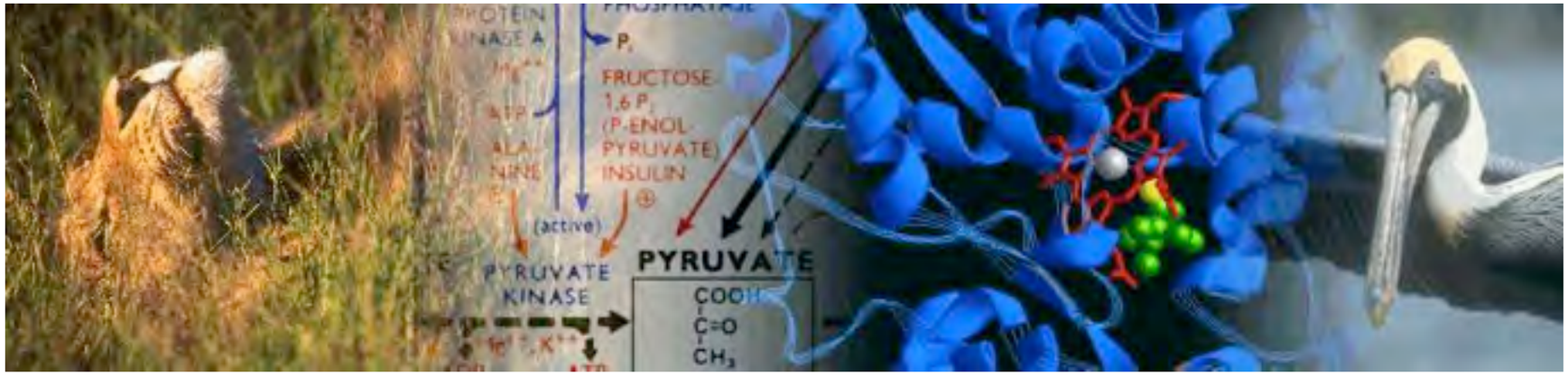
Tutorial: Modelling and Simulation of Quantitative Biological Models



JWS Online and OneStop

Dawie van Niekerk and Jacky Snoep

JWS Online team at SU and VU: Danie Palm, Johann Eicher, Carla Breytenbach and Cor Stoof

SysMO team at University of Manchester and at HITS

JWS Online and OneStop

- model repository (curated published models SBML)
- web based simulator (ODE type models)
- simple tool to build SBML, SBGN, MIRIAM model (OneStop)
- SED-ML enabled (save simulation specification and run)
- links experimental data and models (construction and validation data)
- linked to scientific journals (FEBSJ, IET-SB, Metabolomics, Microbiology)

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http://jjj.bio.vu.nl
http://jjj.mib.ac.uk
http://jjj.biochem.sun.ac.za

