Metabolomics

- Novel solutions for Metabolomics, Lipidomics and high-throughput Phenomics

Powerful Yet Intuitive

The metabolome is the final manifestation of biochemical pathways. It shows an extremely large variety of structural classes as it includes the complete set of metabolites of all cellular processes.

Changes in the metabolite composition reflect the outcome (phenotype) of interactions at the genomic, transcriptomic and proteomic levels. Therefore, studying the phenome is a cornerstone to gain deeper insights related to e.g. diseases, therapeutic interventions or environmental influences.

MetaboScape helps to find regulated biomarkers in the global profiling of large sample cohorts and offers tools for automated and confident identification.

MetaboScape software delivers key advantages such as:

- Intuitive **T-ReX** algorithm (**T**ime aligned **R**egion complete **eX**traction) for fully automatic calibration, retention time alignment, adduct management and recursive feature extraction

- T-ReX offers universal processing skills:
  New! T-ReX² for MALDI-QTOF-MS
  T-ReX 2D for FIA-MRMS and MALDI-MRMS
  T-ReX 3D LC-QTOF-MS and LC-MRMS
  T-ReX 4D LC-TIMS-MS

- Processing of **large data sets** (> 1000 LC-MS injections) e.g. for ultra-fast chromatography-free FIA-MRMS workflows of > 200 samples/day

- "**Annotation Quality**" scoring boosts confidence in compound identification with up to five specific indicators of data quality

- Workflow integration with SCiLS Lab Pro for identification and spatial distribution mapping of specific metabolites and lipids. This data processing pipeline supports unique timsTOF fleX (MALDI-QTOF-MS) and MALDI-MRMS data

Confidently venture into the unknown

Metabolomics and high-throughput Phenomics

Flow Injection Analysis - MRMS provides high sample throughput for phenomics research with ~5 min cycle time per sample (including both polarities) - more than a factor of 10x faster than conventional LC-MS methods. FIA-MRMS can generate thousands of molecular formulae for metabolites in every sample and reveals additional compounds not detectable via LC-MS. scimaX and solariX platforms also provide complementary MALDI Imaging capabilities for SpatialOMx.

The Phenomics Workhorse

Complementary deep metabolomics by UHPLC-QTOF-MS/MS can 'detect' thousands of features and identify hundreds of metabolites by combining different LC methods and positive and negative ion runs. The impact II is perfectly suited to meet the demands of large profiling studies.

The Phenomics Workhorse featuring TIMS and MALDI Imaging

The technology of the impact II raised to the next dimension: The timsTOF instrument series offers **T**rapped **I**on **M**obility **S**pectrometry and gives access to the exact collisional cross section values for higher confidence in compound IDs. The combined ESI and MALDI source on the novel timsTOF fleX enables direct localization of lipids, metabolites, and drugs for an integrated spatial omics workflow that combines MALDI Imaging and ESI-based metabolomics and lipidomics on the same platform.

NMR based clinical research phenomics

Avance IVDr 600 MHz NMR can measure ~250 plasma or serum samples per day, and reliably identifies and quantitates the ~100+ most abundant metabolites in phenomics research, e.g., in the IPCN*.

For research use only
* IPCN = International Phenome Center Network (led by Prof. Jeremy Nicholson, ICL)

How robust is your data quality over a sequence of several weeks? – The "Phenomics workhorse"

Achieving a high data quality is mandatory for complex profiling experiments. Large batches of samples frequently bring along an increasing build-up of contamination. The larger the batch, the more important a steady data quality becomes for subsequent statistical calculations.

The impact II offers outstanding robustness and excellent long-term stability for long sample sequences typical of large cohort studies, making it truly a phenomics workhorse.

Figure 1 shows the development of data quality over > 1100 injections, covering a time span of more than 14 days [1]. The mass accuracy and the isotopic pattern quality (mSigma value) e.g., of uric acid did not degrade. As well, the peak areas showed no decreasing trends.

