

Tools for Systems Biology Modeling and Data Exchange: SABIO-RK

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Motivation for an enzyme kinetics database

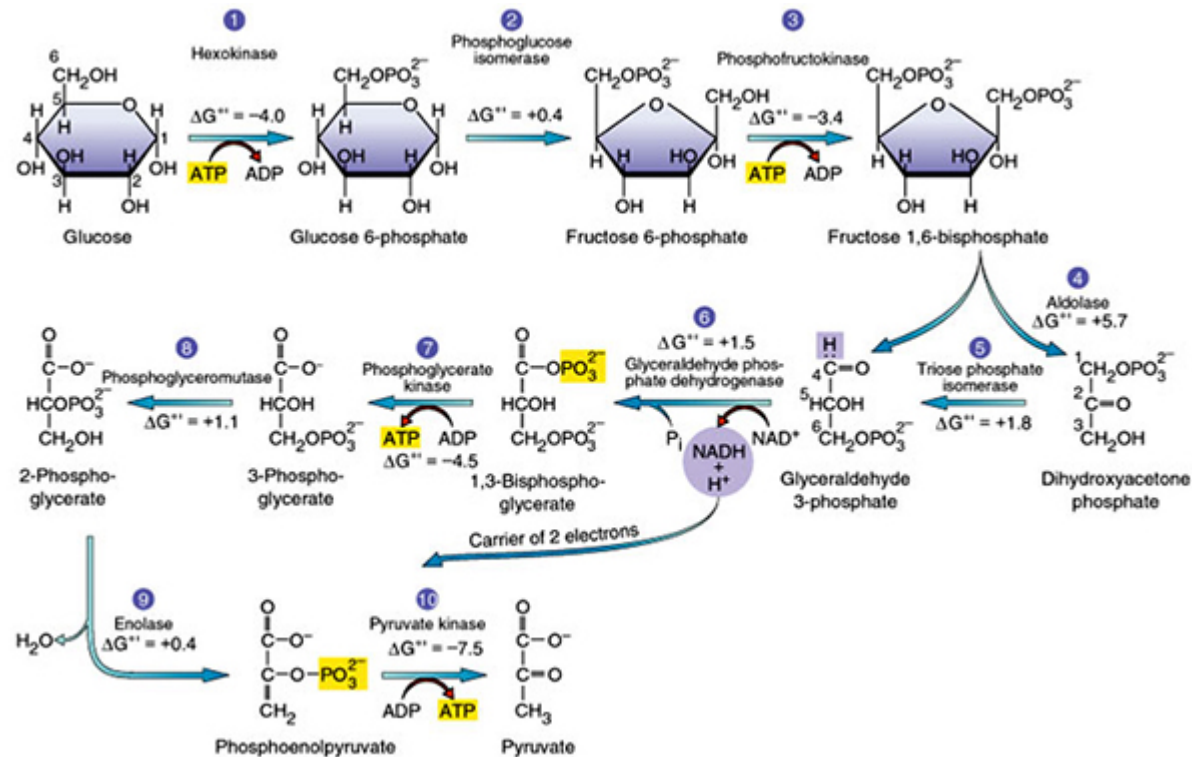
- quantitative data on enzyme kinetics are required e.g. for modellers
- problem: data digging is time consuming / hard to find in literature / partly hidden in figures and tables

=> 2006 start of collecting reaction kinetics data, storage in a public accessible database

