Protein-Protein Interactions

Introduction to Data Processing

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Interaction Data Processing

Topics

- XML parsing
  - Lxml library
  - Xpath
- MIF file structure
  - ‘compact vs ‘expanded’ variants
- Binary expansion of multi-protein interactions
  - ‘spoke’ vs ‘matrix’ expansion
- Extracting data from MIF files
  - Access relevant/useful information
  - Prepare files ready to import into Cytoscape

Interaction Record Formats

XML file anatomy

```
<?xml version="1.0" encoding="UTF-8"?>
<mif:entrySet xmlns:mif="http://psi.hupo.org/mi/mif"
              level="2" version="5" minorVersion="4">
 <mif:entry>
  <mif:source releaseDate="2019-05-13">
   <mif:names>
     <mif:shortLabel>DIP</mif:shortLabel>
     <mif:fullName>Database of Interacting Proteins</mif:fullName>
   </mif:names>
     <mif:xref>
        <mif:primaryRef db="psi-mi" dbAc="MI:0488" id="MI:0465"
                        refType="identity" refTypeAc="MI:0356"/>
        ...
      </mif:xref>
    </mif:source>
     ...
  </mif:entry>
 </mif:entrySet>
```

Namespace

Text

Element

Opening tag

Closing tag

Namespace Prefix

Attribute (name = “value”)

```
<element attribute=“value”/>
is equivalent to
<element attribute=“value”></element>
```

Interaction Data Processing

Lxml library (https://lxml.de/)

```
from lxml import etree
from io import StringIO
```

Only if needed...

```
xml = '<protein acc="P60010"><seq>MKYDDEW...</seq></protein>'
```

```
strDom = etree.fromstring( xml )
              or
strDom = etree.fromstring( StringIO(xml) )
```

Parse String

```
fileDom = etree.parse("doc/test.xml")
              or
fileDom = etree.parse( open("doc/test.xml") )
```

Parse File/URL

.gz files OK

```
print( etree.tostring( strDom ).decode())
```

... and back to String

See lxml web site for more options

Interaction Data Processing

lxml library (https://lxml.de/)

```
from lxml import etree

xml = '<protein acc="P60010"><seq format="fasta">MKYDDEW...</seq></protein>'

xmlDom = etree.fromstring( xml )

for child in xmlDom:
```

```
print( child.tag.decode() )                          Get element tag
print( child.get("format").decode() )                Get attribute
print( child.text.decode() )                         Get text
print( etree.tostring(child).decode() )              Get element as XML
```

See lxml web site for more options

Interaction Data Processing

lxml Xpath support (https://lxml.de/xpathxslt.html)

```
from lxml import etree

xml = '<protein acc="P60010"><seq>MKYDDEW...</seq></protein>'

xmlDom = etree.fromstring( xml )

root = xmlDom.xpath('/protein')          Get top-level 'protein' element
```

NOTE: Returns a list !!!

```
for child in root[0]:
```

```
print( child.tag.decode() )                          Get element tag
print( child.get("format").decode() )                Get attribute
print( etree.tostring(child).decode() )              Get element as XML
```

See lxml web site for more options

Interaction Data Processing

lxml Xpath support (https://lxml.de/xpathxslt.html)

```
from lxml import etree

xml = '<protein acc="P60010"><seq>MKYDDEW...</seq></protein>'

xmlDom = etree.fromstring( xml )
```

```
t1 = xmlDom.xpath('/protein/seq/text()')
```
Get the text of 'seq' elements that are children of the top-level 'protein' element

```
t2 = xmlDom.xpath('//seq/text()')
```
Get the text of ANY 'seq' element

```
e3 = xmlDom.xpath('//protein[@acc="P60010"]/seq')
```
Get 'seq' elements that are children of 'protein' element with 'acc' attribute equals to 'P60010'

```
e4 = e3[0].xpath('./text()')
```
Get the text of the current element

