Flux Balance Model

with Acinetobacter

Outlines

1- Reconstruction of a flux balance model of Acinetobacter

the use of BioCyc as a "middleware" to reconstruct the FBA model of Acinetobacter sp. ADP1 & compare it with high throughput experimental data ;

2- OoCyc:

the development of OoCyc, an additional API design to query/manipulate BioCyc information in an Object Oriented manner ;

Genoscope : Quick History of Genoscope

Centre National de Séquençage

- 18 December 1996: Creation of a Public Interest Group ("Groupement d'intérêt public", GIP) named "Centre national de Séquençage" (CNS, also named Genoscope) for 10 years (Official Journal, 1 January 1997).

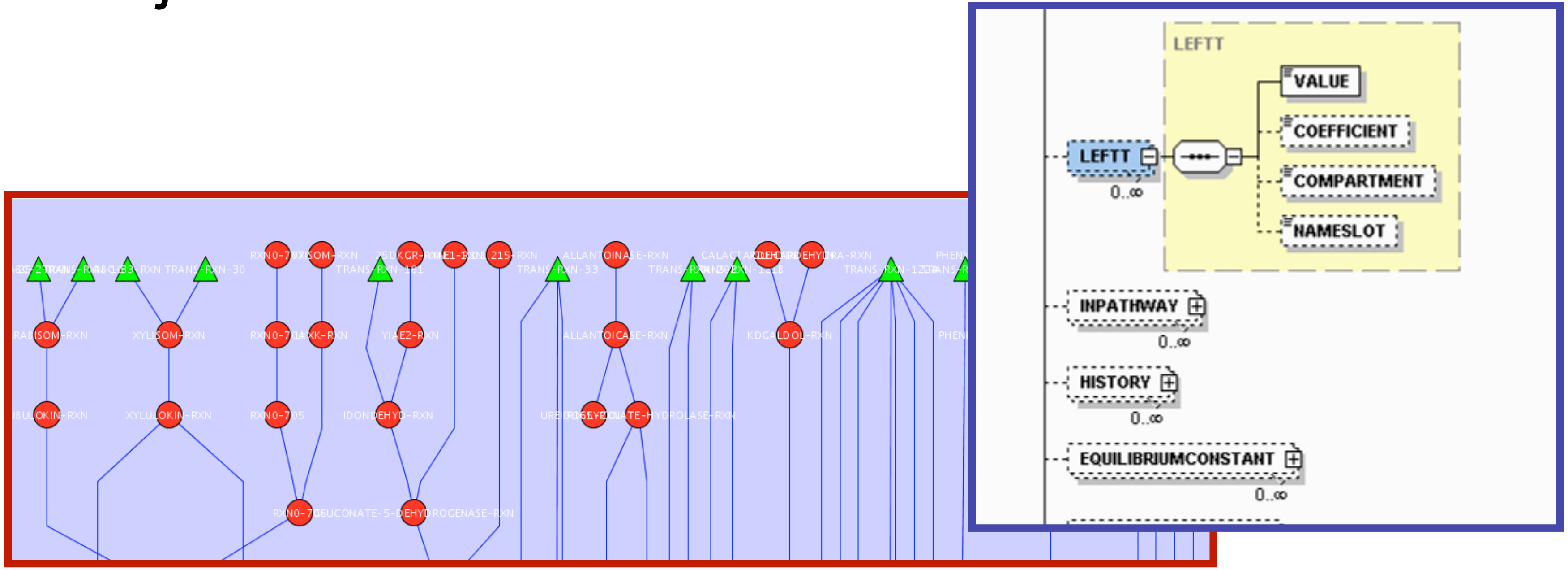
- In 1997, France decided to join the consortium "Human Genome Project" by creating a large sequencing center.

- 1 July 2002: Integration of Genoscope within a new GIP, "Consortium National de Recherche en Génomique" (CNRG), created for 12 years, which also includes the Centre National de Génotypage (CNG) and the Réseau National des Génopoles (RNG).

Part two

OoCyc:

the development of OoCyc, an additional API to query, manipulate BioCyc information in an Object Oriented manner



Ways to access biocyc data?

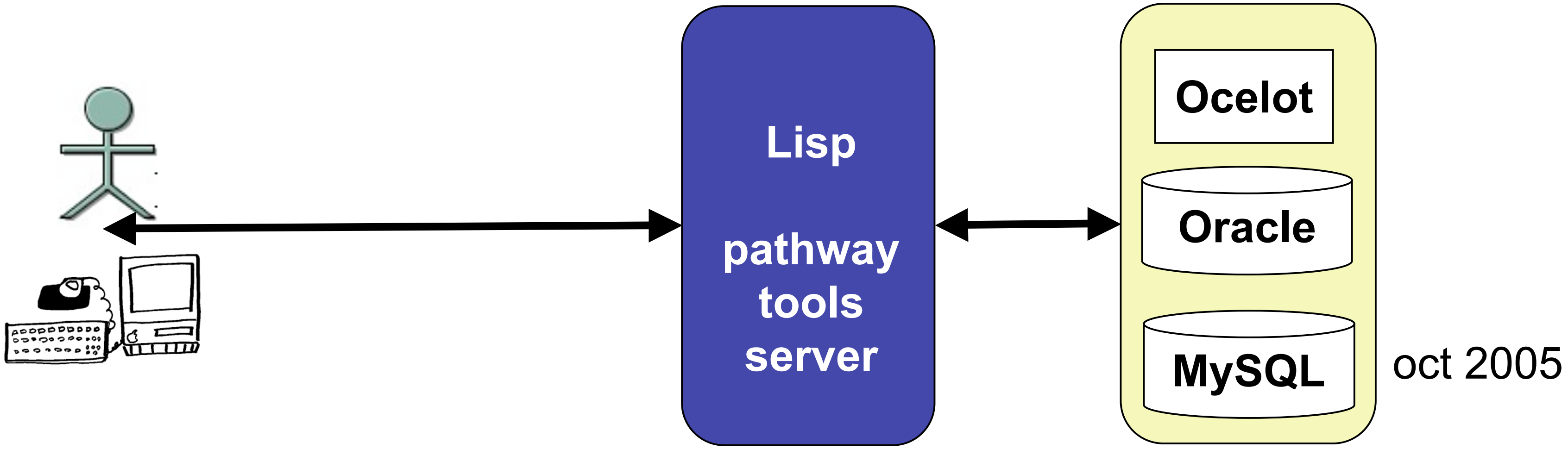
- Graphical Interface
  - Web
  - PathwayTools Interface

- Pathway tools server
  - Lisp api
  - PerlCyc
  - JavaCyc

- Output files
  - text files, attribut -value or tab-delimited
  - sbml
  - biopax

- Biowarehouse
  - SQL

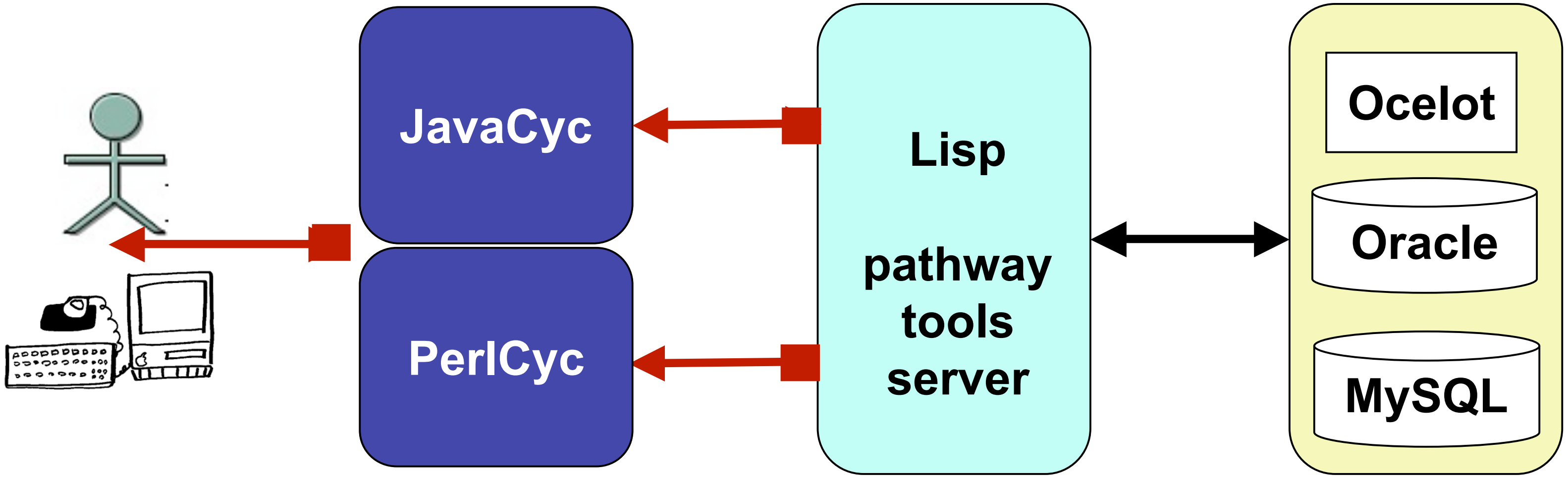
Ways to access biocyc data : Lisp Api



- Lisp is Pathway-tools native language ,
- Multi-user editing,
- Access to a transaction log of all PGDB edits

- Need to know Lisp
- Low level mySQL database schema → SQL queries almost impossible

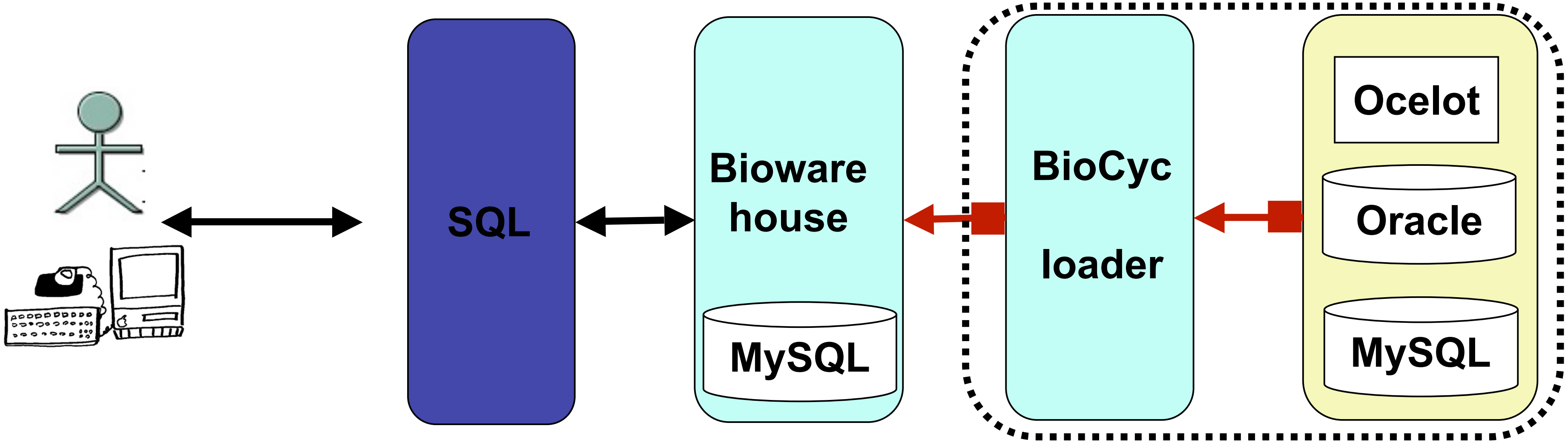
Ways to access biocyc data : JavaCyc and PerlCyc Api



+ ● A first approach to access Lisp fonction throw java or perl.

- ● No implementation of the GFP objects with Perl or Java
- ● Need to run a special socket server
- ● Only one such connection can be opened
- ● Run on Unix only

Biowarehouse Api



+

- relational schema corresponding to biological concepts
- a solution to query BioCyc with the integration of external data
- simple installation,
- fast data upload

-

- **unidirectional** : no modification can be loaded back into biocyc
- **loss** of information in regards of BioCyc model (transcription unit, citation, compound-pathway classification, no multifun …)
- querying is a bit **tedious** as you will see

Our Initial Motivation

1. Overcome some limitations of BioCyc
   - dependency on the OS (Unix)
   - no concurrent access
   - memory management (load all pgdbs in memory)

   ] before released 9.5

2. Manipulate objects corresponding to biological concepts

3. No loss of info with respect to Biocyc

4. Add import / export features

5. Benefit from existing Java tools / packages

What is OoCyc ?

