



Mehr edizininformatik am Meer

Dagmar Waltemath
Professur Medizininformatik



Eingeladener Vortrag auf dem MIRACUM Symposium 2019, 27.-28.03.2019, Mainz, Deutschland

Motivation



Ganz einfache Fragen...

- Wie viele freigegebene Bioproben aus einem Primärtumor enthält die Biobank von Patienten mit einem Prostatakarzinom und einem Grading der Kategorien mäßig, mäßig gut und mittelgradig?
- Automatisiert ermittelte Knochendichte bei Patientenkohorten mit der Diagnose MGUS (Monoklonale Gammopathie unbestimmter Signifikanz) und mit/ohne anschließende Diagnose Multiples Myelom?
- Wie hoch war die 5-Jahres-Überlebensrate von Patienten mit Diffus-Großzelligem Lymphom, die 2010 im UKHD behandelt wurden?
- Wie lange war die durchschnittliche Zeit zwischen letzter Chemotherapie und Todesdatum bei Tumorpatienten am Beispiel Lymphom?
- Bei wie vielen wurde ein Thorax-CT oder eine Broncho-alveoläre Lavage durchgeführt?
- Wie viele Tumorpatienten hatten eine Pneumonie?
- Wie viele stationäre Tumorpatienten bekamen eine Sepsis?

Aus unserer Vorführung des neuen Datawarehouses im Juli 2017

dkfz.



Inhalt



Hintergrund: Systembiologisches
Datenmanagement diesseits und
jenseits von Nord- und Ostsee



Und die Aussichten? MORRE
Medical Informatics



Systembiologisches Datenmanagement diesseits und jenseits von Nord- und Ostsee



Linköpings universitet

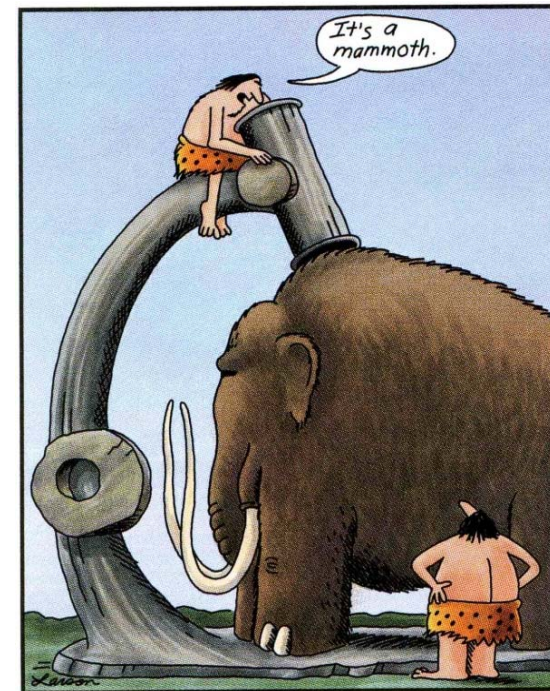


@SemsProject

Systembiologisches Datenmanagement: Systembiologie (-medizin)

Systems biology is the science that studies how *biological function* emerges from the interactions between the components of living systems.

... and how these *emergent properties* enable/constrain the *behavior* of these components.



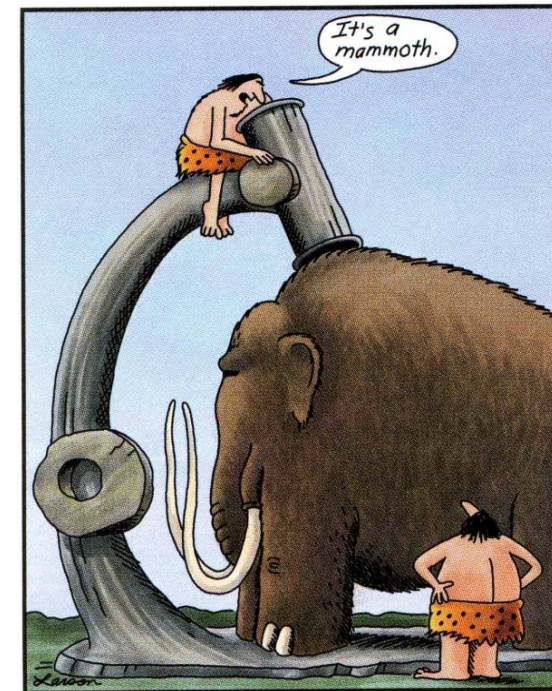
Early microscope

(Folie: [Olaf Wolkenhauer](#))

Systembiologisches Datenmanagement: Systembiologie (-medizin)

Systems biology is the science that studies how *biological function* emerges from the interactions between the components of living systems.

... and how these *emergent properties* enable/constrain the behavior of these components.



Early microscope

(Folie: [Olaf Wolkenhauer](#))

Systembiologisches Datenmanagement: Simulationsmodelle

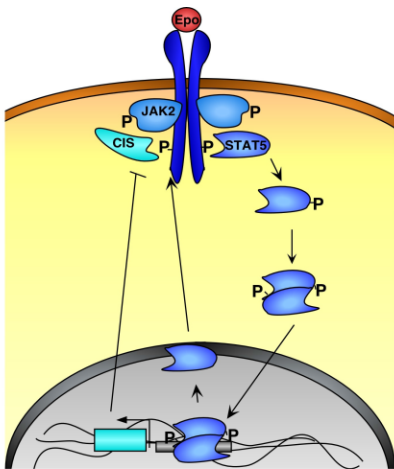


Abb.: Olaf Wolkenhauer

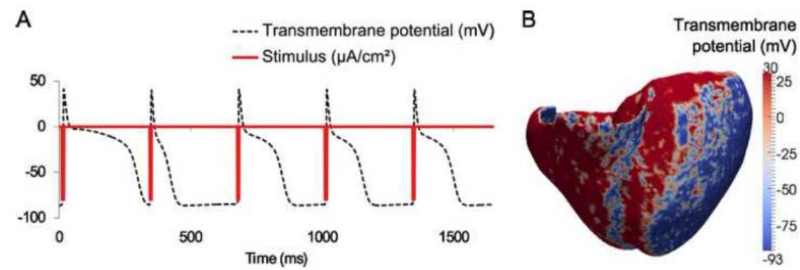


Abb.: Physiologie des Herzens, Chaste,
[Cooper et al 2015](#)



Abb: Menschliches Gehirn, Human Brain
Project, <https://www.humanbrainproject.eu>

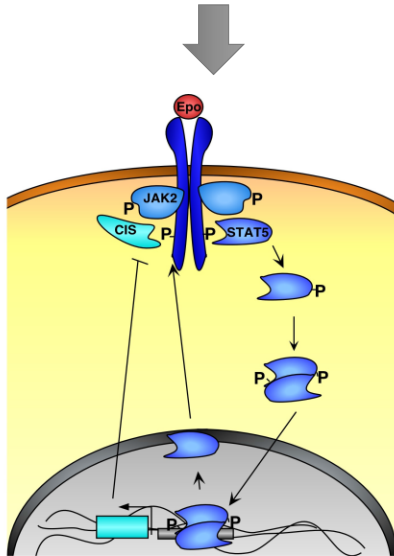
Systembiologisches Datenmanagement: Modelldaten

Research article

Open Access

A systems biology approach to analyse amplification in the JAK2-STAT5 signalling pathway

Julio Vera¹, Julie Bachmann², Andrea C Pfeifer², Verena Becker²,
Jose A Hormiga³, Nestor V Torres Darias³, Jens Timmer⁴, Ursula Klingmüller²
and Olaf Wolkenhauer^{*1}



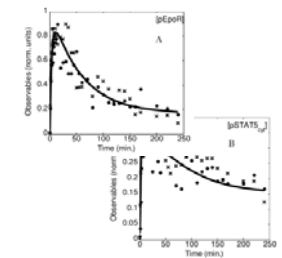
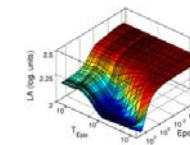
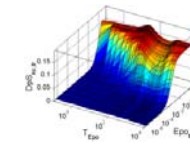
$$\frac{d}{dt} EJ = \gamma_1 - \gamma_2 \cdot EJ^{s_1} \cdot Epo^{s_2} - \gamma_1 \cdot EJ^{s_3} \quad (3.1)$$

$$\frac{d}{dt} pEpf = \gamma_2 \cdot EJ^{s_1} \cdot Epo^{s_2} - \gamma_3 \cdot pEpf^{s_4} \quad (3.2)$$

$$\frac{d}{dt} S = 2 \cdot \gamma_4 \cdot (DpS_{nc}(t - \tau))^{s_5} - 2 \cdot \gamma_5 \cdot S^{s_6} \cdot pEpf^{s_7} \quad (3.3)$$

$$\frac{d}{dt} DpS = \gamma_5 \cdot S^{s_6} \cdot pEpf^{s_7} - \gamma_6 \cdot DpS^{s_8} \quad (3.4)$$

$$\frac{d}{dt} DpS_{nc} = \gamma_6 \cdot DpS^{s_8} - \gamma_4 \cdot (DpS_{nc}(t - \tau))^{s_5} \quad (3.5)$$



Publikationen
(Text, Tabellen)

Reaktionsnetzwerke
(XML, OWL/RDF)

Mathematische Modelle
(MathML / XML)

Simulationsbeschreibungen
(XML, OWL/RDF)

Ergebnisse
(CSV, Excel...)

Systembiologisches Datenmanagement: Aufgaben

Standardisierung / Speicherung

```
<?xml version="1.0" encoding="UTF-8"?>
<sbml xmlns="http://www.sbml.org/sbml/level1" level="1" version="1">
  <model name="Michaelis_Menten_kinetics">
    <listOfCompartments>
      <compartment name="compartment" volume="1"/>
    </listOfCompartments>
    <listOfSpecies>
      <species name="E" compartment="compartment" initialAmount="0.999" boundaryCondition="false"/>
      <species name="S" compartment="compartment" initialAmount="1" boundaryCondition="true"/>
      <species name="P" compartment="compartment" initialAmount="0.001" boundaryCondition="false"/>
    </listOfSpecies>
    <listOfReactions>
      <reaction name="R" reversible="false">
        <listOfReactants>
          <speciesReference species="S" stoichiometry="1"/>
        </listOfReactants>
        <listOfProducts>
          <speciesReference species="P" stoichiometry="1"/>
        </listOfProducts>
        <listOfModifiers>
          <speciesReference species="E" stoichiometry="1" />
        </listOfModifiers>
        [...]
      </reaction>
      [...]
    </listOfReactions>
  </model>
</sbml>
```



Show me models of the Cell Cycle by Tyson that simulate cdk1 concentration!

