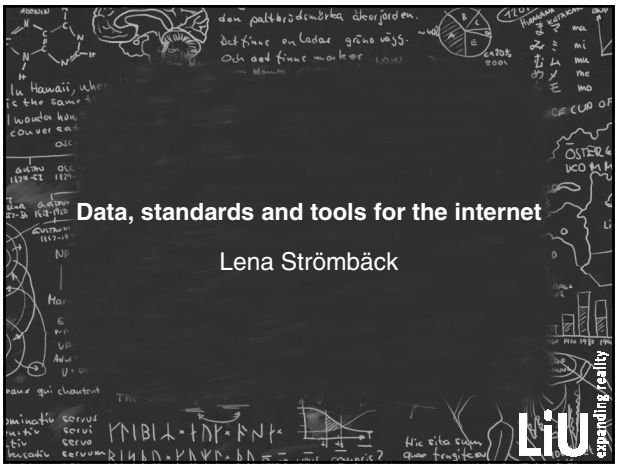
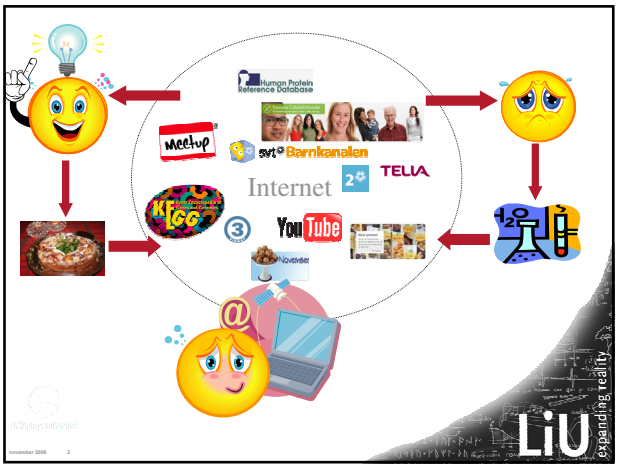
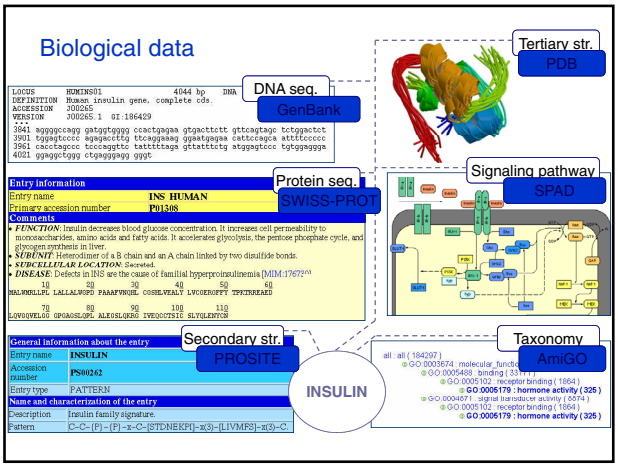


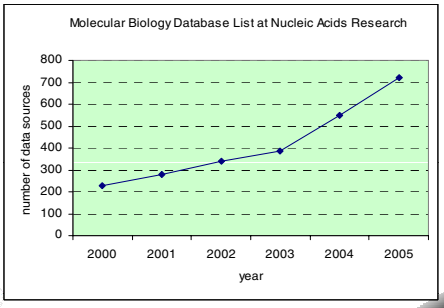


Topics

- Part 1: Data and representation
  - Databases on the web
  - XML standards
  - Minimal Information Standards
- Part 2: Tools
  - General Overview
  - Databases and data mangement
  - Putting things together: Scientific workflows



Biological data sources



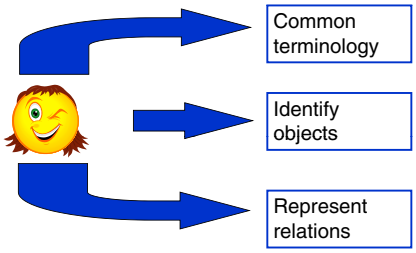
Example of web sources

- Biomodels http://www.ebi.ac.uk/biomodels-main/static-pages.do?page=home
- Reactome http://www.reactome.org/
- IntAct http://www.ebi.ac.uk/intact/site/index.jsf
- KEGG http://www.genome.jp/kegg/
- Uniprot http://www.uniprot.org/
- CheBi http://www.ebi.ac.uk/chebi/

So …

- Availability of web sources within bioinformatics is unique
- How can we make best use of them?

