NCIBI Literature Mining

Behind the Scenes, Web-Based Access

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Introduction

- NCIBI Biomedical Literature and Accessory Databases
- Natural Language Processing Pipeline
- Database Access
- XML Querying

NCIBI Biomedical Literature and Accessory Databases

Source Pubmed Database

- Available from the National Center for Biotechnology Information (NCBI)
- Provides access to citations and abstracts from biomedical literature from ~1950 to present in ~5000 journals
- Publishers participating in Pubmed electronically submit their citations to NCBI prior to or at the time of publication
- Records are indexed with NLM's MeSH
- Abstracts only, not full-text

NCIBI Pubmed Database

- We lease the NLM Pubmed data set, extract the data from the source XML files, and populate our local NCIBI Pubmed database
- Updated nightly (~12K per update, but never more than 30K)
- ~20M documents
- ~19M unique documents
- ~11M abstracts

Source PMCOA Database

- Pubmed Central is the NIH's free digital archive of biomedical and life science literature
- Some articles in PMC are "open access" which means that an article is still protected by copyright, but is distributed under a Creative Commons or similar license that generally allows more liberal use than a traditional copyrighted work
- Full-text documents

NCBI PMCOA Database

- We download the PMCOA data set, extract the data from the source XML files, and populate our local NCIBI PMCOA database
- Updated monthly (~2K documents per update)
- ~107K documents

Accessory Databases

- Entrez Gene - is NCBI's database for gene-specific information
- Journal - all Entrez journals
- Taxonomy - contains names of all organisms represented in the genetic database with at least one nucleotide or protein sequence
- UMLS - Metathesaurus and Semantic Network, very large vocabulary database that contains information about biomedical and health related concepts, their names, and the relationships among them (GO, FMA, ICD9, etc.)
- MeSH - NLM's controlled vocabulary for indexing Pubmed

MeSH

- Medical Subject Headings
- The NLM's controlled vocabulary thesaurus
- Sets of naming descriptors in an eleven-level hierarchical structure that permits searching at various levels of specificity
- ~25K descriptors, 83 qualifiers, ~186K entry terms (synonyms)
- e.g. Ascorbic Acid (descriptor), administration & dosage (qualifier), Vitamin C (entry term), etc.

Natural Language Processing Pipeline

NLP Tools and Pipeline

- We "value add" to the Pubmed and PMCOA databases by doing Natural Language Processing to the data and adding those results to the database
- Sentence segmentation (boundary detection) using MxTerminator
- Named entity tagging using NameTagger, SciMiner, and Genia
- Part of speech, stemming, lemmatizing using Porter-Stemmer and StanfordParser
- Parsing using StanfordParser
- Information extraction using ClairLib and GIN-IE

MxTerminator

- Java based sentence boundary detector
- Written by Adwait Radnaparkhi
- No source code available
- Performs with an accuracy of 93.5% on Medline abstracts with the default model
- The version I use has been trained for biomedical text and has an accuracy of about 96%
- ~92M Pubmed sentences, ~16M PMCOA sentences

Named Entity Tagging

- Looking for important biomedical words or phrases in a sentence
- NameTagger - uses a dictionary approach to tagging gene/protein names and MeSH terms
- SciMiner - uses a dictionary approach to tagging gene/protein and metabolite names
- Genia - statistical tagger trained on 2000 Medline abstracts for tagging protein, DNA, RNA, cell line, and cell type names
  - Hand annotated abstracts selected using *human*, *blood cell*, and *transcription factor* MeSH terms

Ambiguous Tags

- There are Gene symbols and synonyms that are also common words
- E.g. be, is, was, to, and, in, for, not, on, with, he, as, you, do, at, with, this, her, she, an, my, if…
- Mask system based on capitalization, punctuation, gene2pubmed, etc.

POS, Stemming, Lemmatizing

- Determine the part-of-speech and stem or root of a word
- Using Porter-Stemmer and the StanfordParser
- Stemming mainly involves suffix stripping rules
- Lemmatizing applies rules based on POS to determine the lemma or root of a word so is highly dependent on accurate POS
- E.g. “run” is the stem of “running” and “runs,” but “ran” is the stem of “ran”
- E.g. “run” is the lemma of “running,” “runs,” and “ran”

Parsing

- Using the StanfordParser
- Phrase Structure parse and Typed Dependency parse are different ways of representing the structure of a sentence
- Phrase Structure
  - Represents nesting of multi-word constituents (chunks)
- Typed Dependencies Collapsed
  - Represents dependencies between individual words and labels those dependencies with grammatical relations (collapsed prepositions and conjunctions)

