User support and training activities in FAIRDOM

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FAIRDOM Consortium

elixir UNITED KINGDOM

elixir BELGIUM

elixir NORWAY

elixir GERMANY

MANCHESTER 1824
The University of Manchester

VIB

UNIVERSITAS BERGENSIS

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Heidelberg Institute for Theoretical Studies

THE UNIVERSITY of EDINBURGH

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UNIVERSITY

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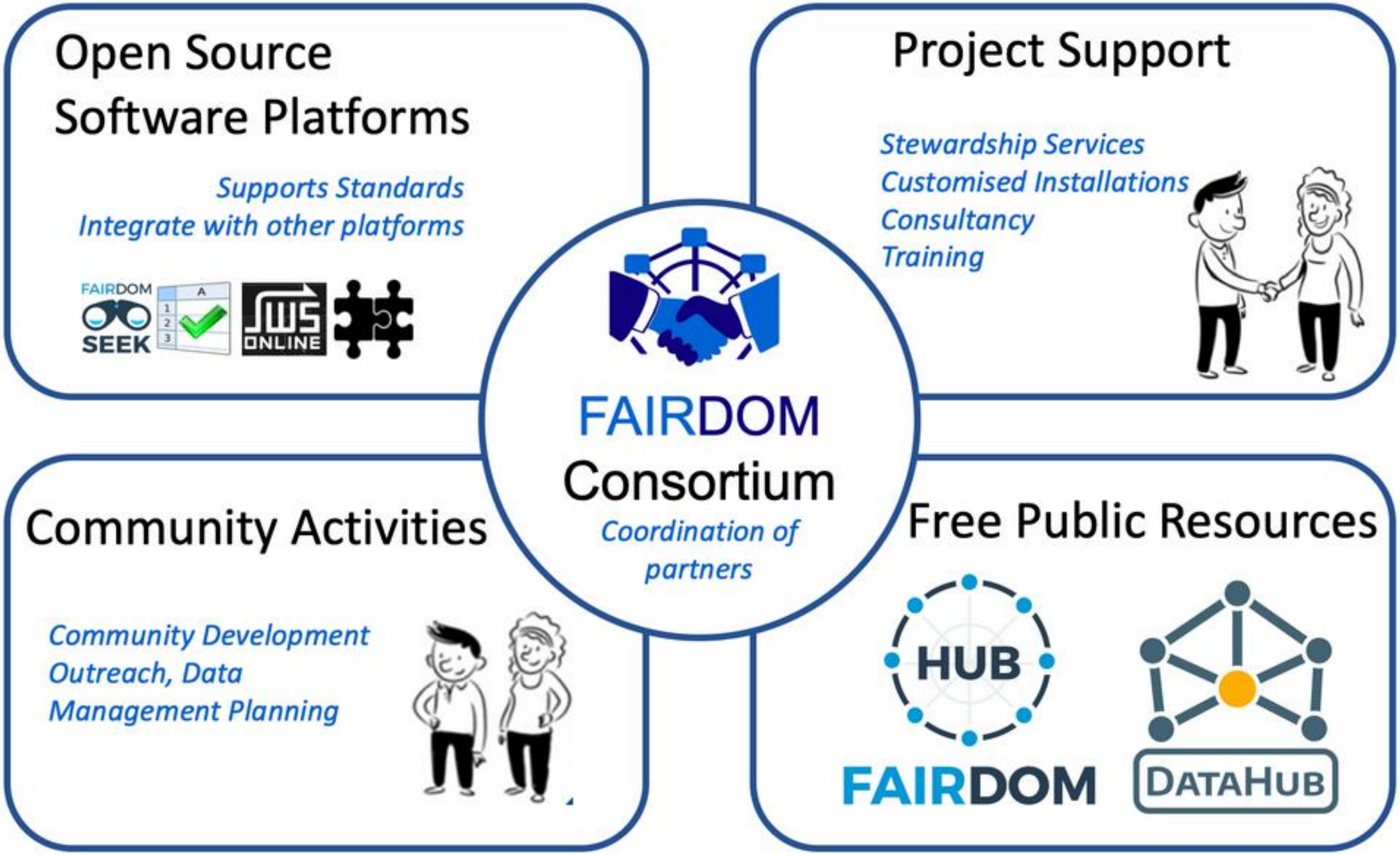
FAIRDOM



