From bulk organic matter profiling to specific metabolite identification: Improving metabolomics data analysis, annotation, interpretation, and integration.

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Overview

Metabolites are the chemical currency of the environment, they are readily used, transformed and exchanged by the microorganisms within a system [1]. Characterizing the metabolome is key to understanding mechanisms driving most ecosystem functions [2]. However, metabolite heterogeneity and complexity make the analysis of metabolomics data a challenging endeavor [3]. Even though metabolomics has long been overshadowed by other 'omics, metabolites are usually at the end of complex biochemical cascades allowing for a better understanding of phenotypic responses [1] by providing a functional snapshot of upstream biological processes that may have been missed by genomics and proteomics. As such, the objective of this work is to develop tools to **optimize**, **streamline**, and **improve** current metabolomics data analysis pipelines.

MetaboDirect

- An Easy-to-use, command line-based pipeline that was developed for the bulk characterization of organic matter by high resolution mass spectrometry (FTICR-MS).
- Designed to facilitate data exploration, visualization, to perform chemodiversity and statistical analysis, and to build mass difference-based transformation networks [4].

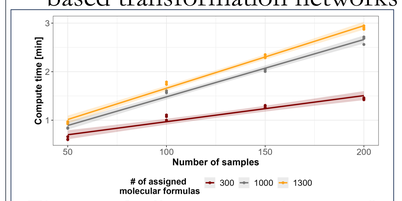
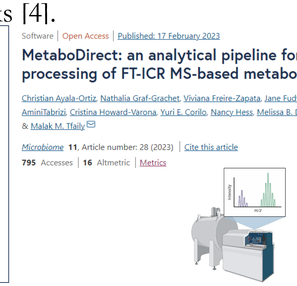


Figure 1. Compute times of MetaboDirect



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What's next for MetaboDirect?

- MetaboDirect will be integrated with CoreMS, a suite of tools focused on MS data processing and management, developed by EMSL at PNNL).
- It will exist as an optional module that can be run along the existing analysis pipelines provided by CoreMS.

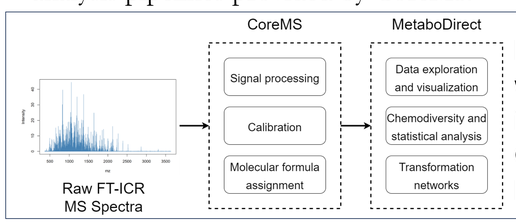

Figure 2. Simplified workflow of the integration of CoreMS and MetaboDirect

MetaboTandem

- This software is currently being developed as both, an R package and a Shiny app for Liquid Chromatography with tandem mass spectrometry (LC-MS/MS).
- Source code will be available from GitHub and as a Docker container.
- This software is currently focused on producing a more-in-depth metabolite annotation by combining the use of custom annotation databases, with public online databases and *in-silico* molecular structure predictions.

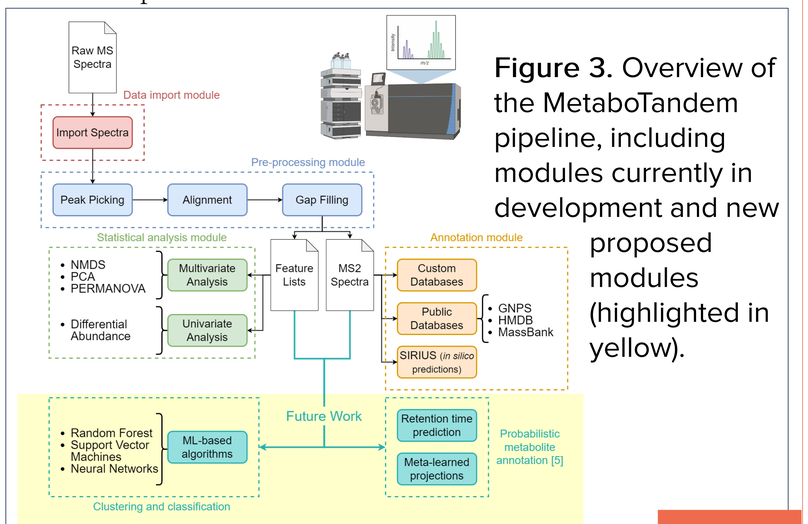

Figure 3. Overview of the MetaboTandem pipeline, including modules currently in development and new proposed modules (highlighted in yellow).

For an example on how ML-based algorithms are being used for: **sample clustering and classification,** please check the poster by **Rajakaruna, et al.**

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Future Work

- Future efforts intend to solve additional challenges in metabolomics: **(A) improvement of metabolite annotation**, and (B) **dealing with larger and more complex data sets by leveraging computer science approaches** (i.e., machine learning) to aid in the analysis of metabolomics data.

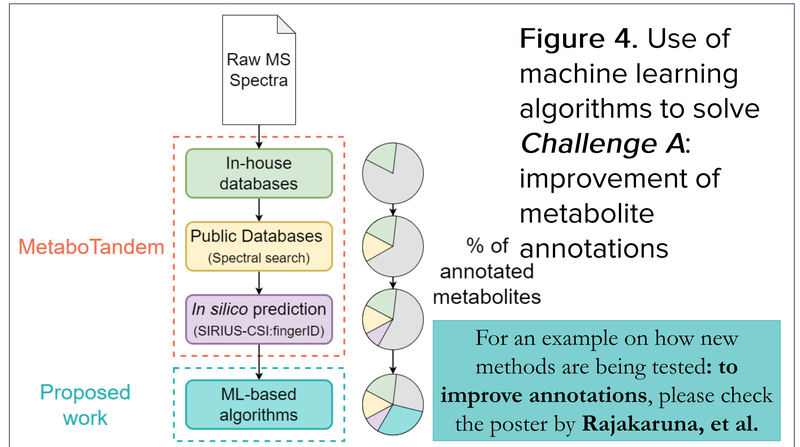

Figure 4. Use of machine learning algorithms to solve ***Challenge A***: improvement of metabolite annotations

For an example on how new methods are being tested**: to improve annotations**, please check the poster by **Rajakaruna, et al.**

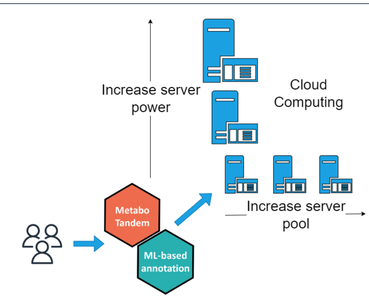

Figure 5. Use of cloud computing to solve ***Challenge B***: handling data of even increasing size and complexity

REFERENCES

1. Fiehn, O., Metabolomics — the link between genotypes and phenotypes, in Functional Genomics, C. Town, Editor. 2002, Springer Netherlands: Dordrecht. p. 155-171.
2. Soule, M.C.K., et al., Environmental metabolomics: Analytical strategies. Marine Chemistry, 2015. 177: p. 374-387.
3. Cooper, W.T., et al., A History of Molecular Level Analysis of Natural Organic Matter by FTICR Mass Spectrometry and The Paradigm Shift in Organic Geochemistry. Mass Spectrometry Reviews, 2022. 41(2): p. 215-239.
4. Ayala-Ortiz, C., et al., MetaboDirect: an analytical pipeline for the processing of FT-ICR MS-based metabolomic data. Microbiome, 2023. 11(1): p. 28.
5. García, C.A., et al., Probabilistic metabolite annotation using retention time prediction and meta-learned projections. Journal of Cheminformatics, 2022. 14(1): p. 33.

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