MSL-ST: Development of Mass Spectral Library Search Tool to Enhance Compound Identification

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Abstract: Identification of new organic compounds through suspect screening (SS) and non-targeted analysis (NTA) became the most challenging task in environmental and metabolomics research in the recent two decades. Identification of thousands of organic compounds is performed using the recent technology advancements in chromatography-mass spectrometry as the core analytical platform, assisted by multitude of cheminformatics-assisted approaches. As many of those approaches rely on mass spectral libraries (MSLs) search, the availability of comprehensive MSLs with engines for batch search and export of MS data and batch search engines for simultaneous search and export of MS data from multiple MSLs is of crucial importance. In lack of such, analysts perform this step in a laborious, time-consuming manual manner, importing significant risk of compound misidentification.

This paper presents MSL-ST, the first tool for automated batch search and storage of MS spectra that uses two of the largest publicly available MSLs as data source, the MassBank of North America (MoNa) and the MassBank of Europe. MSL-ST assembles large amount of MS data in an automated, time- and cost-effective manner in a format which allows its further processing, especially for the purpose of compound identification. The tool, accompanied with user manual, is publicly available on GitHub.

1 INTRODUCTION

The typical targeted analysis of organic compounds, based on the identification of the presence and determination of the concentration of a predetermined list of organic compounds is the golden standard in all monitoring analyses of organic compounds. Despite it, over the last two decades, SS and NTA have evolved into effective screening strategies for “known unknowns” and ”unknown unknowns” compounds in complex environmental samples, respectively. In addition to the challenge of developing sensitive generic analytical methods able to identify as many analytical signals as possible that correspond to organic compounds, the next major challenge is to identify the compounds to which these analytical signals correspond. Appropriate data processing and compound identification tools have to be employed for this task in order to avoid false positive or false negative identifications, most frequently due to the presence of interfering singals. Acquisition of signals of thousands of compounds in a single environmental or biological sample is achieved by employing two analytical platforms: nuclear magnetic resonance (NMR) and gas chromatography (GC) or liquid chromatography (LC) coupled to mass spectrometry (MS). While the first analytical platform performs nondestructive and noninvasive sample analysis with concentration-dependent sensitivity, GC/LC-MS analytical platforms offer sensitive detection of thousands of analyte signals, accompanied with various established cheminformatics-assisted approaches for their annotation and identification. High resolution-accurate mass MS (HR/AM-MS) became the indispensable analytical platform for accurate and reliable compound identification. GC and LC are the analytical techniques used for selective compound separation, that, when coupled to various HR/AM-MS ana-

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lyzers with high mass accuracy, resolving power and sensitivity and wide linear range ensure reliable compound identification across a wide mass and concentration range.

One of the main applications of cheminformatics is generating methods for storage and retrieval of chemical structures of compounds. Effective search through structural information for compounds involves the use of information tools (data search and machine learning), as well as knowledge in the field of graph theory (or more precisely, chemical graph theory). The automated retrieval and storage of chemical, structural compound information is an important step that would facilitate and speed up the process that is currently being performed manually. In recent decade, multitude of cheminformatics approaches are developed that perform compound identification using MS data as initial input data. Numerous tools, such as MOLGEN-MS (Schymanski et al., 2008), the GMD algorithm (Hummel et al., 2010), FT-BLAST (Rasche et al., 2012) and NEIMS (Wei et al., 2019) include MSL(s) search of the MS spectra of the candidate compound, followed by comparison of the measured MS spectra of the unknown compound with the MS spectra of the candidate compounds contained in the searched MSLs. As NTA often results with identification of hundreds to thousands of analyte signals, identical is the number of candidate compounds for which MS data should be searched across one or multiple MSLs. The automation of the MSL(s) search, as well as improvements in spectrum search tools in terms of user interface, search algorithms, speed and IT support are the future challenges addressed in this research. Literature reviews from the last decade indicate difficulties that persist to this day. Namely, in order to enable the development of data-driven algorithms for identification of small molecules, it is necessary that all sets of MS spectra are available for public use through appropriate MSLs. The fact that most MSLs do not allow data download, ie. batch data download suggests that for optimal use of MSL data, research communities should embrace new technologies and mechanisms that support interoperability, and promote the advancement of an ”open data sharing” culture. They would find even more frequent use as input data on several ML models (Scheubert et al., 2013). The entries of spectral data in MSLs is often accompanied by rich metadata annotations, including compound structure, name, molecular descriptors (InChI, InChIKey, SMILES), instrument type, ionization mode, operation conditions (e.g. GC oven temperature program, LC method, collision energy etc.), adduct ion type and product ion annotations. An extensive overview of the literature on MSLs and the identification of peptides and small molecules using cheminformatics-assisted approaches indicates that the lack of ability to search and retrieve batch mass spectra from publicly available MSLs significantly impedes the development of new ML models for predicting molecular mass, MF and / or the structure of small organic compounds, thus preventing the identification of new organic compounds. Hence the main impetus for the development of an MSLs search tool, used for the identification of organic compounds, which has the option of batch search of mass spectra for more data and their automated retrieval.

The paper first discusses some of the notable tools related to the problem at hand (section 2), moves forward to the presentation of the main data sources and methods used for the tool development (Section 3) and of the comprehensive functionality of the tool (Section 4) and concludes the directions of further development (section 5).

2 RELATED WORK

Searching and providing high quality chemical information from multiple data sources is an extreme challenge, but also essential before performing SS and NTA, given that the direct approach to identifying compounds is to search for one or more MSLs. Challenges for chemical DBs of compounds include attaching high quality data and thus providing access to chemical structures and related metadata (experimental/predicted properties, toxicity data, literature data, etc.). The publication of chemical metadata with an appropriate molecular descriptor (eg SMILES, InChI, InChI Key, PubChem ID, ChemSpider ID, Dashboard DTXSID, CAS numbers or MOL files) is extremely important for unique self-identification display, but also for in the database.

Most MSLs are publicly available, including METLIN (Guijas et al., 2018), MassBank, GMD (Hummel et al., 2007), although many do not allow batch download. Some MSLs are specific to a specific research area, such as Human Metabolome Database (HMDB) (Wishart et al., 2007), which includes the MS / MS spectrum of human metabolites, and ReSpect (Sawada et al., 2012) contains mass spectra of plant metabolites. Also, depending on the type of chromatography, for GH-MS large MSLs are routinely used, while for LC-MS MSLs are used which usually contain a smaller number of mass spectra for a smaller number of compounds.

