Metabolomics

- Powering Comprehensive Studies
The accurate determination of changes in small molecule profiles related to a disease, therapeutic intervention, genetic modification or environmental variation is central to all metabolomics studies.

Bruker remains the leader in integrated solutions for metabolomics with its latest innovations for hyphenated NMR, LC-MS and GC-MS technologies. These systems can be used for a multitude of metabolomics studies and are very well equipped to detect, identify, and quantify metabolites across the large chemical diversity of compounds building the metabolome.

Many different pieces of information have to be linked in metabolomics experiments. Bruker provides all you need in a comprehensive, integrated system adjustable to your growing requirements.

**Bruker’s analytical systems for targeted and non-targeted metabolomics are used in:**

- Clinical research
- Public health studies
- Plant science
- Nutrition & food
- Microbial research
- Environmental & ecology research
- Drug discovery & development
- Biochemistry
- Systems biology
Bruker solutions for the main Metabolomics workflows:

**Non-targeted profiling**

Maximum coverage of the metabolome’s chemical space can be achieved by utilizing Bruker’s high performance LC-MS, GC-MS and NMR systems in conjunction with dedicated software for data evaluation. These systems combine all necessary tools for feature extraction, statistical evaluation and compound identification. The unique hyphenation of high resolution MS and NMR, the MetabolicProfiler™, enables rapid biomarker detection and identification by combined statistical evaluation of MS and NMR data.

**Targeted analysis - biomarker validation**

Identified biomarkers can be validated in targeted metabolomics experiments, where a limited number of compounds are quantified.

For such tasks, Bruker offers both dedicated triple quadrupole MS systems with excellent sensitivity and powerful quantitation capabilities as well as more versatile ESI-UHR-QTOF MS systems that provide highly accurate data with a wide dynamic range and excellent resolution for the simultaneous analysis of both high- and low-abundance metabolites.

Bruker’s NMR based food screening solutions are best suited for sample classification e.g. for food quality control and can be combined with Bruker’s MS solutions for food safety studies.

**impact II™ – omics knowledge generation**

Equipped with the latest of Bruker’s time-of-flight technology, the impact II delivers the best of what only TOF can do: combined resolution, sensitivity, mass accuracy and dynamic range, over the full mass range.

Because biology’s diversity demands versatility …
Transform Your Data into Knowledge

Non-targeted Metabolomics – Detect and ID possible Biomarkers using ProfileAnalysis

- Increased productivity using “Find Molecular Features” – automatically extract all relevant information from complex LC-MS datasets
- Ease of use for handling complex data sets –
  - Retention time alignment
  - Different scaling, normalization & filtering options
- Quickly pinpoint relevant information by supervised and unsupervised statistics: PCA, t-Test, ANOVA, PLS-DA, etc.

De novo identification of target compound X

A) Accurate mass and isotopic fidelity in MS and MS/MS spectra; B) SmartFormula3D™ - unique molecular formula generation capabilities by combining accurate mass and isotopic pattern information in MS and MS/MS spectra; C) In-silico Fragmentation via direct Link to MetFrag (IPB Halle, Germany); D) Detailed evaluation using the FragmentExplorer supports the in-silico fragments generated by MetFrag.; E) Verification of the identity with reference standard.
Combine Targeted and Non-Targeted Workflows for Deeper Insights

- Hypothesis driven targeted data evaluation quickly turns LC-QTOF-MS data into knowledge
- Rapidly screen for known metabolites
- Biochemical pathway driven workflows
- Deeper insights by sample batch processing and retrospective data analysis

Get twice the answers from Compass PathwayScreener.