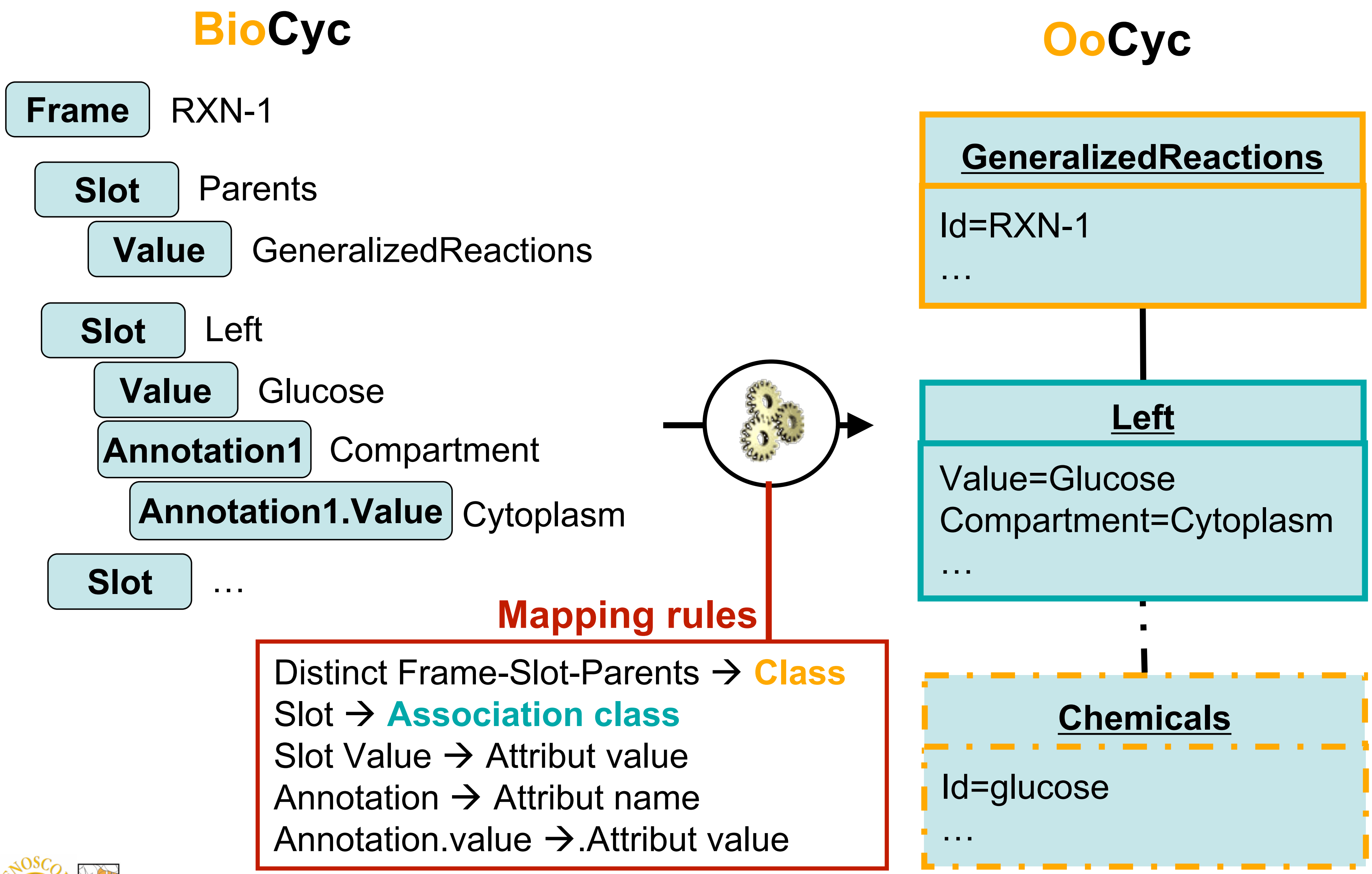
- OoCyc is an Object Oriented Cyc (api design to manipulate biocyc biological object)

- OoCyc is a pipeline

- OoCyc is a relational database in your favorite RDBMS

- OoCyc is an import / export of Biocyc in xml or in your database

From Frame … … to Java classes



BioCyc

Frame RXN-1

Slot Parents

Value GeneralizedReactions

Slot Left

Value Glucose

Annotation1 Compartment

Annotation1.Value Cytoplasm

Slot …

OoCyc

GeneralizedReactions

Id=RXN-1
…

Left

Value=Glucose
Compartment=Cytoplasm
…

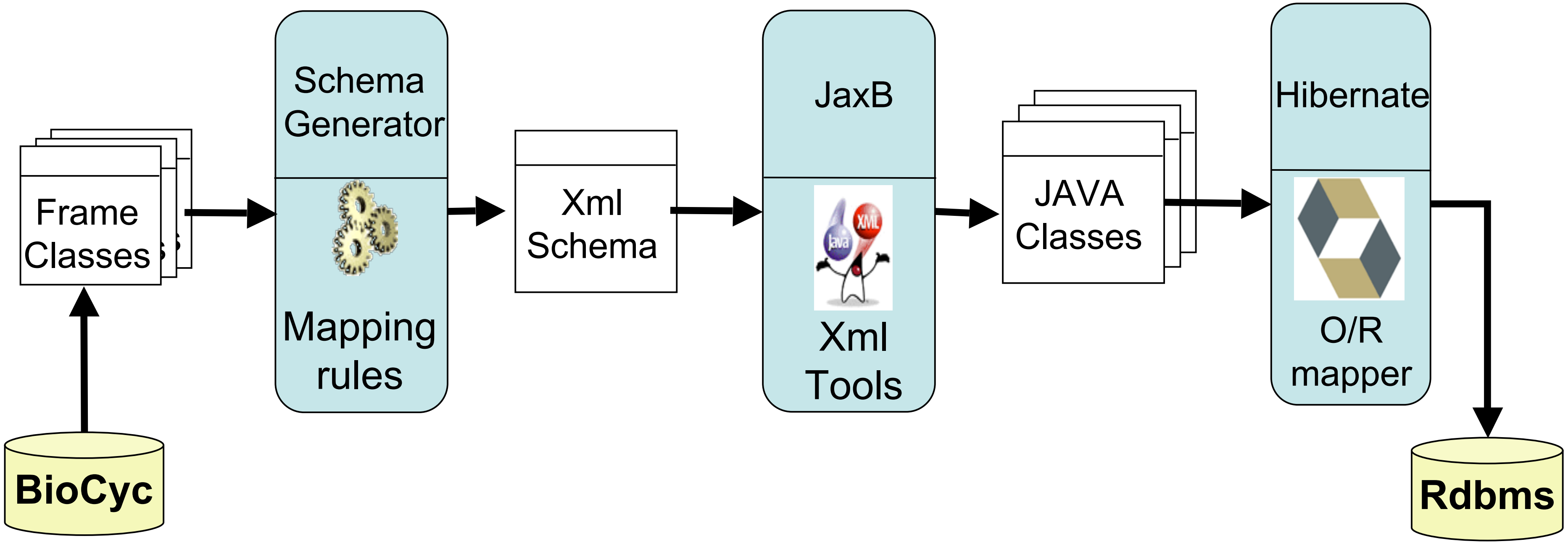
Chemicals

Id=glucose
…

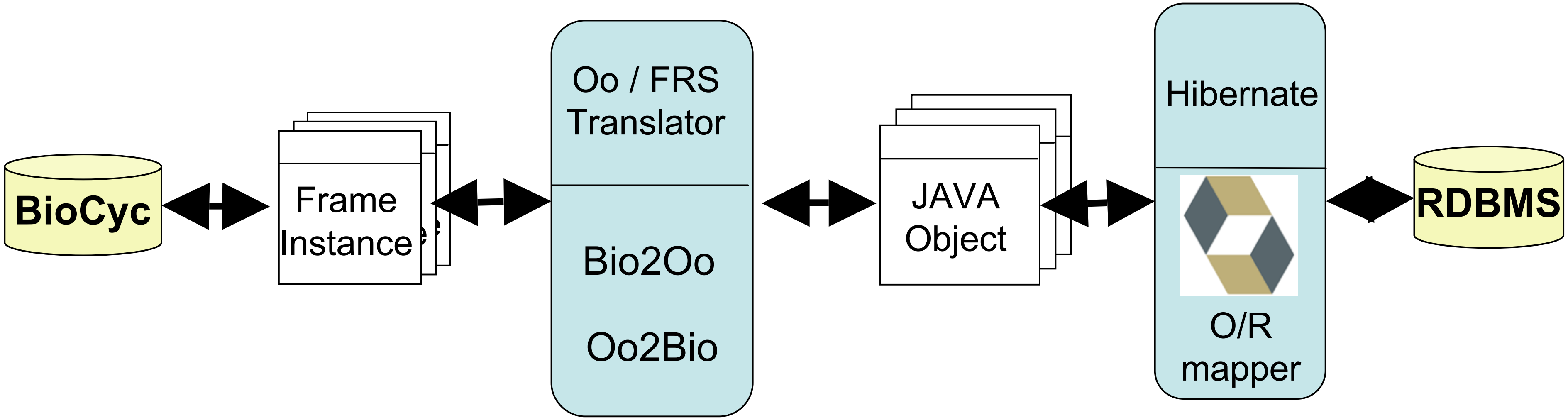
Mapping rules

Distinct Frame-Slot-Parents → **Class**
Slot → **Association class**
Slot Value → Attribut value
Annotation → Attribut name
Annotation.value →.Attribut value

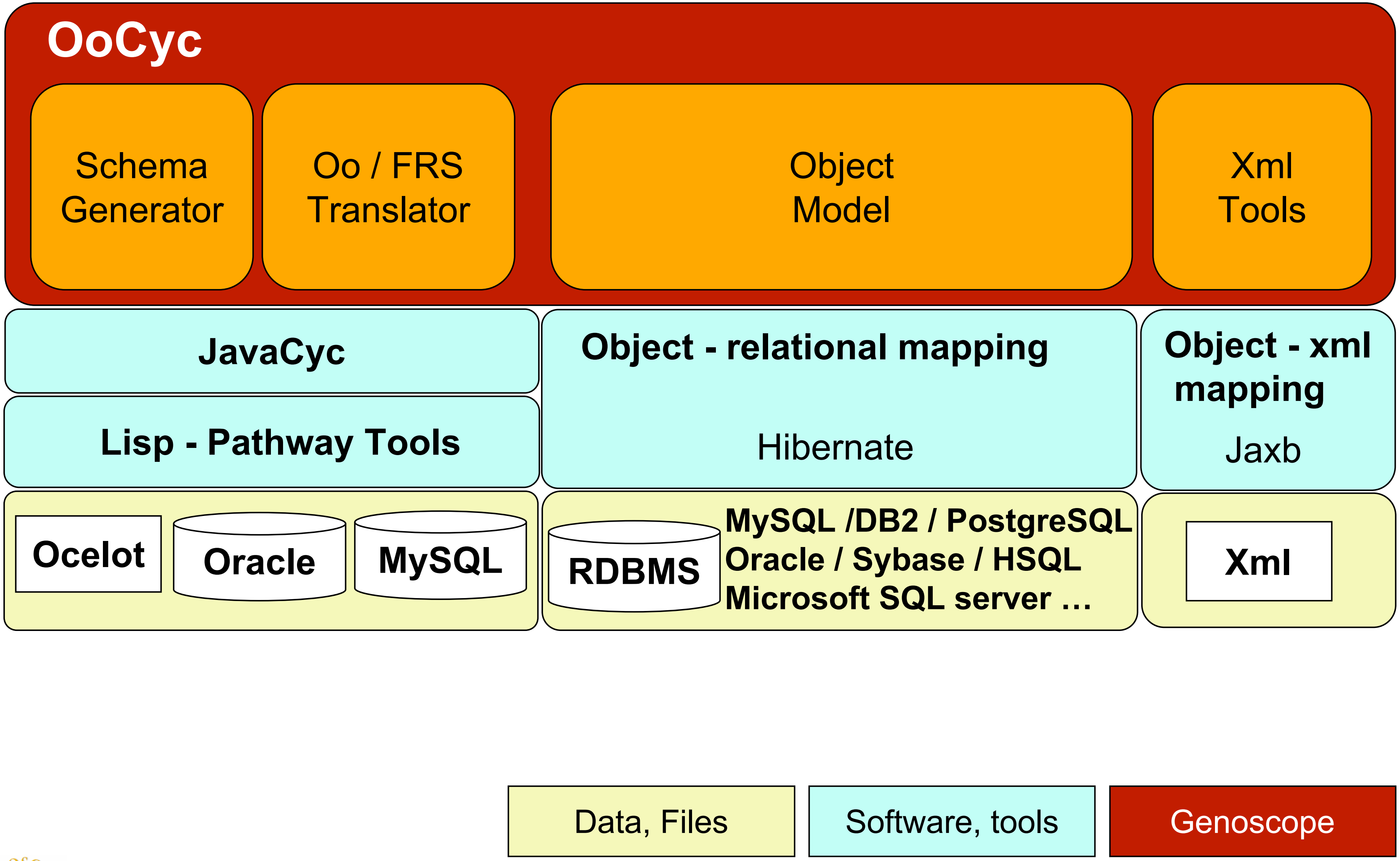
OoCyc's pipeline - initial step: code and database generation