Auffindbarkeit / Retrieval

Systembiologisches Datenmanagement: Aufgaben

Versionierung / Provenance

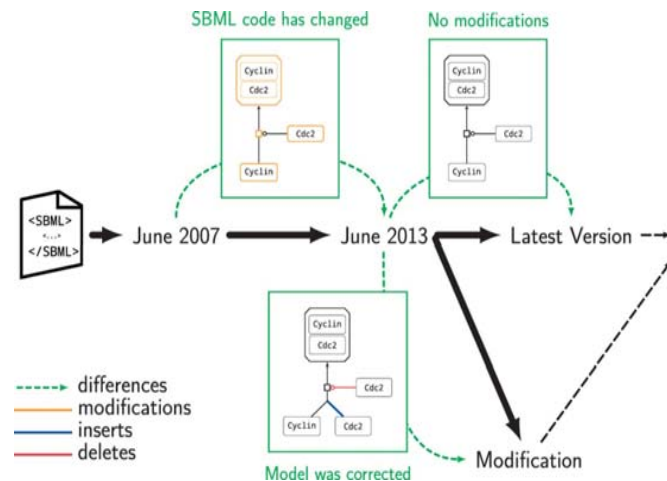


Abb.: [Waltemath et al 2013](#)

Weiterverwendbarkeit

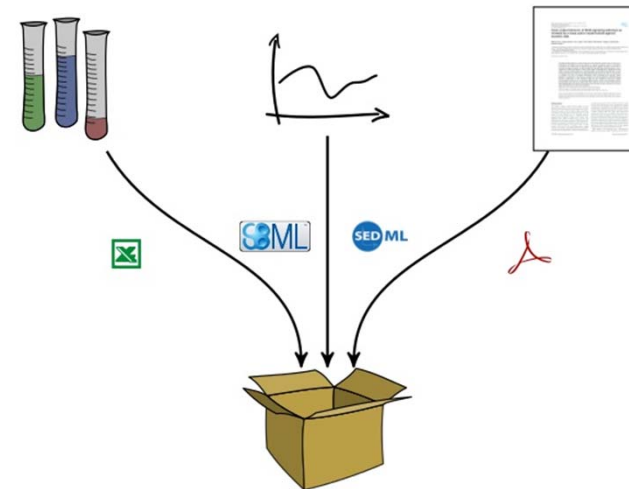


Abb.: Martin Scharm, [FAIRDOM webinar series 2016](#)

Systembiologisches Datenmanagement: Standardisierung

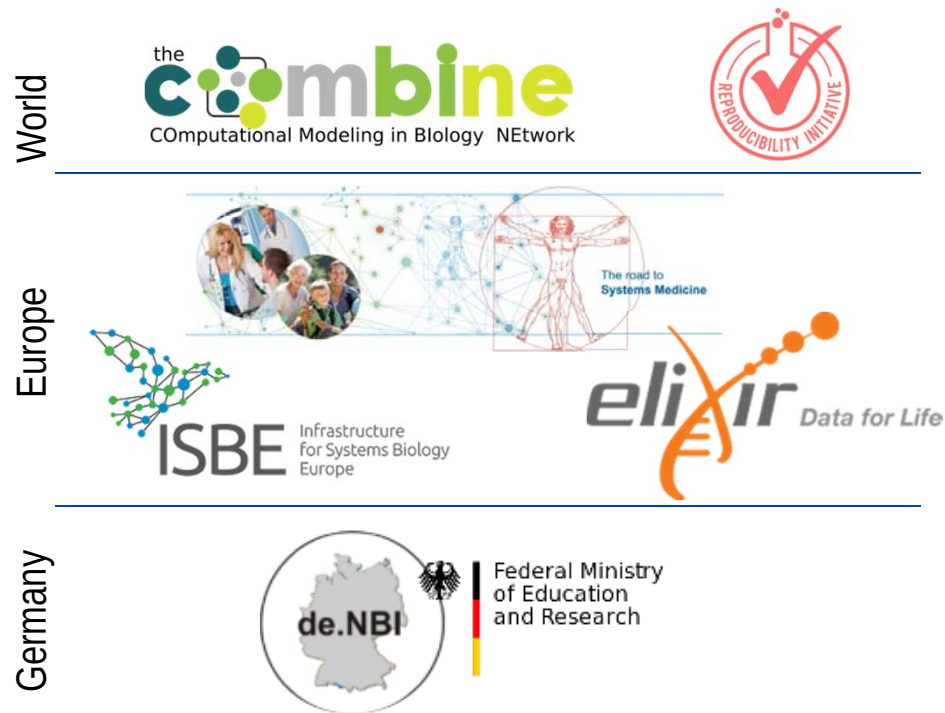
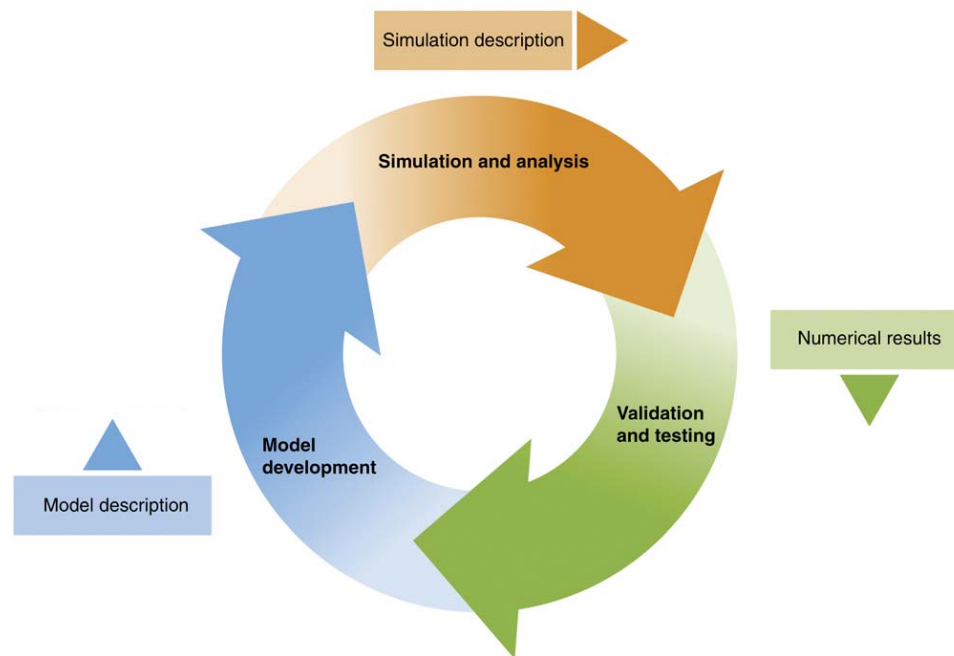


