Metabolomics Identification Report Standards

A Metabolomics unknown feature identification report industry standards from BioNovoGene corporation.

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1. Definition and background

There is a general consensus that supports the need for standardized reporting of metadata or information describing large-scale metabolomics data sets. Reporting of standard metadata provides a biological and empirical context for the data, enables the reinterrogation and comparison of data by others, which is also could let us interpret the result in a more clearly way.

This article is mainly address at the unknown metabolite identification in LC-MS experiment, and proposes the reporting standards related to the chemical analysis aspects of metabolomics experiments its metabolite identification.

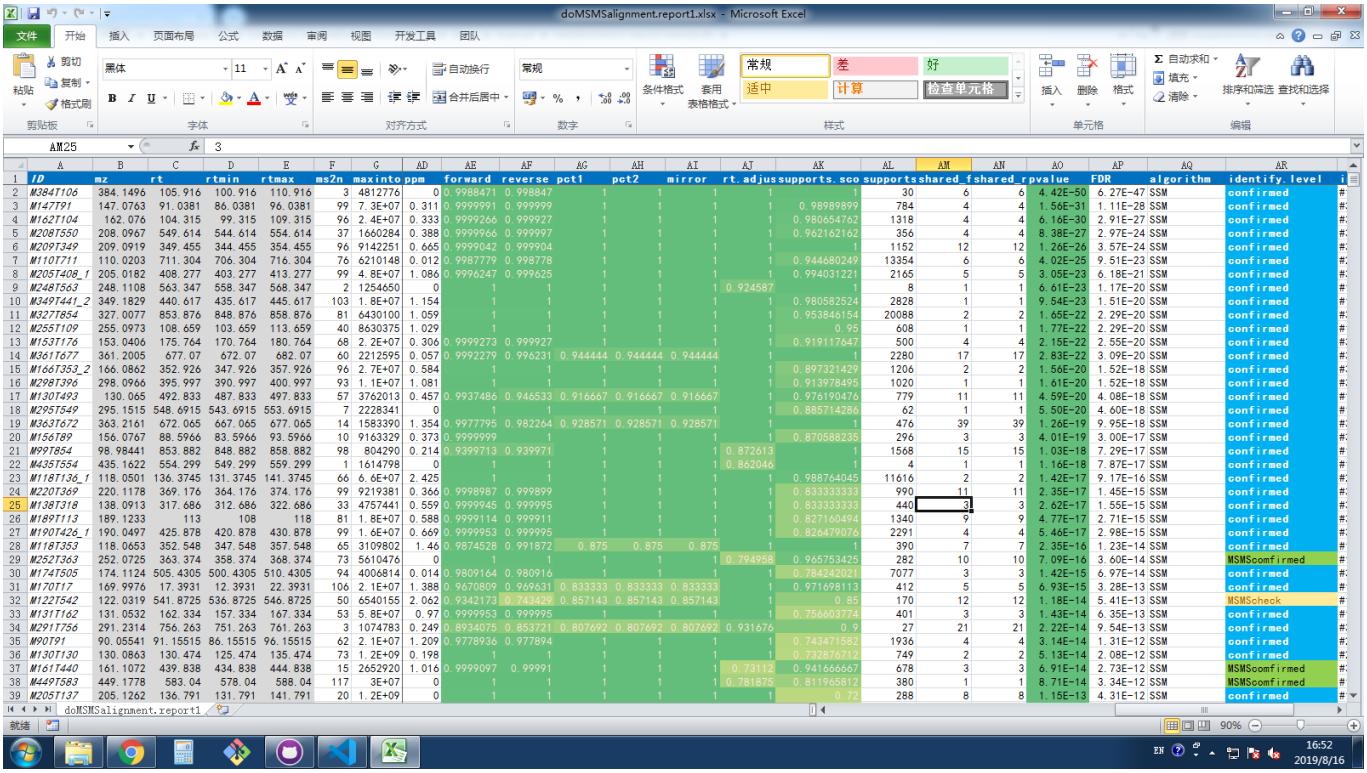
Some terms in this article that address to:

- `feature`, the term **feature** in this article is refer to a parent ion in LC-MS experiment result raw data. Where a parent ion feature is a peak in chromatography data, which is consist of mass to charge ratio in ms1 level and its retention time (with a range of lower bound and upper bound) in chromatography experiment result.
- `annotation`, the term **annotation** in this article is refer to the multidimensional information about the metabolite that assigned to a unknown **feature**, which such multidimensional information consist with the metabolite its cross reference id in different database, common name, basic chemical data like mass and formula composition and its molecule structure information, etc.
- `alignment`, the term **alignment** means a kind of operation that use to compare the similarity of the mass spectrum data between user sample and the reference standard library. Such similarity comparison result is the most important evidence that use for unknown **feature** its identification.
- `score`, the term **score** is a kind of numeric value that produced by the **alignment** comparison calculation. Literally, the higher score the **alignment** it produce, the better the result it is.