Hypothesis based pathway driven analysis – PathwayScreener™

Hypothesis generation

Full scan LC-MS data (MS/MS)

Non-targeted data evaluation

Unknown ID

Novel hypothesis

Pathway directed targeted data evaluation

Knowledge

Tailored views enable straightforward data review

Batch of samples

Chromatogram

Analytes

Area

Analysis

Read more:
Bruker Daltonics
Application Note ET-38
Accelerate Known Target Compound Identification

- Accelerate data analysis in metabolomics research with this tandem mass spectrometry accurate-mass library
- Increase your productivity with high-confidence identification based on manually curated MS/MS spectra
- Obtain deeper insights with links to external repositories for bringing identified molecules quickly into a biological context

“We are delighted to have collaborated with Bruker to produce a new Human Metabolite MS/MS accurate-mass library with much improved spectral quality. This library, along with an automated spectral acquisition and processing strategy, allows researchers to identify metabolites very quickly and with highest confidence.”

Dr. Liang Li, Professor of Chemistry, University of Alberta, (co-PI of the Human Metabolome Database (HMDB) project) explained.
**Enhanced Metabolite Profiling by GC-MS**

... use the same QTOF MS for LC and GC analysis

Metabolomics studies based on gas chromatography-mass spectrometry (GC-MS) are well-established and typically employ electron impact (EI) ionisation. Unfortunately, many possible biomarkers detected in these experiments cannot be identified due to the lack of EI reference spectra for a majority of biologically relevant compounds.

Hyphenating GC with HRAM TOF-MS technology by soft atmospheric pressure ionisation (APCI) can preserve the molecular ion information and deliver accurate mass and isotopic pattern information. This data enables identification of possible biomarkers which remained “unknowns” up until now.

**GC-APCI-MS: Identification by accurate mass and isotopic pattern**

![Graph showing accurate mass and isotopic pattern](image)

“GC-APCI II is expected to reveal more significantly regulated metabolites in metabolic fingerprinting and subsequently to enable their sensitive quantification.”

Dr. Katja Dettmer, Institute of Functional Genomics, Regensburg University, Germany

**Novel GC-APCI II source for**

- Improved LLQQ and dynamic range by optimized source chamber design
- Revealing more significantly regulated metabolites
- Improved unknown ID capabilities by automated calibration routines
- Increased ease of use by tool free switching between GC and LC mode

Read more:
- Bruker Daltonics Application Note ET-22
- "Enhanced metabolite profiling using a redesigned atmospheric pressure chemical ionization source for gas chromatography coupled to high-resolution time-of-flight mass spectrometry"

Christian J. Wachsmuth, Thomas A. Hahn, Peter J. Oefner, Katja Dettmer
Analytical and Bioanalytical Chemistry 2015 in press
eXtreme Resolution for Deeper Insights

Spatial Metabolomics by MALDI Imaging
- Direct localization of lipids, metabolites, drugs, and peptides
- High selectivity using extreme resolution
- High specificity through unparalleled mass accuracy

In this rat testis dataset, the two displayed lipid signals have a mass difference of only 3 mDa. The signal shown in green is found in the seminiferous tubules, the one in red is seen in the interstitial space. At a resolving power of 470k the signals are clearly resolved.

Elemental composition by IFS – Isotopic Fine Structure
- Read out elemental compositions based on eXtreme Resolution
- Create powerful streamlined workflows to efficiently discover and ID new metabolites
  - Read more: Bruker Daltonics Application Note FTMS-43

Rapid profiling by USP – Ultra Fast Statistical Profiling
- Rapid profiling of complex metabolic extracts
- Automated data acquisition by ESI or MALDI
- Increased sample throughput 10-100x
  - Read more: Bruker Daltonics Application Note FTMS-51
Unambiguously Identify Unknown Compounds by MS + NMR

Fully integrated and automated NMR and HRAM-MS

- Generate complementary metabolomics data for statistical analysis as well as for the identification of unknown compounds
- Combine the structural capabilities and highest reproducibility of NMR with mass accuracy and sensitivity of MS - enabling identification and quantification of metabolites for biomarker discovery

“Mass spectrometry and NMR are the two major platforms used for unknown identification in metabolomics research because they provide complementary information for de novo identification”

Professor Kazuki Saito
Group Director of the Metabolomics Research Group, RIKEN Center for Sustainable Resource Science, Yokohama, Japan, Professor of the Graduate School of Pharmaceutical Sciences Chiba University, Japan

Read more:
Bruker Daltonics Application Note LCMS-85

Verify Your Small Molecule Structures

The Bruker FUSION-SV™ software solution for rapid automatic structure verification allows scientists to easily integrate and combine high resolution accurate mass (HRAM) mass spectrometry and complementary NMR data.