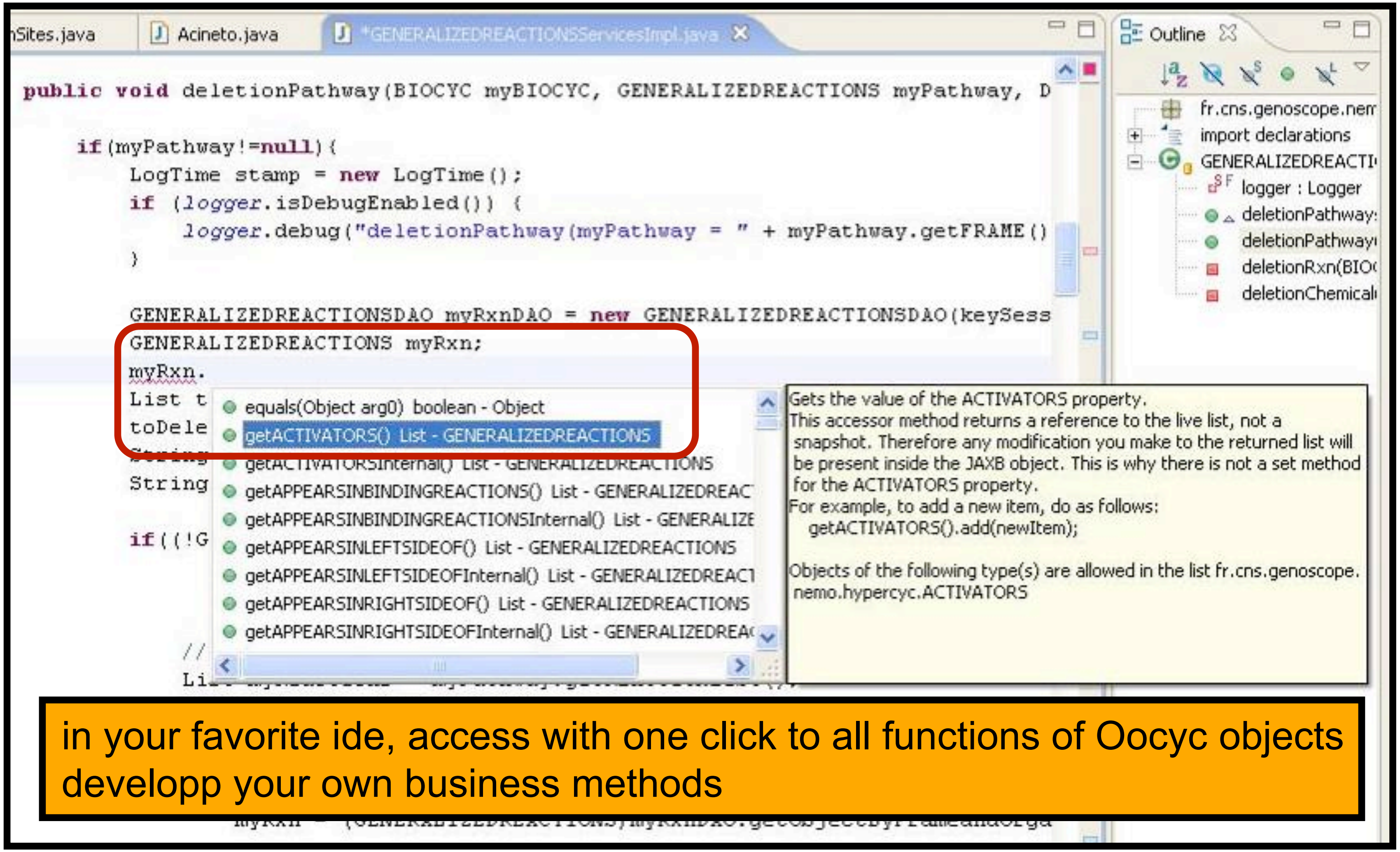
OoCyc's pipeline - daily step: Data Synchronization



OoCyc's architecture



Beneficits of using OoCyc :
Java Object Api matching biological concept



```
public void deletionPathway(BIOCYC myBIOCYC, GENERALIZEDREACTIONS myPathway, D

    if(myPathway!=null){
        LogTime stamp = new LogTime();
        if (logger.isDebugEnabled()) {
            logger.debug("deletionPathway(myPathway = " + myPathway.getFRAME()
        }

        GENERALIZEDREACTIONSDAO myRxnDAO = new GENERALIZEDREACTIONSDAO(keySess
        GENERALIZEDREACTIONS myRxn;
        myRxn.
        List t
        toDele
        String
        String

        if((!G

            //
            Li
```

```
equals(Object arg0) boolean - Object
getACTIVATORS() List - GENERALIZEDREACTIONS
getACTIVATORSInternal() List - GENERALIZEDREACTIONS
getAPPEARSINBINDINGREACTIONS() List - GENERALIZEDREAC
getAPPEARSINBINDINGREACTIONSInternal() List - GENERALIZE
getAPPEARSINLEFTSIDEOF() List - GENERALIZEDREACTIONS
getAPPEARSINLEFTSIDEOFInternal() List - GENERALIZEDREACT
getAPPEARSINRIGHTSIDEOF() List - GENERALIZEDREACTIONS
getAPPEARSINRIGHTSIDEOFInternal() List - GENERALIZEDREA
```

Gets the value of the ACTIVATORS property.
This accessor method returns a reference to the live list, not a snapshot. Therefore any modification you make to the returned list will be present inside the JAXB object. This is why there is not a set method for the ACTIVATORS property.
For example, to add a new item, do as follows:
getACTIVATORS().add(newItem);

Objects of the following type(s) are allowed in the list fr.cns.genoscope.nemo.hypercyc.ACTIVATORS

in your favorite ide, access with one click to all functions of Oocyc objects
developp your own business methods

Beneficits of using OoCyc :
Query in OQL (Object Query Language)

OQL is a powerful and easy-to-use SQL-like query language with special features dealing with complex objects, values and methods.

Lisp : Find all enzym for which ATP is an inhibitor

```
(defun atp-inhibits ()
 ;; We check every instance of the class
 (loop for x in (get-class-all-instances |Enzymatic-Reactions|)
 ;; Test for whether the INHIBITORS-ALL slot contains the
                                              compound frame ATP
  when (member-slot-value-p x INHIBITORS-ALL ATP)
   ;; Whenever the test is positive, we collect the value of the
   slot ENZYME The collected values are returned as a list, once
                                        the loop terminates.
   collect (get-slot-value x 'ENZYME))
)
;; invoking the query:
(select-organism :org-id 'ECOLI)
(atp-inhibits)
```

Beneficits of using OoCyc : Query in OQL (Object Query Language)

PerlCyc : Find all enzym for which ATP is an inhibitor

```
use perlcyc;
my $cyc = perlcyc -> new("ECOLI");
my @enzrxns = $cyc -> get_class_all_instances("|Enzymatic-
                                                Reactions|");
## We check every instance of the class
foreach my $er (@enzrxns) {
## We test for whether the INHIBITORS-ALL slot contains
the                                     compound frame ATP
   my $bool = $cyc -> member_slot_value_p($er,"Inhibitors-
                                             All", "Atp");
   if ($bool) {
     ## Whenever the test is ≥0, we collect the value of
     the slot ENZYME. The results are printed in
theterminal
     my $enz = $cyc -> get_slot_value($er, "Enzyme");
     print STDOUT "$enz\n";
   }
}
```

Beneficits of using OoCyc :
Query in OQL (Object Query Language)

JavaCyc : Find all enzym for which ATP is an inhibitor

```java
import java.util.*;
public class JavacycSample {
public static void main(String[] args) {
 Javacyc cyc = new Javacyc("ECOLI");
 ArrayList enzrxns = cyc.getClassAllInstances("|Enzymatic-Reactions|");
   for (int i = 0; i < enzrxns.size(); i++) {
     String er = (String)enzrxns.get(i);
     boolean bool = cyc.memberSlotValueP(er, "Inhibitors-All","Atp");
     if (bool) {
        String enz = cyc.getSlotValue(er, "Enzyme");
        System.out.println(enz);
     }
    }
  }
}
```

Beneficits of using OoCyc :
Query in OQL (Object Query Language)

Biowarehouse : Find all enzym for which ATP is an inhibitor

```
SELECT DISTINCT DBID.xid
FROM DBID, Protein, EnzymaticReaction, Chemical, DataSet,
                             EnzReactionInhibitorActivator
WHERE DataSet.name=EcoCyc
AND DataSet.wid=EnzymaticReaction.datasetwid
AND EnzymaticReaction.proteinwid = Protein.wid
AND EnzymaticReaction.wid =
          EnzReactionInhibitorActivator.enzymaticreactionwid
AND EnzReactionInhibitorActivator.compoundwid=Chemical.wid
AND EnzReactionInhibitorActivator.inhibitoractivate=I
AND Chemical.name=ATP
AND DBID.otherwid = Protein.wid
```

Beneficits of using OoCyc : Query in OQL (Object Query Language)

HQL is fully object-oriented, understanding notions like inheritence, polymorphism and association.

OoCyc : Find all enzym for which ATP is an inhibitor

```
 SELECT er FROM ENZYMATICREACTIONS er
LEFT JOIN er.INHIBITORSALLInternal inhibitors
WHERE er.ORGANISM.VALUE LIKE :organism
        AND
        "Atp" = inhibitors.VALUE
```

Comparative Matrix

	BioCyc		Biowarehouse	OoCyc
Representation System	FRS		Relational model	**Object** model
Storing System	Ocelot	mySQL oracle	mySQL	mySQL , Oracle Sybase, PostgreSQL …
Query	Lisp (perl/java)	SQL	SQL	**OQL** SQL Java
API	Lisp		-	**Java**
BioCyc Compatibilty	-		not full	**full** (- class)
Import / Export to BioCyc	-		Yes / No	**Yes / Yes**
Independent of Pathway tools	No		Yes	**Yes**

What can you do with OoCyc? : Bioinformatics applications

- **Easy data extraction from BioCyc:**
  - to mix them with different types of data (clusters of transcription units, pathways, complexes, regulon db...)
  - to build FBA models by:
    - grouping together Pathways for map design in Flux Analyser,
    - assemble elementary bricks of the metabolic network, based on reactions / genes / compounds found in BioCyc,

- **Link easily Biocyc to new systems :**
  - example : Genoscope's LIMS use BioCyc compounds repository as a language of media representation,
  - algorithm for inferrence: protein complexes.

- **Modify or implement new housekeeping functions in a PGDB:**
  - add / updates data from a given annotation database (e.g. multifun, cellular localization of genes products, pubmed links...), actualy not feasible with pathologic format,
  - delete / annotate pathways known not to exist, and keep those informations unless new BioCyc updates.

Ongoing work - Roadmap

- Extends the mapping rule between FRS and Java Object
- Future work: a software plateform dedicated to FBA models
  - Easy management of FBA models (define reactions, objective functions…)
  - Convenient handling of environments
  - Extensible perturbation framework (systematic mutants)
  - Pluggable analysis modules (topological analyses, phenotype predictions…)

Open questions

- Are you convince of this interest of OoCyc?
  - access with java to biocyc object
  - store your PGDBs in your favorite rdbms
  - manipulate classes representing biological concept
  - use efficient mapping object -relational (Hibernate)
  - …
- If yes to at least one, how to deliver OoCyc?
  - jar files
  - eclipse project
  - eclipse plugin
  - open a new sourceforge project

Thanks to …

Jean Weissenbach

Info
Ali Boudani
Laurent SainteMarthe
Claude Scarpelli

NeMo

Pierre-Yves Bourguignon
Cyril Combe
Maxime Durot
Matthias Heinig
Francois Le Fevre
Benjamin Pinaud
Serge Smidtas

Vincent Schachter

NEtwork MOdeling

NeMo@genoscope.cns.fr

Metabolic Thesaurus
Allain Perret
Valérie Barbe
Gorges Cohen
Annett Kreimeyer
Nuria Fonknechten
Marcel Salanoubat
Veronique De Bernardinis

AGC
David Vallenet
Claudine Médigue

HyperJaxB
Aleksei Valikov

SRI
Peter Karp
Thomas Lee
Monica Riley
Suzanne Paley
John Lowrance

References

- **Flux balance analysis**
  - •Metabolic modelling of microbial strains *in silico* ; Covert et al ; Trends in Biochemical Sciences 2001, 26(3):179-186.
  - •Genome-Scale Metabolic Model of *Helicobacter pylori* 26695 ; Schilling et al ; Journal of Bacteriology 2002, 184(16):4582-459
  - •Metabolic pathways in the post-genome era ; Papin et al ; Trends in Biochemical Sciences 2003, 28:250-258.
  - •Theory for the Systemic Definition of Metabolic Pathways and their use in Interpreting Metabolic Function from a Pathway-Oriented Perspective ; Schilling et al ; J. theor. Biol. 2000, 203:229-248.
  - •Assessment of Metabolic capabilities of *Haemophilus influenzae* Rd through a genome-scale pathway analysis ; Schilling et al ; J. theor. Biol. 2000, 203:249-283.
  - •Metabolic network structure determines key aspects of functionality and regulation ; Stelling et al ; Nature 2002, 420:190-193.
  - •Characterizing the Metabolic Phenotype: A Phenotype Phase Plane Analysis ; Edwards et al ; Biotechnology and Bioengineering 2002, 77:27-36.
  - •*In silico* predictions of *Escherichia coli* metabolic capabilities are consistent with experimental data ; Edwards et al ; Nature 2001, 19:125-130.

