RDF processing for Bioconductor: *Redland*

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1 Introduction

Resource Description Framework (RDF) is a graphical model for information. RDF statements are ordered triples of the form (subject, predicate, object). Subjects and objects are viewed as nodes in a directed graph, and predicates are viewed as arcs in the graph. RDF is a key component of current developments towards a semantic web, with considerable work completed on web resource metadata representation and exchange using RDF. A richer metadata model is provided by OWL (Web Ontology Language), but most OWL models are serialized using XML/RDF. Thus, as we will illustrate, various public OWL resources can be processed by this package.

Redland is the name of an open source software project downloadable from [librdf.org](http://librdf.org). Redland is a C language library with bindings provided to a variety of other languages. Redland is highly modular, and allows developers to drop in components to substitute for base functionalities. Because metadata resources can be very voluminous, such flexibility is important. A solution to the problem of persistent storage of indexed metadata is provided through the use of BerkeleyDB serializations of Redland models.

*Redland* is an R package that provides interfaces to facilities of Redland. Configuration support is currently limited. You will be able to use Rredland if you do a stock...
installation of librdf and BerkeleyDB. If you have these resources in nonstandard locations, you can set the Makevars variables in src to reflect your configuration. You may need to set LD_LIBRARY_PATH.

2 Illustration

2.1 Simple manipulations with a fragment of GO

Eric Jain of ISB-CH has provided an RDF serialization of the UniProt database and associated annotation resources, including an RDF serialization of GO. A fragment of this serialization is distributed with the Rredland package.

> library(Rredland)

A redland RDF world has been created in package:Rredland as ..GredlWorld.

> gofrag <- system.file("RDF/gopart.rdf", package = "Rredland")

Here we dump the first 10 lines of this document as text:

> readLines(gofrag, n = 10)

This could be processed as an XML document, but let's use Redlands modeling facilities. First we need to set up a URI object for the model source document.

> gouri <- makeRedlURI(paste("file:\", gofrag, sep = ""))

Now we read from this document. We will set the useCore option to use in-memory storage.

> gof <- readRDF(gouri)
> gof
redlModel object, status=open.

We are handed back an S4 object of class redlModel.

> getClass("redlModel")

Slots:

Name:       ref storagetype stateEnv world
Class: externalptr character environment redlWorld

We need to use the model accessor to get to the model reference.

We can easily compute the number of statements (also computed with show()):

> size(gof)

[1] 69

We can also transform to a data frame:

> godf <- as(gof, "data.frame")
> godf[1:4, ]

subject
1 urn:lsid:uniprot.org:go:0000001
2 urn:lsid:uniprot.org:go:0000001
3 urn:lsid:uniprot.org:go:0000001
4 urn:lsid:uniprot.org:go:0000001

predicate
1 http://www.w3.org/1999/02/22-rdf-syntax-ns#type
2 http://www.w3.org/2000/01/rdf-schema#label
3 http://www.w3.org/2000/01/rdf-schema#comment
4 http://www.w3.org/2000/01/rdf-schema#subClassOf

1
2
3 "The distribution of mitochondria, including the mitochondrial genome, into daughter..."
4

We see that long text strings can cause a problem for rendering.

> as.character(godf[1:4, 3])

