Heidelberg Institute for
Theoretical Studies

SYCAMORE

http://sycamore.eml.org

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SYCAMORE

Outline

- motivation
- implementation
- main features
- interaction with other applications

SYCAMORE

"**SY**stems biology's **C**omputational **A**nalysis and **M**Odeling **R**esearch **E**nvironment"

Motivation

- to facilitate the set-up, simulation and analysis of new biochemical models, particularly by non-expert users
- facilitates building and modification of biochemical models
- view, analysis and refinement of models
- allows quick simulations
- interaction with other tools

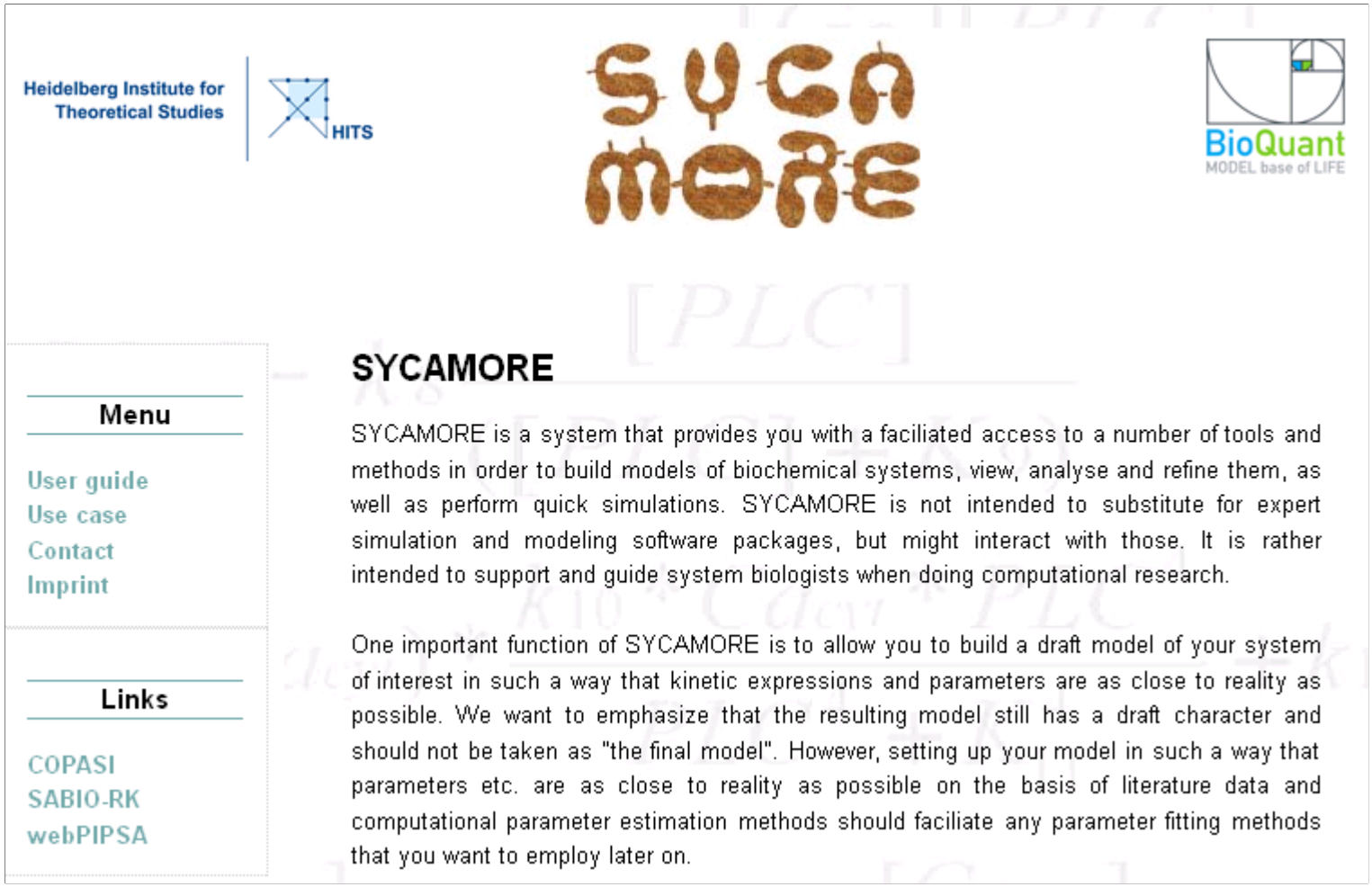
SYCAMORE

Implementation features

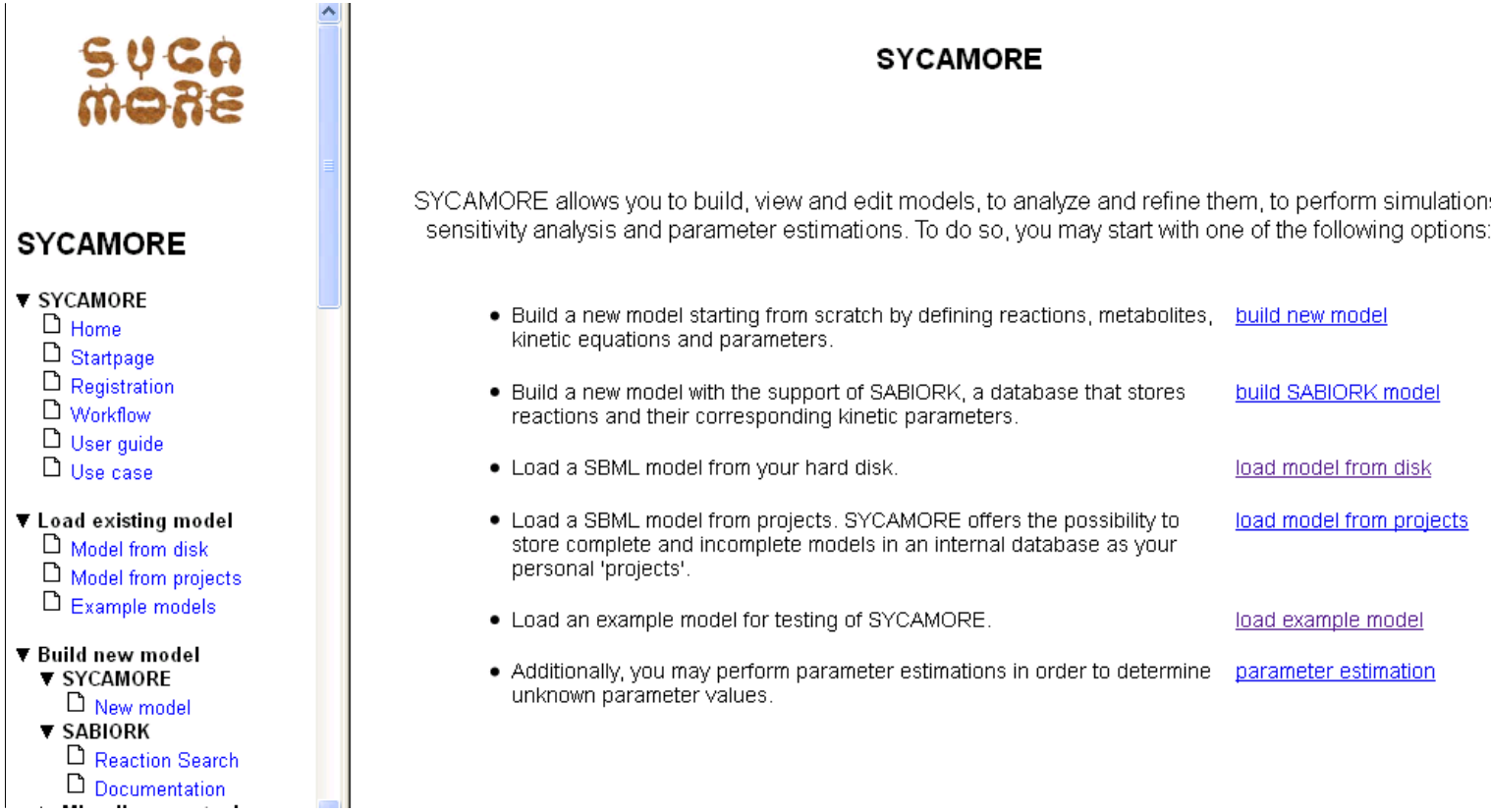
- no installation required: web application
- database supported modelling: SABIO-RK
- one platform for different programs, including
  - Copasi for simulation & sensitivity analysis
  - JWS online for simulation & visualization
  - qPIPSA for parameter estimation

