Uniting metabolomics data processing and highly confident annotation across six MS instrumental set ups: MetaboScape 5.0

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Introduction

Metabolomics approaches may be motivated in a variety of ways, pushing different criteria into foreground: speed (throughput), separation, and/or accuracy. Tailored to these prioritized criteria different instrumental set ups will fall into favor. Combining different platforms, complementing their respective strengths, ultimately closes the gap between high-throughput and in-depth analysis methods. MetaboScape 5.0, including the feature extraction and ion deconvolution algorithms T-ReX 2D, 3D, 4D, and T-ReX² integrates the processing-, dereplication- and unknown annotation-workflows for FIA-MRMS, LC-MRMS, LC-ESI-TOF, and LC-ESI-TIMS-TOF and SpatialOMx in a single software.

Feature processing and ion deconvolution across hundreds of analyses

Due to its speed, especially FIA-MRMS is suited to create experiments containing several hundreds of measurements. The T-ReX algorithms perform feature picking, deisotoping, and deadducting across all these measurements. Where LC is involved, retention time alignments are computed to ensure solid feature tables. The deadducting is designed to create unanimous ion interpretation across all analyses. This is even true for feature tables combined from positive and negative polarity. Intelligent filter parameters provide an option to account for multifactorial designs during feature assessment.

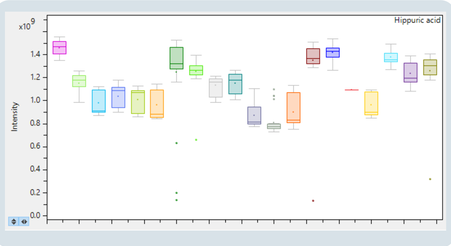

Fig. 2 Boxplot of Hippuric acid intensities of 20 groups and in total 560 FIA-MRMS spectra from urine samples, measured in negative mode. Statistics and visualizations profit from experimental designs.

MetaboScape combines the key features of MS instruments in one single software

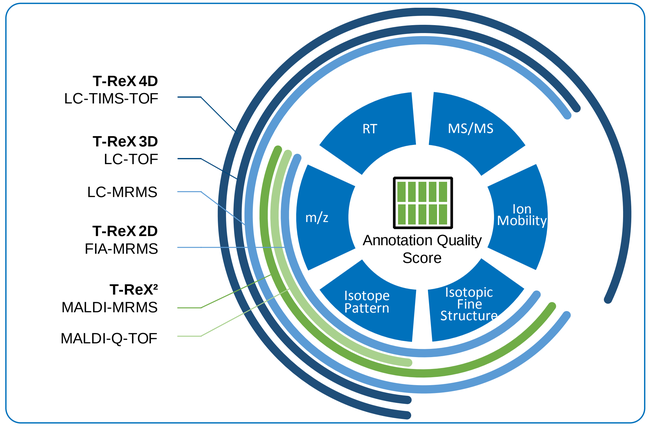

Fig. 1 (left)
MetaboScape and the T-ReX workflows support different instrument types, exploiting the respective strengths of each: For the sake of separation, annotation quality, or throughput. The wheel on the left focuses on the annotation quality criteria, MetaboScape extracts from each platform and reports to quantify the confidence in any annotation. Profit from all the bits and pieces of information in 4D Metabolomics and 4D Lipidomics experiments.

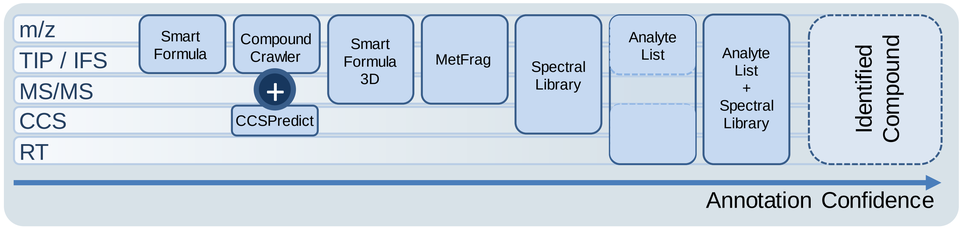

Fig. 3 (below)
In MetaboScape, compound identification is supported by a variety of (semi-) automated tools, which are highly integrated and enable the creation of annotations at increasing levels of specificity and confidence.

