The 2019 COMBINE MEETING

Heidelberg
15-19 July 2019

Heidelberg Institute for Theoretical Studies

Welcome to Heidelberg!

In 2010, the first *COMBINE Forum* was held in Edinburgh (UK). Since then, the meeting took place as the annual meeting of the whole COMBINE community. We are very proud to host the tenth COMBINE Forum in Heidelberg this year at the Heidelberg Institute for Theoretical Studies (HITS) from July 15th to July 19th, 2019. More than 100 guests from around the globe will celebrate with us, exchanging their ideas, approaches and implementations for improved data and modelling standards in the life sciences. We will as well discuss further needs for standardization and harmonization in order to further improve data and model interoperability. A combination of keynote lectures, invited talks and interactive breakout discussions, as well as contributed talks, posters and lightning talks, selected from submitted abstracts, provides the basis for the meeting, offering diverse formats to work on interoperability problems.

One special focus this year is on the standardization need in systems medicine, which has been recognized as a necessity for computer-assisted personalized medicine. To direct the scientific communitys attention to this topic, the *European standardization framework for data integration and data-driven in silico models* (EU-STANDS4PM) organizes a workshop as part of COMBINE 2019.

Also, reproducibility in modelling is a main topic this year, as reflected by several sessions and workshops, like the *FAIRDOM PALs and user workshop*, the inaugural meeting of the *Model eXchange consortium* and breakout sessions on data and model reproducibility, as well as on metadata specifications. Besides these focus themes, also sessions, workshops and breakout discussions around single standards, their further development and their interoperability help to advance the standardization, standing in the tradition of COMBINE.

We invite you to celebrate the tenth anniversary of the COMBINE Forum this year with us and wish you a productive meeting, fruitful discussions and a wonderful time in Heidelberg.

Martin Golebiewski & Dagmar Waltemath
(on behalf of the organizing team of COMBINE 2019)

Funding is gratefully provided by:

Welcome by the HITS management

On behalf of the HITS management, we are pleased to welcome all delegates and visitors to the campus for the 10th COMBINE meeting which runs from 15-19 July at the Studio Villa Bosch, right next to the Heidelberg Institute for Theoretical Studies (HITS).

There is some history of COMBINE at HITS. After our institute was founded by Klaus Tschira and Andreas Reuter in 2010, the following year already saw the hosting of the second meeting at HITS. It was a major effort for the young institute as it was then, since COMBINE has been the combined conference on standards in computational modelling of biological systems.

The COMBINE community has returned to HITS stronger than ever for its 10th anniversary meeting.

We are delighted that we will be host to this event again and we hope you will join us to make this anniversary meeting a memorable event.

Dr. Gesa Schönberger (HITS Managing Director) &
Priv.-Doz. Dr. Wolfgang Müller (HITS Scientific Director)

About HITS

The Heidelberg Institute for Theoretical Studies (HITS) was established in 2010 by the physicist and SAP co-founder Klaus Tschira (1940-2015) and the Klaus Tschira Foundation as a private, non-profit research institute. HITS conducts basic research in the natural sciences, mathematics and computer science, with a focus on the processing, structuring, and analyzing of large amounts of complex data and the development of computational methods and software. The research fields range from molecular biology to astrophysics. The shareholders of HITS are the HITS-Stiftung, which is a subsidiary of the Klaus Tschira Foundation, Heidelberg University and the Karlsruhe Institute of Technology (KIT). HITS also cooperates with other universities and research institutes and with industrial partners. The base funding of HITS is provided by the HITS Stiftung with funds received from the Klaus Tschira Foundation. The primary external funding agencies are the Federal Ministry of Education and Research (BMBF), the German Research Foundation (DFG), and the European Union.

About COMBINE

Standards for exchange of scientific data are critical to the development of any field. They enable researchers and practitioners to transport information reliably, to apply a variety of tools to their problems, and to reproduce scientific results. Over the past two decades, a range of standards have been developed to facilitate the exchange and reuse of information in the domain of representation and modeling of biological systems, especially in the fields of systems biology and systems medicine. These standards are complementary, so the interactions between their developers increased over time. By the end of the last decade, the research community decided that more interoperability is required between the standards, and that common development is needed to make better use of effort, time, and money devoted to these activities.

As a consequence, the COmputational MOdeling in Biology NEtwork (COMBINE) was created beginning of 2010 to enable the sharing of resources, tools, and other infrastructure, and to coordinate standardization efforts for modeling in biology. COMBINE began with four core standards, and it has since expanded to eight, and coordinates with a number of other related standardization efforts. COMBINE brings standard communities together around activities that are mutually beneficial. These activities include making specification documents available from a common location, providing a central point of contact, and organizing regular face-to-face meetings.

To this end, the COMBINE network organizes an annual conference style meeting (the COMBINE Forum) and annual hackathon style events called HARMONY (Hackathon on Resources for Modeling in Biology), as well as tutorials at the International Conference on Systems Biology (ICSB) and related meetings.

Contact us

Website: `http://co.mbine.org/`
Get in touch with the editors: combine-coord@googlegroups.com

Contents

Welcome to Heidelberg! **iii**
Funding is gratefully provided by: . . . iv
Welcome by the HITS management . . . v
About HITS . . . v

Conference venue **1**
Directions . . . 1
Room names and location . . . 2
Conference Dinner . . . 2

Meeting Agenda **3**

Keynote Talks **13**
Computational Physiology and the Physiome Project (***Peter Hunter***) . . . 13
Implementing Open Science in publishing (***Thomas Lemberger***) . . . 13
Modeling projects across platforms - the reality and how reality should be (***Ursula Kummer***) . . . 14
Let's go on a FAIR asset management safari (***Carole Goble***) . . . 14
From data via models to personalized medicine - An example in Pediatric Oncology (***Norbert Graf***) . . . 15

Invited Talks **17**
The History of COMBINE (***Michael Hucka***) . . . 17
How (not) to Apply (COMBINE) Standards in Agent-Based Modeling (***Judith Wodke***, *Jens Hahn, Jorin Diemer, Edda Klipp*) . . . 17
Computational modeling of liver function tests - Stratification and individualization based on semantic annotations of models and data (***Matthias König***, *Jan Grzegorzewski*) . . . 18
Research software engineers and their role for open and reproducible research (***Heidi Seibold***) . . . 19
A Standard Enabled Workflow for Synthetic Biology (***Chris Myers***) . . . 20
BIOROBOOST: A last chance for standardisation in Biology? (***Manuel Porcar Miralles***) . . . 20
The Center for Reproducible Biomedical Modeling (***Herbert Sauro***,*Michael L. Blinov, John H. Gennari, Arthur P. Goldberg, Jonathan R. Karr, Ion I.Moraru, David P. Nickerson*) . . . 21

A personalized modeling pipeline for cardiac electrophysiology simulations of cardiac resynchronization therapy in infarct patients (***Caroline Mendonça Costa****, Aurel Neic, Eric Kerfoot, Bradley Porter, Benjamin Sieniewicz, Justin Gould, Baldeep Sidhu, Zhong Chen, Gernot Plank, Christopher A. Rinaldi, Martin J. Bishop, Steven A. Niederer*) 22

CellDesigner: A modeling tool for biochemical networks (***Akira Funahashi***) 23

Virtual Cell: Modeling and Visualization of Reaction Rules (***Michael Blinov***) 23

EU-STANDS4PM: A pan-European Expert Forum joined forces to tackle the complexity of big data integration for in silico methodologies in personalised medicine (***Marc Kirschner***) 25

Standards in Biobanking (***Petr Holub***) 25

Standards for Clinical Data and Systems Medicine (***Søren Brunak***) . . . 26

A Bird's Eye view of Legal and Ethical aspects of EU-STANDS4PM (***Katharina Ó Cathaoir***) 26

In silico medicine and the VPH Institute: bringing the community together and the field forward (***Liesbet Geris***) 27

Semantic annotation in the Physiome Model Repository (***David Nickerson****, Dewan Sarwar, Tommy Yu, Anand Rampadarath, Koray Atalag*) 28

Gene Ontology Causal Activity Modeling (GO-CAM) (***Huaiyu Mi****, Paul D. Thomas, David P. Hill, David Osumi-Sutherland, Kimberly Van Auken, Seth Carbon, James P. Balhoff, Laurent-Philippe Albou, Benjamin Good, Pascale Gaudet, Nomi L. Harris, Suzanna E. Lewis, Christopher J. Mungall*) 28

Sharing standardised models and data on the Open Source Brain platform (***Padraig Gleeson***) 29

Multi-method modelling of synaptic plasticity and the challenges it brings (***Melanie Stefan***) 29

Contributed Talks **31**

Analyzing Genetic Circuits for Hazards and Glitches (***Pedro Fontanarrosa****, Hamid Hosseini; Amin Borujeni, Yuval Dorfan, Chris Voigt, Chris Myers*) 31

SBOL and its applicability in partially and fully automated design workflows: Three success stories (***Ernst Oberortner***) 31

Physiome - Publish your models curated for reproducibility and reusability to increase research quality for everyone (***Karin Lundengård****, Peter Hunter, David Nickerson*) 32

Reproducibility in model construction, validation and analysis workflows in systems biology projects; Xylose metabolism in Caulobacter crescentus as a case study, using JWS Online and the FAIRDOMHub (***Jacky Snoep****, Lu Shen, Bertina Siebers, Dawie van Niekerk, Wolfgang Müller, Carole Goble*) 33

Causal, Mechanistic Pathway Based Analysis of -Omic Profiles (***Emek Demir***, *Özgün Babur, Funda Durupinar Babur, Hannah Manning, Michal Grzadkowski, Joseph Estabrook, Olga Nikolova, Kevin Watanabe-Smith*) 34
Predictive in-silico multiscale analytics to support cancer personalized diagnosis and prognosis, empowered by imaging biomarkers (***Polyxeni Gkontra***, *Leonor Cerd Alberich, Gracia Mart Besa, Luis Mart Bonmat*) 34
Datanator: Tools for Aggregating Data for Large-Scale Biomodeling (***Yosef Roth***, *Zhouyang Lian, Saahith Pochiraju, Jonathan Karr*) 36
Simulation and Sensitivity Analysis for Large Kinetic Models in AMICI (***Fabian Fröhlich***) 36
OpenCOR: current status and future plans (***Alan Garny***, *David Brooks, Peter Hunter*) 37
Visualization of Part Use in SynBioHub (***Jeanet Mante***, *Zach Zundel, Chris Myers*) 37
PySB framework: Tools to build, calibrate and visualize biochemical models (***Oscar O. Ortega***, *Carlos F. Lopez*) 38
Visualization, Access, and Exploration of Biological Pathway Information from Pathway Commons (***Augustin Luna***, *Emek Demir, Igor Rodchenkov, Özgün Babur, Jeffrey Wong, Chris Sander, Gary Bader*) . . 38
ELIXIR Cloud & AAI: Standardised and Interoperable Services for Human Data Communities (***Susheel Varma***, *Shubham Kapoor, Ania Niewielska, Alexander Kanitz, Jinny Chien, Andrea Cristofori, Sarah Butcher, Foivos Gypas, Kevin Sayers, Juha Törnroos, Marco Tangaro, Giacinto Donvito, Yasset Perez-Riverol, Bjorn Gruning, Jennifer Harrow, Jonathan Tedds, Salvador Capella, Tommi Nyrönen, Steven Newhouse*) 40
BioModels Parameters: A resource to search and access parameters from published systems models (***Sheriff Rahuman***, *Chinmay Arankalle, Mihai Glont; Tung Nguyen, Henning Hermjakob*) 41
Two universes one world: Community standards vs. formal standards in systems biology and systems medicine (***Martin Golebiewski***) . . . 41
Model curation and annotation (***Anand Rampadarath***) 42
Identifiers.org Compact Identifiers for robust data citation (***Henning Hermjakob***, *Sarala Wimalaratne, Manuel Bernal Llinares, Javier Ferrer, Nick Juty*) 42
Principles for declarative multicellular modelling (***Jörn Starruß***, *Walter de Back, Martin Golebiewski, Lutz Brusch*) 43
Flapjack: an open-source tool for storing, visualising, analysing and modelling kinetic gene expression data (***Guillermo Yanez***, *Isaac Nunez, Tamara Matute, Fernan Federici, Timothy Rudge*) 43

Workshops and Breakouts **45**
Sharing experiences in building a standards community (*Dagmar Waltemath, Mike Hucka*) 45

SED-ML Script: a Proposal (*Lucian Smith, Herbert Sauro*) 45
COMBINE as Legal Entity (*Martin Golebiewski, Herbert Sauro*) 46
SBGN workshop (*Falk Schreiber, Michael Blinov*) 47
MIRIAM 2 & the OMEX Metadata Specification (*Dagmar Waltemath, David Nickerson*) 47
SBOL breakout (*Ernst Oberortner, Chris Myers*) 48
Model eXchange consortium: Inaugural meeting (*Rahuman Sheriff, Henning Hermjakob*) 48
EU-STANDS4PM workshop (*Marc Kirschner, Martin Golebiewski*) 49
Something old, something new: constraint-based modelling and SBML (*Brett G. Olivier, Frank T. Bergmann*) 50
SBML L3 Packages - An Introduction to SBML packages (*Sarah Keating*) 50
FAIRDOM PALs and User Workshop (*Olga Krebs*) 51
Model eXchange consortium: Inaugural meeting (*Rahuman Sheriff, Henning Hermjakob*) 51

Lightning Talks **53**
Systems Biology Graphical Notation (SBGN) (***Michael Blinov***) 53
SBML Level 3 Version 2 and SBML Level 3 packages (***Michael Hucka***) . 53
WebProv: A web-based tool to access, store, and display provenance information of simulation models (***Kai Budde***, *Jacob Smith, Andreas Ruscheinski, Adelinde M. Uhrmacher*) 54
MIRIAM 2 & the OMEX Metadata Specification (***Dagmar Waltemath***, *David Nickerson*) 54
A Virtual Cohort of Heart Failure Patients Four-chamber Heart Meshes for Cardiac Electro-mechanics Simulations (***Marina Strocchi***, *Christoph Augustin, Matthias Gsell, Orod Razeghi, Anton Prassl, Edward Vigmond, Jonathan Behar, Justin Gould, Sidhu Baldeep, Aldo Rinaldi, Martin Bishop, Gernot Plank, Steven Niederer*) 55
WebLab update (***Sarah Keating***) 55
NESTML: A domain-specific language for biologically realistic neuron and synapse models (***Charl Linssen*** , *Jochen M. Eppler, Abigail Morrison*) 56
BioModels 2019 (***Mihai Glont***, *Henning Hermjakob, Rahuman Sheriff, Krishna Tiwari, Tung Nguyen, Manh Tu Vu*) 57
Minibatch optimization: a method for training mechanistic models using large data sets (***Paul Stapor***, *Leonard Schmiester, Jan Hasenauer, Daniel Weindl*) 57
Modelling pancreas - Computational modelling and analysis of altered metabolism in the pancreas and its relationship to disease (***Deepa Maheshvare*** *Soumyendu Raha, Matthias König, Debnath Pal*) . . . 58
PK-DB 1.0: a pharmacokinetics database for individualized and stratified modeling (***Jan Grzegorzewski***, *Matthias König*) 58
Standardised meta-data in Hospital Information Systems unlock clinical data for research purposes A real-world example (*Robert Gött, Kai Fitzer, Torsten Leddig,* ***Dagmar Waltemath***, *Thomas Bahls*) . . . 59

Development of python visualization package DNAplotlib (***Sunwoo Kang***) 60
Cy3SBML: a Cytoscape app for SBML (***Matthias König***, *Nicolas Rodriguez, Andreas Dräger*) 60

Posters **61**
Review of software tools and data sources supporting the Systems Biology Graphical Notation (SBGN) standard (***Michael Blinov***, *Adrien Rougny, Andreas Dräger, Vasundra Touré, Ugur Dogrusoz, Alexander Mazein*) 61
WebProv: A web-based tool to access, store, and display provenance information of simulation models (***Kai Budde***, *Jacob Smith, Andreas Ruscheinski, Adelinde M. Uhrmacher*) 61
Comprehensive mathematical modeling of sphingolipid metabolism by integration of lipidomics and proteomics data (***Canan Has***, *Thorsten Hornemann, Robert Ahrends*) 62
The Systems Biology Graphical Notation: a standardised representation of biological maps (***Andreas Dräger***, *Vasundra Touré, Alexander Mazein, Adrien Rougny, Ugur Dogrusoz, Michael Blinov, Augustin Luna*) 62
AMICI and PESTO - A strong couple for simulation and parameter estimation in computational and systems biology (***Erika Dudkin***, *Paul Stapor, Daniel Weindl, Benjamin Ballnus, Sabine Hug, Carolin Loos, Anna Fiedler, Sabrina Krause, Sabrina Hroß, Yannik Schälte, Leonard Schmiester, Dantong Wang, Elba Raimndez Alvarez, Simon Merkt, Fabian Fröhlich, Jan Hasenauer*) 63
Analyzing Genetic Circuits for Hazards and Glitches (***Pedro Fontanarrosa***, *Hamid Hosseini; Amin Borujeni, Yuval Dorfan, Chris Voigt, Chris Myers*) 64
YoMoSt - Statistics for you local model versions (***Tom Gebhardt***, *Martin Scharm, Olaf Wolkenhauer*) 65
PK-DB 1.0: a pharmacokinetics database for individualized and stratified modeling (***Jan Grzegorzewski***, *Matthias König*) 65
EnzymeML - a SBML-based exchange format for biocatalytic data (***Colin Halupczok***, *Jürgen Pleiss*) 65
The JSBML project: a fully featured Java API for working with systems biology models (***Thomas M. Hamm***, *Nicolas Rodriguez, Roman Schulte, Leandro Watanabe, Ibrahim Y. Vazirabad, Victor Kofia, Chris J. Myers, Akira Funahashi, Michael Hucka, Andreas Dräger*) . 66
Identifiers.org Compact Identifiers for robust data citation (***Henning Hermjakob***, *Sarala Wimalaratne, Manuel Bernal Llinares, Javier Ferrer, Nick Juty*) 67
Experiences with Developing Digital Registries for Contraceptive Care using the Collaborative Requirements Development Methodology (***Esther Inau***) 67
Virtual patient (***Fedor Kolpakov***) 68

FAIRDOM approach for Systems Biology Data and Model Management (***Olga Krebs***, *Martin Golebiewski, Stuart Owen, Maja Rey, Natalie Stanford, Ulrike Wittig, Xiaoming Hu, Katy Wolstencroft, Jacky L. Snoep, Bernd Rinn, Wolfgang Müller, Carole Goble*) 69

NESTML: A domain-specific language for biologically realistic neuron and synapse models (***Charl Linssen*** , *Jochen M. Eppler, Abigail Morrison*) 69

