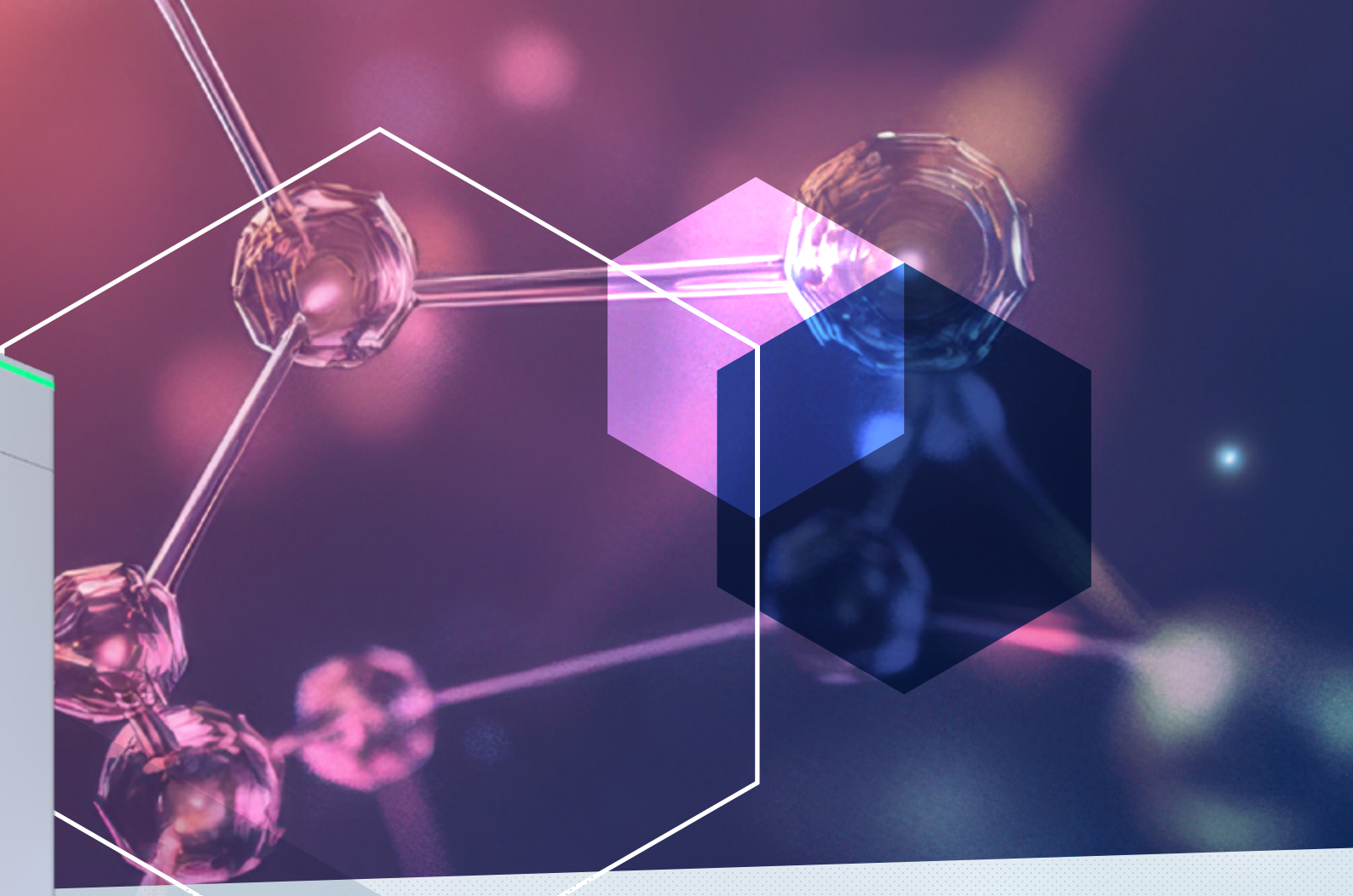
The timsMetabo brings numerous technological innovations together in a benchtop system.

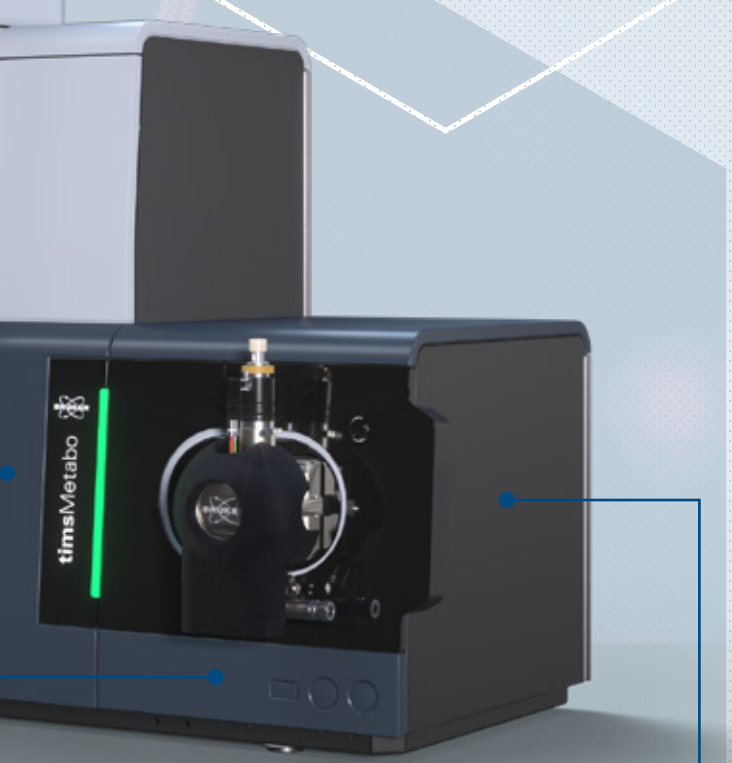
Key Features

Precision detection system for **reliable profiling and quantitation**, at speed and scale.

The **Athena Ion Processor (AIP)** works synergistically with TIMS in 4D-omics workflows to deliver MS and MS/MS sensitivity enhancement.

VIP-HESI ion source for maximum signal intensity and sensitivity.





The **TIMS-MX analyzer** and **Mobility Range Enhancement (MoRE)** bring a three-fold advantage to small molecule analysis in 4D-Metabolomics and 4D-Lipidomics workflows:

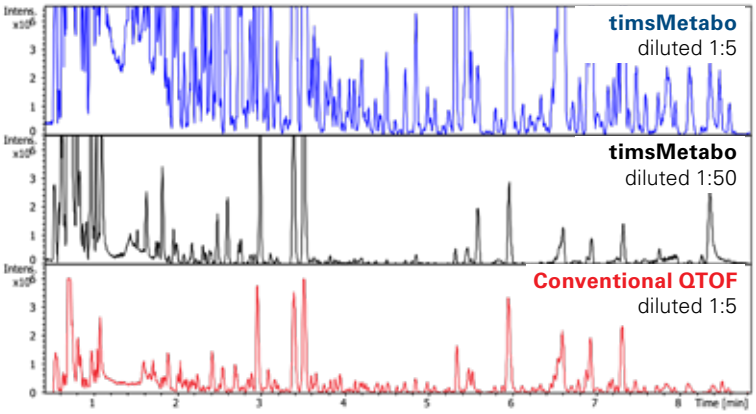
- Increased **ion separation capacity** enables resolution of isomers, isobars and interferences for enhanced measurement selectivity and reduced incidence of chimeric MS/MS spectra.
- Sensitivity and MS/MS speed are boosted by ion handling efficiency enabled by **mobility-based ion sorting**.
- Accurate and reproducible collisional cross section (CCS) measurements provide additional molecular descriptors for more **confident metabolite annotation**.

The power to see MoRE metabolism

The timsMetabo is uniquely designed to enable discovery in small molecule research. Bruker´s technology and workflow innovations combine depth and selectivity for the ultimate in profiling and targeted applications.

Enhanced Sensitivity, enabling deeper and more accurate profiling with less sample.