Sycamore Homepage

http://sycamore.eml.org/

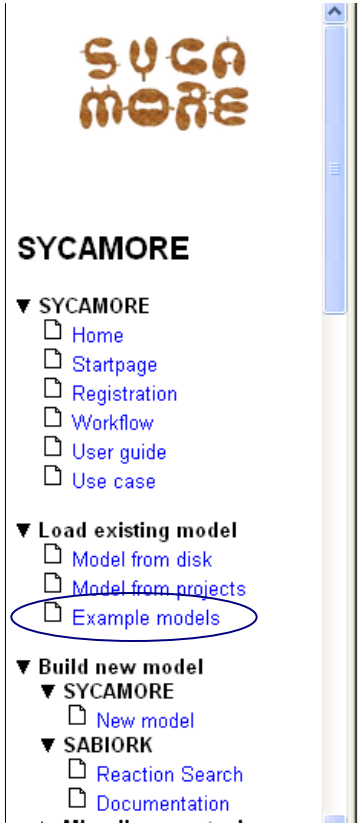


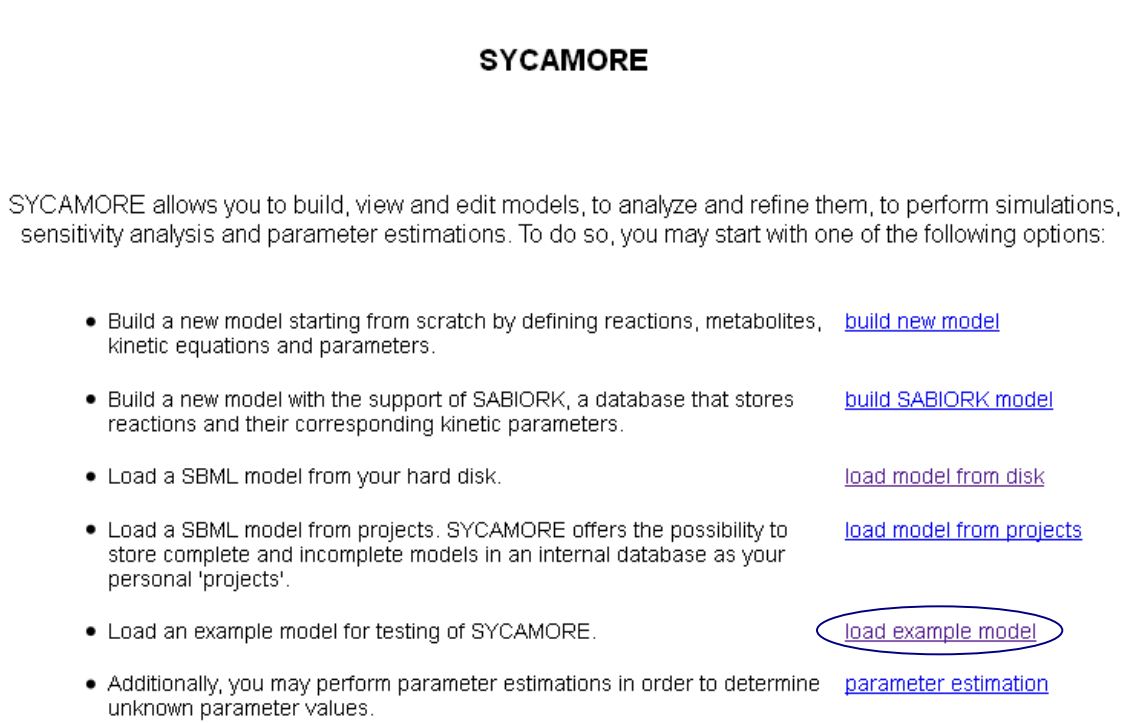
Sycamore start screen



Sycamore start screen

