Exchanging Experimental Kinetic Data via SabioML

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Heidelberg Institute for Theoretical Studies
HITS gGmbH, Germany

COMBINE Meeting 2010, October 6-9, Edinburgh (UK)
- Kinetic data from literature and directly from experiments merged with data describing biochemical reactions and pathways from other resources
- Data about metabolic and signalling reactions, as well as reaction mechanisms
- Data is unified, structured, normalized, interrelated and annotated
- Access through a web-based user interface and through web-services (API)
- Proprietary levels can be defined to restrict access to sensitive data
- Data export possible in Systems Biology Markup Language (SBML)
SabioML: Exchange Format for Experimental Kinetic Data

Extensible Markup Language (XML) based exchange file format

- Developed for data import into the SABIO-RK database
- Data schema mapped to the SABIO-RK database model → Data can be directly integrated into SABIO-RK
- Uses Controlled vocabulary (Constraints)
- Supports standardized annotations for many data types → Compliant with the MIRIAM standard (Minimal Information Required In the Annotation of Models)
- Data model flexible and conferrable for exchanging experimental kinetic data between databases and tools
SabioML: Exchange Format for Experimental Kinetic Data

SabioML: Exchange Format for Experimental Kinetic Data

```xml
<compound>
  <location description="UNDEFINED" />
</compound>

<species>
  <species name="2-(alpha-Hydroxyethyl)thiamine diphosphate" role="Product" stoichiometricvalue="1.0" speciesid="species3">
    <compound name="2-(alpha-Hydroxyethyl)thiamine diphosphate" compoundtype="simpleMolecule" stoichiometricvalue="1.0">
      <inchi_string>InChI=1/C14H32N4O8P2S/c1=8-12(4-5-25-28(23,24)26-27(20,21)22)29-14(9(2)19)18(6)7-11-6-16-10(3)17-13(11)15/h6,9,19H,4-5,7H2,1-3H3,(H4,-15,16,17,20,21,22,23,24)/p+1/InChI=1/C14H32N4O8P2S/h20-21,23H,15H2/q+1"/>
    </compound>
  </species>
</specie>

<complementaryinfo>
  <annotation url="urn:miriam:obo.chebi" elemid="CHEBI%3A978" />
  <annotation url="urn:miriam:kegg.compound" elemid="C05125" />
</complementaryinfo>

<compound>
  <location description="UNDEFINED" />
</compound>

<species>
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    <compound name="PDC1" compoundtype="ProteinPeptide" stoichiometricvalue="1.0">
      <complementaryinfo>
        <annotation url="urn:miriam:uniprot" elemid="P06169" />
      </complementaryinfo>
    </compound>
  </species>
</species>

<complementaryinfo>
  <annotation url="urn:miriam:kegg.reaction" elemid="R00755" />
</complementaryinfo>

<reaction>
  <protein_in_reaction name="Pyruvate decarboxylase isozyme 1" uniprotid="P06169" wildtype="wildtype" recombinant="recombinant" expressed_in="Saccharomyces cerevisiae" />
</reaction>
</reaction>
```
Direct Data Submission

Spreadsheet (data and metadata) → NOVOstar data parser

Java data model

KineticsWizard

Experimental data + meta data

MeMo-RK → Web / web service

SabioML

Kinetic parameters + meta data

SABIO-RK → Web / web service

SBRML

SBRML Browser

SBML
Enzyme kinetics informatics: from instrument to browser

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Additional Information (Show All)

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†+ These authors contributed equally to this work
SABIO-RK Web Interface

Search with Reactant(s)

Search in Pathway(s)

Search having Enzyme(s)

Use wildcard "%" to display e.g. all kinases in the selection list (type "%kinase%").

Search criteria:
- Reactant:
- Pathway:
- Enzyme:
- Publication:
- Protein:
- Sign. modific.:
- Sign. event:
- Organism:
- Tissue:
- Cell. loc.:
- Exp. cond.:
- Kin. data:

Join entries with AND or OR

2.1.1.45:Thymidy late synthase

in Publication

related to Protein (UniProtID)

for Signalling

in Organism(s)

in Tissue(s)/Cell Type(s)

in (Intra/Extra)Cellular Location(s)
Kinetic Data Available for Reaction:
D-Glucose 6-phosphate <-> D-Fructose 6-phosphate
Show only kinetic data matching the search criteria

Expanding the entry...

### Entry Nr. 29390

**Organism:** Saccharomyces cerevisiae (strain BY4700 transformed in Y258)

**Tissue:**

**EC Class:** 5.3.1.9

**Recombinant:** wildtype Glucose-6-phosphate isomerase

**Substrates**

<table>
<thead>
<tr>
<th>name</th>
<th>location</th>
<th>comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>D-Fructose 6-phosphate</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Products**

<table>
<thead>
<tr>
<th>name</th>
<th>location</th>
<th>comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>D-Glucose 6-phosphate</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Modifiers**

<table>
<thead>
<tr>
<th>name</th>
<th>location</th>
<th>effect</th>
<th>comment</th>
<th>protein complex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose-6-phosphate isomerase (Enzyme)</td>
<td></td>
<td>Modifier-Catalyst</td>
<td>(P12709)*2</td>
<td></td>
</tr>
</tbody>
</table>

**Kinetic Law**

- **type:** Michaelis-Menten
- **formula:** $k_{cat} \cdot E_t \cdot S / (K_s + S)$