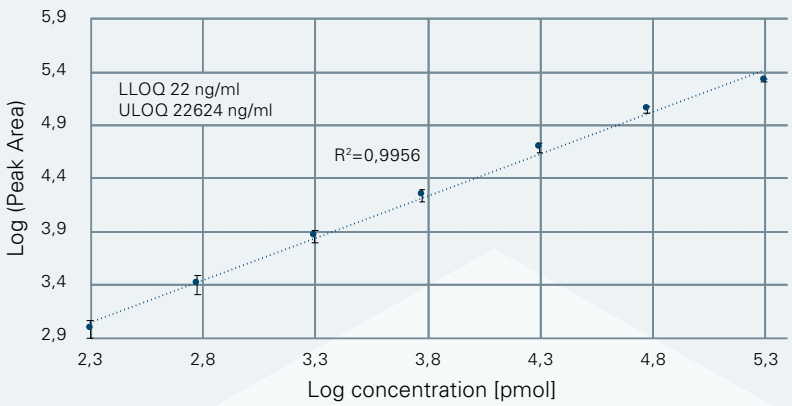
A refined ion path geometry builds on successive generations of timsTOF design, enabling efficient ion sampling for incredible sensitivity with analytical scale LC compatibility.



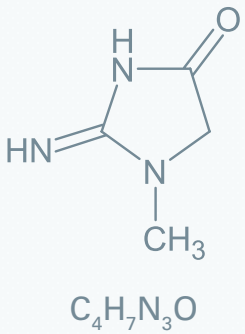
SRM 3672 reference urine analysis on timsMetabo requires ten times less concentrated sample amount injections for achieving similar BPC intensities.

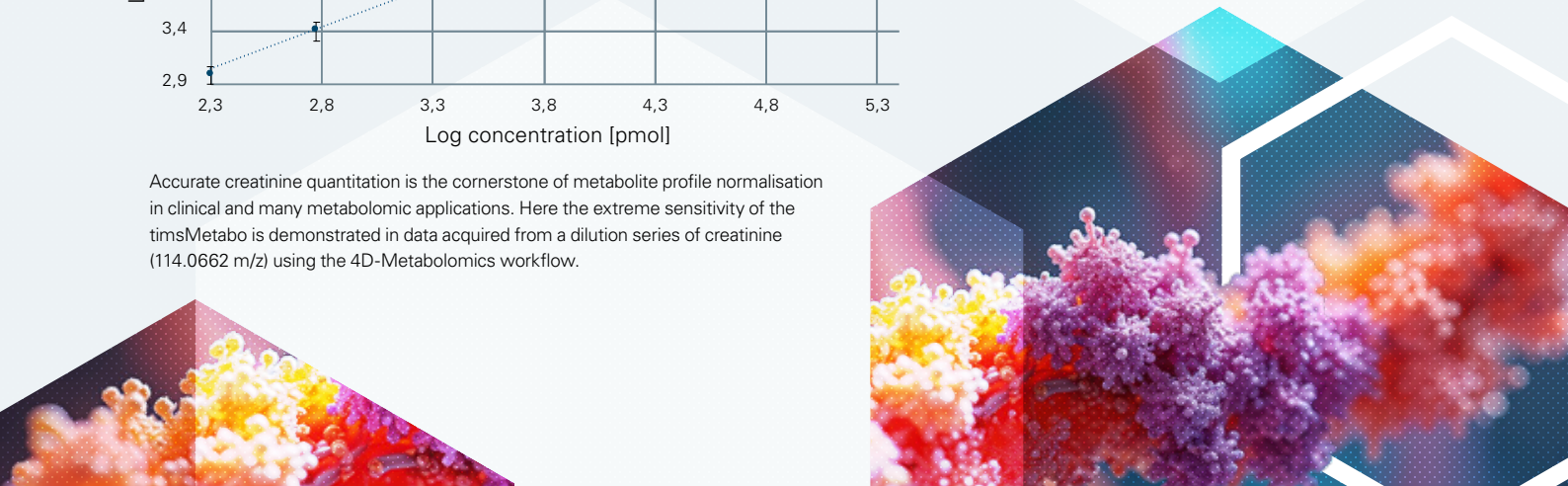
Achieve accurate quantitation with low limits of detection for small molecules while using 4D-Metabolomics workflows that simultaneously and routinely deliver accurate m/z and CCS measurements for high confidence metabolite annotation.

Creatinine Dilution



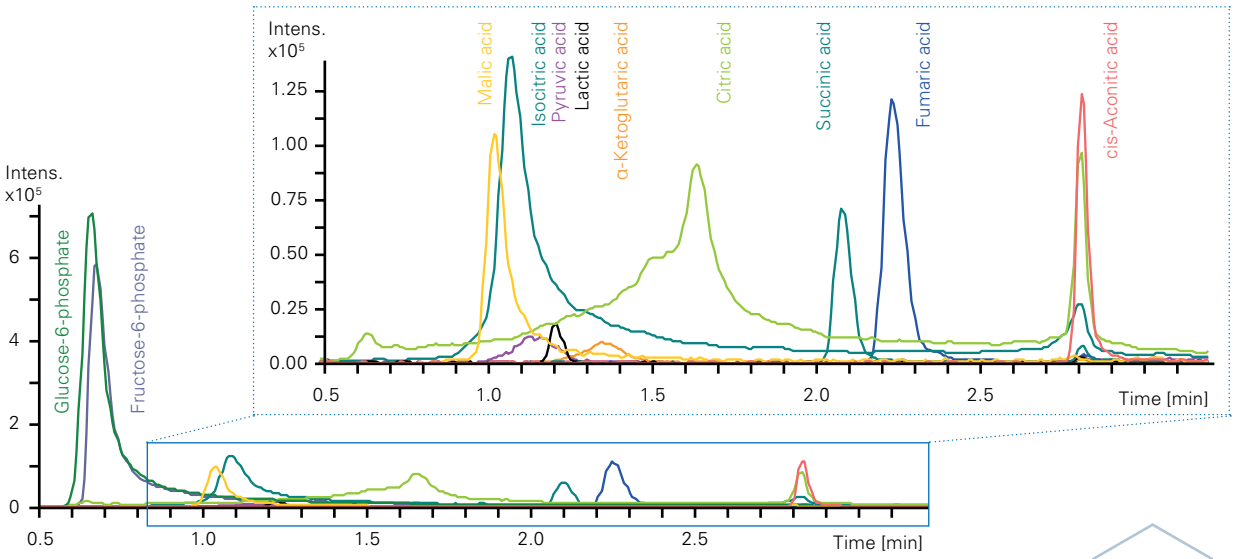
Accurate creatinine quantitation is the cornerstone of metabolite profile normalisation in clinical and many metabolomic applications. Here the extreme sensitivity of the timsMetabo is demonstrated in data acquired from a dilution series of creatinine (114.0662 m/z) using the 4D-Metabolomics workflow.