Physiome - Publish your models curated for reproducibility and reusability to increase research quality for everyone (***Karin Lundengård***, *Peter Hunter, David Nickerson*) 70

Modelling pancreas - Computational modelling and analysis of altered metabolism in the pancreas and its relationship to disease (***Deepa Maheshvare*** *Soumyendu Raha, Matthias König, Debnath Pal*) . . . 70

Enhancing the computational based function annotation of thiamine diphosphate dependent enzymes (***Stephan Malzacher***, *Patrick Buchholz, Colin Halupczok, Saskia Bock, Dörte Rother, Jürgen Pleiss*) 70

Visualization of Part Use in SynBioHub (***Jeanet Mante***, *Zach Zundel, Chris Myers*) 71

Comprehensive Modelling Platform (***Lukrécia Mertová***, *Matej Troják, Jan Červený, Marek Havlı, Matej Hajna, Radoslav Doktor, Ondřej Lošták*) 71

PySB framework: Tools to build, calibrate and visualize biochemical models (***Oscar O. Ortega***, *Carlos F. Lopez*) 72

The Center for Reproducible Biomedical Modeling (***Anand Rampadarath***, *David Nickerson, Michael Blinov, John Gennari, Arthur Goldberg, Jonathan Karr, Herbert Sauro*) 72

Datanator: Tools for Aggregating Data for Large-Scale Biomodeling (***Yosef Roth***, *Zhouyang Lian, Saahith Pochiraju, Jonathan Karr*) 72

Standardizing Electronic Laboratory Notebooks to improve their integration with data from the biomedical domain (***Max Schröder***, *Dagmar Waltemath, Frank Krüger, Sascha Spors*) 73

Minibatch optimization: a method for training mechanistic models using large data sets (***Paul Stapor***, *Leonard Schmiester, Jan Hasenauer, Daniel Weindl*) 73

A Virtual Cohort of Heart Failure Patients Four-chamber Heart Meshes for Cardiac Electro-mechanics Simulations (***Marina Strocchi***, *Christoph Augustin, Matthias Gsell, Orod Razeghi, Anton Prassl, Edward Vigmond, Jonathan Behar, Justin Gould, Sidhu Baldeep, Aldo Rinaldi, Martin Bishop, Gernot Plank, Steven Niederer*) 74

SABIO-RK: kinetic data for systems biology (***Andreas Weidemann***, *Ulrike Wittig, Maja Rey, Wolfgang Müller*) 74

Flapjack: an open-source tool for storing, visualising, analysing and modelling kinetic gene expression data (***Guillermo Yanez***, *Isaac Nunez, Tamara Matute, Fernan Federici, Timothy Rudge*) 74

Standardised meta-data in Hospital Information Systems unlock clinical data for research purposes A real-world example (*Robert Gött, Kai Fitzer, Torsten Leddig,* ***Dagmar Waltemath****, Thomas Bahls*) . . . 75

Conference venue

COMBINE 2019 will be held at the conference facilities of Studio Villa Bosch in Heidelberg. The address is Schloss-Wolfsbrunnenweg 33, 69118 Heidelberg, Germany.

Directions

- **By plane:** You travel to the international airport of Frankfurt/Main. From there, you take the Lufthansa-Bus (leaving in front of terminal 1, section B) to Heidelberg or Mannheim/Heidelberg (depending on the time of the day). In approximately one hour it will bring you to the Crowne Plaza in Heidelberg. From there you can take a taxi for a 15 minute ride to Studio Villa Bosch in the Schloss-Wolfsbrunnenweg.

- **By train:** You travel to Heidelberg Hauptbahnhof. From there you can either take public transport, as mentioned below, or a taxi to the Studio Villa Bosch.

- **By bus:** You can reach HITS and Studio Villa Bosch directly with the bus number 30, the so called science-bus, which runs hourly from Monday to Friday. At Heidelberg main station you take the train S2 (direction Eberbach), S1 (direction Osterburken) or S5 (direction Eppingen Bahnhof) and get off at Heidelberg-Altstadt station. There you change to bus number 30, direction Schlierbach (HD), HITS. Please get off the bus at the bus stop "Villa Bosch".

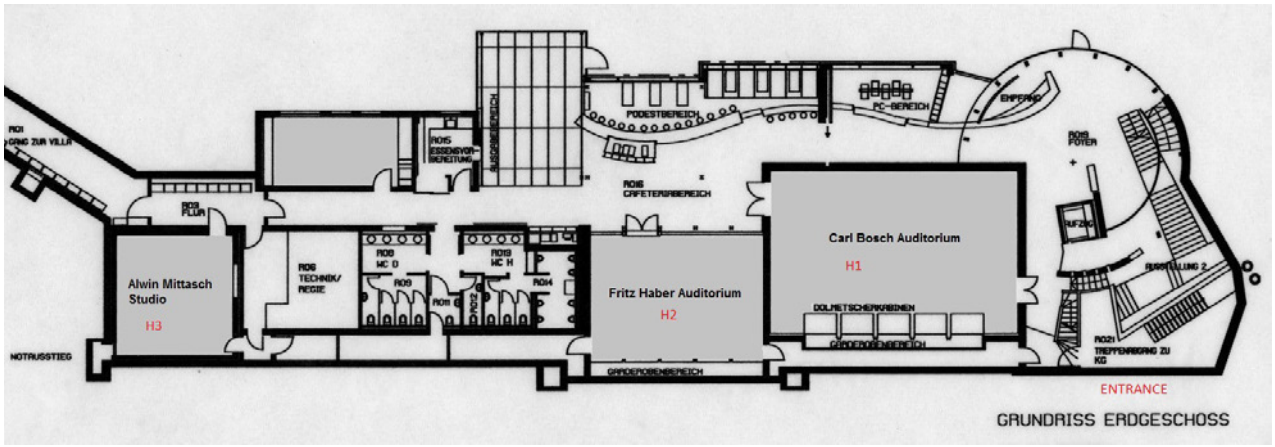
  At the main station you can also take:

  - bus number 32 (direction Universittsplatz). You get off at the bus stop Universittsplatz and change to bus number 30, direction Schlierbach (HD), HITS.
  - bus number 33 (direction Ziegelhausen, Kpfel). You leave at the bus stop Peterskirche and change to bus number 30, direction Schlierbach (HD), HITS.

- **By car:** You travel on the Autobahn to the Heidelberger Kreuz (Heidelberg crossing), from there on route A 656 directly to Heidelberg. At the end of the Autobahn you turn left and then right; you are now on B 37, which you will follow some minutes, until Heidelberg downtown ends (ca. 5 km). After a few hundred meters, you will see a pointer to HITS, which leads you upwards to the right, across the railway. Then turn left and follow the streets Am Rosenbusch and Hausackerweg, always climbing upwards the serpentine

curves. The Hausackerweg ends by joining the Schloss-Wolfsbrunnenweg at the Hotel Atlantic. Turn left, following the HITS pointer onto the Schloss-Wolfsbrunnenweg. 300 m further at your left you have reached the gateway to the Villa Bosch. The HITS campus is about 200 meters farther, on the left-hand side. Parking: in the garage Unter der Boschwiese, opposite to the Villa Bosch.

Room names and location



Conference Dinner

Restaurant 'S' Kastanie, Elisabethenweg 1 in Heidelberg

Wednesday, July 17th, 2019 - 19:00 - 23:00

Registered accompanying persons (payable IN CASH at the restaurant): 70 Euro

Meeting Agenda

Monday, July 15th 2019

time		Plenary	
Room:	Foyer	Carl Bosch Auditorium (H1)	
09:15-10:00	*Registration & Coffee*		
10:00 – 11:00		**Opening Session**; Chair: Martin Golebiewski (Heidelberg, D)	
10:00 - 10:05		Martin Golebiewski, HITS, Heidelberg (D)	Welcome by the host
10:05 - 10:20		Gesa Schönberger and Wolfgang Müller, HITS, Heidelberg (D)	Welcome addresses from the HITS Management
10:20 - 11:00		**Michael Hucka**, California Institute of Technology, Pasadena, CA (USA)	The History of COMBINE (invited talk)
11:00 – 12:00		**HITS Colloquium**; Chair: Wolfgang Müller (Heidelberg, D)	
11:00 - 12:00		**Peter Hunter (Auckland, New Zealand)**	**Keynote**: Computational Physiology and the Physiome Project
12:00 - 13:00	*Lunch*		
13:00 – 15:00		**COMBINE Colloquium**; Chair: Martin Golebiewski (Heidelberg, D)	
13:00 - 13:45		**Thomas Lemberger** (EMBO press, D)	**Keynote:** Implementing Open Science in publishing
13:45 - 14:30		**Ursula Kummer**, University of Heidelberg (D)	**Keynote:** Modeling projects across platforms - the reality and how reality should be
14:30 - 15:00		**Lightning talks (1)**	*3 min talks selected from the submitted abstracts*
15:00 - 15:30	*Poster Session & Coffee Break*		
15:30 – 17:30		**de.NBI Colloquium**; Chair: Dagmar Waltemath (Greifswald, D)	
15:30 - 16:00		**Judith Wodke**, Humboldt University Berlin (D)	How (not) to Apply (COMBINE) Standards in Agent-Based Modeling
16:00 - 16:30		**Matthias König**, Humboldt University Berlin (D)	Computational modeling of liver function tests - Stratification and individualization based on semantic annotations of models and data
16:30 - 17:00		**Heidi Seibold**, Ludwig-Maximilians-Universität München (D)	Research software engineers and their role for open and reproducible research
17:00 - 17:30		**Lightning talks (2)**	*3 min talks selected from the submitted abstracts*
17:30 - 19:00	*Poster Session & Welcome Reception: 10 years COMBINE - Happy Birthday !*		

Tuesday, July 16th 2019

time		Plenary/Breakout session 1		Breakout session 2	Breakout session 3
Room:	Foyer	Carl Bosch Auditorium (H1)		Fritz Haber Auditorium (H2)	Alwin Mittasch Studio (H3)
09:30 – 11:10	**Session 1:**	**Synthetic Biology**; Chairs: Ernst Oberortner (Berkeley, CA, USA) & Chris Myers (Salt Lake City, UT, USA)			
09:30 - 10:00		**Chris Myers**, University of Utah, Salt Lake City, UT (USA)	A Standard Enabled Workflow for Synthetic Biology (invited talk)		
10:00 - 10:30		**Manuel Porcar Miralles**, Institute for Integrative Systems Biology, València (Spain)	BioRoboost: A last chance for standardisation in biology? (invited talk)		
10:30 - 10:40		Pedro Fontanarrosa, University of Utah, Salt Lake City, UT (USA)	Analyzing Genetic Circuits for Hazards and Glitches		
10:40 - 10:50		Ernst Oberortner, Lawrence Berkeley Nat. Laboratory (USA)	SBOL and its applicability in partially and fully automated design workflows: Three success stories		
10:50 - 11:05		all speakers of Session 1	Discussion		
11:05 - 11:30	***Poster Session & Coffee***				
11:30 – 13:00	**Session 2:**	**Reproducibility in Synthetic and Systems Biology**; Chairs: Dagmar Waltemath (Greifswald, D) & David Nickerson (Auckland, NZ)			
11:30 - 12:00		**Herbert Sauro**, University of Washington, Seattle, WA (USA)	The Center for Reproducible Biomedical Modeling (invited talk)		
12:00 - 12:10		Karin Lundengård, University of Auckland (NZ)	Physiome - Publish your models curated for reproducibility and reusability to increase research quality for everyone		
12:10 - 12:20		Jacky Snoep, Stellenbosch University (South Africa)	Reproducibility in model construction, validation and analysis workflows in systems biology projects; Xylose metabolism in Caulobacter crescentus as a case study, using JWS Online and the		
12:20 - 12:30		Emek Demir, Oregon Health and Science University, Portland (USA)	Causal, Mechanistic Pathway Based Analysis of -Omic Profiles		
12:30 - 12:40		Polyxeni Gkontra, La Fe Health Research Institute (IIS La Fe), Valencia (Spain)	Predictive in-silico multiscale analytics to support cancer personalized diagnosis and prognosis, empowered by imaging biomarkers		
12:40 - 13:00		all speakers of Session 2	Discussion		

time		Plenary/Breakout session 1	Breakout session 2	Breakout session 3
Room:	Foyer	Carl Bosch Auditorium (H1)	Fritz Haber Auditorium (H2)	Alwin Mittasch Studio (H3)
13:00 - 14:00	*Lunch*			
14:00 – 15:30	Session 3:	**Sharing experiences in building a standards community**; Chairs: Dagmar Waltemath (Greifswald, D) & Mike Hucka (Pasadena, CA, USA)	**Reproducibility - SED-ML Script: a Proposal**; Chairs: Herbert Sauro & Lucian Smith (Seattle, WA, USA)	
15:30 - 16:00	*Poster Session & Coffee*			
16:00 – 17:30	Session 4:	**COMBINE as Legal Entity**; Chairs: Martin Golebiewski (Heidelberg, D) & Herbert Sauro (Seattle, WA, USA)		
17:30 - 17:45		**Plenary Wrapup**		

18:30 - 20:30 *Guided Tour through the old town of Heidelberg (optional)*

Wednesday, July 17th 2019

time		Plenary/Breakout session 1		Breakout session 2	Breakout session 3
Room:	Foyer	Carl Bosch Auditorium (H1)		Fritz Haber Auditorium (H2)	Alwin Mittasch Studio (H3)
09:30 – 11:00	**Session 5:**	**Modeling Approaches and Tools**; Chairs: Matthias König (Berlin, D) & Melanie Stefan (Edinburgh, UK)			
09:30 - 10:00		**Caroline Mendonça Costa**, King's College London (UK)	A personalized modeling pipeline for cardiac electrophysiology simulations of cardiac resynchronization therapy in infarct patients (invited talk)		
10:00 - 10:10		Yosef Roth, Icahn School of Medicine at Mount Sinai, New York City, NY (USA)	Datanator: Tools for Aggregating Data for Large-Scale Biomodeling		
10:10 - 10:20		Fabian Fröhlich, Harvard Medical School, Boston, MA (USA)	Simulation and Sensitivity Analysis for Large Kinetic Models in AMICI		
10:20 - 10:30		Alan Garny, University of Auckland (NZ)	OpenCOR: current status and future plans		
10:30 - 10:45		all speakers of Session 5	Discussion		
10:45 - 11:15	***Poster Session & Coffee***				
11:15 – 13:00	**Session 6:**	**Visualization**; Chairs: Falk Schreiber (Konstanz, D) & Michael Blinov (Farmington, CT, USA)			
11:15 - 11:45		**Akira Funahashi**, Keio University, Yokohama (Japan)	CellDesigner: A modeling tool for biochemical networks (invited talk)		
11:45 - 12:15		**Michael Blinov**, UConn Health, Farmington, CT (USA)	Virtual Cell: Modeling and Visualization of Reaction Rules (invited talk)		
12:15 - 12:25		Jeanet Mante, University of Utah, Salt Lake City, UT (USA)	Visualization of Part Use in SynBioHub		
12:25 - 12:35		Oscar O Ortega, Vanderbilt University, Nashville, TN (USA)	PySB framework: Tools to build, calibrate and visualize biochemical models		
12:35 - 12:45		Augustin Luna, Harvard Medical School, Boston, MA (USA)	Visualization, Access, and Exploration of Biological Pathway Information from Pathway Commons		
12:45 - 13:00		all speakers of Session 6	Discussion		
13:00 - 14:00	***Lunch***				

time		Plenary/Breakout session 1		Breakout session 2	Breakout session 3
Room:	Foyer	Carl Bosch Auditorium (H1)		Fritz Haber Auditorium (H2)	Alwin Mittasch Studio (H3)
14:00 – 15:30	Session 7:	**SBGN workshop**; Chairs: Falk Schreiber (Konstanz, D) & Michael Blinov (Farmington, CT, USA) EVERYBODY IS INVITED TO ATTEND	https://sbgn.github.io/sbgn12	**MIRIAM 2 & the OMEX Metadata Specification**; Chairs: Dagmar Waltemath (Greifswald, D) & David Nickerson (Auckland, NZ)	**SBOL**; Chairs: Ernst Oberortner (Berkeley, CA, USA) & Chris Myers (Salt Lake City, UT, USA)
15:30 - 16:00	*Poster Session & Coffee*				
16:00 – 17:30	Session 8:	**SBGN workshop**; Chairs: Falk Schreiber (Konstanz, D) & Michael Blinov (Farmington, CT, USA) EVERYBODY IS INVITED TO ATTEND	https://sbgn.github.io/sbgn12	**Model eXchange consortium: Inaugural meeting**; Chairs: Henning Hermjakob & Rahuman Sheriff (EMBL-EBI, Hinxton, UK)	**SBOL**; Chairs: Ernst Oberortner (Berkeley, CA, USA) & Chris Myers (Salt Lake City, UT, USA)
17:30 - 17:45		**Plenary Wrapup**			

19:30 - 23:00 *Conference Dinner at the restaurant S'Kastanie (address: Elisabethenweg 1 in Heidelberg): https://www.restaurant-s-kastanie.de*

