Techno	logies, methods and challenges
14 1 16 24	ective public data sharing and
	Mark D Wilkinson Mark D Wilkinson Medical Genetics, UBC Pl Bioinformatics Heart + Lung Institute at St. Paul's Hospital markw@illuminae.com http://wilkinsonlab.ca

1 51/52 + 0 10 0 1

485

 $0 \pm -$

Thanks in advance

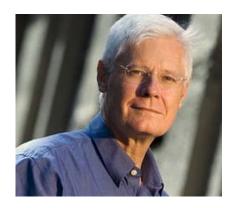
(very few of these ideas are my own!)



Paul Gordon – Sun Center of Excellence, U Calgary

Carole Goble – University of Manchester



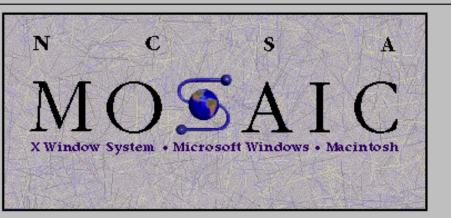


Charles Petrie – Stanford University

We've come a long way!!

In the beginning...

S NCSA Mosaic for MS Windows	_ 🗆 ×
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Document Title: NCSA Mosaic Home Page	
Document URL: http://www.ncsa.uiuc.edu/SDG/Software/Mosaic/NCS/	\square



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Link Integration

Show All 🔻	entries		Show/hide columns		Filter:	
Name 🕴	Transcript ID 🕴	Length (bp)	Protein ID	Length (aa) 🗦	Biotype 🍦	CCDS 🔶
BRCA1-001	ENST0000357654	7094	ENSP00000350283	1863	Protein coding	CCDS11453
BRCA1-003	ENST00000497488	779	ENSP00000418986	177	Protein coding	-
BRCA1-004	ENST00000477152	1980	ENSP00000419988	622	Protein coding	-
BRCA1-005	ENST00000471181	5939	ENSP00000418960	1885	Protein coding	-
BRCA1-006	ENST00000493795	5732	ENSP00000418775	1816	Protein coding	-
BRCA1-007	ENST0000468300	3273	ENSP00000417148	699	Protein coding	-
BRCA1-008	ENST00000493919	1948	ENSP00000418819	572	Protein coding	-
BRCA1-009	ENST00000478531	1972	ENSP00000420412	623	Protein coding	-
	ENST00000470026	2108	ENSP00000419274	649	Protein coding	-
	ENST00000494123	1612	ENSP00000419103	473	Protein coding	-
	ENST00000491747	2376	ENSP00000420705	758	Protein coding	-
	ENST00000484087	1495	ENSP00000419481	498	Protein coding	-
	ENST00000489037	455	ENSP00000420781	98	Protein coding	-
BRCA1-017	ENST00000476777	769	ENSP00000417554	222	Protein coding	-
BRCA1-018	ENST00000473961	958	ENSP00000420201	319	Protein coding	-
BRCA1-019	ENST00000487825	800	ENSP00000418212	266	Protein coding	-
BRCA1-022	ENST00000461574	726	ENSP00000417241	242	Protein coding	-
BRCA1-201		7173	ENSP00000310938	1567	Protein coding	CCDS11459
BRCA1-202	ENST0000346315	6456	ENSP00000246907	1624	Protein coding	CCDS11455
BRCA1-203		3624	ENSP00000338007	680	Protein coding	CCDS11454
	ENST00000352993	3747	ENSP00000312236	721	Protein coding	-
	ENST0000353540	7050	ENSP0000013772	1822	Protein coding	-
	ENST0000354071	6378	ENSP00000326002	1598	Protein coding	CCDS11456
BRCA1-207	ENST0000393680	7236	ENSP00000377285	1354	Protein coding	-
BRCA1-208		6484	ENSP00000377288	1567	Protein coding	CCDS11459
BRCA1-209		7370	ENSP00000377294	1863	Protein coding	CCDS11453
BRCA1-210		7167	ENSP00000397145	1863	Protein coding	CCDS11453
BRCA1-002		1584	ENSP00000420253	59	Nonsense mediated decay	-
	ENST00000461221	5693	ENSP00000418548	63	Nonsense mediated decay	-
BRCA1-020		582	ENSP00000417988	63	Nonsense mediated decay	-
	ENST00000467274	4497	No protein product	-	Retained intron	-
BRCA1-021	ENST00000472490	561	No protein product	-	Retained intron	-

Integration of What?