[1] "urn:lsid:uniprot.org:ontology:Concept"
[2] ""mitochondrion inheritance"
[3] "The distribution of mitochondria, including the mitochondrial genome, into daughter..."
The data frame representation is useful for splitting up the statement set.

```r
> bypred <- split(godf, as.character(godf$predicate))
> names(bypred)

[1] "http://www.w3.org/1999/02/22-rdf-syntax-ns#type"
[2] "http://www.w3.org/2000/01/rdf-schema#comment"
[4] "http://www.w3.org/2000/01/rdf-schema#subClassOf"
```

```r
> sapply(bypred, nrow)

<table>
<thead>
<tr>
<th>Name</th>
<th>Rows</th>
</tr>
</thead>
<tbody>
<tr>
<td><a href="http://www.w3.org/1999/02/22-rdf-syntax-ns#type">http://www.w3.org/1999/02/22-rdf-syntax-ns#type</a></td>
<td>16</td>
</tr>
<tr>
<td><a href="http://www.w3.org/2000/01/rdf-schema#comment">http://www.w3.org/2000/01/rdf-schema#comment</a></td>
<td>15</td>
</tr>
<tr>
<td><a href="http://www.w3.org/2000/01/rdf-schema#label">http://www.w3.org/2000/01/rdf-schema#label</a></td>
<td>19</td>
</tr>
<tr>
<td><a href="http://www.w3.org/2000/01/rdf-schema#subClassOf">http://www.w3.org/2000/01/rdf-schema#subClassOf</a></td>
<td>17</td>
</tr>
<tr>
<td>urn:lsid:uniprot.org:ontology:obsolete</td>
<td>2</td>
</tr>
</tbody>
</table>
```

The `subClassOf` predicate helps determine the DAG structure:

```r
> bypred$"http://www.w3.org/2000/01/rdf-schema#subClassOf"[, -2]

<table>
<thead>
<tr>
<th>Subject</th>
<th>Object</th>
</tr>
</thead>
<tbody>
<tr>
<td>urn:lsid:uniprot.org:go:0000012</td>
<td>urn:lsid:uniprot.org:go:0006281</td>
</tr>
</tbody>
</table>
```
2.2 BioPAX Level 1

The BioPAX pathway ontologies are available.

```r
> bp1 <- makeRedlURI(paste("file:", system.file("RDF/biopax-level1.owl", + package = "Rredland"), sep = ""))
> bp1m <- readRDF(bp1)
> size(bp1m)

[1] 630
```

This is a manageable object, so we convert to data frame:

```r
> bp1df <- as(bp1m, "data.frame")
> sapply(bp1df[1:5, ], substring, 1, 70)

subject
[1,] "http://www.biopax.org/release/biopax-level1.owl"
[2,] "http://www.biopax.org/release/biopax-level1.owl"
[3,] "http://www.biopax.org/release/biopax-level1.owl#physicalEntityParticip"
[4,] "http://www.biopax.org/release/biopax-level1.owl#chemicalStructure"
[5,] "http://www.biopax.org/release/biopax-level1.owl#physicalEntityParticip"

predicate
[1,] "http://www.w3.org/1999/02/22-rdf-syntax-ns#type"
[2,] "http://www.w3.org/2000/01/rdf-schema#comment"
[3,] "http://www.w3.org/1999/02/22-rdf-syntax-ns#type"
[4,] "http://www.w3.org/1999/02/22-rdf-syntax-ns#type"
[5,] "http://www.w3.org/2002/07/owl#disjointWith"

object
[1,] "http://www.w3.org/2002/07/owl#Ontology"
[2,] "This is version 1.4 of the BioPAX Level 1 ontology. The goal of the "
[3,] "http://www.w3.org/2002/07/owl#Class"
[4,] "http://www.w3.org/2002/07/owl#Class"
[5,] "http://www.biopax.org/release/biopax-level1.owl#chemicalStructure"
```

The namespace qualifications make the strings difficult to render. A simple approach uses substitution up to the pound sign, preceded by eliminating any XSD postfix information.

```r
> strip2pound <- function(x) gsub(".*#", ",", cleanXSDT(as.character(x)))
> sapply(bp1df[1:5, ], strip2pound)

subject
[1,] "http://www.biopax.org/release/biopax-level1.owl" "type"
[2,] "http://www.biopax.org/release/biopax-level1.owl" "comment"
```
Working with a data frame, it is easy to filter statements of interest. Suppose we wish to determine all the instances of \texttt{owl\#Class} in the model.

```r
> isTypeOwlClass <- grep("owl\#Class", as.character(bp1df[, 3]))
> strip2pound(bp1df[isTypeOwlClass, 1])
```

We see a number of decipherable terms, and some tokens of the form (rnnn...). The latter are called blank nodes. These are created to define classes that have no names, but that are implicitly defined in the model. For example, a class that is the union of entity and physicalEntity is a blank node in this model.