Abb.: The Economist,
[Trouble at the lab](#), 2013

Systembiologisches Datenmanagement: Standardisierung

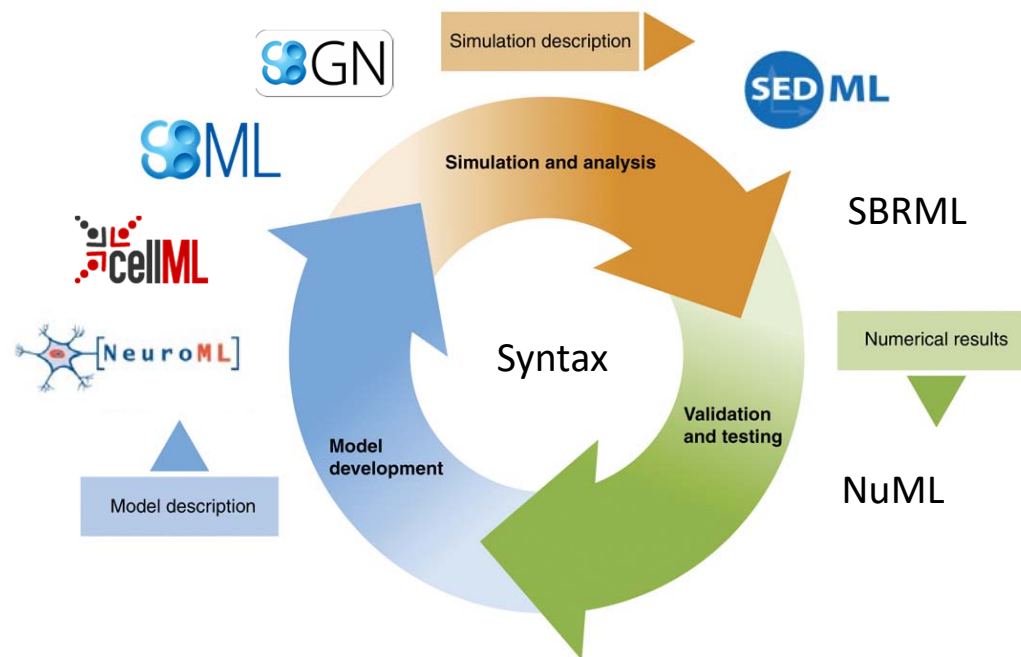


Systembiologisches Datenmanagement: Standardisierung



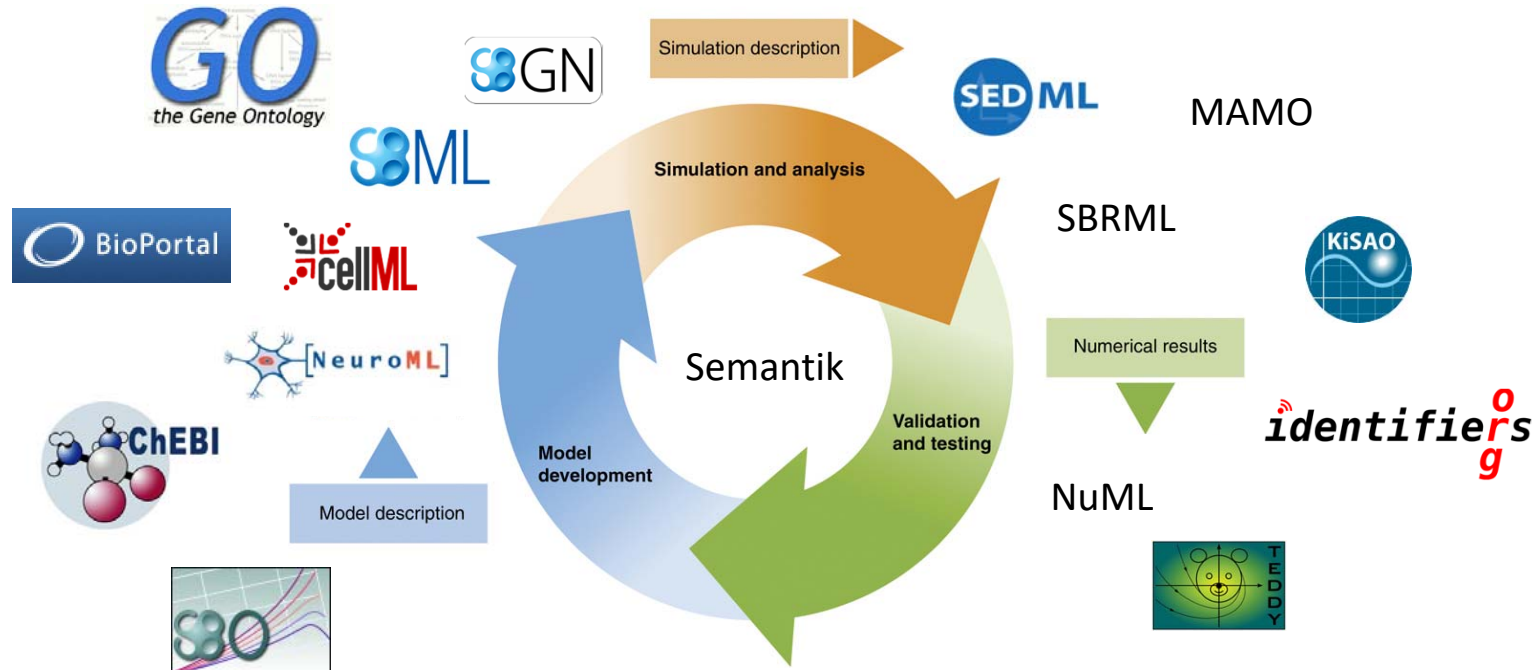
(Abb. angelehnt an [Courtot et al 2011](#))

Systembiologisches Datenmanagement: Standardisierung



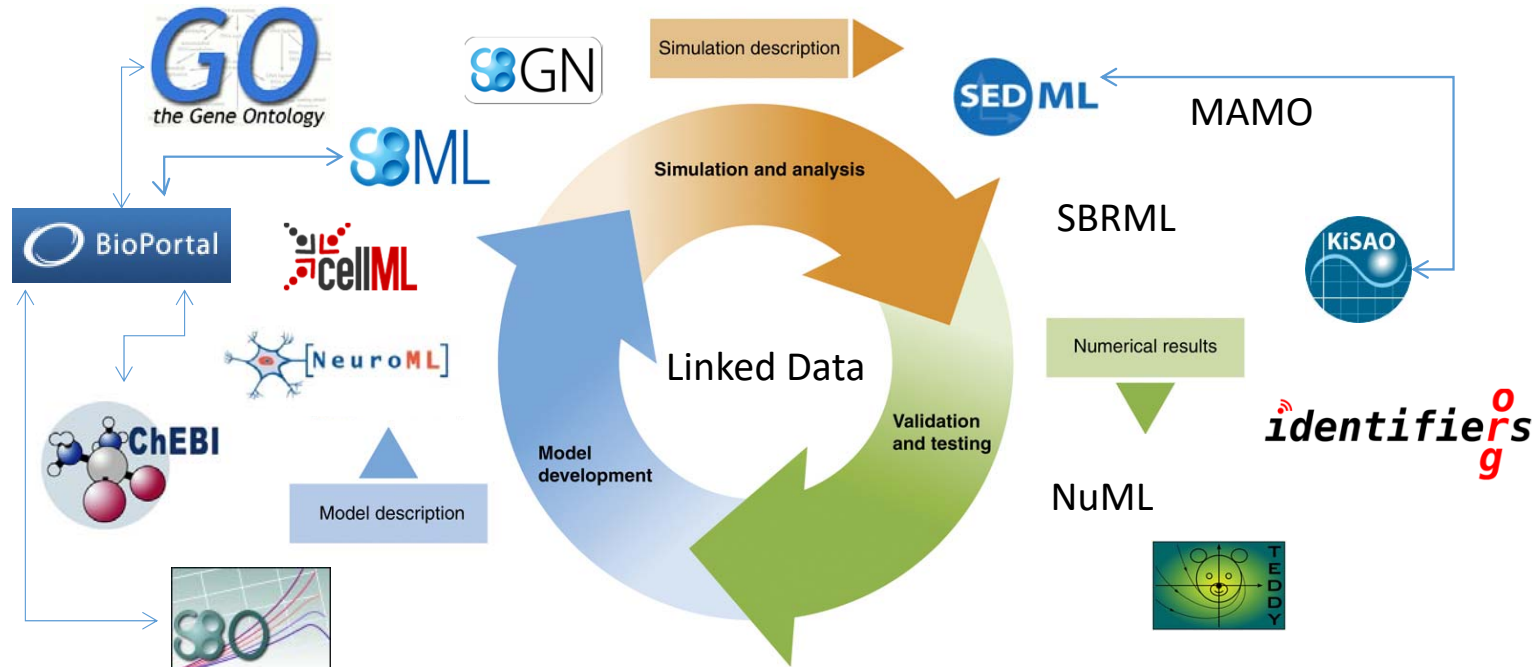
(Abb. angelehnt an [Courtot et al 2011](#))

Systembiologisches Datenmanagement: Standardisierung



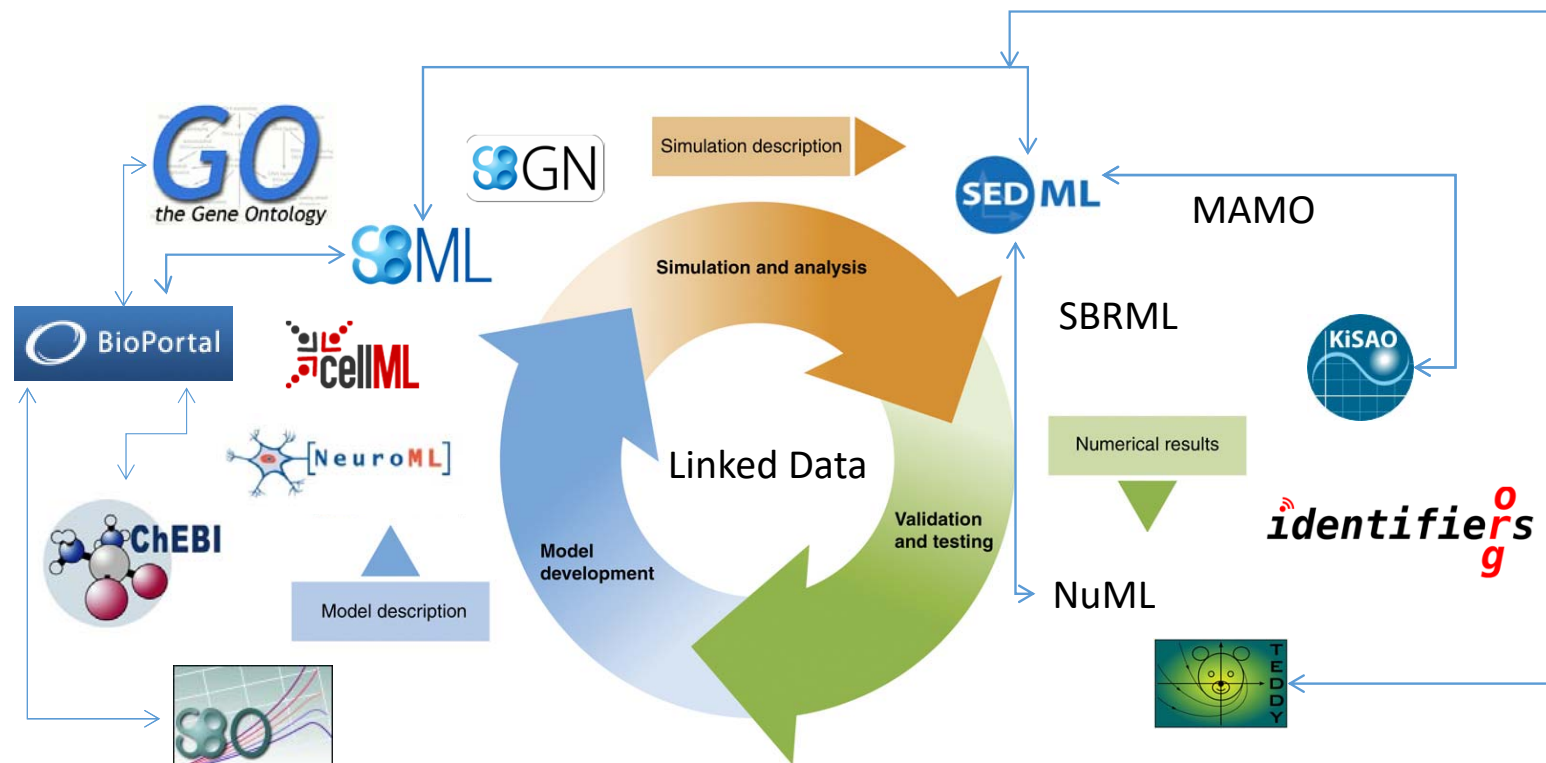
(Abb. angelehnt an [Courtot et al 2011](#))

Systembiologisches Datenmanagement: Standardisierung



(Abb. angelehnt an [Courtot et al 2011](#))