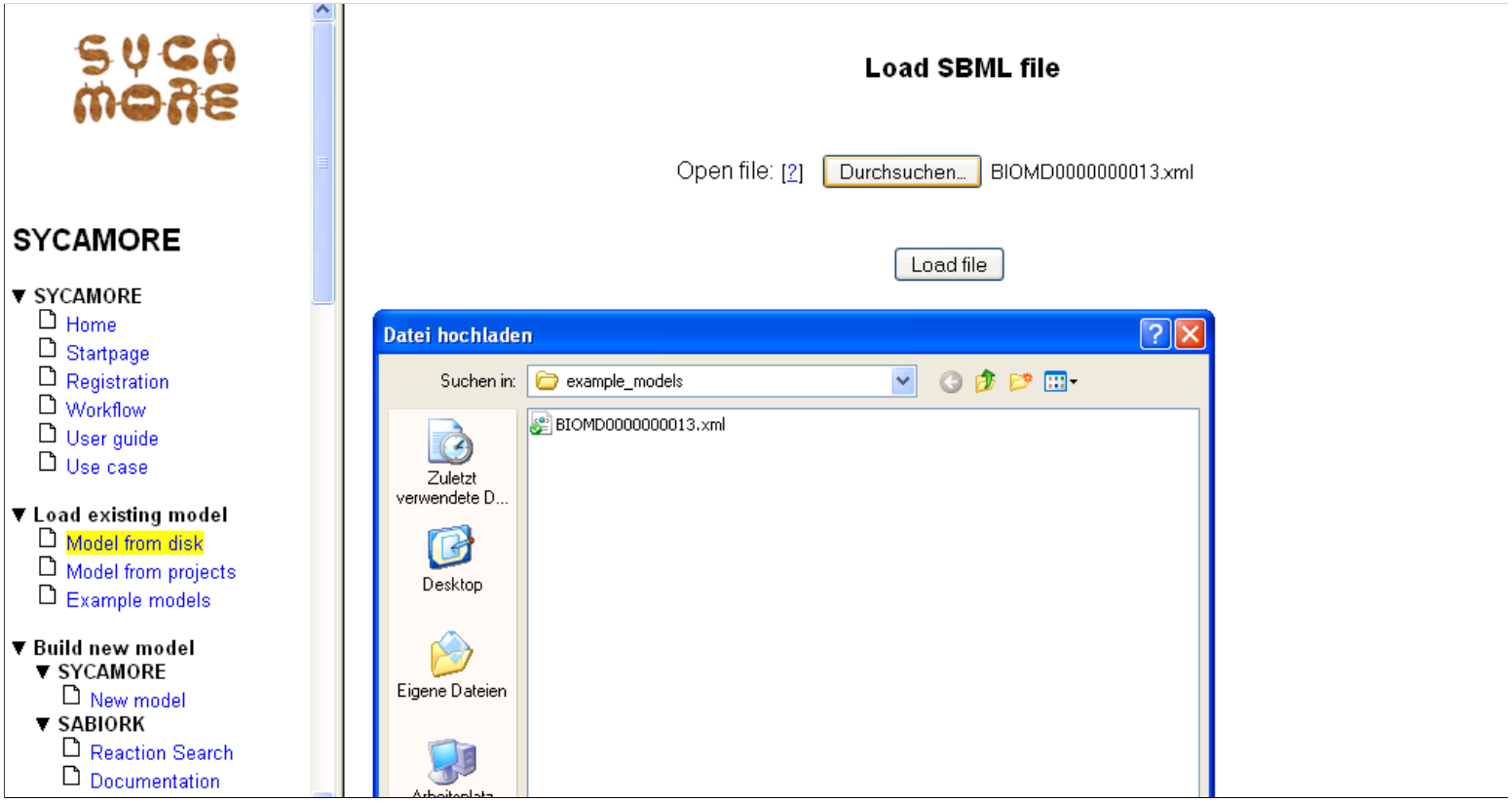
Example models provided for testing





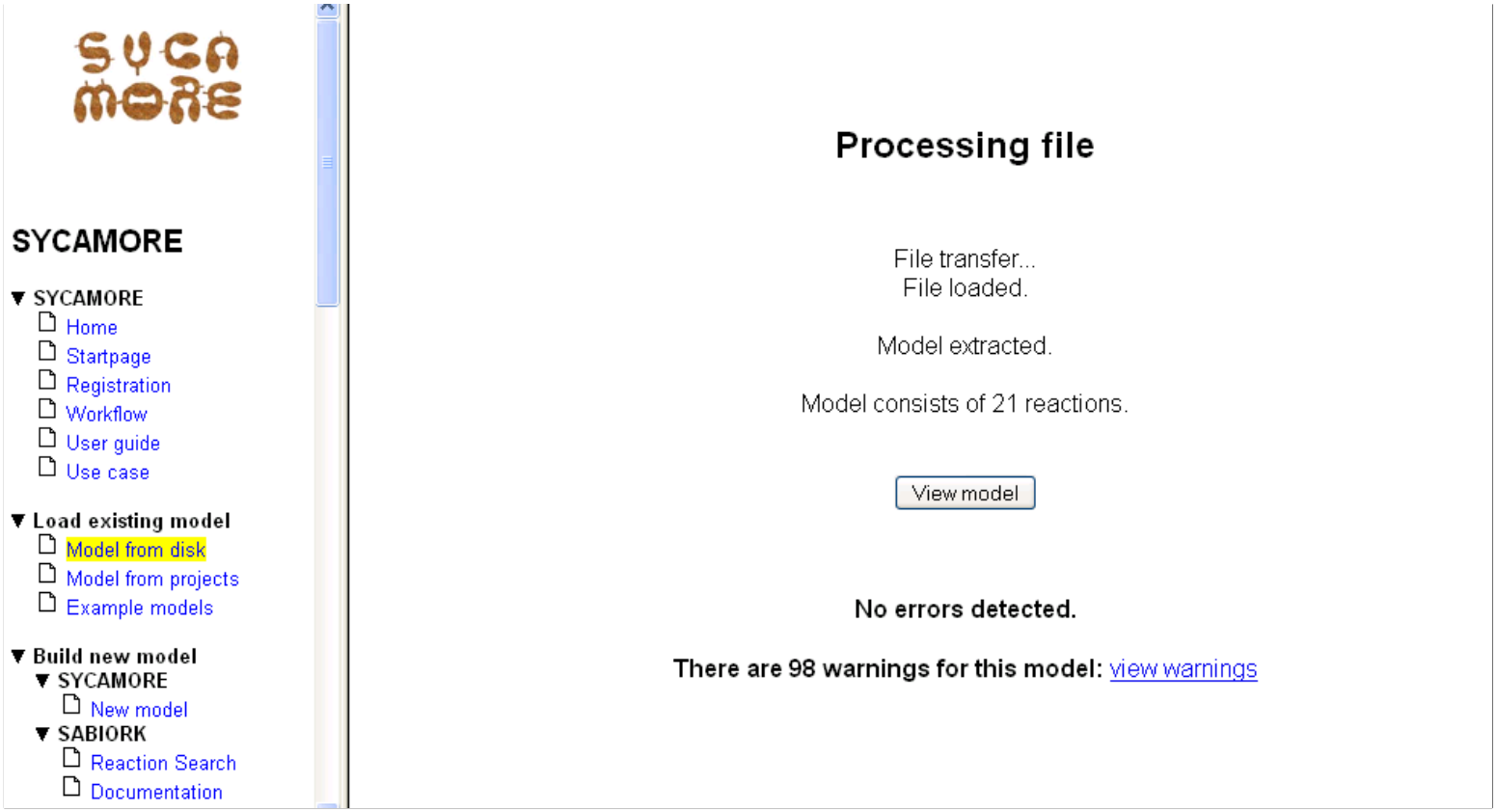
Model import

Upload of models (SBML format)