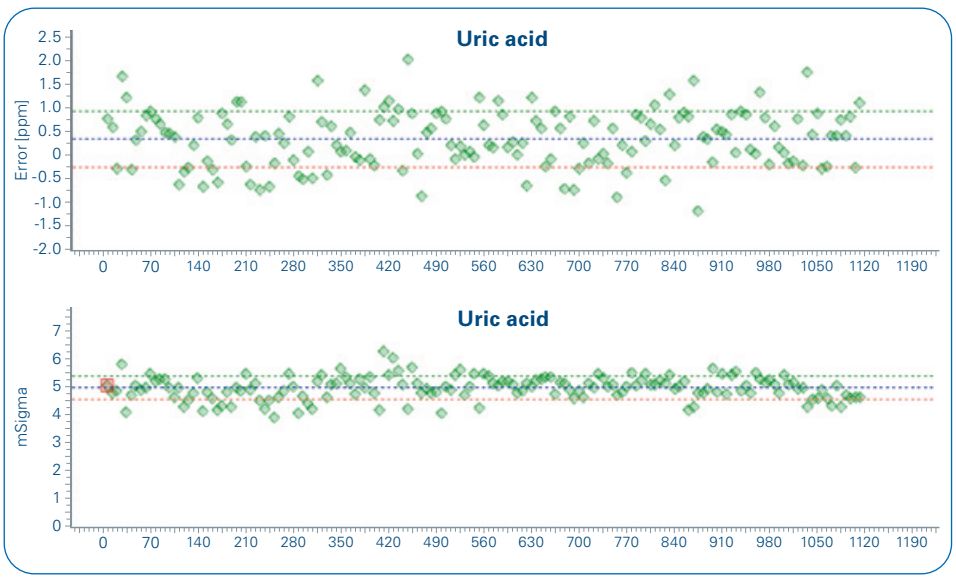


Figure 1: Development of mass accuracy and isotopic pattern quality over > 1100 injections. Every 7th data point is shown

The Phenomics workhorse delivers:

- Unmatched long-term stability of data quality
- No compromise Full Sensitivity Resolution
- InstantExpertise™ for simultaneous acquisition of MS and MS/MS information in "one shot"
- Isotopic pattern fidelity, facilitating molecular formula generation
- Dynamic range of > 4 orders of magnitude for quantitative performance without limitations

[1] The data was acquired following a fixed standard operating procedure: M.R. Lewis, J.T.M. Pearce, K. Spagou, M. Green, A.C. Dona, A.H.Y. Yuen, M. David, D.J. Berry, K. Chapell, V. Horneffer-van der Sluis, R. Shaw, S. Lovestone, P. Elliott, J. Shockcor, J.C. Lindon, O. Cloarec, Z. Takats, E. Holmes, J.K. Nicholson, *Analytical Chemistry* (2016), **88**, 9004-9013

Simplified T-ReX LC-QTOF solution for non-targeted Metabolomics

Confidently identifying compounds relevant for metabolic processes relies on several crucial steps, including sample preparation, data acquisition, data pre-processing and data evaluation.
In order to simplify and harmonize this workflow, Bruker developed the **T-ReX LC-QTOF solution**:

1. Sample preparation

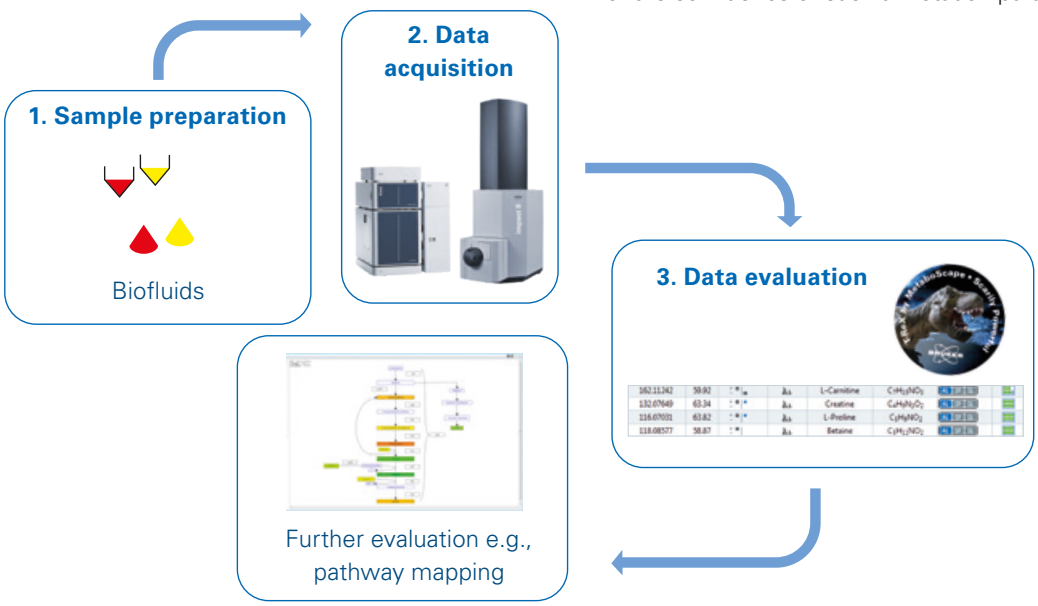
- Standard Operating Procedures (SOPs) for the preparation of typical clinical research samples, e.g., urine and plasma