To get the detailed commentary on a class definition, the following function can be used:

```r
> getClassComment <- function(term, df, nsPref = "http://www.biopax.org/release/biopax-level1.owl#", +    commPred = "http://www.w3.org/2000/01/rdf-schema#comment",
```
doChop = TRUE, nword = 12) {
  ind <- which(as.character(df[, 1]) == paste(nsPref, term, sep = "") & as.character(df[, 2]) == commPred)
  chopLong(cleanXSDT(as.character(bp1df[ind, 3])), nword = nword)
}

> cat(getClassComment("chemicalStructure", bp1df))

"A utility class that defines a small molecule structure. An instance of this class can also define additional information about a small molecule, such as its chemical formula, names, and synonyms. This information is stored in the slot STRUCTURE-DATA, in one of two formats: the CML format (see URL www.xml-cml.org) or the SMILES format (see URL www.daylight.com/dayhtml/smiles/). The STRUCTURE-FORMAT slot specifies which format is used. An example is the following SMILES string, which describes the structure of glucose-6-phosphate:

'C(OP(=O)(O)O)CH1(CH(O)CH(O)CH(O)CH(O)O1)'."

> cat(getClassComment("biochemicalReaction", bp1df))

"A conversion interaction in which one or more entities (substrates) undergo covalent changes to become one or more other entities (products). The substrates of biochemical reactions are defined in terms of sums of species. This is what is typically done in biochemistry, and, in principle, all of the EC reactions should be biochemical reactions.

Example: ATP + H2O = ADP + Pi.

In this reaction, ATP is considered to be an equilibrium mixture of several species, namely ATP4-, HATP3-, H2ATP2-, MgATP2-, MgHATP–, and Mg2ATP. Additional species may also need to be considered if other ions (e.g. Ca2+) that bind ATP are present. Similar considerations apply to ADP and to inorganic phosphate (Pi). When writing biochemical reactions, it is important not to attach charges to the biochemical reactants and not to include ions such as H+ and Mg2+ in the equation. The reaction is written in the direction specified by the EC nomenclature system, if applicable, regardless of the physiological direction(s) in which the reaction proceeds. (This definition from EcoCyc)

NOTE: Polymerization reactions involving large polymers whose structure is not explicitly specified should generally be represented as unbalanced reactions in which the monomer is consumed but the polymer remains unchanged, e.g. glycogen + glucose = glycogen."
2.3 BioPAX level 2

Here we check the classes available in BioPAX level 2.

```r
> bp2 <- makeRedlURI(paste("file:", system.file("RDF/biopax-level2.owl", + package = "Rredland"), sep = ""))
> bp2m <- readRDF(bp2)
> size(bp2m)

[1] 910

> bp2df <- as(bp2m, "data.frame")
> isTypeOwlClass <- grep("owl#Class", as.character(bp2df[, 3]))
> strip2pound(bp2df[isTypeOwlClass, 1])

[1] "dataSource"           "openControlledVocabulary"
[3] "xref"                 "bioSource"
[5] "externalReferenceUtilityClass" "dnaParticipant"
[7] "rnaparticipant"        "dna"
[9] "physicalEntityParticipant" "proteinParticipant"
[11] "complexParticipant"    "smallMoleculeParticipant"
[13] "transportWithBiochemicalReaction" "biochemicalReaction"
[15] "transport"             "complexAssembly"
[17] "conversion"            "physicalEntity"
[19] "interaction"           "entity"
[21] "pathway"               "unificationXref"
[23] "relationshipXref"      "publicationXref"
[25] "physicalInteraction"   "smallMolecule"
[27] "protein"               "rna"
[29] "complex"               "sequenceLocation"
[31] "confidence"            "evidence"
[33] "chemicalStructure"     "utilityClass"
[35] "pathwayStep"           "sequenceInterval"
[37] "sequenceSite"          "sequenceFeature"
[39] "modulation"            "catalysis"
[41] "control"               "experimentalForm"
[43] "(r1209547402r28139r141)" "(r1209547402r28139r156)"
[45] "(r1209547402r28139r159)" "(r1209547402r28139r166)"
[47] "(r1209547402r28139r170)" "(r1209547402r28139r173)"
[49] "(r1209547402r28139r176)" "(r1209547402r28139r182)"
[51] "(r1209547402r28139r186)" "(r1209547402r28139r189)"
[53] "(r1209547402r28139r201)" "(r1209547402r28139r204)"
[55] "(r1209547402r28139r207)" "(r1209547402r28139r211)"
```
2.4 HumanCyc