Bruker FUSION-SV Features

- Fully automatic structure verification for small organic molecules synergizing NMR and MS data into one result
- Structure centric workflow which guides chemists straight to a clear and meaningful report
- Bruker FUSION-SV’s intuitive operation enables the rapid deployment of structure verification workflows

Read more:
Bruker Daltonics FUSION-SV Flyer

Configurable Workbench layout
Boost Your Metabolomics Impact

MetabolicProfiler
Fully integrated and automated NMR and HRAM-MS generate complementary metabolomics data for statistical analysis as well as for the identification of unknown compounds.

GC-APCI Source
Unique combination of high-resolution accurate mass MS with GC enables identification of unknowns in GC-MS based metabolomics.

Triple Quadrupole Mass Spectrometers
Deliver exceptional sensitivity, precision, accuracy, linearity, and a wide dynamic range for targeted metabolomics.

solariX XR FT-ICR-MS
Providing eXtreme Resolution (XR™) to reveal the fine structure (IFS-MS) in isotopic patterns that are uniquely specific to the exact molecular formulae of the detected compounds. Gain unique insights into highly complex samples.

ESI–QTOF mass spectrometers featuring Instant Expertise™
High performance ESI-TOF-MS instruments for full sensitivity and resolution at fast scan speeds to detect, resolve, identify and quantify even low-level metabolites.
Recommended Metabolomics Publications

**Plant Metabolomics**
Combination of liquid chromatography-Fourier transform ion cyclotron resonance-mass spectrometry with $^{13}$C-labeling for chemical assignment of sulfur-containing metabolites in onion bulbs.

Annotating unknown components from GC/EI-MS-based metabolite profiling experiments using GC/APCI(+)-QTOFMS

**Bacterial Metabolomics**
Microbial strain prioritization using metabolomics tools for the discovery of natural products

Myxoprincimide, a novel natural product from *myxococcus xanthus* discovered by a comprehensive secondary metabolome mining approach

**Clinical Metabolomics**

Molecular cartography in acute *chlamydia pneumoniae* infections – a non-targeted metabolomics approach.

**Food & Environmental**
Apple peels, from seven cultivars, have lipase-inhibitory activity and contain numerous ursenoic acids as identified by LC-ESI-QTOF-HRMS

Ultra high performance liquid chromatography-time of flight mass spectrometry for analysis of avocado fruit metabolites: Method evaluation and applicability to the analysis of ripening degrees

**Lipidomics**
Optimizing a ultrahigh pressure liquid chromatography-time of flight mass spectrometry approach using a novel sub-2μm core-shell particle for in depth lipidomic profiling of *caenorhabditis elegans*.

**Invertebrate Metabolomics**
Metabolomic changes in *caenorhabditis elegans* lifespan mutants as evident from GC–EI–MS and GC–APCI–TOF–MS profiling

A novel ion pairing LC/MS metabolomics protocol for study of a variety of biologically relevant polar metabolites

**Spatial Metabolomics**
Molecular cartography of the human skin surface in 3D
Think Biology!

In the past decade modern metabolomics has quickly grown and become widely adopted. The growing number of detectable and identifiable substances increase the need for comprehensive workflows.

Bruker remains the leader in integrated solutions for metabolomics with its latest innovations for hyphenated NMR, LC-MS and GC-MS technology.

Gain Deeper Insights

“We are pushing the boundaries of metabolite identification in our lab with Bruker’s hyphenated UHPLC-UV-MS-SPE-NMR system. A combination of complementary MS and NMR technology will be used to accelerate identification of unknown compounds.”

Professor Lloyd W. Sumner
Samuel Roberts Noble Foundation Ardmore, OK, USA