Systembiologisches Datenmanagement: Standardisierung



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Systembiologisches Datenmanagement: Standardisierung

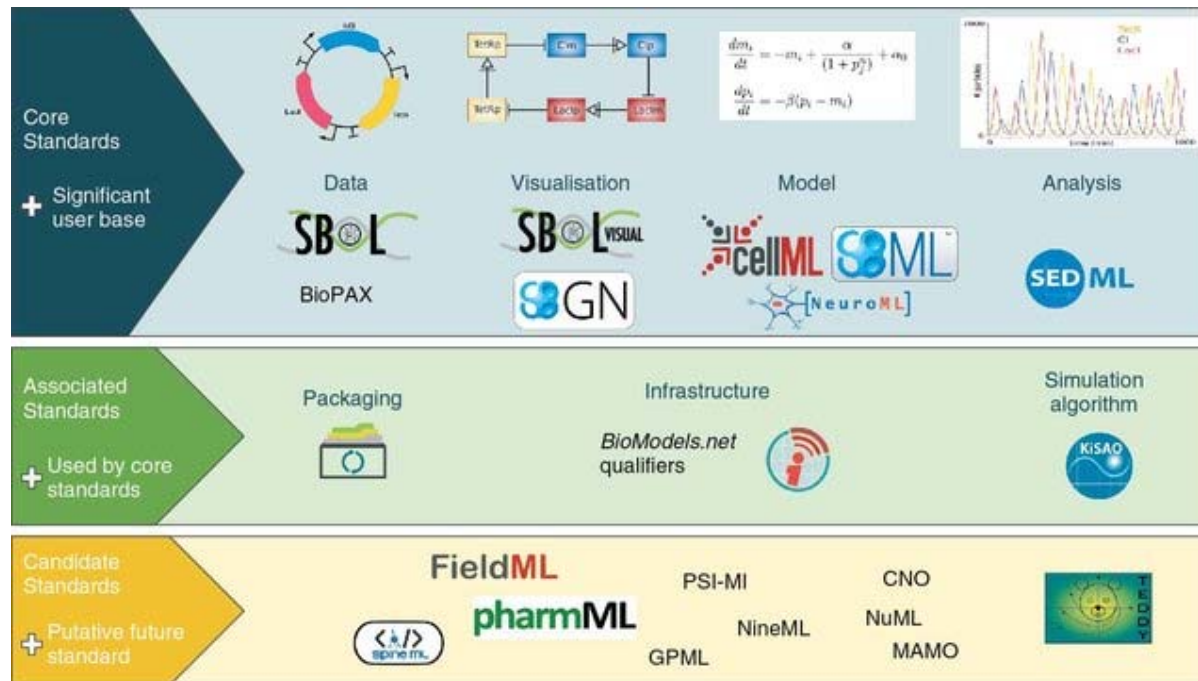


Abb.: [Schreiber et al 2017](#)

Systembiologisches Datenmanagement: Graph-basierte Speicherung

```
<?xml version="1.0" encoding="UTF-8"?>
<sbml xmlns="http://www.sbml.org/sbml/level1" level="1" version="1">
  <model name="Michaelis-Menten_kinetics">
    <listOfCompartments>
      <compartment name="compartment" volume="1"/>
    </listOfCompartments>
    <listOfSpecies>
      <species name="E" compartment="compartment" initialAmount="0.999" boundaryCondition="false"/>
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      <species name="P" compartment="compartment" initialAmount="0.001" boundaryCondition="false"/>
    </listOfSpecies>
    <listOfReactions>
      <reaction name="R" reversible="false">
        <listOfReactants>
          <speciesReference species="S" stoichiometry="1"/>
        </listOfReactants>
        <listOfProducts>
          <speciesReference species="P"/>
        </listOfProducts>
        <listOfModifiers>
          <speciesReference species="E"/>
        </listOfModifiers>
      </reaction>
    </listOfReactions>
  </model>
</sbml>
```

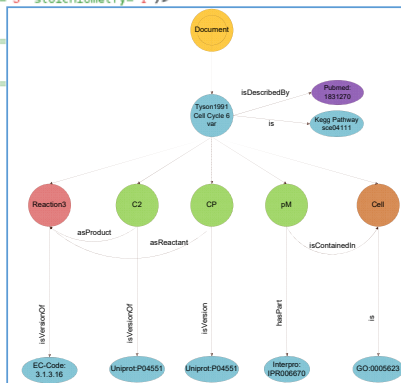


Abb.: [Henkel et al. INFORMATIK2012](#) (2012)

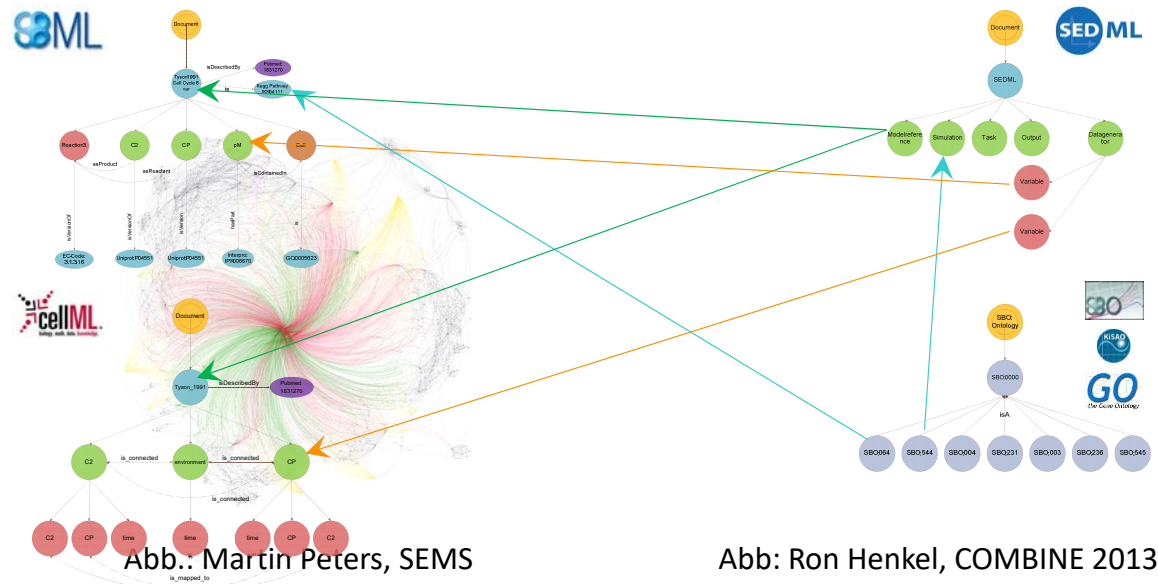
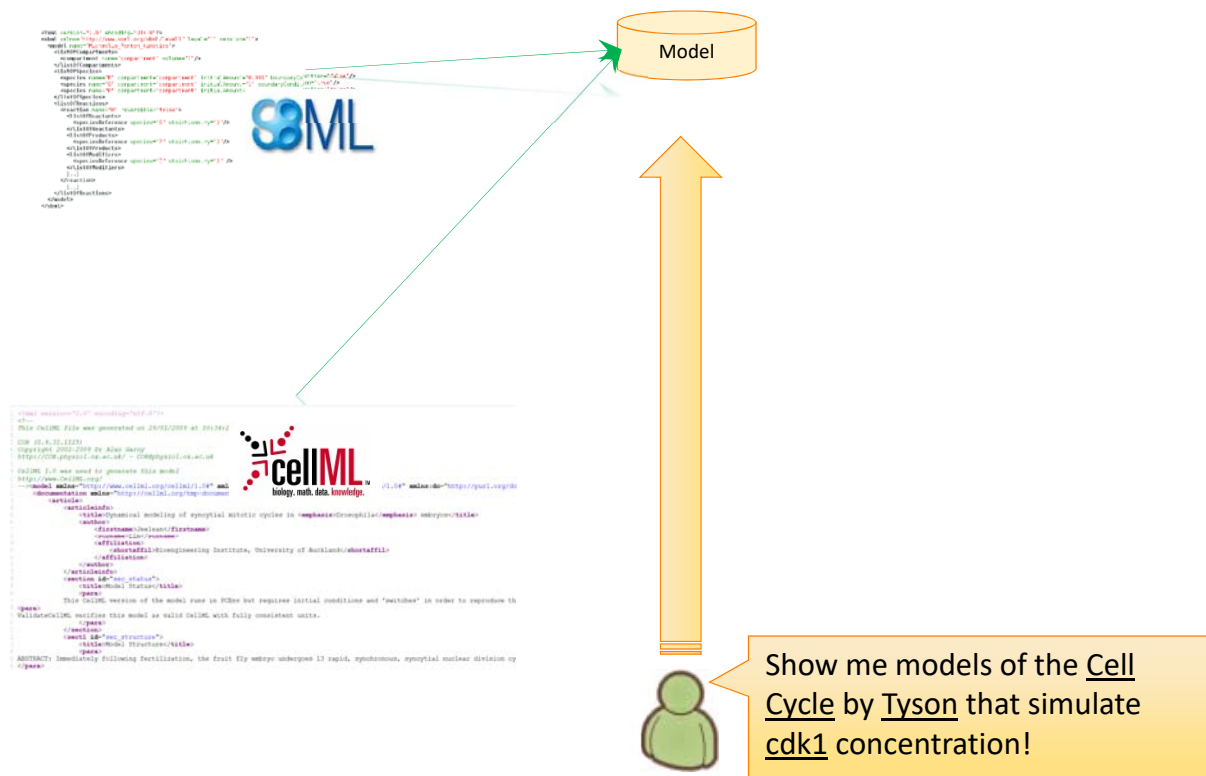