MSLs can be classified according to various criteria, such as resolution (low/high), number and type of mass analyzers used to generate mass spectra (MS^1, MS^2, ..., MS^n) (method type of ionization, type of chromatography (GH, LH), number and type of compounds with mass spectra included in MSLs, taking into account their physicochemical properties and source (human, animal, plant, synthetic compound, environmental pollutant).

Statistical processing of the information extracted from the relevant scientific literature in 2015 shows that EI-MS libraries for volatile compounds (such as NIST (NIST: National Institue of Standard and Technology, 2020) / EPA / NIH, Wiley (McLafferty and Stauffer, 2009), GMD (Hummel et al., 2007), MassBank (Horai et al., 2020)) are most commonly cited and used MSLs (82%), followed by ESI-MS / MS MSLs (such as METLIN (Guijas et al., 2018) and HMDB (Wishart et al., 2007)) for non-volatile compounds (16%) (Ljoncheva, Milka and Stepišnik, Tomaž and Džeroski, Sašo and Kosjek, Tina, 2020).

GC-MS spectra have a great advantage over LC-MS/MS spectra due to their higher reproducibility, which makes the generated mass spectra comparable, regardless of whether they are generated using mass analyzers of different configuration and/or manufacturer, which in turn allows the application of comprehensive MBSs. The limited use of the GC-MS analytical platform for the analysis of volatile compounds leads to a reduced number of GH-MS spectra in MSLs. Namely, Mass Bank of Europe (Horai et al., 2020) contains mass spectra of 15000 non-volatile organic compounds out of a total of 41,092 compounds, METLIN (Guijas et al., 2018) only 12,057 out of 242,032 compounds, compared to libraries with volatile compounds such as NIST (NIST: National Institue of Standard and Technology, 2020), Wiley (McLafferty and Stauffer, 2009), MassBank of Europe (Horai et al., 2020), Fiehn Lib (Kind et al., 2009), and the Golm Metabolome Database (Hummel et al., 2007), containing a significantly larger number of compounds.

3 MATERIALS AND METHODS

3.1 Materials

3.1.1 MassBank of Europe

MassBank of Europe (Horai et al., 2020) is the first publicly available MSL containing comprehensive corpus of MS data generated using versatile analytical platforms, such as LC-ESI-QTOF, LC-ESI-ITFT, LC-ESI-QFT, EI-B, LC-ESI-QQ, LC-ESI-Q, LC-ESI-QQQ and GC-EI-TOF. As of December 2020, electrospray ionization (ESI) (60.0%), electron ionization (EI) (30.0%), chemical ionization (CI) (2.0%), atmospheric-pressure chemical ionization (APCI) (1.6%) and matrix-assisted laser desorption/ionization (MALDI) (1.5%) mass spectra represent the most valuable MS data from the 88 168 unique spectra (19 981 MS^1, 67 188 MS^2, 929 MS^3 and 70 MS^4 spectra) of 14 838 unique compounds this MSL includes, making it one of the most comprehensive MS data repository available MassBank (Horai et al., 2020). MassBank of Europe's unique feature is the inclusion of merged spectra, that are spectra containing MS data from numerous spectra of a single compound generated under different instrumental conditions (usually at different ionization energies). MassBank of Europe is also repository for trial and unknown MS data, that are of great importance for SS and NTA. Despite being especially user-friendly and with versatile search options, including name, exact mass, molecular formula, peak list, peak differences, InChIKey and SPLASH search, the search engine of this MSL does not offer batch data search and export.

3.1.2 MoNa

The MassBank's version of North America,MoNa (Mehta, 2020) is the most exhaustive readily-downloadable MS data repository. As of December 2020, it contains 672 751 MS spectra of more than 90 300 organic compounds (20 756 MS^1, 635 129 MS^2, 929 MS^3 and 70 MS^4 spectra), 490 087 of which *in silico* and 179 535 experimental spectra. MoNa's search engine apart from offering quick spectra search by compound name, compound class, molecular formula and/or exact mass includes the unique feature of searching for spectra similar to the one of the user, but lacks to offer batch search and download of spectral data and accompanying metadata.

3.2 Methods

MSL-ST relies on both Python and Django framework, and the concept of simulating human approach for data assessment. This approach saves significant amount of time otherwise used for manual spectral data download. The process itself involves fetching the web page and downloading data by utilising Python libraries, which is automating the scenario when the web page would have been displayed to the user through a web browser. Once data is downloaded, the extraction begins. The content of the page can be parsed, searched, and reformatted.

Python is often described as the "batteries included" language because of its comprehensive standard library and modules for variety of tasks (DeBill, 2010). Besides being the main tool for the automated data extraction functionality, it was as well selected as the most appropriate programming language for developing MSL-ST by using the Django free open source framework, which follows the model-view-template (MVT) architectural pattern (Holovaty and Kaplan-Moss, 2009), including usage of Python even for the configuration files and data models. Django was selected as web framework due to the emphasizing reusable components, shorter codes, rapid development and principle of non-repetition, which lead to facilitated creation of complex data-driven web pages.

The source code of MSL-ST is available at GitHub *https : //github.com/gerasimoska/mass_spectra*, and is also hosted and can be accessed at the following link *https : //massspectra.dev/*.

4 MSL-ST FUNCTIONALITY

In this section, the functionality of MSL-ST is presented by depicturing two experimental scenarios of obtaining data from the two possible sources: the first one represents batch search and export from MoNa and the second one from MassBank of Europe.

The web interface of MSL-ST (Fig. 1) consists of:
(1) Mass spectral library section, in which the user selects the MSL to be searched against. Selecting one among the two MSLs (one-at-a-time) enables parts of the interface that correspond with the selected library, that are searching parameters valid for the library at hand. Selecting MoNa as source MSL enables the Library filter section, where the user is allowed to select one or more of the sub-MSLs included in MoNa (Fig. 2). Selecting MassBank of Europe as source MSL, on the other hand, enables the mass Spectra Library filter section, the Other Instrument Types filter, which is only available when searching the Mass Bank, is no longer blurred and disabled (Fig. 3);
(2) Search parameter filter sections, used to custom the search parameters according to the user's requirements. Apart from the library-specific parameters made available after MSL selection, other filters are available for both MSLs, including:

- The ion mode filter, that allows the selection of the type of ionization in MS, positive or negative;
- The MS Type filter which indicates the number and type of mass spectrometers used to generate MS and
- The Source Introduction filter that allows the selection of the type of chromatography, whether it is gas chromatography, liquid chromatography, or capillary electrophoresis.

offering selection of ion mode (positive/negative), MS type (MS^1, MS^2, MS^3, MS^4) and source introduction (LC, GC, capillary electrophoresis (CE)). The search filters are represented as tabs where the header is the name of the filter, and the available options that can be selected are radio buttons (only one of the offered options is allowed), or, checkboxes (one or more of the offered options are allowed). Since we already described the different contents the .csv file might contain, the user has to select the type of input data: InChiKey, molecular formula or exact mass. Selection of exact mass as input data triggers another input number field requiring the user to define the mass difference tolerance level of the exact mass variation (in Da);
(3) Upload file section, which allows attachment of a .csv file with a list of compound names, molecular formulae, InChIKeys or molecular masses of compounds for which MS data is required. The file upload is performed by clicking the Browse button, which allows attachment of files locally stored on the device. After selecting the file, the window closes automatically and the name of the selected file is written in the Upload File tab and thus is visible for the user.