<http://sabiork.h-its.org>

Enzyme kinetics data

example: Glycolysis pathway, conversion of Glucose into Pyruvate



Enzyme kinetics data

$$v = \frac{d[P]}{dt} = \frac{V_{\max}[S]}{K_M + [S]}.$$

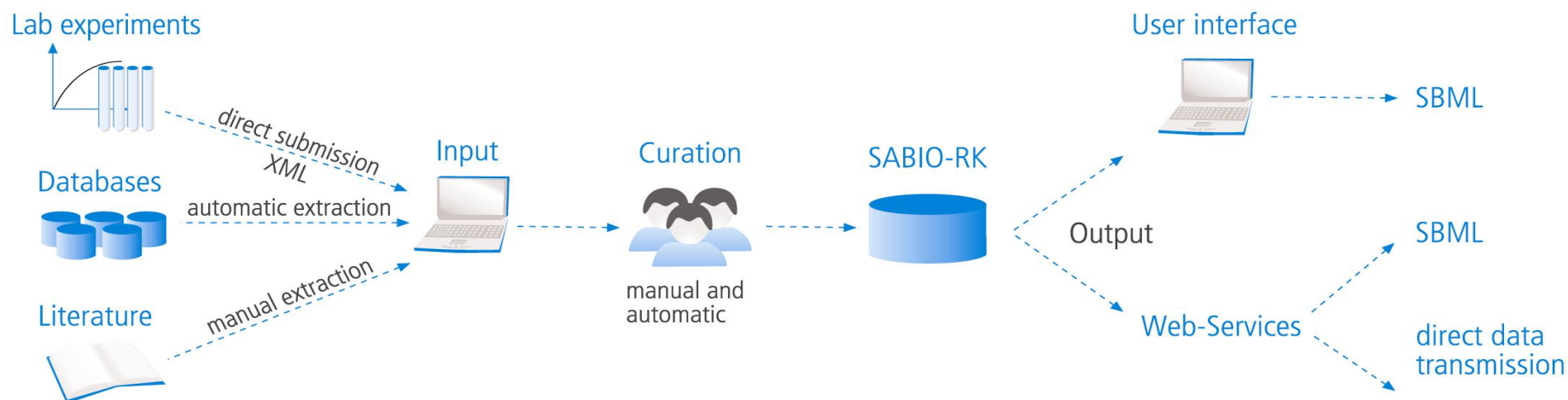
example: Michaelis–Menten kinetics

equation describing the rate of enzymatic reactions

v rate: formation of product P from substrate S

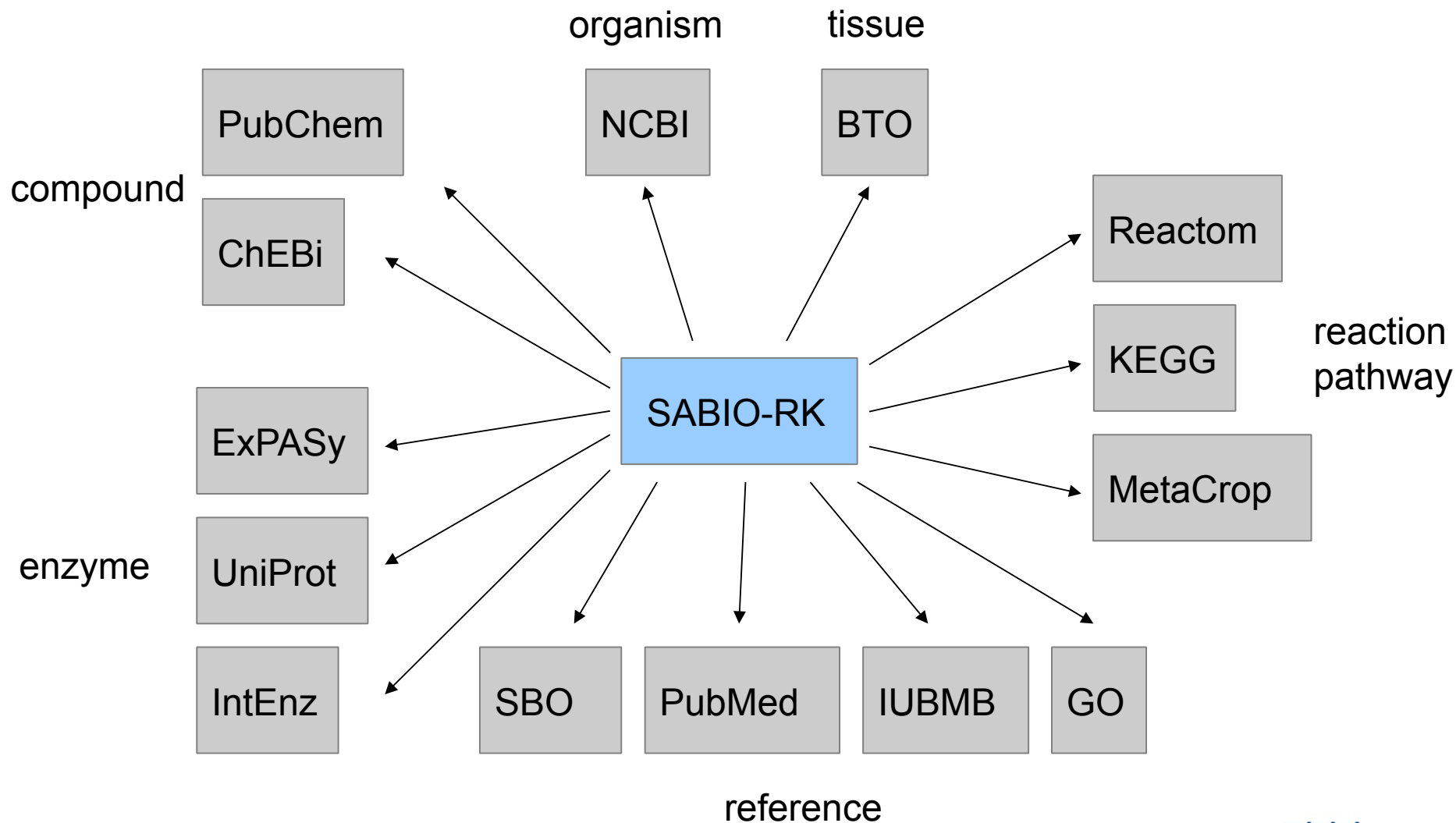
K_M , V_{\max} : specific constants for this reaction

SABIO-RK: data workflow



- kinetic data from literature and from experiments entered in a structured manner
- data are unified, normalized and annotated
- access by a web-based user interface and by web-services


Annotations



SABIO-RK homepage

(System for the Analysis of BIOchemical Pathways - Reaction Kinetics)

<http://sabiork.h-its.org>




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Welcome!