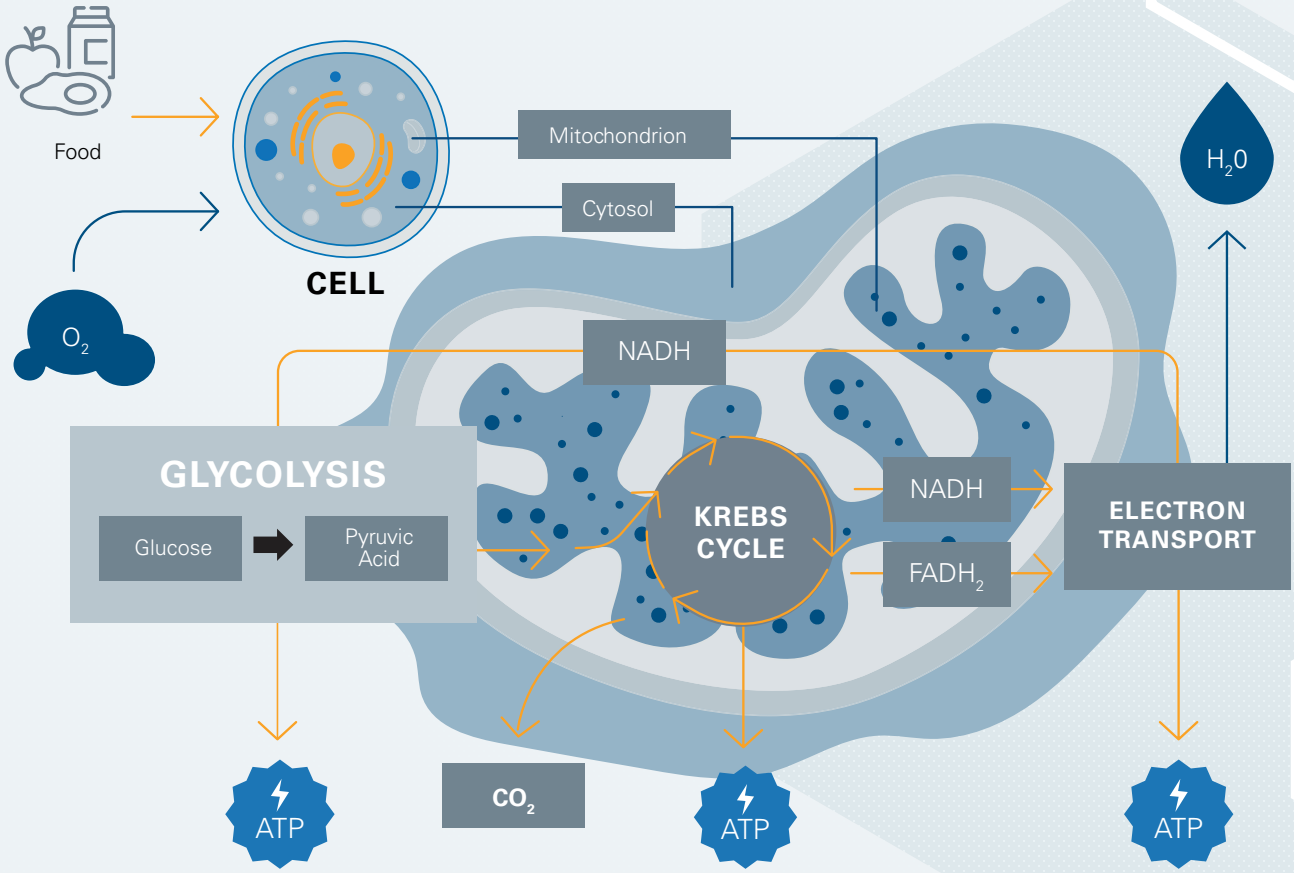


Extended mobility capability for 4D-Metabolomics

Mobility Range Enhancement (MoRE) and the TIMS-MX analyzer enhance small molecule transmission for broad metabolome coverage in 4D-Metabolomics workflows.



Extracted ion chromatogram for TCA cycle and glycolysis standards

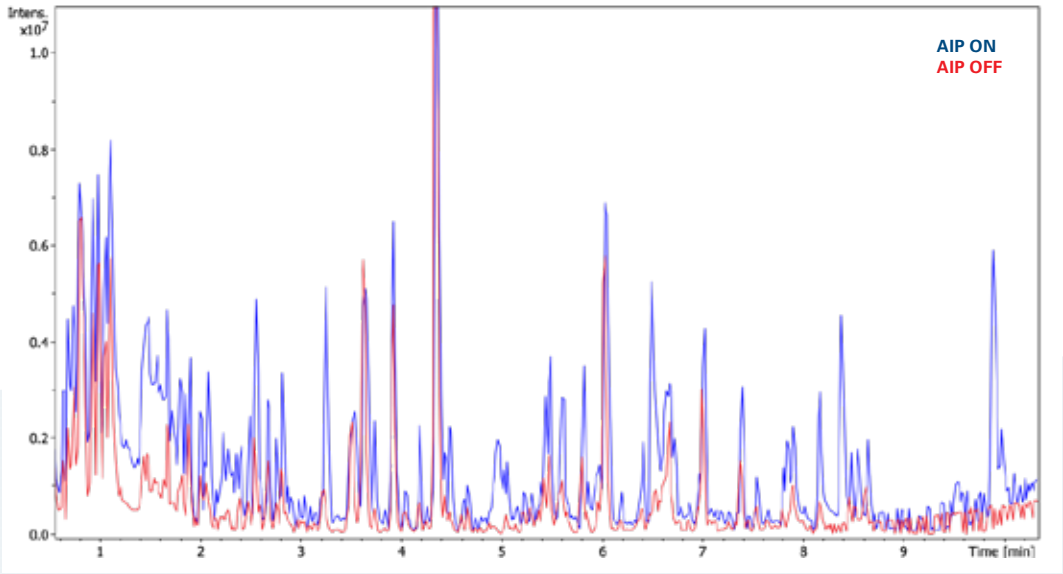


Enhanced sensitivity with the synergistic integration of TIMS and the Athena Ion Processor

Introduction of the AIP extends sensitivity gains in both MS and MS/MS modes, providing advantages for both profiling and targeted analysis workflows.

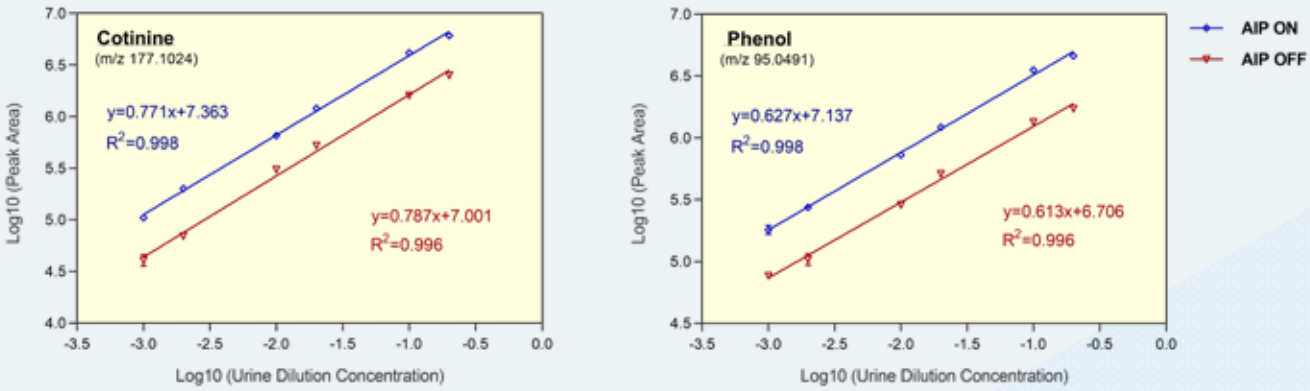
AIP synchronisation with TIMS-MX mobility-based ion sorting and enrichment maximizes this effect for 4D-Metabolomics and 4D-Lipidomics workflows. Sensitivity gains by AIP enable MS/MS spectra matching even for data acquired from low sample amounts.

Profiling

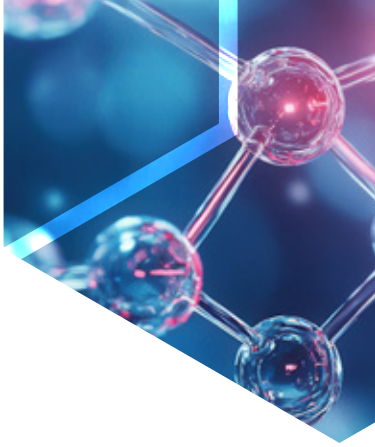


A comparison of 4D-Metabolomics data using the equivalent of 0.2 µl NIST SRM 3671 urine and MoRE acquisition with AIP on or off highlights the sensitivity enhancement provided by AIP.

Quantitation

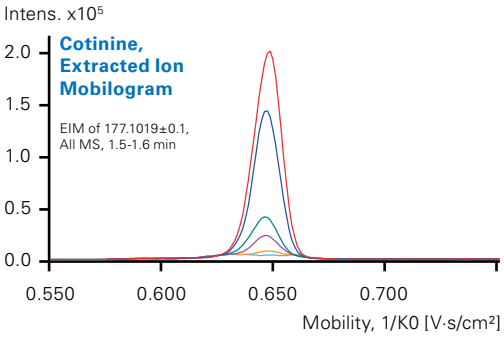


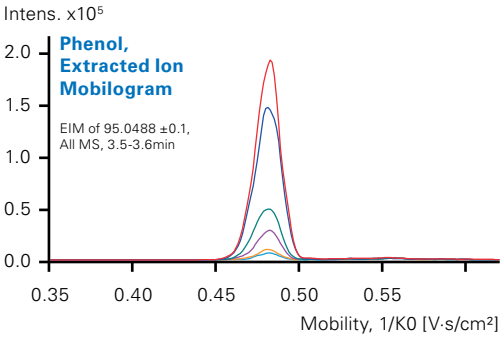
Biomarkers of tobacco smoking exposure in NIST SRM 3671 human urine dilutions from 0.4 µl to 0.002 µl equivalent injected on column.



TIMS-Enhanced Mobilogram-based Quantitation

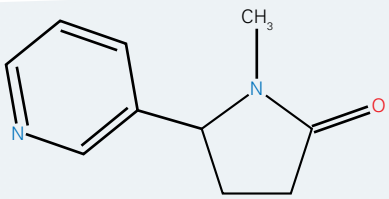
Extracted ion mobilograms for biomarkers of tobacco smoking exposure in NIST SRM 3671 human urine dilutions (from 0.4 µl to 0.002 µl equivalent injected on column).



