

# Standardization in distributed research networks: The Virtual Liver Experience

Martin Golebiewski & the SDBV team  
Heidelberg Institute for Theoretical Studies (HITS)  
Heidelberg, Germany

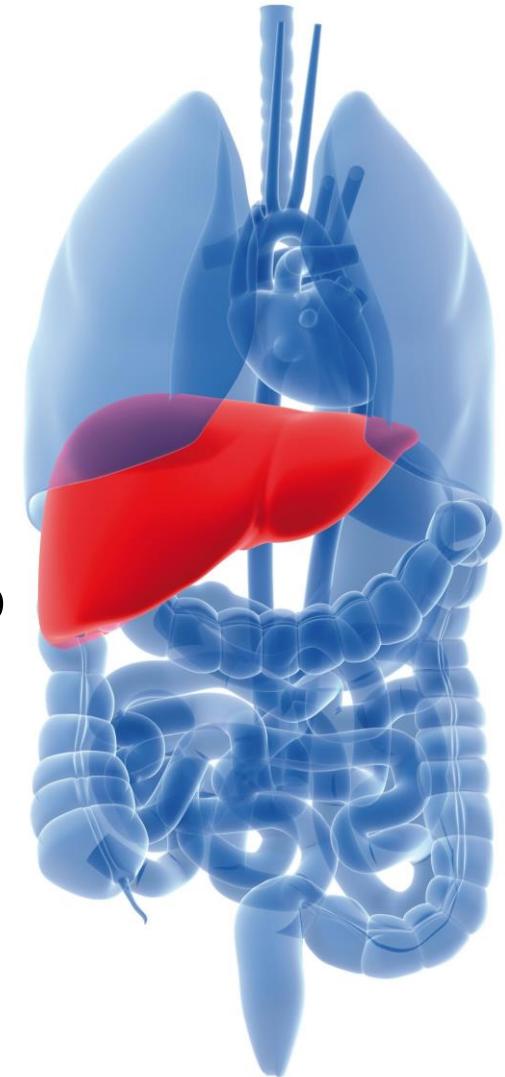
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# The Virtual Liver Mission

To create

- Dynamic mathematical model that represents, rather than fully replicates human liver physiology, morphology and function
- A model that integrates quantitative data from all scales, from sub-cellular levels to the whole organ (and beyond)
- A model that has a specific focus on applications in medicine



# The Virtual Liver Objectives

**Cellular level → Whole organ**

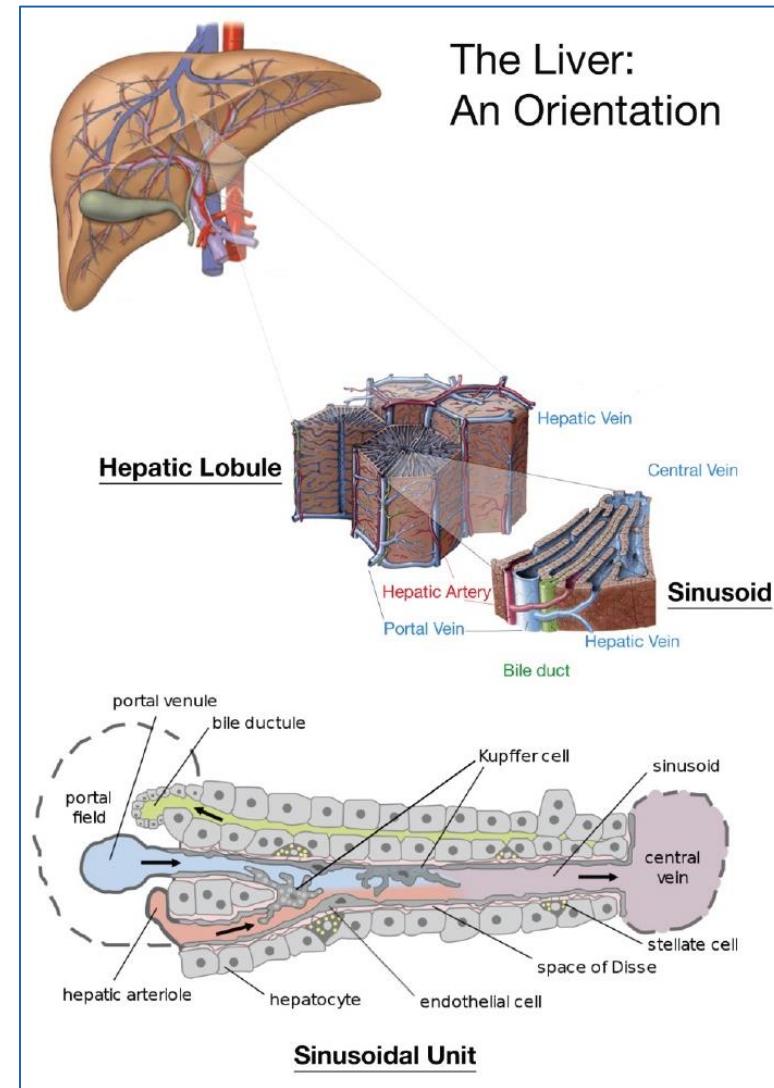
**True multi-scale representation  
of liver physiology**

- Modular
- Flexible
- Modifiable

**Deliver novel tools & processes**

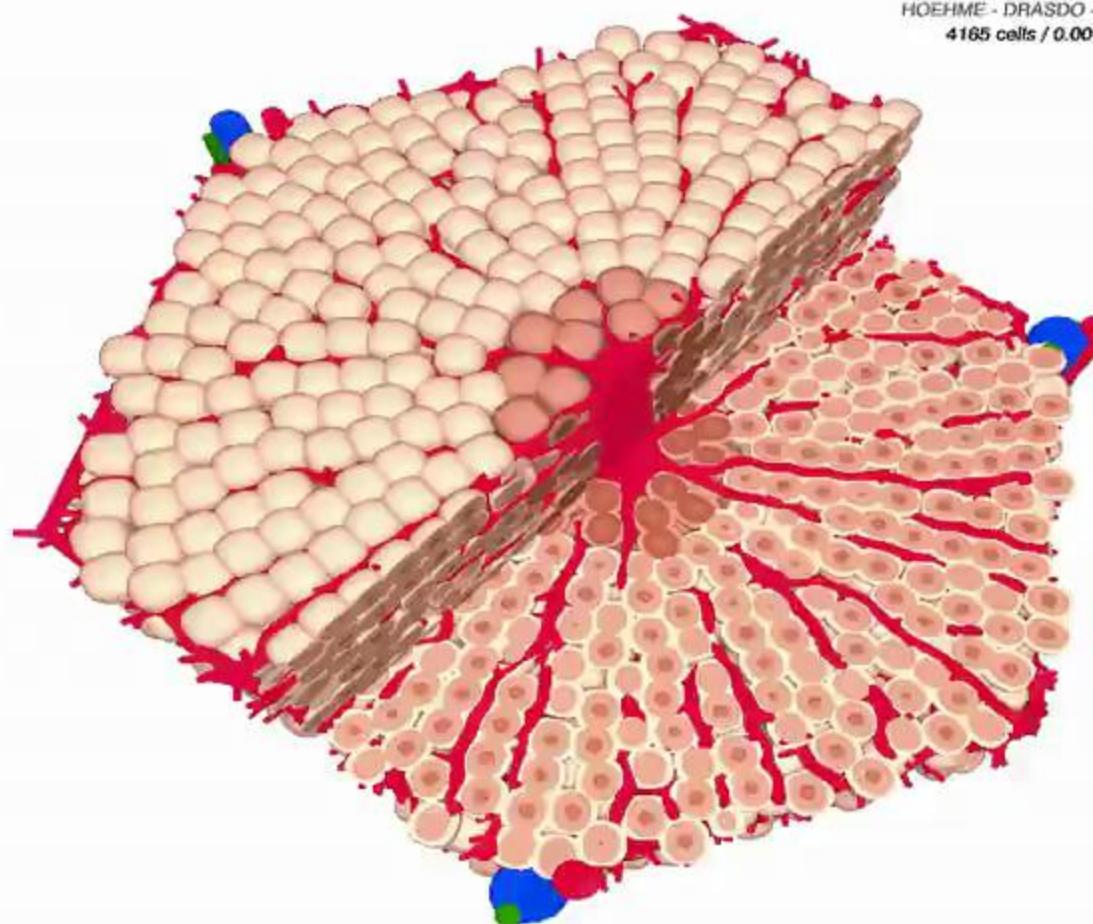
**Impact on medicine:**

- Non alcoholic fatty liver disease
- Regeneration
- Inflammation

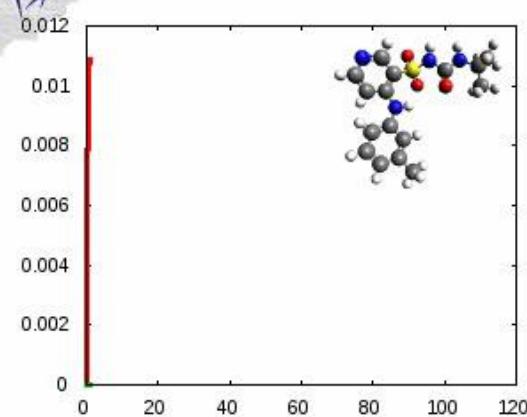
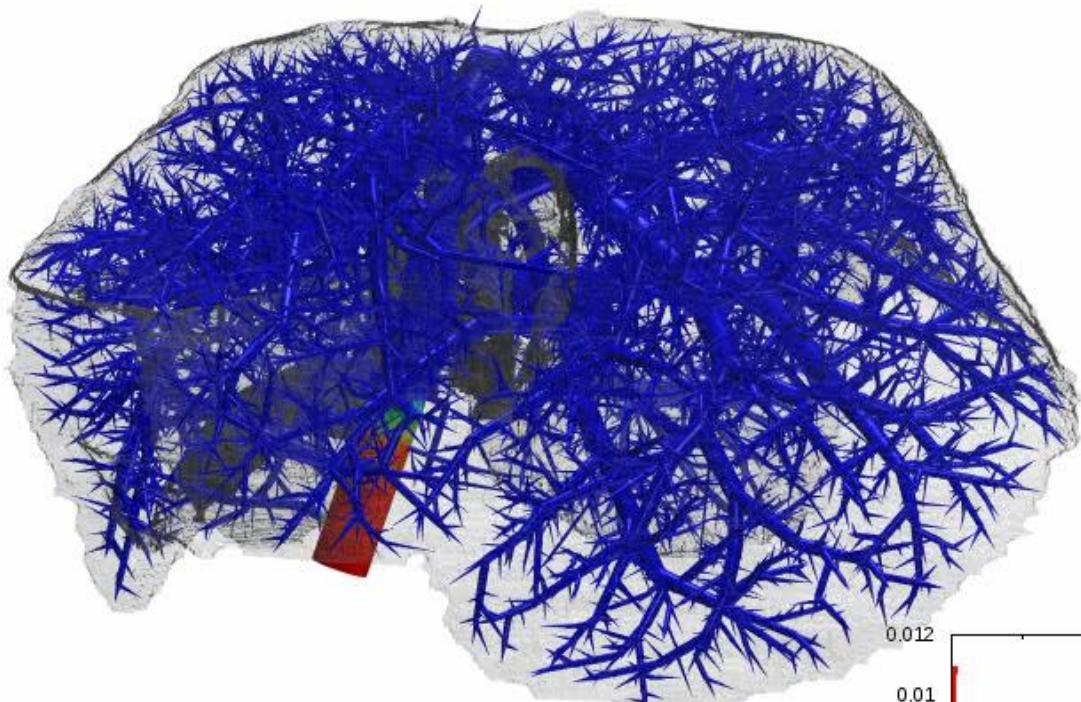