SABIO-RK is a curated database that contains information about biochemical reactions, their kinetic rate equations with parameters and experimental conditions.




SABIO-RK database search

News

[STRENDAB data in SABIO-RK](#)
03-23-2018
Integration of **STRENDAB** data according to the "Standards for Reporting Enzymology Data" [more>>](#)

[SABIO-RK in de.NBI course](#)
01-31-2018
Tools for systems biology modeling and data management in Magdeburg, Germany [more>>](#)



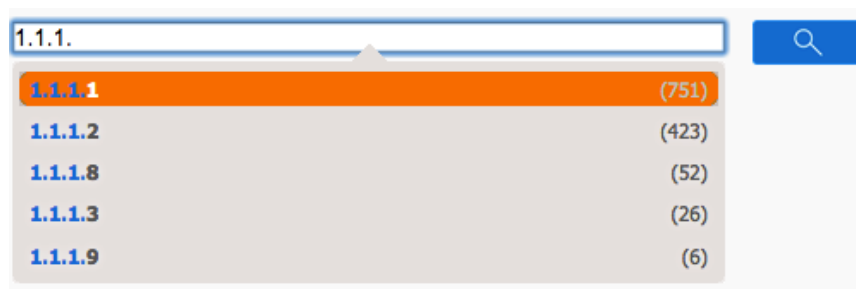
[New SABIO-RK](#)
11-06-2017
[more>>](#)

[More export formats supported](#)
10-12-2017
[more>>](#)



Public search interface

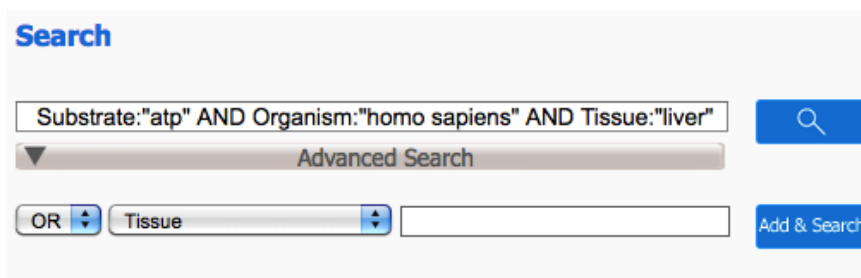
simple free-text search, eg EC number



A screenshot of a search interface. At the top, there is a text input field containing "1.1.1." and a blue search button with a magnifying glass icon. Below the input field, a dropdown menu is open, showing a list of EC numbers and their corresponding counts in parentheses. The first item, "1.1.1.1", is highlighted in orange and has a count of "(751)". The other items are "1.1.1.2" (423), "1.1.1.8" (52), "1.1.1.3" (26), and "1.1.1.9" (6).

| EC Number | Count |
|-----------|-------|
| 1.1.1.1 | (751) |
| 1.1.1.2 | (423) |
| 1.1.1.8 | (52) |
| 1.1.1.3 | (26) |
| 1.1.1.9 | (6) |

alternatively, many options for detailed search



A screenshot of a more complex search interface. It features a "Search" header in blue. Below it is a text input field containing the query "Substrate:"atp" AND Organism:"homo sapiens" AND Tissue:"liver"". To the right of the input field is a blue search button with a magnifying glass icon. Below the input field is a button labeled "Advanced Search" with a downward arrow. At the bottom, there is a section for adding filters. It starts with an "OR" button, followed by a dropdown menu currently set to "Tissue", and then an empty text input field. To the right of this section is a blue button labeled "Add & Search".