Open Source Software Platforms

Supports Standards
Integrate with other platforms

Project Support

Stewardship Services
Customised Installations
Consultancy
Training

FAIRDOM Consortium

Coordination of partners

Community Activities

Community Development
Outreach, Data Management Planning

Free Public Resources

FAIRDOM-SEEK

FAIRDOM
SEEK

Storing
Interlinking
Sharing
Publishing

SEEK

Models

People

Data files
Documents

Samples

Programmes
Projects

SOPs

Publications

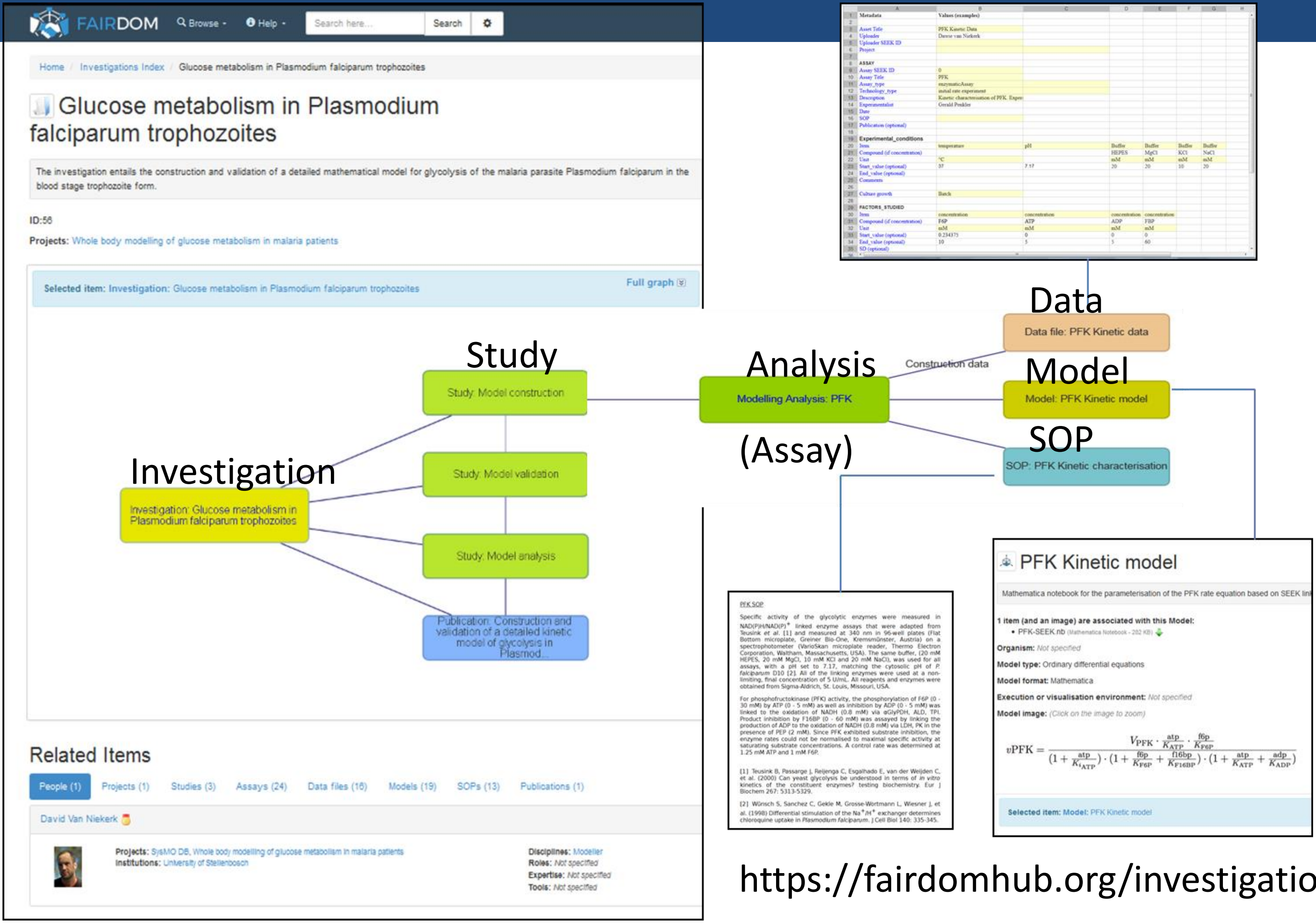
Events

Presentations

Workflows

https://fairdomseek.org

FAIRDOM-SEEK



Glucose metabolism in Plasmodium falciparum trophozoites

The investigation entails the construction and validation of a detailed mathematical model for glycolysis of the malaria parasite Plasmodium falciparum in the blood stage trophozoite form.