Thursday, July 18th 2019

EU-STANDS4PM
standards for in silico models for personalised medicine

time		Plenary/Breakout session 1		Breakout session 2	Breakout session 3
Room:	Foyer	Carl Bosch Auditorium (H1)		Fritz Haber Auditorium (H2)	Alwin Mittasch Studio (H3)
09:30 – 11:00	**Session 9:**	**Model and Data Management**; Chairs: Wolfgang Müller & Ulrike Wittig (Heidelberg, D)			
09:30 - 10:15		**Carole Goble**, University of Manchester (UK)	**Keynote:** Let's go on a FAIR asset management safari		
10:15 - 10:25		Susheel Varma, EMBL-EBI, Hinxton (UK)	ELIXIR Cloud & AAI: Standardised and Interoperable Services for Human Data Communities		
10:25 - 10:35		Rahuman Sheriff, EMBL-EBI, Hinxton (UK)	BioModels Parameters: A resource to search and access parameters from published systems models		
10:35 - 10:45		Martin Golebiewski, HITS, Heidelberg (D)	Two universes – one world: Community standards vs. formal standards in systems biology and systems medicine		
10:45 - 11:00		all speakers of Session 9	Discussion		
11:00 - 11:30	***Poster Session & Coffee***				
11:30 – 13:00	**Session 10:**	**Standards for Personalized Medicine**; Chairs: Marc Kirschner (Jülich, D) & Martin Golebiewski (Heidelberg, D)			
11:30 - 11:45		**Marc Kirschner**, PTJ (Germany) and **Ingrid Skelton Kockum**, Karolinska Institutet (Sweden)	EU-STANDS4PM: A pan-European Expert Forum joined forces to tackle the complexity of big data integration for in silico methodologies in personalised medicine		
11:45 - 12:15		**Norbert Graf**, Saarland University Medical Center, Homburg (D)	**Keynote:** From data via models to personalized medicine – An example in Pediatric Oncology		
12:15 - 12:30		**Petr Holub**, BBMRI-ERIC, Masaryk University (Czech Republic)	Standards in Biobanking (invited talk)		
12:30 - 12:45		**Søren Brunak**, University of Copenhagen (DK)	Standards for Clinical Data and Systems Medicine		
12:45 - 13:00		**Katharina Eva Ó Cathaoir**, University of Copenhagen (DK)	A Bird's Eye view of Legal and Ethical aspects of EU-STANDS4PM		

time		Plenary/Breakout session 1		Breakout session 2	Breakout session 3
Room:	Foyer	Carl Bosch Auditorium (H1)		Fritz Haber Auditorium (H2)	Alwin Mittasch Studio (H3)
13:00 - 14:00	*Lunch*			COMBINE coordinators' meeting	
14:00 - 14:30		**Liesbet Geris**, Executive Director VPH Institute, KU Leuven (Belgium)	In silico medicine and the VPH institute: bringing the community together and the field forward (invited talk)	**Something old, something new: constraint-based modelling and SBML**; Chair: Brett Olivier (VU University Amsterdam, NL)	**SBOL**; Chairs: Chris Myers & Ernst Oberortner
14:30 – 15:30	**Session 11:**	**EU-STANDS4PM workshop**; Chairs: Marc Kirschner (Jülich, D) & Martin Golebiewski (Heidelberg, D) EVERYBODY IS INVITED TO ATTEND	Link to the agenda: http://co.mbine.org/system/files/EU-STANDS4PM_COMBINE_workshop_published_0.pdf		
15:30 - 16:00	*Poster Session & Coffee*				
16:00 – 17:30	**Session 12:**	**EU-STANDS4PM workshop**; Chairs: Marc Kirschner (Jülich, D) & Martin Golebiewski (Heidelberg, D) EVERYBODY IS INVITED TO ATTEND	Link to the agenda: http://co.mbine.org/system/files/EU-STANDS4PM_COMBINE_workshop_published_0.pdf	**SBML L3 Packages - An Introduction to SBML packages**; Chair: Sarah Keating (University College London, UK)	**SBOL**; Chairs: Chris Myers & Ernst Oberortner
17:30 - 17:45		**Plenary Wrapup**			

Friday, July 19th 2019

time		Plenary/Breakout session 1		Breakout session 2	Breakout session 3
Room:	Foyer	Carl Bosch Auditorium (H1)		Fritz Haber Auditorium (H2)	Alwin Mittasch Studio (H3)
09:30 – 11:00	**Session 13:**	**Semantic Model Annotation**; Chair: Dagmar Waltemath (Greifswald, D)			
09:30 - 10:00		**David Nickerson**, Auckland Bioengineering Institute, University of Auckland (New Zealand)	Semantic annotation in the Physiome Model Repository (invited talk)		
10:00 - 10:30		**Huaiyu Mi**, Keck School of Medicine of the University of Southern California (USC), Los Angeles, CA (USA)	Gene Ontology Causal Activity Modeling (GO-CAM) - invited talk		
10:30 - 10:40		Anand Rampadarath, University of Auckland (NZ)	Model curation and annotation		
10:40 - 10:50		Henning Hermjakob, EMBL-EBI, Hinxton (UK)	Identifiers.org Compact Identifiers for robust data citation		
10:50 - 11:00		all speakers of Session 13	Discussion		
11:00 – 11:30	*Poster Session & Coffee*				
11:30 – 13:00	**Session 14:**	**Emerging Standardization Needs and Multicellular Modeling**; Chair: Tim Johann (Dortmund, D)			
11:30 - 11:50		**Padraig Gleeson**, University College London (UK)	Sharing standardised models and data on the Open Source Brain platform (invited talk)		
11:50 - 12:10		**Melanie Stefan**, University of Edinburgh (UK)	Multi-method modelling of synaptic plasticity and the challenges it brings (invited talk)		
12:10 - 12:20		Jörn Starruß, TU Dresden (D)	Principles for declarative multicellular modelling		
12:20 - 12:30		Guillerm Yanez, Pontificia Universidad Católica de Chile (CL)	Flapjack: an open-source tool for storing, visualising,analysing and modelling kinetic gene expression data		
12:30 - 12:45		all speakers of Session 14	Discussion		
12:45 – 13:00		**CLOSING PLENARY;** Chairs: Martin Golebiewski (HITS, Heidelberg, D) & Dagmar Waltemath (University of Greifswald, D)			

time		Plenary/Breakout session 1		Breakout session 2	Breakout session 3
Room:	Foyer	Carl Bosch Auditorium (H1)		Fritz Haber Auditorium (H2)	Alwin Mittasch Studio (H3)
13:00 - 14:00	*Lunch*				
14:00 – 15:30	Session 15:	**FAIRDOM PALs and User Workshop**; Chair: Olga Krebs (HITS, Heidelberg, D)	**EVERYBODY IS INVITED TO ATTEND:** https://fair-dom.org/events/fairdom-pals-users-meeting-2019/	**Model eXchange consortium**; Chairs: Henning Hermjakob & Rahuman Sheriff (EMBL-EBI, Hinxton, UK)	
15:30 - 16:00	*Poster Session & Coffee*				
16:00 – 17:30	Session 16:	**FAIRDOM PALs and User Workshop**; Chair: Olga Krebs (HITS, Heidelberg, D)	**EVERYBODY IS INVITED TO ATTEND:** https://fair-dom.org/events/fairdom-pals-users-meeting-2019/		
17:30	**END OF MEETING**				

Keynote Talks

Computational Physiology and the Physiome Project

July 15
11:00am
H1

Peter Hunter[1]

[1]Auckland Bioengineering Institute, University of Auckland (New Zealand)

Computational physiological models deal with multiple physical processes (coupled tissue mechanics, electrical activity, fluid flow, etc) at multiple spatial and temporal scales. In many cases the goal is to understand integrative biological function in terms of underlying tissue structure and molecular mechanisms. These models are intended both to help understand physiological function and to provide a basis for diagnosing and treating pathologies in a clinical setting. The Physiome Project is developing model and data encoding standards, web accessible databases and open source software for multiscale modelling (e.g. www.cellml.org). A new journal called Physiome will soon be launched to publish reproducible and reusable models. The talk will discuss the current state of the Physiome Project, including a summary of a multi-physics mathematical framework based on port-Hamiltonians for modelling physiology, and a project to map the pathways of the autonomic nervous system (commonfund.nih.gov/sparc).

Implementing Open Science in publishing

July 15
1:00pm
H1

Thomas Lemberger[1]

[1]EMBO Press, Heidelberg (Germany)

Computational physiological models deal with multiple physical processes (coupled tissue mechanics, electrical activity, fluid flow, etc) at multiple spatial and temporal scales. In many cases the goal is to understand integrative biological function in terms of underlying tissue structure and molecular mechanisms. These models are intended both to help understand physiological function and to provide a basis for diagnosing and treating pathologies in a clinical setting. The Physiome Project is developing model and data encoding standards, web accessible databases and open source software for multiscale modelling (e.g. www.cellml.org). A new journal called Physiome will soon be launched to publish reproducible and reusable models. The talk will discuss the current state of the Physiome Project, including a summary of a multi-physics mathematical framework based on port-Hamiltonians for modelling physiology, and a project to map the pathways of the autonomic nervous system (commonfund.nih.gov/sparc).

July 15
1:45pm
H1

Modeling projects across platforms - the reality and how reality should be

Ursula Kummer[1]

[1]Heidelberg University (Germany)

With the establishment of SBML many years ago a first and important step was taken to be able to perform modeling projects across platforms. Thus it is now possible to set up a model using one software and perform specific analyses in other software. However, despite the progress done, in reality there are still often traps and boundaries one wouldn't expect. In this talk examples from real world problems are given and suggestions made how we could tackle the still existing problems.

July 18
9:30am
H1

Let's go on a FAIR asset management safari

Carole Goble[1]

[1]University of Manchester (UK)

FAIR: Findable Accessable Interoperable Reusable. The "FAIR Principles" for research data, software, computational workflows, scripts, or any other kind of Research Object one can think of, is now a mantra; a method; a meme; a myth; a mystery. FAIR is about supporting and tracking the flow and availability of data across research organisations and the portability and sustainability of processing methods to enable transparent and reproducible results. All this is within the context of a bottom up society of collaborating (or burdened?) scientists, a top down collective of compliance-focused funders and policy makers and an in-the-middle posse of e-infrastructure providers.

Making the FAIR principles a reality is tricky. They are aspirations not standards. They are multi-dimensional and dependent on context such as the sensitivity and availability of the data and methods. We already see a jungle of projects, initiatives and programmes wrestling with the challenges. FAIR efforts have particularly focused on the "last mile" - "FAIRifying" destination community archive repositories and measuring their "compliance" to FAIR metrics (or less controversially "indicators"). But what about FAIR at the first mile, at source and how do we help Alice and Bob with their (secure) data management? If we tackle the FAIR first and last mile, what about the FAIR middle? What about FAIR beyond just data like exchanging and reusing pipelines for precision medicine?

Since 2008 the FAIRDOM collaboration [1] has worked on FAIR asset management and the development of a FAIR asset Commons for multi-partner researcher projects [2], initially in the Systems Biology field. Since 2016 we have been working with the BioCompute Object Partnership [3] on standardising computational records of HTS precision medicine pipelines.

So, using our FAIRDOM and BioCompute Object binoculars let's go on a FAIR safari! Let's peruse the ecosystem, observe the different herds and reflect what where we are for FAIR personalised medicine.

[1] http://www.fair-dom.org

[2] http://www.fairdomhub.org
[3] http://www.biocomputeobject.org

From data via models to personalized medicine - An example in Pediatric Oncology

July 18
11:45am
H1

Norbert Graf[1]

[1]Saarland University Medical Center, Homburg (Germany)

Medicine is undergoing a paradigm shift from phenotyping to genotyping. This is supported by systems approaches to disease, modeling and visualization technologies, and new computational and mathematical tools. An open, modular architectural framework for tools, models and services is necessary to design and develop models for translational medicine. Such a framework needs to share and handle efficiently the enormous personalized data sets to ensure that policies for privacy, non-discrimination, and access to data, services, tools and models are implemented to maximize data protection and data security to enable standardization and semantic data interoperability to integrate models from system biology to guarantee that tools, services and models are clinically driven and do enhance decision support to provide tools for large-scale, privacy-preserving data mining, and literature mining to enhance patient empowerment. In addition, all models need to be evaluated and validated by end-users and have to be tested in concrete clinical research projects that target urgent topics of the medical community. To sustain such a translational infrastructure realistic use-cases have to offer tangible results for end-users. Teaching and educational programs should be implemented to facilitate the use of the models. The large scale integrating transatlantic CHIC project (http://www.chic-vph.eu/) developed a suite of tools, services and a secure infrastructure that supports accessibility and reusability of mathematical and computational hypermodels and fulfills the above-mentioned criteria. One of these models is the Nephroblastoma (Wilms Tumor) Multimodeller Hypermodel. This model is answering the question, if preoperative chemotherapy will reduce the tumor size of a nephroblastoma in an individual patient. For that purpose, different hypomodels are developed, including a vascular, metabolic, biomechanical, molecular model and the Wilms Tumor Oncosimulator. All of them compose the final multimodeler hypermodel. A clinical Research Application Framework (CRAF) allows a clinician to run the hypermodel in individual patients, by selecting the model and the data that are needed. Currently we are starting to prospectively evaluate the model by comparing response to chemotherapy in reality with the predicted response by the hypermodel in individual patients with nephroblastoma.

Invited Talks

Monday

The History of COMBINE

15 July
10:20am
H1

Michael Hucka[1]
[1]Caltech, Pasadena (USA)

In this presentation, I will summarize COMBINE (the COmputational Modeling in BIology NEtwork), the history of its formation, and its status today.

How (not) to Apply (COMBINE) Standards in Agent-Based Modeling

July 15
3:30pm
H1

Judith Wodke[1], Jens Hahn[1], Jorin Diemer[1], Edda Klipp[1]
[1]Humboldt-Universität zu Berlin, Theoretische Biophysik (Germany)

Agent-based modeling (ABM) has recently become of great interest in different research areas, especially when modeling stochastic processes or when aiming at single molecule-resolution. The advantages of ABM are clear: i) modeling is centered around the system entities, which can hold any properties the modeler is able to give them, ii) (system) state transitions are defined by functions iii) the level of detail is limited by computer power only. However, this liberty in terms of possibilities is paid for by a total lack of standardized methods and tools. There is no 'Copasi for ABM', not a simple plotting function is pre-defined. Also, no list of species/reactions/parameters is created automatically. Even worse, parameters are often hidden in different files and at least hundreds of lines of code. Because no user interface (UI) exists that provides easy access to the model and its simulation options, accessibility and usability of agent-based models are highly limited. A modeler aiming at the application of modeling standards has to hard-code them within the model and/or its supplements (analysis and plotting tools, (G)UI, etc.). Thus, while the systems biology/modeling community successfully increased the level of standardization in mathematical modeling for years now, ABM poses a new challenge to this noble aim. Usability of agent-based models and reproducibility of results from ABM simulations highly depend on capacities and disposition of the individual modeler who not only has to put a significant effort in commenting the code but needs to provide access and analysis tools along with the model. In summary, while ABM allows us to model processes not describable by kinetic rate laws

only, it requires a significant amount of extra time and (wo)man power to apply a minimum of (COMBINE) modeling standards.

Computational modeling of liver function tests - Stratification and individualization based on semantic annotations of models and data

July 15
4:00pm
H1

Matthias König[1], Jan Grzegorzewski[1]

[1]Humboldt-Universität zu Berlin (Germany)

Quantitative dynamical liver function tests evaluate the function of the liver via the clearance of a given test substance, thereby providing in vivo information on the metabolic capacity of the liver. Within this work we used multi-scale SBML models (core and comp package) for the description of whole-body physiological models of absorption, distribution, metabolization and elimination of test substances used in dynamical liver function tests. Assessment of liver function is a key task in hepatology but accurate quantification of hepatic function has remained a clinical challenge. Dynamic liver function tests are a promising tool for the non-invasive evaluation of liver function in vivo. One class of such tests are breath tests based on the conversion of 13C-labeled substrates by the liver to 13CO2 subsequently measured in the breath. A commonly applied substrate is 13C-methacetin, converted to paracetamol and 13CO2 via cytochrome P450 1A2 (CYP1A2), used orally in the methacetin breath test (MBT) and intravenously in the LiMAx test. An important clinical question is which factors can affect MBT and LiMAx results. The aim of our study was to answer this question using computational modeling to derive basic information for a better understanding of the methacetin breath test and factors influencing its results. The liver function test based on caffeine is known for long, but its clinical usability is hampered by large interindividual variability and dose-dependency. In this work we developed a detailed physiologically based pharmacokinetics model (PBPK) for the evaluation of the caffeine clearance test, assessing hepatic conversion of caffeine to paraxanthine via cytochrome P450 CYP1A2. The model is able to reproduce results from a wide range of reported studies under varying caffeine doses and application routes. The model accounts for interindividual differences based on distributions of CYP1A2 and modification of CYP1A2 activity via lifestyle factors, e.g. smoking, and pharmacological interactions, e.g. oral contraceptives. Validation was performed with an independent clinical trial (EudraCT 2011-002291-16, ClinicalTrials.gov NCT01788254) demonstrating an improved prediction using individualized models accounting for smoking status and contraceptive use. Hereby, we could reduce the large variability in the test results providing the basis for better sensitivity and specificity in diagnosing subjects with liver problems.

Research software engineers and their role for open and reproducible research

July 15
4:30pm
H1

Heidi Seibold[1]

[1]LMU Munich (Germany)

Many of the proposed solutions to the reproducibility crisis are technical solutions. Open and reproducible research require researchers to learn new technical skills. In this talk I will show some of the tools and strategies I use to make my research open and reproducible. I argue that not all researchers can become experts in these tools and strategies. Instead we need research software engineers (RSEs) and reproducibility support.

Tuesday

July 16
9:30pm
H1

A Standard Enabled Workflow for Synthetic Biology

Chris Myers[1]

[1]University of Utah, Salt Lake City (USA)

A synthetic biology workflow is composed of data repositories that provide information about genetic parts, sequence-level design tools to compose these parts into circuits, visualization tools to depict these designs, genetic design tools to select parts to create systems, and modeling and simulation tools to evaluate alternative design choices. Data standards enable the ready exchange of information within such a workflow, allowing repositories and tools to be connected from a diversity of sources. This talk describes one such workflow that utilizes the growing ecosystem of software tools that support the Synthetic Biology Open Language (SBOL) to describe genetic designs, and the mature ecosystem of tools that support the Systems Biology Markup Language (SBML) to model these designs. In particular, this presentation will demonstrate a workflow using tools including SynBioHub, SBOLDesigner, and iBioSim. SynBioHub (http://synbiohub.org) is a database designed for storing synthetic biology designs captured using the SBOL data model, and it provides both a RESTful API for computational access and a user-friendly Web-based frontend. SBOLDesigner is a sequence editor that allows the designer to fetch parts from a SynBioHub repository and compose them to construct larger designs. Finally, iBioSim is genetic modeling, analysis, and design tool that provides a means to construct SBML models for these designs that can be simulated and analyzed using a variety of techniques. Both SBOLDesigner and iBioSim also support uploading these larger system designs back to the SynBioHub repository. Finally, this talk will demonstrate how this workflow can be utilized to produce a complete record of a genetic design facilitating reproducibility and reuse.

July 16
10:00am
H1

BIOROBOOST: A last chance for standardisation in Biology?

Manuel Porcar Miralles[1]

[1]University of Valencia (Spain)

Synthetic Biology is an engineering research field aiming at (re)designing biological circuits for applied purposes. SynBio strongly relies on the use of well-defined, universal and robust standard components. Despite the outstanding success of synthetic biology in the last years, the difficulties in defining biological standards are well known. Some of the difficulties to achieve standardisation include the cultural "tribalisation" of synthetic biology, a field involving mainly biologists/biotechnologists and engineers; the intrinsic features of live such as mutation, noise, metabolic promiscuity, emergent properties, fitness biasses, variability and, finally, evolution. BIOROBOOST proposes to finally overcome cultural issues and to dramatically advance in solving technical difficulties by i) gathering the most relevant stakeholders

of all the aspects of standardisation in biology in a co-creation scenario; ii) by empirically testing cultural (lab-centric) standardisation practices and by promoting a consensus conceptual and technical redefinition of biological standards; and, finally, iii) by fostering a realistic and flexible toolbox of standard biological parts, including a reduced set of specialised chassis for specific applications as well as a renewed conceptual framework to inform policy makers, scientific and other societal actors.