Phrase Structure

- Colony-stimulating factor-1 (CSF-1) is essential for macrophage growth, differentiation and survival.

```
(ROOT
  (S
    (NP
      (NP (JJ Colony-stimulating) (NN factor-1))
      (PRN (-LRB- -LRB-)
        (NP (NN CSF-1))
        (-RRB- -RRB-)))
    (VP (VBZ is)
      (ADJP (JJ essential)
        (PP (IN for)
          (NP
            (ADJP (NN macrophage) (NN growth))
            (, ,) (NN differentiation)
            (CC and)
            (NN survival)))))
    (. .)))
```

```
S: Simple Declarative Clause
NP: Noun Phrase
JJ: Adjective
NN: Noun
PRN: Parenthetical
VP: Verb Phrase
VBZ: Verb, 3rd person singular present
ADJP: Adjective Phrase
PP: Prepositional Phrase
IN: Preposition
CC: Coordinating Conjuction
```

Typed Dependencies Collapsed

- Colony-stimulating factor-1 (CSF-1) is essential for macrophage growth, differentiation and survival.

```
amod(factor-1-2, Colony-stimulating-1)
nsubj(essential-7, factor-1-2)
appos(factor-1-2, CSF-1-4)
cop(essential-7, is-6)
prep_for(essential-7, macrophage-9)
dep(macrophage-9, growth-10)
conj_and(macrophage-9, differentiation-12)
conj_and(macrophage-9, survival-14)
```

```
amod: adjectival modifier
nsubj: nominal subject
appos: appositional modifier
coop: copula
prep_for: prepositional modifier
conj_and: conjuct
dep: dependent
```