See *https://en.wikipedia.org/wiki/XPath* and *https://www.w3.org/TR/xpath-10* for more details

Interaction Data Processing

lxml Xpath namespace support (https://lxml.de/xpathxslt.html)

```
from lxml import etree

xml = '''<mif:protein xmlns:mif="http://psi.hupo.org/mi/mif" acc="P60010">
           <mif:seq>MKYDDEW...</mif:seq>
       </mif:protein>'''

xmlDom = etree.fromstring( xml )

e = xmlDom.xpath('/m:protein/m:seq',
                 namespaces={'m': 'http://psi.hupo.org/mi/mif'})
```

```
print( e[0].tag.decode())
```
Get qualified (i.e. with namespace) tag

```
qname = etree.QName(e[0])

print( qname.localname.decode() )
print( qname.namespace.decode() )
```
Split qualified tag into namespace and local name

Interaction Data Processing

PSI-MI XML (MIF) file anatomy

Compact MIFs use references to interactors and/or experiments

```
<entry Set>
  <entry>
    <source releaseDate='2019-05-22'>...</source>
    <interactorList>
      <interactor id='1'>...</interactor>
      <interactor id='2'>...</interactor>
      ...
    </interactorList>
    <experimentList>
      <experiment id='1'>...</experiment>
      <experiment id='2'>...</experiment>
      ...
    </experimentList>
    <interactionList>
      <interaction id='1' imexId='IM-123456-1'>
        <experimentList>
          <experimentRef id='1'/>
        </experimentList>
        <participantList>
          <participant id='1'>
            <interactorRef id='2'/>
            <biologicalRole>...</biologicalRole>
            <experiemntalRole>...</experimentalRole>
            ....
          </participant>
          <participant id='2'>...</participant>
          ....
        </participantList>
      </interaction>
      <interaction id='2' imexId='IM-123456-12'>...</interaction>
      ...
    </interactionList>
  </entry>
  ...
</entrySet>
```

Record source (database)

List of interactors

List of experimental methods/protocols

List of interactions

Reference to experimental method/protocol

Reference to interactor

Participant (e.g. protein)
- Describes the state of the molecule as used in the experiment
- Refers to 'interactor' – the reference description of the molecule (e.g. UniprotKB)

Interaction Data Processing

PSI-MI XML (MIF) file anatomy

Expanded MIFs describe interactors and experiments within each interaction

```
<entry Set>
  <entry>
    <source releaseDate='2019-05-22'>...</source>
    <interactionList>
      <interaction id='1' imexId='IM-123456-1'>
        <experimentList>
          <experiment id='1'/>...</experiment>
        </experimentList>
        <participantList>
          <participant id='1'>
            <interactor id='2'>...</interactor>
            <biologicalRole>...</biologicalRole>
            <experiemntalRole>...</experimentalRole>
            ....
          </participant>
          <participant id='2'>...</participant>
          ....
        </participantList>
      </interaction>
      <interaction id='2' imexId='IM-123456-12'>...</interaction>
      ...
    </interactionList>
  </entry>
  ...
</entrySet>
```

Record source (database)

List of interactions

Experimental method/protocol description

Interactor description

Participant (e.g. protein)
- Describes the state of the molecule as used in the experiment
- Refers to 'interactor' – the reference description of the molecule (e.g. UniprotKB)

Interaction Data Processing

PSI-MI XML (MIF) file anatomy

Compact MIFs use references to interactors and/or experiments

Description of the experimental method (explicit or a reference)