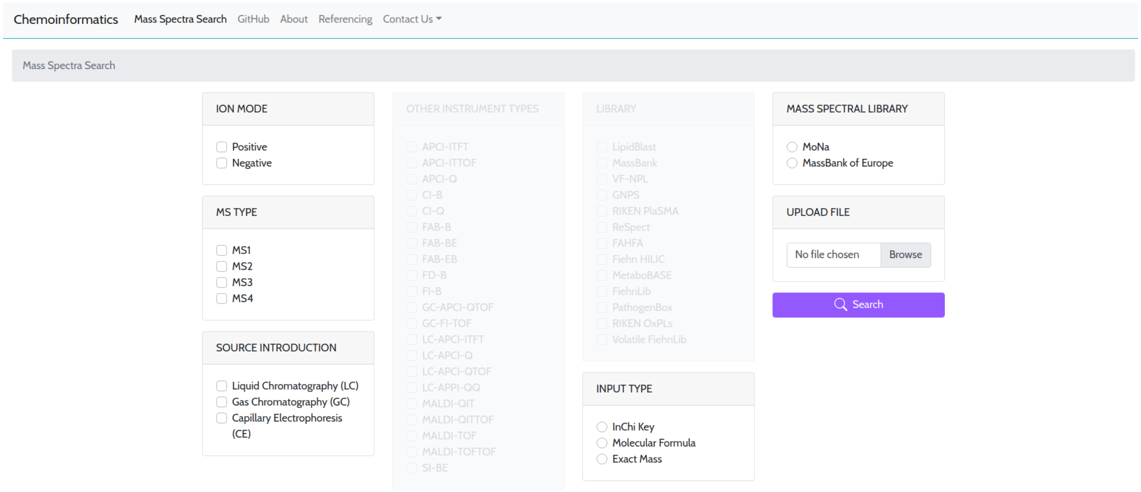
Furthermore, MSL-ST implements validation of the attached file, approving attachment only of files with .csv or .txt extension. This feature warns the user fo attaching inappropriate file format by displaying an error message in a warning window.

After uploading and selecting the desired filter options, by clicking the Search button, the request is submitted and the data retrieval process begins, after which a file is automatically generated and downloaded (Fig. 8). In case the file is not in the appropriate format, and the source is not selected from the Mass Spectral Library filter, this button remains disabled.

After clicking Search, a POST request is sent and a message for successful processing is displayed in a warning window. This means that an HttpRequest object is passed from the displayed template as an argument in the function of the view pointed from the URL. The view expects an HttpResponse that will be returned after executing the function for data retrieval.

As soon as the OK button is clicked, all filters are disabled and a spinner is displayed, while the request is processed and an output file is generated.

The data retrieval process, as shown in Fig. 5 starts by scrolling through all the input items, and invoking the corresponding function from additional helpers file in the system. Input arguments are the values of selected filters from the application (ION MODE, MS TYPE, SOURCE INTRODUCTION, LIBRARY), while the other arguments are initialized



ION MODE
□ Positive
□ Negative

MS TYPE
□ MS1
□ MS2
□ MS3
□ MS4

SOURCE INTRODUCTION
□ Liquid Chromatography (LC)
□ Gas Chromatography (GC)
□ Capillary Electrophoresis (CE)

OTHER INSTRUMENT TYPES
□ APCI-ITFT
□ APCI-ITTOF
□ APCI-Q
□ CI-B
□ CI-Q
□ FAB-B
□ FAB-BE
□ FAB-EB
□ FD-B
□ FI-B
□ GC-APCI-QTOF
□ GC-FI-TOF
□ LC-APCI-ITFT
□ LC-APCI-Q
□ LC-APCI-QTOF
□ LC-APPI-QQ
□ MALDI-QIT
□ MALDI-QITTOF
□ MALDI-TOF
□ MALDI-TOFTOF
□ SI-BE

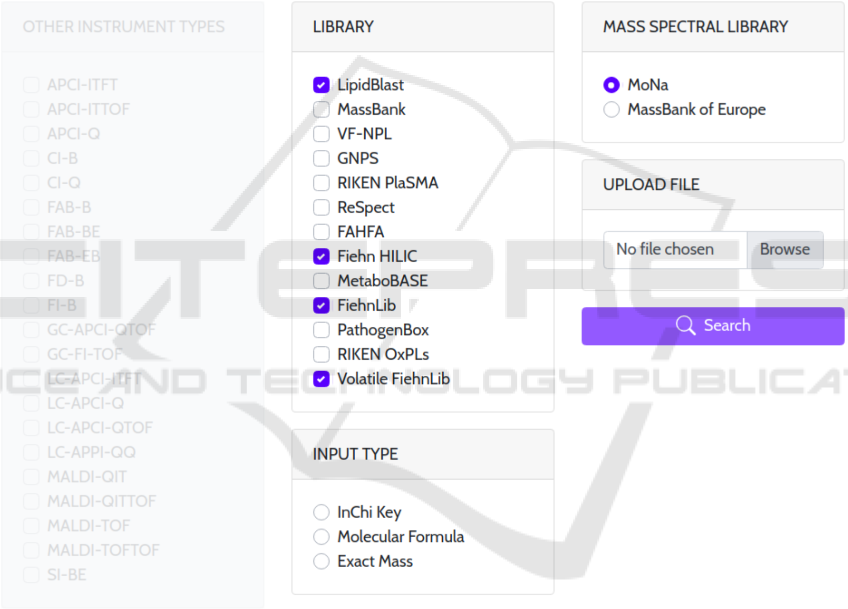
LIBRARY
□ LipidBlast
□ MassBank
□ VF-NPL
□ GNPS
□ RIKEN PlaSMA
□ ReSpect
□ FAHFA
□ Fiehn HILIC
□ MetaboBASE
□ FiehnLib
□ PathogenBox
□ RIKEN OxPLs
□ Volatile FiehnLib

INPUT TYPE
○ InChi Key
○ Molecular Formula
○ Exact Mass

MASS SPECTRAL LIBRARY
○ MoNa
○ MassBank of Europe

UPLOAD FILE
No file chosen

Figure 1: MSL-ST web interface.



