Vers une annotation RMN 1D et 2D ciblée à partir de matrices de référence

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Towards NMR 1D and 2D targeted annotation from reference matrices

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Introduction

1D proton NMR spectroscopy is largely used to characterize **extracts** or **biofluids for metabolomic analyzes**. A 1D proton NMR spectrum of a complex mixture is a signature or fingerprint resulting from the superposition of the spectra of all the molecules constituting this mixture weighed by their concentrations.

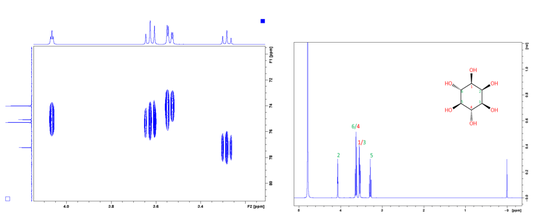
- The **identification of a compound** is sometimes only based on one or two resonances, that cannot be validated without using 2D NMR experiments such as JRES or HSQC to comply with the Metabolomics Standards Initiative guidelines (MSI) on the identification of metabolites[1, 2].
- **Identification and quantification** of more numerous compounds require a very good knowledge of the composition of the studied matrix.
- **Search for candidate compounds** in a 1D proton-NMR spectra library covering all species and many metabolic pathways provides a very rich but inextricable information without the look of an expert.

Purpose: Annotate a NMR Spectrum of Complex Mixture by relying on a Metabolic Profile

The main strategy is to capitalize on experts' knowledge
for each model matrix defined as a metabolic profile annotated with all the reference compounds of interest

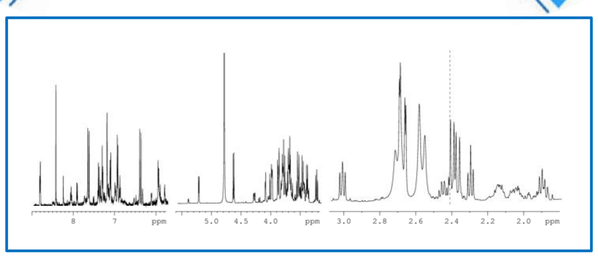
- Constitution of a **reference compound database : PeakForest** (peakforest.org)
- **Associated with protocols :** same condition as sample preparation

- Constitution of a **reference NMR profile database**
- Initially curated and supplied by the **four MetaboHUB platforms** with their model matrices (tomato, human tissues, …)

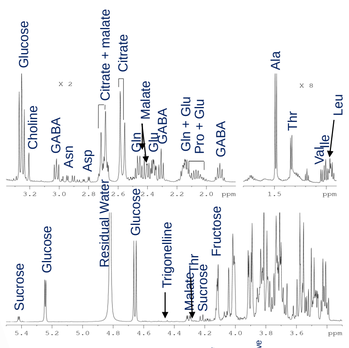


*1D- proton and 2D NMR spectra of a **reference compound** e.g. Myo Inositol for tomato matrix.*

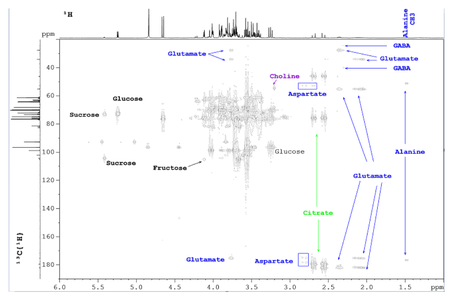
Other reference compound databases e.g HMDB

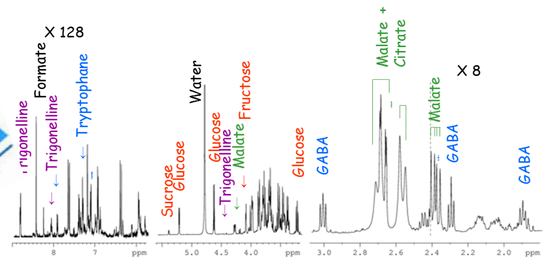


*The1D proton **NMR spectrum of complex mixtur**e to annotate*



*A selected 1D- proton and 2D NMR **reference** **NMR Profile***





Annotated NMR profile spectrum

ENRICHMENT of the reference compound database

ENRICHMENT of the reference profile database

1. **Comparison** between query spectrum and a reference profile
2. **Retrieval** of the corresponding **set of reference compounds**
3. **Comparison** between query spectrum and the set of metabolites
4. **Comparison** with other reference compounds from external libraries
5. **Annotation** of the query spectrum

Implementation Roadmap

- Establish **a library of reference 1D and 2D NMR spectra of interest compounds** constituting each NMR Profile, and acquired in the same conditions of pH and similar ionic strength[1, 2],
- Implement **"peak matching" algorithms** [3] for targeted candidate searching on the library of the corresponding NMR Profile.
- All the **NMR spectra** of reference compounds and profiles will be modeled, **stored and managed in the "PeakForest database"**
  (See **Poster P1 " PEAKFOREST " , Nils Paulhe et al.**)

References

Literature cited

1. Summer L.W. et al. Proposed minimum reporting standards for chemical analysis. Metabolomics, 2007. 3:211
2. Salek R. et al., The role of reporting standards for metabolite annotation and identification in metabolomic studies. GigaScience, 2013. 2:13
3. Jacob D. et al. An efficient spectra processing method for metabolite identification from 1H-NMR metabolomics data. Analytical and Bioanalytical Chemistry, 2013. 405:5049

ANR -11- INBS -0010 project