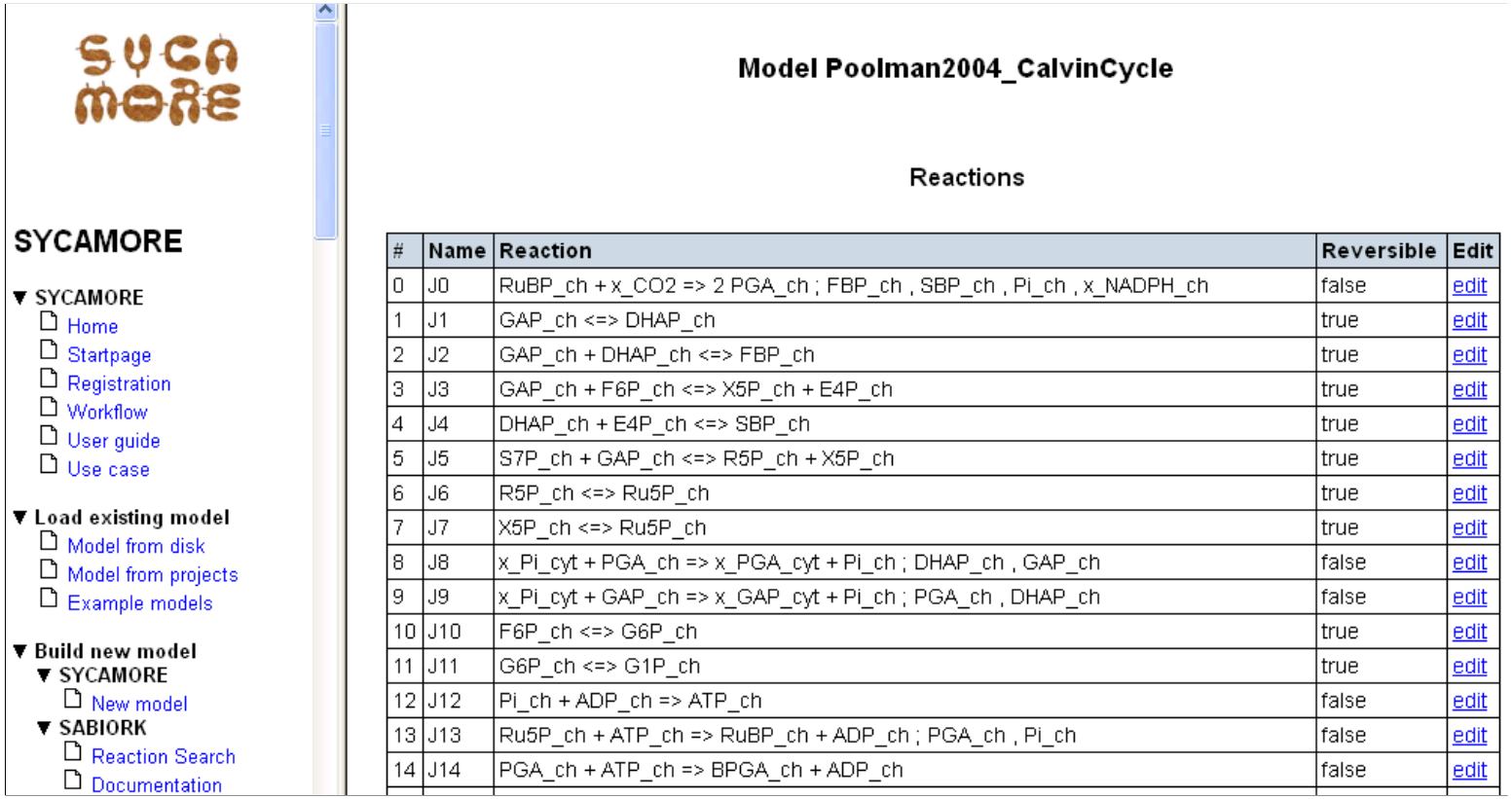
Model import

Model validation: http://sbml.org/validator/ (F. Bergmann)



Model editing

Display of all model data



SYCAMORE

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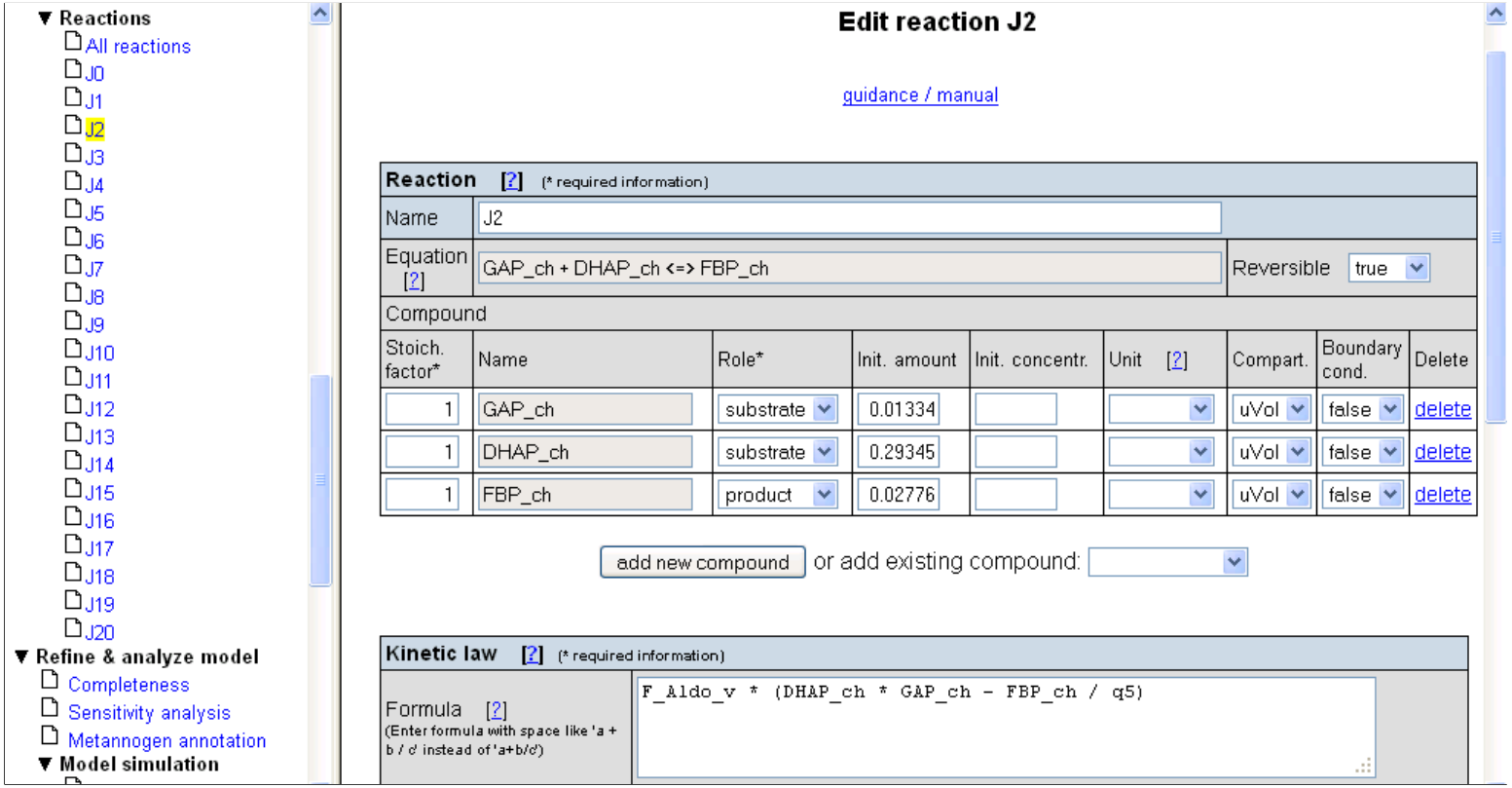
Model Poolman2004_CalvinCycle

