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On the integration of biomedical knowledge bases: problems and solutions

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Outline

- A collaboration between:
  - *Systems and Technologies for Automated Reasoning laboratory, DIST, University of Genoa*
  - *Bioengineering and Bioimages laboratory (Biolab), DIST, University of Genoa*
- Brief introduction to the problem
- Our research goal
- The different possible solutions
- BioGIS (Bioinformatic GAV Integration System)
  - Rewriting rules
  - Front end
  - Internal structure
- Conclusions

Data Sources Integration

"The user should be able to focus on what he is looking for rather than thinking how to obtain it"(A. Levy)

- Issues:
  - Overlapping and mismatching
  - Syntactic difference between sources
  - Different layout of the sources (chart based, text based, etc.)
  - Lacking of a common exchange format
  - Unknown data source internal structure
  - Internet is not a stable environment
  - Sometimes hard identifying the same element in different systems

BioGIS

- The goal:
  - Integration of the human metabolic pathways
- The sources:
  - KEGG (M. Kanehisa et al., 2002)
  - Reactome (G. Joshi-Tope et al., 2005)
- The user:
  - Biolab portal (http://grid.bio.dist.unige.it)

Modelling the data sources

Global as view (Garcia-Molina et al., 1997)

- Two data sources:
  - DB1 (Pathway_Name, Pathway_ID1, Description, Molecule)
  - DB2 (Pathway_ID2, Pathway_Name, Organism)
- Mediated schema relations:
  - Pathway (Pathway_Name, Description, Organism) :- DB1(Pathway_Name,Pathway_ID1, Description, Molecule), DB2(Pathway_ID2, Pathway_Name, Organism)
  - Connection_Molecule (Pathway_Name, Molecule) :- DB1(Pathway_Name,Pathway_ID1, Description, Molecule)

Modelling the data sources

Local as view (O. Duschka et al., 1997)

- DB1 (Pathway_Name, Pathway_ID1, Description, Molecule) :-

  Pathway (Pathway_Name, Description, Organism, *Pathway_ID1, Pathway_ID2*),

  Connection_Molecule (Pathway_Name, Molecule, Class), Class = “genes”

- DB2 (Pathway_ID2, Pathway_Name, Organism) :-

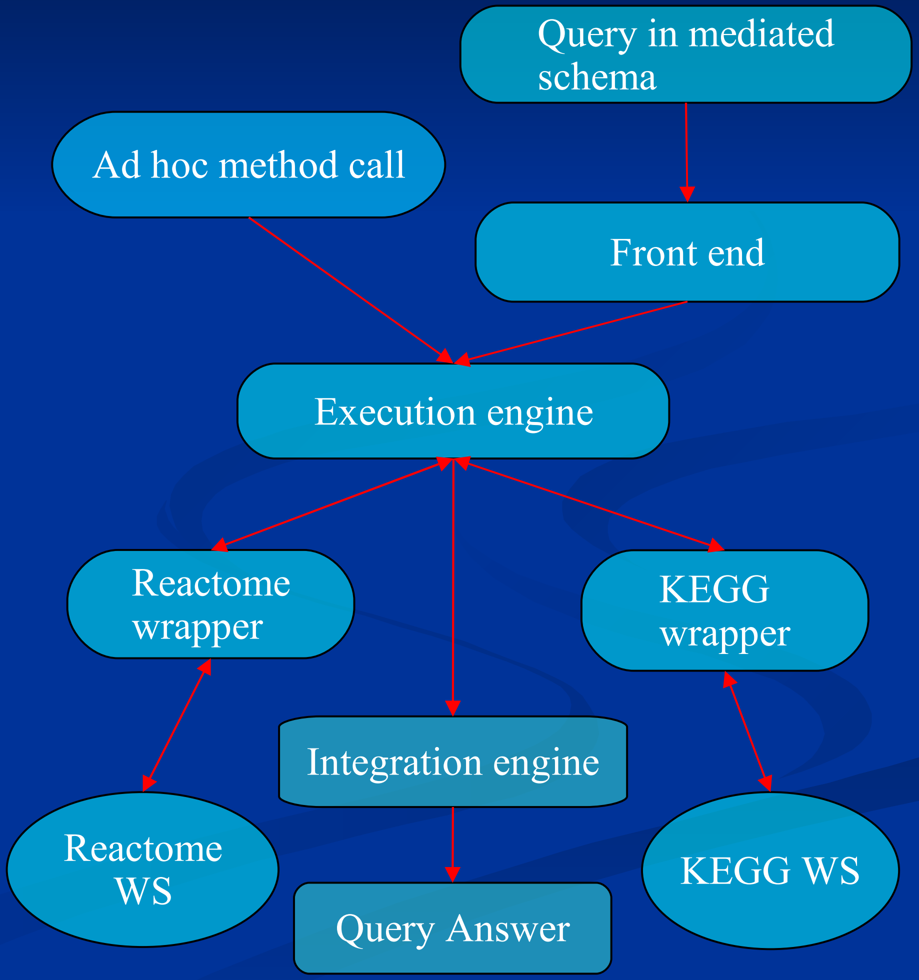
  Pathway (Pathway_Name, Description, Organism, *Pathway_ID1, Pathway_ID2*), Organism = “homo sapient”