2. Data acquisition

- ELUTE UHPLC for analyzing large sample cohorts with high retention time stability
- Metabolomics Reverse Phase column kit to enable matching of retention times to the Bruker HMDB Metabolite Library 2.0
- impact II QTOF-MS system, with a robust performance for large profiling studies of complex samples

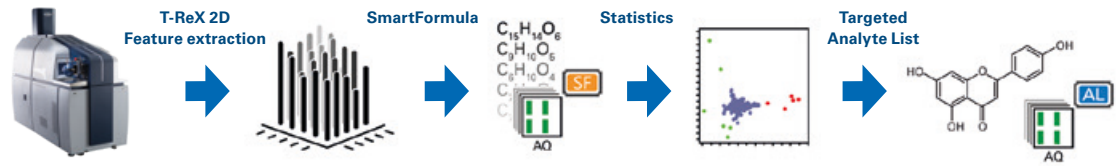
3. Data evaluation

- MetaboScape software for automatic identification of known compounds, incl. the T-ReX 3D algorithm for a minimized false negative rate in statistical analysis
- Bruker HMDB Metabolite Library 2.0, providing MS/MS spectra for > 880, and retention time information for > 600 metabolites, as prerequisite for confident identification of relevant markers
- Bruker MetaboBASE Personal Library 3.0: MS/MS spectra from more than 100,000 compounds – endogenous metabolites, drugs, pesticides and other chemical entities
- Annotation Quality Scoring: A fast overview of the confidence of each annotation parameter



Dr. Liang Li, Professor of Chemistry, University of Alberta, Canada
"We are delighted to have collaborated with Bruker to produce the comprehensive **T-ReX LC-QTOF solution**. *The complete out of the box solution provides the basis for high confidence identification of relevant known endogenous metabolites and enables to set these into a biological context using pathway mapping. This solution will provide researchers a head start in non-targeted metabolomics for typical research samples like urine or plasma."*

Achieve high sample throughput with MRMS aXelerate ...



LC free MRMS measurements with sub-ppm mass accuracy

Feature Matrix incl. Isotopic Patterns and Isotopic Fine Structure

Unique Molecular Formulae Annotation incl. Annotation Quality Scoring

Determine Compounds of Interest

Putative Structure Annotations

Perfect for Metabolomics, Phenomics or any other large-scale sample evaluation:

MRMS aXelerate is based on the extreme resolving power of the scimaX MRMS system and uses MetaboScape to enable a powerful chromatography-free solution.

The FIA-MRMS approach enables the measurement of > 200 samples per day in both, positive and negative ion modes.

The extreme resolution allows for direct sample analysis and enables true high sample throughput complementary to established NMR based solutions. From the largest unknown to the smallest, MRMS aXelerate utilizes a combination of ultra-high mass accuracy, True Isotope Pattern, and Isotopic Fine Structure to ensure confident assignments of molecular formulae at any level.