ID:56

Projects: Whole body modelling of glucose metabolism in malaria patients

Selected item: Investigation: Glucose metabolism in Plasmodium falciparum trophozoites

Related Items

David Van Niekerk

Projects: SysMO DB, Whole body modelling of glucose metabolism in malaria patients
Institutions: University of Stellenbosch

Disciplines: Modeller
Roles: *Not specified*
Expertise: *Not specified*
Tools: *Not specified*

	A	B	C	D	E	F	G
1	**Metadata**	**Values (examples)**					
2							
3	Asset Title	PFK Kinetic Data					
4	Uploader	Dawie van Niekerk					
5	Uploader SEEK ID						
6	Project						
7							
8	**ASSAY**						
9	Assay SEEK ID	0					
10	Assay Title	PFK					
11	Assay_type	enzymaticAssay					
12	Technology_type	initial rate experiment					
13	Description	Kinetic characterisation of PFK. Exper					
14	Experimentalist	Gerald Penkler					
15	Date						
16	SOP						
17	Publication (optional)						
18							
19	**Experimental_conditions**						
20	Item	temperature	pH	Buffer	Buffer	Buffer	Buffer
21	Compound (if concentration)			HEPES	MgCl	KCl	NaCl
22	Unit	°C		mM	mM	mM	mM
23	Start_value (optional)	37	7.17	20	20	10	20
24	End_value (optional)						
25	Comments						
26							
27	Culture growth	Batch					
28							
29	**FACTORS_STUDIED**						
30	Item	concentration	concentration	concentration	concentration		
31	Compound (if concentration)	F6P	ATP	ADP	FBP		
32	Unit	mM	mM	mM	mM		
33	Start_value (optional)	0.234375	0	0	0		
34	End_value (optional)	10	5	5	60		
35	SD (optional)						

PFK SOP

Specific activity of the glycolytic enzymes were measured in NAD(P)H/NAD(P)$^+$ linked enzyme assays that were adapted from Teusink *et al.* [1] and measured at 340 nm in 96-well plates (Flat Bottom microplate, Greiner Bio-One, Kremsmünster, Austria) on a spectrophotometer (VarioSkan microplate reader, Thermo Electron Corporation, Waltham, Massachusetts, USA). The same buffer, (20 mM HEPES, 20 mM MgCl, 10 mM KCl and 20 mM NaCl), was used for all assays, with a pH set to 7.17, matching the cytosolic pH of *P. falciparum* D10 [2]. All of the linking enzymes were used at a non-limiting, final concentration of 5 U/mL. All reagents and enzymes were obtained from Sigma-Aldrich, St. Louis, Missouri, USA.

For phosphofructokinase (PFK) activity, the phosphorylation of F6P (0 - 30 mM) by ATP (0 - 5 mM) as well as inhibition by ADP (0 - 5 mM) was linked to the oxidation of NADH (0.8 mM) via αGlyPDH, ALD, TPI. Product inhibition by F16BP (0 - 60 mM) was assayed by linking the production of ADP to the oxidation of NADH (0.8 mM) via LDH, PK in the presence of PEP (2 mM). Since PFK exhibited substrate inhibition, the enzyme rates could not be normalised to maximal specific activity at saturating substrate concentrations. A control rate was determined at 1.25 mM ATP and 1 mM F6P.

[1] Teusink B, Passarge J, Reijenga C, Esgalhado E, van der Weijden C, et al. (2000) Can yeast glycolysis be understood in terms of *in vitro* kinetics of the constituent enzymes? testing biochemistry. Eur J Biochem 267: 5313-5329.

[2] Wünsch S, Sanchez C, Gekle M, Grosse-Wortmann L, Wiesner J, et al. (1998) Differential stimulation of the Na$^+$/H$^+$ exchanger determines chloroquine uptake in *Plasmodium falciparum*. J Cell Biol 140: 335-345.