Reactions

#	Name	Reaction	Reversible	Edit
0	J0	RuBP_ch + x_CO2 => 2 PGA_ch ; FBP_ch , SBP_ch , Pi_ch , x_NADPH_ch	false	edit
1	J1	GAP_ch <=> DHAP_ch	true	edit
2	J2	GAP_ch + DHAP_ch <=> FBP_ch	true	edit
3	J3	GAP_ch + F6P_ch <=> X5P_ch + E4P_ch	true	edit
4	J4	DHAP_ch + E4P_ch <=> SBP_ch	true	edit
5	J5	S7P_ch + GAP_ch <=> R5P_ch + X5P_ch	true	edit
6	J6	R5P_ch <=> Ru5P_ch	true	edit
7	J7	X5P_ch <=> Ru5P_ch	true	edit
8	J8	x_Pi_cyt + PGA_ch => x_PGA_cyt + Pi_ch ; DHAP_ch , GAP_ch	false	edit
9	J9	x_Pi_cyt + GAP_ch => x_GAP_cyt + Pi_ch ; PGA_ch , DHAP_ch	false	edit
10	J10	F6P_ch <=> G6P_ch	true	edit
11	J11	G6P_ch <=> G1P_ch	true	edit
12	J12	Pi_ch + ADP_ch => ATP_ch	false	edit
13	J13	Ru5P_ch + ATP_ch => RuBP_ch + ADP_ch ; PGA_ch , Pi_ch	false	edit
14	J14	PGA_ch + ATP_ch => BPGA_ch + ADP_ch	false	edit