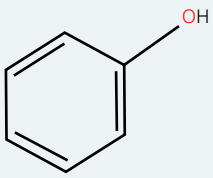


CCS-Predict Pro

CCS value matching vs. measured reference or predicted values can increase annotation confidence.

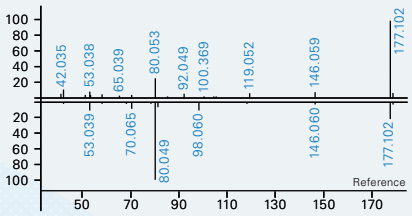


Ion Notation	Measured	Prediction	CSS [%]
[M+H]+	144.3	138.9	3.7

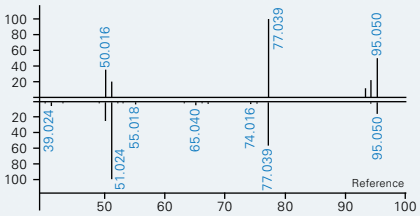


Ion Notation	Measured	Prediction	CSS [%]
[M+H]+	113.4	117.5	-3.6

High Quality TIMS-Enhanced MS/MS



timsMetabo MS/MS from **0.004 µl** equivalent human urine injected on column as compared to a reference spectrum **(Bruker HMDB Metabolite Library 2.0)**.



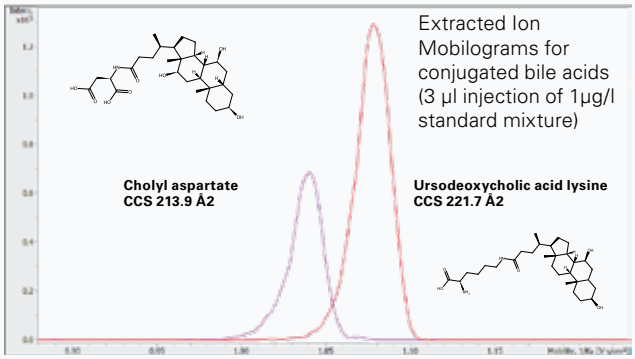
timsMetabo MS/MS from **0.002 µl** equivalent human urine injected on column as compared to a reference spectrum **(Bruker MetaboBase Personal Library 3.0)**.

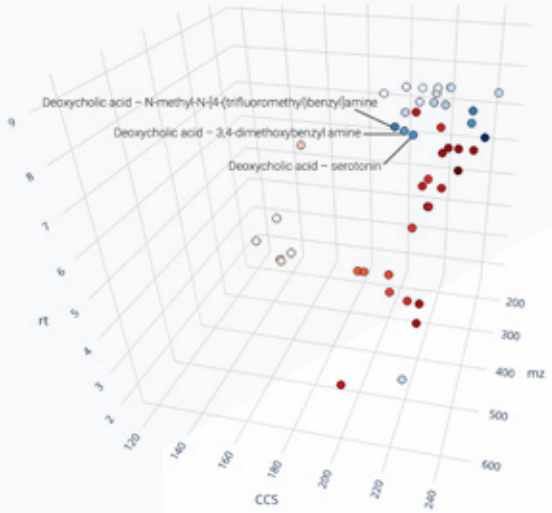
TIMS-enabled 4D workflows deliver the measurement selectivity needed for complex biological sample analysis

High-capacity multidimensional metabolite mapping in LC, TIMS and HRMS space enables accurate and descriptive metabolome measurement in both untargeted and targeted analyses.

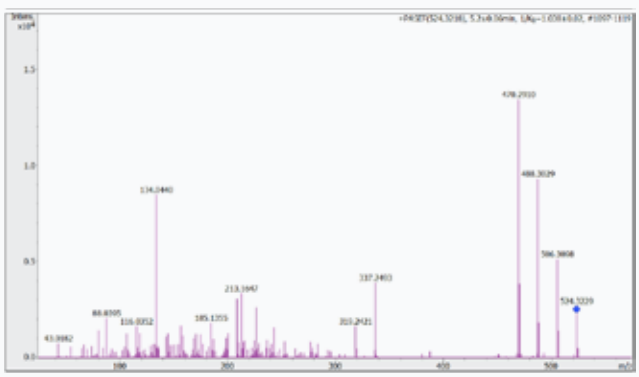
Advanced Profiling and Quantification of Novel Bile Acids

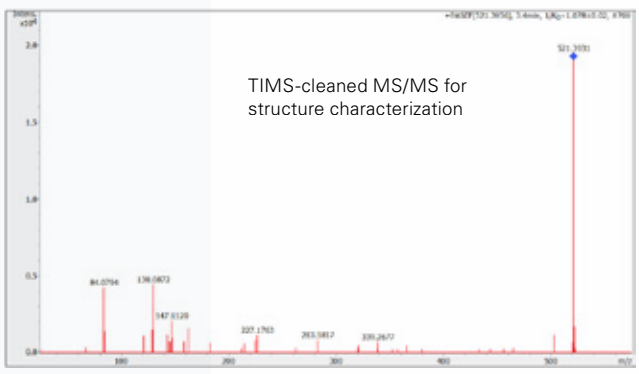
Newly discovered, amino acid conjugated bile acids are involved in gut microbe-host interactions. Characterizing these novel and structurally similar compounds is imperative for deciphering their biological function.





Multi-dimensional metabolite map leveraging TIMS separation for complete resolution of novel amino acid-conjugated bile acids within chromatographic retention time (RT), m/z and CCS axes.





Prof. Pieter Dorrestein

UC San Diego, California, USA

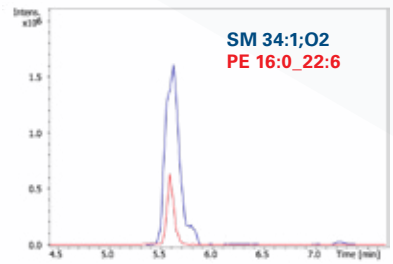
"Bile acids are a diverse and biologically important class of molecules involved in nutrient transport, immune regulation, and are altered in response to medications, diet, and disease. Thousands of distinct bile acid structures – including newly discovered microbially modified forms – are now being revealed. Ion mobility, enhanced by CCS values alongside chromatography and MS/MS, is unlocking this hidden complexity, advancing our understanding of bile acid biology, clinical research, and therapeutic discovery. The technology within the timsMetabo will help us better understand this biologically diverse class of molecules routinely, and this is an exciting combination."

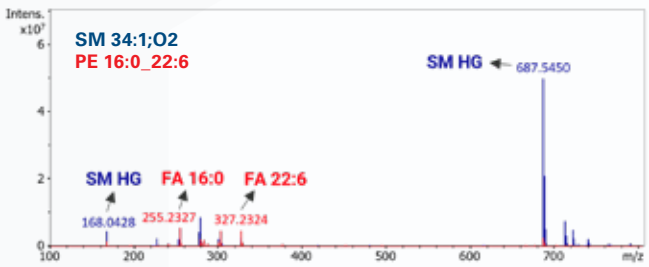
TIMS-Enhanced MS/MS

TIMS-enhancement enables resolution of isomers, isobars and interferences, reducing the incidence of chimeric MS/MS spectra for high-confidence automated annotation.

Lipid and metabolite annotation benefits from clean MS/MS spectra, especially in automated downstream workflows utilising spectral libraries and *in-silico* fragmentation (4D-Metabolomics) and rule-based annotation (4D-Lipidomics). Here, co-eluting and co-isolated lipid species, measured using dia-PASEF 4D-Lipidomics, are mobility separated, producing distinctive and characteristic MS/MS fragmentation spectra for each. These cleaned spectra form the cornerstone of accurate annotation, interpretation and reporting.