# Modelling Lobular Regeneration

Heidelberg Institute for  
Theoretical Studies



# Modelling Drug Distribution in the Liver



 **Fraunhofer**  
MEVIS



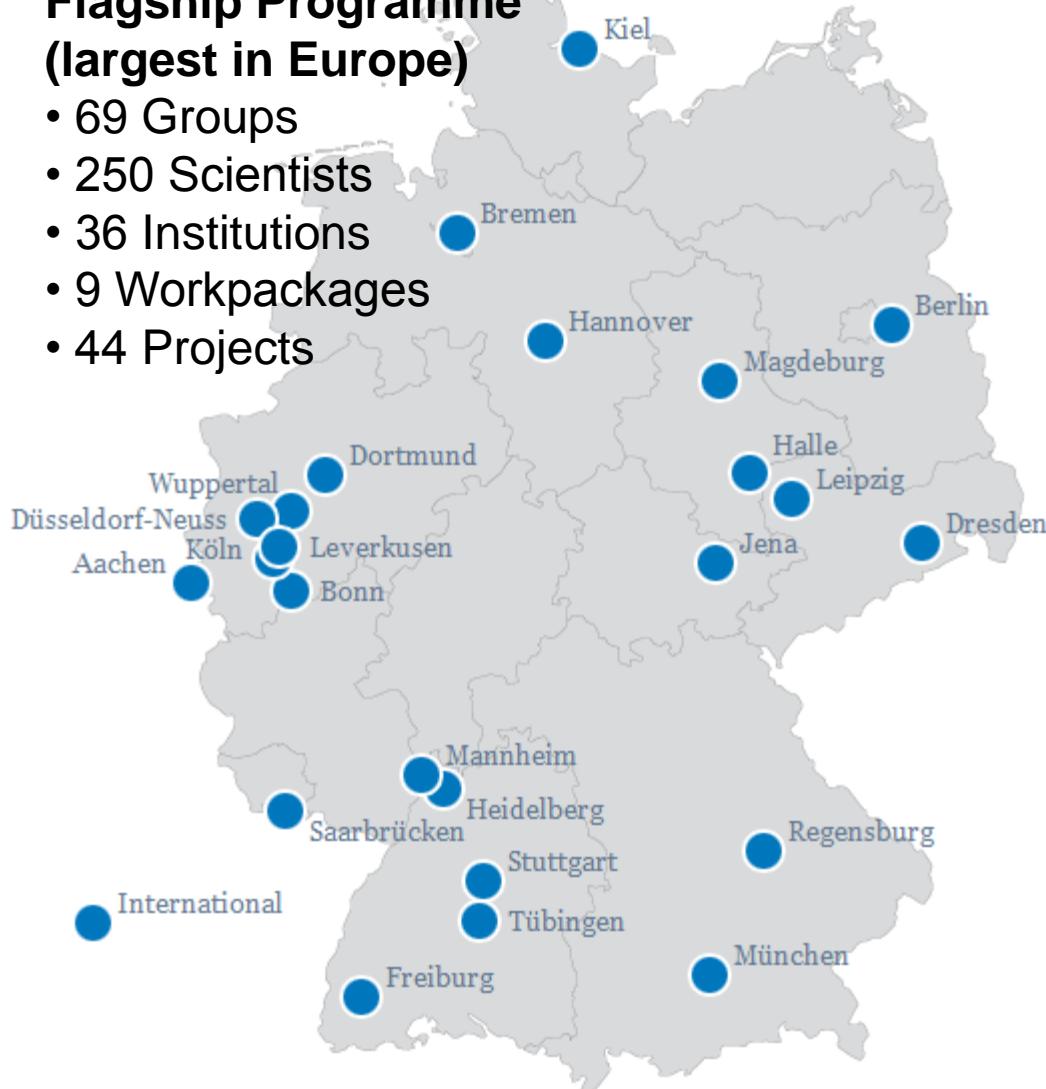
Bayer Technology Services



# Virtual Liver Network

## German Systems Biology Flagship Programme (largest in Europe)

- 69 Groups
- 250 Scientists
- 36 Institutions
- 9 Workpackages
- 44 Projects



## Experimentalists, Modelers, Clinicians and Industry

### Different scales:

#### The Liver Cell

- Metabolism
- Signalling
- Functions

#### Beyond the Cell:

- Intercellular
- Liver lobule
- Whole organ

#### Integration and Translation:

- Model integration
- Data management
- Clinical translation

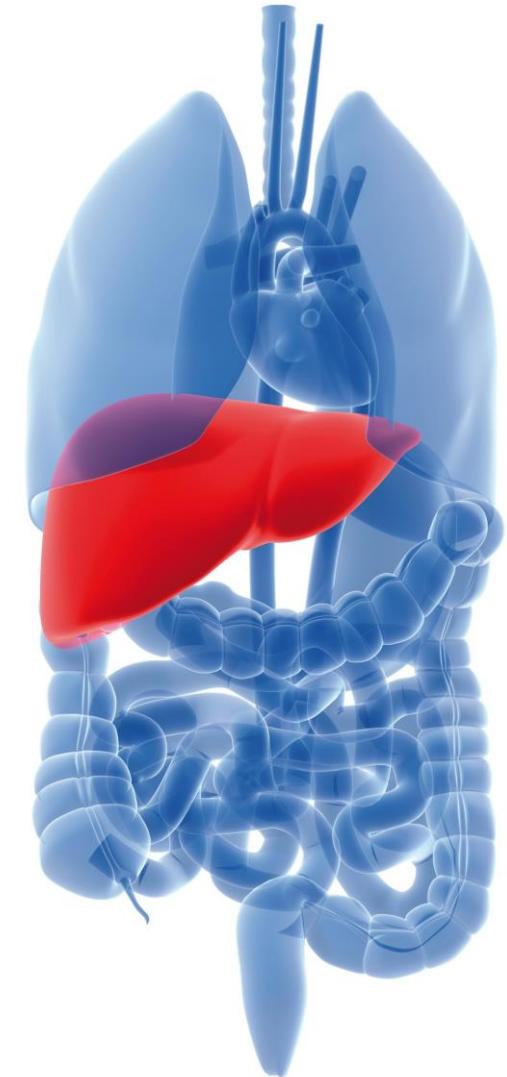
# The Data Management Challenges

## Technical: Standardisation

- Protocols (SOPs)
- Data formats
- Model formats
- Metadata for data and models
- Interfaces
- Tools for integration -> **multi-scale modelling**

## Social: Communication

- Complex project organisation structure
- Geographically dispersed
- Diverse scientific background
- Managing expectations
- Benefits for the users?
- Internal communication
- Outreach



Most common:

**MATLAB code**

**Problems:**

- Reusability
- Model exchange
- Model integration

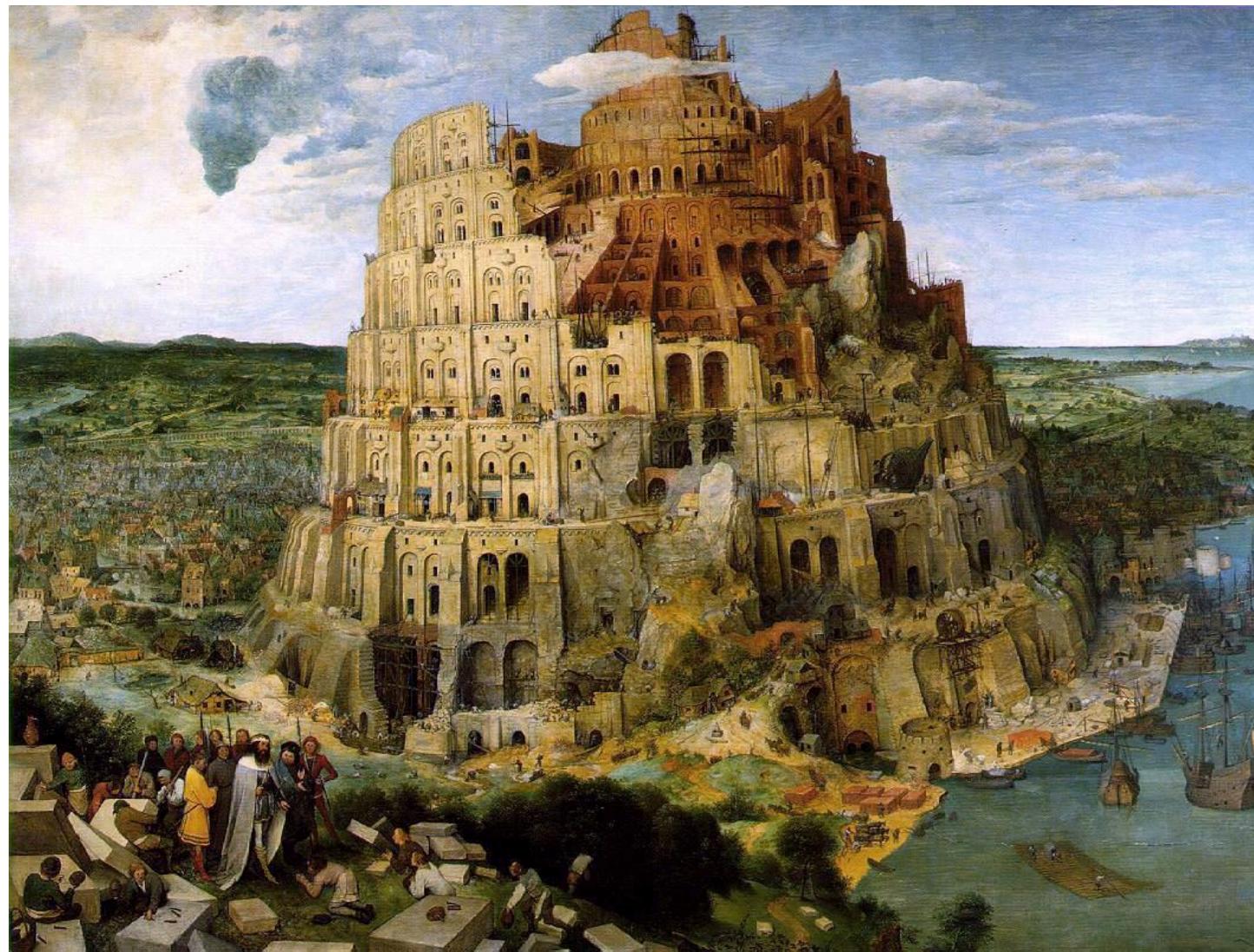
## Metadata: Data describing data or models

- Context & Environment
- Entities & Elements

→ SEMANTICS

Helps to connect the dots (data, models...)

