MS2Snoop: a R package for automatic extraction and curation of MS/MS spectra in metabolomics

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Introduction

Omics approaches including metabolomics generate huge datasets requiring powerful processing tools. In the field of non-targeted mass spectrometry metabolomics, HRMS data mining has been the subject of much work, with the development of powerful interactive tools, including Workflow4Metabolomics (W4M) [1-2]. One of the main bottlenecks of current workflows lies in the complexity of the interpretation of results, in particular a lack of reliable MS/MS spectral reference databases (DBs) to be used for confident identification (level 1 and 2 according to the metabolomics standard initiative). Creating reliable and well curated spectral DBs remains a laborious and challenging task, but necessary to ensure the quality of the reference spectra. In this work, we present a tool inspired by expert manual curation allowing the export of MS/MS data from both targeted and data dependent (DDA) fragmentation methods to laboratory spectral DBs, named “MS2Snoop”.

- **Workflow (R):**
  - **XCMS**
    - Peak picking
      - From mzML file(s) containing MS & MS/MS
      - Use of xcmsSet & group functions of XCMS
      - Generation of an x-cmsSet - object (.tsv)
    - Precursors quality
      - From same mzML file(s)
      - Use of purityA function to evaluate the purity of precursors [3]
      - Generation of a purityA - object (.tsv)
  - **msPurity**
  - **frag4feature**
    - Association of fragment ions with precursor by merging - purityA - and xcmsSet - objects
    - Generation of .tsv files for fragment & precursor ions
  - **FilterFrag**
  - **MS2snoop**
    - Fragment ions Filtration
      - Definition of detection level of fragment ions (intensity, S/N ratio)
      - Generation of .tsv files for fragment & precursor ions
    - MS/MS spectra reconstruction
      - Merging of fragment & precursor ions with list of expected compounds
      - Correlation of fragment intensity with precursor intensity

- **Examples of applications**
  - Targeted MS/MS by resonant CID achieved on a LTQ-Orbitrap XL using ESI in the positive mode
    - Fragment ions successfully associated with the expected resonant protonation by MS2snoop
    - Interference ions: Detected by manual curation & successfully eliminated by MS2snoop

- **Conclusions**

MS2Snoop already allows extracting and cleaning MS/MS datasets using commonly used metabolomics data processing steps as a starting point, then combined with inputs of a list of expected compounds and MS/MS raw data deconvoluted by MSpurity. Firstly developed and validated with targeted MS/MS spectra from about 30 compounds, MS2snoop is compatible with DDA spectra, although limited by the number of MS/MS scans acquired. This package will allow high throughput extraction of MS/MS spectra in order to feed the PeakForest project [4]. Preliminary results obtained with MS2snoop allowed considering it as a valuable tool for confident annotation of metabolites on chromatographic methods coupled to non-targeted mass spectrometry.

A beta version of this original package is already publicly available on W4M (https://workflow4metabolomics.org/) and recent update allows –fragments ions formula annotation with Sinus.

References


Acknowledgments

HRMS analyses were achieved in the frame of the French national infrastructure MetabolHUB (MetaboHUB-ANR-11-INBS-0010). Special thanks to JF Martin for his long career and the good times!