EIC



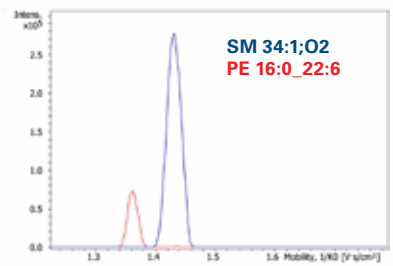


3D-Lipidomics

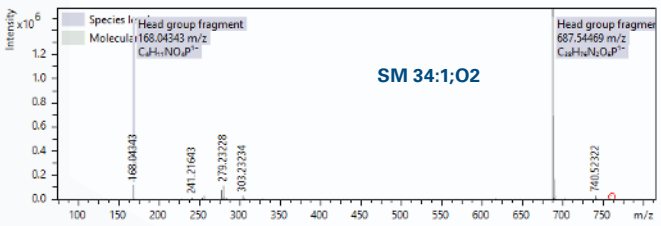
4D-Lipidomics

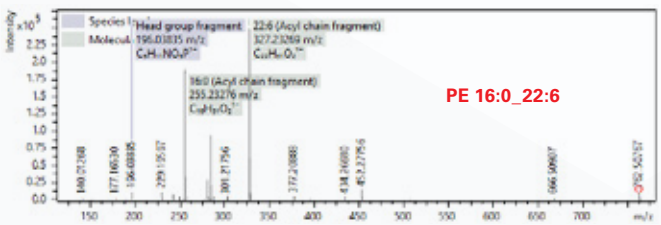
TIMS

EIM



Species co-elute but can be separated with TIMS





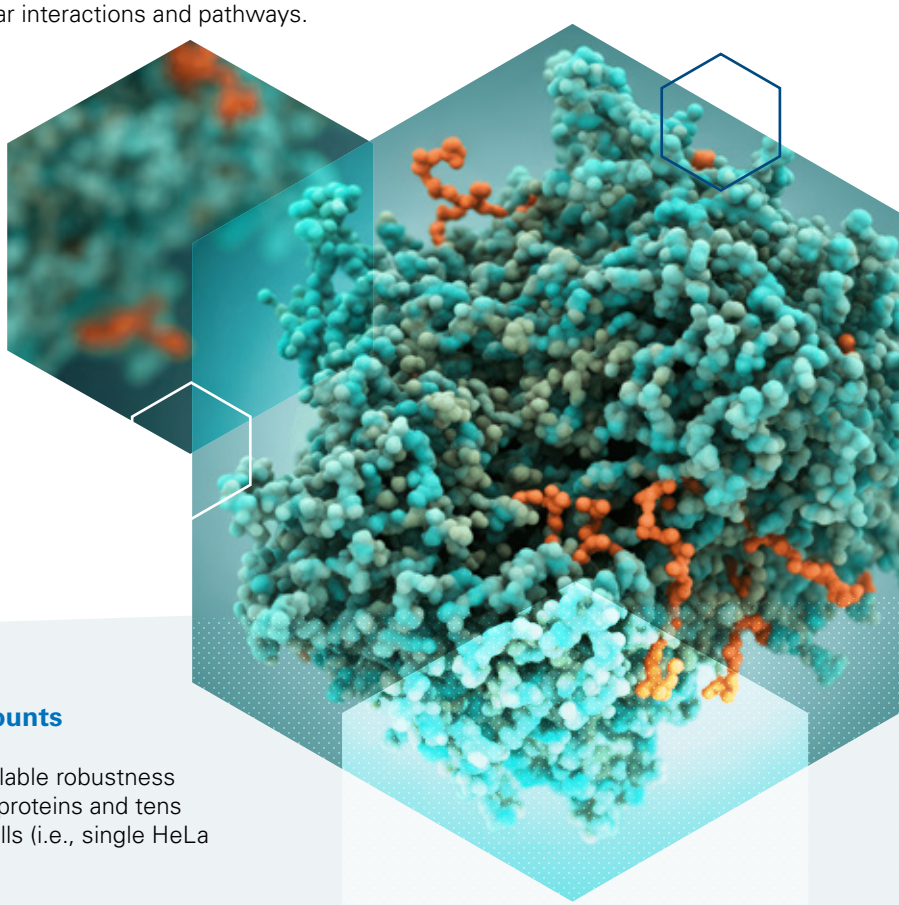
DIA-PASEF resolves precursor lipids providing clean MS/MS spectra for high confidence annotation

Annotation of DIA-based co-isolated lipids PE 16:0_22:6 and SM 34:1;O2 (Δm/z = 0.926) in negative ion mode.

Unlock Comprehensive Proteomics Insights with timsMetabo

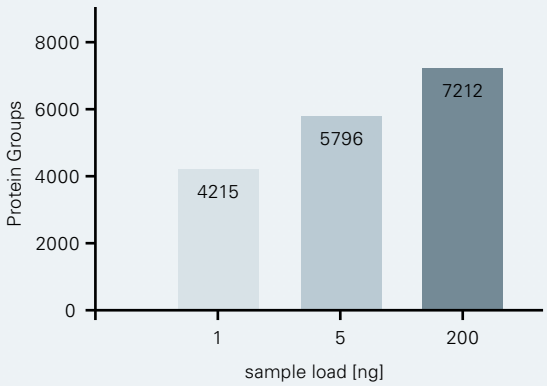
timsMetabo is designed to excel in lipidomics and metabolomics while preserving the unique proteomics research capabilities of the timsTOF family. By integrating multiomics capabilities in a single platform, this system offers uniquely comprehensive insights into biological processes, enabling researchers to uncover complex molecular interactions and pathways.

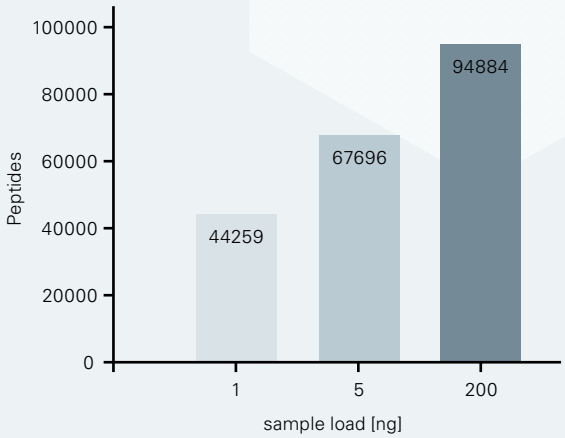
Whether you're exploring lipid profiles, metabolic changes, or protein functions, timsMetabo empowers you to achieve comprehensive, precise, and accurate multiomics insights at scale, driving advancements in biomedical research and personalized medicine.



Deep Insights Down to Small Sample Amounts

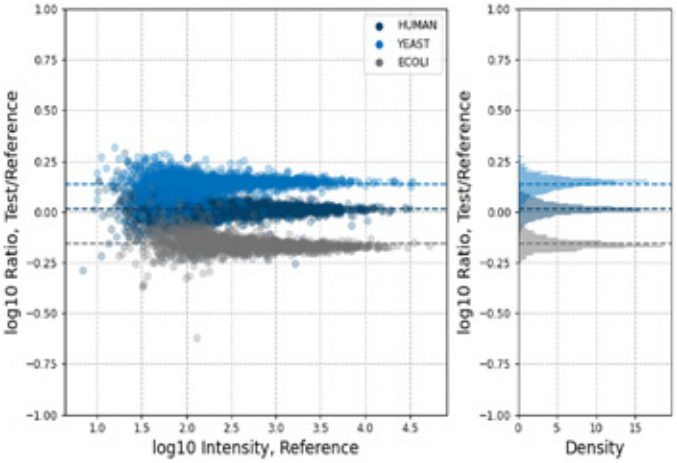
Discover the complexity of the proteome with scalable robustness and sufficient sensitivity to quantify thousands of proteins and tens of thousands of peptides from just a few single cells (i.e., single HeLa cell ~0.25 ng).

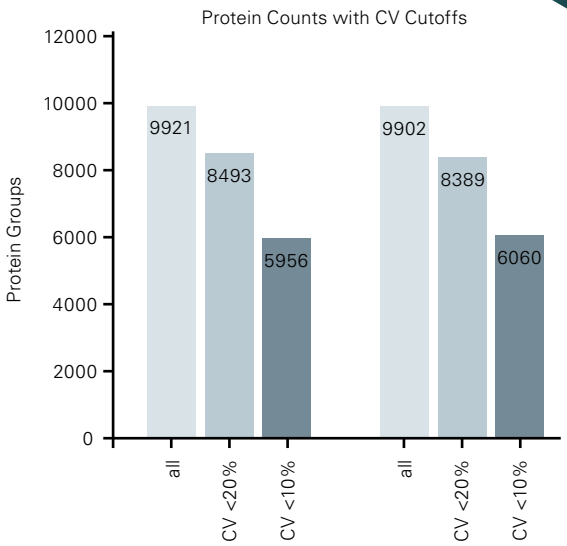




Robust Quantification Discerning Smallest Proteome Differences

Quantify thousands of proteins and peptides with highest fold-change accuracy and precision to discover biologically relevant protein regulations confidently.