A Comparison

- GAV
  - Does not require containment checking (fast and reliable)
  - Somehow awkward modelling the system
  - Difficult to extend
- LAV
  - Easy to extend
  - Useless details in the model of the system
  - Requires containment checking (slow)
  - The algorithm may be even intractable
- GLAV (M Friedman et al., 1999)
  - Same complexity than LAV
  - Solved some drawbacks in the modelling phase

BioGIS

- Front end or ad hoc methods
- Execution engine which iteratively calls the wrappers
- A wrapper for each data source
- Integration engine

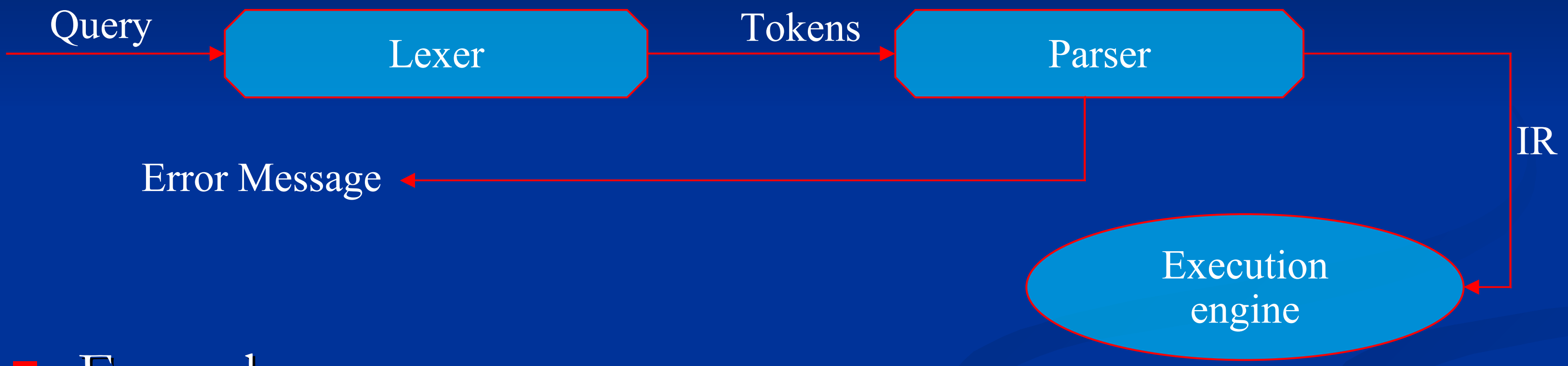


The information extracted

- Two ad hoc family of methods:
  - getMoleculesForPathway
  - getPathwayForMolecules
- Three global schema relations:
  - Pathway
  - Connection_Molecule
  - Reaction