Our metabolite identification report consist with two parts of data which present to our user:

1. Report excel table that contains the raw sample information and the meta annotation information of the metabolite.
2. Data visual plot for the mass spectrum alignment details.

2. Report Table Format



2.1. section1: basic info of ion feature

field	type	description
ID	name	The unique id of current ion, which can be generated from `xcms` R package
mz	double	m/z ratio of the ion in ms1 result
rt	double	rt in seconds of the ion in liquid chromatography result
rtmin	double	rt its lower bounds of the ion peaks
rtmax	double	rt its upper bounds of the ion peaks
ms2n	integer	Number of ms/ms spectrum that matched by current ms1 ion
maxinto	double	The max intensity of current ion between samples
index	name	The row index
feature	name	The feature of the best ms/ms spectrum in raw file, in format like: `rawfile_name#scan_number`

2.2. section2: annotation information

In this section, includes three parts of annotation information to describ the resulted metabolite.

2.2.1. part1. the basic meta information

field	type	description
BioDeepID	term	A unique database reference id of current assigned metabolite
name	name	The common name of the assigned metabolite
exact_mass	double	The exact mass of the assigned metabolite
formula	term	The chemical formula of the assigned metabolite

2.2.2. part2. the external database cross reference id

field	type	description
KEGG	term	The KEGG id
hmdb	term	The HMDB main id
pubchem	term	The pubchem compound id (not substrate id)
chebi	term	The chebi main id
CAS	term	The CAS registry number
metlin	term	The metlin metabolite id

2.2.3. part3. the chemical structure information of target

field	type	description
InChIKey	name	The hash key of the InChI calculate result
InChI	name	The InChI identifier of the molecule structure of current metabolite
SMILES	name	The SMILES string of the molecule structure of current metabolite
kingdom	term	The chemical structure classify result in *kingdom* level from `ClassyFire` database
super_class	term	The chemical structure classify result in *super class* level from `ClassyFire` database
class	term	The chemical structure classify result in *class* level from `ClassyFire` database

field	type	description
sub_class	term	The chemical structure classify result in *sub class* level from `ClassyFire` database
molecular_framework	term	The chemical structure classify result in *molecular framework* level from `ClassyFire` database

2.3. section3: annotation score

This section of data consist with two parts of information. First part of the information is the alignment information for the metabolite identification, includes: the reference standard source trace in the reference library, and multiple dimensions of the scores of current identification.

field	type	description
libname	name	The best alignment its unique id in mass spectrum reference library
library	name	The library name
lib.mz	double	The m/z ratio value of the ion in reference library
precursor_type	term	The `precursor type` calculation result base on the sample mz and the exact mass value
ppm	score	The ppm value between sample mz and target reference libibrary mz
forward	score	The `query vs reference` SSM socre
reverse	score	The `reference vs query` SSM score
shared_forward	score	The number of shared fragment in direction `query vs reference`
shared_reverse	score	The number of shared fragment in direction `reference vs query`
pct1	score	The shared fragment ratio in direction `query vs reference`
pct2	score	The shared fragment ratio in direction `reference vs query`
mirror	score	The mirror score between query and reference
rt.adjust	score	The robust rt adjustment score between sample and reference
supports	score	The spectrum alignment supports count of current metabolite cross over multiple standard spectrum database
supports.score	score	The ratio of supports against the max likelihood supports score

And then, is the final identification confidence result for current alignment.

field	type	description
pvalue	score	The max likelihood hyper-geometric pvalue test result
FDR	score	FDR controls of the pvalue

field	type	description
algorithm	enum	The algorithm name for produce current identification score: `SSM`/`shared_hits`/`metaDNA`
identify.level	enum	The confidence level of current identification result: `confirm`, `MSMSconfirmed`, `MSMScheck` and `ms2hit`

The result of `identify.level` have literal values for the representation of the identification its confidence level:

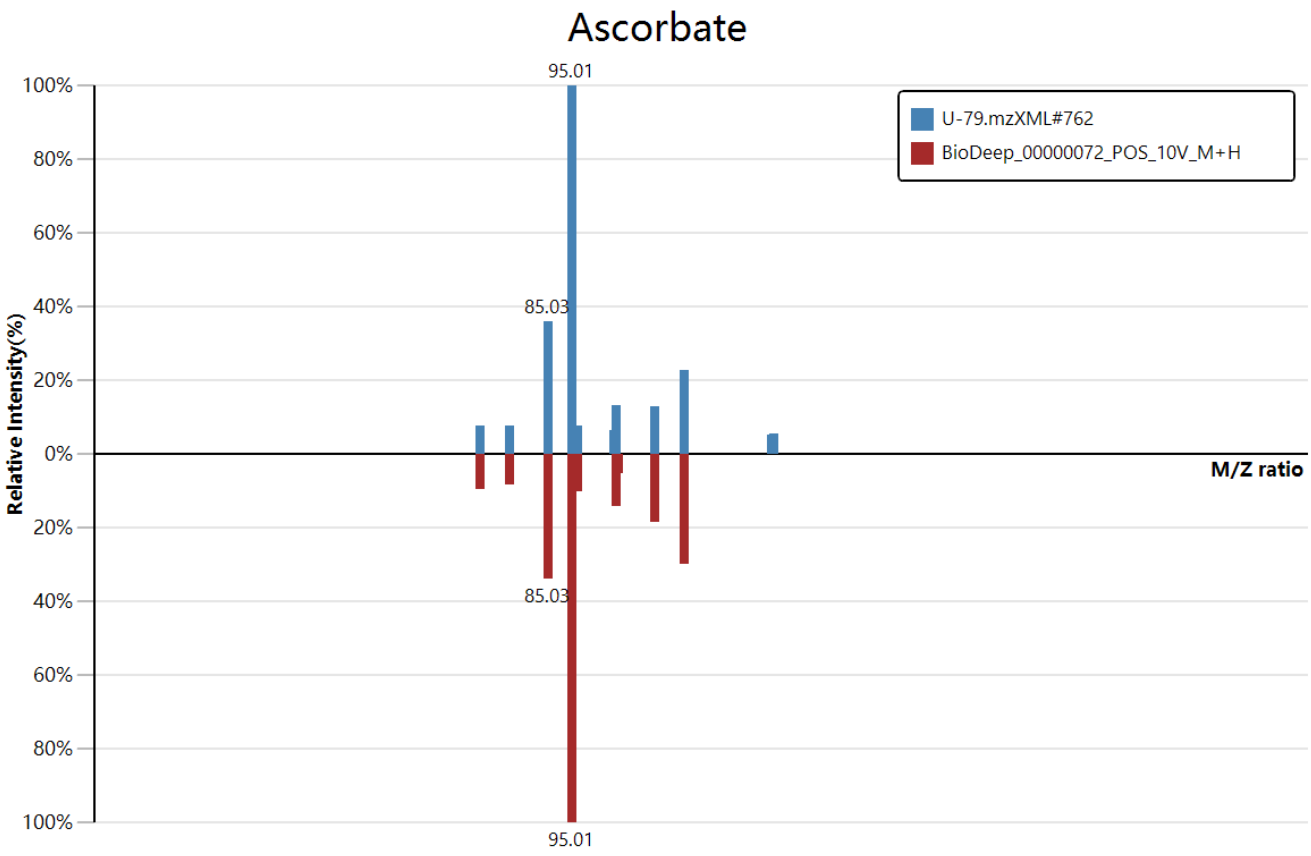
- confirm: the unknown feature is *confirm* as the assigned metabolite both in ms1 level and ms2 level
- MSMSconfirmed: the unknown feature is *confirm* as the assigned metabolite in ms2 level, and ms1 m/z ratio, but not match in rt relative adjustment result value.
- MSMScheck: the unknown feature is probably *confirm* as the assigned metabolite in ms2 level and ms1 m/z ratio, but have low score in ms2 alignment and rt also not match.
- ms2hit: the unknown feature is probably *confirm* as the assigned metabolite, but have low score in ms2 alignment and rt match, we only sure that the alignment have the relative high number of shared fragments between the user sample and the reference library.

> 1. `SSM` algorithm is original defined in this literature article: "MetDIA: Targeted Metabolite Extraction of Multiplexed MS/MS Spectra Generated by Data-Independent Acquisition." ***DOI: 10.1021/acs.analchem.6b02122***
> 2. `pvalue` is tested from the `BHR` score vector, which is original defined in this literature article: "KAAS: an automatic genome annotation and pathway reconstruction server." ***DOI: 10.1093/nar/gkm321***

3. Alignment Visual

Due to the reason of mass spectrum alignment is the most important part in unknown metabolite identification, so it is important to make a clear presentation of the alignment result to user.

The mass to mass spectrum alignment reuslt can be visual by bi-direction barplot, where the top part of the plot which in blue is the ms2 mass spectrum in user sample; and the bottom half of the plot which in brown color is the ms2 mass spectrum of the reference in standards library.



> Only the molecule fragment its intensity value greater than 30%, then its mz ratio will be display on this barplot.