Search results

reaction-centered list of results

| <div>Entry View</div> <div>Reaction View</div> <div>Visual Search</div> | | | | | | | | | | |
|--|---|----------|--------------------------|----------|--------------------------|------------------------------|-----------------------------------|-------------|-----|--------------------------|
| Total number of kinetic law entries found: 1534 <input type="checkbox"/> expand all displayed entries | | | | | | | | | | |
| 1 2 3 4 5 6 7 8 9 10 .. 103 Next | | | | | | | display 15 entries per page | | | |
| Kinetic data | Reaction | Enzyme | | | Tissue | Organism | Parameter (besides concentration) | Environment | | Add to export cart? |
| | | ECNumber | Protein | Variant | | | | °C | pH | |
| ▶ | Glucose + ATP = ADP + Glucose 6-phosphate | 2.7.1.1 | Q6SYC5 ↗ | wildtype | muscle ↗ | Ascaris suum | Km | 30.0 | 7.4 | <input type="checkbox"/> |
| ▶ | ATP + D-Fructose = ADP + D-Fructose 6-phosphate | 2.7.1.1 | Q6SYC5 ↗ | wildtype | muscle ↗ | Ascaris suum | Km | 30.0 | 7.4 | <input type="checkbox"/> |
| ▶ | Glucose + ATP = ADP + Glucose 6-phosphate | 2.7.1.1 | Q6SYC5 ↗ | wildtype | muscle ↗ | Ascaris suum | Ki | 30.0 | 7.5 | <input type="checkbox"/> |
| ▶ | Glucose + ATP = ADP + Glucose 6-phosphate | 2.7.1.1 | Q6SYC5 ↗ | wildtype | muscle ↗ | Ascaris suum | Ki | 30.0 | 7.5 | <input type="checkbox"/> |
| ▶ | Glucose + ATP = ADP + Glucose 6-phosphate | 2.7.1.1 | Q6SYC5 ↗ | wildtype | muscle ↗ | Ascaris suum | Ki | 30.0 | 7.5 | <input type="checkbox"/> |

Stored data I

| Kinetic data | Reaction | Enzyme | | | Tissue | Organism | Parameter (besides concentration) |
|--------------|---|----------|--------------------------|----------|--------------------------|--------------|-----------------------------------|
| | | ECNumber | Protein | Variant | | | |
| ▼ | Glucose + ATP = ADP + Glucose 6-phosphate | 2.7.1.1 | Q6SYC5 ↗ | wildtype | muscle ↗ | Ascaris suum | Km |

Entry ID: 10020

General information

| | |
|-------------------|--|
| Organism | Ascaris suum |
| Tissue | muscle ↗ |
| EC Class | 2.7.1.1 |
| SABIO reaction id | 6915 |
| Variant | wildtype |
| Experiment Type | in vitro |
| Pathways | Glycolysis classical Glycolysis/Gluconeogenesis |
| Event Description | - |

Substrates

| name | location | comment |
|-------------------------|----------|---------|
| Glucose | - | - |
| ATP | - | - |

Products

| name | location | comment |
|-------------------------------------|----------|---------|
| Glucose 6-phosphate | - | - |
| ADP | - | - |

Modifiers

| name | location | effect | comment | protein complex |
|--------------------|----------|-------------------|---------|---------------------------|
| hexokinase(Enzyme) | - | Modifier-Catalyst | - | Q6SYC5 ↗; |

Enzyme (protein data)

| | UniProtKB_AC | name | mol. weight (kDa) | deviation (kDa) |
|---------|--------------|------|-------------------|-----------------|
| subunit | Q6SYC5 | - | - | - |
| complex | - | - | 100.0 | - |

Stored data II

| name | location | effect | comment | protein complex |
|--------------------|----------|-------------------|---------|---------------------------|
| hexokinase(Enzyme) | - | Modifier-Catalyst | - | Q6SYC5 ↗; |

Enzyme (protein data)

| | UniProtKB_AC | name | mol. weight (kDa) | deviation (kDa) |
|---------|--------------|------|-------------------|-----------------|
| subunit | Q6SYC5 | - | - | - |
| complex | - | - | 100.0 | - |

Kinetic Law

| type | formula | annotation |
|------|---------|------------|
| - | - | - |

Parameter

| name | type | species | start val. | end val. | deviat. | unit | comment |
|------|---------------------------------|---------|------------|----------|---------|------|---------|
| B | concentration ↗ | Glucose | 0.0 | 50.0 | - | mM | - |
| A | concentration ↗ | ATP | 0.0 | 4.0 | - | mM | - |
| Kma | Km ↗ | ATP | 0.22 | - | - | mM | - |
| Kmb | Km ↗ | Glucose | 4.7 | - | - | mM | - |

Experimental conditions

| | start value | end value | unit |
|-------------|---|-----------|------|
| temperature | 30.0 | - | °C |
| pH | 7.4 | - | - |
| buffer | 50 mM Tris, 0.75 mM NADP, 8 mM MgCl ₂ , 0.5 U/ml Glucose 6-phosphate dehydrogenase | | |
| comment | - | | |

Reference

| title | author | year | journal | volume | pages | PubMed |
|--|-----------------------|------|----------------------|--------|-------|---------------------------|
| Ascaris suum hexokinase: purification and possible function in compartmentation of glucose 6-phosphate in muscle | Supowit SC, Harris BG | 1976 | Biochim Biophys Acta | 422 | 48-59 | 1247596 ↗ |

RESTful web-services

programmatic search using RESTful web services

Example URL:

[http://sabiork.h-its.org/sabioRestWebServices/searchKineticLaws/sbml?q=Tissue:"spleen" AND Organism:"Homo sapiens"](http://sabiork.h-its.org/sabioRestWebServices/searchKineticLaws/sbml?q=Tissue:)

Data export formats

- manual search, export of result set:

- SBML format

- PDF

- XML

- Tables (Excel)

- Matlab, Octave,...



