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Untargeted metabolomic approach by GC-QTOF : From low to high resolution

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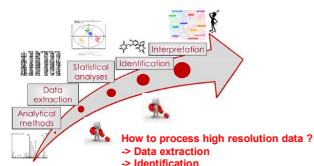
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Untargeted metabolomic approach aims to gather information on as many metabolites as possible in biological systems by taking into account all informations present in the data sets. This approach is essential to pinpoint modifications of metabolic pathways associated to nutritional, health or environmental status for identifying biomarkers.

GC is often coupled to single quadrupole analyzers, which offer high sensitivity, good dynamic range but operate with slower scan rates and lower resolution compared to Time of Flight (ToF) systems. GC coupled with ToF Mass Spectrometry is increasingly used for metabolic profiling because of fast acquisition rates, particularly useful for an accurate deconvolution of overlapping peaks obtained from complex mixtures.

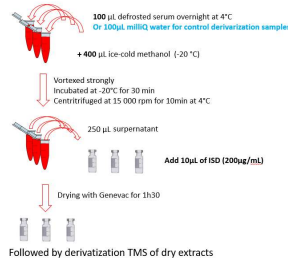
Untargeted metabolomic approach



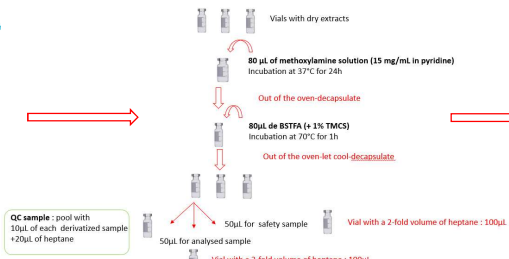
	Low Resolution	High Resolution
Sensitivity	-	+
Resolution	-	+
Acquisition Rate	+	++
Databases	NIST, GOLM, FIEHN and in-house databases	MassBank and In-house databases



Sample preparation*



Trimethylsilylation Derivatization*



GC Conditions :

Injection system: 2 µL split 1/20, T = 250 °C
 Column: HP5-MS (30 m x 0.25 mm x 0.25 µm)
 Carrier gas: He 5.5, 1 mL / min constant debit.

GCMS Analysis*

Oven temperature:

Temp	Time	Temp	Time	Temp	Time
Temp 1	30	300	2	300	20
Temp 2	40	300	2	300	20
Temp 3	200	300	2	300	20

Total run time : 49 min

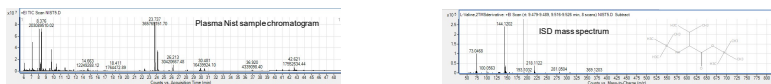
MS Conditions:

EI ion source temperature : 230°C, full scan mode (m/z 50-800)
 Quad parameters
 EI ion source temperature: 230°C
 Quadrupole Temperature: 150°C
 Electron energy: 70eV