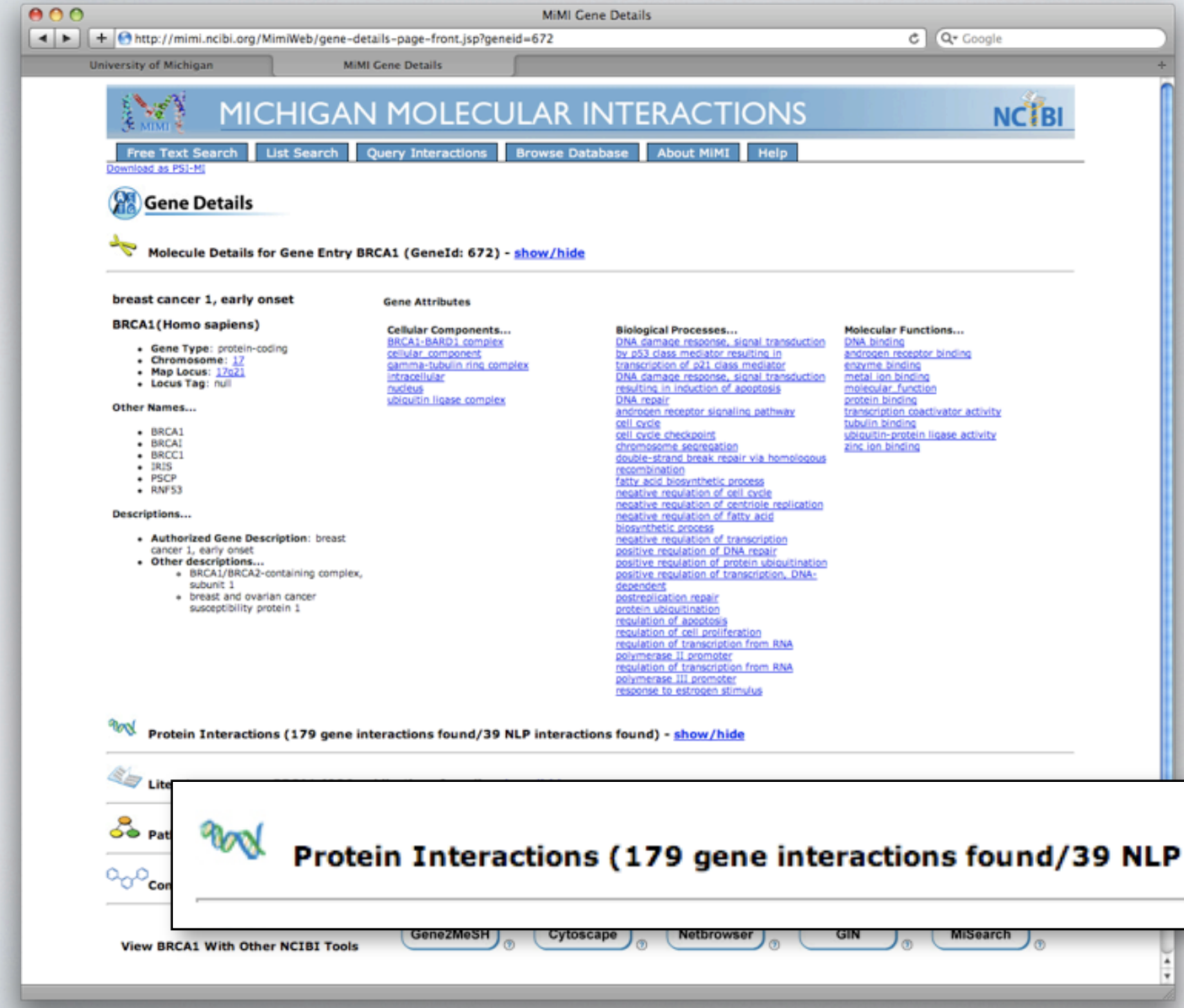
GIN-IE

- Uses the sentences, tags, and parse data to extract and annotate protein-protein interactions
- Results are available as an RSS feed (recently published documents) and within MiMI (soon to be all documents)
- E.g. The partial results of GIN-IE on sentences tagged for BRCA1
  - We finally demonstrated by immunoprecipitation of ACCA in cells, that the whole BRCA1 protein interacts with ACCA when phosphorylated on Ser1263.
  - In contrast, BRCA1-p53 interaction is weak or other mechanisms operate.
  - We documented an in vivo association of the endogenous BRCA1 with PR isoforms A and B and a direct in vitro interaction between BRCA1 and PR, which was partially mapped.
  - BRCA1 colocalized with TRF2 in telomerase-positive cells and with a small subset of ALT-associated PML bodies (APBs) in ALT cells.

