psims - A Declarative Writer for mzML and mzIdentML for Python

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Brief
A Python library for writing and transforming mzML 1.1 and mzIdentML 1.2 XML documents and traversing controlled vocabularies. Builds the document declaratively and manages referential integrity over an XML stream.

Graphical Abstract

Highlights

• Incrementally build mzML 1.1, and mzIdentML 1.2 files in Python over a file stream.

• Traverse controlled vocabularies using common mapping patterns.

• Generate byte offset index as the document streams.

• Manage referential integrity on-the-fly.
psims - A Declarative Writer for mzML and mzIdentML for Python*

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Summary: mzML and mzIdentML are commonly used, powerful tools for representing mass spectrometry data and derived identification information. These formats are complex, requiring non-trivial logic to translate data into the appropriate representation. Most published implementations are tightly coupled to data structures. The most complete implementations are written in compiled languages that cannot expose the complete flexibility of the implementation to external programs or bindings. To our knowledge, there are no complete implementations for mzML or mzIdentML available to scripting languages like Python or R. We present psims, a library written in Python for writing mzML and mzIdentML. The library allows writing either XML format using built-in Python data structures. It includes a controlled vocabulary resolution system to simplify the encoding process and an identity tracking system to manage entity relationships. The source code is available at https://github.com/mobiusklein/psims, and through the Python Package Index as psims, licensed under the Apache 2 common license. Molecular & Cellular Proteomics 18: 571–575, 2019. DOI: 10.1074/mcp.RP118.001070.

The proliferation of data processing and identification methods in mass spectrometry has led to ever increasing complexity for tools that need to describe their results. Over the last decade and a half, the community-driven XML standards for representing spectral data, mzML (1), and peptide/protein identification, mzIdentML (2), have become core to computational methods development (3). These formats combine a complex XML schema for defining the structure of the information contained with a flexible vocabulary of terms for describing the contents (4).

Although this combination makes these tools powerful, it comes at the cost of increased complexity in implementation. There are a small number of comprehensive C/C++ implementations for these formats, the dominant two being ProteoWizard (5) and OpenMS (6), and Java implementations including ms-data-core-api/mzML and MSFTBX (7, 8), among other statically typed compiled languages. In higher-level languages, readers of these formats are often implemented directly on top of generic XML parsing libraries (9, 10) or as bindings for the implementation in a lower level language (11, 12). When readers are implemented, often writers are implemented as being templated on some read-in data, or not implemented at all. These libraries cannot be used to generate files “from native data,” which means that users cannot easily write tools to produce these file formats because the data to produce are not immediately connected with an input template. For implementations using bindings on lower level languages, there are limits on the range of constructs that can be expressed, such as the inability to describe a new complex structure that is not part of the lower level library’s bindings or type system. This may be because of a violation of the single responsibility principle, or intentionally covering only those parts of the specification that are considered useful by the implementors. To our knowledge, the only template-free writers are found in the above listed C++ libraries and in several published and unpublished Java or C# implementations. To write mzML and mzIdentML files from native data using a scripting language like Python or R, one must use bindings OpenMS through pyOpenMS (11) and ProteoWizard through mzR (12) and MSnbase (13) respectively. This adds unnecessary complexity to the creation and deployment of mass spectral data processing tools.

We implemented a declarative writer for mzML 1.1 and mzIdentML 1.2 in Python, with a wider range of expression than previously available implementations for the language (11, 12). The document writers use context managers to express the logical nesting of components, dynamically translates common Python types, and tracks referential integrity of the document for the user. The document is generated as a stream of enclosing contexts, which can only influence actions taken inside themselves, making document construction referentially transparent. Our writers automatically resolve controlled vocabulary terms by name or accession number, including unit information where appropriate. These writers store only the identity map for maintaining referential integrity, decoupling document size from the bounds of available memory by writing the document incrementally as elements are attached to the document writer. This library includes the option to perform validation against the appropriate XML schema, but validation is not made mandatory. This allows its
users to provide additional information to downstream applications if both have an agreed upon structure to parse, extending the document format used, if needed. The decision to step outside the defined schema should not be made lightly, as this may make the file unusable by other software. Additionally, semantic validation has not been implemented, as this functionality is available through stand-alone tools in OpenMS (6) as well as those provided with the mzML and mzIdentML format specification (1, 2).