Front End

- Queries have to follow a precise grammar



- Examples:
  - PATHWAY { GOTerm = " alanine metabolism " } END
  - PATHWAY { ReactomePathwayID = " 109606 " } , CONNECTION_MOLECULE { ReactomePathwayID = " 109606 " } END
  - CONNECTION_MOLECULE { UniqueID = " Q92934 " } END

Internal structure

- Execution engine:
  - Simple unfolding of the queries according to the GAV methodology
  - Ad hoc methods: concurrent threads which query in parallel the wrappers
- Wrappers:
  - A class for every different data source relation. The information is retrieved from the sources and structured into objects.
- Integration engine:
  - Pathways merged using the pathway names and the Gene Ontology terms
  - Molecules merged using the UniProt and COMPOUND ids

Performances

- Vary according to several factors:
  - The number of hits of the query
    - “Retrieve all the genes that take part to a pathway which matches the keyword “pyruvate” ”: around 65 hits – 1 minute
    - “Retrieve all the genes that take part to a pathway which matches the keyword “metabolism” ”: thousands of hits – half an hour
  - The state of the Reactome cache
  - The network latency
- Better to be used in a chain of web services than as a standalone service available through a browser

Conclusions

- GAV approach:
  - Yet possible easy extensions of the wrappers thanks to the modelling of the same knowledge base as more relations
  - Good approach in case of few stable sources and limited extension
- Web service approach
- Future work:
  - Extension to allow a more expressive grammar
  - Extension to another data source (BioCyc)
  - Extension to take advance also XML format together with web services

Thanks for your kind attention

Any question?

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The grammar

- goal → relations END
- relations → relation rel'
- Rel' → , relation rel

  | ε
- relation → namerelation { bindings }
- Namerelation → PATHWAY

  | CONNECTION MOLECULE

  | REACTION
- bindings → binding bin'
- bin' → , binding bin'

  | ε
- binding → string = “ string ”
- string → [azA-Z0-9[ ] +, ()-]

The global schema: Pathway

- Pathway (PathName, KEGGPathwayID, ReactomePathwayID, Description, Organism, GOTerm) :- KEGG1 (PathName, KEGGPathwayID, Organism), Reactome1 (PathName, ReactomePathwayID, Description, Organism, GOTerm)
- Pathway (PathName, KEGGPathwayID, ReactomePathwayID, Description, Organism, GOTerm) :- KEGG1 (PathName, KEGGPathwayID, Organism),
- Pathway (PathName, KEGGPathwayID, ReactomePathwayID, Description, Organism, GOTerm) :- Reactome1 (PathName, ReactomePathwayID, Description, Organism, GOTerm)

The global schema: Connection_Molecule

- Connection_Molecule (ReactomePathwayID, KEGGPathwayID, ReactomeMoleculeID, MoleculeNameR, KEGGMoleculeID, MoleculeNameK, UniqueID, Database, Definition, Class, Description) :-
  Reactome3 (ReactomePathwayID, ReactomeMoleculeID , MoleculeNameR, UniqueID, Database),
  KEGG2 (KEGGMoleculeID, MoleculeNameK, UniqueID , Definition, Class, Description),
  KEGG3 (KEGGPathwayID, KEGGMoleculeID, Class)
- Connection_Molecule (ReactomePathwayID, KEGGPathwayID, ReactomeMoleculeID, MoleculeNameR, KEGGMoleculeID, MoleculeNameK, UniqueID, Database, Definition, Class, Description) :-
  Reactome3 (ReactomePathwayID, ReactomeMoleculeID , MoleculeNameR, UniqueID, Database)
- Connection_Molecule (ReactomePathwayID, KEGGPathwayID, ReactomeMoleculeID, MoleculeNameR, KEGGMoleculeID, MoleculeNameK, UniqueID, Database, Definition, Class, Description) :-
  KEGG2 (KEGGMoleculeID, MoleculeNameK, UniqueID , Definition, Class, Description),
  KEGG3 (KEGGPathwayID, KEGGMoleculeID, Class)

The global schema: Reaction

Reaction (PathName, ReactomePathwayID, Reaction) :-
Reactome1 (PathName, ReactomePathwayID, Description, Organism, GOTerm),
Reactome2 (ReactomePathwayID, Reaction)