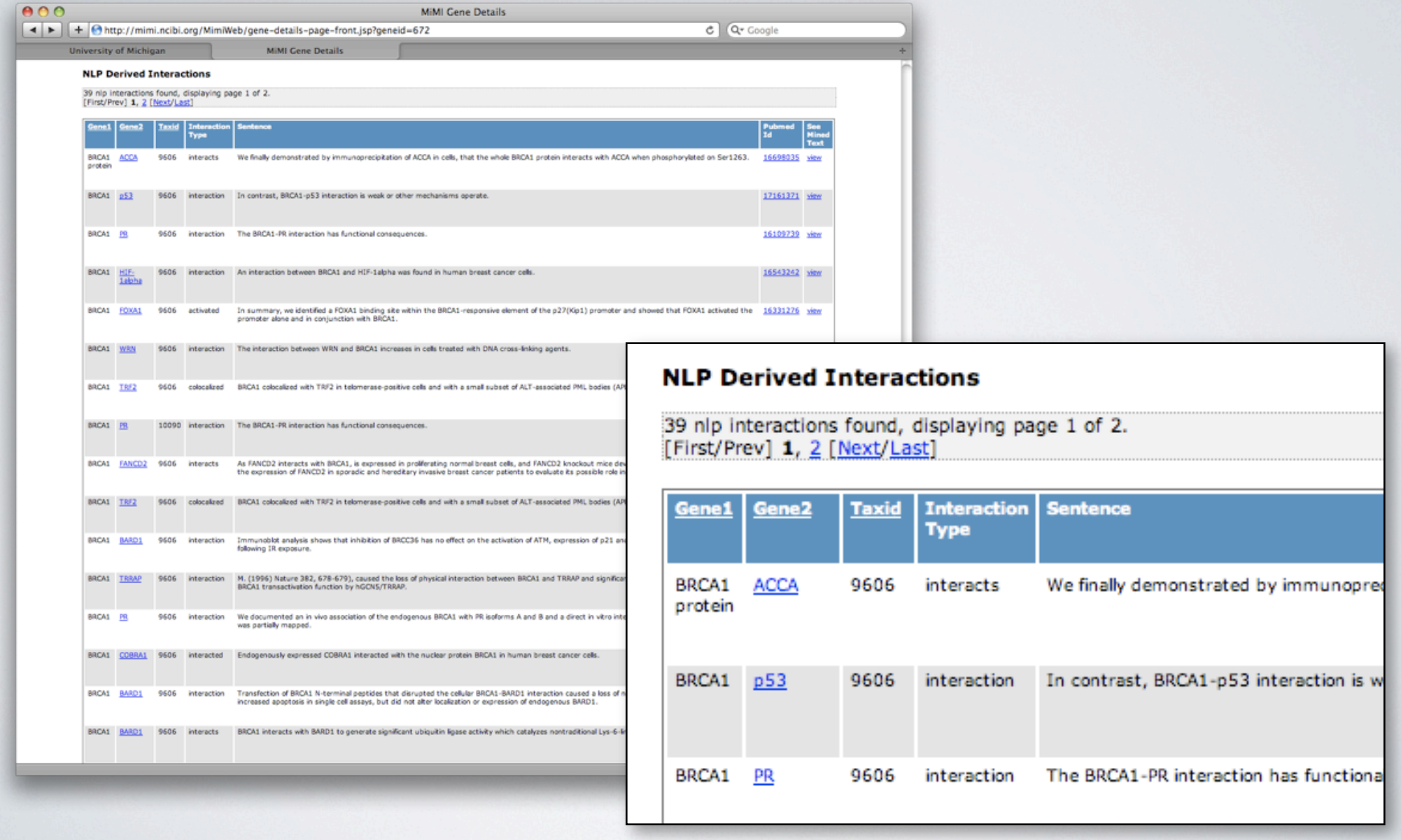
GIN-IE RSS Feed

- http://gin.ncibi.org/rss/gin-ie/interactions.rss
- RSS 2.0 format
- Contains only the interactions from recently published documents in Pubmed
- ~4700 interactions in the feed

GIN-IE Data in MiMI



GIN-IE Data in MiMI



Database Access

NCIBI NLP Web Service

- NCIBI NLP web service provides programmatic access to the Pubmed and PMCOA databases
- Loosely modeled after NCBI's eUtils because many biomedical researchers are familiar with that service
- Build a URL based query using a base URL and a set of parameters
- Returns an XML result set
- http://nlp.ncibi.org/about.html

NCIBI-WS Future Work

- Query for SciMiner tags in Pubmed
- Query for Nametagger and SciMiner tags in PMCOA
- Add Metadata to the Article (e.g. authors, title)
- Support for multiple, comma separated identifiers in a single query (e.g. pmid=1234,5678,9101)
- Add support for querying GIN-IE interaction data

XML Result (PMID)

http://nlp.ncibi.org/fetch.php?pmid=17523140

```
<?xml version="1.0"?>
<NCIBI>
   <BioNLP>
      <Request type="fetch">
         <ParameterSet>
            <PMID>17523140</PMID>
            <Limit>1000</Limit>
         </ParameterSet>
      </Request>
      <Response>
         <ResultSet>
            <Result>
               <Article pmid="17523140">
                  <Section type="abstract">
                     <Paragraph>
                        <Sentence>Heat stress causes severe constraints on numerous physiological...</Sentence>
                        <Sentence>In this study, we performed proteomic profiling of a nuclear...</Sentence>
                        <Sentence>We found 10 protein spots whose expression had changed after heat...</Sentence>
                        <Sentence>Seven of those protein spots, periodic tryptophan protein 1 homolog...</Sentence>
                        <Sentence>We focused on the downregulation of two splicing factors, which might...</Sentence>
                     </Paragraph>
                  </Section>
               </Article>
            </Result>
         </ResultSet>
      </Response>
   </BioNLP>
</NCIBI>
```

XML Result (Tagged PMID)

http://nlp.ncibi.org/fetch.php?pmid=17523140&tagger=nametagger&type=gene

```
<?xml version="1.0"?>
<NCIBI>
   <BioNLP>
      <Request type="fetch"><ParameterSet><PMID>17523140</PMID><Limit>1000</Limit></ParameterSet></Request>
      <Response><ResultSet><Result>
         <Article pmid="17523140">
            <Section type="abstract">
               <Paragraph>
                  <Sentence>Heat stress causes severe constraints on numerous physiological...</Sentence>
                  <Sentence>In this study, we performed proteomic profiling of a nuclear...</Sentence>
                  <Sentence>We found 10 protein spots whose expression had changed after heat...</Sentence>
                  <Sentence>Seven of those protein spots, <Gene type="entrez" id="11137">periodic tryptophan protein 1</
Gene> homolog (<Gene type="entrez" id="11137">PWP1</Gene>), <Gene type="entrez" id="3837">importin beta-1 subunit</Gene>,
sumoylated protein, <Gene type="entrez" id="10946">splicing factor 3a subunit 3</Gene> (<Gene type="entrez"
id="10946">SF3a3</Gene>), <Gene type="entrez" id="23435">TAR DNA-binding protein 43</Gene>, <Gene type="entrez"
id="26854,6066,26853,26855">U2</Gene> small nuclear ribonucleoprotein auxiliary factor 35 kDa subunit (<Gene
type="entrez" id="7307">U2AF35</Gene>) and small ubiquitin-related modifier-1 (<Gene type="entrez" id="7341">SUMO-1</
Gene>) were downregulated, while three other protein spots, Protein SET, 40S <Gene type="entrez" id="3921">ribosomal
protein SA</Gene> and <Gene type="entrez" id="6175">60S acidic ribosomal protein P0</Gene> were upregulated by the heat
stress.</Sentence>
                  <Sentence>We focused on the downregulation of two splicing factors, which might...</Sentence>
               </Paragraph>
            </Section>
         </Article>
      </Result></ResultSet></Response>
   </BioNLP>
</NCIBI>
```