The Center for Reproducible Biomedical Modeling

July 16
11:30am
H1

Herbert Sauro[1],Michael L. Blinov, John H. Gennari, Arthur P. Goldberg, Jonathan R. Karr, Ion I.Moraru, David P. Nickerson

[1]University of Washington, Seattle (USA)

The Center for Reproducible Biomedical Modeling is a NIH-funded center which aims to enable comprehensive predictive models of biological systems, such aswhole-cell models, that can guide medicine and bioengineering. Achieving this goal requires new tools, resources, and best practices for systematically, scalably, and collaboratively building, simulating and applying models, as well as new researchers trained in comprehensive modeling. To meet theseneeds, the center is developing new technologies for comprehensive modeling, working with journals to provide authors, reviewers, and editors model annotation and validation services, and organizing courses and meetings totrain researchers to model systematically, scalably, and collaboratively. For more information see: https://reproduciblebiomodels.org/. The talk will include the latest developments from the centers efforts.

Wednesday

A personalized modeling pipeline for cardiac electrophysiology simulations of cardiac resynchronization therapy in infarct patients

July 17
9:30am
H1

Caroline Mendonça Costa[1], Aurel Neic[2], Eric Kerfoot[1], Bradley Porter[1], Benjamin Sieniewicz[1], Justin Gould[1], Baldeep Sidhu[1], Zhong Chen[1], Gernot Plank[2], Christopher A. Rinaldi[1,3], Martin J. Bishop[1], Steven A. Niederer[1]

[1]King's College London (UK), [2]Medical University of Graz (Austria), [3]Guy's and St. Thomas' Hospital, London (UK)

Cardiac Resynchronization Therapy (CRT) is an effective treatment for heart failure. However, CRT increases the risk of ventricular tachycardia (VT) in patients with ischemic cardiomyopathy (ICM) when the left ventricular (LV) epicardial lead is implanted in proximity to scar. To determine the mechanisms underpinning this risk, we investigate the effects of pacing on local electrophysiology (EP) in relation to scar that provides a substrate for VT in ICM patients undergoing CRT. Investigating the role of pacing location during CRT on VT risk in the clinical setting is hampered by the anatomy of the coronary sinus veins, which limits where CRT pacing leads can be implanted. Computational models provide full flexibility, thus, allowing a detailed and systematic investigation of the role of pacing location. However, building clinically relevant models that include realistic anatomy and scar morphology, and simulating cardiac electrophysiology (EP) at clinical time-scales remains a challenging task. Therefore, we developed a personalization pipeline, which allows fast development of infarct model cohorts and EP simulations. The developed pipeline was used to build 24 image-based models of left ventricular anatomy and scar morphology. The pipeline allows fast (2 hours) creation of models in a standardized fashion. Moreover, the developed pipeline allows selecting lead locations consistently across models, improving control of simulation conditions. The models built were used to investigate the role of pacing location on dispersion of repolarization, as a surrogate for VT risk. Our simulation results predict that pacing adjacent to a scar increases dispersion of repolarization in its vicinity, which provides a mechanistic explanation for increased VT risk in CRT patients with infarct. Moreover, our simulations predict that pacing 3.5 cm or more from a scar is likely to avoid increasing VT risk in CRT patients.

CellDesigner: A modeling tool for biochemical networks

July 17
11:15am
H1

Akira Funahashi[1]

[1]Keio University (Japan)

Understanding the logic and dynamics of gene-regulatory and biochemical networks is a significant challenge of systems biology. To facilitate this research topic, we have developed a modeling/simulating tool called CellDesigner.

CellDesigner primarily has capabilities to visualize, model, and simulate gene-regulatory and biochemical networks. Two significant characteristics embedded in CellDesigner boost its usability to create /import/export models: (1) Solidly defined and comprehensive graphical representation (Process Diagram) of network models and (2) Systems Biology Markup Language (SBML) as a model-describing basis, which function as inter-tool media to import/export SBML-based models.

Since its initial release in 2004, we have extended various capabilities of CellDesigner. For example, we integrated the third party Garuda enabled simulation/analysis software packages. CellDesigner also supports simulation and parameter scan, supported by integration with SBML ODE Solver, COPASI and Simulation Core Library enabling users to simulate through our sophisticated graphical user interface. Users can also browse and modify existing models by referring to existing databases (ex. BioModels.net) directly through CellDesigner.

Those extended functions empower CellDesigner as not only a modeling/simulating tool but also an integrated analysis suite. CellDesigner is implemented in Java and thus supports various platforms (i.e., Windows, Linux, and MacOS X). CellDesigner version 4.4.2 is freely available via our web site http://celldesigner.org, and a new version of CellDesigner is under development, which will support spatial modeling.

Virtual Cell: Modeling and Visualization of Reaction Rules

July 17
11:45am
H1

Michael Blinov[1]

[1]UConn School of Medicine, Farmington (USA)

Rule-based approach allows representation and simulation of biological systems accounting for molecular features (molecular sites of binding and modifications) and site-specific details of molecular interactions. While rule-based description is very precise and can define very fine molecular details (like how phosphorylation status of a single residue in a multi-protein complex can affect affinity of another binding site of another protein within the same complex), it comes with a cost. Combining all the assumptions scribed in multiple rules into a single diagram is a daunting task. Here we present the approach and software for precise and compact representation of rule-based models implemented in Virtual Cell modeling and simulation tool. It is based on the three basic concepts that allow scalability: molecular pattern (molecules that participate or affect the rule), rule center (molecular sites that are directly modified by a rule), and rule context (molecular sites that affect the rule). We also provide an approach for a complete visualization of rule-based modeling

in Systems Biology Graphical Notations (SBGN)-compliant Process Diagram (PD) conventions, suggesting a possible SBGN-PD extension for rule-based models.

Thursday

EU-STANDS4PM: A pan-European Expert Forum joined forces to tackle the complexity of big data integration for in silico methodologies in personalised medicine

July 18
11:30am
H1

Marc Kirschner[1]

[1]Forschungszentrum Jülich (Germany)

On January 1st 2019 the Horizon2020 Coordinating and Support Action *EU-STANDS 4PM - A European standardization framework for data integration and data-driven in silico models for personalized medicine* launched activities with support by the European Commission Directorate-General for Research & Innovation. During the next three years EU-STANDS4PM will initiate an EU-wide mapping process to assess and evaluate strategies for data-driven in silico methodologies for personalised medicine. This process is the foundation to assemble specific recommendation and guidelines (including formal standard documents) for data harmonization and integration strategies as well as data-driven in silico approaches to interpret human disease and health data. EU-STANDS4PM is an open network and seeks input from all relevant stakeholders that have an interest in advancing in silico methodologies in personalised medicine through broadly applicable standards as well as coordinated procedures for integration and harmonization of heterogeneous health data. This will help to sustain the competitiveness of the European Research Area and ensure a leading role for the European personalized medicine community of stakeholders in the transition from current reactive medical practice to a data-driven and predictive medicine of the future. EU-STANDS4PM receives funding from the European Commission under grant agreement 825843.

Standards in Biobanking

July 18
12:15pm
H1

Petr Holub[1]

[1]BBMRI-ERIC (Austria) and Masaryk University (Czech Republic)

Standardization efforts for Biobanking will be discussed, including activities of the European research infrastructure for biobanking BBMRI-ERIC (Biobanking and Biomolecular Resources Research Infrastructure European Research Infrastructure Consortium) and standardization efforts within the technical committee for biotechnology standards of the international standardization organization ISO (ISO/TC 276 Biotechnology).

July 18
12:30pm
H1

Standards for Clinical Data and Systems Medicine

Søren Brunak[1]

[1]University of Copenhagen (Denmark)

Standardization efforts for clinical data will be discussed, especially with regard to preparing the data for their use in systems medicine and computer modelling in the context of personalized medicine.

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18 July
12:45pm
H1

A Bird's Eye view of Legal and Ethical aspects of EU-STANDS4PM

Katharina Ó Cathaoir[1]

[1]University of Copenhagen (Denmark)

This presentation will introduce the work-in-progress of Work Package 3: legal and ethical framework for data-driven in silico models in personalized medicine. The overarching aim of this work package is to provide comprehensive guidance on the legal, ethical and policy considerations arising from the use of in silico modelling for personalised medicine through mapping overlapping but distinct regulations and conventions: the European Union General Data Protection Regulation (GDPR) (2016), the EU Clinical Trials Regulation (2014) and Council of Europe conventions on patients rights, such as the Convention on Human Rights and Biomedicine (1997). The purpose of the presentation is to highlight the legal significance of the source of the data used in in silico modelling. For example, certain legal and ethical principles apply to data gathered in the doctors office, while other rules apply to data gathered in connection with clinical trials. From a GDPR perspective, the basis upon which the data was originally processed can be significant, for example, whether consent was given, and if so, what form of consent. At international and European levels patient and research subjects rights are underpinned by separate principles, yet this system of governance is weaker, in light of more modest means of enforcement, which will be outlined. Finally, one can also question the extent to which these frameworks remain applicable to Big Data research.

In silico medicine and the VPH Institute: bringing the community together and the field forward

18 July
14:00pm
H1

Liesbet Geris[1]

[1]VPH Institute (Belgium)

Nearly a decade after its official incorporation, the VPH institute, a scientific organization by and for researchers working the field of in silico medicine, is getting every closer to fulfilling its mission: ensuring the adoption of in silico technologies in all aspects of healthcare, from prevention to clinical translation. Hereto, the institute works together with a wide variety of stakeholders, from researchers to clinicians, from industry to the regulators, and from policy makers to funders. In recent years, the field of in silico medicine has gotten a serious boost owing to a number of activities at the translational side. For instance, in 2016, FDA published guidelines on reporting of computer models used in the context of medical devices. More recently, in 2018, ASME published a standard on verification and validation of computer models, again in the context of medical devices, but quite generic in terms of the underlying philosophy. Guidelines and standards such as these do not only reinforce the confidence of industrial and clinical stakeholders in the potential of in silico models, they should also be adopted by the research community in order to increase the quality and reproducibility of the scientific work that is published.

Friday

July 19
9:30am
H1

Semantic annotation in the Physiome Model Repository

David Nickerson[1], Dewan Sarwar[1], Tommy Yu[1], Anand Rampadarath[1], Koray Atalag[1]

[1]Auckland Bioengineering Institute, University of Auckland (New Zealand)

The Physiome Model Repository (PMR) contains over 800 publicly available and version controlled workspaces. These primarily consist of published computational models encoded in the CellML format, some including descriptions of simulation experiments encoded in the SED-ML format. Here I will briefly introduce our recent efforts to curate and annotate these models with detailed biological semantics as well as some high-level workspace annotations. I will then demonstrate how these annotations can be utilised to improve the discovery and comprehension of models in the PMR and then how they aid the model building tasks. I will conclude with some thoughts on how models built in this manner can be verified against similarly annotated simulation experiments or experimental data.

July 19
10:00am
H1

Gene Ontology Causal Activity Modeling (GO-CAM)

Huaiyu Mi[1], Paul D. Thomas, David P. Hill, David Osumi-Sutherland, Kimberly Van Auken, Seth Carbon, James P. Balhoff, Laurent-Philippe Albou, Benjamin Good, Pascale Gaudet, Nomi L. Harris, Suzanna E. Lewis, Christopher J. Mungall

[1]University of Southern California (USA)

The Gene Ontology was developed to conceptualize and describe the functions of genes. The broad aims were (1) comprehensive representation of how genes function in biological systems to enable computational analysis of genomic datasets, and (2) representation of biological concepts consistently across the broad range of model organisms to enable the identification of evolutionarily shared genetic programs, and to use this information to shed light on the functions of human genes. GO annotations are regarded as the most comprehensive structured representation of gene functions, and are widely used in the interpretation of genome-wide experimental data. However, the current GO annotation data structure allows association of GO terms to individual gene product, so it limits the expressiveness of annotations and their application in computational analysis of experimental data. To address this limitation, the GO Consortium has developed a framework, GO Causal Activity Modeling (GO-CAM), for linking multiple GO annotations into an integrated model of a biological system. The fundamental framework of GO-CAM is to connect molecular functions associated to different gene products with causal relationships. GO-CAM supports modeling at multiple levels, from individual gene products to complex regulatory and metabolic pathways, and can be applied in network analysis and systems biology modeling. In addition, GO-CAM is actively working with other standards (BioPAX/SBGN) and resources (Reactome) with regard to interoperability and compatibility.

Sharing standardised models and data on the Open Source Brain platform

July 19
11:30am
H1

Padraig Gleeson[1]

[1]University College London (UK)

I will present the latest functionality of the Open Source Brain platform (OSB; http://www.opensourcebrain.org). OSB was created for sharing and collaboratively developing models in computational neuroscience. Models of cells and circuits in standardised formats (NeuroML) can be visualised, analysed and simulated through a standard web browser. The aim has been to improve the quality, accessibility and scientific rigour of models used to investigate brain function. Following a renewal of our funding from the Wellcome Trust, we are expanding the functionality of the platform to also enable sharing of the experimental data behind the models. I will present how we are using the Neurodata Without Borders (NWB) standard to facilitate sharing of cellular neuroscience data and will outline our vision for a platform of complex yet accessible neuronal models which are shared along with the experimental recordings used to constrain them.

Multi-method modelling of synaptic plasticity and the challenges it brings

July 19
11:50am
H1

Melanie Stefan[1]

[1]University of Edinburgh (UK)

We can look at processes underlying learning and memory at a variety of different scales: from investigating molecular interactions within synapses to studying networks of neurons, to looking at how students learn in classrooms. Computational modelling has proven to be a promising tool at all those levels. But an increasingly important question is how those levels interact with each other and how we can combine different types of models as well as experimental data to answer this question. Addressing this question requires thinking about interfaces both between levels of analysis, and between different methods. I will present some of our preliminary work and future directions in this area.

Contributed Talks

Tuesday

Analyzing Genetic Circuits for Hazards and Glitches

July 16
10:30am
H1

Pedro Fontanarrosa[1], Hamid Hosseini[2]; Amin Borujeni[2], Yuval Dorfan[2], Chris Voigt[2], Chris Myers[1]

[1]University of Utah (USA), [2]MIT, Boston (USA)

A hazard is the possibility of an unwanted or unexpected variation of the output of a combinational logic network before it reaches steady-state. A glitch is the actual observance of such a problem. These terms are used mostly for electronic circuits, though glitches have been observed for genetic regulatory networks (GRNs) as well. A glitch is a transient behavior that corrects itself as the system reaches a steady-state. Nonetheless, this glitching behavior can have drastic consequences if this transient output of the GRN causes an irreversible change in the cell such as a cascade of responses within or with other cells, or if it induces apoptosis. Therefore, avoiding glitching behavior can be crucial for safe operation of a genetic circuit.To better understand glitching behavior in genetic circuits, this work utilizes a version of our dynamic model generator that automatically generates a mathematical model composed of a set of ordinary differential equations (ODEs) that are parameterized using characterization data found in a Cello genetic gate library. Simulation of a dynamic model allows for the prediction of glitches that cannot be observed with steady-state analysis. This work is done using data-standards such as SBOL, SBML and SED-ML. For more information visit: https://journal.physiomeproject.org

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SBOL and its applicability in partially and fully automated design workflows: Three success stories

July 16
10:40am
H1

Ernst Oberortner[1]

[1]DOE Joint Genome Institute (JGI), Berkeley Labs (USA)

The Synthetic Biology Open Language (SBOL) and its recently added W3C Provenance Ontology (PROV-O) extension enable to exchange data in a standardized format and to track the activities, entities and data across the entire, iterative life cycles of synthetic biology Design-Build-Test-Learn (DBTL) workflows. An integrated design workflow is required when managing various large-scale, complex projects simultaneously, as we experience at the U.S. Department of Energy (DOE)

Joint Genome Institute (JGI). The dilemma is, however, to address the varying requirements across the simultaneous projects, to define the activities of each projects DBTL workflow, and to incorporate frequently changing requirements due to improved technologies and scientific discoveries. In this presentation, I will survey the design of three projects with varying requirements and workflows. The projects focus on the design of a few small proteins to pathways with multiple operons, such as in refactored gene clusters. The design workflow was either performed using a partially or fully automated approach including the adoption of SBOL for exchanging designs and tracking design activities. The design tasks of the projects range from (i) codon optimizing the genes for expression in the target host organism over (ii) grouping genes into operons to modulate their expression using regulatory elements (e.g., promoters, terminators) to (iii) specifying the synthesis limitations as well as the assembly and cloning instructions of the design. When designing a pathway, then various design alternatives need to be considered. We experienced designs ranging from explicitly specified pathway variants to combinatorial designs that need to be sampled either randomly, algorithmically or based on constraints. Lastly, I will also touch on our approach of using SBOL for the specification of build instructions (i.e., synthesis, assembly, cloning) for the three projects. Although in its infancy, this approach could enable to order the physical construction of a design and desired build instructions to downstream manufacturing facilities, such biofoundries or commercial DNA synthesis providers.

July 16
12:00pm
H1

Physiome - Publish your models curated for reproducibility and reusability to increase research quality for everyone

Karin Lundengård[1], Peter Hunter[1], David Nickerson[1]

[1]Auckland Bioengineering Institute, University of Auckland (New Zealand)

Physiome is a journal committed to reproducibility and reusability of mathematical models of physiological processes. Every article published in Physiome is connected to a curated and permanent version of the model code with a persistent identifier. Through the Physiome paper, the code necessary to run the model is easily accessible by just clicking a link, to be reused as it is or as a module in a bigger model. It is also connected to a primary paper published in a domain specific journal, where the validation and scientific value of the model is discussed. A Physiome publication is a complement to your primary article that ensures reproducibility, reusability and discoverability of you model. The format encourages modularity that facilitates combination of different models to develop the next level of systems understanding. And all the models are in one place, easy to find and accessible. Reproducibility and confirmation of results is crucial for useful science and should be one of the supporting pillars of good research. Yet, publication of it is rarely incentivised, often treated as a secondary result at best, which undermines the quality of our work. With the strict formulation of equations and easily shared code, it seems like mathematical models should be reproducible by default, but in fact less than 10% of the models published in scientific journals work when implemented by another group. Waste no more valuable time and effort on trying

to implement models from papers that lack information, or having your results lost because others cannot use them. Publish your models in Physiome and contribute to making science useful in society (and less frustrating for your colleagues). For more information visit: https://journal.physiomeproject.org

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Reproducibility in model construction, validation and analysis workflows in systems biology projects; Xylose metabolism in Caulobacter crescentus as a case study, using JWS Online and the FAIRDOMHub

July 16
12:10pm
H1

Jacky Snoep[1], Lu Shen[2], Bertina Siebers[2], Dawie van Niekerk[1], Wolfgang Müller[3], Carole Goble[4]

[1]Stellenbosch University (South Africa), [2]University Duisburg-Essen (Germany), [3]Heidelberg Institute for Theoretical Studies (HITS) (Germany), [4]University of Manchester (UK)

With the uptake of modelling standards as advocated by the COMBINE community, the description and publication of models in standard formats such as SBML has much improved. Many journals require authors to make their mathematical models available, and the SBML format is often used in Systems Biology studies. However, the requirement to submit a model description does not guarantee that the model simulations shown in the manuscript are reproducible. Usually, reviewers will not check the submitted models, and without clear instructions for simulations, it can be quite challenging to reproduce particular model simulations. Having been active for a long time in technical model curation of scientific manuscripts that contain mathematical models, we need on average about 5 communications with authors to successfuly reproduce their simulation results, and model simulations published in journals without a curation service will very often not be reproducible. Using a standard model simulation description such as SED-ML makes it much easier to check for reproducibility, but not many manuscripts include SED-ML descriptions of model simulations. The JWS Online project includes both a model database and a model simulation database, the tools to construct SBML and SED-ML files, and test for model simulation reproducibility. In addition, it allows for linking experimental data stored on the FAIRDOMHub. Whereas one could consider the reproducibility of model simulations as a minimal requirement, our aims for the scientific process of mathematical modelling should be much higher, including transparancy and reproducibility for the construction, validation and analysis of the model. We will illustrate the approach for a combined experimental and modelling study on xylose metabolism, using initial rate kinetics on isolated enzymes, progress curve analysis, sequential enzyme cascade, one pot cascade and cell extract incubations. All data, model and simulation description files for each of the steps are made available on the FAIRDOMHub, making the complete process reproducible and FAIR.