FT FT FT FT FT FT FT FT FT FT FT FT FT	CDS misc_binding	731212 /db_xref="GDB:135679" /db_xref="GOA:P27361" /db_xref="HGNC:6877" /db_xref="UniProtKB/Swiss-Prot:P27361" /gene="ERK1" /product="protein serine/threonine kinase" /protein_id="CAA42744.1" /translation="MAAAAAQGGGGGEPRRTEGVGPGVPGEVEMVKGQPFDVGPRYTQL QYIGEGAYGMVSSAYDHVRKTRVAIKKISPFEHQTYCQRTLREIQILLRFRHENVIGIR DILRASTLEAMRDVYIVQDLMETDLYKLLKSQQLSNDHICYFLYQILRGLKYIHSANVL HRDLKPSNLLSNTTCDLKICDFGLARIADPEHDHTGFLTEYVATRWYRAPEIMLNSKGY TKSIDIWSVGCILAEMLSNRPIFPGKHYLDQLNHILGILGSPSQEDLNCIINMKARNYL QSLPSKTKVAWAKLFPKSDSKALDLLDRMLTFNPNKRITVEEALAHPYLEQYYDPTDEP VAEEPFTFAMELDDLPKERLKELIFQETARFQPGVLEAP" 13541379 /Affymetrix="probe:HG_U95Av2:1000_at;399:559;" 13661391
FT FT	misc_binding	13661391 /Affymetrix="probe:HG_U95Av2:1000_at;544:185;"

misc_feature	447283484667 /note="Putative prophage; Putative lysogenic prophage region. Best Hits not completed. Putative attL/R; PHAGE01"
gene	<pre>complement(447387448511) /locus_tag="BA0427" /db_xref="GeneID:1087434" /db_xref="prophinder:34501" /db_xref="sherw:116" /db_xref="phage_finder:16305"</pre>
CDS	<pre>complement(447387448511) /locus_tag="BA0427" /note="identified by match to PFAM protein family HMM PF00589" /codon_start=1 /transl_table=11 /product="prophage LambdaBa04, site-specific recombinase, phage integrase family" /protein_id="NP_842969.1" /db_xref="GI:30260592" /db_xref="GeneID:1087434" /db_xref="aclame:protein:vir:6181" /translation="MKGYFRKRGEKWSFTIDIGKDPITGKRKQKTASGFKTKKEAERA CNELIHQFNTGSLVDDKNFTLSEYLQEWLENTAKQRVRETTFTNYKRAINSRIIPVLG SHKLKDLKPLHGQRFVKSLIDEGLSPAYIEYIFIVLKGSLEDAVRWELLFKNPFQHVE IPRPRKVVNSTWSIEETKKFLNRTKFENVIYYHLFLLALNTGMRRGEILGLKWKNFDL NEGKISVTETLIYDENGFRFTEPKTHGSKRLISIDQNLCKEFKSYKAKQNEFKLLFGQ SYEDNDLVFAKETGQPILPRTMTTTFNQFIKKADVPQIRFHDLRHTHATILLKLGINP KIVSERLGHSSIKTTLDTYSHVTIDMQESAVLKLSEALKS" /db_hit="ID=aclame:protein:vir:6181#Eval=6e-77#bits=281"</pre>

GenBankFormat

```
ID
     AB000263 standard; RNA; PRI; 368 BP.
XX
AC
    AB000263;
ΧХ
     Homo sapiens mRNA for prepro cortistatin like peptide, complete cds.
DE
ΧХ
    Sequence 368 BP;
SQ
AB000263 Length: 368 Check: 4514 ...
       1 acaagatgcc attgtccccc ggcctcctgc tgctgctgct ctccggggcc acggccaccg
      61 ctgccctgcc cctggagggt ggccccaccg gccgagacag cgagcatatg caggaagcgg
     121 caggaataag gaaaagcagc ctcctgactt tcctcgcttg gtggtttgag tggacctccc
     181 aggccagtgc cgggcccctc ataggagagg aagctcggga ggtggccagg cggcaggaag
     241 gcgcaccccc ccagcaatcc gcgcgccggg acagaatgcc ctgcaggaac ttcttctgga
     301
          agaccttctc ctcctgcaaa taaaacctca cccatgaatg ctcacgcaag tttaattaca
     361 gacctgaa
```

At least 20 different formats for representing DNA sequences...