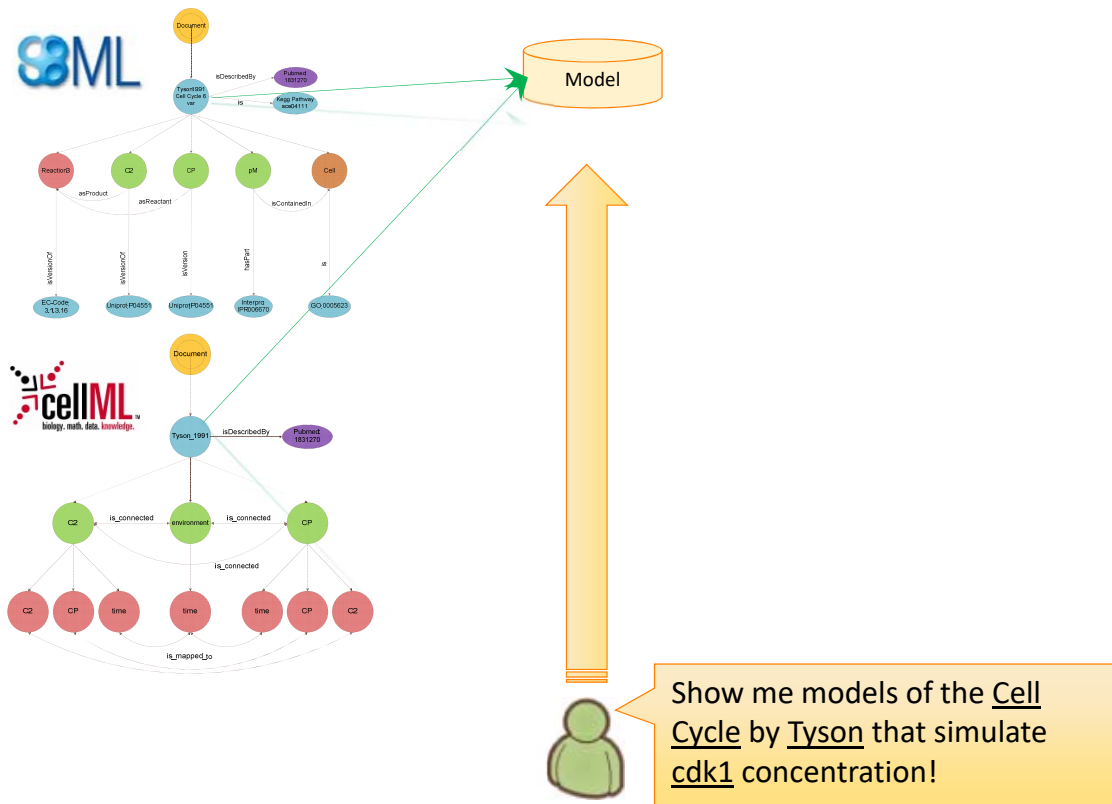
Abb.: Martin Peters, SEMS

Abb: Ron Henkel, COMBINE 2013

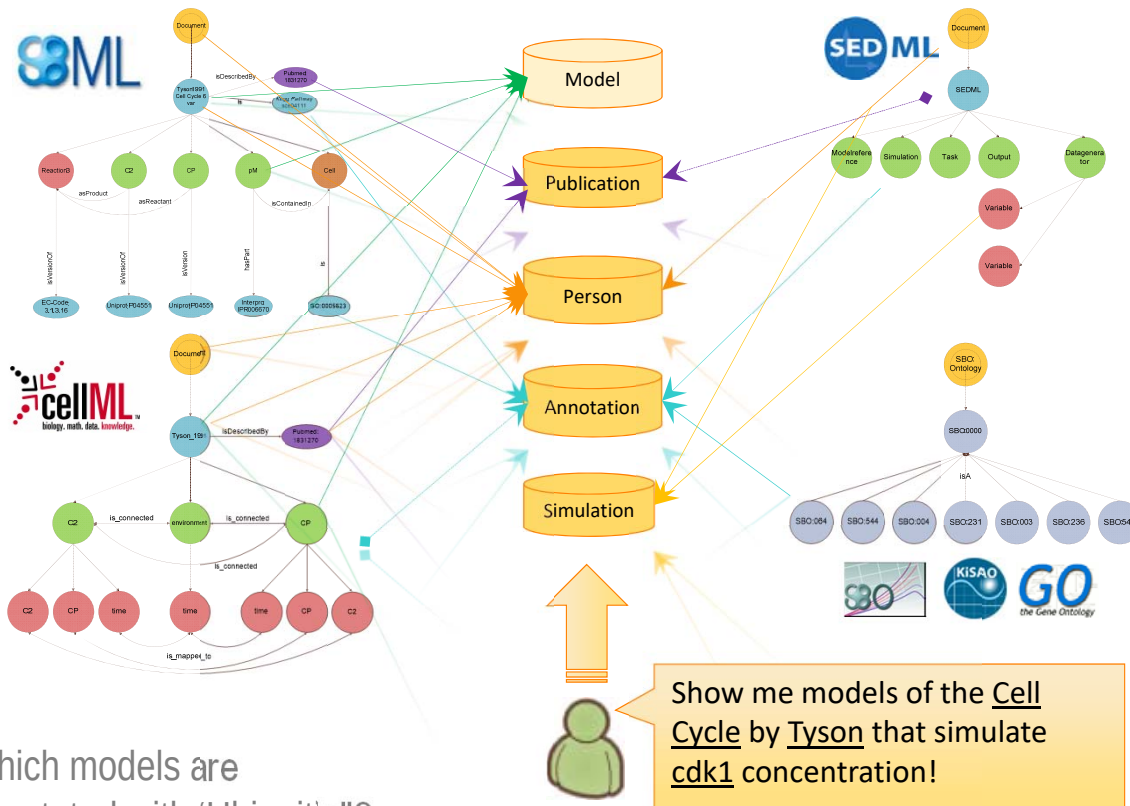
Systembiologisches Datenmanagement: Retrieval und Bewertung (MORRE)



Systembiologisches Datenmanagement: Retrieval und Bewertung (MORRE)



Systembiologisches Datenmanagement: Retrieval und Bewertung (MORRE)



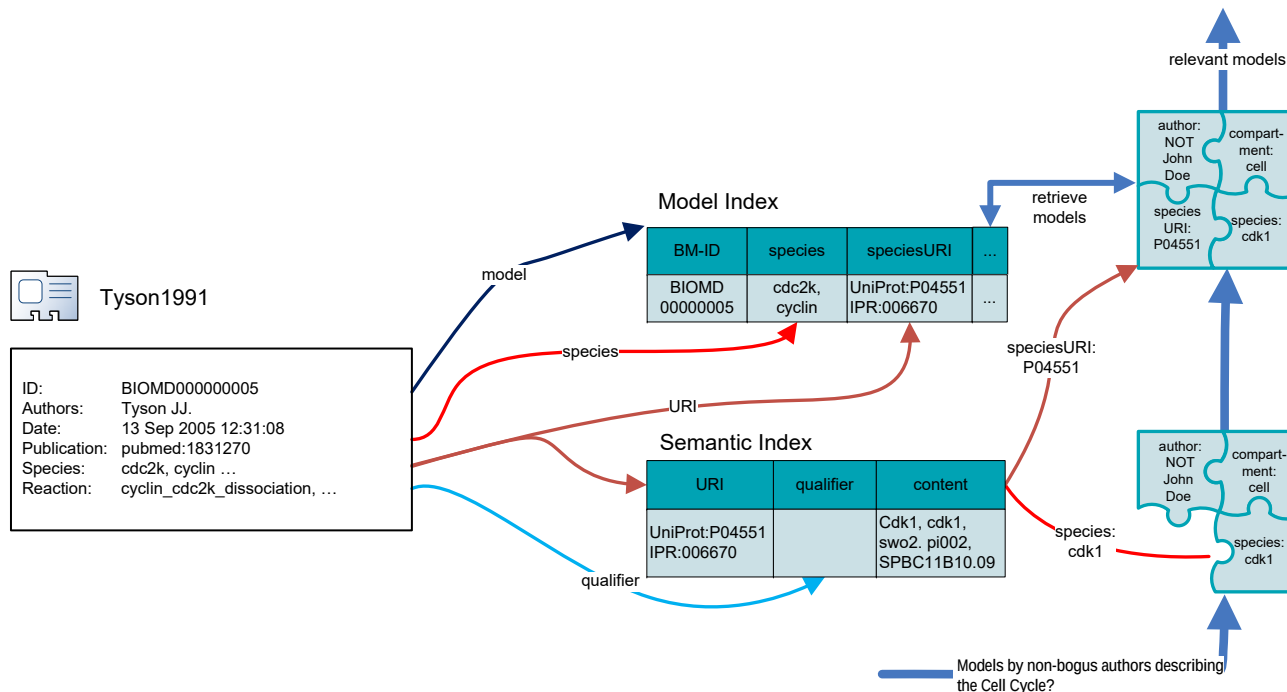
How similar are these two models with respect to structure?

Which models contain reactions with 'ATP' as reactant and 'ADP' as product?

Find good candidates for features describing my model set.

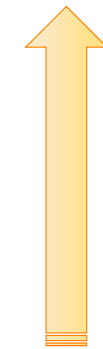
Which are the most frequently used GO annotations in my model set?

Systembiologisches Datenmanagement: Retrieval und Bewertung (MORRE)



(Abb. angelehnt an [Henkel et al \(2010\)](#))

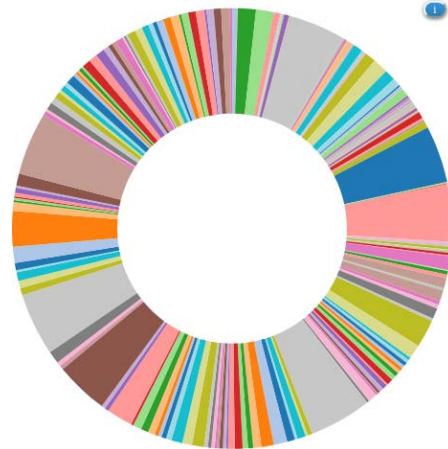
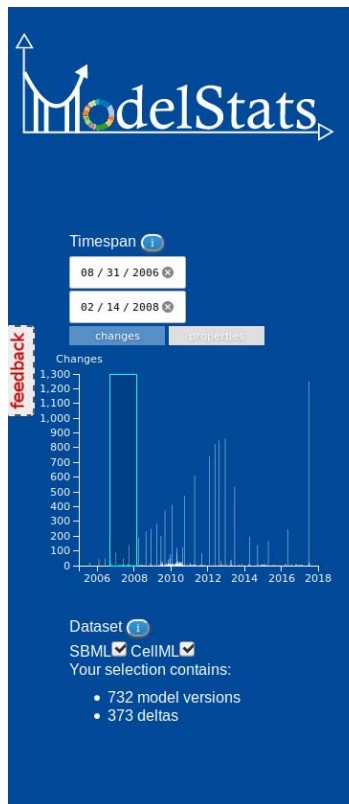
Rank	BioModels ID	Name	Publication ID	Last Modified
1. (0.9071)	BIOMD0000000144	Calzone2007_CellCycle	17667953	2008-01-21T14:59:57+00:00
2. (0.6057)	BIOMD0000000007	Novak1997_CellCycle	9256450	2009-10-15T16:07:54+00:00
3. (0.5662)	BIOMD0000000195	Tyson2001_Cell_Cycle_Regulation	11371178	2009-03-16T14:37:30+00:00
4. (0.5681)	BIOMD0000000005	Tyson1991_CellCycle_6var	1831270	2010-02-12T14:00:50+00:00



Show me models of the Cell Cycle, not by John Doe that contain cdk1 and a compartment cell!