- programatic search using RESTful web services:

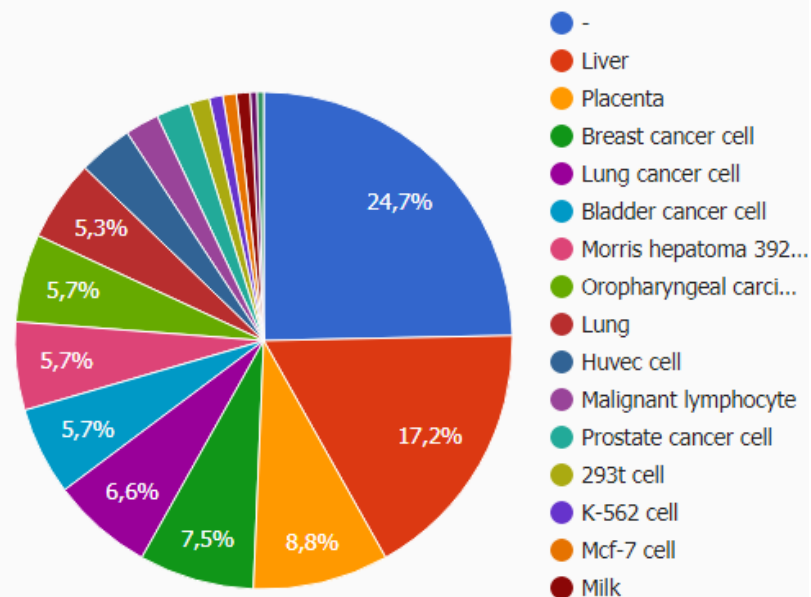
- SBML format

- TSV (Excel)

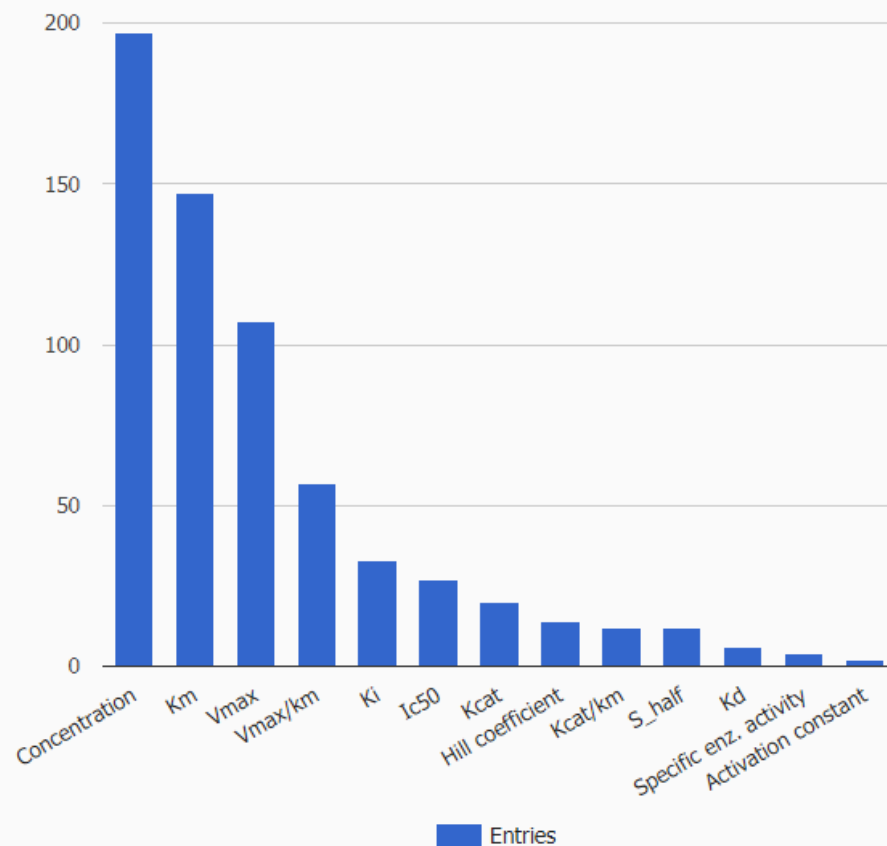
Visual search interface

tissue and parameter distribution for search term 'cancer'

Tissues



Parameter Types



Curation requests as service

SABIO-RK Curation Service

To improve the SABIO-RK database content and to better match user requirements, we encourage you to send us curation requests.