PFK Kinetic model

Mathematica notebook for the parameterisation of the PFK rate equation based on SEEK lin

1 item (and an image) are associated with this Model:
- PFK-SEEK.nb (Mathematica Notebook - 202 KB)

Organism: *Not specified*

Model type: Ordinary differential equations

Model format: Mathematica

Execution or visualisation environment: *Not specified*

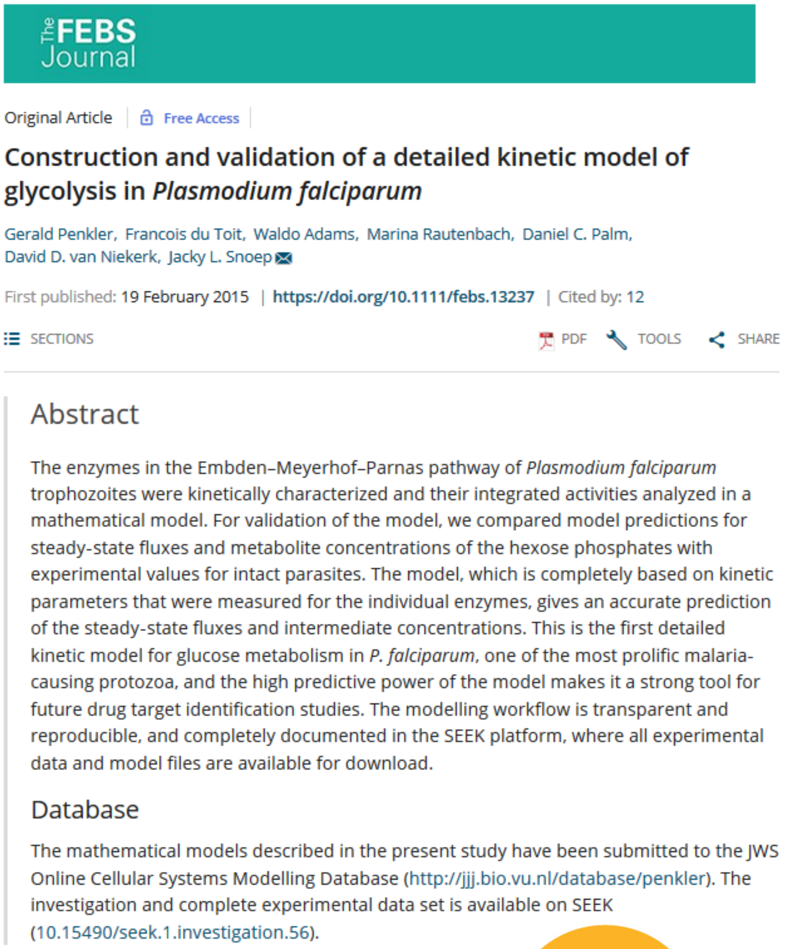
Model image: *(Click on the image to zoom)*

$$vPFK = \frac{V_{PFK} \cdot \frac{atp}{K_{ATP}} \cdot \frac{f6p}{K_{F6P}}}{(1 + \frac{atp}{K_{i_{ATP}}}) \cdot (1 + \frac{f6p}{K_{F6P}} + \frac{f16bp}{K_{F16BP}}) \cdot (1 + \frac{atp}{K_{ATP}} + \frac{adp}{K_{ADP}})}$$

Selected item: Model: PFK Kinetic model

https://fairdomhub.org/investigations/56

More than simple supplementary materials



The FEBS Journal

Original Article | Free Access

Construction and validation of a detailed kinetic model of glycolysis in *Plasmodium falciparum*

Gerald Penkler, Francois du Toit, Waldo Adams, Marina Rautenbach, Daniel C. Palm,
David D. van Niekerk, Jacky L. Snoep

First published: 19 February 2015 | https://doi.org/10.1111/febs.13237 | Cited by: 12

Abstract

The enzymes in the Embden–Meyerhof–Parnas pathway of *Plasmodium falciparum* trophozoites were kinetically characterized and their integrated activities analyzed in a mathematical model. For validation of the model, we compared model predictions for steady-state fluxes and metabolite concentrations of the hexose phosphates with experimental values for intact parasites. The model, which is completely based on kinetic parameters that were measured for the individual enzymes, gives an accurate prediction of the steady-state fluxes and intermediate concentrations. This is the first detailed kinetic model for glucose metabolism in *P. falciparum*, one of the most prolific malaria-causing protozoa, and the high predictive power of the model makes it a strong tool for future drug target identification studies. The modelling workflow is transparent and reproducible, and completely documented in the SEEK platform, where all experimental data and model files are available for download.