How to make use of this data?



How to represent data …

- Representation of structure or relations
- Web data is often less structured than traditional applications
  - Semi structured
  - Integration
- XML is the most common language
- OWL and RDF are alternatives

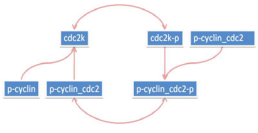
SBML

- Defined by: System Biology Development workbench group.
- Aim: Standard for information exchange.
- Mathematical formulas can be defined, discrete events.

```
<model>
<listOfCompartments>
<listOfSpecies>
<listOfReactions>
  <reaction>
     <listOfReactants>
     <listOfProducts>
     <listOfModifiers>
  </reaction>
</listOfReactions>
</model>
```

XML model example

```
<model id="Tyson1991CellModel_6"
       name="Tyson1991_CellCycle_6var">
 <listOfSpecies>
   + <species id="C2" name="cdc2k" compartment="cell">
   + <species id="M" name="p-cyclin_cdc2" compartment="cell">
   + <species id="YP" name="p-cyclin" compartment="cell"> ...
 </listOfSpecies>
 <listOfReactions>
   <reaction id="Reaction1" name="cyclin_cdc2k dissociation">
     <annotation>
       <rdf:li
     rdf:resource="http://www.reactome.org/#REACT_6308"/>
       <rdf:li
     rdf:resource="http://www.geneontology.org/#GO:0000079"/>
     </annotation>
     <listOfReactants>
       <speciesReference species="M"/>
     </listOfReactants>
     <listOfProducts>
       <speciesReference species="C2"/>
       <speciesReference species="YP"/>
     </listOfProducts>
     <kineticLaw>
       <math xmlns="http://www.w3.org/1998/Math/MathML">
         <apply> <times/> <ci> k6 </ci> <ci> M </ci>  </apply></math>
       <listOfParameters>  <parameter id="k6" value="1">
       </listOfParameters>
     </kineticLaw>
   </reaction>
   + <reaction id="Reaction2" name="cdc2k phosphorylation">
   ... more reactions
 </listOfReactions>
</model>
</sbml>
```



PSI MI

- Defined by: Proteomics Standards Initiative.
- Aim: Standard for representation of molecular interaction.
- Thorough description of experiments and protein structure.

```
<entry>
<experimentList>
<interactorList>
<interactionList>
  <interaction>
    <experimentList>
    <participList>
  </interaction>
</interactionList>
</entry>
```

Available XML standards ….

Name	Ver.	Year	Defined by	Purpose	Tools	Data
SBML	2	2003	Systems Biology Workbench development group.	A computer-readable format for representing models of biochemical reaction networks.	Many tools available.	Data available from many databases, for instance, KEGG and Reactome.
PSI MI	2.5	2005	Proteomics Standards Initiative.	A standard for data representation for protein-protein interaction to facilitate data comparison, exchange and verification.	Tools for viewing and analysis.	Datasets available from many sources, for instace IntAct, DIP and MINT.
BioPAX	2	2005	The BioPAX group.	A collaborative effort to create a data exchange format for biological pathway data.	Existing tools for OWL such as Protégé.	Datasets available from Reactome.
CellML	1.1	2002	University of Auckland and Physiome Sciences, Inc.	Support the definition of models of cellular and subcellular processes.	Tools for publication, visualization, creation and simulation.	CellML Model Repository (~240 models).
CML	2.2	2003	Peter Murray-Rust, Henry S. Rzepa.	Interchange of chemical information over the Internet and other networks.	Molecular browsers, editors.	BioCYC.
EMBLxml	1.0	2005	EBI.	More stability and fine-grained modelling of nucleotide sequence information.	API support in BioJavaX.	EMBL.
INSDseq	1.4	2005	International Nucleotide Sequence Database Collaboration.	The purpose of INSDSeq is to provide a near-uniform representation for sequence records.	API support in BioJavaX.	EMBL, DBJ and GenBank.
Seqentry	n/a	n/a	NCBI.	NCBI uses ASN.1 for the storage and retrieval of data such as nucleotide and protein sequences. Data encoded in ASN.1 can be transferred to XML.	SRI's BioWarehouse and ProteinStructureFactory's ORFer.	Entrez.
BSML	3.1	2002	Labbook.com.	Facilitate the interchange of data for more efficient communication within the life sciences community.	Labbook's Genomic Browser and Sequence Viewer. Converters.	Previously provided by EMBL.
HUP-ML	0.8	2003	JHUPO.	A proteomics-oriented markup language for exchanging proteome data between researchers.	HUP-ML Editor.	
MAGE-ML	1.1	2003	MGED.	To facilitate the exchange of microarray information	Converters.	