The BioCyc project ([www.biocyc.org](http://www.biocyc.org)) is a collection of pathway/genome databases in a variety of structures. The data resources are available to academic researchers, and a registration/download process must be completed for access. We illustrate use of Rredland to work with the BioPAX encoding of HumanCyc. This is 19MB of RDF and an in-core storage model is not likely to be satisfactory. We will use the default BerkeleyDB storage approach.

```r
> humu <- makeRedlURI(paste("file:", "humancyc.owl", sep = "))
> humm <- readRDF(humu, storageType = "bdb", storageName = "hucyc")
```

Note that the vignette cannot assume that you have this OWL file. After the above commands, we have

```
-rw-r--r-- 1 stvjc stvjc  59723776 Jul 28 13:09 test-sp2o.db
-rw-r--r-- 1 stvjc stvjc  39538688 Jul 28 13:07 test-po2s.db
-rw-r--r-- 1 stvjc stvjc  57499648 Jul 28 13:07 test-so2p.db
```

These are the BerkeleyDB hashes representing aspects of the graph.

It is not too difficult to transform into a data frame.

```r
> hudf <- as(humm, "data.frame")
> husubs <- as.character(hudf[, 1])
> hupreds <- as.character(hudf[, 2])
> huobs <- as.character(hudf[, 3])
> table(hupreds)
```

```
hupreds

  http://www.biopax.org/release/biopax-level1.owl#AUTHORS 31432
  http://www.biopax.org/release/biopax-level1.owl#CELLULAR-LOCATION 2800
  http://www.biopax.org/release/biopax-level1.owl#COFACTOR 11
  http://www.biopax.org/release/biopax-level1.owl#COMMENT 1231
  http://www.biopax.org/release/biopax-level1.owl#COMPONENTS 36
  http://www.biopax.org/release/biopax-level1.owl#CONTROL-TYPE 36
  http://www.biopax.org/release/biopax-level1.owl#CONTROLLED 2216
  http://www.biopax.org/release/biopax-level1.owl#CONTROLLER
```

---

9
To find the named pathways,

```r
> isPw <- grep("pathway", husubs)
> isNa <- grep("NAME", hupreds)
> isnp <- intersect(isPw, isNa)
> cleanXSDT(huobs[isnp][1:10])
```

[1] ""biosynthesis of aspartate and asparagine; interconversion of aspartate and asparagine""
[2] ""serine and glycine biosynthesis"
[3] ""alanine biosynthesis II"
[4] ""alanine biosynthesis I"
[5] ""alanine biosynthesis III"
[6] ""superpathway of alanine biosynthesis"
[7] ""arginine biosynthesis III"
[8] ""citrulline biosynthesis"
[9] ""asparagine biosynthesis I"
[10] ""aspartate biosynthesis and degradation"

So we see in the predicate set what kinds of relationships are described, and we get a glimpse of the pathway names addressed in this resource.

Note that there is no need to parse the data once the Berkeley DB hashes are made available. The BDBSexists option on readRedlModel can be used to revive a model-hash association.
3 Future work

We will need to take unions of RDF models and C code will be required for that. We need R interfaces to Redland approaches to model filtering. Some graph/set-theoretic activities can be introduced to bring some RDF/RDFS inferencing in.