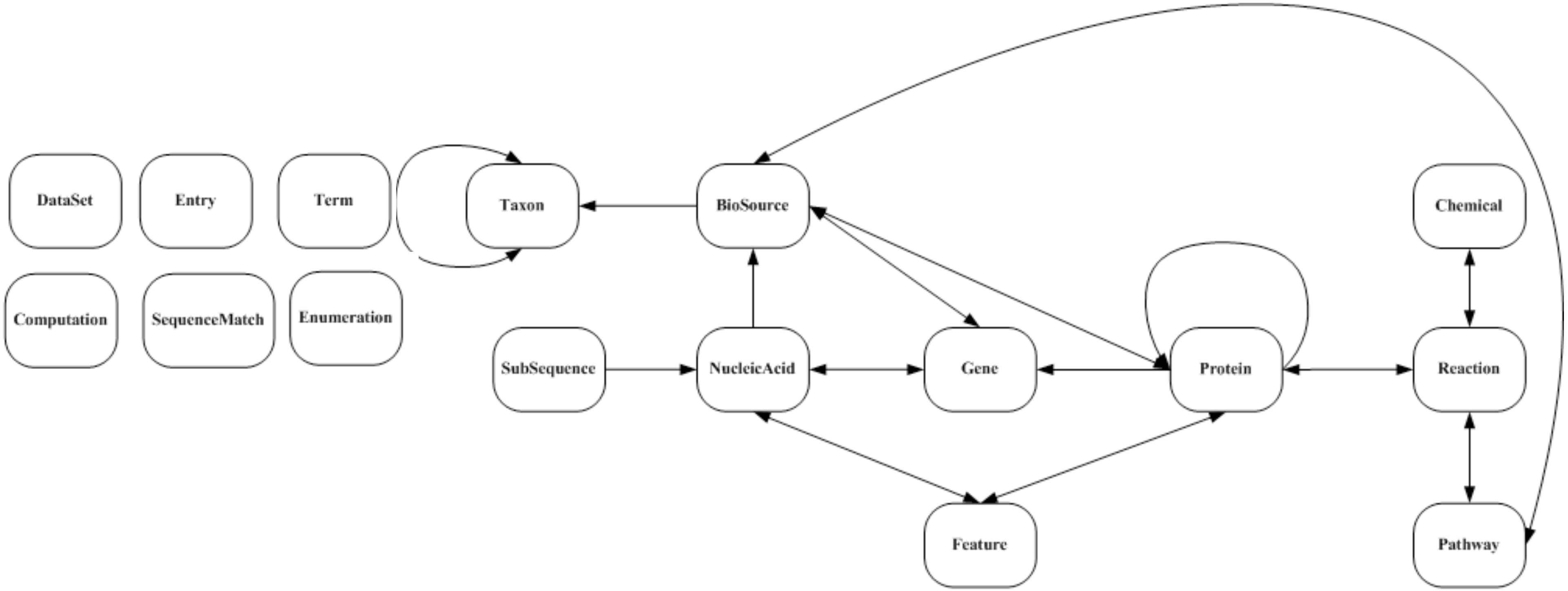
- **Biocyc /MetaCyc /EcoCyc**
  - •Karp P.D., Arnaud M., Collado-Vides J., Ingraham J., Paulsen I.T., Saier M.H. Jr. (2004). "The E. coli EcoCyc Database: No Longer Just a Metabolic Pathway Database." ASM News 70(1): 25-30.
  - •Cynthia J. Krieger, and Peter D. Karp, MetaCyc: a multiorganism database of metabolic pathways and enzymes, Nucleic Acids Research, 32(1):D438-42 2004.
  - • P. Karp, S. Paley, and P. Romero, « The Pathway Tools Software », , Bioinformatics 18:S225-32 2002.
  - • S. Paley and P. Karp, "Evaluation of computational metabolic-pathway predictions for H. pylori, "Bioinformatics 18(5):705-14 2002.
  - • Krummenacker M, Paley S, Mueller L, Yan T, Karp PD. , Abstract Querying and computing with BioCyc databases. Bioinformatics. 15;21(16):3454-5. 2005.

Supplementary Slides

OoCyc

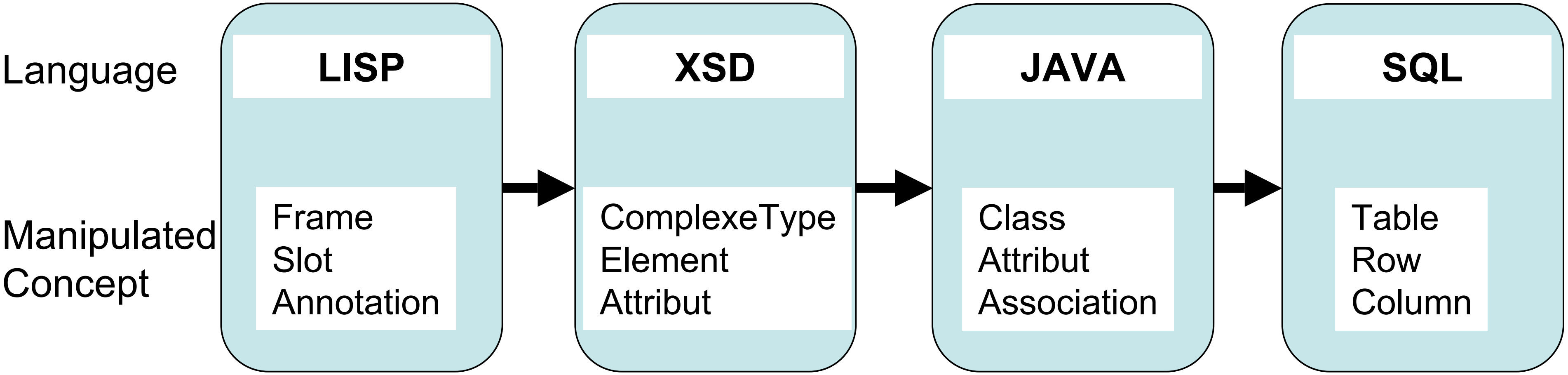
supplementary slides

Biowarehouse, another solution to query biocyc data



supplementary slides

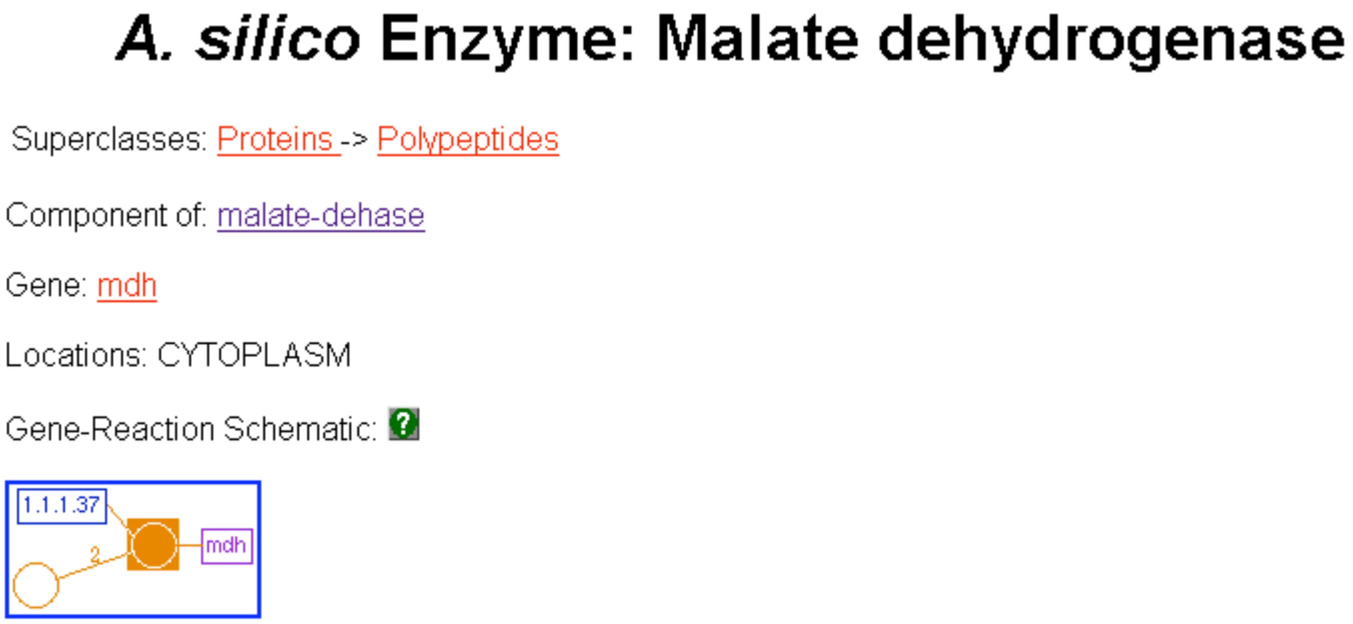
Pipeline for the creation of OoCyc



Language	LISP	XSD	JAVA	SQL
Manipulated Concept	Frame Slot Annotation	ComplexeType Element Attribut	Class Attribut Association	Table Row Column

supplementary slides

Application: complexe inference



A. silico Enzyme: Malate dehydrogenase

Superclasses: Proteins -> Polypeptides

Component of: malate-dehase

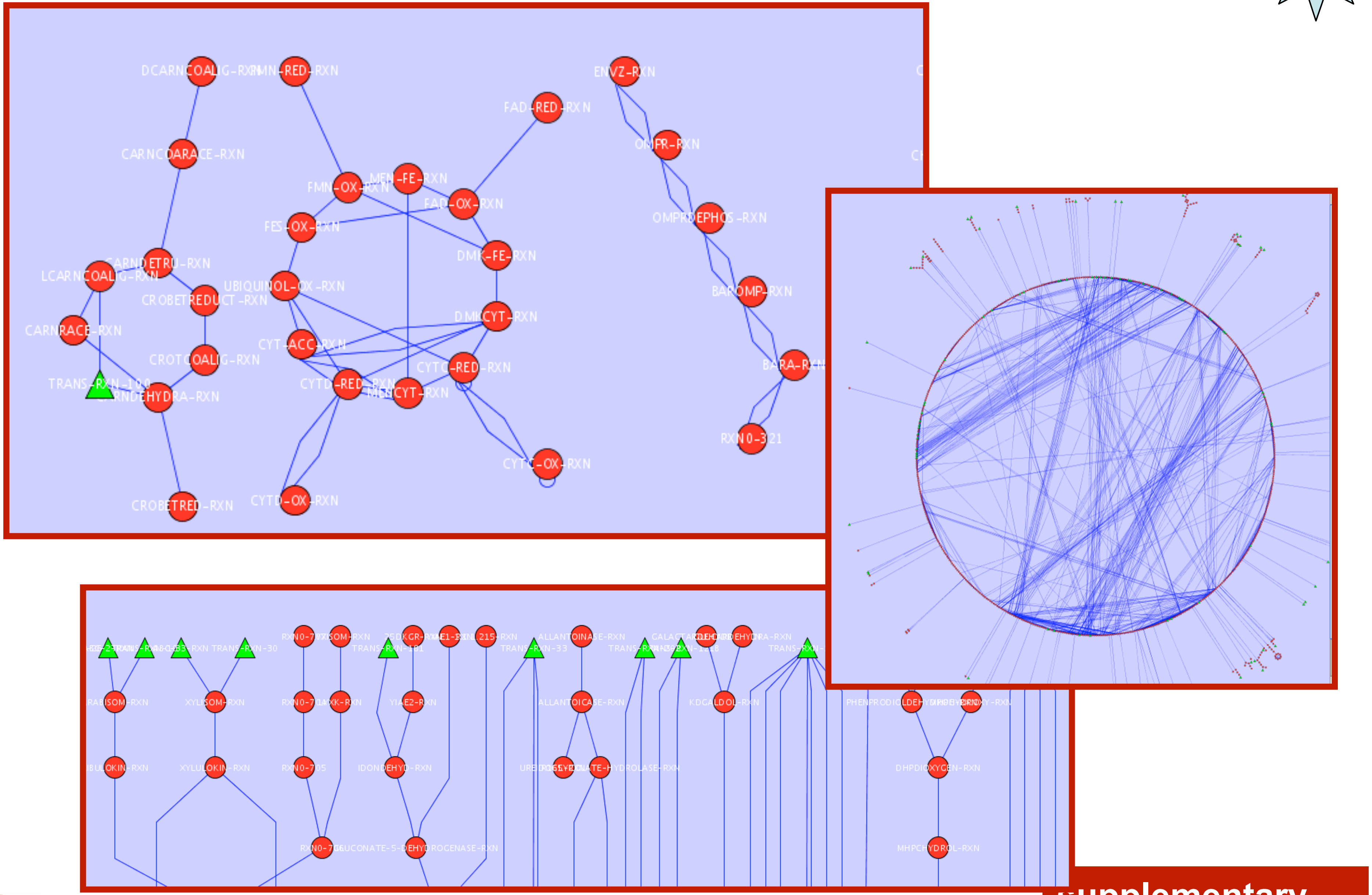
Gene: mdh

Locations: CYTOPLASM

Gene-Reaction Schematic: ?