OTHER INSTRUMENT TYPES
□ APCI-ITFT
□ APCI-ITTOF
□ APCI-Q
□ CI-B
□ CI-Q
□ FAB-B
□ FAB-BE
□ FAB-EB
□ FD-B
□ FI-B
□ GC-APCI-QTOF
□ GC-FI-TOF
□ LC-APCI-ITFT
□ LC-APCI-Q
□ LC-APCI-QTOF
□ LC-APPI-QQ
□ MALDI-QIT
□ MALDI-QITTOF
□ MALDI-TOF
□ MALDI-TOFTOF
□ SI-BE

LIBRARY
☑ LipidBlast
□ MassBank
□ VF-NPL
□ GNPS
□ RIKEN PlaSMA
□ ReSpect
□ FAHFA
☑ Fiehn HILIC
□ MetaboBASE
☑ FiehnLib
□ PathogenBox
□ RIKEN OxPLs
☑ Volatile FiehnLib

INPUT TYPE
○ InChi Key
○ Molecular Formula
○ Exact Mass

MASS SPECTRAL LIBRARY
● MoNa
○ MassBank of Europe

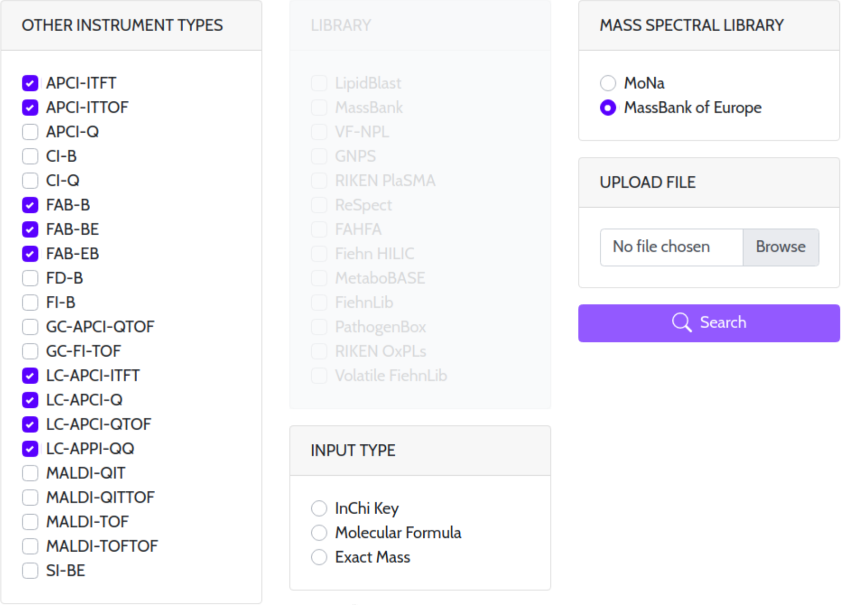
UPLOAD FILE
No file chosen

Figure 2: MSL-ST with MoNa selected as source MSL.

to an empty list. Using the selected filters, a URL where querystring passes the values, is generated and a GET request is sent to it. The response of the request contains list of ids from all of the compounds whose metadata is contained in the selected MSL, that fulfil the selected parameters.

Using the output arguments of the function, it is iterated through each of the received IDs, and a GET request is sent to each of the generated URLs from the ID. The response contains all the data for the given compound (name, exact mass, molecular formula, molecular descriptors etc.) and the metadata corresponding to instrument part and conditions, as shown in Fig. 5. Since the response is in JSON format, using build-in functions of data structure objects eases the process of parsing the data. Additionally, formatting of the retrieved data in an easy-to-use output .csv format is done before download (Fig. 8).

The output .csv file, where the header contains the metadata/parameters name, molecular formula, ions, etc.). The described data retrieval procedure is repeated for all compounds from the input file and the results are added to the output file accordingly. As soon as the data retrieval process is finished for all input items that have been iterated, the Django view that has received the POST HttpRequest as an input argument, returns the response as an output argument of the function. After receiving the response from



OTHER INSTRUMENT TYPES

- ☑ APCI-ITFT
- ☑ APCI-ITTOF
- □ APCI-Q
- □ CI-B
- □ CI-Q
- ☑ FAB-B
- ☑ FAB-BE
- ☑ FAB-EB
- □ FD-B
- □ FI-B
- □ GC-APCI-QTOF
- □ GC-FI-TOF
- ☑ LC-APCI-ITFT
- ☑ LC-APCI-Q
- ☑ LC-APCI-QTOF
- ☑ LC-APPI-QQ
- □ MALDI-QIT
- □ MALDI-QITTOF
- □ MALDI-TOF
- □ MALDI-TOFTOF
- □ SI-BE

LIBRARY

- □ LipidBlast
- □ MassBank
- □ VF-NPL
- □ GNPS
- □ RIKEN PlaSMA
- □ ReSpect
- □ FAHFA
- □ Fiehn HILIC
- □ MetaboBASE
- □ FiehnLib
- □ PathogenBox
- □ RIKEN OxPLs
- □ Volatile FiehnLib

INPUT TYPE

- ○ InChi Key
- ○ Molecular Formula
- ○ Exact Mass

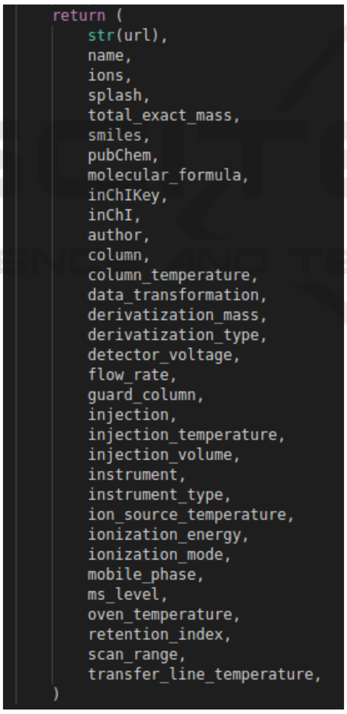
MASS SPECTRAL LIBRARY

- ○ MoNa
- ● MassBank of Europe

UPLOAD FILE

No file chosen | Browse

Figure 3: MSL-ST with MassBank of Europe selected as source MSL.



```
    return (
        str(url),
        name,
        ions,
        splash,
        total_exact_mass,
        smiles,
        pubChem,
        molecular_formula,
        inChIKey,
        inChI,
        author,
        column,
        column_temperature,
        data_transformation,
        derivatization_mass,
        derivatization_type,
        detector_voltage,
        flow_rate,
        guard_column,
        injection,
        injection_temperature,
        injection_volume,
        instrument,
        instrument_type,
        ion_source_temperature,
        ionization_energy,
        ionization_mode,
        mobile_phase,
        ms_level,
        oven_temperature,
        retention_index,
        scan_range,
        transfer_line_temperature,
    )
```