**Parameter**

# SABIO-RK Web Interface

**D-Glucose-6-phosphate**

<table>
<thead>
<tr>
<th>Modifiers</th>
<th>name</th>
<th>location</th>
<th>effect</th>
<th>comment</th>
<th>protein complex</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Glucose-6-phosphate isomerase(Enzyme)</td>
<td>-</td>
<td>Modifier-Catalyst</td>
<td></td>
<td>(P12709)^2</td>
</tr>
</tbody>
</table>

**Kinetic Law**

<table>
<thead>
<tr>
<th>type</th>
<th>formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>Michaelis-Menten</td>
<td>$k_{cat} \times \frac{E_t \times S}{(K_s + S)}$</td>
</tr>
</tbody>
</table>

**Parameter**

<table>
<thead>
<tr>
<th>name</th>
<th>type</th>
<th>species</th>
<th>start val.</th>
<th>end val.</th>
<th>deviat.</th>
<th>unit</th>
<th>comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>kcat</td>
<td>kcat</td>
<td>-</td>
<td>247.2</td>
<td>-</td>
<td>5.1</td>
<td>s^(-1)</td>
<td></td>
</tr>
<tr>
<td>Ks</td>
<td>Km</td>
<td>D-Fructose 6-phosphate</td>
<td>0.307</td>
<td>-</td>
<td>0.021</td>
<td>mM</td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>concentration</td>
<td>D-Fructose 6-phosphate</td>
<td>-</td>
<td>2.0</td>
<td>-</td>
<td>mM</td>
<td></td>
</tr>
<tr>
<td>Et</td>
<td>concentration</td>
<td>Enzyme</td>
<td>6.67E-7</td>
<td>-</td>
<td>-</td>
<td>mM</td>
<td></td>
</tr>
</tbody>
</table>

**Experimental conditions**

<table>
<thead>
<tr>
<th>start value</th>
<th>end value</th>
<th>unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>6.5</td>
<td></td>
</tr>
<tr>
<td>temperature</td>
<td>30.0</td>
<td>°C</td>
</tr>
<tr>
<td>buffer</td>
<td>0.0mM Glucose-6-phosphate 1-dehydrogenase, 100.0mM 2-(N-morpholino)ethanesulfonic acid, 5.0mM magnesium dichloride, 100.0mM potassium chloride, 0.4mM NADP</td>
<td></td>
</tr>
</tbody>
</table>

**Reference**

<table>
<thead>
<tr>
<th>SABIO RK id</th>
<th>title</th>
<th>author</th>
<th>year</th>
<th>direct submission link</th>
</tr>
</thead>
<tbody>
<tr>
<td>2459</td>
<td>Glycolysis</td>
<td>Hanan Messiha and Naglis Malys, Manchester Centre for Integrative Systems Biology (MCISB), UK</td>
<td>2009</td>
<td><a href="http://maureen.mib.manchester.ac.uk:8080/mcisb-web/index.jsp?application=MeMo-RK&amp;directory=Home&amp;experimentId=.14795743_9a81_45eb_ab79_d779a61fa41b">http://maureen.mib.manchester.ac.uk:8080/mcisb-web/index.jsp?application=MeMo-RK&amp;directory=Home&amp;experimentId=.14795743_9a81_45eb_ab79_d779a61fa41b</a></td>
</tr>
</tbody>
</table>
Currently up to **SBML Level 2 Version 4**

- **Reaction Kinetics Warehouse:** Reactions, kinetic equations and parameters (with corresponding units) from different database entries can be exported in one SBML file
- Data is annotated (RDF and SBOterms) according to **MIRIAM**
- Annotations include **SABIO-RK Ids** (reaction and kineticlaw) for tracking
- Optional **normalization of kinetic parameters** to SI base units
- Model can also be exported as human readable PDF → **SBML2LaTeX**
SBML Export

http://www.ra.cs.uni-tuebingen.de/software/SBML2LaTeX/

**Short description:** SBML2LaTeX is a tool to convert files in the System Biology Markup Language (SBML) format into LaTeX files. A convenient web service is available, which allows the user to directly generate various file types from SBML including PDF, TeX, DVI, PS, EPS, GIF, JPG or PNG. SBML2LaTeX can also be downloaded and used locally in batch mode or interactively with its Graphical User Interface or several command line options. The purpose of SBML2LaTeX is to provide a way to read the contents of XML-based SBML files. This is helpful and important for, e.g., error detection, proofreading and model communication.
Currently up to **SBML Level 2 Version 4**

- **Reaction Kinetics Warehouse:** Reactions, kinetic equations and parameters (with corresponding units) from different database entries can be exported in one SBML file.
- Data is fully annotated (RDF and SBOterms) according to **MIRIAM**
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**SBML export of literature data**

**SBML export of direct submission data**
SABIO-RK API Access (Web Services)

- JAW-WS based
- Integration possible in modeling platforms or simulation tools (e.g. CellDesigner)
- Cross-linking with other databases (e.g. ChEBI)
- Data export in SBML supported
SABIO-RK API Access
Integration into Modeling Platforms

http://www.celldesigner.org
Acknowledgements

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Pedro Mendes
Norman W. Paton

http://www.mcisb.org/
If you want to speed up SABIO-RK development

Get Involved

Two software developer positions available in the research group "Scientific Databases and Visualization" (Heidelberg Institute for Theoretical Studies)


To apply, please send CV by 31 October 2010