Lord et al. 2004

Many formats contained a wide variety of related, but different, information

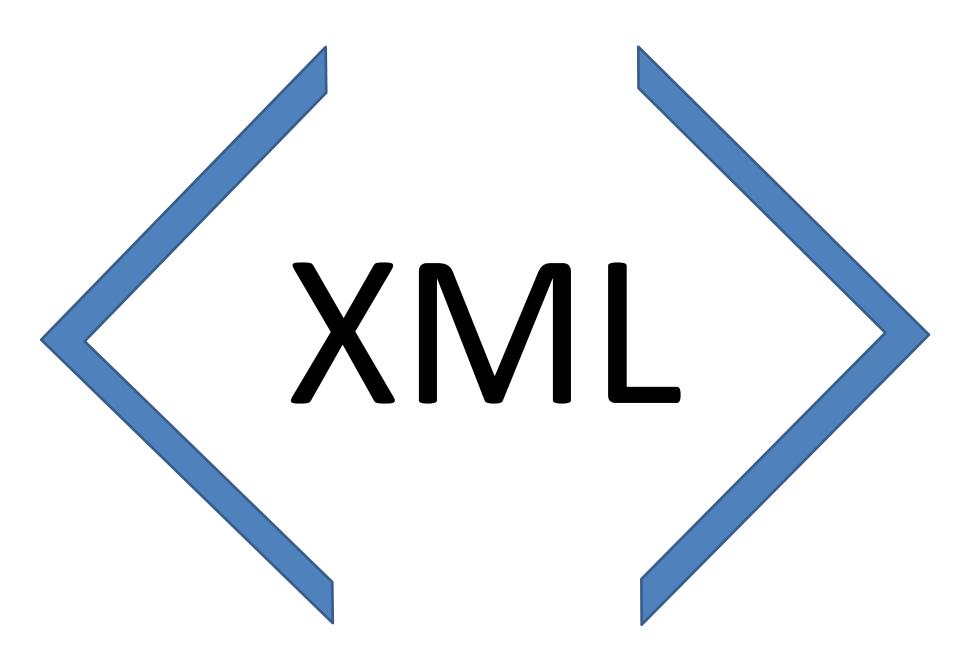
DNA sequence Sequence features Translation Date/time/method Publication cross-references

. . .

. . .

Each file format required it's own parser...

...and that problem wasn't limited to DNA...



What did XML do for us?



"...advent of XML meant that we didn't have to write our own parsers anymore..."

Individual data elements in a file can be automatically located and extracted

Predictable way to represent data

Makes it easier for machines to encode/extract

```
<value>
    BRCA1
   </value>
 </qualifier>
 <qualifier name="product">
   <value>
    breast and ovarian cancer susceptibility
   </value>
 </qualifier>
 <qualifier name="note">
   <value>
    influences susceptibility to breast and ovarian cancer
   </value>
 </qualifier>
 <qualifier name="protein_id">
   <value>
    AAA73985.1
   </value>
 </qualifier>
 <qualifier name="translation">
   <value>
    MDLSALRVEEVQNVINAMQKILECPICLELIKEPVSTKCDHIFCKFCMLKLLNQKKGPSQCPLCKNDITKRSLQESTRFSQLVEELLKIICAFQLDTGLEYANS
   </value>
 </qualifier>
 <location type="single" complement="false">
   <locationElement type="range" accession="U14680" version="1" complement="false">
     <basePosition type="simple">
      120
     </basePosition>
     <basePosition type="simple">
      5711
     </basePosition>
   </locationElement>
 </location>
</feature>
<feature name="exon">
 <qualifier name="gene">
   <value>
                                                           EMBL Record for BRCA1
    BRCA1
   </value>
                                                           In XML
 </gualifier>
 <qualifier name="number">
   <value>
    3
   </value>
 </gualifier>
```

</GBQualifier name> <GBQualifier_value> breast and ovarian cancer susceptibility </GBQualifier value> </GBQualifier> <GBQualifier> <GBQualifier_name> protein_id </GBQualifier name> <GBQualifier_value> AAA73985.1 </GBQualifier value> </GBQualifier> <GBQualifier> <GBQualifier name> db xref </GBQualifier_name> <GBQualifier_value> GI:555932 </GBQualifier value> </GBQualifier> <GBQualifier> <GBQualifier_name> translation </GBQualifier name> <GBQualifier value> MDLSALRVEEVQNVINAMQKILECPICLELIKEPVSTKCDHIFCKFCMLKLLNQKKGPSQCPLCKNDITKRSLQESTRFSQLVEELLKIICAFQLDTGLEYANSYNFAKKEF </GBQualifier_value> </GBQualifier> </GBFeature quals> </GBFeature> <GBFeature> <GBFeature_key> exon </GBFeature key> <GBFeature location> 200..253 </GBFeature_location> GenBank Record for BRCA1 <GBFeature intervals> <GBInterval> <GBInterval from> In XML 200 </GBInterval_from> <GBInterval_to> 253 </GBInterval to> <GBInterval_accession>



```
<qualifier name="translation">
<value>
MDLSALRVEEVQNVINAMQKILECPICLELIKEPVSTKCDHIF
</value>
</qualifier>
```