Figure 4: Obtained metadata for a given compound.

the POST request, when the output file is ready to be downloaded, this option becomes available and easily visible to the user as shown in Fig. 6. In real time, the MS data for all MS entries of the selected MSL will be downloaded and written in the output file. As shown in Fig.7, it contains all the metadata available in both MSLs.

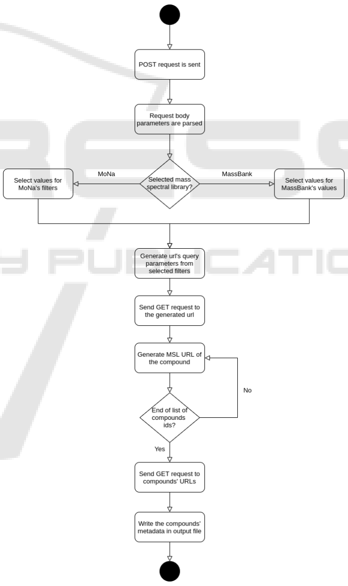
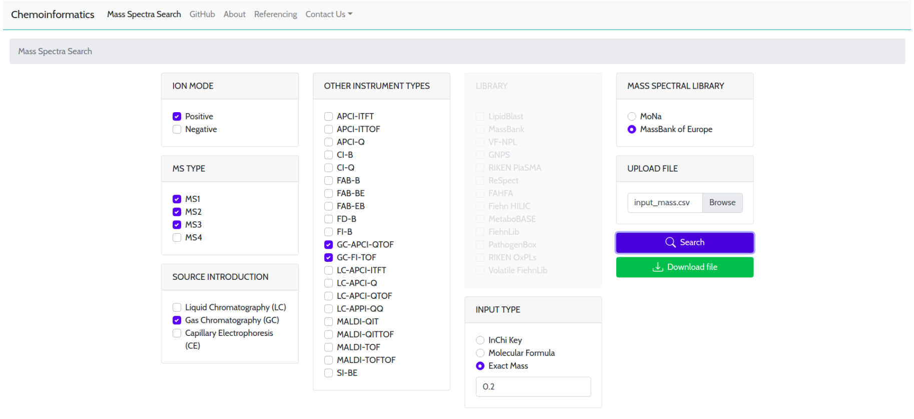

POST request is sent
Request body parameters are parsed
MoNa
Selected mass spectral library?
MassBank
Select values for MoNa's filters
Select values for MassBank's values
Generate url's query parameters from selected filters
Send GET request to the generated url
Generate MSL URL of the compound
No
End of list of compounds ids?
Yes
Send GET request to compounds' URLs
Write the compounds' metadata in output file

Figure 5: UML diagram for the POST request.

Apart from the MSLs search engine, the navigation menu of MSL-ST's interface provides about page with introduction to the project aim, mass spectrometry and organic compound identification, a content aimed to aid the user's experience while utilizing MSL-ST. A link to the GitHub repository and author's contact information are also provided (Fig. 8).

In this way, MSL-ST allows time-effective retrieval of large data quantities, replacing multiple weeks of manual MS data search and export with few minutes of automated gathering of MS data for thou-



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Mass Spectra Search

ION MODE
☑ Positive
☐ Negative

MS TYPE
☑ MS1
☑ MS2
☑ MS3
☐ MS4

SOURCE INTRODUCTION
☐ Liquid Chromatography (LC)
☑ Gas Chromatography (GC)
☐ Capillary Electrophoresis (CE)

OTHER INSTRUMENT TYPES
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☐ FAB-BE
☐ FAB-EB
☐ FD-B
☐ FI-B
☑ GC-APCI-QTOF
☑ GC-FI-TOF
☐ LC-APCI-ITFT
☐ LC-APCI-Q
☐ LC-APCI-QTOF
☐ LC-APPI-QQ
☐ MALDI-QIT
☐ MALDI-QITTOF
☐ MALDI-TOF
☐ MALDI-TOFTOF
☐ SI-BE

LIBRARY
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☐ GNPS
☐ RIKEN PlaSMA
☐ ReSpect
☐ FAHFA
☐ Fiehn HILIC
☐ MetaboBASE
☐ FiehnLib
☐ PathogenBox
☐ RIKEN OxPLs
☐ Volatile FiehnLib

INPUT TYPE
○ InChi Key
○ Molecular Formula
● Exact Mass
0.2

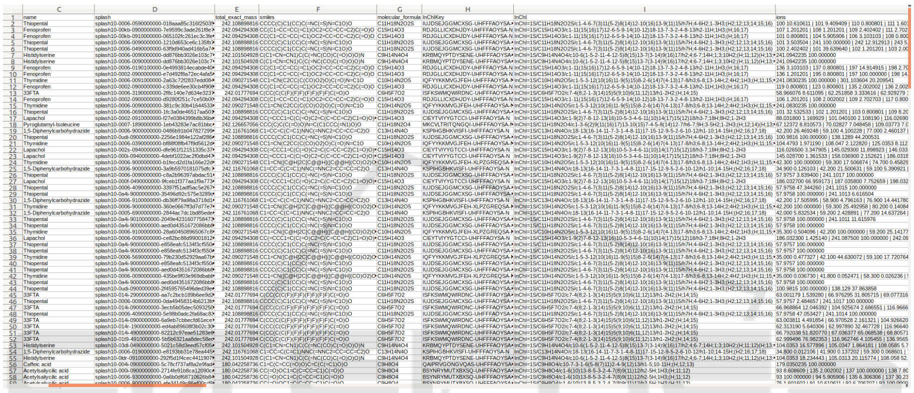
MASS SPECTRAL LIBRARY
○ MoNa
● MassBank of Europe

UPLOAD FILE
input_mass.csv Browse

Search

Download file

Figure 6: Data ready to be downloaded.