JWS Online as a service

Review-service for scientific journals

Teaching

Collaboration with research projects

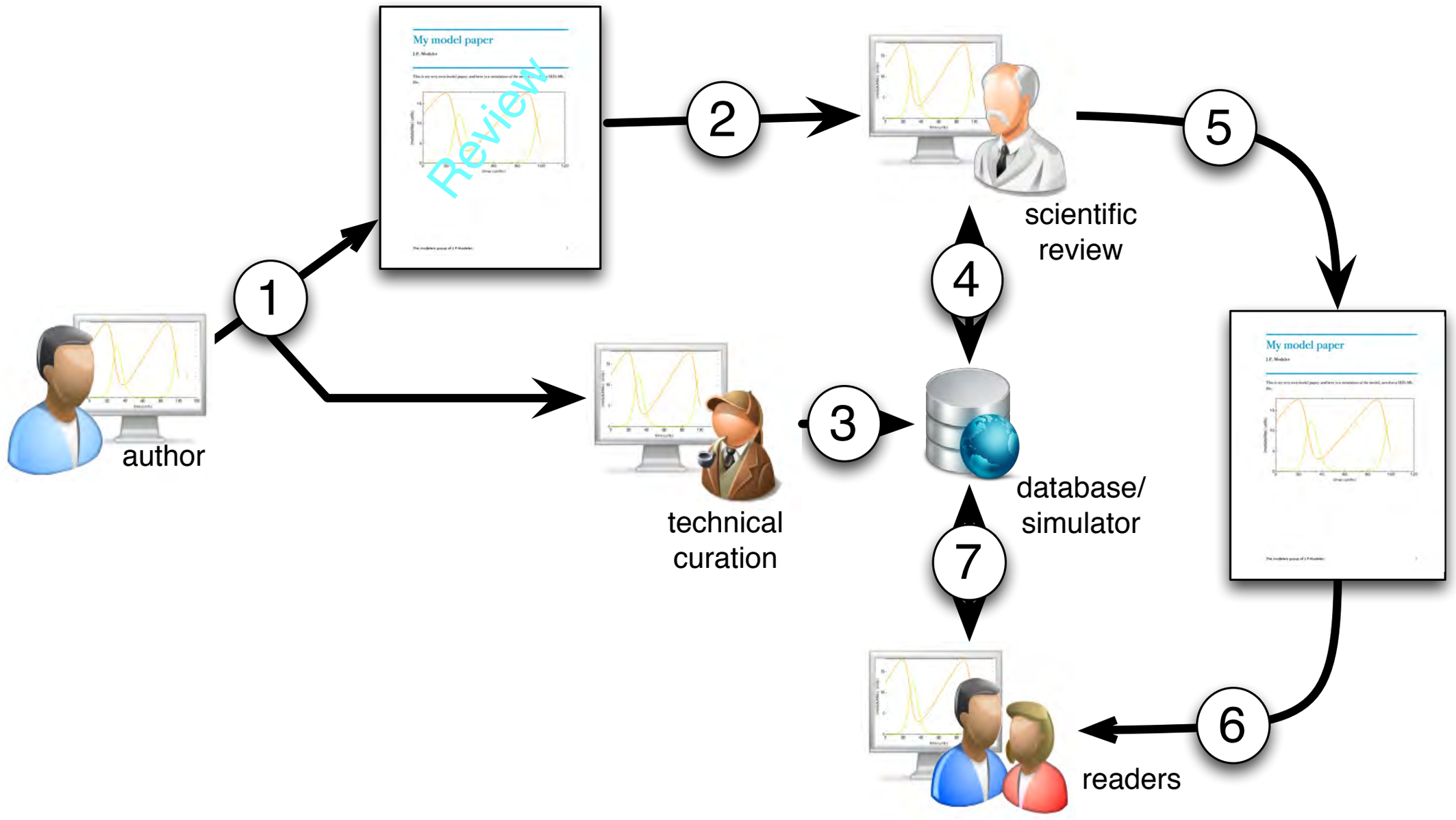
Model database
Web Simulator

Collaboration with research initiatives

Collaboration with research institutes

The Centre for Plant Integrative Biology

JWS Online: link to scientific journals



FEBSJ, IET-SB, Microbiology, Metabolomics

the FEBS Journal

Intermediate instability at high temperature leads to low pathway efficiency for an *in vitro* reconstituted system of gluconeogenesis in *Sulfolobus solfataricus*

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2 Molecular Cell Physiology, Vrije Universiteit, Amsterdam, The Netherlands
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Keywords
carbon loss; mathematical model; thermal instability; thermophile

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Four enzymes of the gluconeogenic pathway in *Sulfolobus solfataricus* were purified and kinetically characterized. The enzymes were reconstituted *in vitro* to quantify the contribution of temperature instability of the pathway intermediates to carbon loss from the system. The reconstituted system, consisting of phosphoglycerate kinase, glyceraldehyde 3-phosphate dehydrogenase, triose phosphate isomerase and the fructose 1,6-bisphosphate aldolase/phosphatase, maintained a constant consumption rate of 3-phosphoglycerate and production of fructose 6-phosphate over a 1-h period. Cofactors ATP and NADPH were regenerated via pyruvate kinase and glucose dehydrogenase. A mathematical model was constructed on the basis of the kinetics of the purified enzymes and the measured half-life times of the pathway intermediates. The model quantitatively predicted the system fluxes and metabolite concentrations. Relative enzyme concentrations were chosen such that half the carbon in the system was lost due to degradation of the thermolabile intermediates dihydroxyacetone phosphate, glyceraldehyde 3-phosphate and 1,3-bisphosphoglycerate, indicating that intermediate instability at high temperature can significantly affect pathway efficiency.

Database
The mathematical models described here have been submitted to the JWS Online Cellular Systems Modelling Database and can be accessed at http://jjj.mib.ac.uk/database/kouril/index.html. The investigation and complete experimental data set is available on the SEEK at https://seek.sysmo-db.org/investigations/51.