EMBL Record for BRCA1 In XML

```
<GBQualifier>
<GBQualifier_name>
translation
</GBQualifier_name>
<GBQualifier_value>
MDLSALRVEEVQNVINAMQKILECPICLELIKEPVSTKCDHIF(
</GBQualifier_value>
</GBQualifier>
```

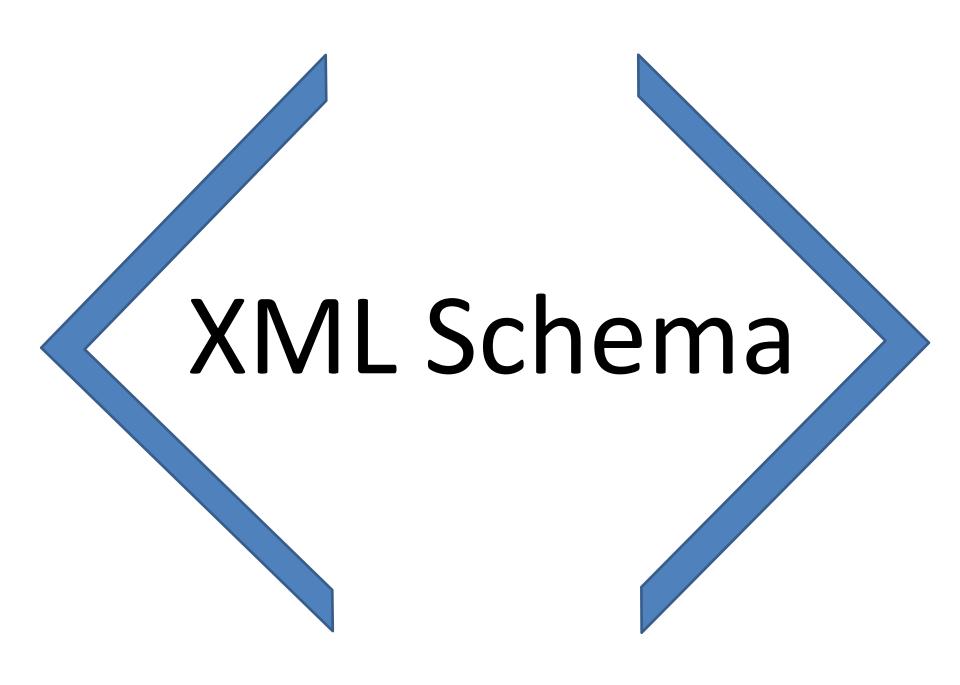
GenBank Record for BRCA1 In XML



...because it isn't (just) a parsing problem...

Various resources have various data models

So... Let's find a way to describe the data models!



```
<qualifier name="translation">
<value>
MDLSALRVEEVQNVINAMQKILECPICLELIKEPVSTKCDHIF
</value>
</qualifier>
```

XML Schema

There will be an element called "qualifier" It will have an attribute called "name" The content of that attribute will be text There will be a child element called "value" The content of that child element will be free-text

<GBQualifier> <GBQualifier_name> translation </GBQualifier_name> <GBQualifier_value> MDLSALRVEEVQNVINAMQKILECPICLELIKEPVSTKCDHIF(</GBQualifier_value> </GBQualifier>