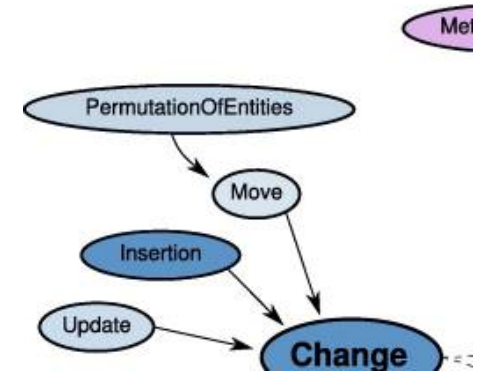
Lucene: species:cdk1, compartment:cell, ...

Analysen: Dokumentation von Änderungen



Comparison of Models

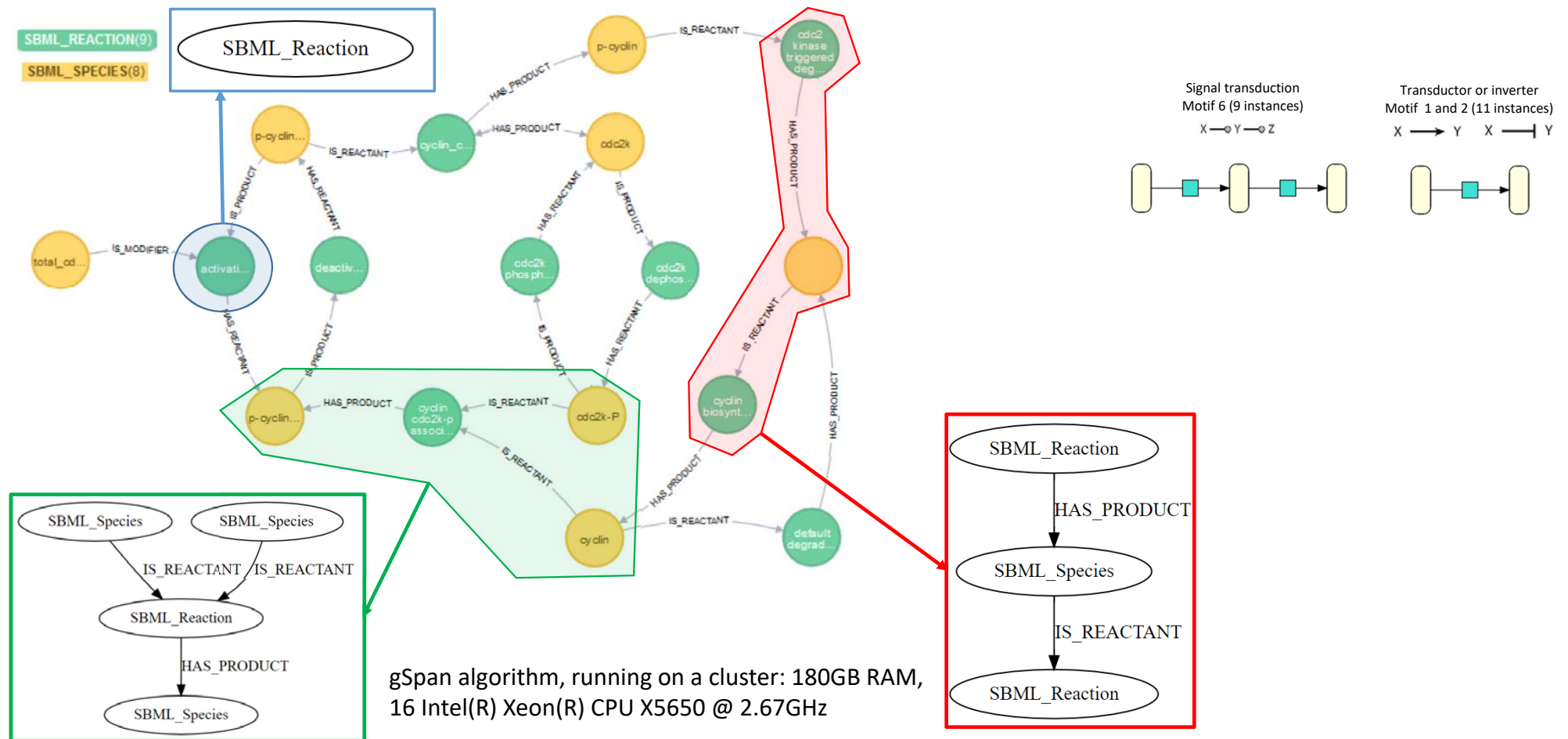
Model	Feist2006_methanogenesis_OptiMethanol	
Version	2006-10-03	2007-01-05
Date	3.9.2006	5.0.2007
Curated	false	false



How often did this model change, when and why?

<https://most.bio.informatik.uni-rostock.de/>

Analysen: Identifikation von häufigen Mustern



Analysen: Modellähnlichkeiten

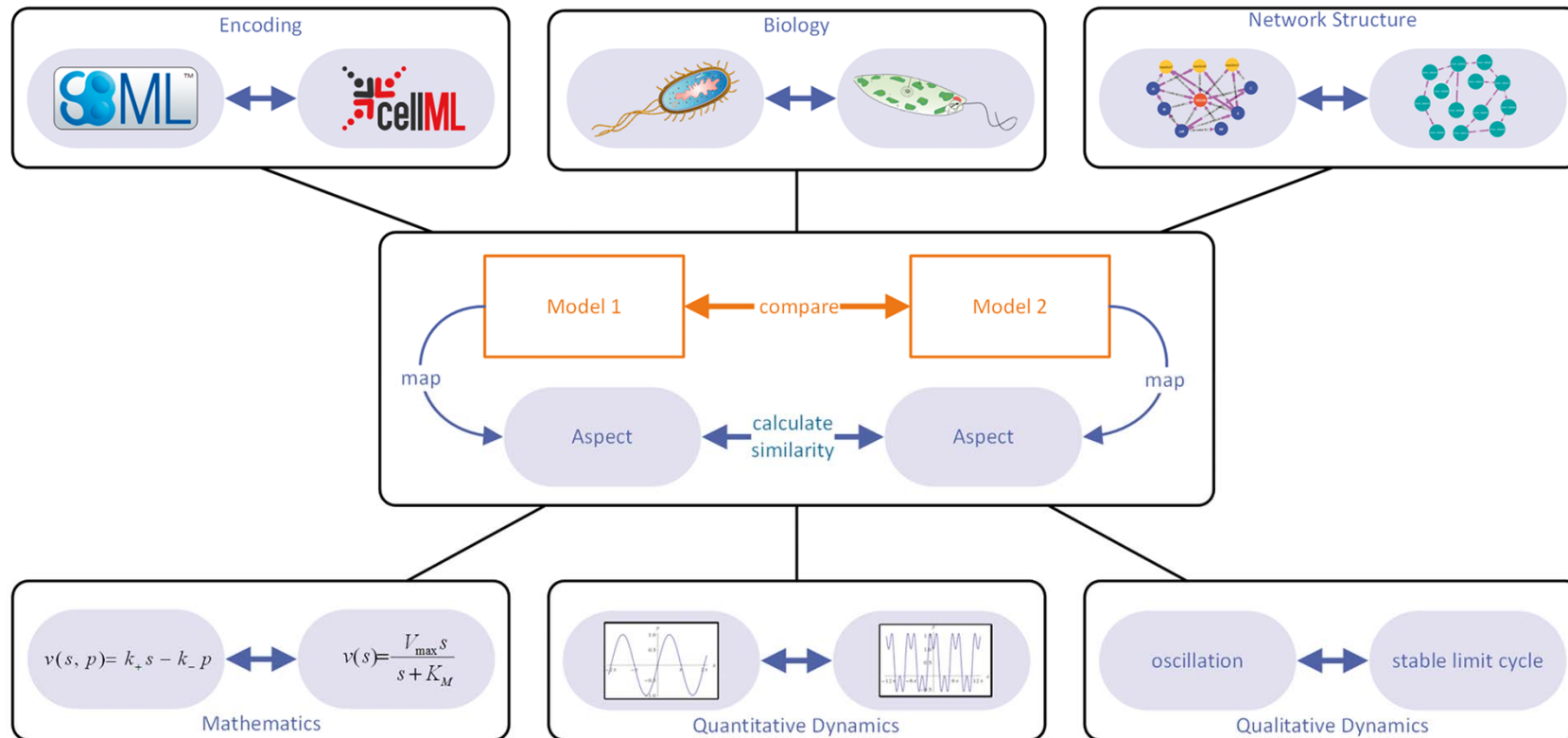


Abb.: [Henkel et al \(2017\)](#)