These requests can be either e.g. PubMed identifiers or a more general request for kinetic data associated e.g. with a particular biochemical pathway, organism or tissue. Currently, this service is still provided without any fee. In case of questions don't hesitate to send us an email. [Contact](#)

[Request for SABIO-RK curation service](#)

Public Curation List

| Topic | Priority | Status | Client Name | Client Address | Request Date | Completed Date | Publ. | Kin. Param. |
|---|----------|---------|-------------|----------------|--------------|----------------|-------|-------------|
| Mycoplasma | medium | pending | - | - | 21-08-2017 | | 37 | |
| Salmo salar, especially fatty acid metabolism | medium | public | - | - | 15-04-2017 | | 10 | |

- users may request for retrieval and storage of kinetic data in SABIO-RK (from literature and exp. data)
- part of the de.NBI initiative (German network supporting bioinformatics infrastructure)
- currently this service is still free of charge

Task I

- search for 'author: Kouril'

Search

▼ Advanced Search

AND Author kou

Add & Search

koukouritaki sb, poch mt,
henderson mc, siddens lk,
krueger sk, vandyke je,
williams de, pajewski nm,
wang t, hines rn (14)

kouril t, esser d, kort j,
westerhoff hv, siebers b,
snoep jl (4)

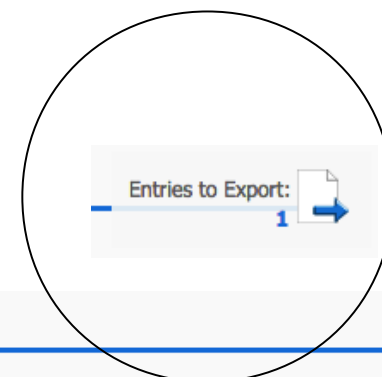
Task I

- search for 'author: Kouril'
- select 'add to export cart'
- select 'entries to export'

| <div>Entry View</div> <div>Reaction View</div> <div>Visual Search (beta)</div> | | | | | | | | | | |
|---|---|----------|--------------------------|----------|--------|---|-----------------------------------|-------------|-----|--------------------------|
| Total number of kinetic law entries found: 4 <input type="checkbox"/> expand all displayed entries <div>display 15 entries per page</div> | | | | | | | | | | |
| Kinetic data | Reaction | Enzyme | | | Tissue | Organism | Parameter (besides concentration) | Environment | | Add to export cart? |
| | | ECNumber | Protein | Variant | | | | °C | pH | |
| ▶ | D-Fructose 1,6-bisphosphate = D-Glyceraldehyde 3-phosphate + Glycerone phosphate | 4.1.2.13 | Q980K6 ↗ | wildtype | - | Sulfolobus solfataricus | Km Vmax | 70.0 | 6.5 | <input type="checkbox"/> |
| ▶ | D-Glyceraldehyde 3-phosphate = Glycerone phosphate | 5.3.1.1 | Q97VM8 ↗ | wildtype | - | Sulfolobus solfataricus | Ki Km Vmax | 70.0 | 6.5 | <input type="checkbox"/> |
| ▶ | ATP + 3-Phospho-D-glycerate = ADP + 3-Phospho-D-glyceroyl phosphate | 2.7.2.3 | P50317 ↗ | wildtype | - | Sulfolobus solfataricus | Ki Km Vmax | 70.0 | 6.5 | <input type="checkbox"/> |
| ▶ | H+ + 3-Phospho-D-glyceroyl phosphate + NADPH = D-Glyceraldehyde 3-phosphate + Phosphate + NADP+ | 1.2.1.13 | P39460 ↗ | wildtype | - | Sulfolobus solfataricus | Hill coefficient Km Vmax | 70.0 | 6.5 | <input type="checkbox"/> |
| <div>display 15 entries per page</div> | | | | | | | | | | |

Task I

- search for 'author: Kouril'
- select 'add to export cart'
- select 'entries to export'



| <div> <div>Entry View</div> <div>Reaction View</div> <div>Visual Search (beta)</div> </div> | | | | | | | | | | |
|---|---|----------|--------------------------|----------|--------|---|-----------------------------------|-------------|-----|--------------------------|
| Total number of kinetic law entries found: 4 <input type="checkbox"/> expand all displayed entries <div>display 15 entries per page</div> | | | | | | | | | | |
| Kinetic data | Reaction | Enzyme | | | Tissue | Organism | Parameter (besides concentration) | Environment | | Add to export cart? |
| | | ECNumber | Protein | Variant | | | | °C | pH | |
| ▶ | D-Fructose 1,6-bisphosphate = D-Glyceraldehyde 3-phosphate + Glycerone phosphate | 4.1.2.13 | Q980K6 ↗ | wildtype | - | Sulfolobus solfataricus | Km Vmax | 70.0 | 6.5 | <input type="checkbox"/> |
| ▶ | D-Glyceraldehyde 3-phosphate = Glycerone phosphate | 5.3.1.1 | Q97VM8 ↗ | wildtype | - | Sulfolobus solfataricus | Ki Km Vmax | 70.0 | 6.5 | <input type="checkbox"/> |
| ▶ | ATP + 3-Phospho-D-glycerate = ADP + 3-Phospho-D-glyceroyl phosphate | 2.7.2.3 | P50317 ↗ | wildtype | - | Sulfolobus solfataricus | Ki Km Vmax | 70.0 | 6.5 | <input type="checkbox"/> |
| ▶ | H+ + 3-Phospho-D-glyceroyl phosphate + NADPH = D-Glyceraldehyde 3-phosphate + Phosphate + NADP+ | 1.2.1.13 | P39460 ↗ | wildtype | - | Sulfolobus solfataricus | Hill coefficient Km Vmax | 70.0 | 6.5 | <input type="checkbox"/> |
| <div>display 15 entries per page</div> | | | | | | | | | | |