XML Result (Gene ID)

http://nlp.ncibi.org/fetch.php?tagger=nametagger&type=gene&id=11137

```
<?xml version="1.0"?>
<NCIBI>
   <BioNLP>
      <Request type="fetch">
         <ParameterSet><Tagger>nametagger</Tagger><Type>gene</Type><ID>11137</ID><Limit>1000</Limit></ParameterSet>
      </Request>
      <Response>
         <ResultSet>
            <Result>
               <Article pmid="7828893">
                  <Section type="abstract">
                     <Paragraph>
                        <Sentence>We have cloned and expressed in vaccinia virus a cDNA encoding an...</Sentence>
                        <Sentence>Database searching indicated that <Gene type="entrez" id="11137">IEF SSP...</Sentence>
                     </Paragraph>
                  </Section>
               </Article>
            </Result>
            <Result>
               <Article pmid="11850830">
                  <Section type="abstract">
                     <Paragraph>
                        <Sentence>The transcript encoding endonuclein, the human homolog of yeast <Gene...</Sentence>
                     </Paragraph>
                  </Section>
               </Article>
            </Result>
            ...
```

XML Querying

XPath

- Defined by the World Wide Web consortium
- XPath is a query language for XML
- XPath is used to navigate through the nodes and attributes in an XML document
- Implementations available for the major bioinformatics programming languages (e.g. Perl, Python, Java)

XPath Example (NCIBI)

```
URL ncibiws = new URL(“http://nlp.ncibi.org/fetch.php?pmid=17523140&tagger=nametagger&type=gene”);
URLConnection connection = ncibiws.openConnection();

InputStream inputStream = connection.getInputStream();

DocumentBuilderFactory factory = DocumentBuilderFactory.newInstance();
Document document = factory.newDocumentBuilder().parse(inputStream);

inputStream.close();

XPath xpath = XPathFactory.newInstance().newXPath();
String expression = “//Sentence”;

NodeList nodes = (NodeList)xpath.evaluate(expression, document, XPathConstants.NODESET);

for (int i = 0; i < nodes.getLength(); i++) {
     System.out.println(nodes.item(i).getTextContent());
}
```

XPath Example (NCIBI + eUtils)

```
URL entrezws =
     new URL("http://eutils.ncbi.nlm.nih.gov/entrez/eutils/esearch.fcgi?db=pubmed&term=ade%20a[au]");

// will return a nodelist of PMIDs where I'm an author
String expression = "//IdList/Id";

NodeList pmidNodes = (NodeList)xpath.evaluate(expression, document, XPathConstants.NODESET);

for (int i = 0; i < pmidNodes.getLength(); i++) {
     String PMID = pmidNodes.item(i).getTextContent();

     URL ncibiws = new URL("http://nlp.ncibi.org/fetch.php?pmid=" + PMID);

     // will return a nodelist of Sentences that have a Gene tag
     expression = "//Gene/parent:node()";

     NodeList sentenceNodes = (NodeList)xpath.evaluate(expression, document, XPathConstants.NODESET);

     for (int k = 0; k < sentenceNodes.getLength(); k++) {
          System.out.println(sentenceNodes.item(i).getTextContent());
     }
}
```

More XPath Expressions

```
// pubmed

// parameters pmid, tagger, type

String expression = “//Sentence”;
String expression = “//Gene”;
String expression = “//Gene/parent::node()”;
String expression = “//Gene[@id=‘11137’]/parent::node()”;

// parameters tagger, type, id

String expression = “//Article/@pmid”;


// pmcoa (soon)

// parameters pmcid, tagger, type

String expression = “//Section[@type=‘results’]//Gene/parent::node()”;
```

Thank You!

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