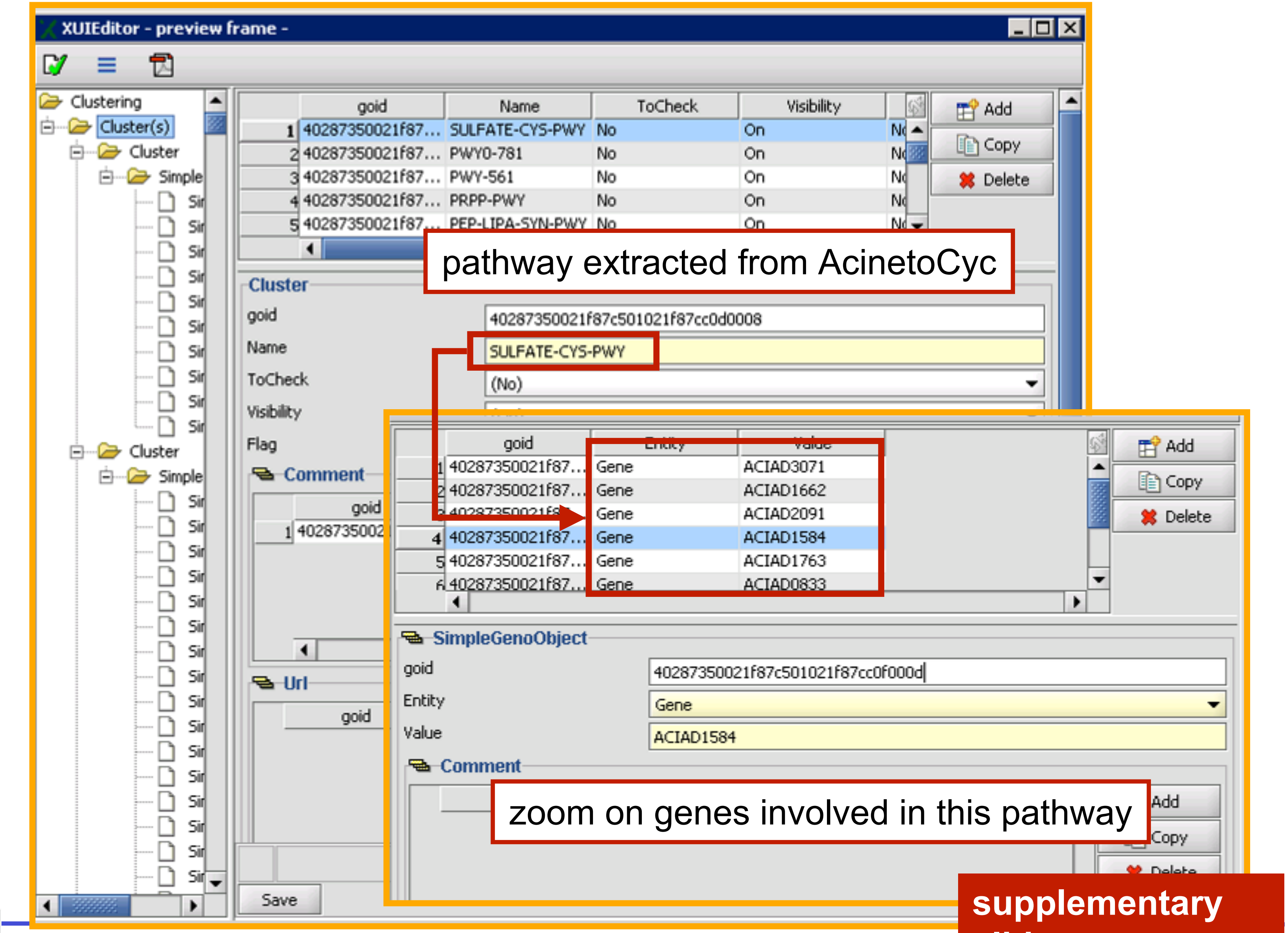
supplementary slides

Application: extraction of graph



supplementary slides

Application: extraction de clusters : genes by pathway



	goid	Name	ToCheck	Visibility	N
1	40287350021f87...	SULFATE-CYS-PWY	No	On	N
2	40287350021f87...	PWY0-781	No	On	N
3	40287350021f87...	PWY-561	No	On	N
4	40287350021f87...	PRPP-PWY	No	On	N
5	40287350021f87...	PEP-LIPA-SYN-PWY	No	On	N

pathway extracted from AcinetoCyc

Cluster

goid: 40287350021f87c501021f87cc0d0008

Name: SULFATE-CYS-PWY

ToCheck: (No)

Visibility

Flag

	goid	Entity	Value
1	40287350021f87...	Gene	ACIAD3071
2	40287350021f87...	Gene	ACIAD1662
3	40287350021f8...	Gene	ACIAD2091
4	40287350021f87...	Gene	ACIAD1584
5	40287350021f87...	Gene	ACIAD1763
6	40287350021f87...	Gene	ACIAD0833

SimpleGenoObject

goid: 40287350021f87c501021f87cc0f000d

Entity: Gene

Value: ACIAD1584

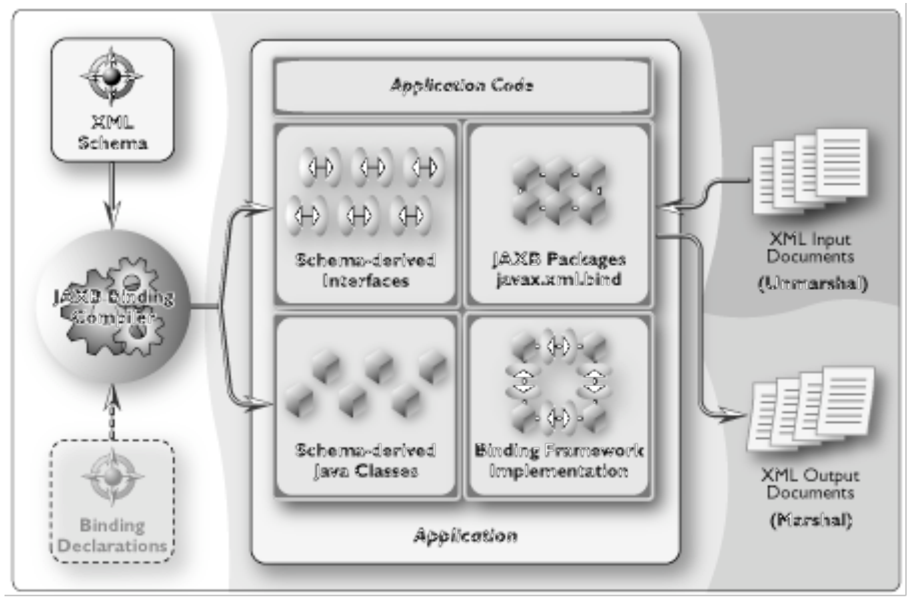
zoom on genes involved in this pathway

supplementary slides

OoCyc : rules for mapping the world of xml schema to java world: JAXB

Java Architecture for XML Binding (JAXB) provides a convenient way to bind an XML schema to a representation in Java code. This makes it easy for you to incorporate XML data and processing functions in applications based on Java technology without having to know much about XML itself

http://java.sun.com/webservices/jaxb/


XML Schema
JAXB Binding Compiler
Binding Declarations
Application Code
Schema-derived Interfaces
JAXB Packages javax.xml.bind
Schema-derived Java Classes
Binding Framework Implementation
Application
XML Input Documents (Unmarshal)
XML Output Documents (Marshal)

supplementary slides

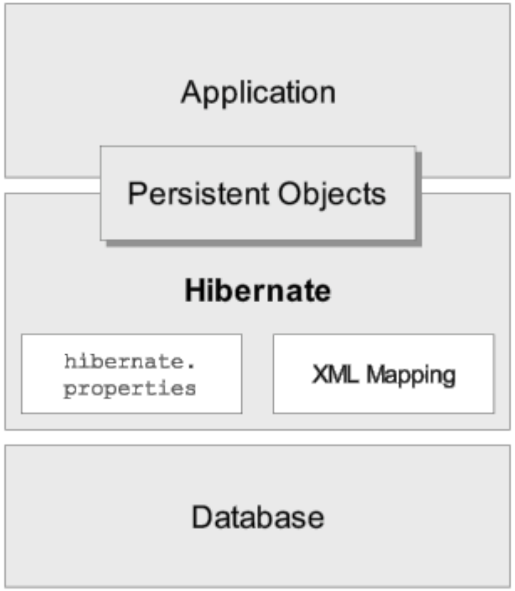
OoCyc : rules for mapping the world of java world to sql world : HIBERNATE

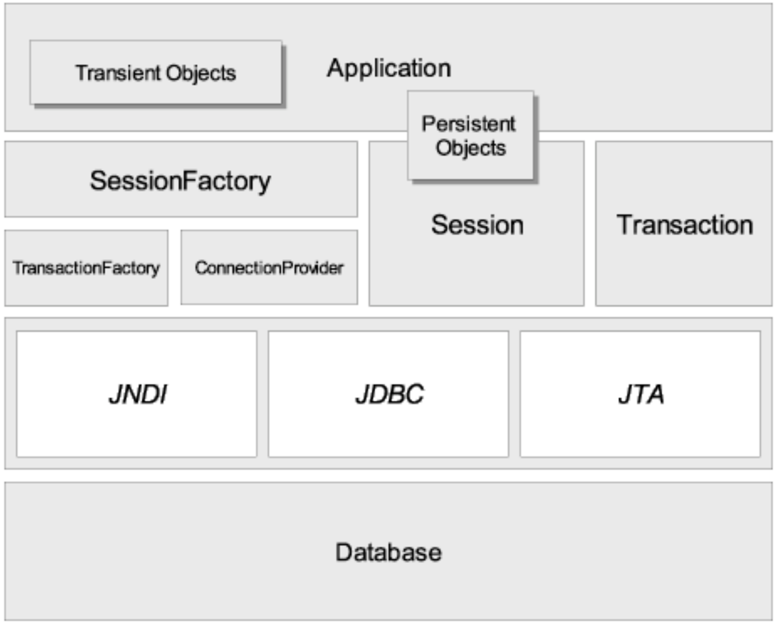
Hibernate is a powerful, ultra-high performance object/relational persistence and query service for Java.

Hibernate lets you develop persistent classes following common Java idiom - including association, inheritance, polymorphism, composition, and the Java collections framework.

Hibernate allows you to express queries in its own portable SQL extension (HQL), as well as in native SQL, or with Java-based Criteria and Example objects. Unlike many other persistence solutions,

Hibernate does not hide the power of SQL or JDBC from you and guarantees that your investment in relational technology and knowledge is as valid as always.





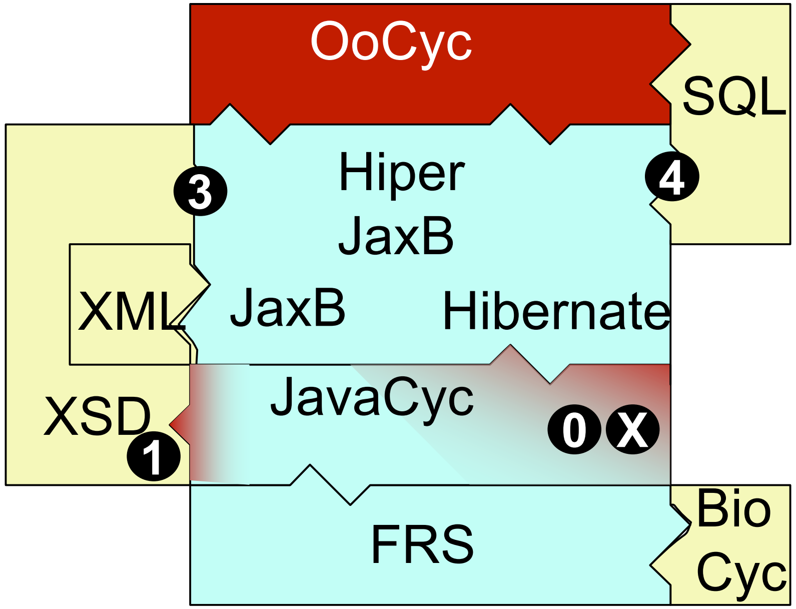
HIBERNATE

http://www.hibernate.org/

supplementary slides

OoCyc : pipeline for the creation of …

Made in Genoscope
Software, tools
Data, Files



1 Populate the mysql db and java classes

1a Extension of JavaCyc: getAnnot()

1b Query of PGDB to build a xml schema

From xsd to java classes

From java classes to hibernate mapping

From hibernate mapping to sql design

2 Upload

2a Import all Frame of a PGDB

2b Save it in MySql

3 Querying & modification of your PGDB

4 Upload your OoCyc into BioCyc

4a Extension of JavaCyc: createFrame()

FLF: Attention je confond cote pipeline et user!!

supplementary slides

OoCyc : rules for mapping the world of frame to the world of xml schema

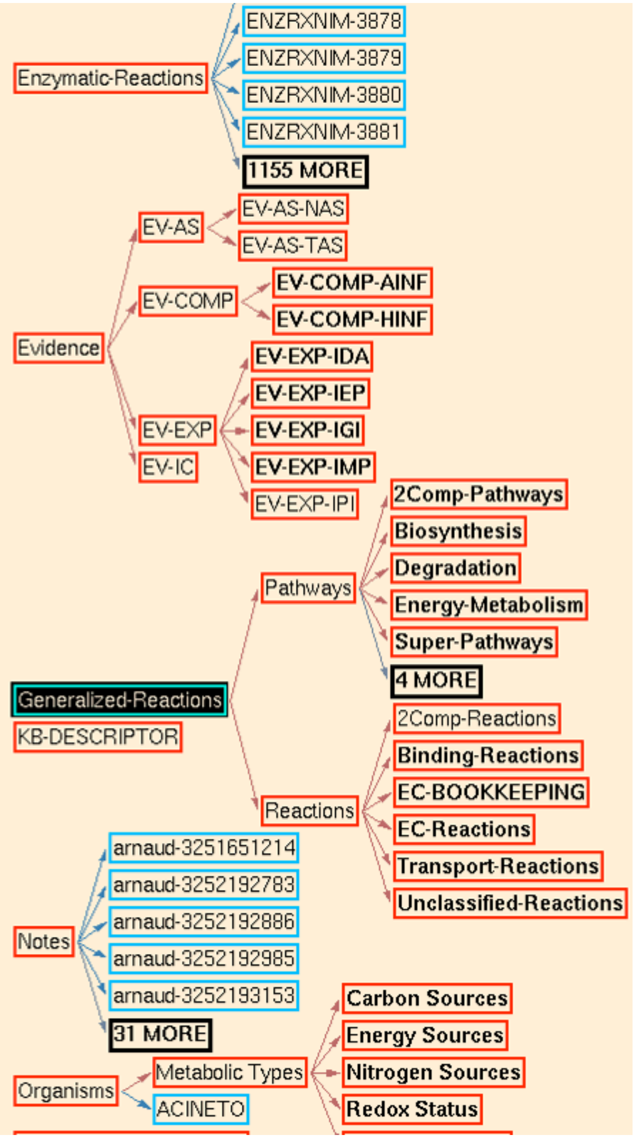
```
(FRAMEID NIL (
        (SLOT S.Value)
        ((SLOT S.Value Annotation A.value))
)
```