	C	D	E	F	G	H
1	name	splash	total_exact_mass	smiles	molecular_formula	InChIKey
2	Thiopental	splash10-0006-0590000000-018aaa85c316f25035	242.108898816	CCCC(C)C1(CC)C(=NC(=S)N=C1O)O	C11H18N2O2S	IUJDSEJGGMCXSG-UHFFFAOYSA-
3	Fenoprofen	splash10-00kb-0900000000-7e9599c3ade261f8e7	242.094294308	CC(C1=CC=CC(=C1)OC2=CC=CC=C2)C(=O)O	C15H14O3	RDJGLLICXDHJDY-UHFFFAOYSA-N
4	Fenoprofen	splash10-00kb-0910000000-065102fc261ec3c3fe	242.094294308	CC(C1=CC=CC(=C1)OC2=CC=CC=C2)C(=O)O	C15H14O3	RDJGLLICXDHJDY-UHFFFAOYSA-N
5	Thiopental	splash10-0006-0090000000-1210d653ce6c135fb7	242.108898816	CCCC(C)C1(CC)C(=NC(=S)N=C1O)O	C11H18N2O2S	IUJDSEJGGMCXSG-UHFFFAOYSA-
6	Thiopental	splash10-0006-0490000000-63f9d940ad416b5a74	242.108898816	CCCC(C)C1(CC)C(=NC(=S)N=C1O)O	C11H18N2O2S	IUJDSEJGGMCXSG-UHFFFAOYSA-
7	Histidylserine	splash10-0006-0090000000-dd876bb3026e103c7	242.101504928	C(C1=CN=CN1)C(C(=NC(CO)C(=O)O)O)N	C9H14N4O4	KRBMQYPTDYSENE-UHFFFAOYSA
8	Histidylserine	splash10-0006-0090000000-dd876bb3026e103c7	242.101504928	C(C1=CN=CN1)C(C(=NC(CO)C(=O)O)O)N	C9H14N4O4	KRBMQYPTDYSENE-UHFFFAOYSA
9	Fenoprofen	splash10-0006-0190100000-0e4993814ecabde40	242.094294308	CC(C1=CC=CC(=C1)OC2=CC=CC=C2)C(=O)O	C15H14O3	RDJGLLICXDHJDY-UHFFFAOYSA-N
10	Fenoprofen	splash10-0002-0900000000-e7d492f8a72ec4afa5	242.094294308	CC(C1=CC=CC(=C1)OC2=CC=CC=C2)C(=O)O	C15H14O3	RDJGLLICXDHJDY-UHFFFAOYSA-N
11	Thymidine	splash10-0006-0091000000-2a63c72f2837edd084	242.090271548	CC1=CN(C2CC(C(CO)O2)O)C(=O)N=C1O	C10H14N2O5	IQFYYKKMVGJFEH-UHFFFAOYSA-
12	Fenoprofen	splash10-0002-0900000000-c339de6ee30cb4f90e	242.094294308	CC(C1=CC=CC(=C1)OC2=CC=CC=C2)C(=O)O	C15H14O3	RDJGLLICXDHJDY-UHFFFAOYSA-N
13	33FTA	splash10-0006-3190000000-2f8c140e7d634e3237	242.01777694	C(CC(C(C(F)(F)F)(F)F)(F)F)C(=O)O	C6H5F7O2	ISFKSWMQWIRDNC-UHFFFAOYSA
14	Fenoprofen	splash10-0002-0900000000-d9280f251c7ce50b00	242.094294308	CC(C1=CC=CC(=C1)OC2=CC=CC=C2)C(=O)O	C15H14O3	RDJGLLICXDHJDY-UHFFFAOYSA-N
15	Thymidine	splash10-0006-0090000000-381c9c30b41644533	242.090271548	CC1=CN(C2CC(C(CO)O2)O)C(=O)N=C1O	C10H14N2O5	IQFYYKKMVGJFEH-UHFFFAOYSA-
16	Thiopental	splash10-0006-0690000000-1fc3a0de46517aa50	242.108898816	CCCC(C)C1(CC)C(=NC(=S)N=C1O)O	C11H18N2O2S	IUJDSEJGGMCXSG-UHFFFAOYSA-
17	Lapachol	splash10-0002-0910000000-f27e0384399b8b36be	242.094294308	CC(=CCC1=C(C(=O)C2=C(C=CC=C2)C1=O)O)	C15H14O3	CIEYTVIYYGTCCI-UHFFFAOYSA-N
18	Pyroglutamyl-Isoleucine	splash10-0007-1890000000-1eb43283e7ac81bbc	242.126657056	CCC(C)C(C(=O)O)N=C(C1CCC(=N1)O)O	C11H18N2O4	MKCVLTRITQNGQI-UHFFFAOYSA-
19	1;5-Diphenylcarbohydrazide	splash10-0006-9000000000-0486b91b047827299	242.116761068	C1=CC=C(C=C1)NNC(=NNC2=CC=CC=C2)O	C13H14N4O	KSPIHGBHKVISFI-UHFFFAOYSA-N
20	Thiopental	splash10-0udi-0900000000-2256e1984e122af286	242.108898816	CCCC(C)C1(CC)C(=NC(=S)N=C1O)O	C11H18N2O2S	IUJDSEJGGMCXSG-UHFFFAOYSA-
21	Thymidine	splash10-0006-0390000000-bf88f08fb47f9d5612d	242.090271548	CC1=CN(C2CC(C(CO)O2)O)C(=O)N=C1O	C10H14N2O5	IQFYYKKMVGJFEH-UHFFFAOYSA-
22	Lapachol	splash10-002s-0940000000-dfe961f12151335c37	242.094294308	CC(=CCC1=C(C(=O)C2=C(C=CC=C2)C1=O)O)	C15H14O3	CIEYTVIYYGTCCI-UHFFFAOYSA-N
23	Lapachol	splash10-000i-0940000000-4debf1022ac2f0dbd47	242.094294308	CC(=CCC1=C(C(=O)C2=C(C=CC=C2)C1=O)O)	C15H14O3	CIEYTVIYYGTCCI-UHFFFAOYSA-N
24	Thymidine	splash10-0006-9000000000-b1fecd2d1fa166e22d	242.090271548	CC1=CN([C@H]2C[C@@H]([C@@H](CO)O2)O	C10H14N2O5	IQFYYKKMVGJFEH-XLPZGREQSA-
25	1;5-Diphenylcarbohydrazide	splash10-0006-9000000000-3a9b5970181075dfc7	242.116761068	C1=CC=C(C=C1)NNC(=NNC2=CC=CC=C2)O	C13H14N4O	KSPIHGBHKVISFI-UHFFFAOYSA-N
26	Thiopental	splash10-0006-0090000000-c8a2b96397abdac51	242.108898816	CCCC(C)C1(CC)C(=NC(=S)N=C1O)O	C11H18N2O2S	IUJDSEJGGMCXSG-UHFFFAOYSA-
27	Lapachol	splash10-000f-0490000000-9fceb1f377aa1f9a773	242.094294308	CC(=CCC1=C(C(=O)C2=C(C=CC=C2)C1=O)O)	C15H14O3	CIEYTVIYYGTCCI-UHFFFAOYSA-N
28	Thiopental	splash10-0006-4090000000-3397f51adf5ac5e267	242.108898816	CCCC(C)C1(CC)C(=NC(=S)N=C1O)O	C11H18N2O2S	IUJDSEJGGMCXSG-UHFFFAOYSA-
29	Thiopental	splash10-0a4i-9000000000-35496d92c575e3289	242.108898816	CCCC(C)C1(CC)C(=NC(=S)N=C1O)O	C11H18N2O2S	IUJDSEJGGMCXSG-UHFFFAOYSA-