Causal, Mechanistic Pathway Based Analysis of -Omic Profiles

July 16
12:20pm
H1

Emek Demir[1], Özgün Babur, Funda Durupinar Babur, Hannah Manning, Michal Grzadkowski, Joseph Estabrook, Olga Nikolova, Kevin Watanabe-Smith

[1]Oregon Health & Science University (USA)

Genomics and imaging data produced by large NIH projects now reaches to Exabyte scale. Current mechanisms of knowledge representation and scientific communication in biology cannot adequately deal with the complexity and volume of this informationa serious bottleneck for developing a causal, predictive understanding of the cell. To address this need we have developed multiple algorithms and tools over the years that bridges causal mechanistic knowledge obtained through decades of low-throughput biology research with big data. Over the last two years these tools are being actively used for molecular tumor boards and cancer precision medicine within the OHSU's SMMART program. In this talk, we will describe the current analysis workflows, how they are facilitated by BioPAX and SBGN, initial tumor board results as well as our future plans.

Predictive in-silico multiscale analytics to support cancer personalized diagnosis and prognosis, empowered by imaging biomarkers

July 16
12:30pm
H1

Polyxeni Gkontra[1], Leonor Cerd Alberich[1], Gracia Mart Besa[1], Luis Mart Bonmat[1]

[1]La Fe Health Research Institute (IIS La Fe), Valencia (Spain)

PRIMAGE (PRedictive In-silico Multiscale Analytics to support cancer personalized diaGnosis and prognosis, Empowered by imaging biomarkers) is a novel, highly innovative H2020 project (GA- 826494) aiming at providing cloud-based computational solutions to the diagnosis, prognosis, choice and follow-up of treatment for two of the most common paediatric cancers with high societal impact, neuroblastoma (NB) and Diffuse Intrinsic Pontine Glioma (DIPG). NB is the most frequent solid cancer in childhood, while DIPG is the leading cause of brain tumour-related death in children. Due to the highly complex nature of both tumours, their diagnosis, prognosis and monitoring require the combination of several sources of data such as biological, clinical, multi-omics and imaging. Apart from the data itself, adequate data infrastructures ensuring secure and anonymized data management, storage and sharing, as well as computational approaches for the effective data exploitation are of paramount importance. Particularly in the case of imaging data, automated high-throughput quantitative image analysis approaches (radiomics) and artificial intelligence are essential in order to translate the huge amount of highly complex images acquired by todays imaging systems into quantitative information. This information can be used to identify novel imaging biomarkers for disease diagnosis, monitoring of progression, choice and response to therapy. In this context, PRIMAGE will develop a functional prototype cloud-based platform offering predictive tools to assist management of NB and DIPG. Multi-modal real-word imaging

data (MRI, CT, MIBG/SPECT, PET-FDG if MIBG is negative) from hospitals around Europe will be used to identify and validate reliable and reproducible imaging biomarkers for NB and DIPG using cutting-edge technologies. The data infrastructures, imaging biomarkers identified, as well as the computational solutions developed within PRIMAGE, including models for in-silico medicine research, will be validated in the context of NB and DIPG, but their application is not limited in these types of cancers but can be extended in a large variety of cancers.

Wednesday

Datanator: Tools for Aggregating Data for Large-Scale Biomodeling

July 17
10:00am
H1

Yosef Roth[1], Zhouyang Lian[1], Saahith Pochiraju[1], Jonathan Karr[1]
[1]Icahn School of Medicine at Mount Sinai (USA)

Systems biology aims to understand how genotype influences phenotype. Comprehensive mechanistic models, such as whole-cell models, can be used to explore cell dynamics. However, the data required to construct these models are contained across many different databases – often with inconsistent identifiers and formats. In addition, the time required to manually collect this data impedes the creation of large-scale models. To accelerate whole-cell modeling, we developed Datanator, an integrated database and search engine. Datanator allows a modeler to input a desired biological parameter (e.g. molecular concentration, reaction rate, etc.) with desired search criteria (e.g. organism, environmental conditions, etc.), and Datanator returns a list of the most relevant observations together with a single consensus value that can be directly used in a model. To accomplish this, Datanator integrates genomic data (RefSeq, Ensembl), transcriptomic data (ArrayExpress), proteomic data (Pax-DB), kinetic data (SABIO-RK), and metabolite concentration data (ECMDB, YMDB). Datanators search engine can identify the most relevant data from a combination of search criteria: genetic similarity (KEGG orthology), taxonomic similarity (NCBI taxonomy), molecular similarity (tanitomo string comparison), reaction similarity (EC number), and environmental similarity. Datanator enable scaleable model creation and consistent provenance tracking. In addition to using Datanator to build a WC model of Mycoplasma pneumoniae, we have shown that Datanator can find missing parameters for ODE models, augment FBA models with kinetic bounds, and recalibrate models to similar organisms. Availability: https://github.com/KarrLab/datanator

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Simulation and Sensitivity Analysis for Large Kinetic Models in AMICI

July 17
10:10am
H1

Fabian Fröhlich[1]
[1]Harvard Medical School (USA)

In recent years, large, kinetic, multi-pathway models with hundreds to thousands of species and parameters have become increasingly abundant. These large kinetics models are often constructed with the aim to deepen our mechanistic understanding of signaling pathways. Yet, calibration of these models poses a major computational challenge, which limits our ability to work with these models in practice. Gradient-based methods such as quasi-Newton optimization or Hamiltonian Monte-Carlo have been demonstrated to work well for high-dimensional problems, but require methods to robustly compute parameter sensitivities. To address this issue, we developed AMICI (Advanced Multilanguage Interface to CVODES and IDAS),

a C++ library tailored to the simulation and sensitivity analysis of large Ordinary Differential Equation and Differential Algebraic Equation models. AMICI provides python and MATLAB interfaces that allow compilation of simulation executables from SBML and BNGL formats. For gradient computation, AMICI implements symbolic processing of model equations to provide efficient local sensitivity analysis using forward, adjoint and steady-state sensitivity analysis. So far AMICI has been applied for simulation and model calibration in 27 publications. To highlight AMICI features that are essential for model simulation and sensitivity analysis for large models, I will showcase several examples, which includes multi-pathway signaling models with hundreds to thousands of species, reactions and parameters.

OpenCOR: current status and future plans

July 17
10:20am
H1

Alan Garny[1], David Brooks[1], Peter Hunter[1]
[1]University of Auckland (New Zealand)

OpenCOR: current status and future plans","OpenCOR is an open source cross-platform modelling environment. It can be used to organise, edit, simulate and analyse models encoded in the CellML format. Partial support for SED-ML and COMBINE archives is also available. In this talk, we will give an overview of OpenCOR and illustrate how it fits within the overall COMBINE effort. We will then share some of our future plans for OpenCOR.

Visualization of Part Use in SynBioHub

July 17
12:15pm
H1

Jeanet Mante[1], Zach Zundel[1], Chris Myers[1]
[1]University of Utah (USA)

We present a visualization plugin to assist designers in finding components for their designs from SynbioHub instances. In particular, our plugin displays up to four graphs per part page. First, there is a Sankey diagram that shows other components that are commonly used with this component sort by their type. Second, there is another Sankey diagram that indicates which of these parts commonly come before or after the component of interest. Third, there is a histogram that shows how commonly used this component is relative to most commonly used components. Finally, there is a histogram that shows the commonality of this component relative to other commonly used components of the same type.

July 17
12:25pm
H1

PySB framework: Tools to build, calibrate and visualize biochemical models

Oscar O. Ortega[1], Carlos F. Lopez[1]

[1]Vanderbilt University (USA)

Computational models are used to understand the dynamics and behavior of complex biological network processes. In order to study cellular network processes, mechanistic models need to be built, calibrated to experimental data, and analyzed to generate hypotheses about the mechanisms that control different cellular processes. Here we present the PySB modeling framework of tools to build, calibrate and visualize models. PySB is a Python-based programming framework for systems biology, and it builds on BioNetGen and Kappa rule-based languages as well as Python libraries to enable model definition as functions that represent biological processes. PySB comprises three different tools for model calibration to experimental data: SimplePso uses the Particle Swarm Optimization algorithm, PyDREAM uses the Differential Evolution Adaptive Metropolis (DREAM) algorithm to obtain posterior distributions of calibrated parameters, and Gleipnir that uses nested sampling algorithms for Bayesian parameter inference. Additionally, PySB contains a tool to obtain static and dynamic representations of model networks and their simulated dynamics. Importantly, the entire PySB framework can be employed within Jupyter Notebooks thus facilitating reproducibility and shareability of complete analysis pipelines. Therefore, we believe that the PySB framework enables users to obtain important mechanistic insights about complex biological processes that could be potentially used for the development of novel therapies to treat different human diseases.

July 17
12:35pm
H1

Visualization, Access, and Exploration of Biological Pathway Information from Pathway Commons

Augustin Luna[1], Emek Demir[2], Igor Rodchenkov[3], Özgün Babur[2], Jeffrey Wong[3], Chris Sander[1], Gary Bader[3]

[1]Dana-Farber Cancer Institute/Harvard Medical School (USA), [2]Oregon Health & Science University (USA), [3]University of Toronto (Canada)

Pathway Commons (pathwaycommons.org) serves researchers by integrating data from public pathway and interaction databases and disseminating this data in a uniform fashion. The knowledge base is comprised of metabolic pathways, genetic interactions, gene regulatory networks and physical interactions involving proteins, nucleic acids, small molecules, and drugs. Alongside attempts to increase the scope and types of data, a major focus has been the creation of user-focused tools, resources, and tutorials that facilitate access, discovery, and application of existing pathway information to aid day-to-day activities of biological researchers. Pathway Commons offers a number of tools for accessing and searching the integrated datasets that are provided as file downloads in the Biological Pathway Exchange (BioPAX), Simple Interaction Format (SIF) and gene set (GMT) formats. This data is also provided via web services that allow for integration with external tools (e.g., CyPath2,

a Cytoscape app, and the paxtoolsr R package; each is a network analysis tool). Discussion of Pathway Commons will, in part, focus on reusable web application visualization components that are built upon cytoscape.js and the Systems Biology Graphical Notation Markup Language (SBGN-ML). The components are the basis for our web-based 'Search' application that enables users to query pathways by keyword and visualize returned pathways using SBGN with an automated layout. Additionally, these components are used for the ongoing development of various pathway visualization applications, such as the online Newt SBGN pathway editor (newteditor.org). Overall, these software components enhance the accessibility to pathways from third-party applications wishing to integrate support for pathway visualization and interpretation.

Thursday

July 18
10:15am
H1

ELIXIR Cloud & AAI: Standardised and Interoperable Services for Human Data Communities

Susheel Varma[1], Shubham Kapoor[1], Ania Niewielska[1], Alexander Kanitz[1], Jinny Chien, Andrea Cristofori, Sarah Butcher, Foivos Gypas, Kevin Sayers[1], Juha Törnroos, Marco Tangaro, Giacinto Donvito, Yasset Perez-Riverol, Bjorn Gruning, Jennifer Harrow, Jonathan Tedds, Salvador Capella, Tommi Nyrönen, Steven Newhouse

[1]European Bioinformatics Institute (EMBL-EBI) (UK)

Currently, patient data are geographically dispersed, difficult to access, and often, patient data are stored in siloed project-specific databases preventing large-scale data aggregation, standardisation, integration/harmonisation and advanced disease modelling. The ELIXIR Cloud and Authentication & Authorisation Infrastructure (AAI) for Human Data Communities project aim to leverage a coordinated network of ELIXIR Nodes to deliver a Global Alliance for Genomic Health (GA4GH) standards-compliant federated environment to enable population scale genomic and phenotypic data analysis across international boundaries and a potential infrastructure to enable 1M Genome analysis. The ELIXIR Cloud & AAI project will lay the groundwork to deliver the foundational capability of federation of identities, sensitive data access, trusted hybrid cloud providers and sensitive data analysis services across ELIXIR Nodes by underpinning the bi-directional conversation between partners with the GA4GH standards and specifications and ELIXIR trans-national expertise. The project is also developing a framework for secure access and analysis of sensitive human data based on national federations and standardised discovery protocols. The secure authentication and authorisation process alongside guidelines and compliance processes is essential to enable the community to use these data without compromising privacy and informed consent. The project therefore provides a globally available curated repository to store bioinformatics software containers and workflows (Biocontainers - GA4GH TRS), a service to discover and resolve the locations of datasets (RDSDS - GA4GH DRS) and distributed workflow and task execution service (WES-ELIXIR/TESK - GA4GH WES/TES) to leverage the federated life-science infrastructure of ELIXIR. The ambition of the project is to provide a global ecosystem of joint sensitive data access and analysis services where federated resources for life science data are used by national and international projects across all life science disciplines, with widespread support for standard components securing their long-term sustainability. Connecting distributed datasets via common standards will allow researchers unprecedented opportunities to detect rare signals in complex datasets and lay the ground for the widespread application of advanced data analysis methods in the life sciences.

BioModels Parameters: A resource to search and access parameters from published systems models

July 18
10:25am
H1

Sheriff Rahuman[1], Chinmay Arankalle[1], Mihai Glont[1]; Tung Nguyen[1], Henning Hermjakob[1]

[1]European Bioinformatics Institute (EMBL-EBI) (UK)

Systems biology models of cell signalling, metabolic and gene regulatory networks have been shown to divulge mechanistic insight into cellular regulation. One of the major bottlenecks in building systems models is identification of model parameters. Searching for model parameters from published literature and models is essential, yet laborious task. To address this, we have developed a new resource, BioModels Parameters, that can facilitate easy search and retrieval of parameters values from models stored in BioModels (Chelliah et al. 2015).

Two universes one world: Community standards vs. formal standards in systems biology and systems medicine

July 18
10:35am
H1

Martin Golebiewski[1]

[1]Heidelberg Institute for Theoretical Studies (HITS) (Germany)

Given the increasing flood and complexity of data in life sciences, standardization of these data and their documentation are crucial. This comprises the description of methods, biological material and workflows for data processing, analysis, exchange and integration (e.g. into computational models), as well as the setup, handling and simulation of models. Hence, standards for formatting and describing data, workflows and computer models have become important, especially for data integration across the biological scales for multiscale approaches.

To this end many grassroots standards for data, models and their metadata have been defined by the scientific communities and are driven by standardization initiatives such as COMBINE and others. For providing the potential users with an overview and comparable information about such standards we develop information resources, such as the NormSys registry for modelling standards (http://normsys.h-its.org).

For facilitating the integration of data and models, standards have to be harmonized to be interoperable and allow interfacing between the datasets. To support this, we drive and lead the definition of novel standards of the International Organization for Standardization (ISO) in the technical ISO committee for biotechnology standards (ISO/TC 276) in order to define a framework and guideline for community standards and their application. With our activities we aim at enhancing the interoperability of community standards for life science data and models and therefore facilitating complex and multiscale data integration and model building with heterogenous data gathered across the domains.

Friday

July 19
10:30am
H1

Model curation and annotation

Anand Rampadarath[1]

[1]Auckland Bioengineering Institute (New Zealand)

In an attempt to curtail the ongoing problem of irreproducibility of published work, the Center for Reproducible Biomedical Modeling has introduced an annotation and curation service to help journal authors, reviewers, and editors publish reproducible, reusable models. Manuscripts received from partner journals will be curated to make sure that any author supplied code will faithfully reproduce the results presented in the manuscript. In this talk I will give a quick description of this curation and annotation process as well as give an update on the service.

July 19
10:40am
H1

Identifiers.org Compact Identifiers for robust data citation

Henning Hermjakob[1], Sarala Wimalaratne[1], Manuel Bernal Llinares[1], Javier Ferrer[1], Nick Juty[2]

[1]European Bioinformatics Institute (EMBL-EBI) (UK), [2]University of Manchester (UK)

Compact identifiers have been informally and widely used for referencing life science data for many years, though the practice has been largely been through ad hoc implementations, serving specific use cases. We describe our implementation, which has already begun to be adopted by publishers.

Compact Identifiers consist of an (Identifiers.org) assigned unique prefix in combination with a locally (database) assigned accession number (prefix:accession). Compact Identifiers are resolved to database records using information that is stored in an underlying Registry, which contains high quality, manually curated information on over 700 data collections. This information includes the assigned unique prefix, a description of the data collection, identifier pattern, and a list of hosting resources or resolving locations. When a Compact Identifier is presented to the Identifiers.org Resolver, it is redirected to a resource provider, taking into consideration information such as the uptime and reliability of all available hosting resources. For example, pdb:2gc4, GO:0006915, doi:10.1101/101279, orcid:0000-0002-5355-2576 etc.

In addition, a formal agreement with N2T resolver, based in California Digital Library has been struck to provide backup resolution services. Users can therefore resolve Compact Identifiers using Identifiers.org (https://identifiers.org) or N2T (https://n2t.net/) resolvers. This implementation of Compact Identifiers has been adopted by Nature Scientific Data for data citations when linking to biomedical datasets with accession numbers [2].