Database

The mathematical models described in the present study have been submitted to the JWS Online Cellular Systems Modelling Database (http://jjj.bio.vu.nl/database/penkler). The investigation and complete experimental data set is available on SEEK (10.15490/seek.1.investigation.56).

16 datafiles (kinetic, flux inhibition, runout)

19 models (kinetics, validation)

13 Protocols

3 studies (model analysis, construction, validation)

24 assays/analyses (simulations, model characterisations)

FAIRDOM

Open Source Software Platforms

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FAIRDOM SEEK

JWS ONLINE

Project Support

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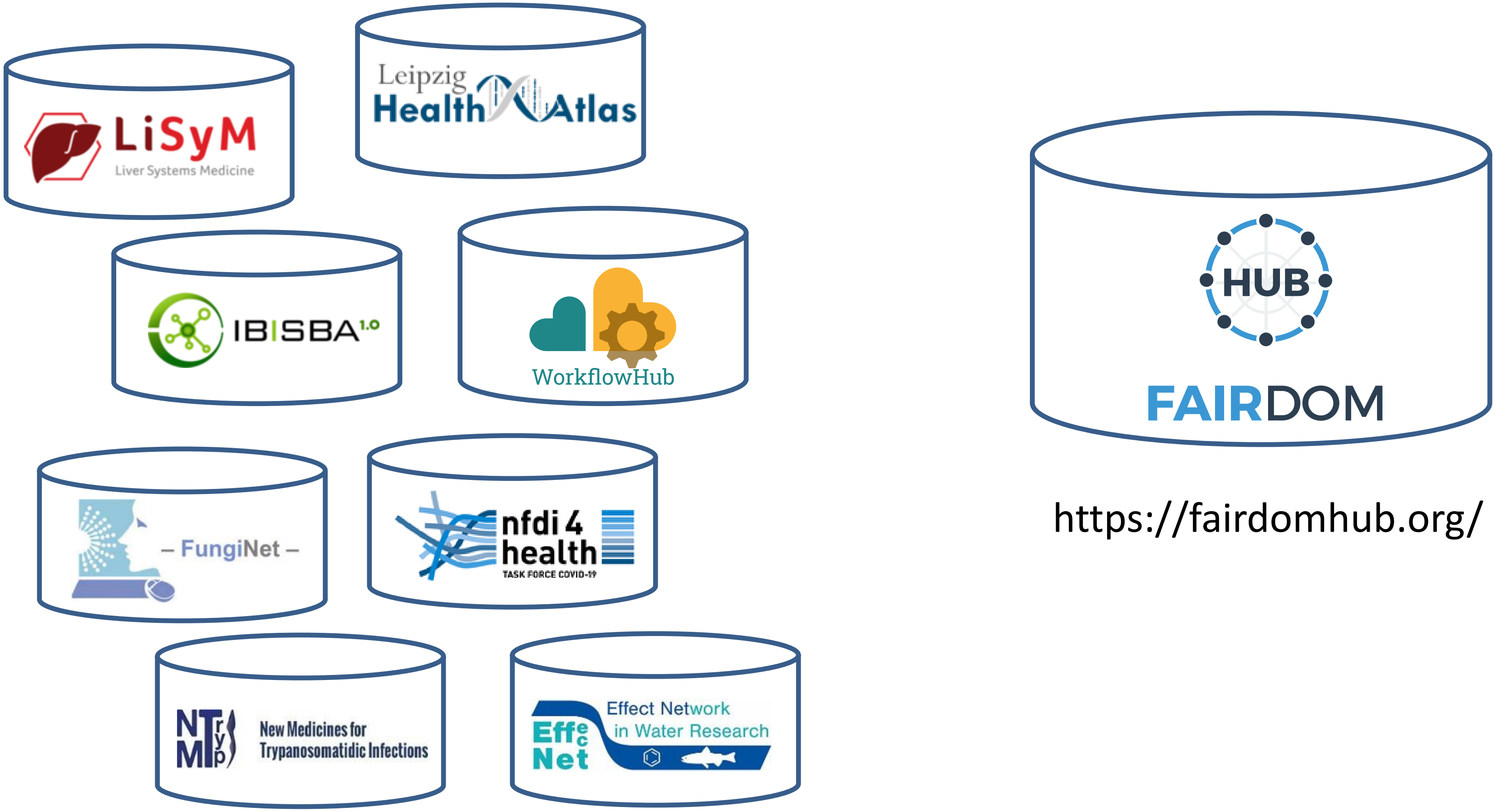
Free Public Resources