The library, psims, was written using lxml, a powerful XML handling library (14), which implements incremental document writing, NumPy (15) to handle binary data arrays, and SQLAlchemy (16) for relational schema representation in some cases where the semantic term graph was not applicable. We demonstrate examples using Pyteomics (9) and it is used extensively in our test suite, providing readers for both mzML and mzIdentML, psims is available under the Apache 2 common license and its source code is freely available at https://github.com/mobiusklein/psims as is its documentation. The library is compatible with both Python 2 and Python 3 across platforms.

The only alternative to this library within Python is to use pyOpenMS, Python bindings generated for the excellent C++ OpenMS library. Although the underlying data model in OpenMS may be as flexible within the standard as ours, the Python-level API was only able to expose some of this after release 2.2. Even with this, the user cannot extend the format, being able to only represent those entities that have a mapping to an OpenMS data structure.

**Table I**

| Example file name       | Format       | Producer          | File source                      |
|-------------------------|--------------|-------------------|----------------------------------|
| small.mzML              | mzML 1.1.0   | ProteoWizard      | proteowizard.sourceforge.net/   |
| only_ms2_mzml.mzML      | mzML 1.1.0   | Bruker CompassXport|                                |
| combined_fdr_1.2.mzid   | mzIdentML 1.2.0 | mzIdLib         | HUPO-PSI/mzIdentML               |
| MSGFplus_tandem.pia.1.2.mzid | mzIdentML 1.2.0 | PIA             | HUPO-PSI/mzIdentML               |
| xIFDR-CrossLinkExample_single_run.mzid | mzIdentML 1.2.0 | xi                | HUPO-PSI/mzIdentML               |
| Mudpit_170119_02_P8_SP_STM_G1_1.mzid | mzIdentML 1.1.0 | Scaffold         | PXD008280                       |
| 2017-10-03-MEM-AGP-0016.raw_20171220_Byonic.mzid | mzIdentML 1.1.0 | Byonic           |                                   |
| AGP_Proteomics2.mzid    | mzIdentML 1.1.0 | PEAKS Studio     |                                   |

* Original File Validated.

To enable automatic derivation of controlled vocabulary terms, we first loaded each CV from either a URI specified by the user during document initialization, or a static file included with the library’s source code during packaging if the network request fails. The library includes a configurable caching mechanism to choose to store the vocabulary source files on the file system after first retrieving them from their providers or from the installed package. Except for Unimod (20), we parsed each CV in OBO format (21), constructing a term graph in memory. We parsed Unimod’s database from the XML export of their relational database. The URIs used to obtain the files included in the packaged distribution are shown in Table II. Next, we indexed each term base. The URIs used to obtain the files included in the packaged distribution are shown in Table II. Next, we indexed each term base. The UrIs used to obtain the files included in the packaged distribution are shown in Table II.

- Mass accuracy and 0.1 Da production mass accuracy. The output was written to pickle format. We used the example identipy_mzid.py to convert the pickle file into mzIdentML format.

**Generality Test**—To demonstrate generality, we constructed two scripts for reading in mzML and mzIdentML files from and output the same document semantically unchanged. We detected material differences in the generated XML by performing a recursive comparison of the parsed data from each source file and its duplicated pair. We assessed semantic difference manually from any detected material differences.

To test the mzML writer, we included a script transform_mzml.py (see supplementary information) that reads in an mzML document using pyteomics, then translated the extracted data back into mzML, followed by XSD validation and a test for content equivalence. We ran this test on small.mzML, an mzML file produced by ProteoWizard from the original mzML specification test data, and on only_ms2_mzml.mzML produced by Bruker’s CompassXport. This translation process included appropriate updating of the software List and dataProcessingList to include the additional processing steps included in the translation procedure. Validation was performed using OpenMS v2.3.0 (6).