[1] Sarala M. Wimalaratne et al. Uniform resolution of compact identifiers for biomedical data. Sci. Data 5:180029 doi:10.1038/sdata.2018.29 (2018)

[2] Open Editorial. On the road to robust data citation. Sci. Data 5:180095 doi:10.1038/sdata.2018.95 (2018)

Principles for declarative multicellular modelling

July 19
12:10pm
H1

Jörn Starruß[1], Walter de Back[1], Martin Golebiewski[2], Lutz Brusch[1]
[1]TU Dresden (Germany),
[2]Heidelberg Institute for Theoretical Studies (HITS) (Germany)

New insights into multicellular processes in tissues and organs, like tissue regeneration, can be gained using spatially resolved modelling and simulation. Correspondingly, many international Systems Medicine projects are developing spatially resolved multicellular models and new simulation software. Exchange, reproducibility and archiving of spatially resolved multicellular models among different projects with different software tools would mean a great leap forward for the community. However, that would require an appropriate and fully declarative model definition language for this class of models. We present our considerations for the design of such a modelling language based on our declarative modelling experience with Morpheus(ML) [1] and highlight central concepts to represent the multicellular complexity.

[1] Morpheus(ML) - http://morpheus.gitlab.io

Flapjack: an open-source tool for storing, visualising, analysing and modelling kinetic gene expression data

July 19
12:20pm
H1

Guillermo Yanez[1], Isaac Nunez[1], Tamara Matute[1], Fernan Federici[1], Timothy Rudge[1]
[1]Pontificia Universidad Catolica de Chile (Chile)

Engineering design cycles based on accurate parameter estimation from experimental data are key for predictable assembly of complex genetic circuits. In particular, as dynamical systems the reliable design of genetic circuits requires analysis of kinetic gene expression data. This data is often distributed across many institutions, in different file formats, repositories and databases, which makes it difficult to collate and reduces the power of analysis. Thus there is a need for data repositories that can store kinetic gene expression data, link this data to circuit designs, and allow analysis that combines multiple studies and experiments to reliably estimate parameters. Here we present Flapjack, a web-based open-source tool for storing, visualising, analysing and modelling kinetic gene expression data. Flapjack enables users to flexibly query experimental data based on metadata, for example extracting all measurements related to a particular DNA sequence, all growth curves for a given strain, etc. These queries return all relevant data irrespective of the particular study or experiment, or may be restricted to specific experiments of interest. Using the web app users may then visualize the experimental time series using interactive plots (time courses, kymographs, heatmaps), apply analyses such as calculation of expression rates, growth rates, and parameterise transfer functions or induction curves. For custom analysis queried data can be downloaded in CSV, JSON or XML file formats. Currently, Flapjack supports upload of Synergy HTX and BMG Labtech microplate reader data, but can easily be extended to accommodate any

data format. We propose a data repository and set of analysis tools that enables scaleable data analysis, visualization and parameter estimation, collating data between institutions, studies, experiments, and individual researchers. Flapjack will thus significantly enhance data sharing, management and analysis for synthetic and systems biology.

Workshops and Breakouts

Tuesday

Sharing experiences in building a standards community

July 16
14:00pm
H1

Dagmar Waltemath[1], Mike Hucka[2]
[1]University Medicine Greifswald (Germany),
[2]Caltech, Pasadena (USA)

COMBINE is now 10 years old and consists of 8 core standards, plus an additional 5 associated standards. Some of these standards have a much longer history. Common to all standards is their bottom-up, community-based approach to developing, evaluating and refining the information to be shared about a piece of research in computational biology modeling and related fields. Our experience when presenting COMBINE at workshops, conferences and meetings is that there is substantial interest in how communities can be built in such a sustainable and open manner. In this breakout session, we invite long-term members of the community to get together and collect with us hints & tips for community building in a scientific, data-driven field of research. We intend to provide the tips to the public afterwards, hoping that others can benefit from our experiences. As an additional topic of discussion, we will discuss how we can improve our communication, not only about community-building processes across different scientific fields, but also about the benefits of COMBINE itself in research fields relating to computational modeling in biology.

SED-ML Script: a Proposal

July 16
14:00pm
H2

Lucian Smith[1], Herbert Sauro[1]
[1]University of Washington (USA)

SED-ML was first introduced 10 years ago. As the next levels and versions are being developed, perhaps it is time to consider a procedural format, instead of the existing declarative format. SED-ML Script is a developing project by Herbert Sauro and Lucian Smith at the University of Washington that attempts to take what we've learned in the past ten years and turn it into a script form. Discussion encouraged.

July 16
16:00pm
H1

COMBINE as Legal Entity

Martin Golebiewski[1], Herbert Sauro[2]

[1]Heidelberg Institute for Theoretical Studies (HITS) (Germany), [2]University of Washington, Seattle, WA (USA)

Options for the COMBINE community to become a legal entity will be discuss. The aim of the session is to develop a roadmap for a sustainable future for the COMBINE network. An expected outcome of the meeting is to decide on concrete actions to be taken in order to establish a legal COMBINE entity. Such a legal entity can appear as partner in research proposals and receive corresponding funding for the further development, implementation and promotion of modelling standards in the life sciences. A COMBINE entity can thus provide a formal home for the COMBINE core standards and comparable standardization activities.

Wednesday

SBGN workshop

July 17
14:00pm
H1

Falk Schreiber[1], Michael Blinov[2]
[1]University of Konstanz (Germany), [2]UConn School of Medicine (USA)

The following topics will be discussed at the workshop:

- Tools and databases supporting SBGN
- Features that SBGN need
- Specifications
- Outreach and funding

See the workshop webpage for details: https://sbgn.github.io/sbgn12

MIRIAM 2 & the OMEX Metadata Specification

July 17
14:00pm
H2

Dagmar Waltemath[1], David Nickerson[2]
[1]University Medicine Greifswald (Germany), [2]University of Auckland (New Zealand)

The Minimum Information Requested In the Annotation of Biochemical Models (MIRIAM) is a widely accepted and referenced Minimum Information Guideline for annotating computational models. MIRIAM was released in 2005 and has been adhered to by major curation services and modeling teams. However, with the creation of the OMEX archive, models are no longer necessarily at the center of a shared research project. Instead, collections of files belonging to a virtual experiment offer a way to package a model with all necessary information for reproducing simulation experiments. Recently, COMBINE community members published recommendations for harmonizing semantic annotations stored in OMEX archives, offering a consensus approach for capturing the meaning of elements within the various types of resources shared in these archives. We propose to run a breakout session at COMBINE to discuss updating the MIRIAM guidelines in light of the recent semantic annotation recommendations as well as how to implement the revised guidelines in annotation software packages. We invite representatives from all modeling standards, curators from model repositories, modelers, and other interested parties for an initial brainstorming session and a potential launch of a working group to coordinate the revision of the original MIRIAM guidelines.

July 17
14:00pm
H3

SBOL breakout

Ernst Oberortner[1], Chris Myers[2]
[1]DOE Joint Genome Institute (JGI), Berkeley Labs (USA), [2]University of Utah (USA)

July 19
16:00pm
H2

Model eXchange consortium: Inaugural meeting

Rahuman Sheriff[1], Henning Hermjakob[1]
[1]European Bioinformatics Institute (EMBL-EBI) (UK)

Model repositories play an essential role in making models easily sharable and accessible. Searching for a model requires users to visit multiple repositories and look for a model of their interest. A common platform that will allow modellers to search for models across all existing repositories is the need of the hour. This requires model repositories to share the model metadata in a common platform where searches can be performed by users. Following the search, users can be redirected to the appropriate repository to download the models of their interest. Henning's presentation at HARMONY 2019 to form a consortium of modelling repositories to collaboratively develop a common search platform gained interest from many. Model exchange consortium will also facilitate development of common and shared curation standards and pipelines as well as opportunity for repositories to support each other. To move forward, we agreed to invite all interested repositories and organise an inaugural meeting for the Model eXchange consortium in a breakout session at COMBINE 2019.

Thursday

EU-STANDS4PM workshop

July 18
14:00pm
H1

Marc Kirschner[1], Martin Golebiewski[2]
[1]Forschungszentrum Jülich (Germany), [2]Heidelberg Institute for Theoretical Studies (HITS) (Germany)

One of the major goals of EU-STANDS4PM is to assess and evaluate national standardization strategies for interoperable health data integration as well as data-driven in silico modelling approaches for personalized medicine with the aim to bundle European standardization efforts. The project will produce an in depth EU-wide mapping of relevant European initiatives with regard to data sources (WP1) as well as in silico models (WP2). This process is the foundation to assemble specific recommendation and guidelines (including EU standard documents) for data harmonization and integration strategies as well as data-driven in silico approaches to interpret human disease/health data.

The current EU-STANDS4PM workshop at the annual COMBINE meeting is embedded in the context of work package 1 "Data sources and standards for predictions in personalized medicine" with the objective to initiate and consolidate a pan-European standardization framework for in silico methodologies applied in personalized medicine. A central aim of WP1 is to drive harmonization and interoperability of domain-specific standards (scientific bottom-up/community standards and standards set by national and international standardization bodies) in personalized medicine in order to facilitate data integration to enable predictive in silico modeling on a broader European level.

Through the workshop EU-STANDS4PM will consult the COMBINE community to put a focus on (i) analyzing interoperability and scalability of data and metadata standards relevant in COMBINE and (ii) reflect on possibilities for cross-domain and cross-technology data integration to facilitate in silico modelling approaches in personalized medicine.

To discuss these topics interactive parallel discussions in smaller groups ("world cafes") will collect and debate on several key points:

- Data and model standards - Which of them are relevant for personalized medicine
- Reproducibility - Standards as drivers
- Integration of clinical and research data - Approaches, problems and standardization gaps
- Pitfalls in developing and harmonizing standards
- Transformation/Transition from community standards to formal standards
- Using patient-derived data for personalized medicine: Legal and ethical aspects

Something old, something new: constraint-based modelling and SBML

July 18
14:00pm
H2

Brett G. Olivier[1], Frank T. Bergmann[2]
[1]AIMMS VU University Amsterdam (Netherlands),[2] BioQuant/COS, Heidelberg University (Germany)

The SBML Level 3 Flux Balance Constraint package (FBC) is now swiftly moving towards its third https://www.overleaf.com/project/5d15d2564d30874b7e91ed70 version. The Version 3 iteration further extends the types of constraint-based models that can be encoded in SBML. Furthermore, new elements are introduced that enable the encoding and annotation of genome-scale, metabolic reconstructions. As this is the FBC package's 10th birthday we also reflect on how the development of the FBC package has mediated a productive collaboration between two diverse communities. Leveraging the strengths of this collaboration has led to FBC being one SBML's most actively developed packages.

SBML L3 Packages - An Introduction to SBML packages

July 18
16:00pm
H2

Sarah Keating[1]
[1]University College London (UK)

SBML is the community-developed format for enabling the exchange and reuse of compuational models in biology. SBML Level 3, has a modular structure, with a core suited to representing reaction-based models, and packages that extend the core with features suited for a variety of model types. This allows the encoding of constraint-based models, reaction-diffusion models, logical network models, and rule-based models. Many L3 packages have been finalised, a couple are approaching the final stage of the process and there are still some packages where more work is required.

The development process requires a written specification and two implementations that can demonstrate exchange of models and reproducibility of results, if appropriate. The SBML Editors then review the document and implementations in order to ratifiy the package.

This talk will give a brief overview of the development process and the capabilities of all SBML L3 packages, both those that have been finalised and those still in development. The floor will then be open to continue the discussion of packages approaching finalisation: Spatial Processes and Distributions; discussion of packages requiring more input: Arrays; and discussion of packages that are not currently progressing: Dynamic Processes and Math. The aim of the session is to move things forward or identify and propose solutions to any impediments.

Participants are also welcome to suggest improvements and/or additional packages that are necessary for their own modelling.

Friday

FAIRDOM PALs and User Workshop

July 19
14:00pm
H1

Olga Krebs[1]

[1]Heidelberg Institute for Theoretical Studies (HITS) (Germany)

FAIRDOM is a research infrastructure offering data management support. The SEEK software is designed as registry and storage place for data, models, biological samples, processes, publications and presentations, and at the same time as yellow pages for projects, people and events. SEEK is implemented as central data management platform FAIRDOMhub (https://www.fairdomhub.org).

In this meeting, FAIRDOM team will present project's current status and future plans, high-profile users of FAIRDOM software will share their data management practices. Finally, we will hold informal discussions and breakouts where the audience, and their needs will define what we discuss. Detailed agenda https://fairdom.org/events/fairdom-pals-users-meeting-2019/

You will have direct contact with the FAIRDOM Community and Tech Team, who can give you personalised advice on your data and model management, and using FAIRDOM.

The meeting welcomes everybody whether you are a PhD student or a professor, a current FARIDOM user or just curious about data and model management.

Model eXchange consortium: Inaugural meeting

July 19
16:00pm
H2

Rahuman Sheriff[1], Henning Hermjakob[1]

[1]European Bioinformatics Institute (EMBL-EBI) (UK)

Model repositories play an essential role in making models easily sharable and accessible. Searching for a model requires users to visit multiple repositories and look for a model of their interest. A common platform that will allow modellers to search for models across all existing repositories is the need of the hour. This requires model repositories to share the model metadata in a common platform where searches can be performed by users. Following the search, users can be redirected to the appropriate repository to download the models of their interest. Henning's presentation at HARMONY 2019 to form a consortium of modelling repositories to collaboratively develop a common search platform gained interest from many. Model exchange consortium will also facilitate development of common and shared curation standards and pipelines as well as opportunity for repositories to support each other. To move forward, we agreed to invite all interested repositories and organise an inaugural meeting for the Model eXchange consortium in a breakout session at COMBINE 2019.

Lightning Talks

Systems Biology Graphical Notation (SBGN)

15 July
14:30am
H1

Michael Blinov[1]

[1]UConn School of Medicine, Farmington (USA)

The Systems Biology Graphical Notation (SBGN), is a set standard graphical languages to describe visually biological knowledge. It is currently made up of three languages describing Process Descriptions (PD), Entity Relationships (ER) and Activity Flows (AF).

In this lightning talk, I will briefly summarize the latest edition of SBGN.

SBML Level 3 Version 2 and SBML Level 3 packages

15 July
14:30am
H1

Michael Hucka[1]

[1]Caltech, Pasadena (USA)

The Systems Biology Markup Language (SBML) project is an effort to develop a machine-readable exchange format for computational models in biology. By supporting SBML as an input and output format, different software tools can operate on the same representation of a model, removing chances for errors in translation and assuring a common starting point for analyses and simulations. Today, SBML is the de facto standard in this area, and it is continually being evolved to support more types of models and modeling needs by a community of developers and supporters worldwide.

While SBML was initially developed to exchange non-spatial compartmental models of biochemical reaction networks primarily formulated in terms of chemical kinetics, it was always understood that there existed more types of models. Over time, SBML was expanded to support a broader range of model types, modeling paradigms, and research areas. SBML Level 3 introduced an extensible modular architecture consisting of a central set of fixed features (named SBML Level 3 Core), and a scheme for adding "packages" that can augment the Core by extending existing elements, adding new elements, and adjusting the meaning or scope of elements. This permit layering the core of SBML with new features suited to more types of models, together with a way for individual models to identify which sets of extensions they need for proper interpretation. Twelve SBML Level 3 packages have been proposed to date.

In this lightning talk, I will briefly summarize the latest edition of SBML Level 3 and the current SBML Level 3 packages.

July 15
14:30pm
H1

WebProv: A web-based tool to access, store, and display provenance information of simulation models

Kai Budde[1], Jacob Smith[2], Andreas Ruscheinski[1], Adelinde M. Uhrmacher[1]
[1]University of Rostock (Germany), [2]University of New Brunswick (Canada)

Provenance provides 'information about entities, activities, and people involved in producing a piece of data or thing, which can be used to form assessments about its quality, reliability, or trustworthiness' [1]. For simulation models, provenance includes, for example, information about simulation experiments that have been executed, data that has been used as input for calibration or validation of the simulation model, or other simulation models the simulation model has been based upon [2]. We will present and discuss a first working version of a web-based provenance tool to access, store, and display provenance information of simulation models. The front end includes a query tool that allows the user to search for different keys (e.g., name of cell line) and model dependencies (e.g., model extensions) and displays results graphically and as text. As an example, we relate different Wnt models to one another by capturing provenance information using the PROV data model standard and show detailed graphs for some of the chosen Wnt models.

[1] Groth, P., Moreau, L.: Prov-overview. an overview of the prov family of documents (2013), https://www.w3.org/TR/prov-overview/.

[2] Andreas Ruscheinski, Dragana Gjorgevikj, Marcus Dombrowsky, Kai Budde, and Adelinde. M. Uhrmacher. Towards a PROV ontology for simulation models. In International Provenance and Annotation Workshop, pages 192-195. Springer, 2018.

July 15
14:30pm
H1

MIRIAM 2 & the OMEX Metadata Specification

Dagmar Waltemath[1], David Nickerson[2]
[1]University Medicine Greifswald (Germany), [2]University of Auckland (New Zealand)

see page 47

A Virtual Cohort of Heart Failure Patients Four-chamber Heart Meshes for Cardiac Electro-mechanics Simulations

July 15
14:30pm
H1

Marina Strocchi[1], Christoph Augustin[2], Matthias Gsell[2], Orod Razeghi[1], Anton Prassl[1], Edward Vigmond[3], Jonathan Behar[4], Justin Gould[4], Sidhu Baldeep[4], Aldo Rinaldi[4], Martin Bishop[1], Gernot Plank[2], Steven Niederer[1]

[1]King's College London (UK), [2]Medical University of Graz (Austria), [3]University of Bordeaux and LIRYC Electrophysiology and Heart Modeling Institute (France), [4]King's College London and Guy's and St Thomas' NHS Foundation Trust (UK)

Computational models of the heart are increasingly being used in the development of devices, patient diagnosis and therapy guidance. While software techniques have been developed for simulating single hearts, there remain significant challenges in simulating cohorts of virtual hearts from multiple patients. To facilitate the development of new simulation and model analysis techniques by groups without direct access to medical data, image analysis techniques and meshing tools we have created a virtual cohort of fifteen hearts. Our cohort was built from heart failure patients, age 6815 years and 14 males. We segmented four-chamber heart geometries from end-diastolic CT images. We generated tetrahedral meshes with an average edge length of 1.10.2mm. We added ventricular fibres with a rule-based method with an orientation of -60 and 80 at the epicardium and endocardium, respectively. We ran benchmark electromechanics simulations to test the numerical stability of the meshes. We simulated ventricular electrical activation with a reaction-eikonal model. Passive mechanics of ventricular tissue was represented with a transversely-isotropic Guccione law. All the other tissues were modelled as isotropic. Ventricular preload and afterload were modelled as constant atrial pressure and three-element Windkessel models, respectively. Omni-directional springs were applied at the cropped left pulmonary veins and at the superior vena cava. Normal springs were applied at the ventricular epicardium to represent the effect of the pericardium. The same parameters were used for the fifteen meshes. The electrophysiology simulations resulted in a QRS duration of 13413 ms. The mechanic simulations resulted in a LV and RV ejection fraction of 383 and 283 % and peak LV and RV systolic pressure of 983 and 241 mmHg. Our results prove that our four-chamber meshes are suitable for electromechanics simulations. The virtual cohort will be made publicly available in a future publication.