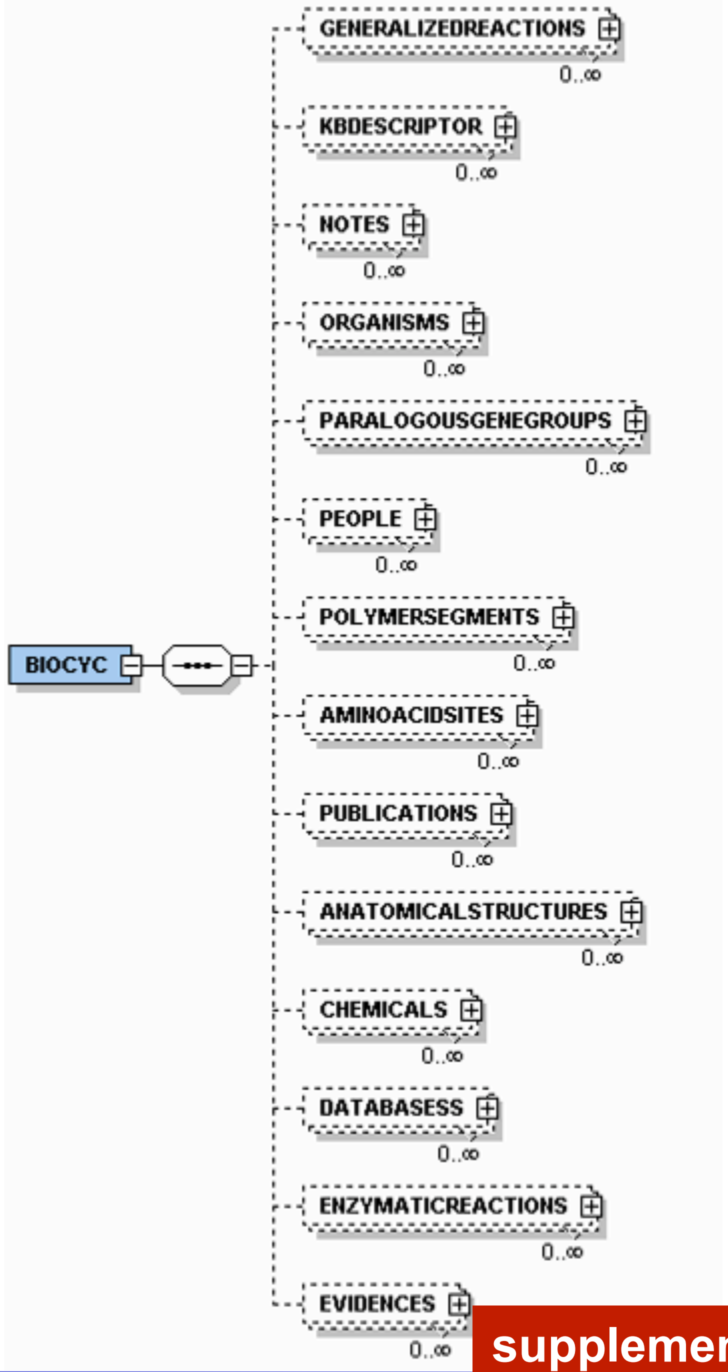
```
<xs:complexType name=“FRAME-CLASS">
    <xs:sequence>
            <xs:element name="FRAMEID" type="xs:string"/>
            <xs:element name=“SLOT" type=“SLOT-TYPE" maxOccurs="unbounded"/>
    </xs:sequence>
</xs:complexType>
```

```
<xs:complexType name=“SLOT-TYPE">
    <xs:sequence>
            <xs:element name=“S.Value" type="xs:string” />
            <xs:element name=“Annotation" type="xs:string" minOccurs="0"/>
    </xs:sequence>
</xs:complexType>
```

supplementary slides

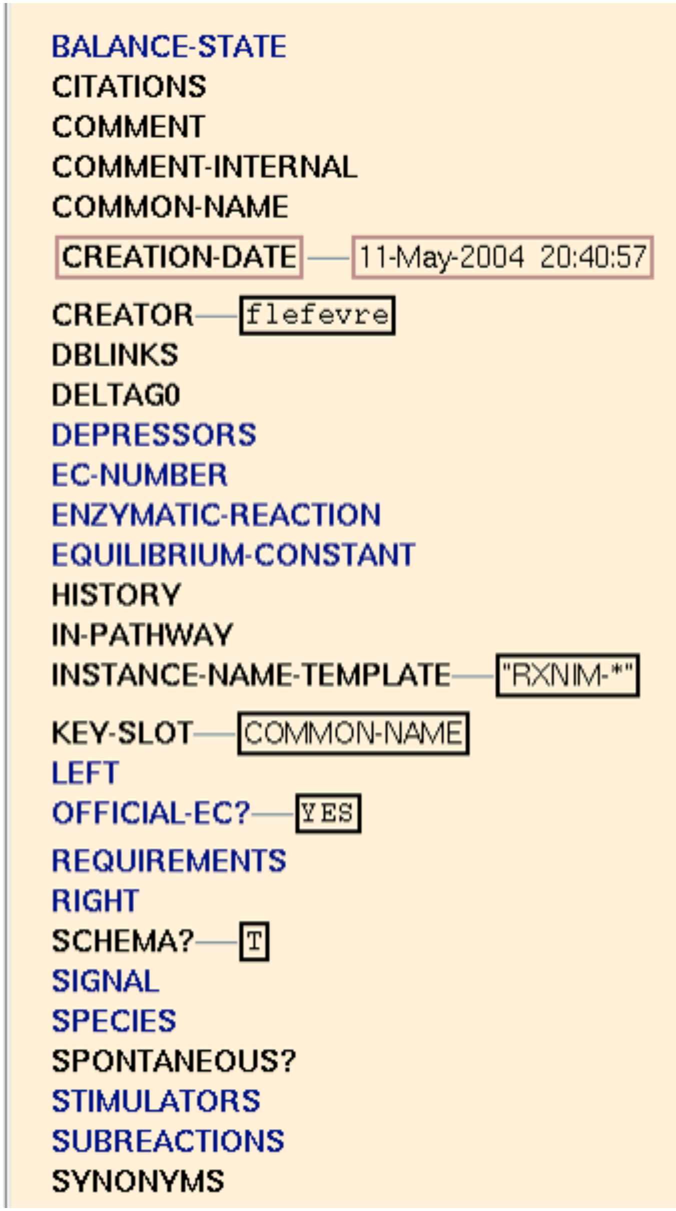
OoCyc : Biocyc FRS into xml schema



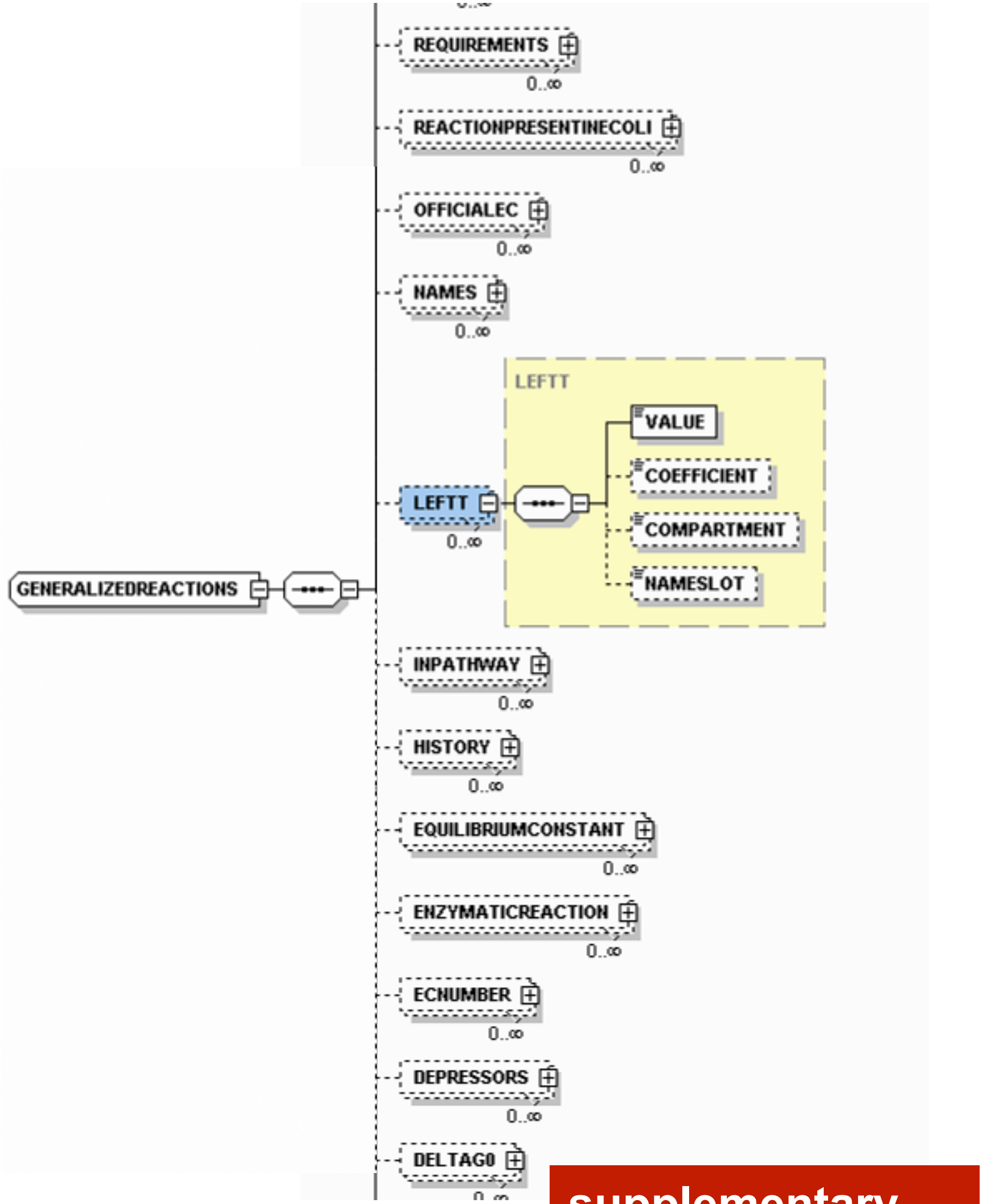


supplementary slides

OoCyc : GeneralizedReactions FRS into xml schema



BALANCE-STATE
CITATIONS
COMMENT
COMMENT-INTERNAL
COMMON-NAME
CREATION-DATE — 11-May-2004 20:40:57
CREATOR — flefevre
DBLINKS
DELTAG0
DEPRESSORS
EC-NUMBER
ENZYMATIC-REACTION
EQUILIBRIUM-CONSTANT
HISTORY
IN-PATHWAY
INSTANCE-NAME-TEMPLATE — "RXNIM-*"
KEY-SLOT — COMMON-NAME
LEFT
OFFICIAL-EC? — YES
REQUIREMENTS
RIGHT
SCHEMA? — T
SIGNAL
SPECIES
SPONTANEOUS?
STIMULATORS
SUBREACTIONS
SYNONYMS