# Metadata: What Are You Talking About?



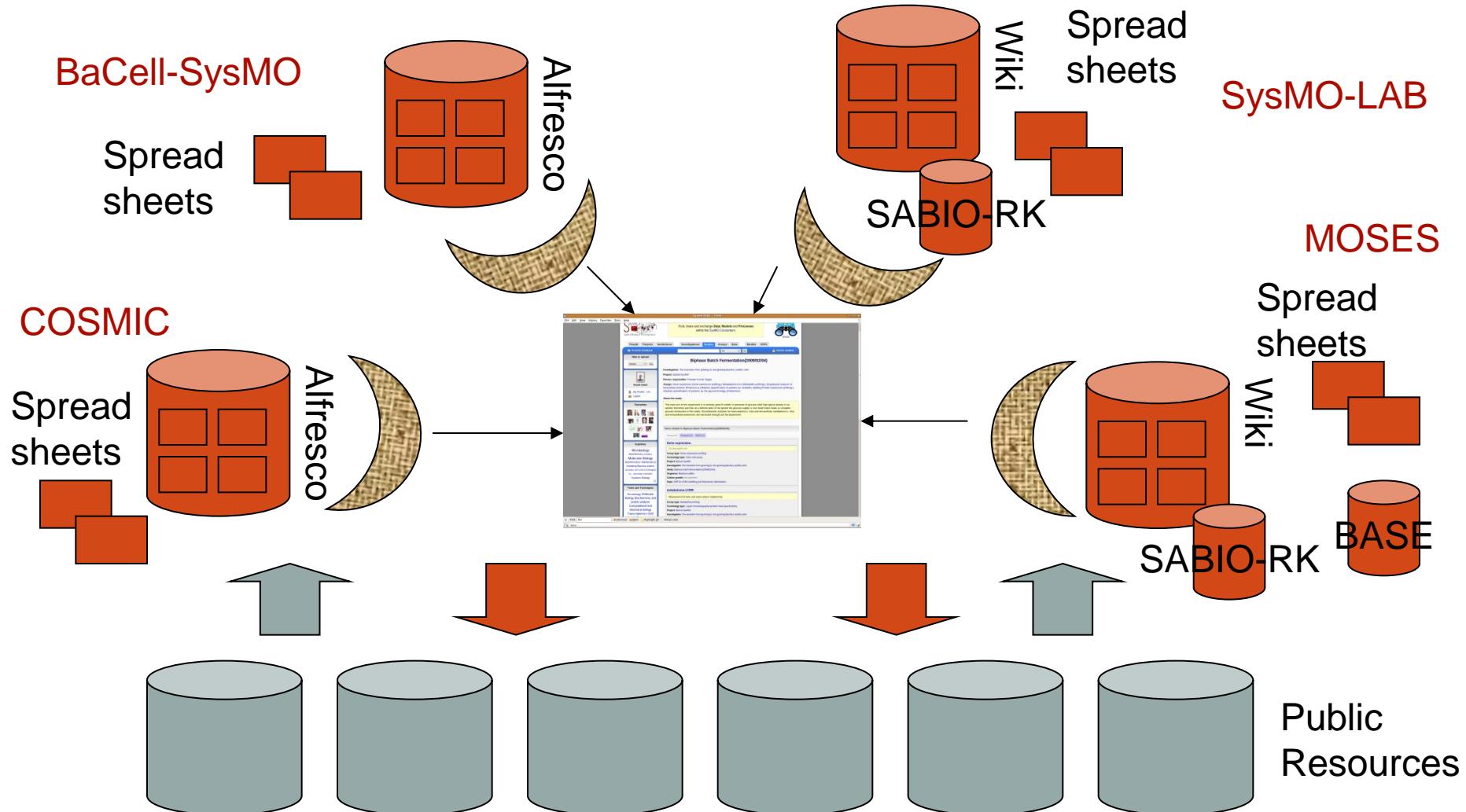
- Interfaces between data, workflows and models
- Interfaces between modules of a model
- Interfaces between different models
- Interfaces between biological scales

**What** information should transmitted?  
(entities, parameters, metadata, ...)

**Which format** is suitable for the transmission?

**How** should the information be integrated?

# SEEK: Systems Biology Data Hub



# SEEK Metadata: Studies & Assays

## Determining the macrophage-derived input on hepatocytes during the LPS-induced inflammatory response

Created at: 26/10/2012 @ 11:27:39 Last updated: 29/10/2012 @ 12:46:32

**Projects:** B1.1: Differential communication of wound healing and hepatotoxic macrophages with the impact of macrophages, B1.2: Reciprocal effect of cell-cell communication with the impact of macrophages, B: Communication of Hepatocytes and Non-Parenchymal Liver Cells, LPS and Inflammation

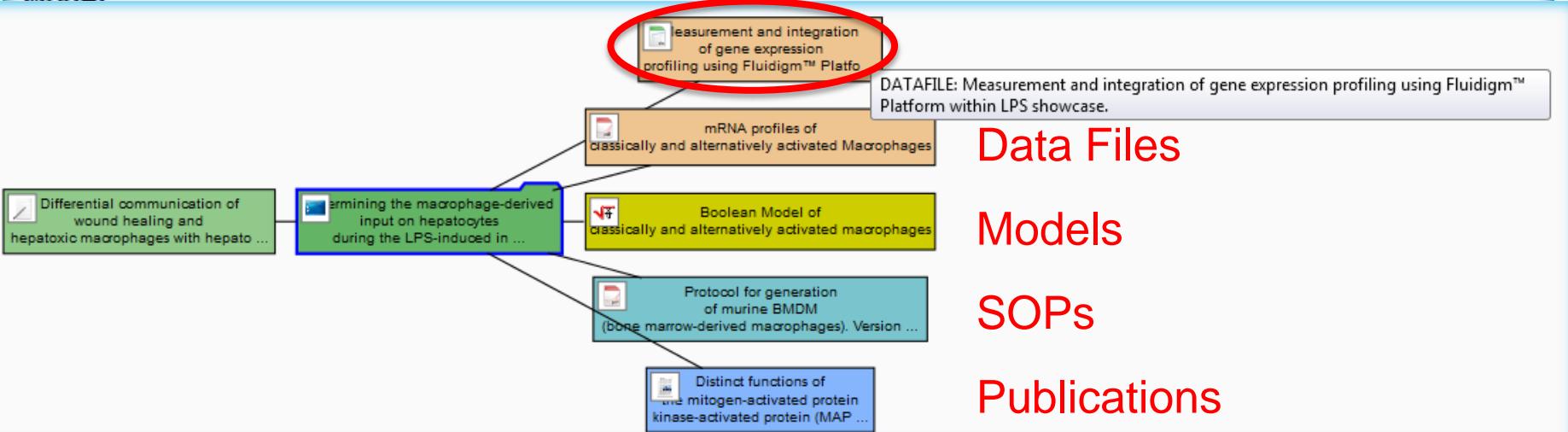
**Investigation:** Intercellular communication of hepatocytes and macrophages (B.1)

**Study:** Differential communication of wound healing and hepatotoxic macrophages with hepatocytes (b.1.1)

**Analysis type:** Gene expression

**Organisms:** Mus musculus : C57/BL6J (wild-type/wild-type)

**Model:**



Items related to Determining the macrophage-derived input on hepatocytes during the LPS-induced inflammatory response.

Projects (5)

Institutions (1) Investigations (1) Studies (1) Data Files (2) Models (1) SOPs (1) Publications (1)

Yellow Pages    Experiments    Biosamples    Assets    Forums    Events    Help

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Announcements

New SEEK version: Improved speed and registration of external links 8 days ago by Martin Golebiewski

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Upload your data to SEEK as email attachment 5 months ago by Martin Golebiewski

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Favourites

Drag an icon here to remember for future reference.

Tags [show all]

CellNetAnalyzer (CNA) data management Flow Cytometry HepatoSys IL-1 IL-6 inflammation Insulin signalling Kinetic Modelling logical modelling metabolism Nuclear receptors ODE primary human hepatocytes ProMoT qPCR Report SAB Meeting Leipzig k.virtual-liver.de/data\_files

Data Models SOPs Publications Presentations

All All Go

Unsubscribe Download Explore Data file

**Measurement and analysis of gene expression profiling using Fluidigm™ Platform within LPS showcase.**

Created at: 24/10/2012 @ 05:45:12   Last used: 29/11/2012 @ 11:46:20   Last updated: 24/10/2012 @ 05:49:16  
 Views: 42   Downloads: 7

**Version 1 (of 1)**

Version created on: 24/10/2012 @ 05:45:13 by: Maria Thomas

**Projects:** B: Communication of Hepatocytes and Non-Parenchymal Liver Cells, Interleukin-6 signalling, Showcase LPS and Inflammation

**File name:** Collection\_Arrays\_Maus.xlsx

**Format:** Spreadsheet

**Description:**

Several high-throughput quantitative Taqman® Fluidigm technology arrays were designed for the simultaneous assessment of 48 transcript-profiles in up to 48 samples. The arrays include the following panels of gene expression assays: 1) main acute phase proteins (designed and purchased by the group of J. Bode); 2) key cytokines/chemokines (designed and purchased by the group of J. Bode); 3) fibrotic genes (designed and purchased by the group of S. Dooley); and 4) important ADME and drug detoxification genes (designed and purchased by the group of U.Zanger). Fluidigm™ platform and dedicated Taqman® arrays represent a powerful advancement for unified high-throughput, high-quality transcriptome analysis of samples generated within the Virtual Liver Network.

 treatment of mouse primary hepatocytes with conditioned medium from mouse bone ma ...