To test the mzIdentML writer, we included a script transform_mzid.py (see supplementary information) that reads in an mzIdentML document using pyteomics, then translated the extracted data back into mzIdentML followed by XSD validation and a test for content equivalence. We ran this test on several mzIdentML 1.1 and 1.2 files from both the mzIdentML specification example collection and from commercial tools, listed in Table I.

**Vocabulary Resolution**—To enable automatic derivation of controlled vocabulary terms, we first loaded each CV from either a URI specified by the user during document initialization, or a static file included with the library’s source code during packaging if the network request fails. The library includes a configurable caching mechanism to choose to store the vocabulary source files on the file system after first retrieving them from their providers or from the installed package. Except for Unimod (20), we parsed each CV in OBO format (21), constructing a term graph in memory. We parsed Unimod’s database from the XML export of their relational database. The URIs used to obtain the files included in the packaged distribution are shown in Table II. Next, we indexed each term base. The UrIs used to obtain the files included in the packaged distribution are shown in Table II. Next, we indexed each term base. The UrIs used to obtain the files included in the packaged distribution are shown in Table II.

**Novel Input Data Preparation**—To demonstrate the facility of the library, we used previously published data from PXD003498. We downloaded AGP-tryp_O16_1.raw and AGP-tryp_O16_1.mgf from PRIDE. We converted AGP-tryp_O16_1.raw to mzXML using Proteowizard (5) with peak picking. Next, we used MS-Deconv (17) to process the mzXML file, using its text output format including MS1 information. Using the example script convert_msdeconv.py to convert the MS-Deconv output into mzXML format.

We used IdentiPy (18) (commit b98a19e) to search AGP-tryp_O16_1.mgf against the Human proteome downloaded from UniProt Release 2017_09 (19) with fixed Carbamidomethyl at Cysteine and variable Oxidation at Methionine. The search was done with trypsin with two missed cleavages. We used 10 ppm precursor mass accuracy and 0.1 Da production mass accuracy. The output was written to pickle format. We used the example identipy_mzid.py to convert the pickle file into mzIdentML format.
1. By single identifier for a term that has no associated value, such as "MSn spectrum" or "ms-ms search." This naturally maps to string value.

2. By paired identifier and a value that has no unit, such as "ms level" and an integer or "peptide sequence-level e-value" and a float. This naturally maps to a Mapping type with as many relevant keys specified as possible.

3. By a fully specified term including an explicit name, value, CV of origin, and optionally a unit identifier and the unit's CV of origin, such as "scan start time" with a float denoting the value, a quantity of time and an identifier of the unit, such as "minute" or "UO:0000031." This maps most naturally to a Mapping type with as many relevant keys specified as possible.

Whenever the document writer would encounter an argument to be interpreted as either a cvParam or userParam, it first determined which of the three idioms was being used, and then queried the controlled vocabulary index in descending order of specificity for each CV, first accession number, then natural name, then synonym until a match was found or no indices remained. See Table III for example term mappings. If a match was found, a controlled vocabulary term was resolved, and a cvParam tag would be rendered to the document, otherwise a userParam would be rendered including with all the fields the user specified. To support mzML's referenceableParamGroup feature, we included a final case, if the provided argument explicitly matched the identifier of a previously registered parameter group, a referenceableParamGroupRef would be rendered instead.

Unit Resolution—When the document writer resolved a controlled vocabulary term, if the term definition specified that the term had a unit through the relationship has_unit, the unit would also be resolved. If only one unit was specified in the controlled vocabulary and the user provided data describing the term did not provide any unit information, the term's defined unit would be used automatically. If multiple units were permitted, as is the case for quantities such as time or signal intensity, instead a warning would be generated, and the first unit option would be used.