HUB FAIRDOM

DATAHUB

FAIRDOM-SEEK Instances



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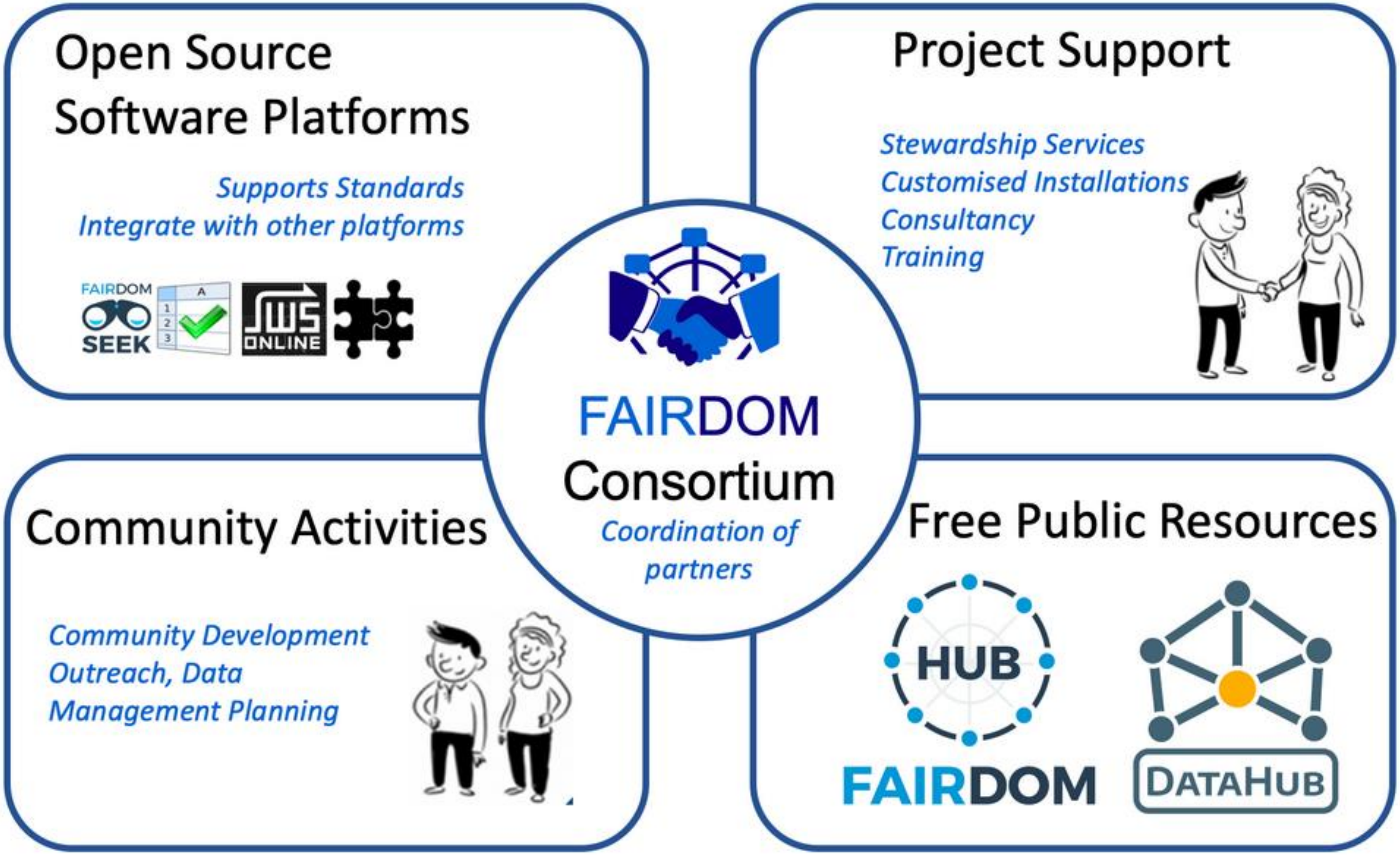
FAIRDOM