supplementary slides

OoCyc : Sample of a frame in xml

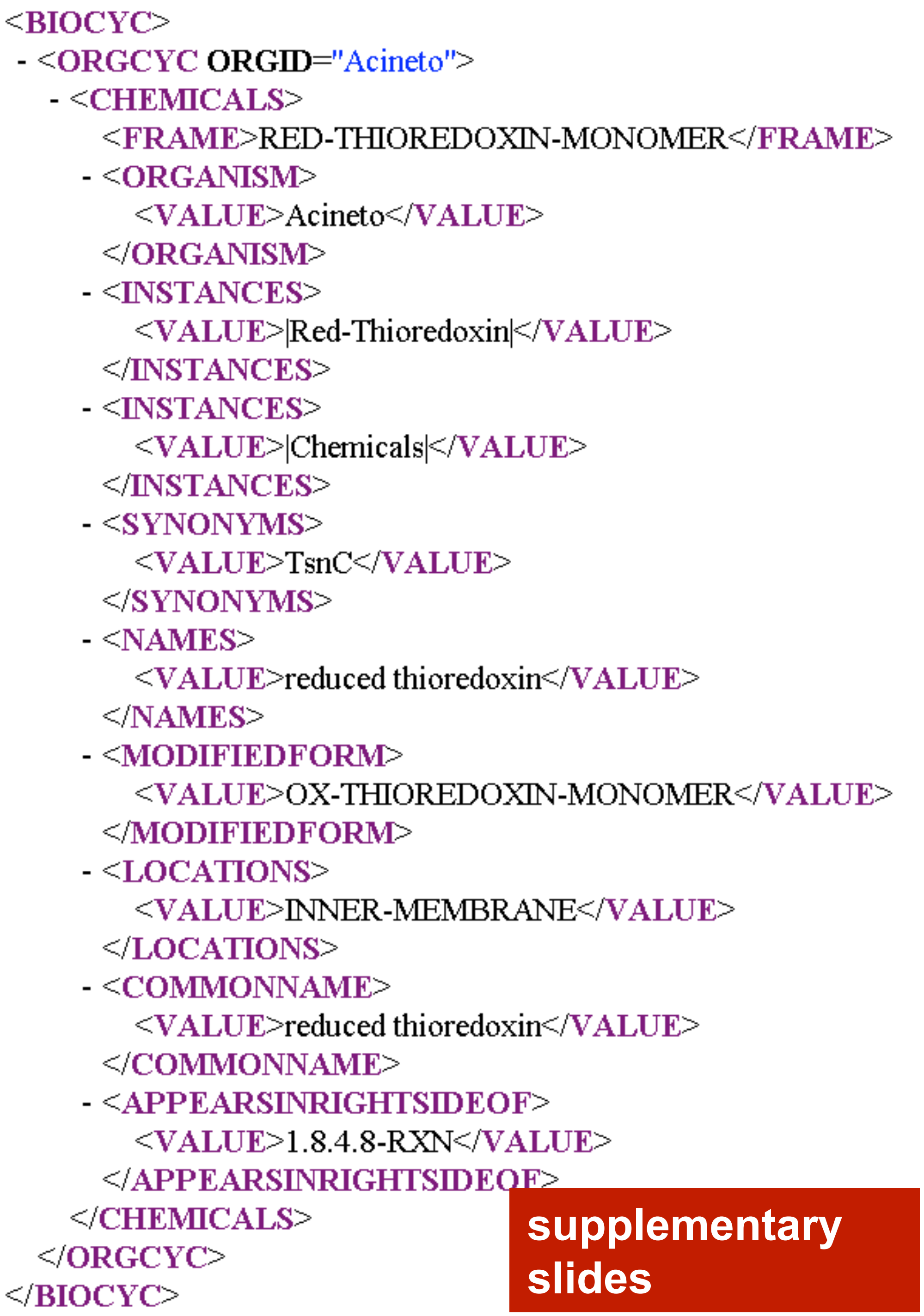
PGDB

Frame

Slot for Inheritance management

Slot-S.Value

Annot-A.Value



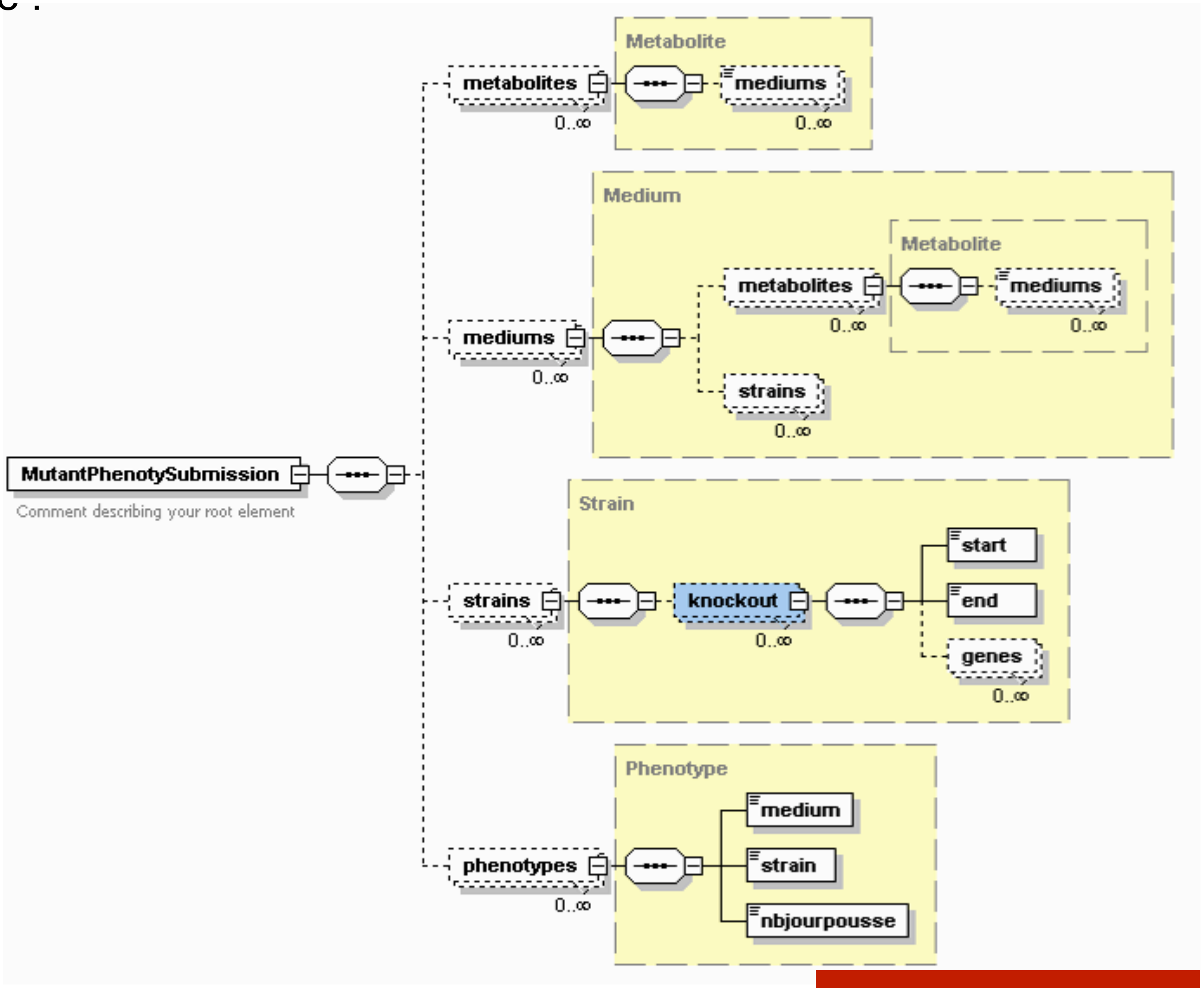
```
<BIOCYC>
 - <ORGCYC ORGID="Acineto">
   - <CHEMICALS>
       <FRAME>RED-THIOREDOXIN-MONOMER</FRAME>
     - <ORGANISM>
         <VALUE>Acineto</VALUE>
       </ORGANISM>
     - <INSTANCES>
         <VALUE>|Red-Thioredoxin|</VALUE>
       </INSTANCES>
     - <INSTANCES>
         <VALUE>|Chemicals|</VALUE>
       </INSTANCES>
     - <SYNONYMS>
         <VALUE>TsnC</VALUE>
       </SYNONYMS>
     - <NAMES>
         <VALUE>reduced thioredoxin</VALUE>
       </NAMES>
     - <MODIFIEDFORM>
         <VALUE>OX-THIOREDOXIN-MONOMER</VALUE>
       </MODIFIEDFORM>
     - <LOCATIONS>
         <VALUE>INNER-MEMBRANE</VALUE>
       </LOCATIONS>
     - <COMMONNAME>
         <VALUE>reduced thioredoxin</VALUE>
       </COMMONNAME>
     - <APPEARSINRIGHTSIDEOF>
         <VALUE>1.8.4.8-RXN</VALUE>
       </APPEARSINRIGHTSIDEOF>
     </CHEMICALS>
   </ORGCYC>
</BIOCYC>
```

supplementary slides

OoCyc : Open discussion - extension of biocyc ontology to capture mutant phenotype

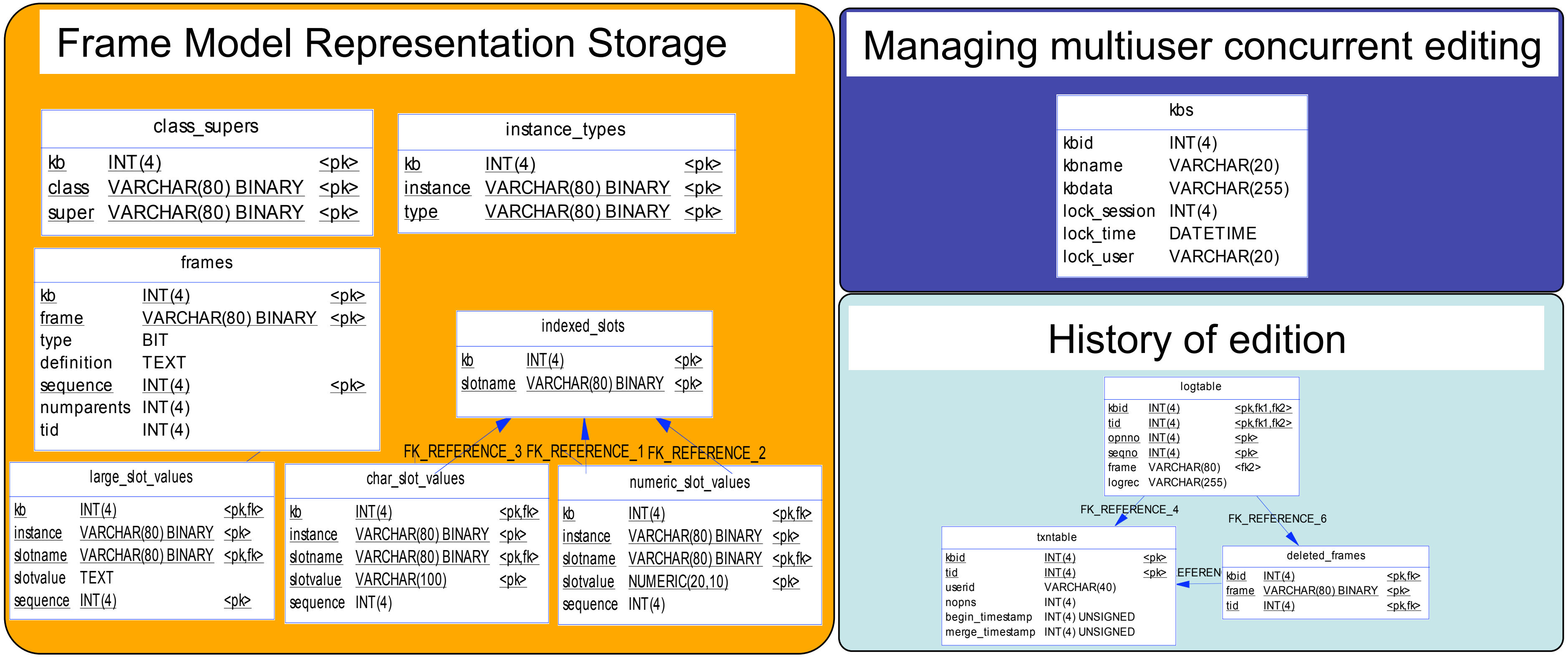
How can we capture :

- growth medium
- mutant strain
- growth phenotype



supplementary slides

BioCyc’s existing database schema



Frame Model Representation Storage

class_supers

kb	INT(4)	<pk>
class	VARCHAR(80) BINARY	<pk>
super	VARCHAR(80) BINARY	<pk>

instance_types

kb	INT(4)	<pk>
instance	VARCHAR(80) BINARY	<pk>
type	VARCHAR(80) BINARY	<pk>

frames

kb	INT(4)	<pk>
frame	VARCHAR(80) BINARY	<pk>
type	BIT	
definition	TEXT	
sequence	INT(4)	<pk>
numparents	INT(4)	
tid	INT(4)	

indexed_slots

kb	INT(4)	<pk>
slotname	VARCHAR(80) BINARY	<pk>

large_slot_values

kb	INT(4)	<pk,fk>
instance	VARCHAR(80) BINARY	<pk>
slotname	VARCHAR(80) BINARY	<pk,fk>
slotvalue	TEXT	
sequence	INT(4)	<pk>

char_slot_values

kb	INT(4)	<pk,fk>
instance	VARCHAR(80) BINARY	<pk>
slotname	VARCHAR(80) BINARY	<pk,fk>
slotvalue	VARCHAR(100)	<pk>
sequence	INT(4)	

numeric_slot_values

kb	INT(4)	<pk,fk>
instance	VARCHAR(80) BINARY	<pk>
slotname	VARCHAR(80) BINARY	<pk,fk>
slotvalue	NUMERIC(20,10)	<pk>
sequence	INT(4)	

Managing multiuser concurrent editing

kbs

kbid	INT(4)
kbname	VARCHAR(20)
kbdata	VARCHAR(255)
lock_session	INT(4)
lock_time	DATETIME
lock_user	VARCHAR(20)

History of edition

logtable

kbid	INT(4)	<pk,fk1,fk2>
tid	INT(4)	<pk,fk1,fk2>
opnno	INT(4)	<pk>
seqno	INT(4)	<pk>
frame	VARCHAR(80)	<fk2>
logrec	VARCHAR(255)	

txntable

kbid	INT(4)	<pk>
tid	INT(4)	<pk>
userid	VARCHAR(40)	
nopns	INT(4)	
begin_timestamp	INT(4) UNSIGNED	
merge_timestamp	INT(4) UNSIGNED	

deleted_frames

kbid	INT(4)	<pk,fk>
frame	VARCHAR(80) BINARY	<pk>
tid	INT(4)	<pk,fk>

+

- fast data access,
- multi-user editing,
- acess to a transaction log of all PGDB edits

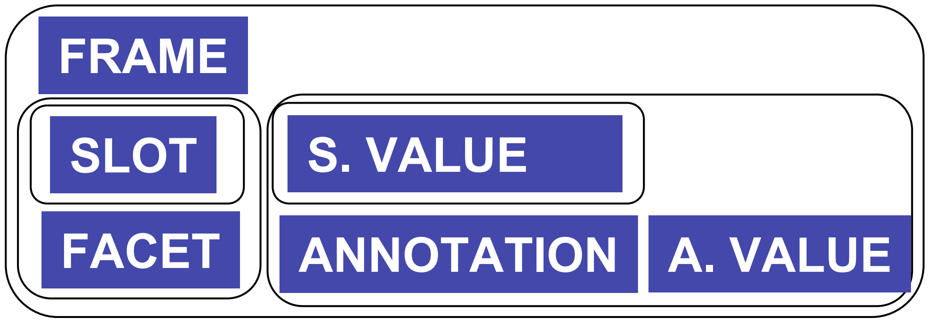
-

- Don’t allow to query biocyc outside pathway-tools software,
- No tables linking to each biology concept