WebLab update

July 15
14:30pm
H1

Sarah Keating[1]

[1]University College London (UK)

WebLab is an online tool that allows users to upload mathematical models and text-based descriptions of experiments (protocols) and run/compare results of using different combinations of the two. We have recently added the ability to upload experimental data and perform fitting of mathematical models to these data in a reproducible fashion.

July 15
14:30pm
H1

NESTML: A domain-specific language for biologically realistic neuron and synapse models

Charl Linssen [1], Jochen M. Eppler[1], Abigail Morrison[2]

[1]Forschungszentrum Jülich (Germany), [2]Institute of Cognitive Neuroscience, Ruhr-University Bochum (Germany)

NESTML [1, 2] was developed to address the maintainability issues that follow from an increasing number of models, model variants, and an increased model complexity in computational neuroscience. Our aim is to ease the modelling process for neuroscientists both with and without prior training in computer science. This is achieved without compromising on performance by the use of automatic source-code generation. While originally developed in the context of the NEST Simulator [31], the language itself as well as the associated toolchain are lightweight, modular and extensible, by virtue of using a parser generator and internal abstract syntax tree (AST) representation. A typical workflow begins by identifying a model of interest, for example, the dynamical behavior of a single neuron, or the plasticity rules concerning a synapse. This model might come in mathematical or textual form, but is subsequently formalised by the neuroscientist following the NESTML syntax. Model entry is facilitated by a compact syntax and language features such as static and dynamic typing, integrated support for physical units, and the ability to directly enter dynamical equations in differential form. Next, invoking the toolchain will generate optimised code for a specified target platform. That code is dynamically loaded or compiled as part of the simulation framework, after which it can be instantiated within a simulation script, written e.g. using the PyNEST API [4], before starting the simulation. NESTML is open sourced under the terms of the GNU General Public License v2.0 and is publicly available at https://github.com/nest/nestml. Extensive documentation and automated testing are in place, both for the language itself as well as the associated processing toolchain. Active user support is provided via the GitHub issue tracker and the NEST user mailing list. Acknowledgements: This project has received funding from the Helmholtz Association through the Helmholtz Portfolio Theme "Supercomputing and Modeling for the Human Brain" and the European Union's Horizon 2020 research and innovation programme under grant agreement No 720270 (HBP SGA1) and No 785907 (HBP SGA2).

1. D. Plotnikov et al. (2016) Modellierung March 2-4 2016, Karlsruhe, Germany.
2. K. Perun et al. (2018). Version 2.4, Zenodo.
3. M.-O. Gewaltig and M. Diesmann (2007) Scholarpedia 2(4), 1430.
4. Y.V. Zaytsev and A. Morrison (2014) Front. Neuroinform. 8:23

BioModels 2019

July 15
14:30pm
H1

Mihai Glont[1], Henning Hermjakob[1], Rahuman Sheriff[1], Krishna Tiwari[1,2], Tung Nguyen[1], Manh Tu Vu[1]

[1]European Bioinformatics Institute (EMBL-EBI) (UK), [2]Babraham Institute (UK)

BioModels is a repository of mathematical models describing biological processes. In this talk I will summarise recent developments.

Minibatch optimization: a method for training mechanistic models using large data sets

July 15
14:30pm
H1

Paul Stapor[1], Leonard Schmiester, Jan Hasenauer, Daniel Weindl

[1]Institute of Computational Biology, Helmholtz Zentrum München (Germany)

In recent years, a number of rich public data bases, such as the Cancer Cell Line Encyclopedia (CCLE), have emerged. They constitute a powerful tool for computational studies of complex diseases such as cancer and make it possible to develop comprehensive mechanistic models, e.g., based on ordinary differential equations (ODEs). Such models are necessary for a detailed understanding of the underlying cellular processes. However, when dealing with ODE-models and big data sets, parameter estimation becomes the limiting factor in model development, as computation time increases linearly with the number of experimental data sets used for model training. This prohibits the use of ODE-models to either small models or limits amount of data to train the model on. Mini batch optimization methods can be employed to circumvent the linear scaling of computation time with the number of the data sets. Although being widely used for model training of deep neural nets, these methods have never been applied for the training of ODE-models, to the best of the authors knowledge. One reason for this may be that this transfer to another scientific field is not straight forward. Typical optimization problems have different properties in both fields, e.g., in ODE-modeling, the underlying ODEs can be numerically not solvable for certain regions of the parameter space. This makes it necessary to adapt mini batch optimization methods for the application to ODE-model training. We show that it is possible to transfer some of the most common mini batch optimization algorithms to the field of ODE-model training. Using adequate adaptations, we can reduce computation and wall time for model training of large-scale ODE-models by up to an order of magnitude, while keeping good convergence properties. We moreover present additional approaches, which may help to further improve the performance of the presented methods.

Modelling pancreas - Computational modelling and analysis of altered metabolism in the pancreas and its relationship to disease

July 15
17:00pm
H1

Deepa Maheshvare[1] Soumyendu Raha[1], Matthias König[2], Debnath Pal[1]
[1]Indian Institute of Science (India), [2]Humboldt-University Berlin (Germany)

An important aspect of many non-infectious diseases are alterations in metabolism. These alterations are a key feature of metabolic disorders such as Diabetes, Obesity, Cardiovascular Disorders, Fatty Liver Disease and arguably, Cancer. Here, we present a model of the islets of Langerhans to study alterations of Human glucose metabolism due to altered pancreatic function (e.g., impaired glucose tolerance and diabetes). Diabetes is characterized by the occurrence of hyperglycemic events as a consequence of altered metabolic processes that control the secretion and uptake of insulin by the pancreatic islets and hepatocytes, respectively. Our metabolic model of the pancreatic beta-cell includes the uptake of nutrients by the cell from the blood, the metabolic processes that trigger the release of hormones like insulin into the blood, and a model of insulin secretion. Our kinetic framework deploys multi-omics data derived from in vitro and in vivo experiments to incorporate human-specific gene-protein-reaction data to assess the transient change in the concentration of biochemical species. Additionally, we apply transcriptomics data to scale the reaction velocities for assessing how the dysregulation of enzymes that regulate the flux through metabolic pathways such as carbohydrates and amino acids, which act as insulin secretagogues, control the exocytosis of insulin granules from the islets of pancreas. Our model will allow us to eventually explore the alterations in Human glucose metabolism that arise due to perturbations in metabolic flux in the pancreatic islets in a disease state versus a healthy state, in a systematic manner.

PK-DB 1.0: a pharmacokinetics database for individualized and stratified modeling

July 15
17:00pm
H1

Jan Grzegorzewski[1], Matthias König[1]
[1]Humboldt University Berlin (Germany)

We present PK-DB, a database for the representation of pharmacokinetics data from clinical trials and pre-clinical research. Data is either curated from the literature or from available raw data. The main focus of PK-DB is to provide high-quality pharmacokinetics data in combination with required meta-information for computational modeling and data integration, i.e., (i) characteristics of studied patient collectives and individuals; (ii) applied interventions (dosing, route,); and (iii) measured pharmacokinetics information and time courses. Important features are the representation of experimental errors and variation, the representation and normalization of units, annotation of information to biological ontologies, and calculation of pharmacokinetics information like apparent clearance, half-life, or area under the curve (AUC) from time course data. We demonstrate the value of PK-DB by (i) a stratified meta-analysis of pharmacokinetics studies for caffeine curated from the

literature, thereby integrating pharmacokinetics information from a wide range of sources; (ii) providing examples for the computational modeling of dynamical liver function tests based on PK-DB data.

Standardised meta-data in Hospital Information Systems unlock clinical data for research purposes A real-world example

July 15
17:00pm
H1

Robert Gött[1], Kai Fitzer[1], Torsten Leddig[1], **Dagmar Waltemath**[1], Thomas Bahls[1]

[1]University Medicine Greifswald (Germany)

Only few commercial Hospital Information Systems (HIS, German: KAS) provide means to encode and use biomedical meta-data thus allowing for Good Epidemiological Practice (GEP) [1]. Moreover, HIS typically encode meta-data as part of the core system, making extraction, reuse, and linkage of meta-data with other data sources a difficult task. A separated, standards-aware or even standards-compliant meta-data repository is more desirable: the meta-data is easily accessible and can be queried by clinical as well as research data providers or consumers. Consistent linkage of data items guarantees fast access to the original data sets as well as to further resources of the HIS environment. Such a knowledge base has the potential to better connect the worlds of systems medicine and medical informatics, and opens up new opportunities for collaborative research in the biomedical domain. As one positive example, the KAS+ project, initiated at the University Medicine Greifswald (UMG), provides an integrated IT infrastructure for hospital (KAS) and research units (the Plus) [2]. It connects patient care and research, making patient care data available for research purposes, and supporting research projects such as clinical studies. A central metadata repository (MDR) stores meta-data of the multitude of heterogeneous clinical data sources, for example using ISO/IEC 11179. Manufacturers of all components of the IT infrastructure supply their own metadata for the MDR in a compatible digital format. Hence, the KAS+ data can be searched, and the extracted data can be linked to external resources (e.g., biobanks, repositories of computational simulation models, or analysis software). On our poster, we demonstrate how meta-data in the MDR is structured, and how it is used to link heterogeneous data sets when addressing complex research questions.

[1] Hoffmann, W., Latza, U., Baumeister, S.E., Brnger, M., Buttmann-Schweiger, N., Hardt, J., Hoffmann, V., Karch, A., Richter, A., Schmidt, C.O. and Schmidtmann, I., 2019. Guidelines and recommendations for ensuring Good Epidemiological Practice (GEP): a guideline developed by the German Society for Epidemiology. European journal of epidemiology, pp.1-17.

[2] Hoffmann W, van den Berg N, Fitzer K, Leddig T, Jackisch M, Bahls T; Enabling Healthcare Data for Health Services Research Recent Developments in Applied Medical Informatics in Germany.

July 15
17:00pm
H1

Development of python visualization package DNAplotlib

Sunwoo Kang[1]

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DNAplotlib is a quick, automated visualization package to support visualization of genetic circuits (mainly transcription & translational level). The current model focuses on visualizing SBOL files, a file type that is widely used in the field of synthetic biology. In the time of python becoming the standard tool for data analysis, DNAplotlib offers a facilitation of communication between researchers and developers about their genetic modules used in their lab.

July 15
17:00pm
H1

Cy3SBML: a Cytoscape app for SBML

Matthias König[1], Nicolas Rodriguez[2], Andreas Dräger[3,4,5]

[1]Humboldt-Universität zu Berlin (Germany), [2]Babraham Institute, Cambridge (UK), [3]University of Tübingen and German Center for Infection Research (DZIF) (Germany)

We present Cy3SBML, a Cytoscape app for the community format SBML. Key features include (i) SBML import of all levels and versions; (ii) support for SBML level 3 packages, specifically for the SBML extensions for Model Layouts (layout), Qualitative Models (qual), Groups (groups), Hierarchical Model Compositions (comp) and Flux Balance Constraints (fbc), (iii) navigation and manipulation of network layouts based on SBML structure, (iii) access to RDF model annotations in MIRIAM format as well as to SBO-based annotations, (iv) REST API for automatization, and (v) validation of SBML. Cy3SBML provides a variety of importers for SBML models with direct access to BioModels and the BiGG database via web services. Cy3SBML is available from the Cytoscape app store and GitHub.

Posters

Review of software tools and data sources supporting the Systems Biology Graphical Notation (SBGN) standard

Poster 1
Poster sessions
Foyer

Michael Blinov[1], Adrien Rougny[2], Andreas Dräger[3], Vasundra Touré[4], Ugur Dogrusoz[5], Alexander Mazein[6]

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Visualisation is a critical part of understanding and conveying biological information. The Systems Biology Graphical Notation (SBGN) is a standard developed to provide a notation, as well as requirements and guidelines, for the visual representation of biomolecular networks. As for the XML-based SBGN Markup Language (SBGN-ML), it was designed to facilitate storage and exchange of SBGN diagrams. Over time, SBGN was adopted by multiple software tools and data sources, allowing biological researchers to create and edit SBGN-compliant diagrams, as well as visualize data originally represented in other systems biology formats (such as SBML, BioPAX, KEGG-ML). We will review software tools and data sources supporting SBGN and SBGN-ML.ions made how we could tackle the still existing problems.

WebProv: A web-based tool to access, store, and display provenance information of simulation models

Poster 2
Poster sessions
Foyer

Kai Budde[1], Jacob Smith[2], Andreas Ruscheinski[1], Adelinde M. Uhrmacher[1]

[1]University of Rostock (Germany), [2]University of New Brunswick (Canada)

see page 53

Comprehensive mathematical modeling of sphingolipid metabolism by integration of lipidomics and proteomics data

Poster 3
Poster sessions
Foyer

Canan Has[1], Thorsten Hornemann[2], Robert Ahrends[1]

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Sphingolipids play an important role in cell membrane composition and lipid raft formation. In addition to that, they exert a vital role in regulating multiple cellular functions including signaling, apoptosis, inflammation. Sphingolipids show antagonistic activities. While ceramide and sphingosine are proapoptotic to benefit growth arrest and apoptosis, ceramide-1-phosphate and sphingosine-1-phosphate are known to promote cell proliferation, transformation and inflammation. The metabolism of sphingolipids, including the all enzymes and lipids involved, has been extensively studied. This metabolic pathway delineates an integrated system linking multiple synthesis and catabolism pathways by centering ceramide. The three main pathways that compose sphingolipid metabolism are de novo synthesis, the hydrolysis of sphingomyelin and recycling of gangliosides also called salvage pathway. The alteration in sphingolipid metabolism results in pathogenicity of several diseases including neurodegenerative diseases and metabolic diseases. Hence, integration of quantitative lipid and protein data along with biochemical reaction kinetics to model sphingolipid metabolism would be crucial to shed light on sphingolipid related disease mechanisms. Here, we propose a comprehensive and extended model of sphingolipid metabolism in mouse. Contrary to the previous studies, we incorporated different long-chain based fatty acid preferences in de novo synthesis of ceramide, considered substrate affinities of enzymes and cross-talk. The rate constants were estimated through parameter estimation via COPASI and the resulting model was fit experimental data for all species. The model validation was performed on lipidomics and proteomics data of RAW264.7 macrophage cell activated by an endotoxin, Kdo2-Lipid A available in the LIPID MAPS consortium. The model we present here will further contribute to our understanding of sphingolipid metabolism and will support to unravel the behavior of sphingolipids in disease models such as Alzheimer and insulin-resistance.

The Systems Biology Graphical Notation: a standardised representation of biological maps

Poster 4
Poster sessions
Foyer

Andreas Dräger[1], Vasundra Touré[2], Alexander Mazein[3], Adrien Rougny[4], Ugur Dogrusoz[5], Michael Blinov[6], Augustin Luna[7]

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Background: Visualization of biological processes plays an essential role in life science research. Over time, diverse forms of diagrammatic representations, akin to

circuit diagrams, have evolved without well-defined semantics potentially leading to ambiguous network interpretations and difficult programmatic processing.

Results: The Systems Biology Graphical Notation (SBGN) is a standard developed to reduce ambiguity in the visual representation of biomolecular networks. It provides specific sets of well-defined symbols for various types of biological concepts. SBGN comprises three complementary languages: Process Description (PD), Entity Relationship (ER), and Activity Flow (AF). SBGN PD is based on reactions and is well-suited for detailed sequential biochemical mechanisms, for instance, to represent metabolic pathways. SBGN AF shows cascades of influences between the activities carried by biomolecular entities (e.g., stimulation, inhibition) and is particularly useful when the precise molecular mechanisms are unknown or do not need to be shown, for instance, to represent signalling pathways and regulatory networks. SBGN ER represents independent interactions between features of biological entities, which avoids combinatorial explosions of represented biological states and interactions. The XML-based SBGN Markup Language (SBGN-ML) facilitates convenient storage and exchange of SBGN maps, supported by the library libSBGN.

Discussion: The SBGN project is an ongoing open community-driven effort coordinated and maintained by an elected international editorial board. Annual workshops, GitHub and mailing lists are used as leading discussion platforms. Major research projects, such as the Virtual Metabolic Human, and pathway databases such as Reactome and WikiPathways display their maps following the SBGN guidelines. Furthermore, a wide range of tools supports SBGN. SBGN regularly offers student coding events through the Google Summer of Code program.

Availability: All documents and source code are freely available at `http://sbgn.org` and `https://github.com/sbgn`. Contributions are welcome.

Contact: sbgn-discuss@googlegroups.com

Keywords: SBGN, circuit diagram, biological network, visualisation, systems biology

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AMICI and PESTO - A strong couple for simulation and parameter estimation in computational and systems biology

Poster 5
Poster sessions
Foyer

Erika Dudkin[1], Paul Stapor[2,3], Daniel Weindl[2], Benjamin Ballnus[2,3], Sabine Hug[2,3], Carolin Loos[2,3], Anna Fiedler[2,3], Sabrina Krause[2,3], Sabrina Hroß[2,3], Yannik Schälte[2,3], Leonard Schmiester[2,3], Dantong Wang[2,3], Elba Raimndez Alvarez[2,3], Simon Merkt[1], Fabian Fröhlich[2,3], Jan Hasenauer[1,2,3]

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Mechanistic models in systems biology are important to gain an understanding of the physical processes in biological systems. Those models are often based on ordinary differential equations. Since large scale-models become increasingly important as more and more data is available, powerful toolboxes are needed. AMICI (Advanced Multilanguage Interface to CVODES and IDAS) is a toolbox employing the numerical solvers CVODES and IDAS from the C-based SUNDIALS package. It has an easy-to-use Python/MATLAB/C++ interface, while ODE integration is

shifted to C to gain speed. Model setup can be done in Python/MATLAB, but also models in the common SBML format can be imported. AMICI can compute first and second order derivatives of functions depending on the ODE solution. To do this accurately and rapidly, it can perform forward and adjoint sensitivity analysis in first and second order. This makes AMICI applicable for large scale problems. AMICI is furthermore able to deal with discrete events and perform sensitivity analysis for them. Events can have particular observables and may depend on the simulated time, but also on the system state or model parameters, which is a unique feature of AMICI. Parameter estimation is a common problem in systems biology. Often, unknown parameters have to be inferred from measurement data. This leads to non-convex and possibly multi-modal optimization problems. PESTO (Parameter EStimation TOolbox) is a highly customizable MATLAB-based toolbox, which presents a wide range of state of the art methods for optimization, such as multi-start local, global or hybrid methods, as well as uncertainty analysis, employing profile likelihoods computed based on different approaches and numerous different Markov-Chain Monte Carlo methods. Confidence or credibility intervals can be computed to user-provided thresholds and all results from either optimization or uncertainty analysis can be visualized using customizable plotting routines. Currently, pyPESTO, a Python-based toolbox is being developed which will have the same functionalities as PESTO with further features such as supporting PEtab a data format for specifying parameter estimation problems in systems biology, as well as parallel computing. AMICI and (py)PESTO are available as open source software and have been used in several publications. They can be easily interfaced with each other, making them a strong couple for fitting mechanistic models in systems and computational biology.