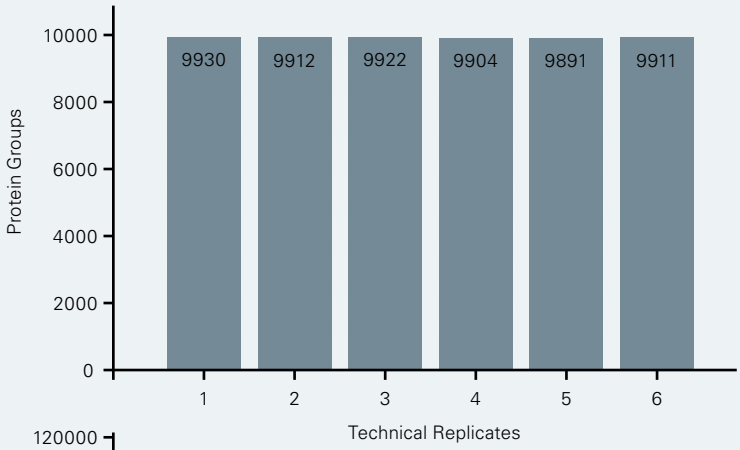


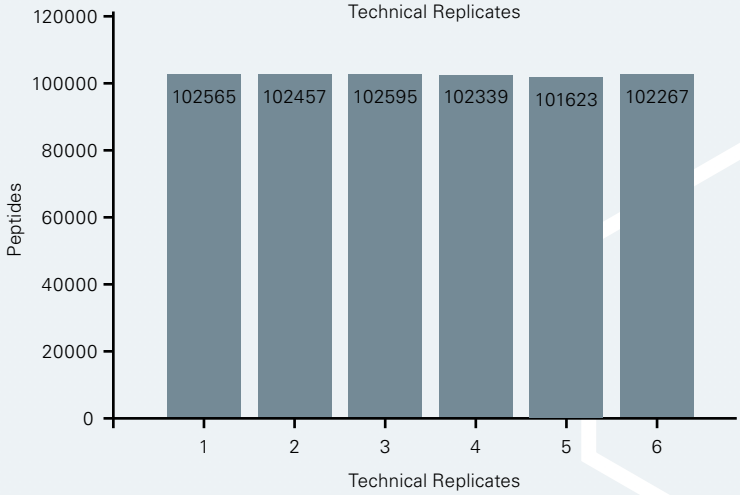


Survey Nuanced Biological Regulations

Our triple proteome study (Yeast, Human, E. coli) showcases exceptional quantification performance, spanning over 4 orders of magnitude. Confident quantification of thousands of proteins and tens of thousands of peptides, providing comprehensive insights into biology.

- **Multiomics Insights:** Gain deeper insights into complex biological processes and regulatory mechanisms.
- **Broad Applicability:** Applicable across various biological systems, enhancing the scope of proteomics research.
- **High Sensitivity:** Detect and quantify low-abundance proteins and peptides with high accuracy.





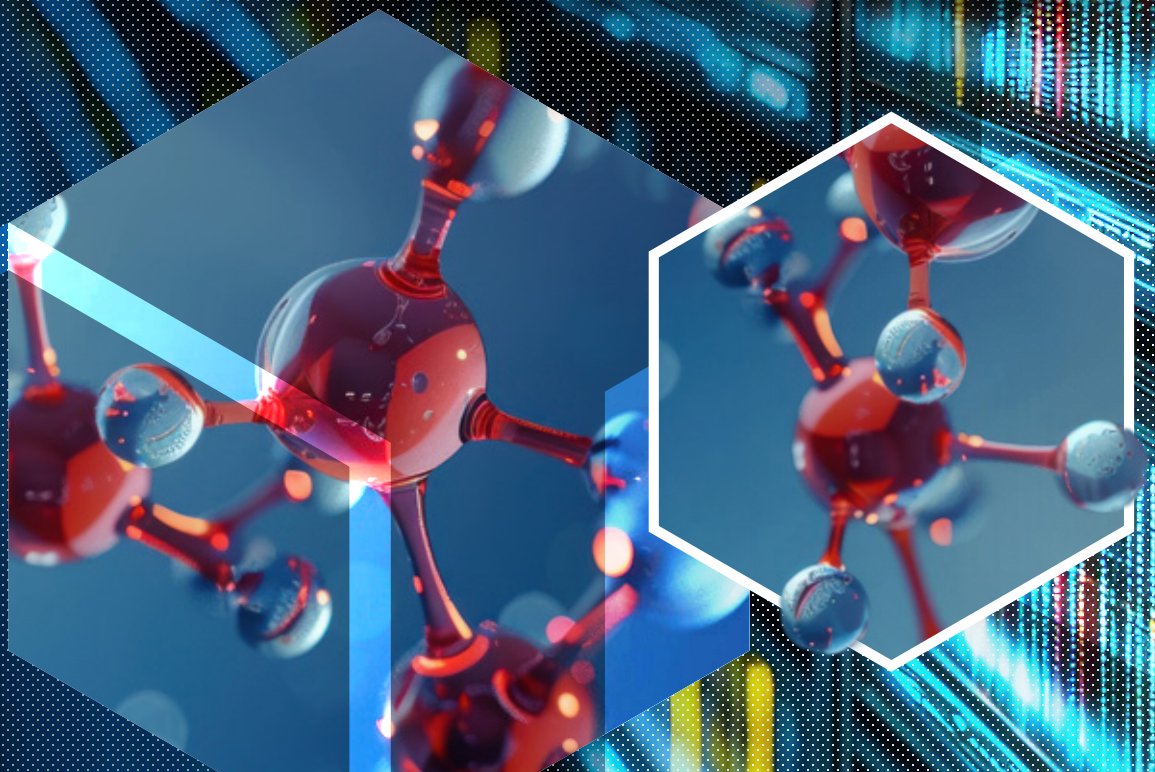
A digital metabolome archive of every sample analysis

The timsMetabo enables simultaneous quantitation and characterisation of the analytes within each sample analysis, virtually eliminating the need for re-acquisition. timsMetabo data enable confident analysis and annotation, and are well suited for AI in metabolomics with machine learning from large-scale, high-quality data sets.

Frédéric Vaz, Ph.D.

Associate Professor, Amsterdam UMC, The Netherlands

"The timsMetabo uniquely combines sensitivity and selectivity, facilitating measurement of known biomarkers and the exploration of new metabolic signatures in research on inborn errors of metabolism."



Multidimensional Metabolite Isolation

LC separation (optional)
Metabolites in complex biofluids and tissue extracts are chromatographically separated prior to ionization.

TIMS-enhancement
Post-ionisation, metabolite ions are concentrated and mobility sorted in each measurement cycle.

TIMS-guided quadrupole isolation
Upstream mobility-based ion sorting enables fast and efficient ion targeting in DDA and DIA modes.

High resolution mass spectrometry
Metabolite ions are separated at high resolution by their mass to charge ratio.