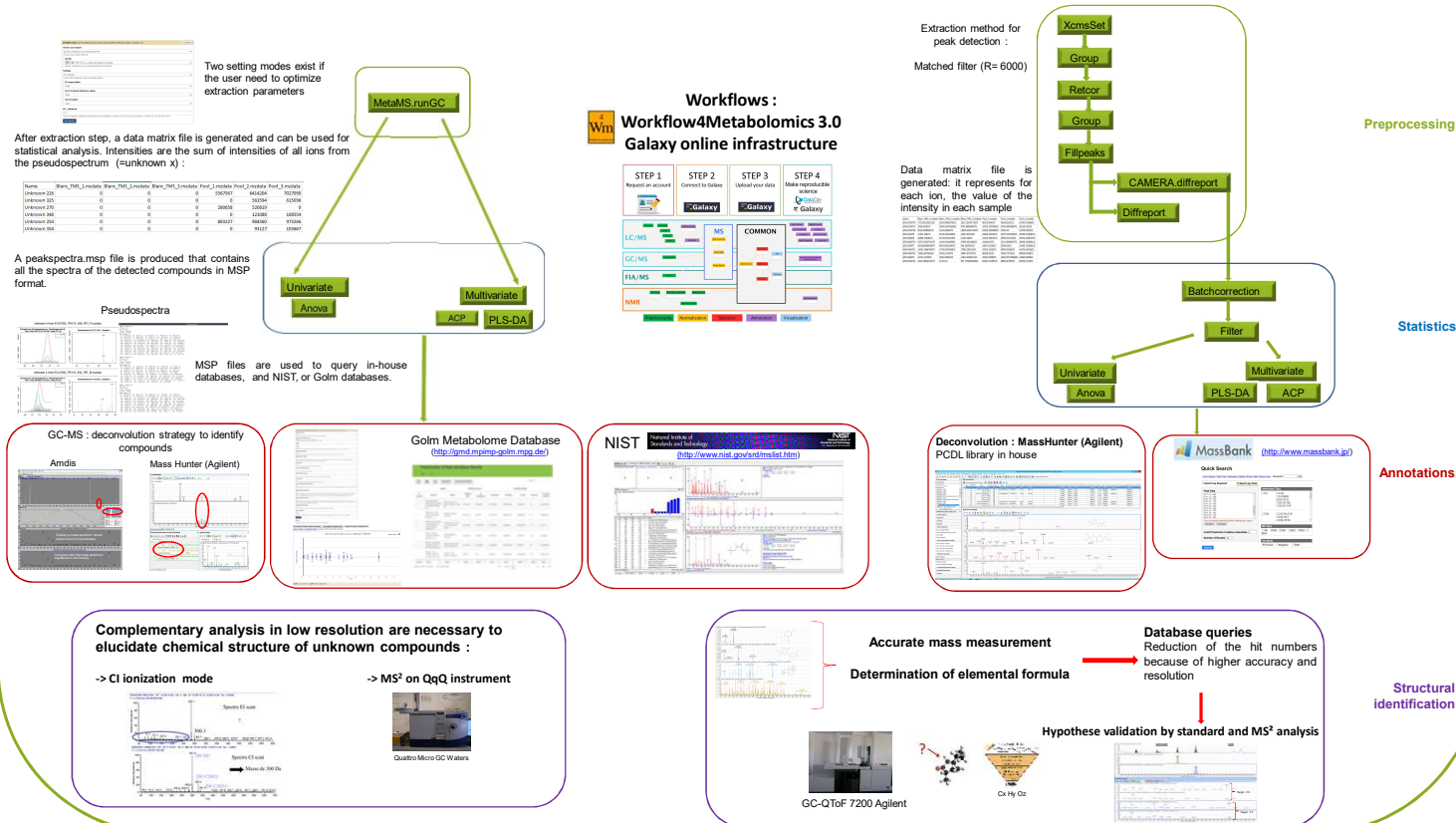
ToF parameters

Acquisition 2GHzEDR with N2 (1.5mL/min)
 Acq rate: 5 spectra/s
 Acq time: 200ms/spectrum
 Transients by spectrum: 2712
 Limits for average PPM error: 3.0 and maximum error: 8.0

Bioinformatic tools : Available workflow to process GS-MS data



Raw data files are processed and converted to mzdata format using the Agilent MassHunter software. Data are processed under the Galaxy web-based platform Workflow4metabolomics, using MetaMS or XCMS packages :



Data extraction :

To process high resolution data using MetaMS package it is necessary to optimize extraction parameters. Therefore, a tool was developed in the lab to realize this step. Several parameters can be considered (e.g : FWHM, similarity threshold,...) one by one or in combination.

Development of new tools

Identification

Reference mass spectra are acquired in high resolution in order to implement Peak Forest database. NIST plasma samples are also analyzed by GC-QToF (MS, MS²) to annotate reference compounds in the matrix.

Conclusion and perspectives

Annotated spectra of reference compounds and biological matrices will be implemented in the metaboHUB national reference database (Peakforest). Accurate mass measurements, as well as the development of new tools for data processing should allow solving the actual bottleneck in biomarker discovery, concerning the identification of metabolites.