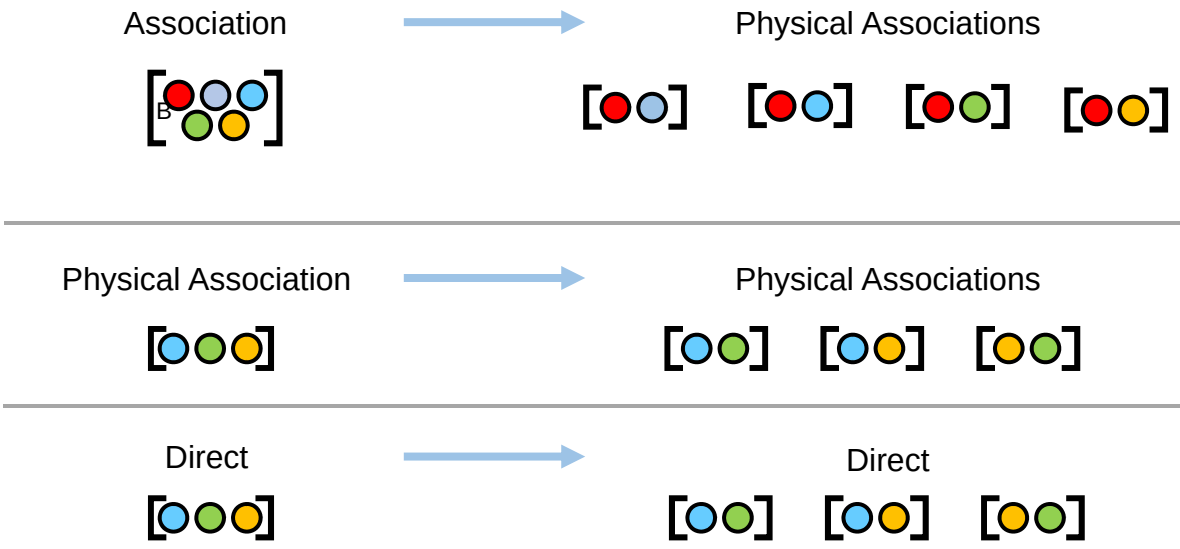
Description of the interactor (explicit or a reference)

Participant (e.g. protein)
- Describes the state of the molecule as used in the experiment
- Refers to 'interactor' – the reference description of the molecule (e.g. UniprotKB)

Features (e.g. mutations)
- Modifications of the molecule relative to the reference state

Interaction Data Processing

Binary Expansion



Interaction Data Processing

XML file parsing

Simple (and less simple but somewhat useful) project ideas

- List UniprotKB (gene names, Entrez gene identifiers, GO terms, etc) identifiers for each protein in a given MIF file
- Generate a FASTA file listing sequences all the bait proteins reported in a given MIF file
- Count interactions of a given protein (or a set of proteins) that are reported in a given MIF file
- Find all direct interactions of a given protein that are reported in a given MIF file
- List all proteins for each interaction reported in a given MIF file excluding proteins annotated (experimental role) as 'ancillary'
- Retrieve GO annotation from XML-formatted UniprotKB record – e.g.

  https://www.uniprot.org/uniprot/P60010.xml
- Retrieve protein cross reference information from EBI PICR service:

  http://www.ebi.ac.uk/Tools/picr/

Interaction Data Processing

References

XML Parsing

- lxml library: https://lxml.de
- XPath: https://en.wikipedia.org/wiki/XPath (and references therein)

MIF (miXML) format specification

- XSD: https://github.com/HUPO-PSI/miXML (2.5/src, 3.0/src directories)
- Publications
  - Hermjakob H *et al*. The HUPO PSI's molecular interaction format--a community standard for the representation of protein interaction data.
    Nat Biotechnol. 22:177-83 (2004). PMID: 14755292
  - Kerrien S et al. Broadening the horizon--level 2.5 of the HUPO-PSI format for molecular interactions.
    BMC Biol. 5:44 (2007). PMID: 17925023
  - Sivade Dumousseau M *et al*. Encompassing new use cases - level 3.0 of the HUPO-PSI format for molecular interactions.
    BMC Bioinformatics. 19:134. doi: 10.1186/s12859-018-2118-1 (2018). PMID: 29642841