**Creators**

  
[Expand](#)

**Tags**

Fluidigm LPS qRT-PCR

[ Add your tags ]

**Scales**

intercellular, cell



Find, share and exchange **Data, Models and Processes** within the [Virtual Liver Network](#).

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Upload your data to SEEK as email attachment 5 months ago by Martin Golebiowski

New Virtual Liver SEEK with extended functionality 5 months ago by Martin Golebiowski

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**Tags [show all]**

- ADME genes CellNetAnalyzer
- (CNA) data management Flow
- Cytometry HepatoSys IL-6
- Kinetic Modelling logical modelling metabolism Microarray analysis Nuclear receptors ODE
- primary human hepatocytes ProMoT qPCR
- Report SAB Meeting Leipzig 2012
- Show Case Steatosis Meeting
- Student Retreat 2011/Hünfeld VLN

**Assets**

[Data](#) [Models](#) [SOPs](#) [Publications](#) [Presentations](#)

D2 [http://www.ncbi.nlm.nih.gov/nuccore/NM\\_007522](http://www.ncbi.nlm.nih.gov/nuccore/NM_007522)

[List Annotations](#) [Add Annotation](#) [Export Data](#) [Plot Data](#) [Clear Selection](#)

K.Breitkopf (Dooley) M.Hahnel (Bode) U.Albrecht (Bode) M.Thomas (Zanger)

	B	C	D	E
1	NCBI Symbol	Genname	Hyperlink	Acession Number (mRNA)
2	Bad	BCL2-associated agonist of cell death [ Mus musculus ]	<a href="http://www.ncbi.nlm.nih.gov/nucc">http://www.ncbi.nlm.nih.gov/nucc</a>	NM_007522
3	Bax	BCL2-associated X protein [ Mus musculus ]	<a href="http://www.ncbi.nlm.nih.gov/nucc">http://www.ncbi.nlm.nih.gov/nucc</a>	NM_007527
4	Bcl2	BCL2-antagonist/killer 1 [ Mus musculus ]	<a href="http://www.ncbi.nlm.nih.gov/nucc">http://www.ncbi.nlm.nih.gov/nucc</a>	NM_007523
5	Bim	BCL2-like 11 (apoptosis facilitator) [ Mus musculus ]	<a href="http://www.ncbi.nlm.nih.gov/nucc">http://www.ncbi.nlm.nih.gov/nucc</a>	NM_207680
6	Birc5	Mus musculus baculoviral IAP repeat-containing 5 (survivin)	<a href="http://www.ncbi.nlm.nih.gov/nucc">http://www.ncbi.nlm.nih.gov/nucc</a>	NM_009689
7	BMP-9	Bone morphogenetic protein 9 [ Mus musculus ]	<a href="http://www.ncbi.nlm.nih.gov/nucc">http://www.ncbi.nlm.nih.gov/nucc</a>	NM_019506
8	CD133	Prominin-1 [ Mus musculus ]	<a href="http://www.ncbi.nlm.nih.gov/nucc">http://www.ncbi.nlm.nih.gov/nucc</a>	NM_001163583
9	Cdh1	Epithelial cadherin [ Mus musculus ]	<a href="http://www.ncbi.nlm.nih.gov/nucc">http://www.ncbi.nlm.nih.gov/nucc</a>	NM_009864
10	Cdh2	Neural cadherin [ Mus musculus ]	<a href="http://www.ncbi.nlm.nih.gov/nucc">http://www.ncbi.nlm.nih.gov/nucc</a>	NM_007664
11	cholesterol 25-hydroxylase	Mus musculus cholesterol 25-hydroxylase	<a href="http://www.ncbi.nlm.nih.gov/nucc">http://www.ncbi.nlm.nih.gov/nucc</a>	NM_009890
12	Col1a1	collagen, type I, alpha 1	<a href="http://www.ncbi.nlm.nih.gov/nucc">http://www.ncbi.nlm.nih.gov/nucc</a>	NM_007742
13	Col3a1	Mus musculus collagen, type III, alpha 1	<a href="http://www.ncbi.nlm.nih.gov/nucc">http://www.ncbi.nlm.nih.gov/nucc</a>	NM_009930
14	Col4a3	Mus musculus collagen, type IV, alpha 3	<a href="http://www.ncbi.nlm.nih.gov/nucc">http://www.ncbi.nlm.nih.gov/nucc</a>	NM_007734
15	Col6a6	Mus musculus collagen, type VI, alpha 6	<a href="http://www.ncbi.nlm.nih.gov/nucc">http://www.ncbi.nlm.nih.gov/nucc</a>	NM_001102607
16	Col8a1	Mus musculus collagen, type VIII, alpha 1	<a href="http://www.ncbi.nlm.nih.gov/nucc">http://www.ncbi.nlm.nih.gov/nucc</a>	NM_007739
17	Ctgf	connective tissue growth factor [ Mus musculus ]	<a href="http://www.ncbi.nlm.nih.gov/nucc">http://www.ncbi.nlm.nih.gov/nucc</a>	NM_010217
18	Cyp2E1	Cytochrome P450 2E1 [ Mus musculus ]	<a href="http://www.ncbi.nlm.nih.gov/nucc">http://www.ncbi.nlm.nih.gov/nucc</a>	NM_021282
19	Edn1	endothelin-1	<a href="http://www.ncbi.nlm.nih.gov/nucc">http://www.ncbi.nlm.nih.gov/nucc</a>	NM_010104
20	FasL	Fas ligand (TNF superfamily, member 6) [ Mus musculus ]	<a href="http://www.ncbi.nlm.nih.gov/nucc">http://www.ncbi.nlm.nih.gov/nucc</a>	NM_001205243
21	Fn1	fibronectin	<a href="http://www.ncbi.nlm.nih.gov/nucc">http://www.ncbi.nlm.nih.gov/nucc</a>	NM_010233
22	Igf1	insulin-like growth factor 1	<a href="http://www.ncbi.nlm.nih.gov/nucc">http://www.ncbi.nlm.nih.gov/nucc</a>	NM_001111276
23	Lama1	Laminin	<a href="http://www.ncbi.nlm.nih.gov/nucc">http://www.ncbi.nlm.nih.gov/nucc</a>	NM_008480
24	<			

# Minimal reporting standards



Find, share and exchange **Data, Models** and **Processes** within the **Virtual Liver Network**.



Yellow Pages

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Tags [show all]

CellNetAnalyzer (CNA) data management Flow Cytometry HepatoSys IL-1 IL-6 inflammation Insulin signalling Kinetic Modelling logical modelling metabolism

## Minimal Information Reporting Guidelines

Help Index > Minimal Information Reporting Guidelines

Here is a list of standards for data description in different technology fields that are strongly recommended:

**<http://seek.virtual-liver.de/help/minimal-information>**

Cellular Assay

MIACA – Minimum Information About a Cellular Assay

Clinical Data

CDISC – Clinical Data Interchange Standards Consortium

Enzymology

STRENDA – Standards for Reporting Enzymology Data

Flow Cytometry (FACS)

MIFlowCyt – Minimum Information about a Flow Cytometry

Genotyping

MIGen – Minimum Information about a Genotyping Experiment

Immunohistochemistry / In Situ Hybridization

MISFISHIE – Minimum Information Specification For In Situ Hybridization

Metabolomics

CIMR – Core Information for Metabolomics Reporting

Microarrays

MIAME – Minimum Information About a Microarray Experiment

Model Annotation

MIRIAM – Minimal Information Required In the Annotation of Models

HOW STANDARDS PROLIFERATE:  
(SEE: A/C CHARGERS, CHARACTER ENCODINGS, INSTANT MESSAGING, ETC)

SITUATION:  
THERE ARE  
14 COMPETING  
STANDARDS.

14?! RIDICULOUS!  
WE NEED TO DEVELOP  
ONE UNIVERSAL STANDARD  
THAT COVERS EVERYONE'S  
USE CASES.  
YEAH!



SOON:

SITUATION:  
THERE ARE  
15 COMPETING  
STANDARDS.

# SEEK: Models



## Boolean Model of classically and alternatively activated macrophages

Created at: 23/10/2012 @ 12:16:39 Last used: 23/11/2012 @ 12:29:22 Last updated: 26/10/2012 @ 08:32:10  
Views: 17 Downloads: 1

### Version 1 (of 1)

Version created on: 23/10/2012 @ 12:16:40 by: Julia Sanwald

Title: Boolean Model of classically and alternatively activated macrophages

All Files (1 in total):  
CNAMacrophage.zip (Zip file)

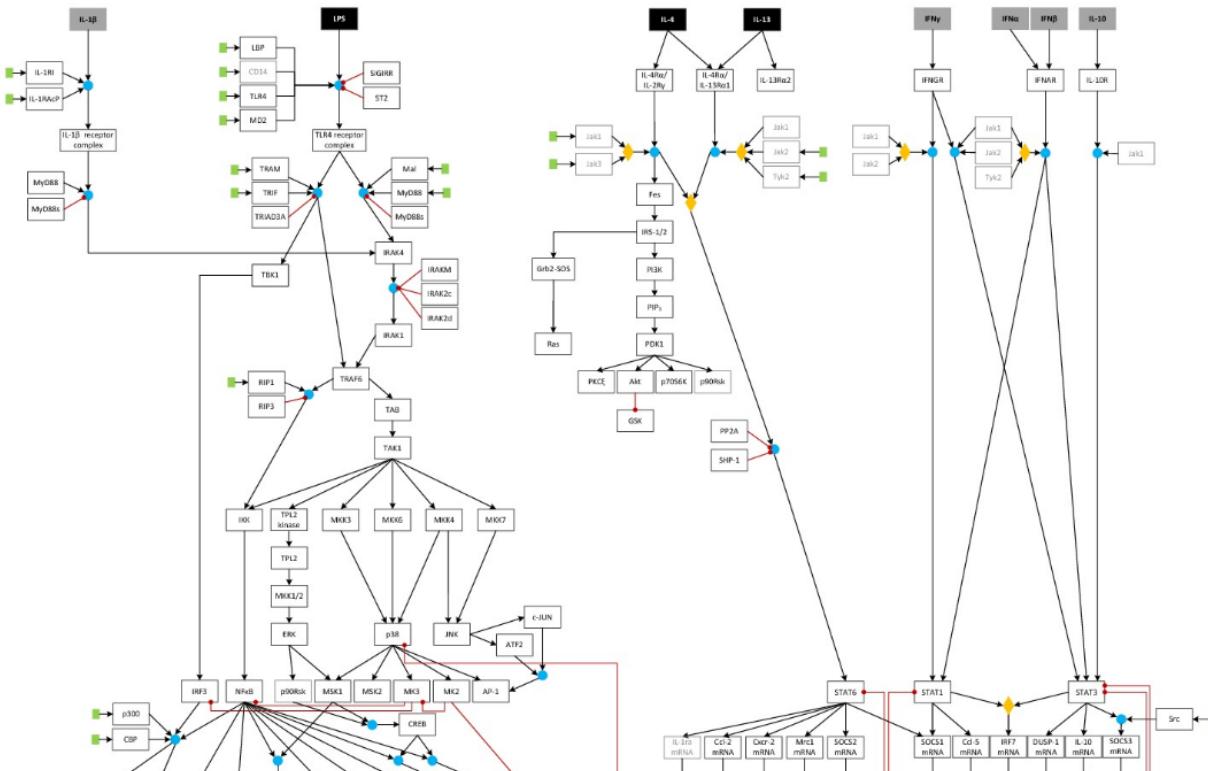
Organism: *Mus musculus*

Model type: Boolean network

Model format: Matlab package

Execution or visualisation environment: CellNetAnalyzer

Model visualization([click it to zoom](#))



### Creators



### Tags

This item has not yet been tagged.