30	1;5-Diphenylcarbohydrazide	splash10-0006-9100000000-db36ff79a98a3718d1	242.116761068	C1=CC=C(C=C1)NNC(=NNC2=CC=CC=C2)O	C13H14N4O	KSPIHGBHKVISFI-UHFFFAOYSA-N
31	Thymidine	splash10-0006-9000000000-360e0667ff3d7d77e7	242.090271548	CC1=CN([C@H]2C[C@@H]([C@@H](CO)O2)O	C10H14N2O5	IQFYYKKMVGJFEH-XLPZGREQSA-
32	1;5-Diphenylcarbohydrazide	splash10-0005-6900000000-2844ac7dc1bd85ede	242.116761068	C1=CC=C(C=C1)NNC(=NNC2=CC=CC=C2)O	C13H14N4O	KSPIHGBHKVISFI-UHFFFAOYSA-N
33	Thiopental	splash10-0a4i-9010000000-2049e4231607758473	242.108898816	CCCC(C)C1(CC)C(=NC(=S)N=C1O)O	C11H18N2O2S	IUJDSEJGGMCXSG-UHFFFAOYSA-
34	Thiopental	splash10-0a4i-9000000000-aed0d4351672086bb8	242.108898816	CCCC(C)C1(CC)C(=NC(=S)N=C1O)O	C11H18N2O2S	IUJDSEJGGMCXSG-UHFFFAOYSA-
35	Thymidine	splash10-0006-9100000000-28a604508965067c8	242.090271548	CC1=CN([C@H]2C[C@@H]([C@@H](CO)O2)O	C10H14N2O5	IQFYYKKMVGJFEH-XLPZGREQSA-
36	Lapachol	splash10-0006-0090000000-ce82bc88d99001812	242.094294308	CC(=CCC1=C(C(=O)C2=C(C=CC=C2)C1=O)O)	C15H14O3	CIEYTVIYYGTCCI-UHFFFAOYSA-N
37	Thiopental	splash10-0a4i-9000000000-e858eafc5134f3cf550	242.108898816	CCCC(C)C1(CC)C(=NC(=S)N=C1O)O	C11H18N2O2S	IUJDSEJGGMCXSG-UHFFFAOYSA-
38	Thiopental	splash10-0a4i-9000000000-e858eafc5134f3cf550	242.108898816	CCCC(C)C1(CC)C(=NC(=S)N=C1O)O	C11H18N2O2S	IUJDSEJGGMCXSG-UHFFFAOYSA-
39	Thymidine	splash10-0006-5690000000-79b230d52929aa67b	242.090271548	CC1=CN([C@H]2C[C@@H]([C@@H](CO)O2)O	C10H14N2O5	IQFYYKKMVGJFEH-XLPZGREQSA-
40	Thiopental	splash10-0a4i-9000000000-e858eafc5134f3cf550	242.108898816	CCCC(C)C1(CC)C(=NC(=S)N=C1O)O	C11H18N2O2S	IUJDSEJGGMCXSG-UHFFFAOYSA-
41	Thiopental	splash10-0a4i-9000000000-aed0d4351672086bb8	242.108898816	CCCC(C)C1(CC)C(=NC(=S)N=C1O)O	C11H18N2O2S	IUJDSEJGGMCXSG-UHFFFAOYSA-
42	Thymidine	splash10-0006-0090000000-435be9f03e969dbabb	242.090271548	CC1=CN([C@H]2C[C@@H]([C@@H](CO)O2)O	C10H14N2O5	IQFYYKKMVGJFEH-XLPZGREQSA-
43	Thiopental	splash10-0a4i-9000000000-aed0d4351672086bb8	242.108898816	CCCC(C)C1(CC)C(=NC(=S)N=C1O)O	C11H18N2O2S	IUJDSEJGGMCXSG-UHFFFAOYSA-
44	Thiopental	splash10-0udi-0900000000-2f4595765496ded39e	242.108898816	CCCC(C)C1(CC)C(=NC(=S)N=C1O)O	C11H18N2O2S	IUJDSEJGGMCXSG-UHFFFAOYSA-
45	33FTA	splash10-014i-2900000000-aa7c2bcb189b6ee9d2	242.01777694	C(CC(C(C(F)(F)F)(F)F)(F)F)C(=O)O	C6H5F7O2	ISFKSWMQWIRDNC-UHFFFAOYSA
46	Thiopental	splash10-0006-0090000000-0da49458314b6213fc	242.108898816	CCCC(C)C1(CC)C(=NC(=S)N=C1O)O	C11H18N2O2S	IUJDSEJGGMCXSG-UHFFFAOYSA-
47	33FTA	splash10-014i-0900000000-3ecb5b05dec5093250	242.01777694	C(CC(C(C(F)(F)F)(F)F)(F)F)C(=O)O	C6H5F7O2	ISFKSWMQWIRDNC-UHFFFAOYSA
48	Thiopental	splash10-0006-4090000000-5e98b0adc2fa68ac83	242.108898816	CCCC(C)C1(CC)C(=NC(=S)N=C1O)O	C11H18N2O2S	IUJDSEJGGMCXSG-UHFFFAOYSA-
49	33FTA	splash10-014i-0900000000-6a9eb7cbbecfd61ece	242.01777694	C(CC(C(C(F)(F)F)(F)F)(F)F)C(=O)O	C6H5F7O2	ISFKSWMQWIRDNC-UHFFFAOYSA
50	33FTA	splash10-014r-1900000000-ed4ab89608f3b02c30	242.01777694	C(CC(C(C(F)(F)F)(F)F)(F)F)C(=O)O	C6H5F7O2	ISFKSWMQWIRDNC-UHFFFAOYSA
51	33FTA	splash10-014i-4900000000-82212c97eae51283e0	242.01777694	C(CC(C(C(F)(F)F)(F)F)(F)F)C(=O)O	C6H5F7O2	ISFKSWMQWIRDNC-UHFFFAOYSA
52	33FTA	splash10-01t9-4910000000-5b5b6321aa8dec58ed	242.01777694	C(CC(C(C(F)(F)F)(F)F)(F)F)C(=O)O	C6H5F7O2	ISFKSWMQWIRDNC-UHFFFAOYSA
53	Histidylserine	splash10-03dl-0490000000-5021c58d3eed57cf05	242.101504928	C(C1=CN=CN1)C(C(=NC(CO)C(=O)O)O)N	C9H14N4O4	KRBMQYPTDYSENE-UHFFFAOYSA
54	1;5-Diphenylcarbohydrazide	splash10-0006-0190000000-e8193bb31e78ea445	242.116761068	C1=CC=C(C=C1)NNC(=NNC2=CC=CC=C2)O	C13H14N4O	KSPIHGBHKVISFI-UHFFFAOYSA-N
55	Histidylserine	splash10-0ldr-0910000000-292f5d1f4cec4411907	242.101504928	C(C1=CN=CN1)C(C(=NC(CO)C(=O)O)O)N	C9H14N4O4	KRBMQYPTDYSENE-UHFFFAOYSA
56	Caffeic acid	splash10-004i-0900000000-5c78cf737af8a2e9fad	180.042258736	C1=C(C=CC(=O)O)C=C(C(=C1)O)O	C9H8O4	QAIPRVGONGVQAS-UHFFFAOYSA
57	Acetylsalicylic acid	splash10-000i-0900000000-2714fe91b8ca12090c	180.042258736	CC(=O)OC1=C(C=CC=C1)C(=O)O	C9H8O4	BSYNRYMUTXBXSQ-UHFFFAOYSA
58	Acetylsalicylic acid	splash10-0006-9300000000-0a6b0df68710626b84	180.042258736	CC(=O)OC1=C(C=CC=C1)C(=O)O	C9H8O4	BSYNRYMUTXBXSQ-UHFFFAOYSA