Both automated and manual tools for metabolite annotation seamlessly adapt to the annotation quality criteria each instrumental platform provides. The chromatographic dimension from LCs is a proven indicator for annotation of knowns. MRMS instruments unlock high-resolution mass accuracy and the power to resolve isotopic fine structure (IFS). Ion mobility serves as an additional indicator for annotations. PASEF-MS/MS acquisition additionally provides a high coverage of MS/MS spectra. To assess the confidence in any annotation, all five criteria are reported in a concise but detailed summary, called the **A**nnotation **Q**uality.

While Smart Formula, Spectral Library and Analyte List are applied to automatically annotate entire feature tables, other tools allow for manual deep-dives, focusing at the identication of single metabolites. Examples are MetFrag[1] and CCSPredict, as depicted in Figs. 5 and 6.

SpatialOMx – SCiLS and MetaboScape: The molecular imaging workflow

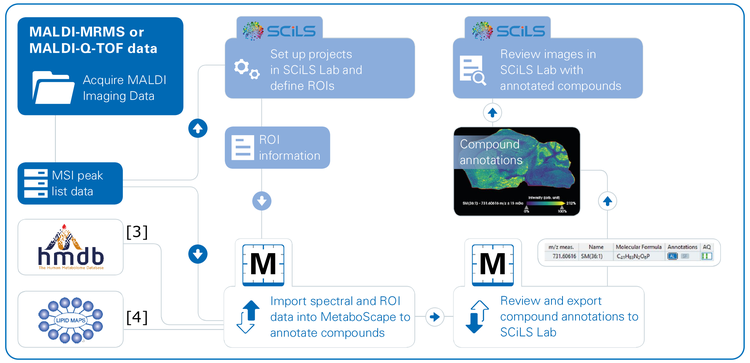

Fig. 4
A novel software workflow for the identification of signals using data from MALDI-Q-TOF or MALDI-MRMS.
Starting in SCiLS Lab, projects can be set up and regions of interest (ROI) can be defined. MetaboScape then allows for the deisotoping, deadducting and annotation of the extracted features by T-ReX². Finally, display the annotated features in the rich User Interface of SCiLS Lab.

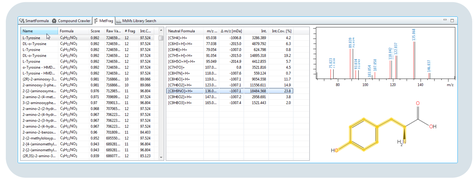

Fig. 5 Verifying structure annotations using MetFrag[1] *in-silico* fragmentation, the MetFrag score and intensity coverage – all available in MetaboScape.

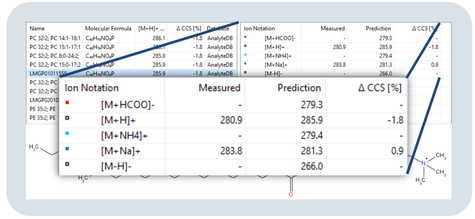

Fig. 6 Comparison of measured and predicted CCS values of lipids[2] adds to annotation confidence.

[1] Ruttkies et al.; J. Cheminf. 2016, 8:3
[2] Zhou et al.; Anal. Chem., 2017, 89 (17)
[3] http://www.hmdb.ca/
[4] http://lipidmaps.org/

Conclusions

- MetaboScape provides consistent processing and annotation workflows for multiple instrument types within a single software solution.
- Process and explore more than a thousand measurements in a single experiment.
- While using high-throughput and automated tools, deep-dives into details are supported, also featuring machine learning based CCS prediction for 4D Lipidomics.

MetaboScape