Component Definition—To avoid locking the document writer into a fixed system forcing an element to be mapped to a single class, XML elements could be created as free tags using the writer's element method that creates a context manager wrapping a light weight element object or using a component type. Component types are fully specified classes, laying out attributes, inter-element relationships, and derived property detection. A component is bound to a document context providing it with access to controlled vocabularies and the document's identity map. Each component constructs one containing element to enclose its contents, but may create multiple inner elements or components automatically, bound to the same document context. Both element and component types implement context managers, so they may be arbitrarily nested and mixed.

Referential Integrity—Each time the document writer constructs an element, it attempts to create an identifier for it for the id attribute. If an element was constructed with an integer identifier, in order to ensure that the identifier is unique, it instead assigned an identifier [TAG_NAME]_[INTEGER]. If the provided identifier was not an integer, it would be used verbatim. If the element was part of the top-level element of a component, it would register a mapping between the user provided identifier and the generated identifier specific to that component type. When constructing a component that references another component, the user would provide the same identifier from their application, and the document writer would map this to the generated identifier, maintaining referential integrity.

If a provided identifier has not been registered prior to being referenced, the document writer would emit a warning to indicate that the reference is missing, though this may be made an error during writer configuration. To avoid generating warnings caused by document ordering elements referencing other elements that have not been written yet, identifiers may be registered independent of element construction with the register method of the document writer. Both register and requesting a missing identifier update the referential integrity map using the same procedure as described during automatic registration, maintaining the same behavior independent of whether an identifier is referenced first or registered first. This makes the registration and query process stateless and serves only as an error checking service.

Streaming and Referential Transparency—Each component object used by the document writer was defined by a class. Each object upon initialization would configure itself and the XML element it represented, register with the referential integrity map of the document, and then await serialization. The component types may call their write method on an XML file stream to serialize themselves and all their child elements, just as in other XML serialization techniques, but this requires first constructing all child elements in memory prior

### Table II

| Controlled vocabulary name | File name      | URI                                           |
|---------------------------|---------------|-----------------------------------------------|
| PSI-MS                    | psi-ms.obo    | https://raw.githubusercontent.com/HUPO-PSI/psi-ms-CV/master/psi-ms.obo |
| UNIT                      | unit.obo      | http://ontologies.berkeleybop.org/uo.obo     |
| PATO                      | pato.obo      | http://ontologies.berkeleybop.org/pato.obo   |
| XLMOD                     | XLMOD.obo     | https://raw.githubusercontent.com/HUPO-PSI/mzIdentML/master/cv/XLMOD.obo |
| UNIMOD                    | unimod_tables.xml | http://www.unimod.org/xml/unimod_tables.xml |

### Table III

Controlled vocabulary synonym mapping examples

| ID          | Name                           | Synonyms                                                   |
|-------------|--------------------------------|------------------------------------------------------------|
| MS:1000128  | Profile spectrum               | Continuous mass spectrum, Continuum Mass Spectrum           |
| MS:1000422  | Beam-type collision-induced dissociation | HCD                                                        |
| UNIMOD:7    | Deamidation                    | Deamidated, Citrullination, phenyllactyl from N-term Phe    |
| UNIMOD:41   | Hex                            | Hexose, Glucose, Galactose, Mannose, Fructose              |
to serialization. Components may also be used as context managers with an XML file stream, writing the component’s opening tag and any content appropriate to their type before yielding control to any nested statements, and finally writes any trailing content such as a list of cvParams and the component’s closing tag. This allows callers to load data into memory incrementally, construct an XML component associated with that data, serialize it, and then release that data from memory.

This pattern also encourages writing code that is referentially transparent, where components are constructed and immediately begin their context, any child elements are incrementally loaded, begun, and ended, before ending themselves. This makes the component effectively immutable, as previously stated when a component is construct and it queries the referential integrity map no tangible state is changed. It also conveys the relationship that any logic within the context manager opened by a component is within that component without constructing the sequence of child components before opening that context. The file writing process we described is declarative by virtue of its referential transparency, it is not monadic, and file operations are performed immediately. Furthermore, the caller can use component objects imperatively, mutating their state repeatedly prior to writing them to the output stream or beginning their context, though the guarantee remains that once begun the component will remain unchanged.