Figure 7: Several columns from the generated output file containing retrieved metadata for the retrieved spectra.

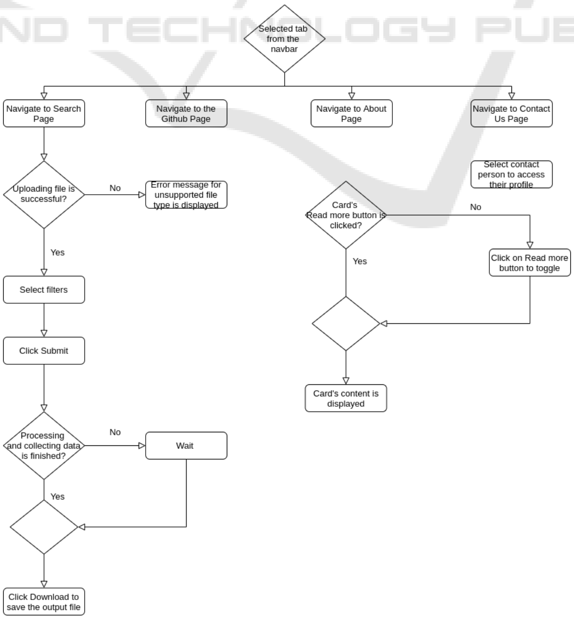

Selected tab from the navbar
Navigate to Search Page
Navigate to the Github Page
Navigate to About Page
Navigate to Contact Us Page
Uploading file is successful?
No
Error message for unsupported file type is displayed
Yes
Select filters
Click Submit
Processing and collecting data is finished?
No
Wait
Yes
Click Download to save the output file
Select contact person to access their profile
Card's Read more button is clicked?
No
Yes
Click on Read more button to toggle
Card's content is displayed

Figure 8: Path diagram of MSL-ST.

sands of compounds. As MSL-ST is the first batch MSLs search and export engine available, no comparative analysis with similar tools can be performed. Due to the lack of batch search option in MassBank of Europe and MoNa, comparison with single MSL batch search and export is also not possible.

5 CONCLUSION

The development of MSL-ST, the first publicly available MS data batch search and export engine using two of the most comprehensive MSLs is pivotal step in MSL-chemoinformatics-based compound identification. By offering a time-, cost- and labour-effective solution for data extraction that can be easily implemented in custom-made workflows, MSL-ST is clearly addressing three of the current challenges of chemoinformatics, that are: **(1)** centralization of multiple MSLs and uniformation of searching through the empirical data they contain; **(2)** enabling search and retrieval of batch data, instead of manually repeating the process, and **(3)** automated download of compound data in a structured tabular format, instead of time-consuming manual storage.

Since MSL-ST is the first MSLs batch search and export engine, it can be easily assumed that the idea of developing such tools in order to aim chemoinformatics-assisted compound identification is in its earliest infancy and thus, many more advancements are to be added to the basic functionalities of MSL-ST available in its first version, presented in this paper. Consequently, its further upgrades would include:

- **Addition of more publicly available MSLs**, that would allow access to larger amount of exeprimental and metadata, thus spreading the capabilities of the MSL(s)-based chemoinformatics tools;

- The MS Type filter which indicates the number and type of mass spectrometers used to generate MS, and

- The Source Introduction filter that allows the selection of the type of chromatography, whether it is gas chromatography, liquid chromatography, or capillary electrophoresis.

This would allow access to a large number of experimental data on compounds of different species (metabolites, peptides, etc.). The process of real-time data extraction would be expanded by searching through other structured databases, using them as a ”living resource” that is updated daily.

The web application provides an easy way to select the characteristics of the mass spectrometry of the whole pile of input compounds, which will be applied in the search in the selected MSL. There is still room for future work in improving the interface of the web application, which would result in a better user experience and easier use of the application.

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