### Add your tags

### Scales

intercellular,  
cell

# SEEK: Models

New or upload

Data file Go

Announcements

2nd VLN Modeling Workshop in Berlin 30/31 May 2013 11 days ago by Martin Golebiowski

Please upload your evaluation presentations and posters to SEEK 22 days ago by Martin Golebiowski

Merry Christmas to all SEEK users and a good start in 2013 about 1 month ago by Martin Golebiowski See all

Favourites

CellNetAnalyzer (CNA) Flow

Cytometry HepatoSys IL-1 IL-6

inflammation Insulin signalling

Kinetic Modelling logical modelling LPS metabolism

MidtermReview Nuclear receptors ODE primary human hepatocytes ProMoT Report

Show Case Steatosis Meeting

VLN VLN Retreat 2012 Hünfeld

Organisms

Homo sapiens

Mus musculus

Rattus norvegicus

Subcribe Download Simulate Model on JWS

Simulate Model on Sycamore

NFkappaB signalling in primary hepatocytes

Created at: 19/10/2012 @ 15:26:26 Last used: 29/01/2013 @ 12:35:40 Last updated: 10/01/2013 @ 09:18:25 Views: 231 Downloads: 42

Version 3 (of 3) View version: 3 (latest)

Version created on: 24/10/2012 @ 13:26:12 by: Katharina Beuke | revision comments

Title: NFkappaB signalling in primary hepatocytes

All Files (2 in total):

NFkappaB signalling in primary hepatocytes.xml (XML document)

NFkappaB signalling in primary hepatocytes.cps (Binary file type)

Organism: Not specified

Model type: Ordinary differential equations (ODE)

Model format: SBML

Execution or visualisation environment: Copasi

Model visualization(click it to zoom)

Simulate (ODE models)

The diagram illustrates the NFκB signalling pathway. It starts with TNFα activating IKKβ. IKKβ then phosphorylates IκBα. The phosphorylated IκBα is targeted for degradation. Free p65 subunits are released and form a complex with IκBα. This complex is also targeted for degradation. The p65 complex is shown in a green box.

Creators

Tags

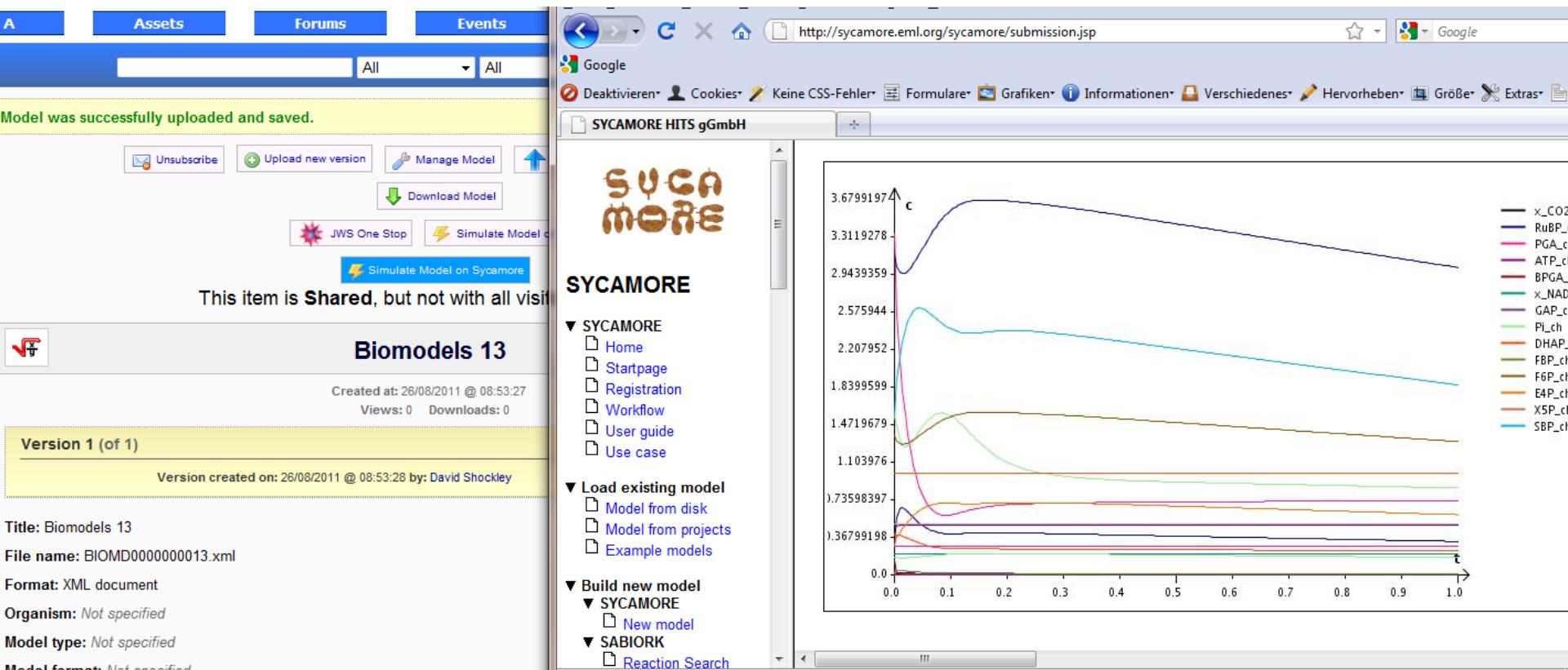
kinetic data primary hepatocytes SBML [ Add your tags ]

Scales

cell

# Integration of Modelling Platforms

Models in SEEK can be directly transferred to and subsequently edited, processed and simulated in JWS online, SYCAMORE or Cytoscape Web



# SEEK Yellow Pages: Projects & People

Virtual Liver F1 PALs: Andreas Dräger, Maria Thomas

Project Coordinators: Ulrich Zanger

**Yellow P** (circled in red)

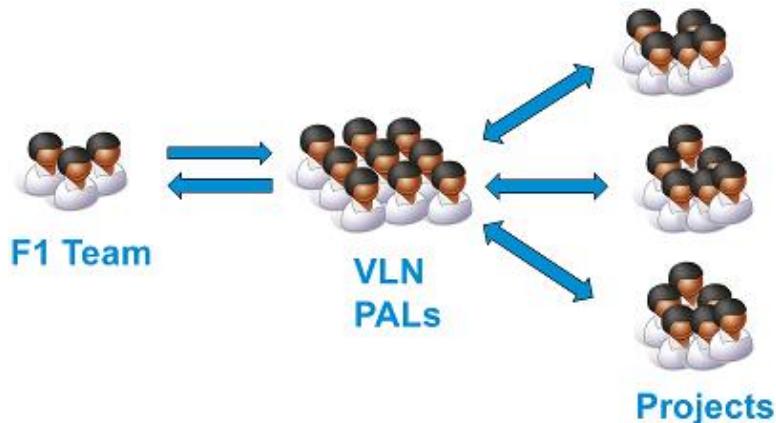
Project Hierarchies (hide):

- Virtual Liver** (254 people)
  - A: Cellular level** (157 people)
    - A1: Cellular metabolism (72 people)
    - A2: Integration of Signalling Pathways in Hepatocellular Response (53 people)
    - A3: Crosslinking signalling metabolism and hepatocyte polarisation** (94 people)
      - A3.1: Integration of signalling gene-regulatory and metabolic network models for guiding the experimental strategies (6 people)
      - A3.2: Cross-talk of signaling pathways and endocytic machinery in hepatocytes: Impact on cell polarity and presence of transporters (55 people)
      - A3.3: Hepatocyte polarity (29 people)
      - A3.4: Linking signalling to metabolic functions (20 people)
      - A3.5: The impact of cell polarity on metabolism detoxification and endocytosis (28 people)
      - A3.6: Transcription factor network and links to metabolism in NAFLD (15 people)
  - B: Communication of Hepatocytes and Non-Parenchymal Liver Cells** (98 people)
  - C: Liver lobule level** (110 people)
  - CTUs** (52 people)
  - D: Whole organ level** (59 people)
  - E: Model integration** (43 people)
  - F: Data management** (24 people)
  - G: Clinical translation** (16 people)
    - HepatoSys (4 people)
    - Interleukin-6 signalling (31 people)
    - PALs Team (16 people)
    - Project Management (28 people)
    - Show cases (90 people)

Project Members(show):

# Tackling the Social Challenge: PALs as Data Management Advocats & Multipliers

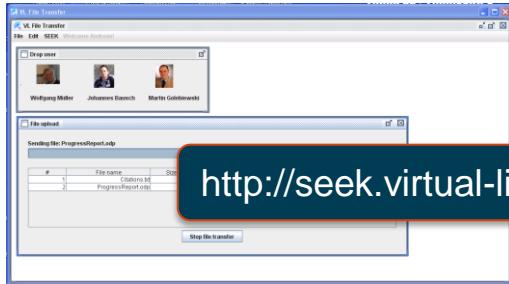
Heidelberg Institute for  
Theoretical Studies



**Virtual Liver PALs Meetings:**  
Dresden, December 9, 2010  
Hünfeld, November 30 – December 1, 2011  
Dortmund, March 6, 2012  
Heidelberg, November 13 – 14, 2012