RESULTS AND DISCUSSION

To demonstrate the facility of making these formats producible by scripting, we translated the result of MS-Deconv (17) from their tab-delimited text format into mzML, preserving as much source file metadata as possible while retaining the deisotoped and charge deconvoluted peak masses and intensities (Fig. 1). We also retained MS-Deconv’s recalculated precursor monoisotopic m/z and charge fields that can correct the precursor monoisotopic peak errors reported by the instrument. The generated mzML file retained the metadata read from the original mzXML file that was passed to MS-Deconv and can be viewed using any tool that can read mzML, such as SeeMS (5). Additionally, during the translation process, we included a set of calculations to look for specific signature ions and include a userParam tag on each MS² scan that contains a desired m/z value.

The convert_msdeconv.py script (see supplementary information) for the workflow described in Fig. 1 also demonstrates the controlled vocabulary resolution process, recognizing partial specifications by name or accession, and packing the structured data into fully specified cvParam tags. In some cases cvParam were automatically derived from other parameters, such as the redundancy between “MSn spectrum” and “ms level”. Finally, the script validates the generated mzML document against the schema definition to ensure each element has all required information and contain the expected elements in the correct order.

We also show that this library can be useful for more complex applications written in Python themselves, including the identify_mzid.py script defining a process for writing the results of IdentiPy to an mzIdentML file (see supplementary information). This script exercises the identifier resolution system to keep track of entities that have no natural identifier or universally unique identifier, and further demonstrates the controlled vocabulary resolution process. As IdentiPy does not use external controlled vocabulary names for post-translational modifications, we include a modification identity resolution procedure to infer Unimod names from the user-provided mass and amino acid specificities, and only emit “unknown modification” when no mapping may be found. IdentiPy does not perform protein inference, so no ProteinDetection or related elements were produced. As with many mzIdentML writers, during the document writing process, the current locations and identifiers of connected external data were recorded in the Inputs element, recording the database and spectral data file used. The native identifiers of the spectra as recorded by IdentiPy were included in the SpectrumIdentificationResult element’s spectrumID attribute. It is compatible with data integration tools like those provided by PRIDE for reconstructing identifications.

We demonstrate generality of the representation and serialization process by parsing data files in mzML 1.1, mzIdentML 1.1, and mzIdentML 1.2 format and re-writing that data back to disk unchanged. In all cases where the original document was structurally and semantically valid the resulting file was also valid. Where manual assessment was necessary, it was caused by the original file leaving an attribute indeterminate or unspecified while we reserialized it explicitly. We assert this shows that a wide variety of workflows and data can be serialized by this library.

CONCLUSION

We presented psims, a library for writing HUPO-PSI standard mzML and mzIdentML and for interacting with the associated controlled vocabularies in Python. We briefly demonstrated its utility for writing an mzML file from tabular data produced by an external tool that consumes raw spectra but cannot return the data to a metadata-rich format, permitting the re-integration of these methods into environments that depend upon this extra information to interpret the described data appropriately. With the increasing number of peptide and protein identification tools including IdentiPy and Ursgal (22)
being written directly in Python, it may be advantageous for future tools to directly write their results to mzIdentML.

psims does not use a DOM-like architecture but it fully supports the published XML schemata and can use them to validate its own generated XML. The library does not strictly enforce the XSD validation at runtime because of its streaming nature, so the user must explicitly request it. We also wanted to provide a flexible system that enables users to write documents that meet their needs, which may not yet be covered by the standard. The ability to experiment with alternative constructs might also lead to better proposals.

* This work was supported by National Institute of Health Grant U01CA221234.

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Author contributions: J.A.K. designed research; J.A.K. performed research; J.A.K. contributed new reagents/analytic tools; J.A.K. analyzed data; J.A.K. and J.Z. wrote the paper.

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