What do the standards contain?

- Information about objects:
  - Proteins/Complexes
  - Genes/DNA
  - Other molecules
- Interaction information
- Information about experiments
  - Kind of experiment
  - Evidence of the experiment
- More ….

BioPAX

- entity
  - physicalEntity
    - dna
    - rna
    - protein
    - complex
    - smallMolecule
  - interaction
    - physicalInteraction
      - conversion
        - complexAssembly
        - biochemicalReaction
          - transportWithBiochemicalReaction
        - transport
          - transportWithBiochemicalReaction
      - control
        - catalysis
        - modulation
  - pathway

- Defined by: The BioPAX working groups.
- Aim: General format for interactions.
- Ontology, implemented in OWL
- Pathway and molecular interactions.

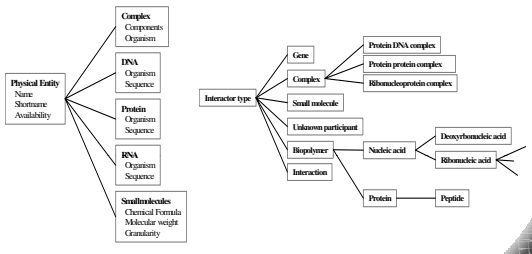
Summary of standards

Name	Substances			Interactions	Pathways	Compartments	Organism	Experiments
	DNA, RNA	Protein	Other					
SBML	UL	UL	UL	SOL	SOL	SL		
PSI MI	SOL	SOL	SOL	SOL		L	SL	S
BioPAX	SOL	SOL	SOL	SOL	S		L	L
CellML	L	L	L	S	S	U	U	
CML			S	S				
EMBLxml	SL	SL					L	
INSDseq	SL	SL					L	
Seqentry	SL	SL					L	
BSML	SL	SL					L	S
HUP-ML	SL	SL					L	S
MAGE-ML	L	L					L	S
mzXML								SO
mzData								S
AGML							U	S

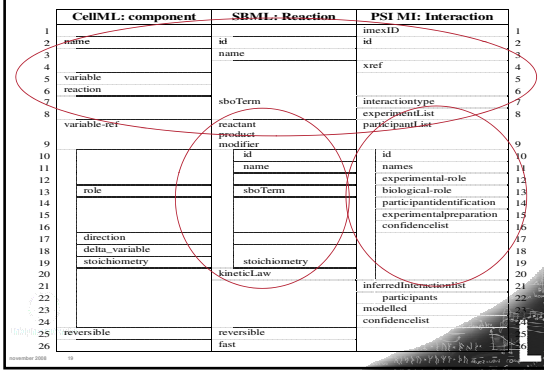
Representation of objects

	SBML: Species	PSI MI: Interactor		CellML:component	
1	id	id		name	1
2	name	names		dc:title dcterms:alternative	2
3		xref		cmeta:bio_entity	3
4	speciesType	interactortype			4
5		organism			5
6			ncbiTaxId		6
7			names	cmeta:species	7
8			celltype		8
9	compartment		compartment	(– group)	9
10			tissue		10
11				cmeta:sex	11
12		sequence			12
13				variable	13
14	initialAmount			initialvalue	14
15	initialConcentration				15
16	substanceUnits			units	16
17	spatialsizeUnits				17
18	hasonlysubstanceUnits				18
19	boundaryCondition				19
20	charge				20
21	constant				21

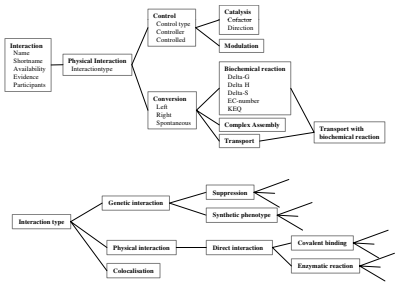
Type of objects



Representation of interactions



Interaction types



Bioinformatics: Minimal Information Standards.