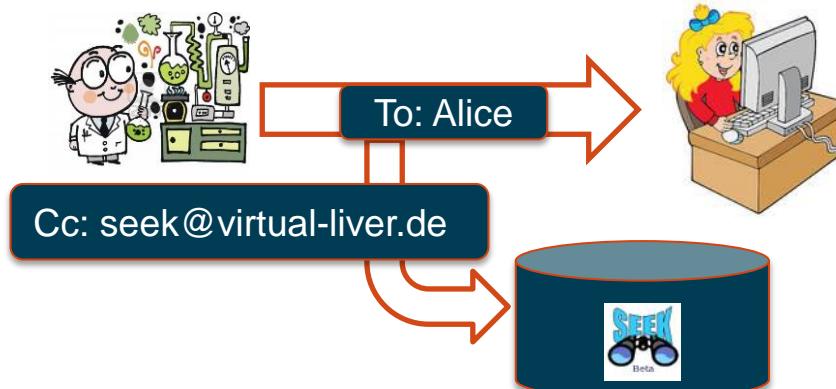
# Simplify data upload

- Submit big data via drag and drop

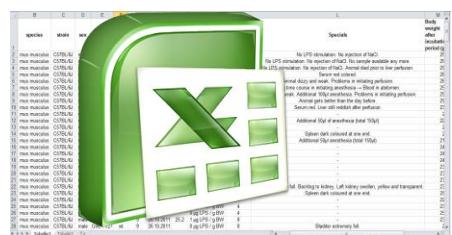


[http://seek.virtual-liver.de/file\\_upload\\_tool/](http://seek.virtual-liver.de/file_upload_tool/)

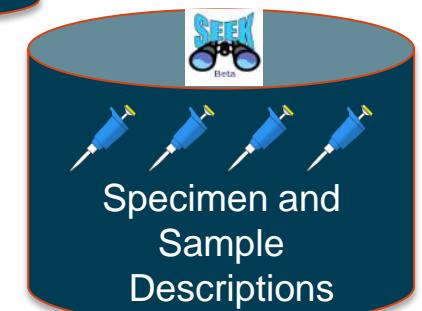
- Submit by mail



- Automated population



Parsing



## Yellow Pages:

- People
- Institutions
- Projects
- Events

## Asset Catalogue:

- Investigations, Studies, Assays
- Data
- Models
- Standardized workflows (SOPs)
- Publications & Presentations
- Biological samples



Heidelberger Institut für  
Theoretische Studien



# SABIO-RK

## Reaction Kinetics

## Database



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Federal Ministry  
of Education  
and Research

# Database for Reaction Kinetics

## Data Input



Literature

Input Interface



Lab Experiments

Automatic submission

## Curation /Annotation



Ontologies



External databases



Rights  
management



Quality  
control

SABIO-RK

## Data Access

User Interfaces



S<sup>3</sup>ML<sup>TM</sup>

Web Services



S<sup>3</sup>ML<sup>TM</sup>



**SABIO-RK**

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

## Biochemical reaction kinetics

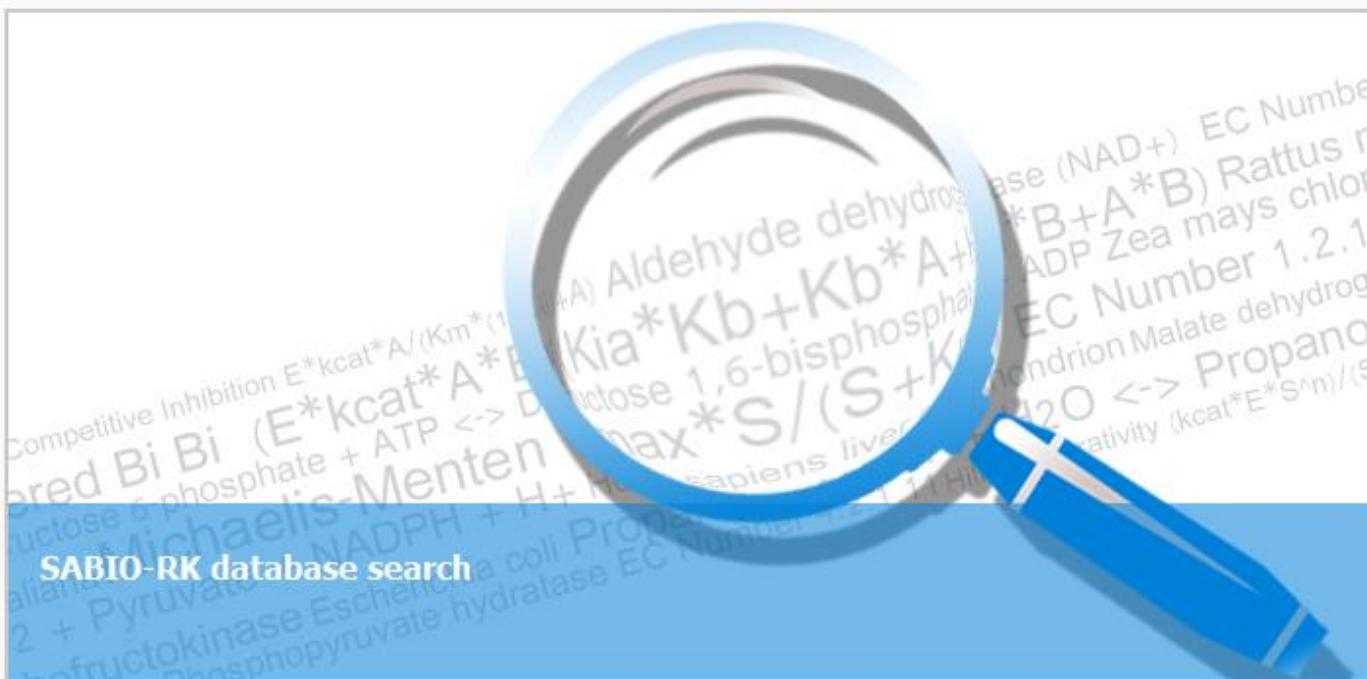
### Data is

- Unified
- Structured
- Curated
- Normalized
- Interrelated
- Annotated



## Welcome!

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



## News

### [Talk on SABIO-RK at VPH2012](#)

14-09-2012

SABIO-RK will be presented in a talk at the VPH Conferences ([VPH 2012](#)) taking place in London (UK) on 18 – 20 September 2012. [more»](#)

### [SABIO-RK tutorial at ICSB2012](#)

31-07-2012

SABIO-RK will be presented at the International Conference on Systems Biology (ICSB) on August 19, 2012, 9:00 am - 2:30 pm as part of the tutorial [Modelling and Simulation of Quantitative Biological Models](#) [more»](#)

**<http://sabio.h-its.org>**



## Search

Organism:"mammalia (NCBI)" AND Tissue:"liver (BTO)" NOT  
UniprotID:P00637 AND Substrate:"D-Fructose 1,6-bisphosphate"



Reset



▼ Advanced Search

AND Substrate

d-fructo

Add & Search

- [d-fructose, 6-\(dihydrogen phosphate\)](#) (0)
- [d-fructose 6-phosphoric acid](#) (0)
- [d-fructose 2,6-bisphosphate](#) (0)
- [d-fructose 6-phosphate](#) (0)
- [d-fructose](#) (0)

[Entry View](#)

[Reaction View](#)

## Filter Options

### Enzyme

Wildtype  Mutant  Recombinant

### Kinetic Data

Rate Equation

### Environmental Conditions

pH: 0 - 14

Temperature: -10 C° - 115 C°

### Source

Direct Submission

Entries inserted since:

15/10/2008



Total number of kinetic law entries found: 40

1 2 3 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	
	D-Fructose 1,6-bisphosphate + H <sub>2</sub> O = D-Fructose 6-phosphate + Orthophosphate	3.1.3.11	<a href="#">Q9N0J6</a>	wildtype	<a href="#">liver</a>	<i>Oryctolagus cuniculus</i>	Kd Km Vmax	25.0	9.5	<input type="checkbox"/>
	H <sub>2</sub> O + D-Fructose 1,6-bisphosphate =	3.1.3.11	<a href="#">Q3SZB7</a>	wildtype	<a href="#">liver</a>	<i>Bos taurus</i>	Km Vmax	28.0	6.5	<input type="checkbox"/>

D-Fructose 1,6-bisphosphate = Glycerone phosphate + D-Glyceraldehyde 3-phosphate	4.1.2.13	<a href="#">P05062 ↗</a>	wildtype aldolase B	<a href="#">liver ↗</a>	Homo sapiens	Vmax Km	22.0	7.6	<input checked="" type="checkbox"/>
--	----------	--------------------------	------------------------	-------------------------	-----------------	------------	------	-----	-------------------------------------

Entry ID: 2175

#### General information

Organism	<a href="#">Homo sapiens</a>		
Tissue	<a href="#">liver ↗</a>		
EC Class	<a href="#">4.1.2.13</a>		
SABIO reaction id	1338		
Variant	wildtype aldolase B		
Recombinant	expressed in Escherichia coli BL21(DE3)		

#### Substrates

name	location	comment
<a href="#">D-Fructose 1,6-bisphosphate</a>	-	-

#### Products

name	location	comment
<a href="#">Glycerone phosphate</a>	-	-
<a href="#">D-Glyceraldehyde 3-phosphate</a>	-	-

#### Modifiers

name	location	effect	comment	protein complex
fructose-bisphosphate aldolase(Enzyme)	-	Modifier-Catalyst	-	<a href="#">(P05062 ↗)*4;</a>

#### Enzyme (protein data)

	UniProt-ID	name	mol. weight (kDa)	deviation (kDa)
subunit	P05062	-	-	-
complex	-	-	-	-

#### Kinetic Law

type	formula
Michaelis-Menten	Vmax*S/(Km+S)

#### Parameter

name	type	species	start val.	end val.	deviat.	unit	comment
S	concentration	D-Fructose 1,6-bisphosphate	-	-	-	-	--
Km	Km	D-Fructose 1,6-bisphosphate	4.0	-	0.6	μM	-