XML Schema

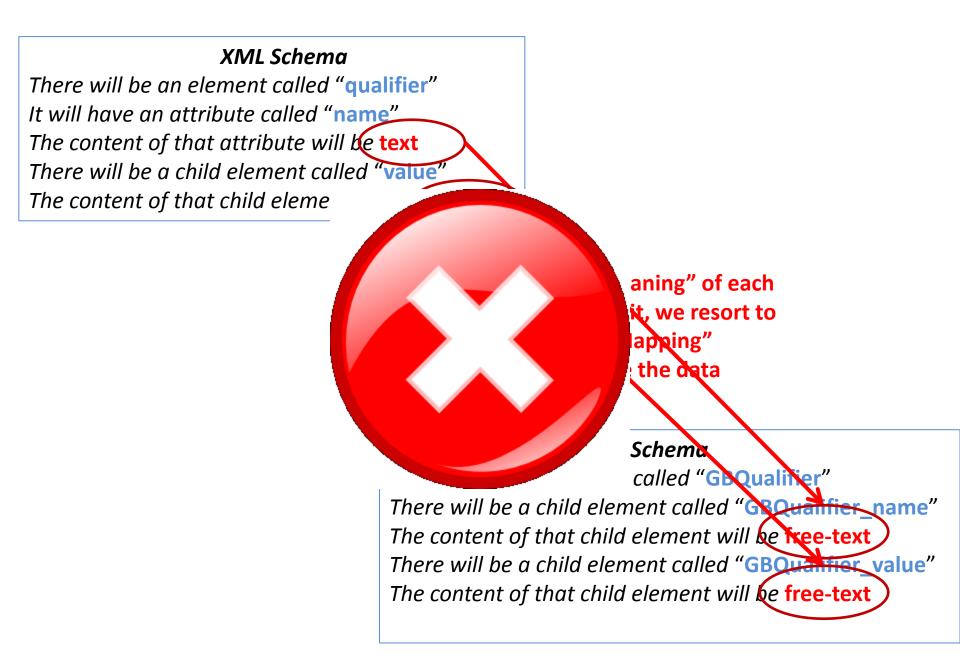
There will be an element called "GBQualifier" There will be a child element called "GBQualifier_name" The content of that child element will be free-text There will be a child element called "GBQualifier_value" The content of that child element will be free-text



What did XML Schema do for us?



"...XML Schema (among other things) allowed us to ~automate the creation of (in-memory) Structures which could hold the given XML-formatted data..." Does not solve the integration or aggregation problem



Nevertheless...



Web Services



"Service Oriented Architectures"



WSDL

(and many other 4-letter words)

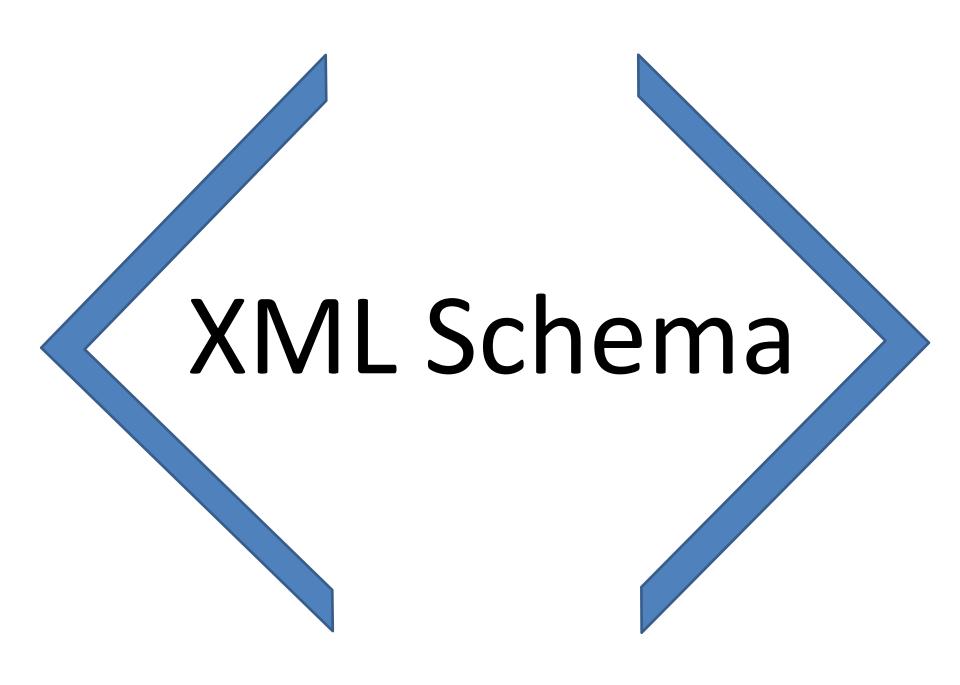


Web Services & SOA's

Allow you to expose software (e.g. a database, analytical tool, or service) on the Web so that others can use it (in their own analytical pipelines)

Excellent!!

But...