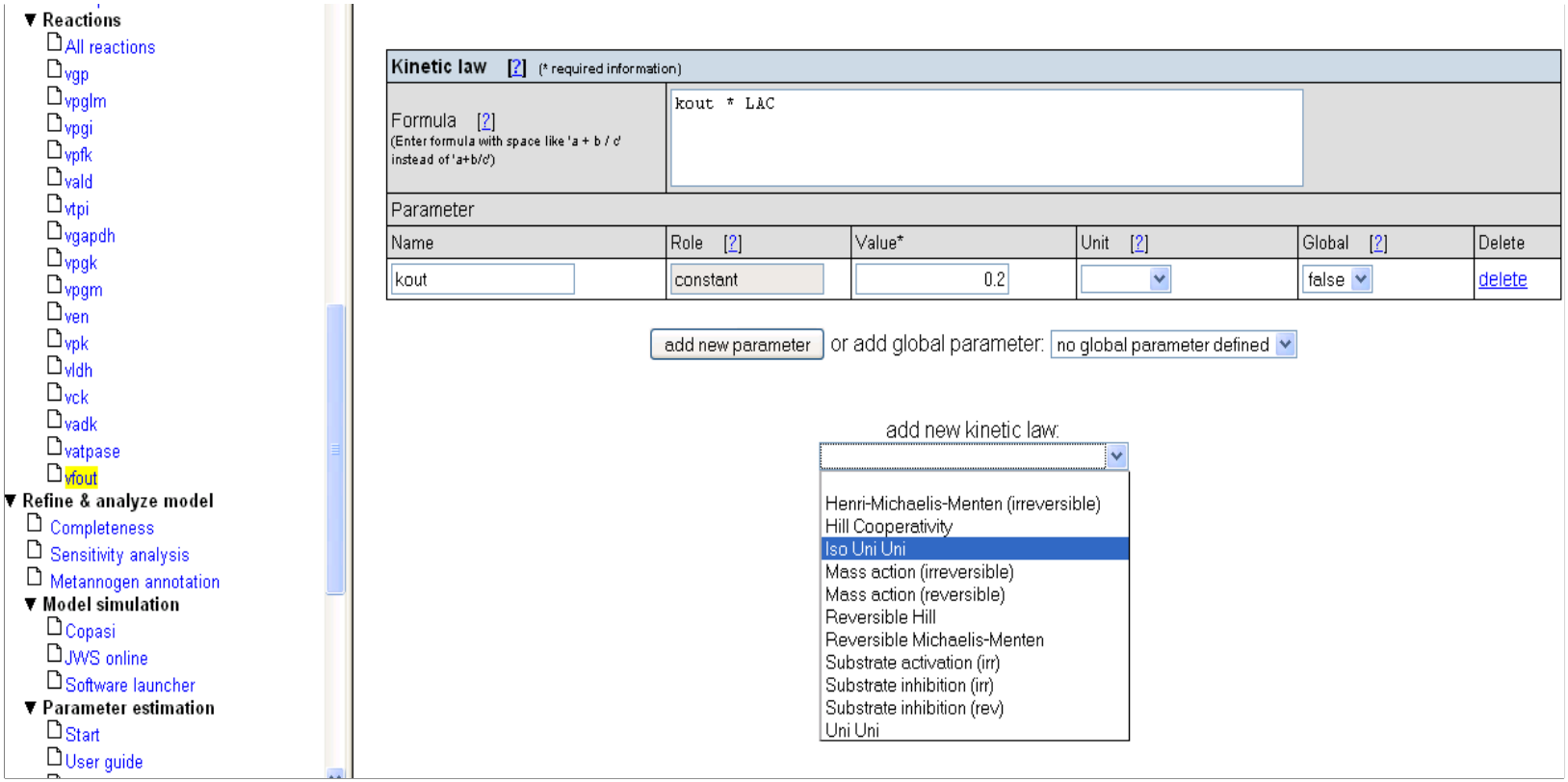
Model editing

Reactions including compounds, kinetic law and parameters



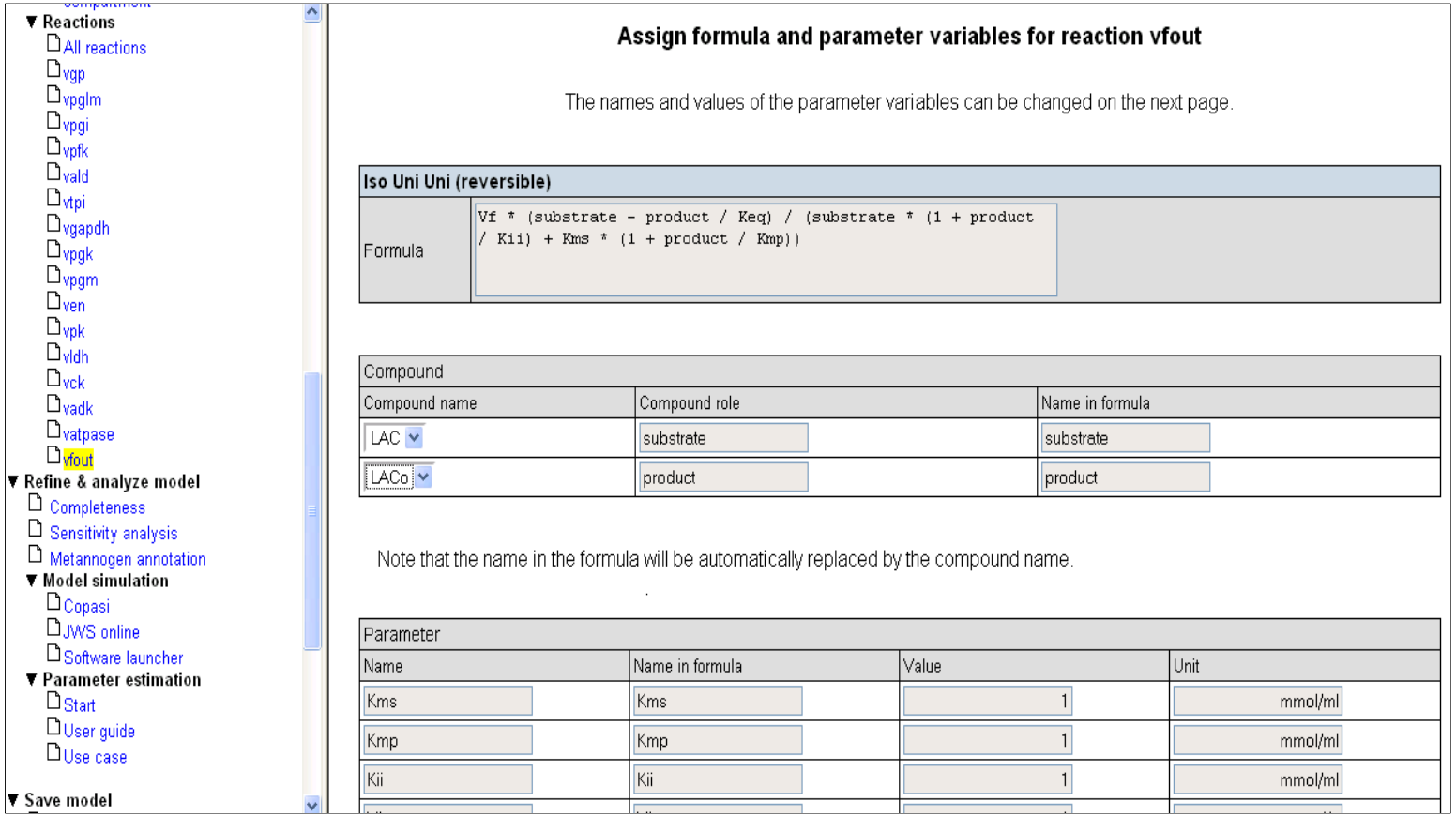
User support: example I

Predefined kinetic law equations
(selection dependent on reaction equation)