- **MIRIAM : Minimal Information Requested in the Annotation of biochemical Models**
- **MIAPE: The Minimum Information About a Proteomics Experiment**
  - **MIAPE: GE**(Gel Electrophoresis)
  - **MIAPE: MS** (Mass Spectrometry)
  - **MIAPE: CC** (Column Chromatography)
  - **MIAPE: CE** (Capillary Electrophoresis)
  - ….
- **MIMIx: The minimum information required for reporting a molecular interaction experiment** ….
- ….

Part 2: Tools

- Many of the standards are supported by software tools:
  - SBML Tools: http://sbml.org/SBML_Software_Guide/SBML_Software_Matrix
  - CellML Tools: http://www.cellml.org/tools
- Data management
- Scientific workflows

Data management of XML data

- How can the data be efficiently stored and accessed?
  - Native XML databases
  - Hybrid solutions

XML as a data model

- XML provides a data model
- The valid XML data structures can be defined by
  - XML Schema
  - DTD
- XML has its own query languages
  - XPath
  - XQuery

Expressing Queries in XQuery

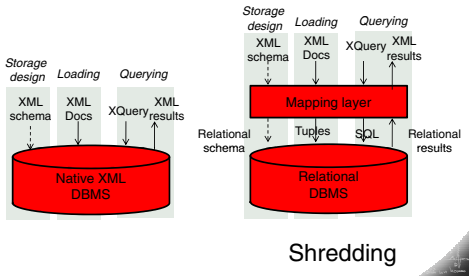
Find information on a given protein. Protein id is given.

```
document("rat_small.xml")//proteinInteractor[@id="EBI-77471"]
```

Find the protein information for the proteins that participate in a given interaction. Interaction id is given.

```
for $ref in document("rat_small.xml")//interaction
    [names/shortLabel="interaction1"]
    /participantList/proteinParticipant/proteinInteractorRef/@ref
  return document("rat_small.xml")//proteinInteractor[@id=$ref]
```

Storage possibilities for XML



Shredding

XML as a data model

- XML is richer than the relational model
  - Tree structure,
  - Order
  - …
- Vary from highly structured to unstructured
  - Database export
  - …
  - Annotated text documents
- Can contain links to other type of entities

How to shred XML?

```
<?xml version="1.0" encoding="UTF-8"?>
<families
xmlns:xsi=http://www.w3.org/2001/XMLSchem
a-instance">
  <family>
    <parent>
      <name>Lena</name>
      <job>Lektor</job>
    </parent>
    <child>
      <name>Ludvig</name>
      <school>Skolan</school>
    </child>
  </family>
</families>
```

Source	Ordinal	attrName	isValue	Value
0	1	Families	False	1
1	1	Family	False	2
2	1	Parent	False	3
3	1	Name	True	Lena
3	2	Job	True	Docent ..