Task II

- search for 'author: Kouril'
- select all 4 entries for export

Selected kinetics data

| Entry ID | Selected Reaction | Organism | Tissue | Kinetic law type | View details | Remove entry (Select all: <input type="checkbox"/>) |
|----------|---|-------------------------|--------|---|----------------------|--|
| 51245 | ATP + 3-Phospho-D-glycerate <-> ADP + 3-Phospho-D-glyceroyl phosphate | Sulfolobus solfataricus | - | Ordered Bi Bi | view | <input type="checkbox"/> |
| 51246 | H+ + NADPH + 3-Phospho-D-glyceroyl phosphate <-> D-Glyceraldehyde 3-phosphate + Phosphate + NADP+ | Sulfolobus solfataricus | - | Reversible Hill Cooperativity | view | <input type="checkbox"/> |
| 51248 | D-Fructose 1,6-bisphosphate <-> D-Glyceraldehyde 3-phosphate + Glycerone phosphate | Sulfolobus solfataricus | - | Random ordered | view | <input type="checkbox"/> |
| 51247 | D-Glyceraldehyde 3-phosphate <-> Glycerone phosphate | Sulfolobus solfataricus | - | Reversible Michaelis-Menten with competitive inhibitors | view | <input type="checkbox"/> |

remove selected Reactions

Back to Results

Write spreadsheet

Write SBML

Write BioPAX



Task III

- search for 'author: Kouril'
- select all 4 entries for export
- export in SBML format / download on disk

Save Model

Enter name of model:

Export parameters normalized to SI base units ☐

Choose the annotation schema *:

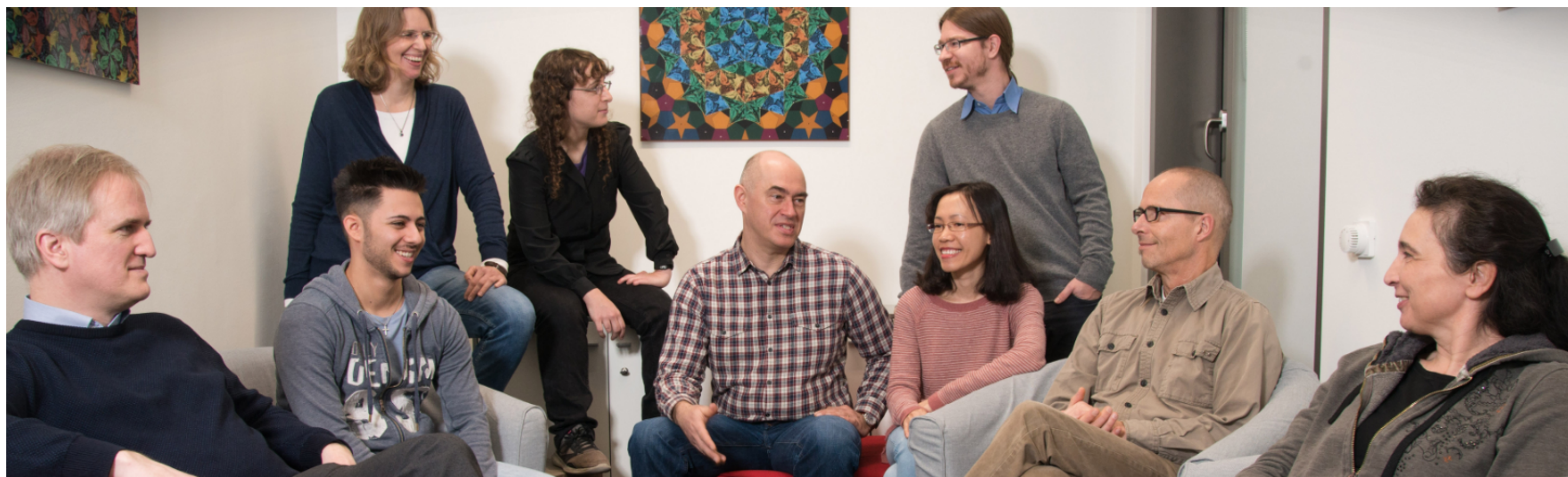
Save Model on Disk as SBML

Save Model on Disk as PDF

Task IV

- search for 'author: Kouril'
- select all 4 entries for export
- export in SBML format / download on disk
- **import into simulation tool like Copasi, CellDesigner, JWS online, ...**