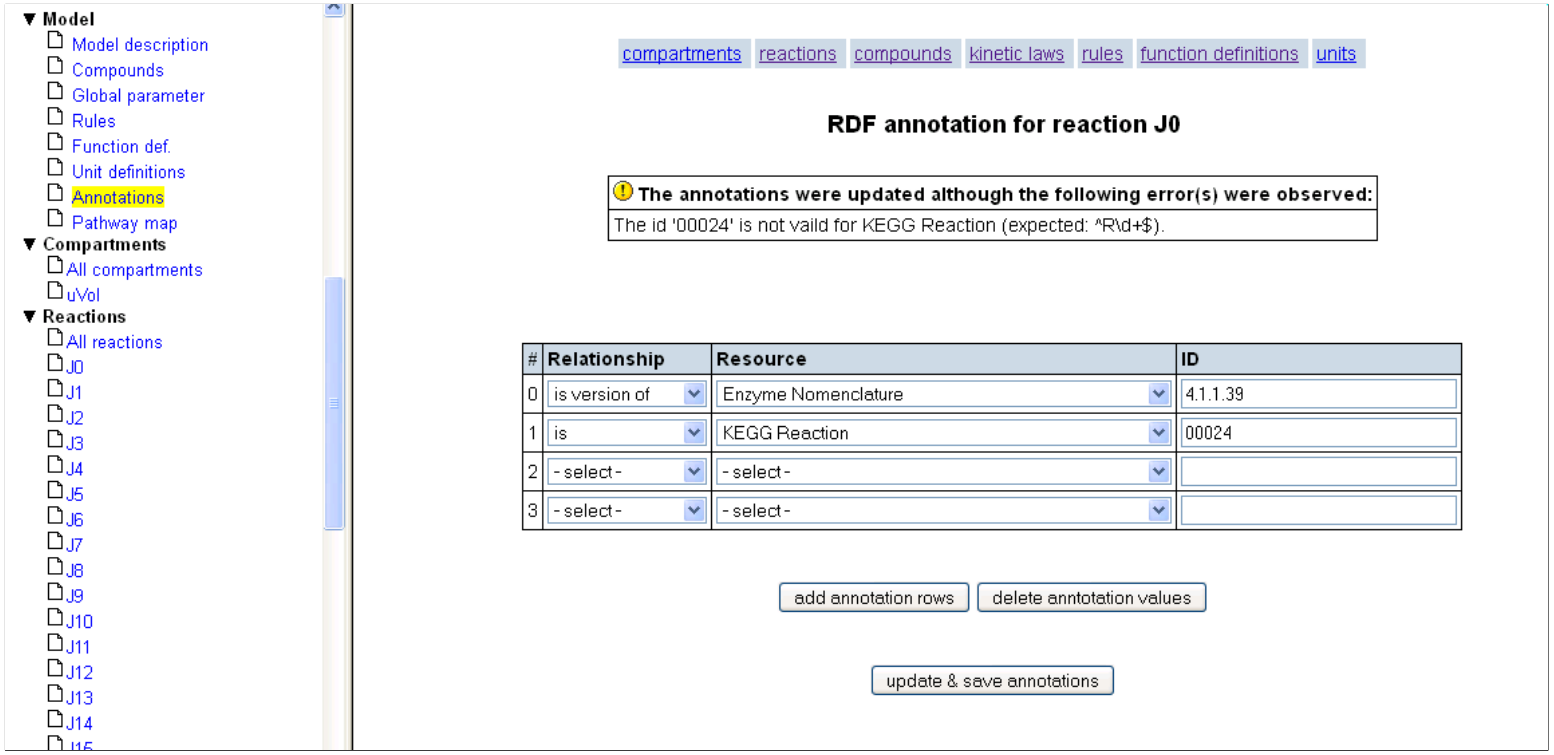
User support: example I

Predefined kinetic law equations



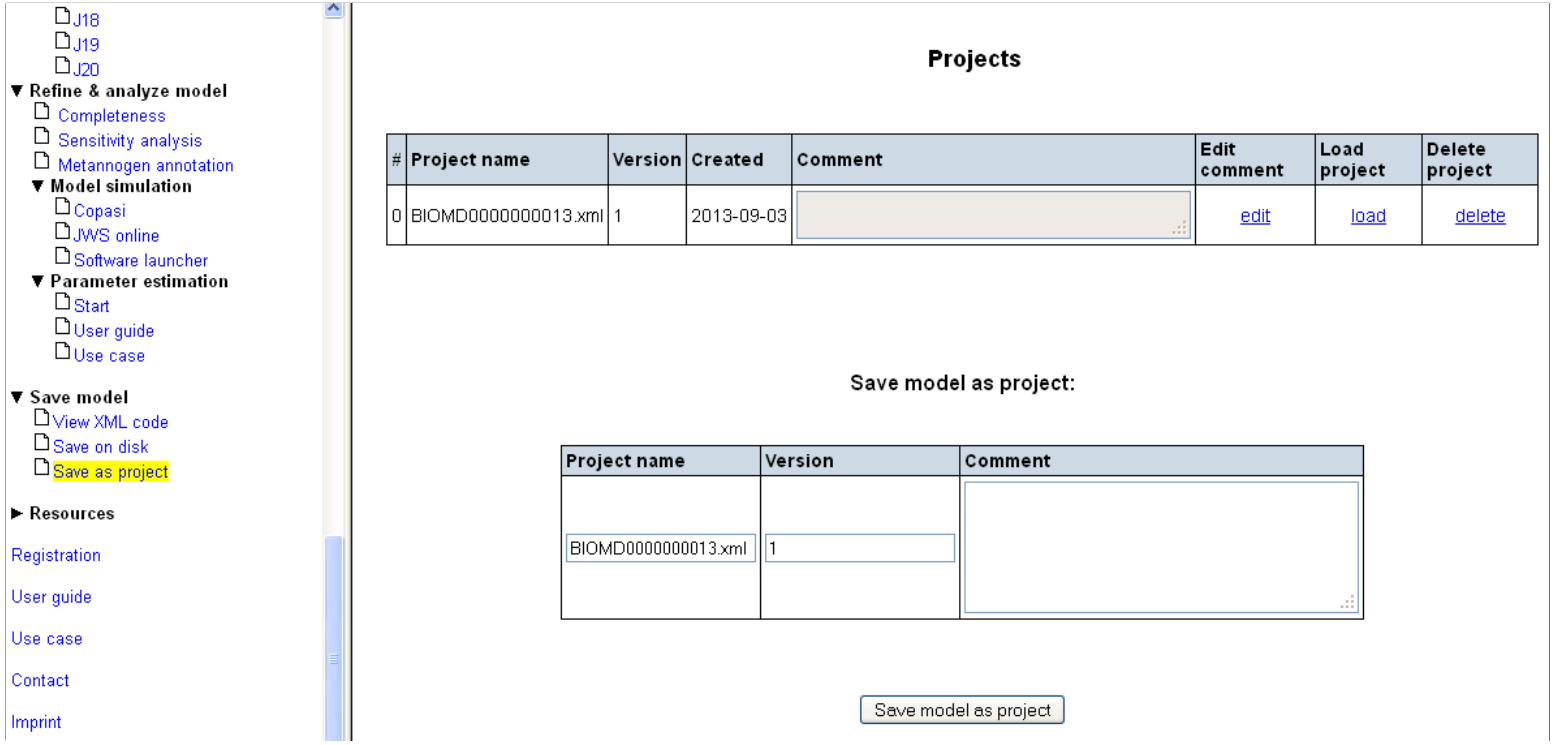
User support: example II

Annotation support (MIRIAM compliant)



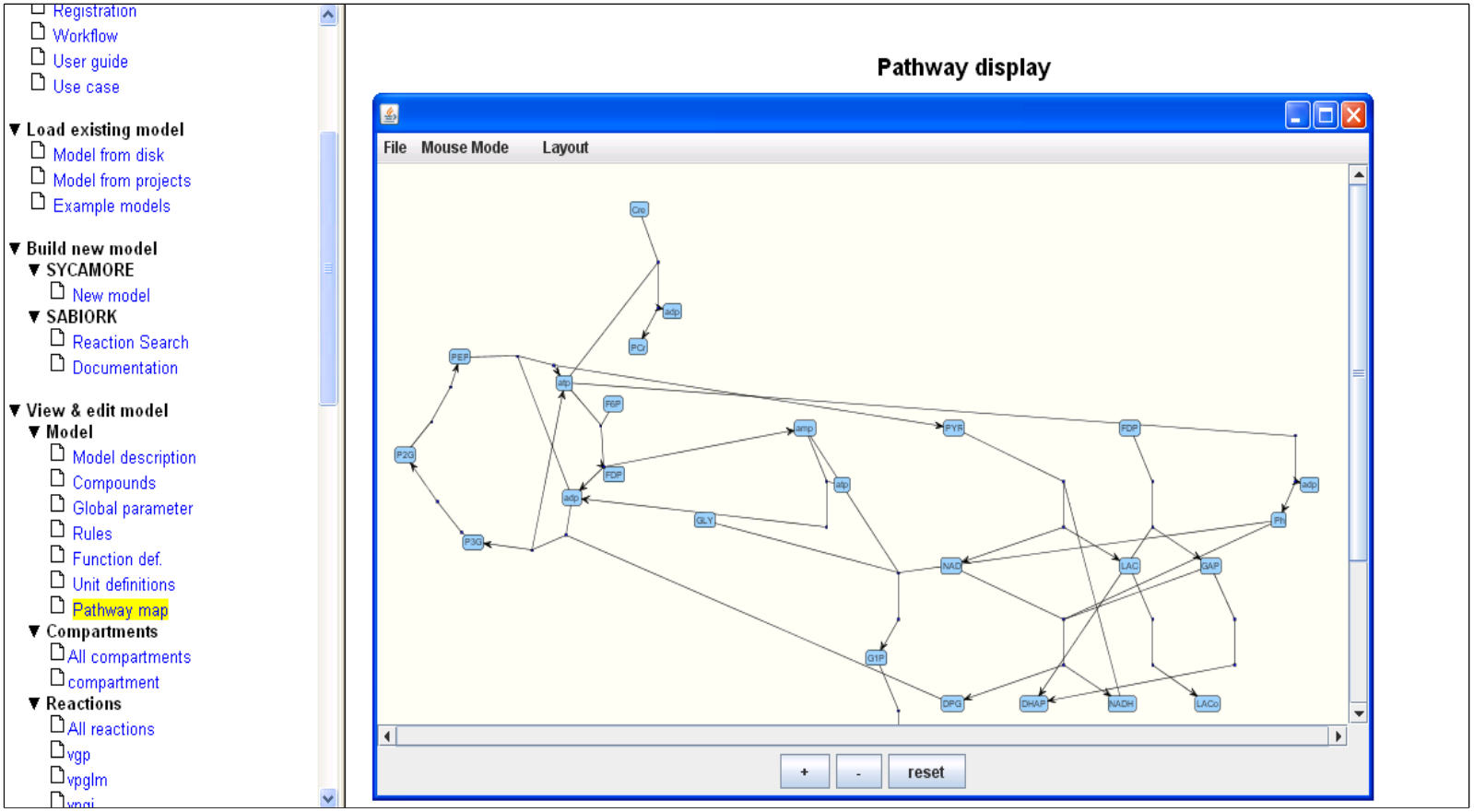
Online storage of models

(registration required)