Families

Id	Pid
0	-

Family

Id	Pid
1	0

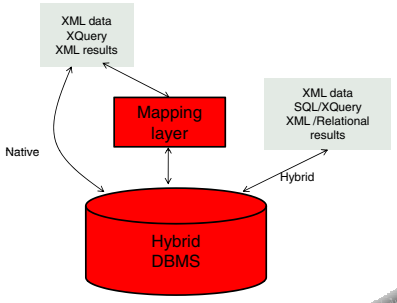
Parent

Id	Pid	Name	Job
2	1	Lena	Lektor

Child

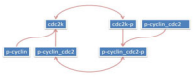
Id	Pid	Name	School
3	1	Ludvig	Skolan

Hybrid XML Storage



New possibilities…

```
<model id="Tyson1991CellModel_6"
       name="Tyson1991_CellCycle_6var">
 <listOfSpecies>
   + <species id="C2" name="cdc2k" compartment="cell">
   + <species id="M" name="p-cyclin_cdc2" compartment="cell">
   + <species id="YP" name="p-cyclin" compartment="cell"> …
 </listOfSpecies>
 <listOfReactions>
  <reaction id="Reaction1" name="cyclin_cdc2k dissociation">
   <annotation>
    <rdf:li
    rdf:resource="http://www.reactome.org/#REACT_6308"/>
    <rdf:li
    rdf:resource="http://www.geneontology.org/#GO:0000079"/>
   </annotation>
   <listOfReactants>
    <speciesReference species="M"/>
   </listOfReactants>
   <listOfProducts>
    <speciesReference species="C2"/>
    <speciesReference species="YP"/>
   </listOfProducts>
   <kineticLaw>
    <math xmlns="http://www.w3.org/1998/Math/MathML">
     <apply> <times/> <ci> k6 </ci> <ci> M </ci>  </apply></math>
    <listOfParameters>  <parameter id="k6" value="1">
    </listOfParameters>
   </kineticLaw>
  </reaction>
  + <reaction id="Reaction2" name="cdc2k phosphorylation">
  … more reactions
 </listOfReactions>
 </model>
</sbml>
```



Species:

Id	Name	Compartment
C2	cdc2k	cell
M	p-cyclin_cdc2	cell
YP	p-cyclin	cell
….	….	….

Reaction:

Id	Name	Annotation	Formula
Reaction1	cyclin_cdc2k dissociation	<annotation ….>	<kinetic_law ….>
Reaction2	cdc2k phosphorylation	<annotation ….>	<kinetic_law ….>
….	….	….	….

Reactants:

Id	Species
Reaction1	M
Reaction2	….
….	….

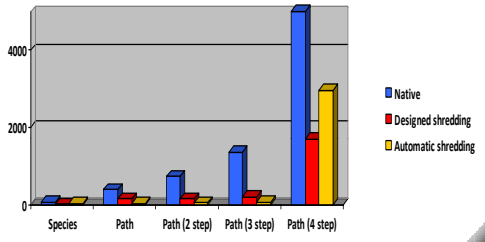
Products:

Id	Species
Reaction1	C2
Reaction1	YP
….	….

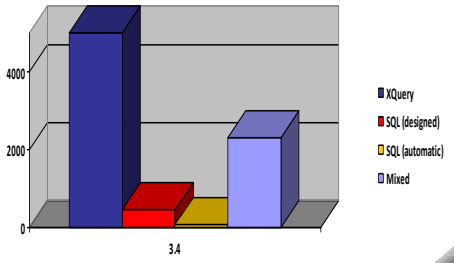
SQL and Xpath/XQuery

```
select, r.name, s.name
from reaction r, products p, species s
where r.id = p.id and p.species=s.id;

xquery
for  $y in db2-fn:xmlcolumn('SBML_DATA.SBML_DOC')
          /model/listOfReactions/reaction/listOfModifiers/modifierSpeciesReference,
     $z in db2-fn:xmlcolumn('SBML_DATA.SBML_DOC')/model/listOfSpecies/species[@id = $y/@species]
return <product> {$y/../../@name} {$z/@name} </product>

SELECT  p.reaction, species.name
from species,
(SELECT X.*
  FROM reactome_data,
  XMLTABLE ('$d/model/listOfReactions/reaction/listOfModifiers/modifierSpeciesReference' passing
      reactome_doc as "d"
  COLUMNS
  product VARCHAR(200) PATH '@species',
  reaction VARCHAR(200)                PATH '../../@id') AS X) p
where p.product=species.id
```