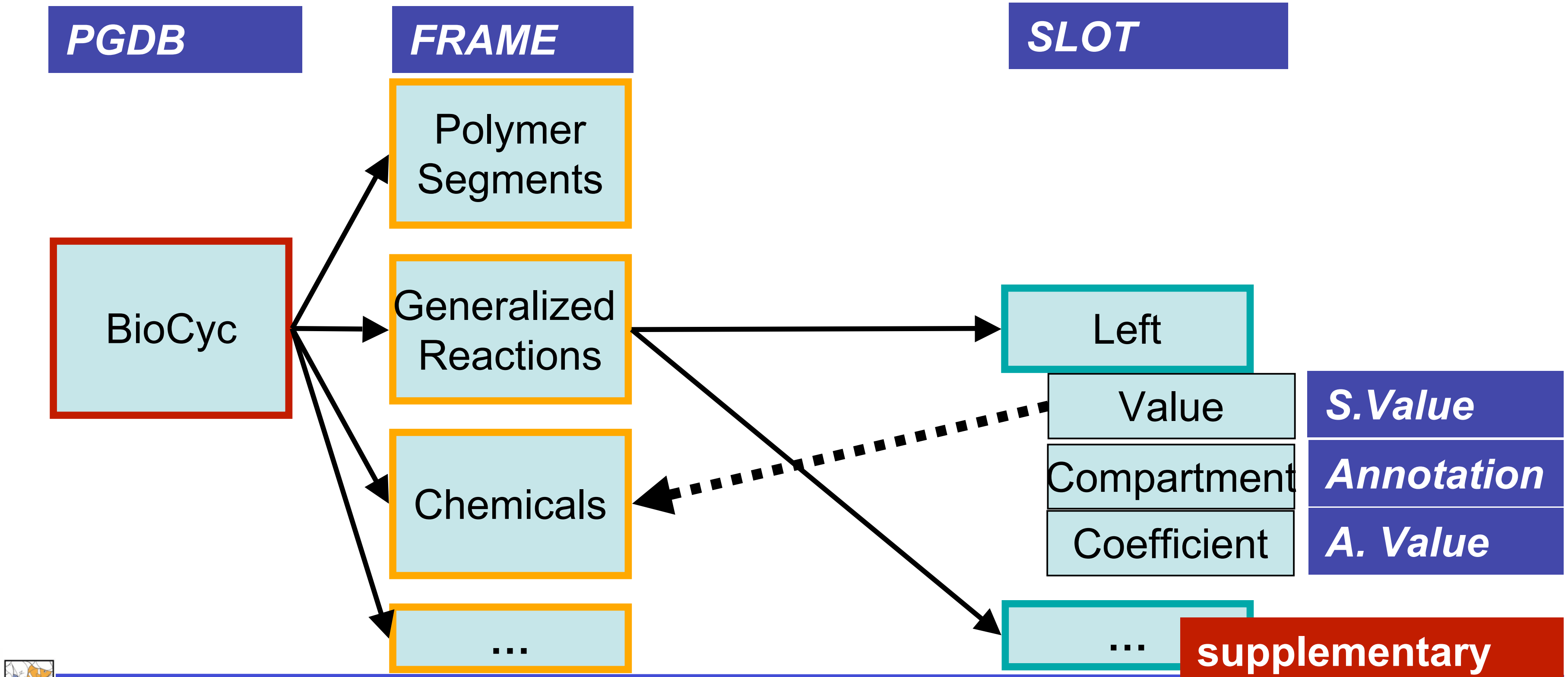
supplementary slides

From FRS to java classes

BioCyc

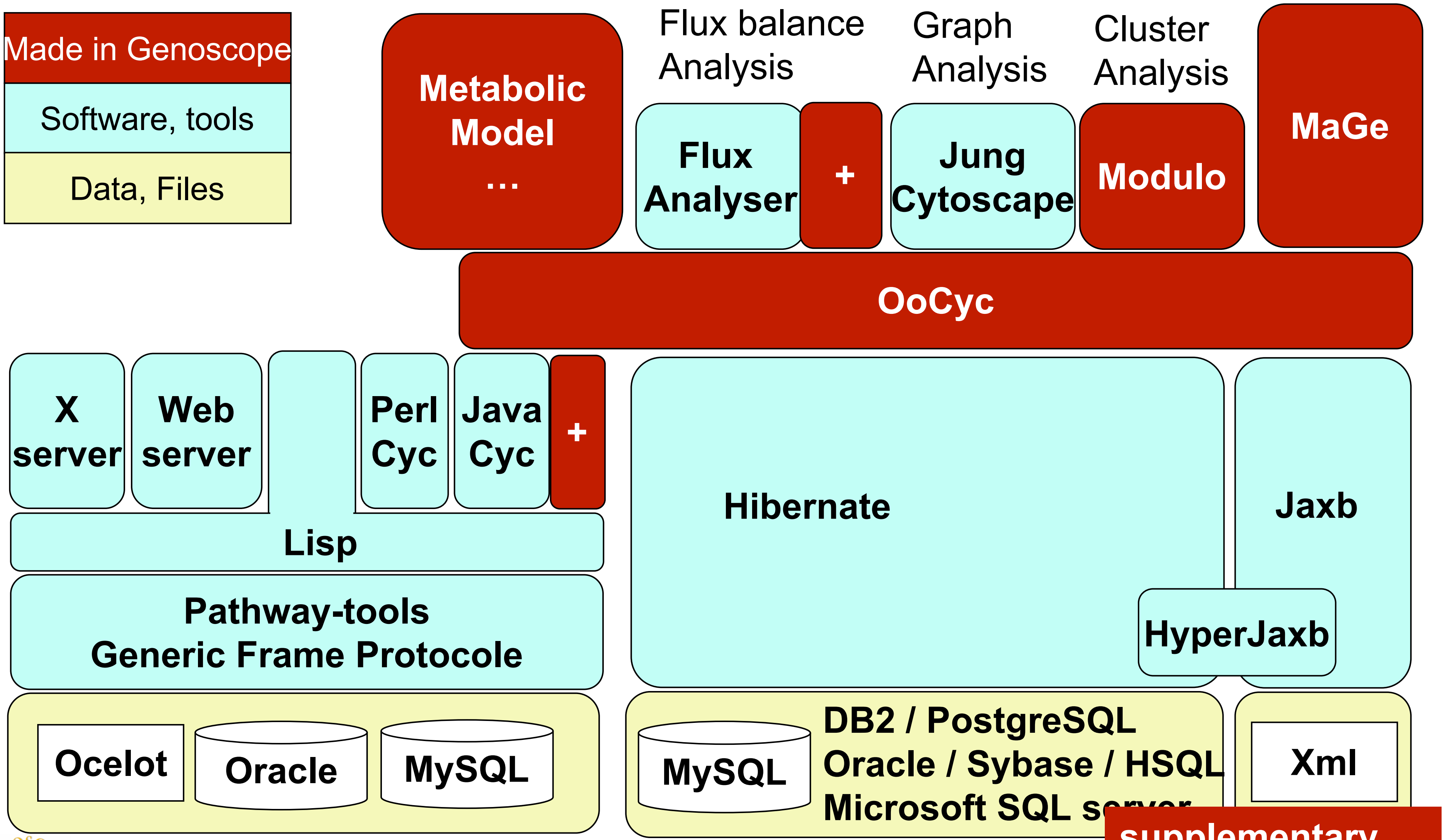


OoCyc



supplementary slides

BioCyc and OoCyc's architecture



Made in Genoscope

Software, tools

Data, Files

Metabolic Model …

Flux balance Analysis

Flux Analyser

+

Graph Analysis

Jung Cytoscape

Cluster Analysis

Modulo

MaGe

OoCyc

X server

Web server

Perl Cyc

Java Cyc

+

Lisp

Pathway-tools Generic Frame Protocole

Ocelot

Oracle

MySQL

Hibernate

Jaxb

HyperJaxb

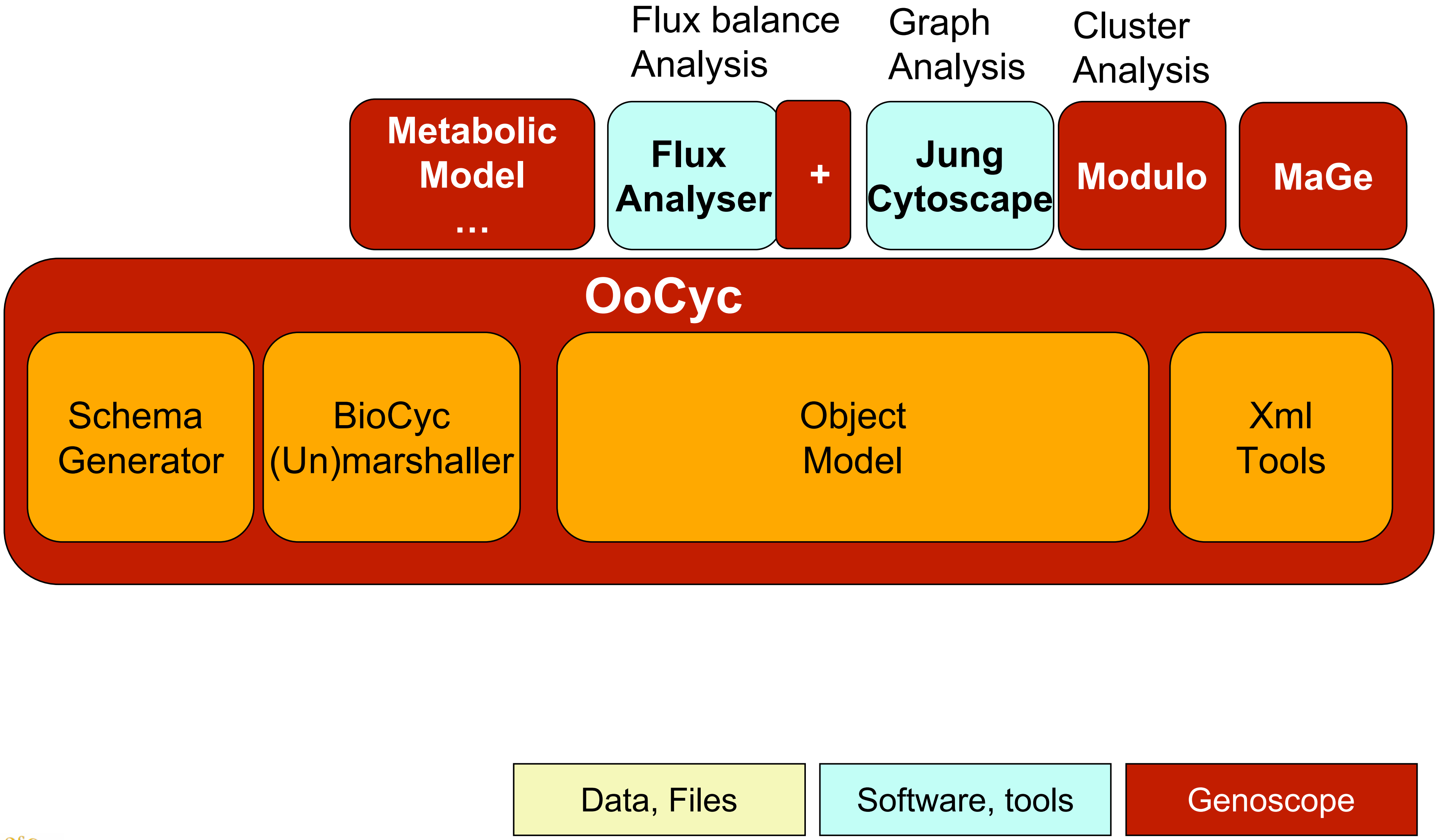
MySQL

DB2 / PostgreSQL
Oracle / Sybase / HSQL
Microsoft SQL se…

Xml

supplementary slides

OoCyc's architecture



Flux balance Analysis

Graph Analysis

Cluster Analysis

Metabolic Model …

Flux Analyser

+

Jung Cytoscape

Modulo

MaGe

OoCyc

Schema Generator

BioCyc (Un)marshaller

Object Model

Xml Tools

Data, Files

Software, tools

Genoscope

True query in OQL

```
public List getAllErInhibitedBy(String org, String inhibitor) {
    try {
            Query hql = HibernateUtil.getSession(keySession).createQuery("select
    distinct er from
    fr.cns.genoscope.nemo.hypercyc.impl.ENZYMATICREACTIONSImpl er "+
                        " join er.INHIBITORSALLInternal inhibitors" +
                        " where " +
                        “ er.ORGANISM.VALUE like :organism and " +
                        “ :inhibitor = inhibitors.VALUE" +
                        “ ");
            hql.setString("organism", org);
            hql.setString("inhibitor", inhibitor);
            return hql.list();
    } catch (HibernateException e) {
            e.printStackTrace();
    }
    return null;
}
```

Java API

```
package fr.cns.genoscope.nemo.hypercyc.cycs.acineto;

public class Acineto {
    public static void main(String[] args) {
            ENZYMATICREACTIONSDAO erdao = new ENZYMATICREACTIONSDAO("hypercyc");
            List r = erdao.getAllErInhibitedBy("ecoli","ATP");
            ENZYMATICREACTIONS er;
            for(int i=0; i < r.size(); i++){
                    er = (ENZYMATICREACTIONS)r.get(i);
                    System.out.println(

    er.getFRAME()+"\t"+((ENZYME)er.getENZYME().get(0)).getVALUE());
    }
}
```