HITS SDBV group @ Heidelberg, Germany



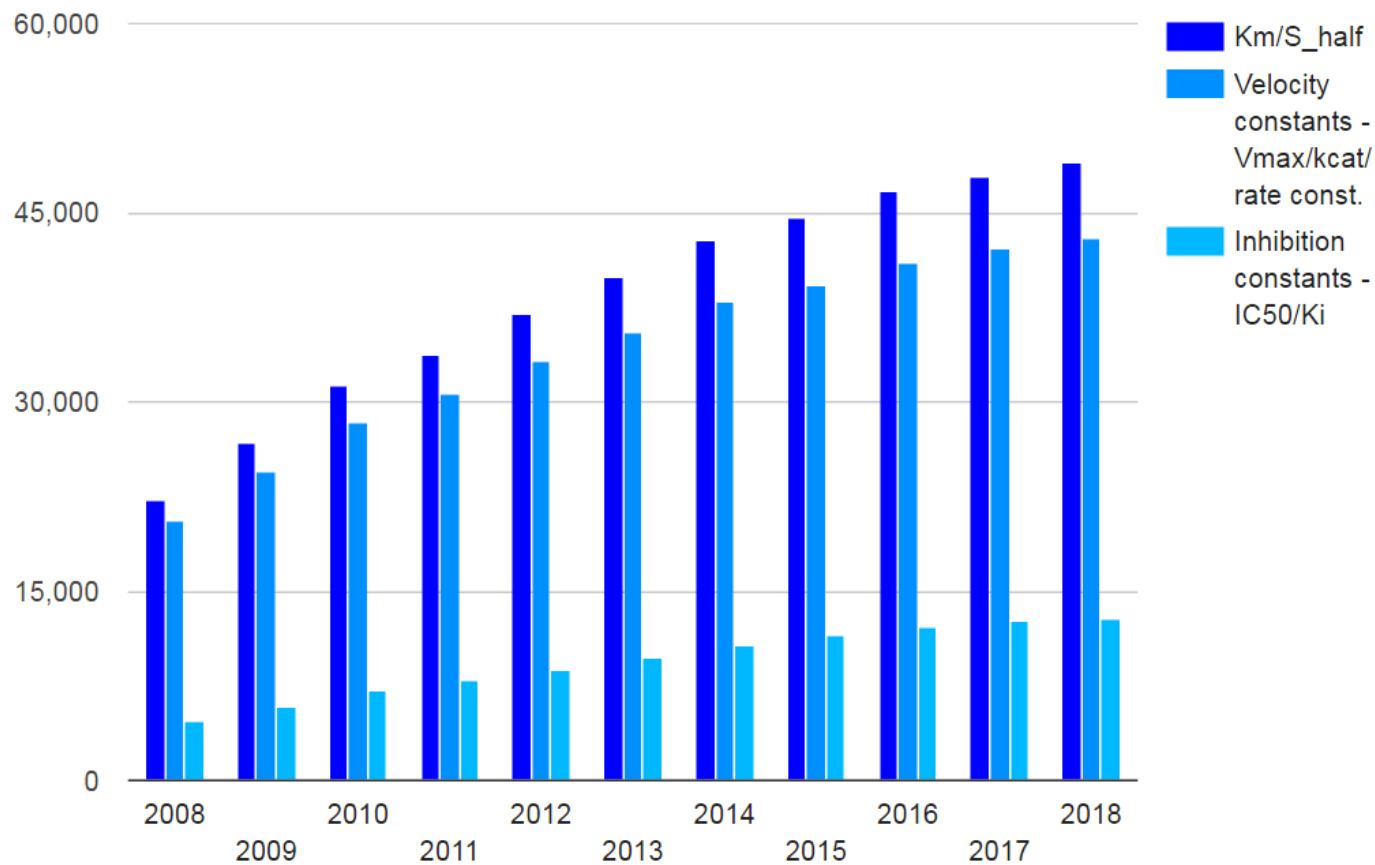
Thank you for your attention!

Data extraction from literature

- kinetics data from literature are manually entered via a web form => standardization
- the data are annotated, e.g. EC number and UniProtKB ID are added => searchable
- further automatic annotations performed: KEGG, PubChem,... => searchable
- additional advantage: many data are also found in figures / figure legends and tables => become searchable

Statistics

Amount of selected kinetic parameters grouped as Km/S_half, velocity constants, and inhibition constants



kinetic parameters March 2018: ~ 128.000