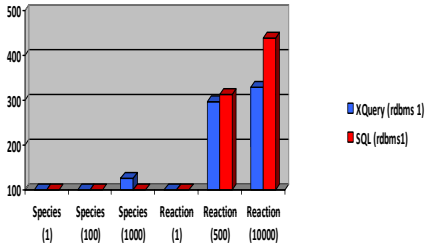
Efficiency: Increasing query complexity



Efficiency: Combining representations



Efficiency: Return the result as XML

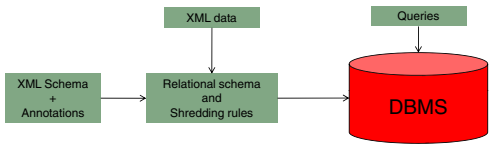


So…

- Native databases –
  - Easy to use but sometimes too inefficient
- Automatic shredding –
  - Can give datamodels that are hard to work with
- Manual shredding /Hybrid solutions –
  - Requires time consuming design

Tool development: ShreX

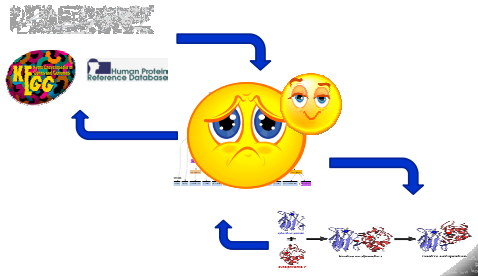
- Need a tool to speed up the process



- Extension of an old tool to allow hybrid storage

Demo ShreX

Workflows for data exploration



Capturing provenance

- Provenance of scientific artifacts is necessary to reproduce, validate and share scientific results
- Provenance can be as important as the results!

Dictionary

prov•e•nance |'prävənəns|

the place of origin or earliest known history of something : *an orange rug of Iranian provenance.*
• the beginning of something's existence; something's origin : *they try to understand the whole universe, its provenance and fate.*
See note at ORIGIN .
• a record of ownership of a work of art or an antique, used as a guide to authenticity or quality : *the manuscript has a distinguished provenance.*

ORIGIN late 18th cent.: from French, from the verb ***provenir 'come or stem from,'*** from Latin ***provenire***, from ***pro- 'forth'*** + ***venire 'come.'***

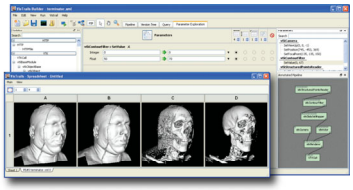
The Vistrails system
(Freire et al. University of Utah)

- *Vision: Provenance enable the world*
- Comprehensive provenance infrastructure for computational tasks
  - Captures provenance transparently
  - Provides intuitive query interfaces for exploring provenance data
  - Supports collaboration
- Designed to support *exploratory tasks such as* visualization and data mining
- VisTrails system is open source: www.vistrails.org
  - >2,000 downloads since beta release in Jan 2007
  - 100% Python--runs on Windows, Linux and Mac

Demo Vistrails

Enhanced functionality

- Parameter exploration
- Query to find workflows of interest
- Compute difference between workflows
- Create an analogy based on computed differences



Interesting issues:

- Reuse of other peoples efforts
  - Provenance server
  - Co-work
- Bio-specific version of Vistrails
  - Handling SBML - Libsbml
  - Annotations – use of ontologies
  - Easy to use module library
  - Combining webdata, own results and visualization

Questions?

Thanks!

Working with ShreX:

```
<?xml version="1.0" encoding="UTF-8"?>
<xs:schema xmlns:xs="http://www.w3.org/2001/XMLSchema"
    xmlns:shrex="http://www.cse.ogi.edu/shrex">

    <xs:element name="families">
      <xs:complexType>
        <xs:sequence maxOccurs="unbounded">
          <xs:element name="family" type="familyType"/>
        </xs:sequence>
      </xs:complexType>
    </xs:element>

    <xs:complexType name="familyType">
      <xs:sequence>
        <xs:element name="parent" type="parentType" >
        <xs:element name="child" type="childType" >
      </xs:sequence>
    </xs:complexType>

    <xs:complexType name="parentType">
      <xs:sequence>
        <xs:element name="name" type="xs:string"/>
        <xs:element name="job" type="xs:string"/>
      </xs:sequence>
    </xs:complexType>

    <xs:complexType name="childType">
      <xs:sequence>
        <xs:element name="name" type="xs:string"/>
        <xs:element name="school" type="xs:string"/>
      </xs:sequence>
    </xs:complexType>
```