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User Support

Understanding the project, its collaborations, its assets, and its workflows

Helping projects promote their project, skills and results

Designing and deploying the technical platforms and the right tools

Maintaining, archiving and securing access to FAIRDOMHub

Working with researchers and technicians to design and adopt practices and procedures and curate models and data.

Customising on-site project installations

Training researchers and students

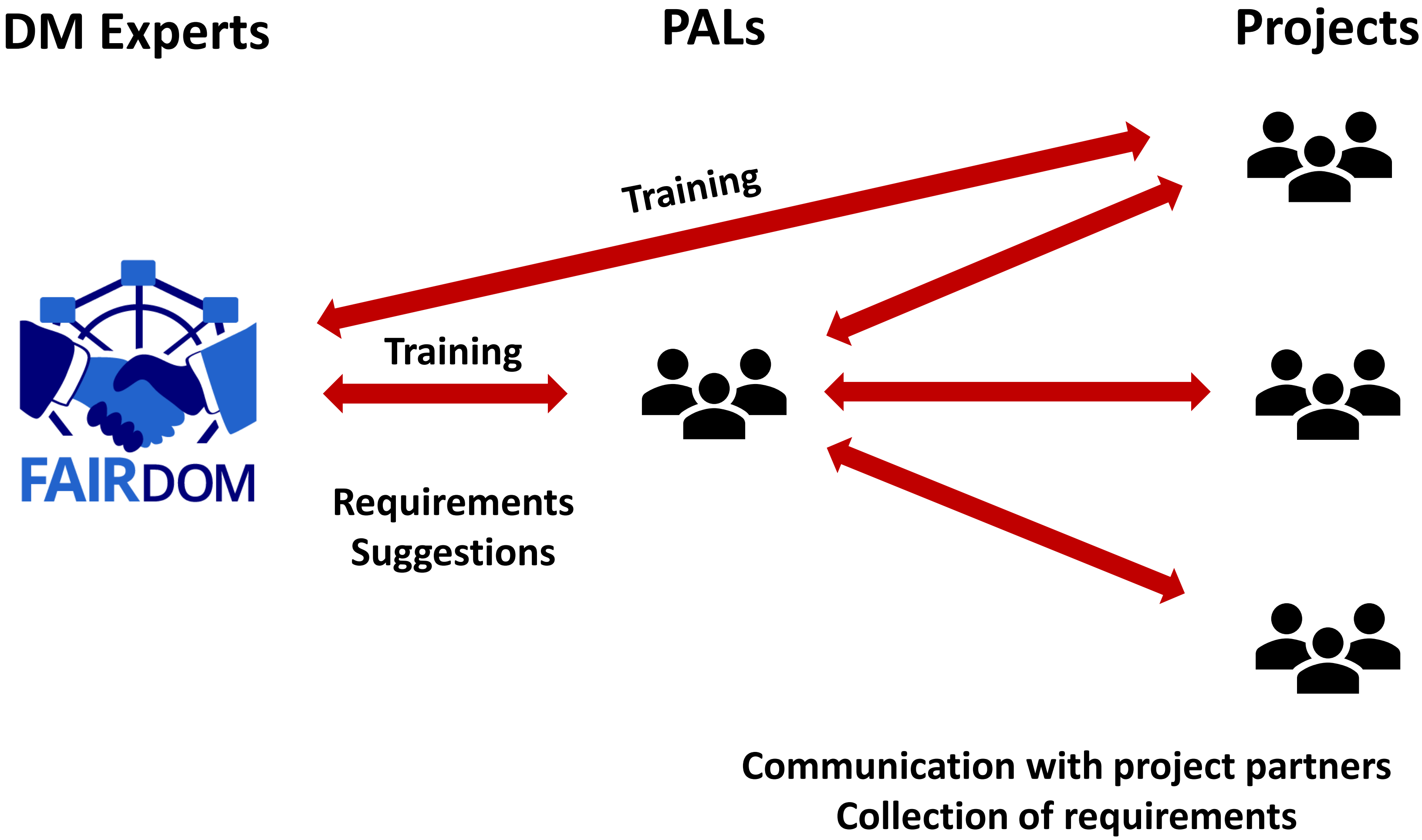
Managing, developing and updating the platforms and tools