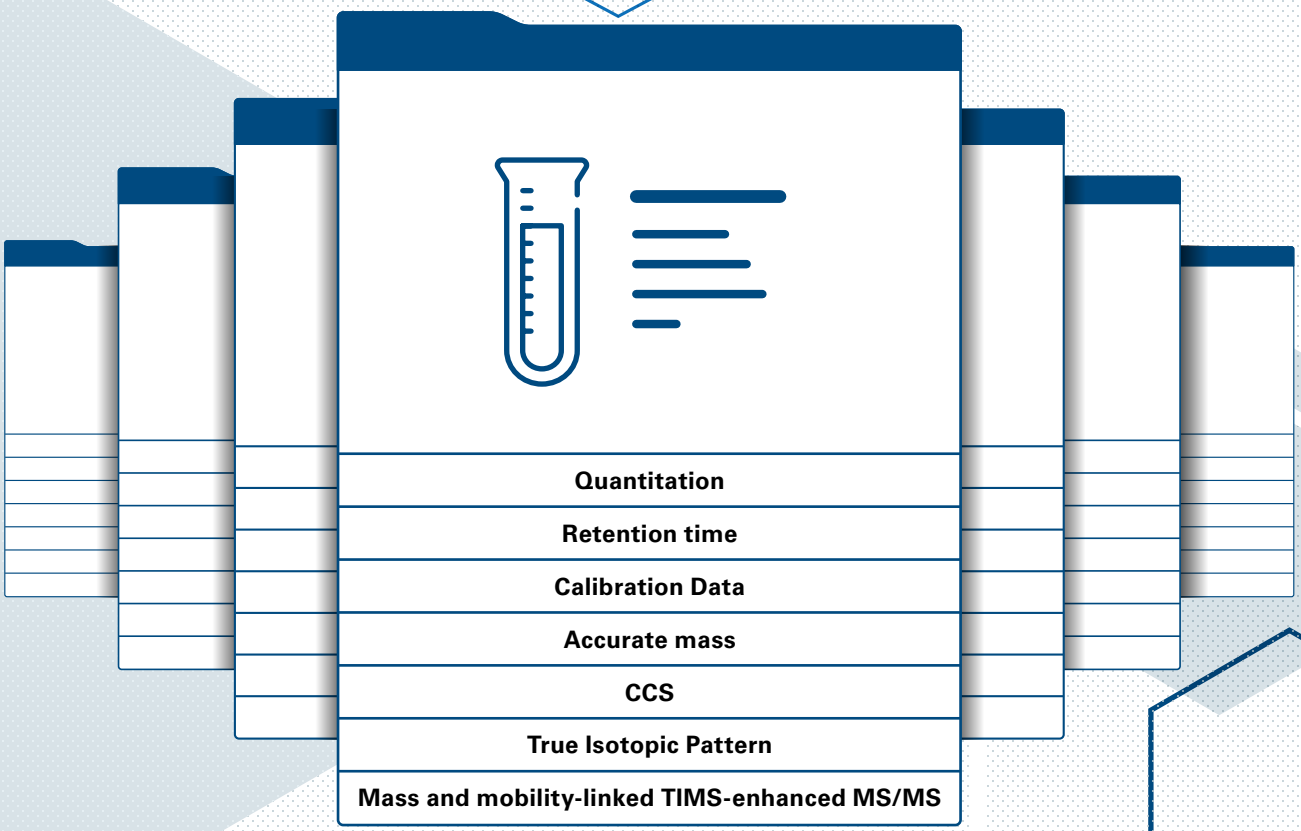
Metabolite Characterisation

TIMS-enhanced MS/MS
CID fragmentation spectra from mobility and mass isolated precursors are acquired with excellent coverage and sensitivity owing to upstream TIMS-enhancement, making them perfect for use in automated spectral library matching.

Metabolite mapping
Chromatographic retention time, CCS, and m/z values are recorded for each isolated metabolite.

Metabolite Quantitation

Quantitation
The abundances of isolated metabolites are measured with accuracy and precision.



Multi-dimensional annotation confidence with timsMetabo and MetaboScape

BRUKER
MetaboScape®

timsMetabo Provides Clean MSMS Spectra

The TIMS separation of precursor ions results in MS/MS spectra that are free from noise signals, enabling more focused spectrum interpretation and reducing negative impacts on MS/MS matching scores. MetaboScape offers various tools for annotating MS/MS spectra, all of which benefit from cleaner spectra.

In-silico fragmentation and SmartFormula3D help in unraveling MS/MS spectra while discovering novel compounds. Spectral Libraries of different sizes and scopes allow matching measured MS/MS spectra to reference spectra.

NIST Library
BRUKER Daltronics

Bruker NIST 2020 Mass Spectral Library is assembled by the National Institute of Standards and Technology (NIST), and contains electron ionization (EI) spectra, gas chromatography retention indices, and tandem mass spectra for a wide range of small molecules.

MetaboBASE Personal Library
BRUKER Daltronics

Bruker MetaboBASE® Personal Library 3.0 contains MS/MS spectra from over 100,000 synthetic or isolated standards derived from the METLIN compound library. It also features in-silico generated MS/MS spectra for more than 233,000 compounds, measured in both positive and negative ionization modes at multiple collision energies.

HMDB Metabolite Library
BRUKER Daltronics

Bruker HMDB Metabolite Library 2.0 offers more than 6,000 MS and MS/MS spectra from over 800 reference standards sourced from the Human Metabolome Database (HMDB). The spectra are manually cureated, ensuring high-quality identification of metabolites found in urine, blood, other biofluids, and cell extracts.

MetaboBASE Plant Library
powerded by BRUKER & Sumner

Bruker MetaboBASE® Plant Library is tailored for plant and food research, providing reference MS/MS spectra and collision cross-section (CCS) values for commercial standards and putatively identified metabolites found in the model legume plant, *Medicago truncatula*.

Unearth the Hidden Gems with 4D-Metabolomics and MetaboScape

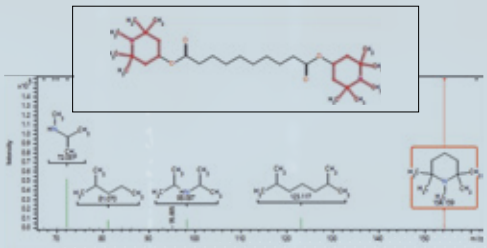
MetaboScape is a comprehensive software platform that enhances discovery Metabolomics by integrating advanced tools like MetFrag[1] *in-silico* fragmentation, CCS-Predict Pro, and BioTransformer.

MetFrag aids in the identification of unknown compound structures by predicting and scoring possible fragment ions, comparing them with experimental data to improve accuracy.

CCS-Predict Pro uses machine learning to predict collision cross section (CCS) values, adding an orthogonal criterion for compound annotation and improving the discrimination between isomers.

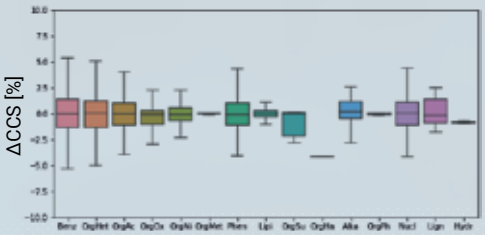
BioTransformer predicts metabolite structures based on known biotransformation reactions, aiding in the identification of drug and xenobiotic metabolites and providing insights into metabolic pathways.

Together, these tools enable MetaboScape to process large datasets efficiently, ensuring high-confidence identification of metabolites. This integrated approach supports the discovery of biomarkers and the understanding of metabolic changes in various biological contexts.



High-quality, information-rich MS/MS spectra combined with powerful automated and interactive annotation tools accelerate streamlined discovery in metabolomics.

CCS-Predict Pro



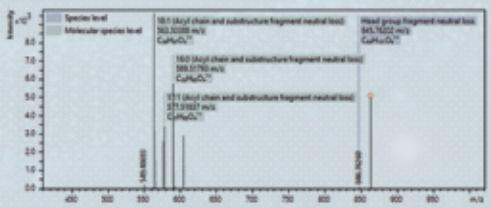
CCS-Predict Pro models are trained specifically for different ion types and improved models are continuously released.

[1] Wolf, Sebastian, et al.; BMC bioinformatics; 2010

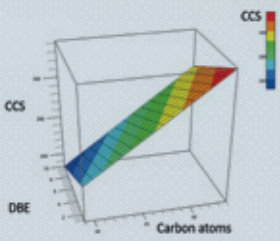
4D-Lipidomics with Rule-Based Annotation

MetaboScape's rule-based lipid annotation follows the guidelines of the Lipidomics Standards Initiative (LSI) to ensure accurate naming of lipid species. By applying selected fragmentation rules, it annotates and visualizes characteristic fragment peaks, supporting both species-level and molecular species-level annotations. This approach minimizes the risk of over-annotation and streamlines the automated identification of lipid features.

Class specific CCS hyperplane models help validating the ion mobility of lipid annotation candidates. Additionally, CCS and RT outlier detection is performed and improves annotation specificity.



MS/MS fragments get interpreted and annotated by MetaboScape's rule-based lipid annotation.



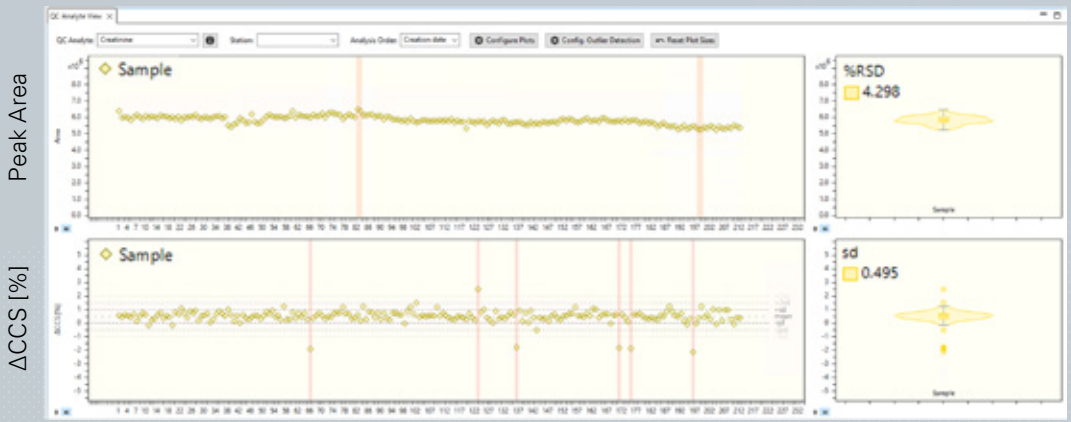
Lipid-class specific CCS hyperplane models validate lipid annotation candidates.