Poster 6
Poster sessions
Foyer

Analyzing Genetic Circuits for Hazards and Glitches

Pedro Fontanarrosa[1], Hamid Hosseini[2]; Amin Borujeni[2], Yuval Dorfan[2], Chris Voigt[2], Chris Myers[1]

[1]University of Utah (USA), [2]MIT, Boston (USA)

see page 31

YoMoSt - Statistics for you local model versions

Poster 7
Poster sessions Foyer

Tom Gebhardt[1], Martin Scharm[2], Olaf Wolkenhauer[3]
[1]University of Rostock (Germany)

Development is often a non-linear process whether you plan buildings, program tools or create biochemical models. Most of the time, one ends up with a set of versions from different approaches and improvements. Especially modellers of biochemical networks may tend to keep older versions of their models due to the pursuance of reproducibility. Thus, they can end up with an individual file structure, which grows in its complexity during the model development. This complicates the tracking of differences and the evaluation of results. While the use of repositories improved the management of model versions, the investigation of currently unpublished models is still tedious manual work. With YoMoSt, we present a pipeline of tools to support studying of locally stored models. Based on the BiVeS algorithm and as an adaption of the MoSt pipeline, we enable the screening of the local model storage, difference detection and the interactive visualisation of the results.

PK-DB 1.0: a pharmacokinetics database for individualized and stratified modeling

Poster 8
Poster sessions Foyer

Jan Grzegorzewski[1], Matthias König[1]
[1]Humboldt University Berlin (Germany)

see page 58

EnzymeML - a SBML-based exchange format for biocatalytic data

Poster 9
Poster sessions Foyer

Colin Halupczok[1], Jürgen Pleiss[1]
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EnzymeML has been designed as an SBML-based exchange format for data on enzyme-catalyzed reactions. It integrates experimental data such as time course of substrates or products and metadata on the enzyme and the reaction conditions with modelling data such as the kinetic model and the kinetic parameters obtained by fitting of the time course data by the kinetic model. Thus, EnzymeML makes data and metadata related to a biocatalytic experiment findable, accessible, interoperable, and reusable (Wilkinson 2016). Most of the biocatalytic data is described by SBML (Hucka et al., 2018) and is enriched by MIRIAM (Novre et al., 2005) annotation and by additional EnzymeML annotations, the SBML file is included into a Combine Archive, which includes additionally the original data on which basis the modeling is made. In EnzymeML the structure of the experiment and the modeling part are separated in different SBML files. This allows the reuse of the same data for different modeling approaches to identify the parameters of the model. EnzymeML is designed to help the experimenters with a standardized file format, which is based

on current standards to easily write, model and publish results of biocatalytic experiments. While experimenters can parse their manual designed experiment tables into EnzymeML, the container file can be used to model the experiment directly in a modeling platform with the attached experiment data. All the results can be published then on different platforms, because EnzymeML contains the most relevant data which is needed by other scientist to do their research.

Hucka, M. et al (2018). The Systems Biology Markup Language (SBML): Language Specification for Level 3 Version 2 Core. Journal of Integrative Bioinformatics, 15(1). https://doi.org/10.1515/jib-2017-0081

Novre, N. Le et al (2005). Minimum information requested in the annotation of biochemical models (MIRIAM). Nature Biotechnology, 23(12), 15091515. https://doi.org/10.1038/nbt1156

Wilkinson, M. D. et al (2016). The FAIR Guiding Principles for scientific data management and stewardship. Scientific Data, 3(1), 160018. https://doi.org/10.1038/sdata.2016.18.

Poster 10
Poster sessions
Foyer

The JSBML project: a fully featured Java API for working with systems biology models

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Background: SBML is the most widely used data format to encode and exchange models in systems biology. The open-source JSBML project has been launched in 2009 as an international collaboration with the aim to provide a feature-rich pure Java implementation for reading, manipulating and writing SBML files.

Results: The JSBML project has matured into a stable, actively developed, and well-documented software project with a large number of contributors around the world. A growing number of applications is now available that uses JSBML as their back-end for data manipulation. These cover diverse areas of use cases, such as model building and graphical display, constraint-based modeling, dynamic simulation, model annotation, and many more. JSBML supports all levels, versions, and releases of SBML and provides numerous utility functions that facilitate working with this standard. JSBML also integrates well with other Java libraries for community standards, such as for SBGN or the COMBINE Archive format.

Discussion: The JSBML team actively maintains and updates the project. JSBML is being used in students education and numerous research projects. Major model databases, such as BioModels or BiGG Models, use JSBML-based tools for their curation pipelines. JSBML is also regularly subject of international students coding events.

Availability: Source code, binaries and documentation for JSBML can be freely obtained under the terms of the LGPL 2.1 from the website `http://sbml.org/Software/JSBML/` and on GitHub `https://github.com/sbmlteam/jsbml/`. The users guide at `http://sbml.org/Software/JSBML/docs/` provides further information about using JSBML.
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Rodriguez, N., et al (2015). JSBML 1.0: providing a smorgasbord of options to encode systems biology models. Bioinformatics, doi:10.1093/bioinformatics/btr361.

Identifiers.org Compact Identifiers for robust data citation

Poster 11
Poster sessions
Foyer

Henning Hermjakob[1], Sarala Wimalaratne[1], Manuel Bernal Llinares[1], Javier Ferrer[1], Nick Juty[2]

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see page 42

Experiences with Developing Digital Registries for Contraceptive Care using the Collaborative Requirements Development Methodology

Poster 12
Poster sessions
Foyer

Esther Inau[1]

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Digital registries linked to standardised medical terminology are increasingly becoming an entry point to adopting patient health records and facilitating population level tracking of health services. They support interoperability and offer a diversity of functionalities including vital events tracking and electronic decision support. However, these systems can only be appropriately designed by first getting a comprehensive picture of the actual tasks and processes associated with service provision; the issues and barriers experienced; and the content and flow of data - all within the local context and aligned with the local infrastructure. This study explores the collaborative requirements development methodology to analyse common workflows of clinicians working in contraceptive care and identify functional user requirements that facilitate development of supportive digital registries. The results of this study can be customized and used as guidance for software professionals developing national digital registries for use in various healthcare settings and contexts worldwide. Keywords: digital registries, medical terminology, workflows, functional user requirements, contraceptive care.

Poster 13
Poster sessions
Foyer

Virtual patient

Fedor Kolpakov[1]

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We have developed a technology for constructing a virtual patient and optimizing the choice of drug therapy using the example of treating arterial hypertension. To achieve this goal we have solved three main tasks:

1) building a modular mathematical model of human biochemistry and physiology with a sufficient level of detail for a given disease. We believe that now it is not realistic to build a "virtual patient" for all occasions. Therefore, our approach is to create a set of basic blocks, and from them to assemble a model for a given patient and illness (as from Lego blocks).

2) for the main classes of antihypertensive drugs: direct inhibitors of renin (aliskiren), calcium channel blockers (amlodipine), angiotensin II receptor antagonists (losartan, azilsartan), angiotensin-converting enzyme inhibitors (enalapril, perindopril, lysinopril) and thiazide-like diuretics, their points of impact on the constructed model were determined and corresponding models of pharmacokinetics and pharmacodynamics were constructed. To validate the resulting model, we used data from clinical studies found in the literature.

3) for model personalization we used data from medical records. However these data are insufficient to estimate values for many model parameters. In order to solve the problem a multitude of virtual patients was built where the unknown parameter values can vary significantly. After that we simulated the effects of the above antihypertensive drugs. Each virtual patient responds to the treatment in his own way, it will not be effective for everyone. Further we can select groups of virtual patients with a similar reaction to the drug and determine which parameters determine the division into these groups.

Using the proposed approach, the treatment of arterial hypertension was modeled for six real patients. The proposed algorithm provides a fairly accurate prediction of the treatment of the selected antihypertensive drug for a particular patient.

As a practical result of the work, a computer program was developed. It works as follows: the available patient data is entered and the program creates many virtual patients for whom it predicts the most likely effect of their treatment and which unknown personal parameters need to be determined in order to make a more accurate choice. However, to implement this program in medical practice, there is still a long way to go - to test it on a large number of patients and go through the certification process.

FAIRDOM approach for Systems Biology Data and Model Management

Poster 14
Poster sessions Foyer

Olga Krebs[1], Martin Golebiewski[1], Stuart Owen[2], Maja Rey[1], Natalie Stanford[2], Ulrike Wittig[1], Xiaoming Hu[1], Katy Wolstencroft[3], Jacky L. Snoep[2,4], Bernd Rinn[5], Wolfgang Müller[1], Carole Goble[2]

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Systems Biologists need a data management infrastructure that enables collaborating researchers to share and exchange information and data as and when it is produced, throughout the entire iterative cycle of experimentation and modelling. We develop and offer integrated data management support for systems biology research within and across research consortia comprising a whole package of solutions. This is applied to large-scale research initiatives in which we are responsible for the scientific data management, like the German Virtual Liver Network (`http://www.virtual-liver.de/`), MESI-STRAT (Systems Medicine of Metabolic-Signaling Networks `https://mesi-strat.eu/`) , and European research networks like ERASysAPP (ERA-Net for Systems Biology Applications), SysMO (Systems Biology of Microorganisms) or NMTrypI (New Medicines for Trypanosomatidic Infections), and Synthetic Biology Centres at Manchester (SynBioChem) and Edinburgh (SynthSys). Our data management concept consists of 4 major pillars: 1) Infrastructure backbone: The SEEK platform as registry and a commons for data, models, processes and resulting publications and presentations, at the same time yellow pages for projects, people and events 2) Terminology: Tailored use of controlled vocabularies and ontologies to describe the data 3) Modelling support: Seamless handling and simulation of models by integrated modelling platforms (JWS-Online, SYCAMORE, Cytoscape) 4) Social support: Data management advocates within the projects for gathering requirements and dissemination The data management concept that we have developed is not only applied in the research consortia that we are responsible for, but also used by other systems biology projects.

NESTML: A domain-specific language for biologically realistic neuron and synapse models

Poster 15
Poster sessions Foyer

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see page 55

Physiome - Publish your models curated for reproducibility and reusability to increase research quality for everyone

Poster 16
Poster sessions Foyer

Karin Lundengård[1], Peter Hunter[1], David Nickerson[1]
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see page 32

Modelling pancreas - Computational modelling and analysis of altered metabolism in the pancreas and its relationship to disease

Poster 17
Poster sessions Foyer

Deepa Maheshvare[1] Soumyendu Raha[1], Matthias König[2], Debnath Pal[1]
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see page 57

Enhancing the computational based function annotation of thiamine diphosphate dependent enzymes

Poster 18
Poster sessions Foyer

Stephan Malzacher[1], Patrick Buchholz, Colin Halupczok, Saskia Bock, Dörte Rother, Jürgen Pleiss
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Thiamine diphosphate (ThDP)-dependent enzymes are potential stereoselective catalysts for the synthesis of pharmaceutical precursors like (S)-phenylacetylcarbinol [1]. Most importantly, the process design for the biocatalytic synthesis of these precursors necessitates the identification of suitable ThDP dependent enzymes. Therefore, public database systems provide a large amount of protein sequences, with a functional annotation by either sequence or structure based homology modelling [2]. However, this functional annotation is error prone. Homology models are created and evaluated by the comparison of experimental data with the protein sequences and structures of already characterised enzymes. These data are generally obtained from peer-reviewed articles. One approach to enhance the accuracy of computational function annotation is to increase the number of protein sequences linked to experimental results. Therefore, the collection of experimental data, optionally directly from the experiments conducted in the laboratories, is desired. Linking these data to information like the formulation of the catalyst, the reaction environment and the analytical methods, enable the reproducibility, comparison and evaluation of the gained results. For this purpose, the thiamine diphosphate-dependent enzyme engineering database (TEED) [3, 4] enables the opportunity to directly transmit data gained from experiments with ThDP-dependent enzymes. Thus, the TEED grants a way for achieving and further process biocatalytic data in a standardised way, enabling reproducibility. This approach not only increases the number of data

linked to ThDP-dependent enzyme sequences, which can be further applied for modelling. Moreover, the negative results of reactions, which are usually not published, can be gathered as an important source for function modelling.
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Visualization of Part Use in SynBioHub

Poster 19
Poster sessions
Foyer

Jeanet Mante[1], Zach Zundel[1], Chris Myers[1]
[1]University of Utah (USA)

see paper 37

Comprehensive Modelling Platform

Poster 20
Poster sessions
Foyer

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Comprehensive Modelling Platform (CMP) combines model building, model analysis, and annotation tasks in a single public site related to a system of interest. Model analysis module is designed to ensure the compatibility with SED-ML to provide exchangeability of simulation experiments.The models are available in the model repository and they are in compliance with SBML level 3. The key feature of the instantiation for a given system relies on mapping kinetic models to Biochemical Space - a precise representation of the related biological knowledge, thereby supporting the systems biological view of the modelled system. Besides the model repository, the platform includes experiments repository and relevant Bioquantities, which improve experimental verification of the models. The general goal of the platform is to respect the need for maintaining existing ODE models but allows to align them with a mechanistic rule-based description that is understandable by biologists, compact in size, executable in terms of allowing basic analysis tasks ensuring consistency of the description, and provides links to existing bioinformatics annotation databases. Such a comprehensive solution allows supporting the effort of modellers in building mathematical models that have clear biochemical meaning and can be easily integrated. Moreover, the mechanistic description can be later used as computational models having all advantages of rule-based modelling. In contrast to existing tools such as Biomodels, CellML, or JWSonline which provide general repositories for biological models, the platform is directly focused on a single system. Moreover, none of these tools is coupled with a systematically organized biological background.

Poster 21
Poster sessions
Foyer

PySB framework: Tools to build, calibrate and visualize biochemical models

Oscar O. Ortega[1], Carlos F. Lopez[1]

[1]Vanderbilt University (USA)

see page 38

Poster 22
Poster sessions
Foyer

The Center for Reproducible Biomedical Modeling

Anand Rampadarath[1], David Nickerson[1], Michael Blinov[2], John Gennari[3], Arthur Goldberg[4], Jonathan Karr[4], Herbert Sauro[3]

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The Center for Reproducible Biomedical Modeling is a NIH-funded center which aims to enable comprehensive predictive models of biological systems, such as whole-cell models, that can guide medicine and bioengineering. Achieving this goal requires new tools, resources, and best practices for systematically, scalably, and collaboratively building, simulating and applying models, as well as new researchers trained in comprehensive modeling. To meet these needs, the center is developing new technologies for comprehensive modeling, working with journals to provide authors, reviewers, and editors model annotation and validation services, and organizing courses and meetings to train researchers to model systematically, scalably, and collaboratively. For more information see: http://reproduciblebiomodels.org.

Poster 23
Poster sessions
Foyer

Datanator: Tools for Aggregating Data for Large-Scale Biomodeling

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see page 36

Standardizing Electronic Laboratory Notebooks to improve their integration with data from the biomedical domain

Poster 24
Poster sessions
Foyer

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The FAIR principles [2] require a semantic documentation of research data. Research datasets following these principles are beneficial for the scientific community as they can be semantically interconnected with other datasets and, thus, be reused. Semantic interoperability, however, requires metadata standards to be employed throughout the entire research process. In the biomedical domain, many experiments are conducted in the wet-lab and documented by laboratory notebooks. The recent shift from paper-based laboratory notebooks to electronic laboratory notebooks (ELNs [1]) enables researchers to build their documentation upon templates to enforce a standardised documentation.

In this poster, we advocate the use of ELNs together with Minimum Information guidelines and standards for laboratory data. The early adoption of standardized vocabularies, taxonomies, and ontologies, such as UMLS, MeSH, or ICD-10 will support the uptake of ELNs and ease the documentation process. The application of standards during the documentation process will in turn ease the creation of FAIR research data, and contribute to the further development of automated mechanisms for data extraction from ELNs.

As a result, research data will gain higher quality and be collected following more standardized operating procedures, thus, fostering the reusability of work done in the laboratory. Beside the standardization of ELNs in the biomedical domain, the clinical domain will benefit from the possibility to create structured, semantically enriched knowledge that could be leveraged in electronic health records.

[1] S. Y. Nussbeck et al. The laboratory notebook in the 21st century: The electronic laboratory notebook would enhance good scientific practice and increase research productivity. EMBO reports, may 2014.
[2] Mark D. Wilkinson et al. The FAIR guiding principles for scientific data management and stewardship. Scientific Data, 3:160018, mar 2016.

Minibatch optimization: a method for training mechanistic models using large data sets

Poster 25
Poster sessions
Foyer

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see page 57

Poster 26
Poster sessions Foyer

A Virtual Cohort of Heart Failure Patients Four-chamber Heart Meshes for Cardiac Electro-mechanics Simulations

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see page 55

Poster 27
Poster sessions Foyer

SABIO-RK: kinetic data for systems biology

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The SABIO-RK database (`http://sabiork.h-its.org/`) supports modelers of biochemical reactions and complex networks and is part of the German bioinformatics network (de.NBI). SABIO-RK represents a repository for structured, curated, and annotated data on reactions and their kinetics. The data are manually extracted from the scientific literature and stored in a relational database. The content comprises both naturally occurring and alternatively measured biochemical reactions, and the data are made available to the public via a web-based search interface. Additionally, web services can be used to automatically access the database, which is also used for the retrieval of kinetics data by third-party software tools and data workflows. These tools include CellDesigner, VirtualCell, Sycamore, SBMLsqueezer, cy3sabiork, Path2Models, LigDig, and FAIRDOMHub. Data are highly interlinked to external databases, ontologies, and controlled vocabularies. Recent work includes the linking to Biomodels (based on Chebi and UniProt identifiers), Rhea, Reactome, MetaCyc and MetaNetX (based on the corresponding reaction identifiers). Additionally, Schema.org semantic markup was added to web pages to improve SABIO-RK data interoperability in life sciences.

Poster 28
Poster sessions Foyer

Flapjack: an open-source tool for storing, visualising, analysing and modelling kinetic gene expression data

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see page 43

Standardised meta-data in Hospital Information Systems unlock clinical data for research purposes A real-world example

Poster 29
Poster sessions
Foyer

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see page 59