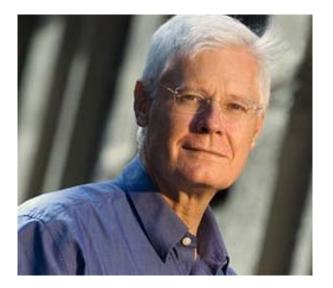
XML Schema

There will be an element called "qualifier" It will have an attribute called "name" The content of that attribute will be text There will be a child attribute called "value" The content of that child attribu

chema

alled "GBQualifi

There will be a child attribute called "GDQuaifier_name" The content of that child attribute will be free-text There will be a child attribute called "GBQuaifier_value" The content of that child attribute will be free-text



"The phrase 'practical Web Services' is not intrinsically an oxymoron, but [I] argue that there are few in existence."

Why?

Because this problem is *so disruptive* that *there is little point* in building "public" Web Services...

They are simply too difficult to integrate with other "public" Web Services.

-- adapted from Petrie, SWSIP 2009

XML Schema

There will be an element called "qualifier" It will have an attribute called "name" The content of that attribute will be text There will be a child attribute called "value" The content of that child attribute will be free-text

XML Schema

There will be an element called "GSQualifier" There will be a child attribute called "GBD- lifier_name" The content of that child attribute will be free-text There will be a child attribute called "GBQualifier_value" The content of that child attribute will be free-text ...and that's pretty much where the world is right now...

But there is hope!

"Linked Data" movement

Resource Description Framework "RDF"

Two new technologies & communities

The "Semantic Web" movement

Web Ontology Language "OWL" (+ RDF)

What does RDF do for us?



"...RDF replaces XML Schema, because RDF says that *there is only one data model*..."

What does OWL do for us?



"...the semantics are **no longer implicit** in the data model..."

XML Scher There will be an element called "qualifier"	na
It will have an attribute called "name" The content of that attribute will be tex- There will be a child attribute called "value" The content of that child attribute will be free-text	
	XML Scheme There where science to all of "SRQualifier There will be a chinary to the colled "SRQualifier
	The content of that child attribute will be free con- There will be a child attribute colled "Goes and year The content of that child attribute will be free con-

So what?

Gives us the opportunity to re-think how we build our health data infrastructures

isn't

"yet another layer of technology"

changes

the way we write software

What to do & How to do it **is no longer encoded in your software**

What to do & How to do it is part of the data

What to do & How to do it is part of a shared, expert understanding

What to do & How to do it IS* PERSONAL!



One piece of software



Any question... Any answer

Let me demonstrate what I mean



Semantic Automated Discovery and Integration http://sadiframework.org





Founding partner



Semantic Health And Research Environment

(a Semantic Web question answerer...)

Example #1

Show me the latest Blood Urea Nitrogen and Creatinine levels of patients **who appear to be rejecting their transplants**

```
?patient l:latestCreatinine ?creat .
```

Likely Rejecter:

A patient who has creatinine levels that are increasing over time

-- Wilkinson "MD"

Likely Rejecter:

...but there is no "likely rejecter" column or table in our database...

Likely Rejecter:

Our database contains various blood chemistry measurements at various time-points

SHARE determines

by itself

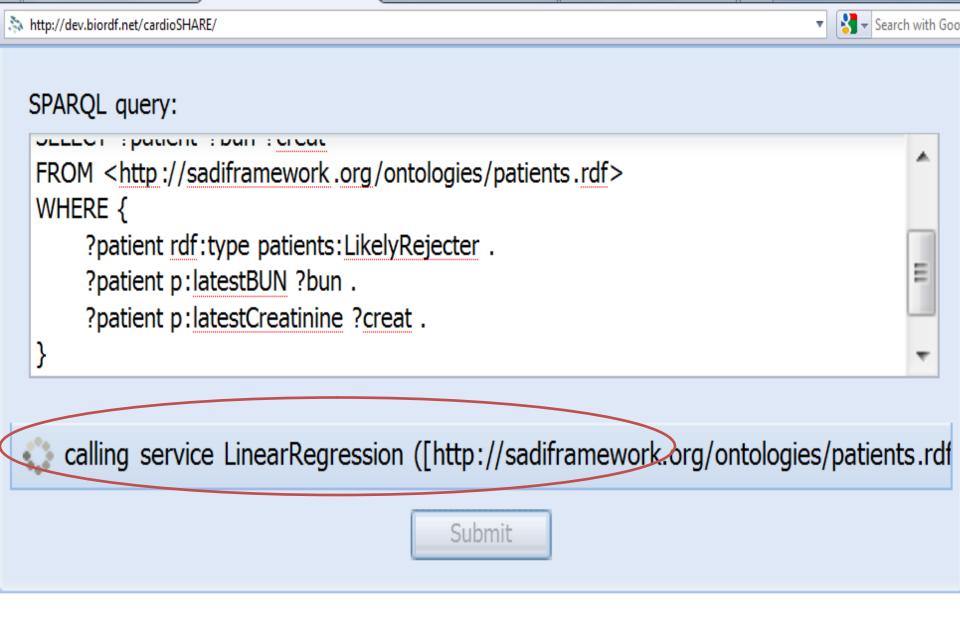
the **need** to do a Linear Regression analysis over Creatinine blood chemistry measurements

SHARE determines

by itself

how and where that analysis can be done

and does it



The SHARE system utilizes Semantics (via SADI) to discover and access analytical services on the Web that do linear regression analysis

SPARQL query:



View results as RDF. There were warnings executing the query. Click for details.