Substrates											
name			location		comment						
<a href="#">D-Fructose 1,6-bisphosphate</a>			-		-						
Products											
name			location		comment						
<a href="#">Glycerone phosphate</a>			-		-						
<a href="#">D-Glyceraldehyde 3-phosphate</a>			-		-						
Modifiers											
name		location	effect	comment	protein complex						
fructose-bisphosphate aldolase(Enzyme)		-	Modifier-Catalyst	-	<a href="#">(P05062</a> ↗)*4;						
Enzyme (protein data)											
	UniProt-ID	name	mol. weight (kDa)	deviation (kDa)							
subunit	P05062	-		-							
complex	-	-		-							
Kinetic Law											
type			formula								
Michaelis-Menten			$V_{max} \cdot S / (K_m + S)$								
Parameter											
name	type	species	start val.	end val.	deviat.	unit					
S	concentration	D-Fructose 1,6-bisphosphate	-	-	-	-					
Km	Km	D-Fructose 1,6-bisphosphate	4.0	-	0.6	μM					
Vmax	Vmax	-	4.787	-	-	μmol/(min*mg)					
Experimental conditions											
	start value		end value		unit						
temperature	22.0		-		°C						
pH	7.6		-		-						
buffer	50 mM Tris-acetate, 0.15 mM NADH, 10 mM EDTA, 100 mg/ml bovine serum albumin, 2 mg/ml alpha-glycerophosphate dehydrogenase/triose phosphate isomerase										
comment	-										
Reference											
title		author	year	journal	volume	pages					
Expression, purification, and characterization of natural mutants of human aldolase B. Role of quaternary structure in catalysis.		Rellos P, Sygusch J, Cox TM.	2000	J Biol Chem	275	1145-51 <a href="#">10625657</a> ↗					

- **Reaction Kinetics Warehouse:**  
Several database entries can be exported in one file
- Export in standard exchange formats:  
**SBML** (Systems Biology Markup Language up to L3 V1) or  
**BioPAX / SBPAX** (Systems Biology Pathway Exchange)
- Data is annotated according to the **MIRIAM annotation standard**  
(*Minimal Information Required In the Annotation of Models*):
  - MIRIAM URN
  - [Identifiers.org](#) (in the next deploy)
- Annotations include **SABIO-RK IDs** (for reaction and entry) for tracking
- Export of kinetic data with **experimental conditions** (SABIO-RK namespace)
- Optional **normalization of kinetic parameters** (to SI base units)
- Export also as **human readable PDF** (SBML2LaTeX) or **spreadsheet table**

```
<sbrk:sabiork xmlns:sbrk="http://sabiork.h-its.org">
<sbrk:modifierType>Modifier-Catalyst</sbrk:modifierType>
</sbrk:sabiork>           <rdf:RDF xmlns:rdf="http://www.w3.org/1999/02/22-rdf-syntax-ns#" xmlns:bqbiol="http://biomodels.net/biology-qualifiers/">
<ns:bqmodel="http://biomodels.net/model-qualifiers/">
    <rdf:Description rdf:about="#META_ENZ_140280_Cell">
        <bqbiol:is>
            <rdf:Bag>
                <rdf:li rdf:resource="http://identifiers.org/uniprot/P05062"/>
            </rdf:Bag>
        </bqbiol:is>
    </rdf:Description>
</rdf:RDF>
</annotation>
</species>
</listOfSpecies>
<listOfReactions>
    <reaction id="REAC_0" metaid="META_REAC_0" reversible="true" fast="false">
        <annotation>
            <rdf:RDF xmlns:rdf="http://www.w3.org/1999/02/22-rdf-syntax-ns#" xmlns:bqbiol="http://biomodels.net/biology-qualifiers/" xmlns:bqmodel="http://biomodels.net/model-qualifiers/">
                <rdf:Description rdf:about="#META_REAC_0">
                    <bqbiol:isVersionOf>
                        <rdf:Bag>
                            <rdf:li rdf:resource="http://identifiers.org/ec-code/4.1.2.13"/>
                        </rdf:Bag>
                    </bqbiol:isVersionOf>
                    <bqbiol:is>
                        <rdf:Bag>
                            <rdf:li rdf:resource="http://identifiers.org/kegg.reaction/R01068"/>
                        </rdf:Bag>
                    </bqbiol:is>
                    <bqbiol:hasTaxon>
                        <rdf:Bag>
                            <rdf:li rdf:resource="http://identifiers.org/taxonomy/9606"/>
                        </rdf:Bag>
                    </bqbiol:hasTaxon>
                    <bqbiol:is>
                        <rdf:Bag>
                            <rdf:li rdf:resource="http://identifiers.org/sabiork.reaction/1338"/>
                        </rdf:Bag>
                    </bqbiol:is>
                </rdf:Description>
</rdf:RDF>
</annotation>
<listOfReactants>
    <speciesReference constant="true" species="SPC_1465_Cell" sboTerm="SBO:0000015" stoichiometry="1"/>
</listOfReactants>
```

# SABIO-RK

## SBML

### Export



```
<?xml version='1.0' encoding='UTF-8' standalone='no'?>
<sbml xmlns="http://www.sbml.org/sbml/level2/version4" level="2" version="4">
  <model name="SABIOmdl24Aug2011127">
    <notes>
      <body xmlns="http://www.w3.org/1999/xhtml">
        <p>
          This model has been created with the help of the SABIO-RK Database
          (http://sabiork.h-its.org/)
          (c) 2005-2010 HITS gGmbH http://www.h-its.org
        </p><br/>
      To cite SABIO-RK Database, please use
      "http://www.ncbi.nlm.nih.gov/pubmed/17822389"
      <br/>
      Wittig U., Golebiewski M., Kania R., Krebs O., Mir S., Weidemann A., Anstein S., Sam
      Lecture Notes in Computer Science, 4075: 94-103.
    </body>
    </notes>
```

```
    <ionDefinitions id="KL_20147">
```

```
      <kineticLaw ... suoterm="SBO:0000020" ...>
        <annotation>
          <sbrk:sabiork xmlns:sbrk="http://sabiork.h-its.org">
            <sbrk:kineticLawID>20147</sbrk:kineticLawID>
            <sbrk:experimentalConditions>
              <sbrk:temperature>
                <sbrk:startValueTemperature>37.0</sbrk:startValueTemperature>
                <sbrk:temperatureUnit>°C</sbrk:temperatureUnit>
              </sbrk:temperature>
              <sbrk:pH>
                <sbrk:startValuepH>8.0</sbrk:startValuepH>
              </sbrk:pH>
              <sbrk:buffer> 50 mM potassium phosphate</sbrk:buffer>
            </sbrk:experimentalConditions>
          </sbrk:sabiork>
            <rdf:RDF xmlns:rdf="http://www.w3.org/1999/02/22-rdf-syntax-ns#">
              <rdf:Description rdf:about="#META_KL_20147">
                <bqbiol:isDescribedBy>
                  <rdf:Bag>
                    <rdf:li rdf:resource="urn:miriam:pubmed:10884298"/>
                  </rdf:Bag>
                </bqbiol:isDescribedBy>
                <bqbiol:isDescribedBy>
                  <rdf:Bag>
                    <rdf:li rdf:resource="urn:miriam:sabiork.kineticrecord:20147"/>
                  </rdf:Bag>
                </bqbiol:isDescribedBy>
              </rdf:Description>
            </rdf:RDF>
          </sbrk:sabiork>
        </annotation>
      </kineticLaw>
    </ionDefinitions>
```

# SBML Import: e.g. BioModels

## Kinetic law

ID	Type	Type ID	Kinetic law	Kinetic law subst.	Reversible	Select	Edit
68535			cytosol*VmGLK/(KmGLKGLC+KmGLKATP)*(GLC+ATP-G6P+ADP/KeqGLK)/((1+GLC/KmGLKGLC+G6P/KmGLKG6P)*(1+ATP/KmGLKATP+ADP/KmGLKADP))		reversible	<input type="checkbox"/>	<a href="#">edit</a>
68536			cytosol*VmPGI_2/KmPGIG6P_2*(G6P-F6P/KeqPGI_2)/(1+G6P/KmPGIG6P_2+F6P/KmPGIF6P_2)		reversible	<input type="checkbox"/>	<a href="#">edit</a>
68537			cytosol*KGLYCOGEN_3		reversible	<input type="checkbox"/>	<a href="#">edit</a>
68538			cytosol*KTREHALOSE		reversible	<input type="checkbox"/>	<a href="#">edit</a>
68539			cytosol*VmPFK*gR*F6P/KmPFKF6P*ATP/KmPFKATP_R_PFK	cytosol*VmPFK*gR*F6P/KmPFKF6P*ATP/KmPFKATP*(1+F6/KmF6P+AT/KmATP+g*F6/KmF6P*AT/KmATP)	reversible	<input type="checkbox"/>	<a href="#">edit</a>
68540			cytosol*VmALD/KmALDF16P*(F16P-KeqTPI/(1+KeqTPI)*TRIO*1/(1+KeqTPI)*TRIO/KeqALD)/(1+F16P/KmALDF16P+KeqTPI/(1+KeqTPI)*TRIO/KmALDGAP+1/(1+KeqTPI)*TRIO/KmALDDHAP+KeqTPI/(1+KeqTPI)*TRIO*1/(1+KeqTPI)*TRIO/(KmALDGAP*KmALDDHAP)+F16P*KeqTPI/(1+KeqTPI)*TRIO/(KmALDGAP+KmALDF16P))		reversible	<input type="checkbox"/>	<a href="#">edit</a>

## Reference

Title	Authors	Journal	Volume	Pages	Year	PubMed	Type	Identifier	Organization	Responsible Person	Contact Email	Contact Phone	Base Url
Can yeast glycolysis be understood in terms of in vitro kinetics of the constituent enzymes? Testing biochemistry.	Teuwink B, Passarge J, Reijenga CA, Esgahade E, van der Weijden CC, Schepper M, Walsh MC, Bakker BM, van Dam K, Westerhoff HV, Snoep JL.	Eur J Biochem	267(17)	5313-29	2000	<a href="#">10951190</a>	BioModel	BIOMD0000000064	Stellenbosch University;California Institute of Technology;EMBL-EBI;	Snoep,Jacky L,Dharuri,Harish,Endler,Lukas,	jls@sun.ac.za,hdharuri@cds.caltech.edu;lukas@ebi.ac.uk;	null	<a href="http://www.ebi.ac.uk/biomodels-main/">http://www.ebi.ac.uk/biomodels-main/</a>