Families

Id	Pid
0	-

Families_family

Id	Pid
1	0

Families_family_parent

Id	Pid	Name	Job
2	1	Lena	Lektor

Families_family_child

Id	Pid	Name	School
3	1	Ludvig	Skolan

Working with ShreX:

```
<?xml version="1.0" encoding="UTF-8"?>
<xs:schema xmlns:xs="http://www.w3.org/2001/XMLSchema"
    xmlns:shrex="http://www.cse.ogi.edu/shrex">

    <xs:element name="families">
      <xs:complexType>
        <xs:sequence maxOccurs="unbounded">
          <xs:element name="family" type="familyType"/>
        </xs:sequence>
      </xs:complexType>
    </xs:element>

    <xs:complexType name="familyType">
      <xs:sequence>
        <xs:element name="parent" type="parentType" >
        <xs:element name="child" type="childType"
                                    shrex:maptoxml="true">
      </xs:sequence>
    </xs:complexType>

    <xs:complexType name="parentType">
      <xs:sequence>
        <xs:element name="name" type="xs:string"/>
        <xs:element name="job" type="xs:string"/>
      </xs:sequence>
    </xs:complexType>

    <xs:complexType name="childType">
      <xs:sequence>
        <xs:element name="name" type="xs:string"/>
        <xs:element name="school" type="xs:string"/>
      </xs:sequence>
```

Families

Id	Pid
0	-

Families_family

Id	Pid	Child
1	0	<child> <name>Ludvig</name> <school>Skolan/school> </child>

Families_family_parent

Id	Pid	Name	Job
2	1	Lena	Lektor

Working with ShreX:

```
<?xml version="1.0" encoding="UTF-8"?>
<xs:schema xmlns:xs="http://www.w3.org/2001/XMLSchema"
    xmlns:shrex="http://www.cse.ogi.edu/shrex">

    <xs:element name="families">
      <xs:complexType>
        <xs:sequence maxOccurs="unbounded">
          <xs:element name="family" type="familyType"/>
        </xs:sequence>
      </xs:complexType>
    </xs:element>

    <xs:complexType name="familyType">
      <xs:sequence>
        <xs:element name="parent" type="parentType"
                                    shrex:tablename="person">
        <xs:element name="child" type="childType"

                                    shrex:tablename="person" >
      </xs:sequence>
    </xs:complexType>

    <xs:complexType name="parentType">
      <xs:sequence>
        <xs:element name="name" type="xs:string"/>
        <xs:element name="job" type="xs:string"/>
      </xs:sequence>
    </xs:complexType>

    <xs:complexType name="childType">
      <xs:sequence>
```

Families

Id	Pid
0	-

Families_family

Id	Pid
1	0

Person

Id	Pid	Name	Job	School
2	1	Lena	Lektor	
3	1	Ludvig		Skolan

Working with ShreX:

```
<?xml version="1.0" encoding="UTF-8"?>
<xs:schema xmlns:xs="http://www.w3.org/2001/XMLSchema"
    xmlns:shrex="http://www.cse.ogi.edu/shrex">

    <xs:element name="families">
      <xs:complexType>
        <xs:sequence maxOccurs="unbounded">
          <xs:element name="family" type="familyType"/>
        </xs:sequence>
      </xs:complexType>
    </xs:element>

    <xs:complexType name="familyType">
      <xs:sequence>
        <xs:element name="parent" type="parentType"
                                    shrex:withparent="true">
        <xs:element name="child" type="childType" >
      </xs:sequence>
    </xs:complexType>

    <xs:complexType name="parentType">
      <xs:sequence>
        <xs:element name="name" type="xs:string"/>
        <xs:element name="job" type="xs:string"/>
      </xs:sequence>
    </xs:complexType>

    <xs:complexType name="childType">
      <xs:sequence>
        <xs:element name="name" type="xs:string"/>
        <xs:element name="school" type="xs:string"/>
      </xs:sequence>
```

Families

Id	Pid
0	-

Families_family

Id	Pid	Name	Job
1	0	Lena	Lektor

Families_family_child

Id	Pid	Name	School
3	1	Ludvig	Skolan