Submit

Query results

VO	

bun	creat	patient
5.861790	1.215768	http://biordf.net/moby/Dumm
17.673603	1.000161	http://biordf.net/moby/Dumm
7.997613	1.146408	http://biordf.net/moby/Dumm
2.977437	0.953866	http://biordf.net/moby/Dumm
10.995189	1.247073	http://biordf.net/moby/Dumm
1.168096	1.185007	http://biordf.net/moby/Dumm
7.570712	0.986164	http://biordf.net/moby/Dumm
44,000004	4 4 40070	http://biomolf.co.gl/co.gl/co.gl/co.gl/

Neither SADI nor SHARE

know anything about

blood chemistry, or mathematics

Example #2

From a (contrived) integrated dataset, retrieve the blood pressure measurements

```
SELECT ?output ?unit ?value
FROM <http://es-01.chibi.ubc.ca/~soroush/framingham/sbpfeb.owl>
WHERE {
```

```
?output rdf:type sbp:BloodPressure .
?output local:hasCanonicalAttribute ?pr .
?pr sio:SIO_000221 ?unit .
?pr sio:SIO_000300 ?value .
```

}

This should be extremely straightforward...

...except for one problem...

<owl:NamedIndividual rdf:about="http://es-01.chibi.ubc.ca/~soroush/framingham/sbpfeb.owl#pressureinstance1"> <rdf:type rdf:resource="&galen;SystolicBloodPressure"/> <resource:SIO_000300>0.137</resource:SIO_000300> <resource:SIO_000221 rdf:resource="&ucum;unit/pressure/meter-of-mercury-column"/> </owl:NamedIndividual>

<owl:NamedIndividual rdf:about="http://es-01.chibi.ubc.ca/~soroush/framingham/sbpfeb.owl#pressureinstance2"> <rdf:type rdf:resource="&galen;SystolicBloodPressure"/> <resource:SIO_000300>12.45</resource:SIO_000300> <resource:SIO_000221 rdf:resource="http://es-01.chibi.ubc.ca/~soroush/framingham/sbpfeb.owl#centi-meter-of-mercury-column"/> </owl:NamedIndividual>

<owl:NamedIndividual rdf:about="http://es-01.chibi.ubc.ca/~soroush/framingham/sbpfeb.owl#pressureinstance3"> <rdf:type rdf:resource="&galen;SystolicBloodPressure"/> <resource:SIO_000300>5.3</resource:SIO_000300> <resource:SIO_000221 rdf:resource="&ucum;unit/pressure/inch-of-mercury-column"/> </owl:NamedIndividual>

```
<owl:NamedIndividual rdf:about="http://es-01.chibi.ubc.ca/~soroush/framingham/sbpfeb.owl#pressureinstance1">
<rdf:type rdf:resource="&galen;SystolicBloodPressure"/>
```

<resource:SIO_000300>0.137</resource:SIO_000300>

<resource:SIO_000221 rdf:resource="&ucum;unit/pressure/**meter-of-mercury**-column"/> </owl:NamedIndividual>

<owl:NamedIndividual rdf:about="http://es-01.chibi.ubc.ca/~soroush/framingham/sbpfeb.owl#pressureinstance2"> <rdf:type rdf:resource="&galen;SystolicBloodPressure"/>

<resource:SIO_000300>**12.45**</resource:SIO_000300>

<resource:SIO_000221 rdf:resource="&ucum;unit/framingham/sbpfeb.owl#**Centi-meter-of-mercury**-colum </owl:NamedIndividual>

<owl:NamedIndividual rdf:about="http://es-01.chibi.ubc.ca/~soroush/framingham/sbpfeb.owl#pressureinstance3"> <rdf:type rdf:resource="&galen;SystolicBloodPressure"/>

<resource:SIO_000300>**5.3**</resource:SIO_000300>

<resource:SIO_000221 rdf:resource="&ucum;unit/pressure/inch-of-mercury-column"/> </owl:NamedIndividual>

Example #2

From a (contrived) integrated dataset, retrieve the blood pressure measurements

SELECT ?output ?unit ?value
FROM <http://es-01.chibi.ubc.ca/~soroush/framingham/sbpfeb.owl>
WHERE {

?output rdf:type sbp:BloodPressure .
?output local:hasCanonicalAttribute ?pr .
?pr sio:SIO_000221 ?unit .
?pr sio:SIO_000300 ?value .