Abbreviations
BPG, 1,3-bis-phosphoglycerate; DHAP, dihydroxyacetone phosphate; EMP, Embden–Meyerhof–Parnas; FBPA/ase, fructose 1,6-bisphosphate aldolase/phosphatase (EC 4.1.2.13); F6P, fructose 6-phosphate; GAP, glyceraldehyde 3-phosphate; GAPDH, glyceraldehyde 3-phosphate dehydrogenase (phosphorylating) (EC 1.2.1.12); GAPN, non-phosphorylating GAPDH; GAPOR, ferredoxin-dependent glyceraldehyde 3-phosphate oxidoreductase; G6P, glucose 6-phosphate; IPTG, isopropyl thio-β-D-galactopyranoside; PEP, phosphoenolpyruvate; 3-PG, 3-phosphoglycerate; PGK, phosphoglycerate kinase (EC 2.7.2.3); TPI, triose-phosphate isomerase (EC 5.3.1.1).

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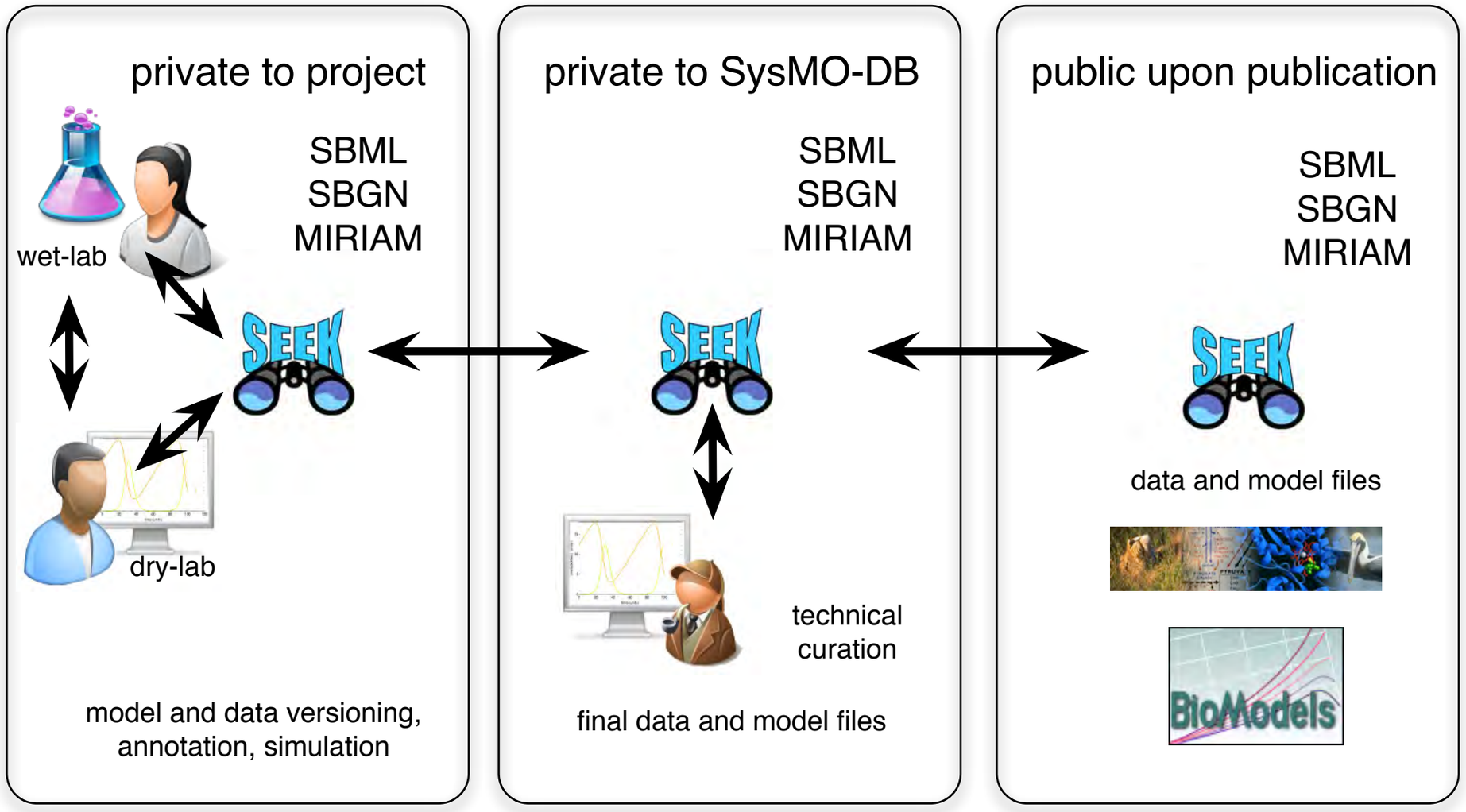
JWS Online: link to SEEK/projects



Thank you!

Heidelberger Institut für Theoretische Studien