SysMO
(Systems Biology for Micro-Organisms)

FAIRDOM supported 13 different research projects in the SysMO consortium (2006-2014):

BaCell-SysMO – The transition from growing to non-growing Bacillus subtilis cells. A systems biology approach.
COSMIC – Systems Biology of Clostridium acetobutylicum – a possible answer to dwindling crude oil reserves.
SUMO – Systems Understanding of Microbial Oxygen Responses.
KOSMOBAC – Ion and solute homeostasis in enteric bacteria: an integrated view from the interface of modelling and experimentation.
SysMO-LAB – Comparative Systems Biology: Lactic Acid Bacteria.
PSYSMO – Systems analysis of biotech induced stresses: towards a quantum increase in process performance in the cell factory Pseudomonas putida.
SCaRAB – Systems Biology of a genetically engineered Pseudomonas fluorescens with inducible exo-polysaccharide production: analysis of the dynamics and robustness of metabolic networks.
MOSES – MicroOrganism Systems Biology: Energy and Saccharomyces cerevisiae.
TRANSLUCENT – Gene interaction networks and models of cation homeostasis in Saccharomyces cerevisiae.
STREAM – Global metabolic switching in Streptomyces coelicolor.
SulfoSYS – Silicon cell model for the central carbohydrate metabolism of the archaeon Sulfolobus solfataricus under temperature variation.
SilicoTryp – The creation of a “Silicon Trypanosome”, a comprehensive, experiment-based, multi-scale mathematical model of trypanosome physiology.
Noisy Strep – Unravelling how transcription fidelity and processivity influences (noisy) gene expression in the human pathogen Streptococcus pneumoniae.

PALs - Project Area Liaisons



DM Experts

PALs

Projects

Training

FAIRDOM

Training

Requirements
Suggestions

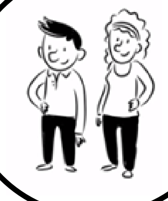
Communication with project partners
Collection of requirements

PALs - Project Area Liaisons

- Small team of “front line” experimentalists, modellers and bioinformaticians from different projects
  → data stewards /data managers
- Easier to disseminate new features and changes
- Communication with projects
- Requirements gathering and reporting
- Reviewing of ideas and prototypes

PALs - Project Area Liaisons

Different Users, Different Support



Independent researchers

EffeNet Effect Network in Water Research
– FungiNet –
SysMO Systems Biology of Microorganisms
virtual liver network
EMPOWER PUTIDA

Projects Programmes

ERASysAPP ERA-Net for Applied Systems Biology
ERA CoBioTech
LiSyM Liver Systems Medicine
NMTrypI New Medicines for Trypanosomatidic Infections

Facilities Centres

EMSL
CENTRE FOR DIGITAL LIFE NORWAY
HITS Heidelberg Institute for Theoretical Studies

Infrastructures

elixir NORWAY
EOSC-Life
IBISBA1.0 Industrial Biotechnology Innovation and Synthetic Biology Accelerator
de.NBI GERMAN NETWORK FOR BIOINFORMATICS INFRASTRUCTURE

FAIRDOM Training

- Customized training:
  - Workshops and hands-on training for research projects with focus on specific research topic
  - DM courses at institutions
  - Individual hands-on training in the institutions or laboratories
  - Individual online support/training

FAIRDOM User Community

- Open community for developers, user communities, and individual users
- For users interested in data management, in any of our platforms, in contributing to our codebase etc.

- Regular FAIRDOM Meetings
  - FAIRDOM Club Meeting: Strategic meeting for resources assignment, collaborations, new projects
  - FAIRDOM Community Workers Meeting: Outreach, training and prioritization of features requests
  - FAIRDOM Developers Meeting: Discussion of technical development
- Communication Channels
  - Slack
  - Github
  - Google groups

Questions?

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FAIRDOM

https://fair-dom.org