My semantic definition of "Blood Pressure" includes the units that I want...

This is enough to trigger SHARE to automatically discover an online unit-conversion service...

<pre>?output rdf:type sbp:BloodPressure . ?output sbp:hasCanonicalAttribute ?pr . ?pr sio:SIO_000221 ?unit . ?pr sio:SIO_000300 ?value . }</pre>	
Submit	
Query results	
outputunitvaluehttp://es-01.chibi.ubc.ca/~soroush/framingham/sbpfeb.ow/#instance3http://es-01.chibi.ubc.ca/~soroush/framingham/sbpfeb.ow/#inilli-meter-of-mercury-column134.6199993999998http://es-01.chibi.ubc.ca/~soroush/framingham/sbpfeb.ow/#instance2http://es-01.chibi.ubc.ca/~soroush/framingham/sbpfeb.ow/#milli-meter-of-mercury-column124.5http://es-01.chibi.ubc.ca/~soroush/framingham/sbpfeb.ow/#instance1http://es-01.chibi.ubc.ca/~soroush/framingham/sbpfeb.ow/#milli-meter-of-mercury-column137.0	<u> </u>
unit	e
http://es-01.chibi.ubc.ca/~soroush/framingham/sbpfeb.ow#milli-meter-of-mercury-column 134.	.61
http://es-01.chibi.ubc.ca/~soroush/framingham/sbpfeb.owl#'milli-meter-of-mercury-column 124.	.5
http://es-01.chibi.ubc.ca/~soroush/framingham/sbpfeb.owl#'milli-meter-of-mercury-column 137.0	.0

Neither SADI nor SHARE

know anything about

units or unit conversions

Many of the challenges to data aggregation and sharing now have solutions that work! What, in my opinion, is the greatest remaining challenge?



To a biologist...

..."data mining" means "this data is mine!"

The challenge to us all

Move from Data Mine-ing

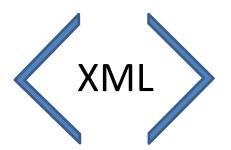
To Data Ours-ing

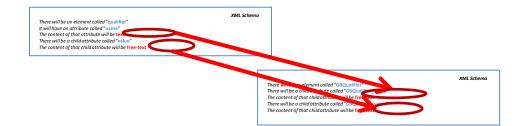
-- Len Silverston, 2007



FT FT FT FT	CDS	731212 /db_xref="GDB:135679" /db_xref="GOA:P27361" /db_xref="HGNC:6877"
FT		/db_xref="UniProtKB/Swiss-Prot:P27361"
FT		/gene="ERK1"
FT		/product="protein serine/threonine kinase"
FT		/protein_id="CAA42744.1"
FT		/translation="MAAAAAQGGGGGEPRRTEGVGPGVPGEVEMVKGQPFDVGPRYTQL
FT		QYIGEGAYGMVSSAYDHVRKTRVAIKKISPFEHQTYCQRTLREIQILLRFRHENVIGIR
FT		DILRASTLEAMRDVYIVQDLMETDLYKLLKSQQLSNDHICYFLYQILRGLKYIHSANVL
FT		HRDLKPSNLLSNTTCDLKICDFGLARIADPEHDHTGFLTEYVATRWYRAPEIMLNSKGY
FT		TKSIDIWSVGCILAEMLSNRPIFPGKHYLDOLNHILGILGSPSQEDLNCIINMKARNYL
FT		OSLPSKTKVAWAKLFPKSDSKALDLLDRMLTFNPNKRITVEEALAHPYLEOYYDPTDEP
FT		VAEEPFTFAMELDDLPKERLKELIF0ETARF0PGVLEAP"
FT	misc_binding	13541379
FT	-	/Affvmetrix="probe:HG_U95Av2:1000_at:399:559:"
FT	misc_bindina	13661391
FT		/Affymetrix="probe:HG_U95Av2:1000_at;544:185;"

We've come a long way!!







TEAM:

Luke McCarthy Benjamin Vandervalk Soroush Samadian



Microsoft Research





New solutions for health