68549		(-cytosol)*VmADH/(KiADHNAD*KmADHETOH)*(NAD*ETOH+NADH*ACE/KeqADH)/(1+NAD/KiADHNAD+KmADHNAD*ETOH/(KiADHNAD*KmADHETOH)+KmADHNADH*ACE/(KiADHNADH*KmADHACE)+NADH/KiADHNADH+NAD*ETOH/(KiADHNAD*KmADHETOH)+KmADHNADH*NAD*ACE/(KiADHNADH*KmADHETOH*KiADHACE)-KmADHNAD*ETOH*NADH/(KiADHNAD*KmADHETOH*KiADHNADH)+NADH*ACE/(KiADHNADH*KmADHACE)+NAD*ETOH*ACE/(KiADHNADH*KmADHETOH*KiADHACE)-ETOH*NADH*ACE/(KiADHETOH*KiADHNADH*KmADHACE))		reversible	<input type="checkbox"/>	<a href="#">edit</a>
68550		cytosol*VmG3PDH/(KmG3PDHDHAP*KmG3PDHNADH)*(1+(1+KeqTPI)*TRIO*NADH+GLY*NAD/KeqG3PDH)/((1+1/(1+KeqTPI)*TRIO/KmG3PDHDHAP+GLY/KmG3PDHGLY)*(1+NADH/KmG3PDHNADH+NAD/KmG3PDHNAD))		reversible	<input type="checkbox"/>	<a href="#">edit</a>
68551	kinetic law type	0 cytosol*KATPASE*ATP		reversible	<input type="checkbox"/>	<a href="#">edit</a>

## Variables

ID	Name	Term	Not replaced	Comment	Edit
68535	ADP	(SUM_P-(P^2*(1-4*KeqAK)+2*SUM_P*P*(4*KeqAK-1)+SUM_P^2)^0.5)/(1-4*KeqAK)	true	species concentration; assignment	<a href="#">edit</a>
68535	ATP	(P-ADP)/2	true	species concentration; assignment	<a href="#">edit</a>
68539	ATP	(P-ADP)/2	true	species concentration; assignment	<a href="#">edit</a>
68539	L_PFK	L*((1+CiATP*AT/KiATP)/(1+AT/KiATP))^2*((1+CAMP*AM/KAMP)/(1+AM/KAMP))^2*((1+CF26BP*F26/KF26BP+CF16BP*F16/KF16BP)/(1+F26/KF26BP+F16/KF16BP))^2		L_PFK	<a href="#">edit</a>
68539	R_PFK	1+F6/KmF6P+AT/KmATP+g*F6/KmF6P*AT/KmATP		R_PFK	<a href="#">edit</a>
68539	T_PFK	1+CATP*AT/KmATP		T_PFK	<a href="#">edit</a>

parsed from BIOMD0000000064

➤ **The jungle of annotation URIs:**

e.g. namespace part:

<http://identifiers.org/go/GO:0015979> (most recent version)

<urn:miriam:obo.go:GO%3A0015979> (level 2 version 3)

<http://www.geneontology.org/#GO:0015979> (level 2 version 1)

e.g. data collection name part: obo.chebi vs. chebi

➤ **Qualifiers confusion:**

is, isVersionOf, isPartOf...

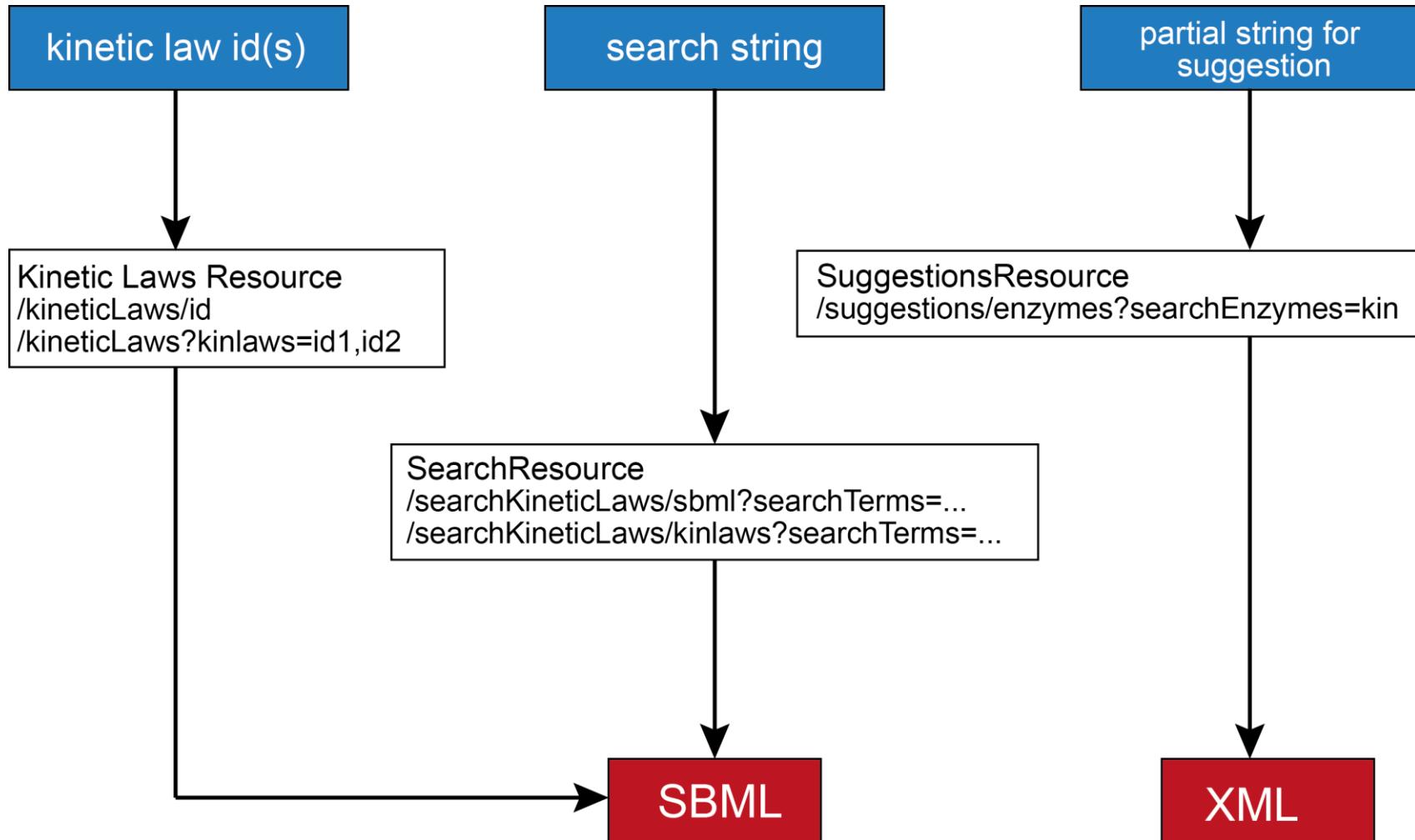
OccursIn, hasTaxon

➤ **No standard place to annotate publication related information.**

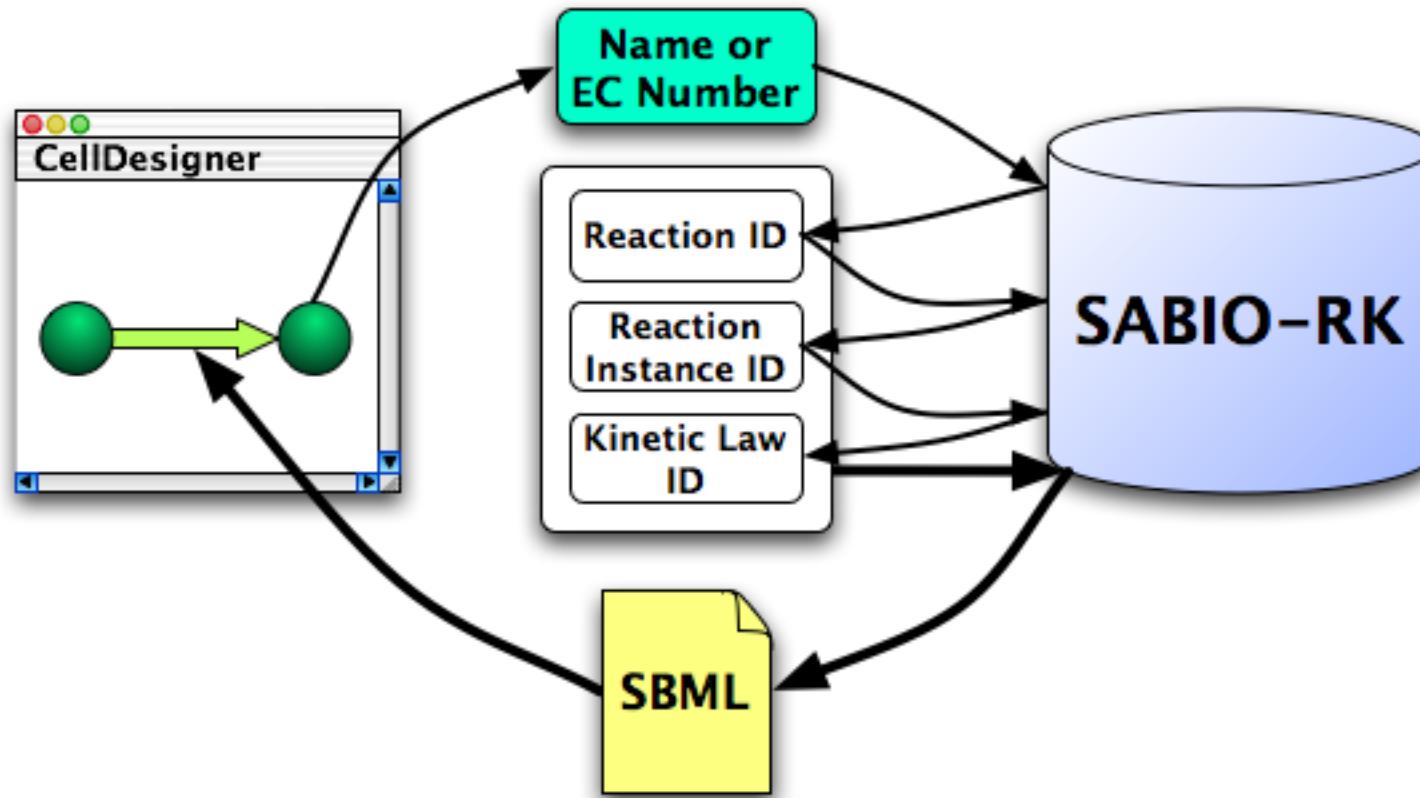
Most of them put them into <notes>, hard to parse.

Currently we grab info from PubMed (if we have the PubMed ID). Otherwise, our curators have to fill it manually.

# Programmatic Access RESTful Web Services



Programmatic access via web services (RESTful)



<http://www.celldesigner.org>

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

.....



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

*Nucleic Acids Research (2012) 40 (D1): D790-D796 (doi: 10.1093/nar/gkr1046)*