- **Accelerate** sample throughput enabling large cohort and longitudinal studies in phenomics research (> 200 samples/day)
- **Simultaneous analysis** of known and unknown metabolites
- **Access compounds** not readily detectable by LC-MS analysis

Prof. Philippe Schmitt-Kopplin, Analytical BioGeoChemistry, Helmholtz Zentrum München, Germany

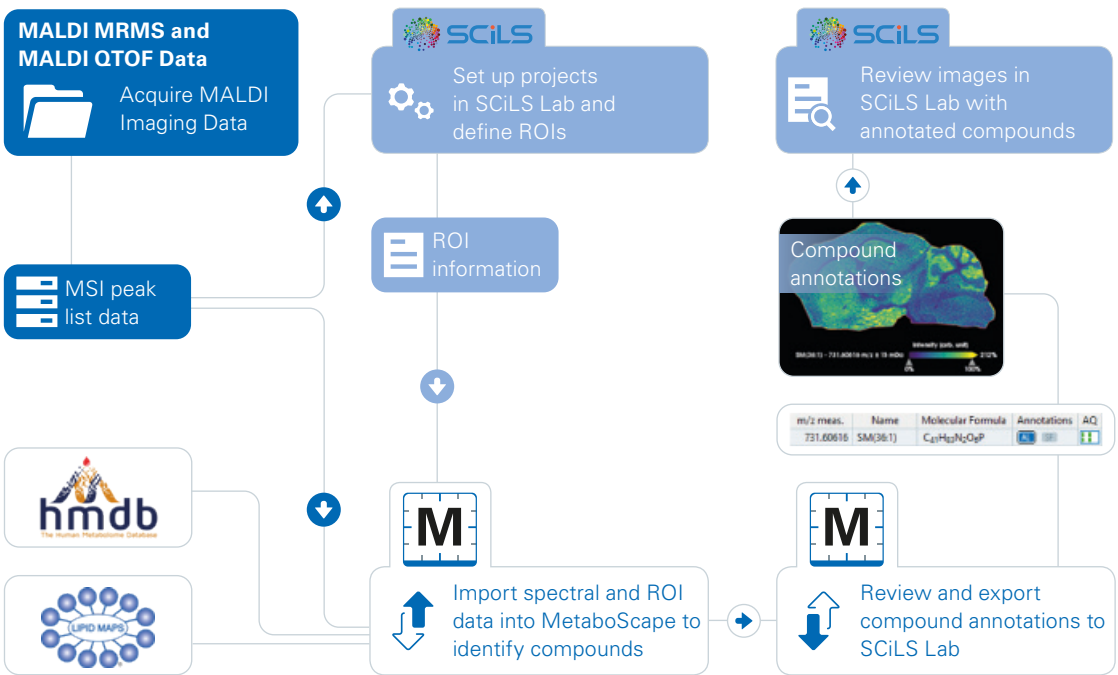
"We set up new discovery approaches to describe the compositional space of any complex system in biology and geochemistry. MRMS eXtreme Resolution enables us to address next generation metabotyping, i.e. simultaneous rapid description of hundreds of known and thousands of new metabolites relevant for dynamic biological/chemical processes. MRMS in combination with MetaboScape will also enable other researchers to shed light to this new exiting research field of this yet dark metabolome."

Discover – Validate – Localize, Think Biology!

Spatial Metabolomics by MALDI Imaging

- Direct localization of lipids, metabolites, drugs, and peptides
- SCiLS Lab and MetaboScape featuring a novel mass spectrometry imaging bioinformatics pipeline for identification of metabolites and lipids from tissue making use of T-ReX²
- Supporting MALDI-MRMS for high selectivity using extreme resolution and providing Isotopic Fine Structure for unambiguous formula assignment
- Leveraging timsTOF fleX by enabling on the same platform:
  - MALDI Imaging for discovering relevant ions
  - Confident identification of targets in MetaboScape
  - Optional validation and improved anno-tation confidences by complementary chromatographic retention times- and ion mobility cross section and PASEF-MS/MS

Novel Mass Spectrometry Imaging Workflow



Novel mass spectrometry imaging workflow: Automated annotation of metabolites and lipids from tissue
**Lipid Maps and HMDB are not Bruker products.*

Look Out!

MetaboScape will provide deeper insights and simplify your metabolomics and lipidomics data processing

The "Phenomics workhorse": the impact II LC-QTOF provides outstanding robustness for large cohort studies

scimaX MRMS aXelerate enables the measurement of > 200 samples per day with chromatography-free acquisitions for large-scale profiling studies

Confidence by powerful T-ReX feature extraction technology

timsTOF fleX provides MALDI Imaging and LC based metabolomics and lipidomics capabilities

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