Analysen: Modellqualität

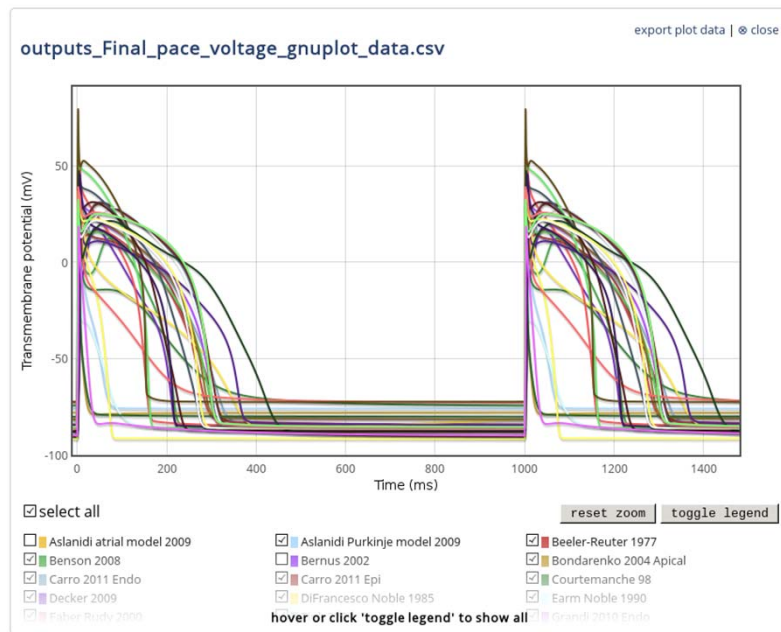
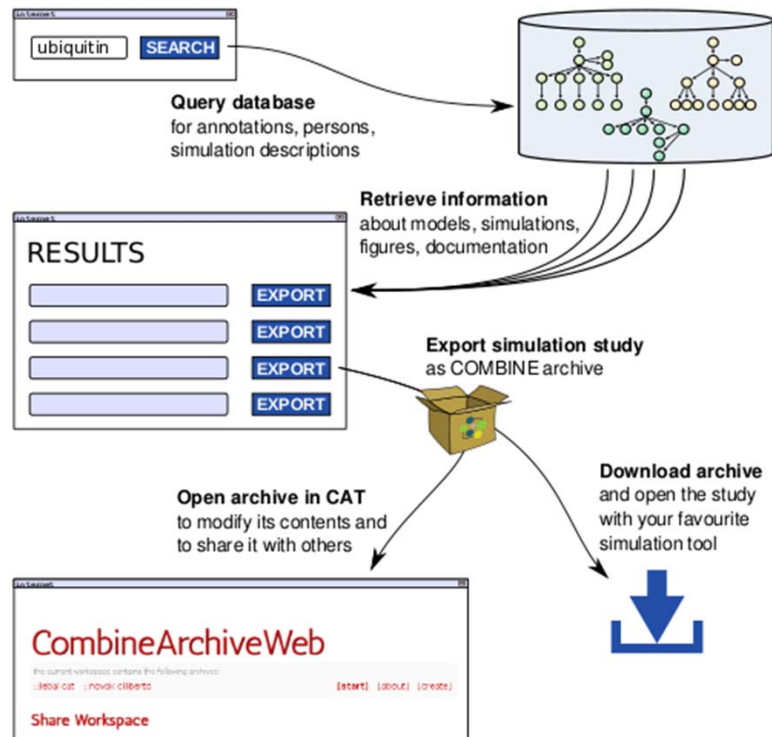


Abb.: Electrophysiology Web Lab, [Cooper et al \(2016\)](#)

Zusammenfassung



Zugreifbar

Mit anderen Standards verknüpfbar

Auffindbar

Wiederverwendbar

In verschiedenen Software-Werkzeugen nutzbar

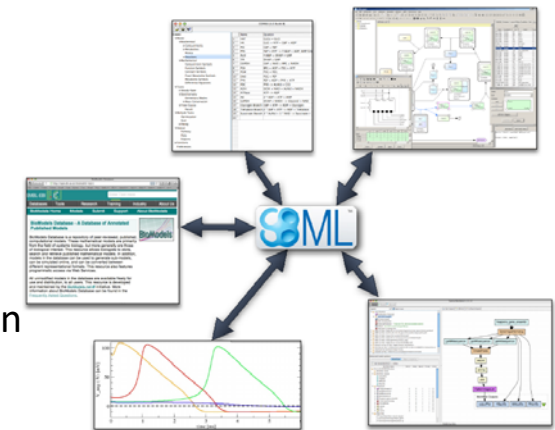
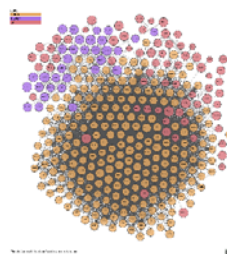
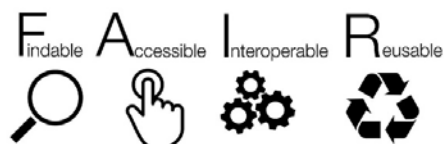


Abb: [Waltemath and Scharm, BTW \(2015\)](#) (links); M. Hucka, [slideshare](#) (rechts)



Und die Aussichten? MORRE Medical Informatics



miracum

Medical Informatics in Research and Care in University Medicine

Standardisierung und Wiederverwendung

FAIRDOM HUB

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⚙

Dagmar Waltemath ▾

[Home](#) / [Projects Index](#) / GMDS Project Group FAIR Data Infrastructures



GMDS Project Group FAIR Data Infrastructures

Overview

Request membership

The GMDS project group bundles activities for health-related FAIR data infrastructures in the fields of biomedical research, clinical data management and medical informatics in Germany. It aims at providing a platform for information exchange about best practice for and implementation of FAIR data management in these fields and constructing a network of FAIR data managements providers in these fields. Through bridging between providers and potential users of such data management platforms within the GMDS it is expected that user requirements are better integrated in the development cycle. Joint activities such as workshop and training events help to synergize

Programme: [German Association for Medical Informatics, Biometry and Epidemiology \(GMDS\)](#)

SEEK ID: <https://fairdomhub.org/projects/133>

Public web page: *Not specified*

Organisms: *No Organisms specified*

FAIRDOM PALs: *No PALs for this Project*

Project administrators: [Martin Golebiewski](#), [Benjamin Löhnhardt](#)

Project created: 17th Jan 2019

Related items

People (7)

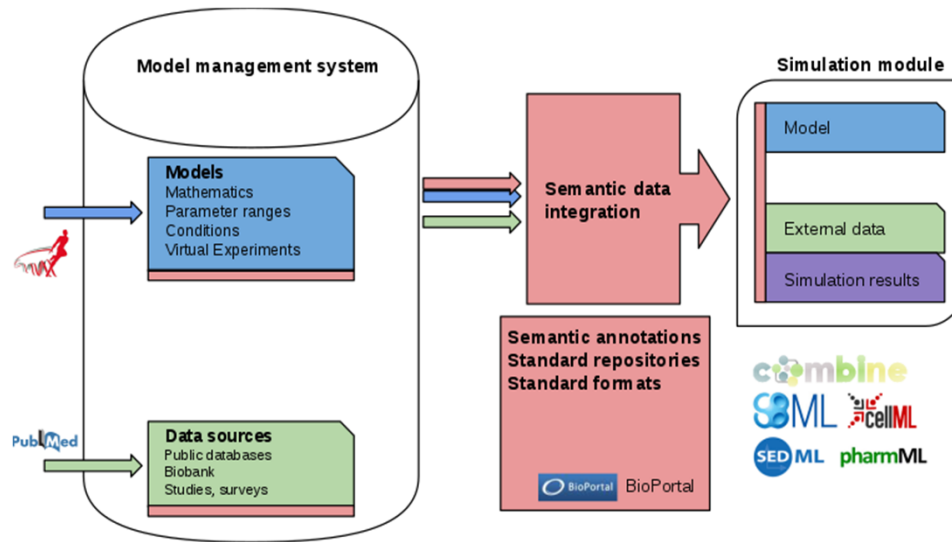
Institutions (3)

Events (0+1)

Documents (0+2)

<https://fairdomhub.org/projects/133>

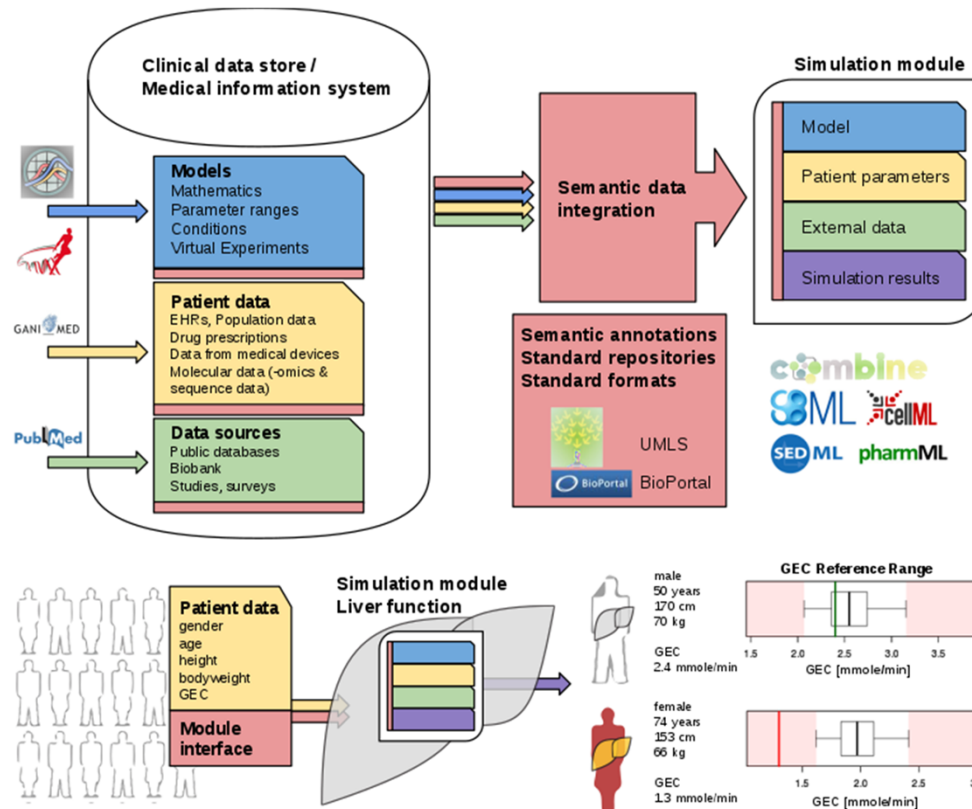
Integration Modelle und klinische Daten



Dr. Matthias König
LiSyM - Systems Medicine of the Liver
<https://livermetabolism.com/>