Data quality monitoring for precision results

BRUKER
TASQ®

Address large cohort studies with **precision**, leveraging Bruker's proven quantitation stability for comparable profiling and quantitation results from the first to the last sample analysed.

TASQ® RealTimeQC



- Replicate injections of 2 µl NIST SRM 3672 reference urine diluted 1 to 50.
- Bruker TASQ RealTimeQC software enabled monitoring of system performance over >200 injected samples.
- Continuous low %RSD values of <5% were achieved for peak areas in the urine sample injections as highlighted for creatinine.
- Deviations in delta CCS values [%] remained low throughout the sequence with standard deviations of 0.5%.

QSee™ 8-mix, Performance Test & TwinScape™

When pushing the boundaries of metabolomics and lipidomics-based discovery research, the importance of data quality is paramount.

The QSee Performance Test Solution offers an easy-to-use Quality Control workflow.

Dedicated columns for metabolomics and lipidomics applications, and compound mixtures, together with Standard Operating Procedures simplify the evaluation of LC-TIMS-MS data quality.

Automatic alignment with TwinScape uncovers trends in system performance over time. Stay on top of your performance!

Dr. Christoph Trautwein

University of Tübingen, Director Core Facility Metabolomics

"By integrating QSee Performance Testing into our lab routine, we're conveniently benchmarking our LC-TIMS-MS system performance before each experiment. The slim and intuitive workflow makes this a straightforward check, and the results provide assurance and peace of mind that we're consistently producing high quality data.

Confidence in our analytical results has never been higher, thanks to this comprehensive solution. It's truly a QC game-changer for our lab."

QSee Performance Test

TwinScape integration allows users to track their instrument performance over time, ensuring consistent performance and providing assurance prior to system use.

BRUKER TwinScape™

- Tracking of QSee results
- Visualization of trends
- Long-term surveillance

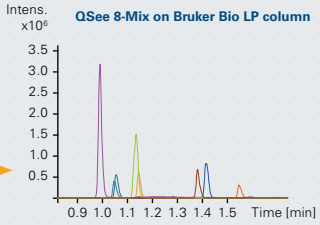
For Long-term surveillance

Longitudinal data can be used for trend analysis

Upload to TwinScape

QSee™ Performance Test

- Data acquisition
- Processing
- Reporting



For Performance Testing

Each QSee test returns a report with a pass or fail feedback

A broader ecosystem for discovery

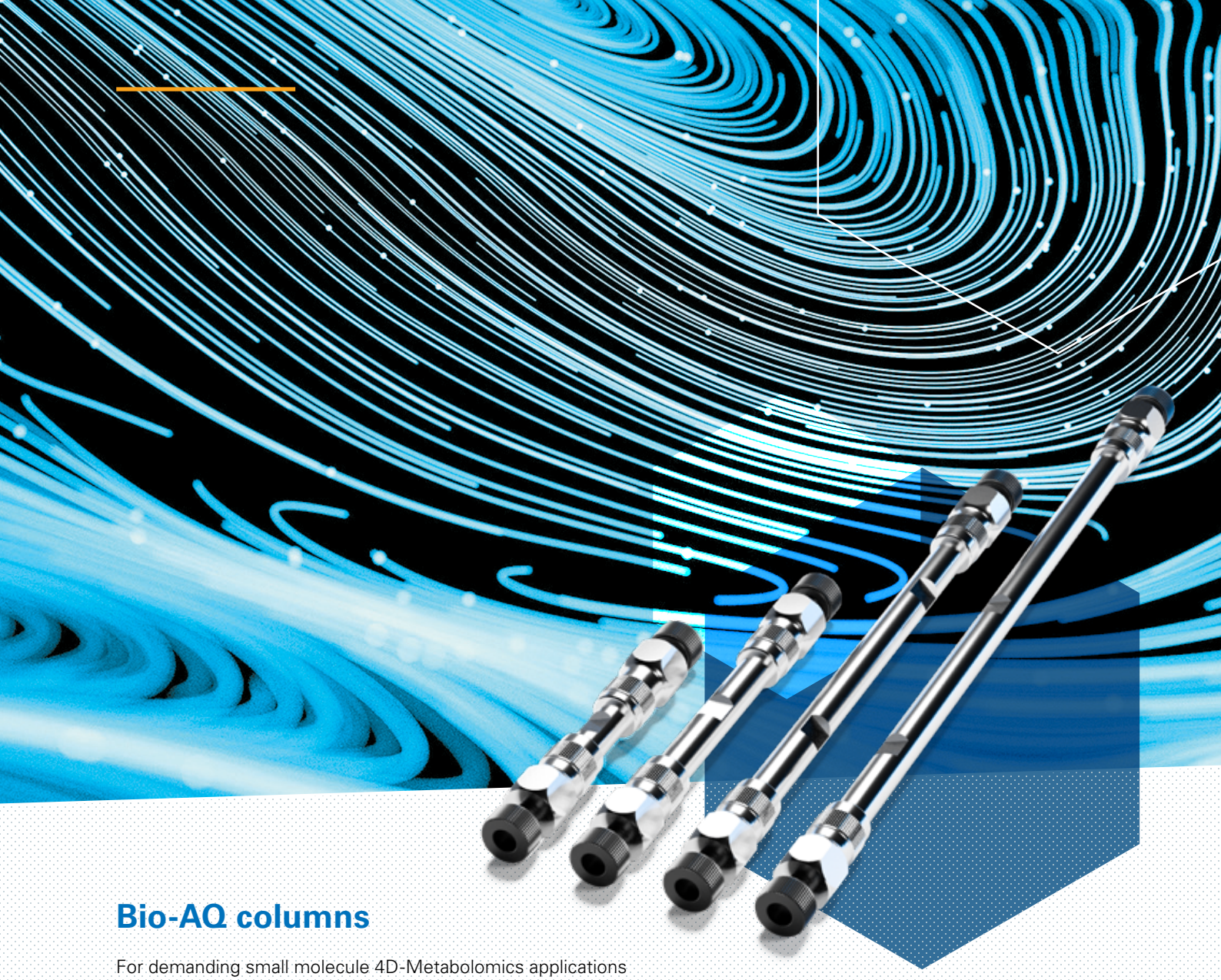
Bio-LP columns

For high confidence 4D-Lipidomics workflows

Product features:

- Bio-LP columns provide fast and high-capacity separations of relevant lipid classes in complex matrices for improved lipidome coverage.
- With PASEF technology, even the smallest LC peaks reveal their secrets—delivering high sensitivity, robustness, and an extra dimension of separation for improved peak capacity.
- Simplified data analysis owing to improved chromatographic peak shapes, peak resolutions and reproducible retention times leads to higher confidence in lipid annotations.
- Low system pressure for reliable performance.

The bonded C8 phase allows excellent retention and separation of a broad range of lipid species found in biofluids and tissue extracts, while also enabling their clean elution from the column with a lower proportion of highly viscous solvent (requiring 50% isopropanol versus the 90% formulation conventionally used for C18-based reversed-phase lipid separations). Together with a lower overall system pressure, these benefits yield higher peak capacity separations with greater reliability for precision lipid profiling.



Bio-AQ columns

For demanding small molecule 4D-Metabolomics applications

Product features:

- Bio-AQ columns enable fast and high-capacity separation of relevant complex matrices for improved metabolome coverage.
- Unique C18-bonded phase with integral polar functionality compatible with 100 % aqueous solvents for improved retention of polar compounds.
- Low system pressure for reliable performance.
- Enhanced data analysis and confidence: Improving chromatographic peak shapes, peak resolutions, and ensuring reproducible retention times foster greater confidence in small molecule annotations.
- Excellent reproducibility and column lifetime featuring ultra high purity, base deactivated silica.

Reversed-phase separations are a stable chromatographic technique in metabolomics workflows owing to their excellent performance characteristics and proven reliability. However, not all C18-based stationary phases are fit for the purpose of maximizing small metabolite retention. With 100% aqueous mobile phase compatibility, polar compound retention is maximized.

Discover MoRE with our next-generation workhorse for 4D-Metabolomics and 4D-Lipidomics

- Game-changing sensitivity for TIMS-enabled small molecule analysis
- 4D LC-TIMS-MS/MS separations and CCS measurements at scale for unprecedented specificity and annotation confidence
- TIMS-enabled confidence in automated analyte annotation
- A digital metabolome archive of every sample analyzed
- Powerful 4D-Lipidomics and 4D-Proteomics capabilities
- Fully featured 4D-enabled quality control and established software ecosystem

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