Abb.: [Koenig et al. \(2016\)](#) ODLS, Halle (Saale)

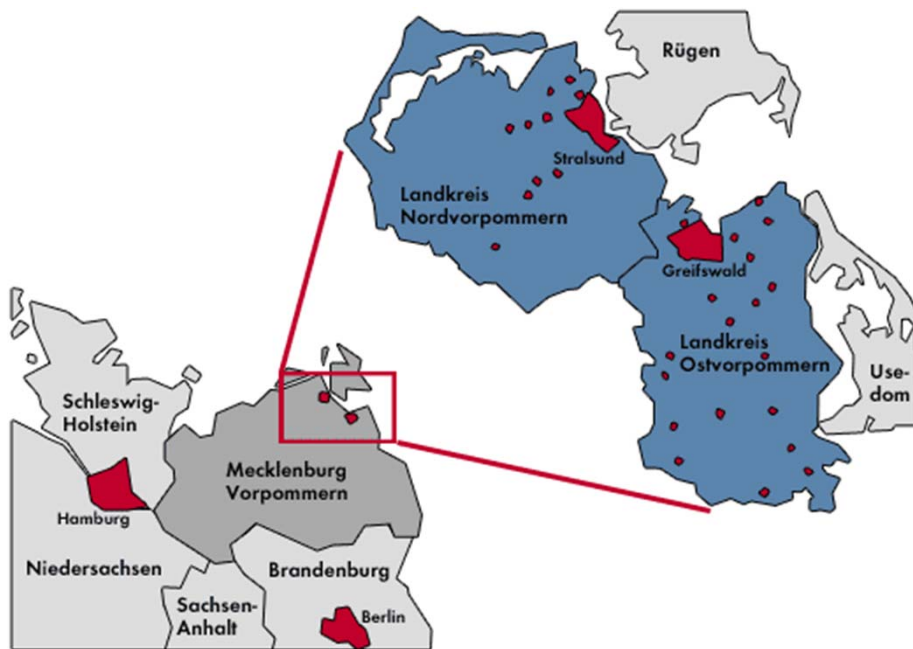
Integration Modelle und klinische Daten



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<https://livermetabolism.com/>

Abb.: [Koenig et al. \(2016\)](#) ODLS, Halle (Saale)

Datensuche, *-retrieval* und -ähnlichkeit

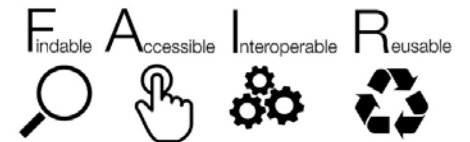


SHIP-Studie, Quelle: <http://www2.medizin.uni-greifswald.de/cm/fv/ship/studienbeschreibung/>

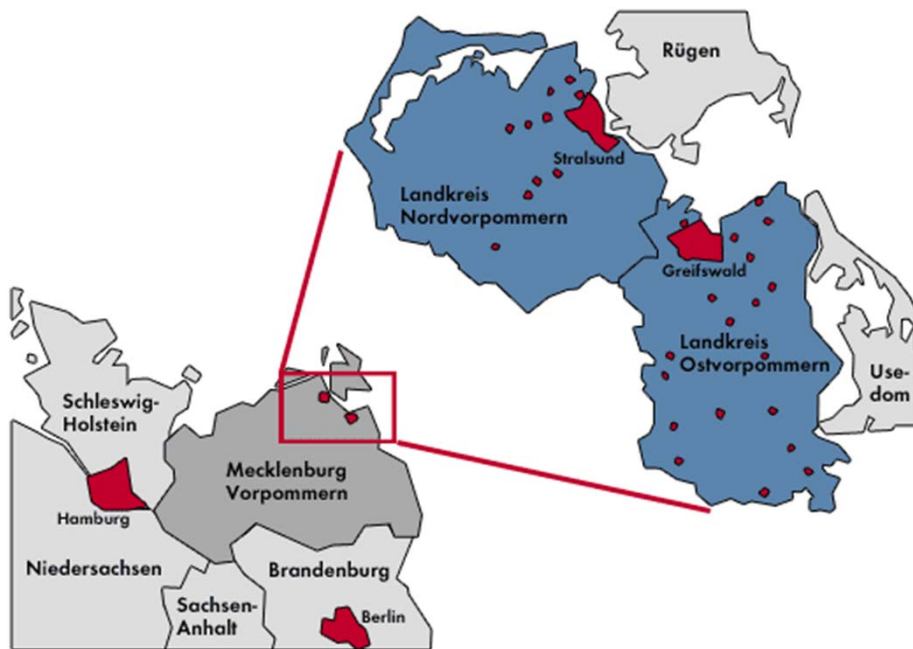


NAKO, Quelle: <https://nako.de/studienteilnehmer/studienzentren/>

KAS+



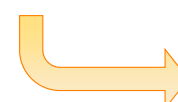
Metadaten-Extraktion



SHIP-Studie, Quelle: <http://www2.medizin.uni-greifswald.de/cm/fv/ship/studienbeschreibung/>



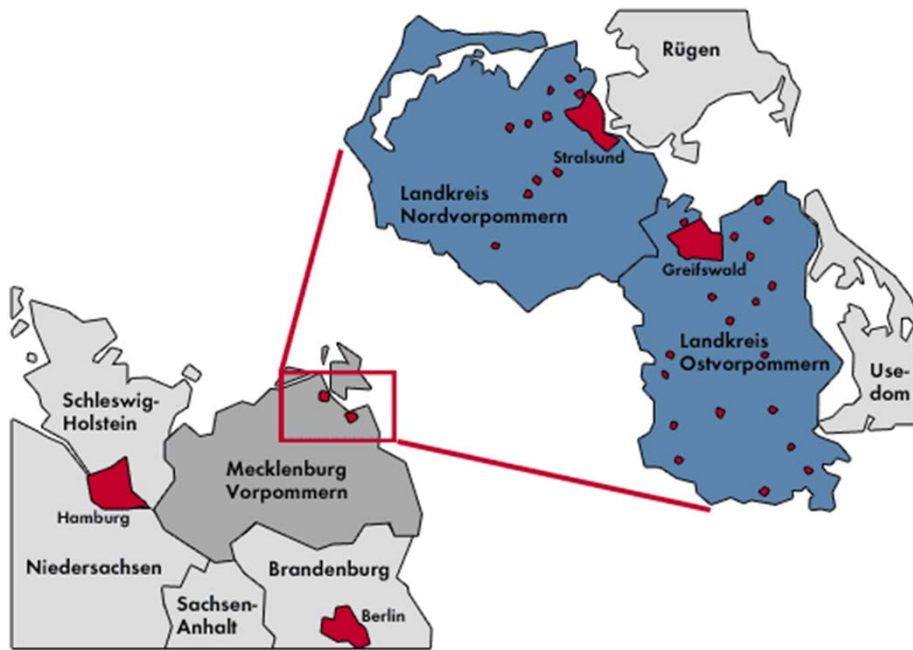
NAKO, Quelle: <https://nako.de/studienteilnehmer/studienzentren/>



KAS+



Semantische Anreicherung



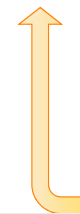
SHIP-Studie, Quelle: <http://www2.medizin.uni-greifswald.de/cm/fv/ship/studienbeschreibung/>



NAKO, Quelle: <https://nako.de/studienteilnehmer/studienzentren/>



KAS+



Metadata on data availability,
analysis options and collaboration
options

<https://www.medizininformatik-initiative.de/en/metadata-data-availability-analysis-options-and-collaboration-options>

MIRACUM - Ausbildung



Whole Cell summer school, Rostock



Data citation & integration, Rostock



Whole Cell 2, Salt Lake City, US



Kinetics on the move,
Heidelberg



Drawing SBGN Maps, Newcastle, UK

Vielen Dank für Ihre Aufmerksamkeit



Dagmar Waltemath

 [0000-0002-5886-5563](https://orcid.org/0000-0002-5886-5563)

 [@dagmarwaltemath](https://twitter.com/dagmarwaltemath)

 <https://semsproject.github.io/>



N.N: Scientific Programmer, Graph Databases

N.N: Biomedical Data Integration

Praktika, Abschlussarbeiten,
Kooperationen, Besucher ...
Herzlich Willkommen!

Software: [MOST](#) [PMR2](#) [JWS Online Simulation](#) [SED-ML Webtools](#)

[Cardiac Electrophysiology Web Lab](#) [FAIRDOMHub](#) [BioModels Database](#)

the  **2019**
Computational Modeling in Biology NETwork

Heidelberg, Germany

15. – 19. Juli 2019

Confirmed Keynote Speakers

- **Carole Goble**, University of Manchester (UK)
- **Peter Hunter**, University of Auckland (New Zealand)
- **Ursula Kummer**, University of Heidelberg (Germany)
- **Thomas Lemberger**, Chief Editor Molecular Systems Biology and Deputy Head EMBO Press, Heidelberg (Germany)

Confirmed Invited Speakers

- **Niklas Blomberg**, Director ELIXIR network, Hinxton (UK) - tentatively confirmed
- **Akira Funahashi**, Keio University, Yokohama (Japan)
- **Michael Hucka**, California Institute of Technology, Pasadena, CA (USA)
- **Sarah Keating**, University of Heidelberg (Germany)
- **Matthias König**, Humboldt University Berlin (Germany)
- **Caroline Mendonça Costa**, King's College London (UK)
- **Manuel Porcar Miralles**, Institute for Integrative Systems Biology (I²SysBio), València (Spain)
- **Chris Myers**, University of Utah, Salt Lake City, UT (USA)
- **David Nickerson**, University of Auckland (New Zealand)
- **Herbert Sauro**, University of Washington, Seattle, WA (USA)
- **Judith Wodke**, Humboldt University Berlin (Germany)

http://co.mbine.org/events/COMBINE_2019



EU-STANDS4PM
standards for personalised medicine