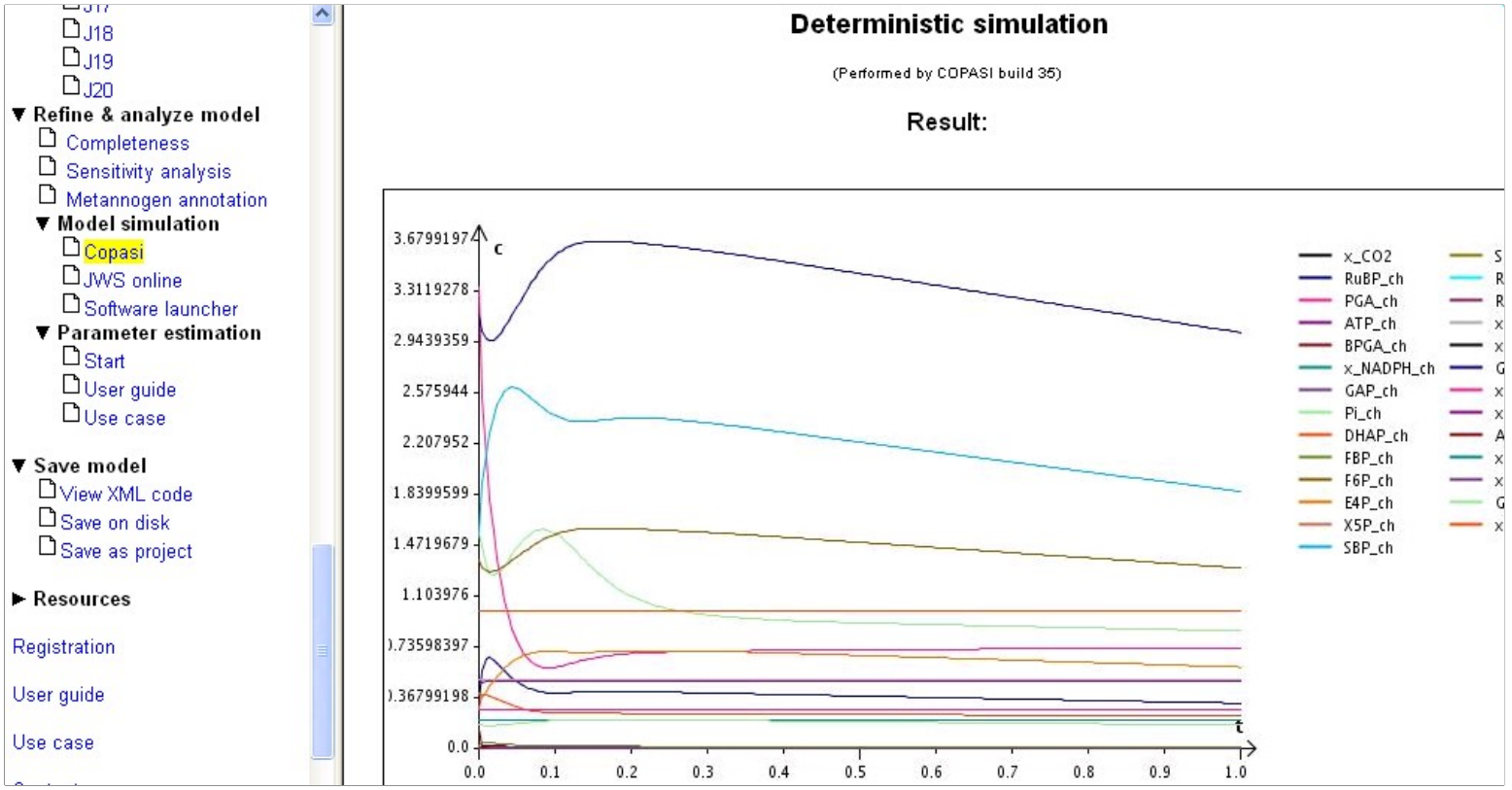
Pathway visualisation

(SBGN import/export/display in next release)



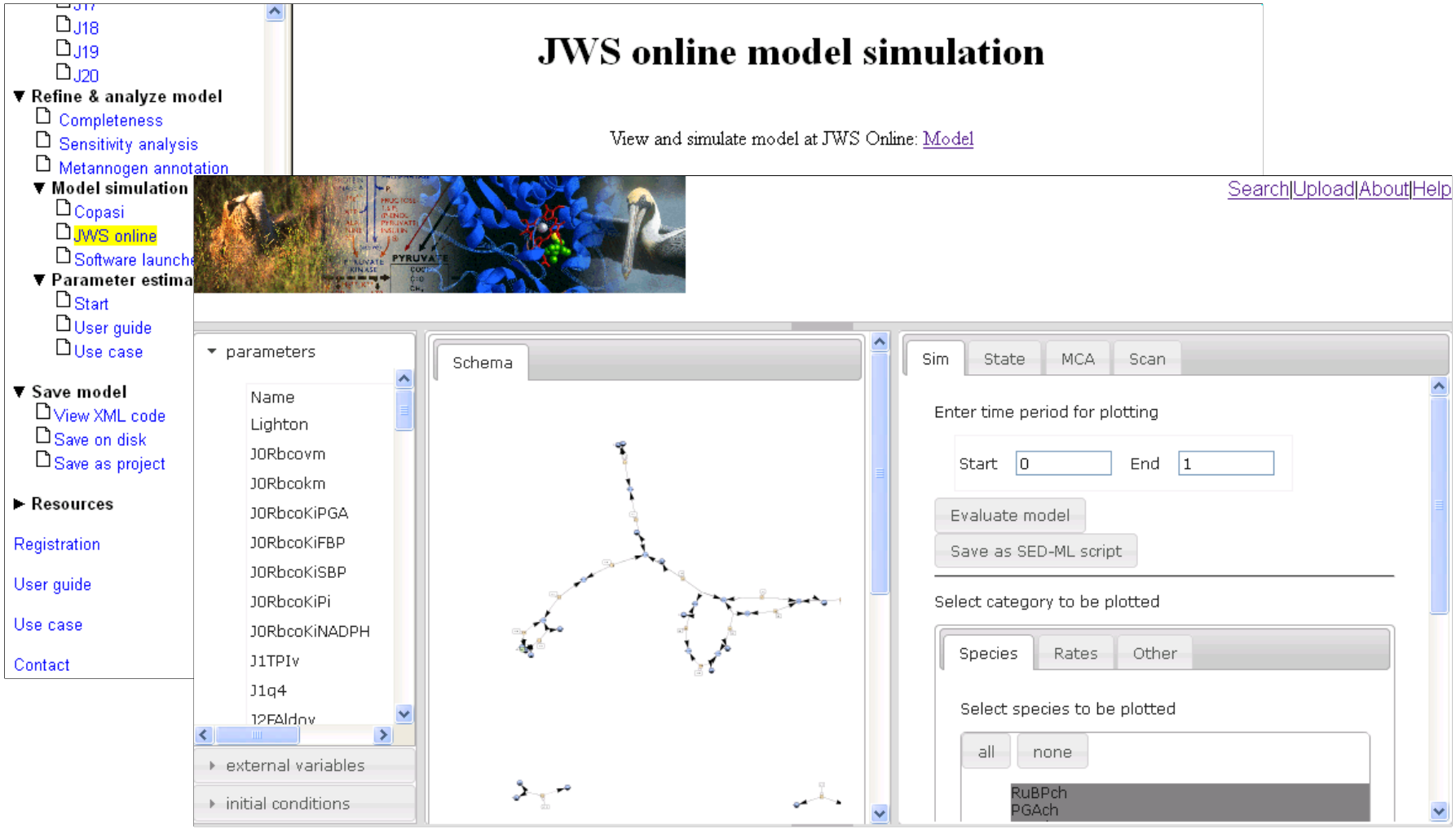
Model simulation

Time course simulation of metabolite concentrations (COPASI)



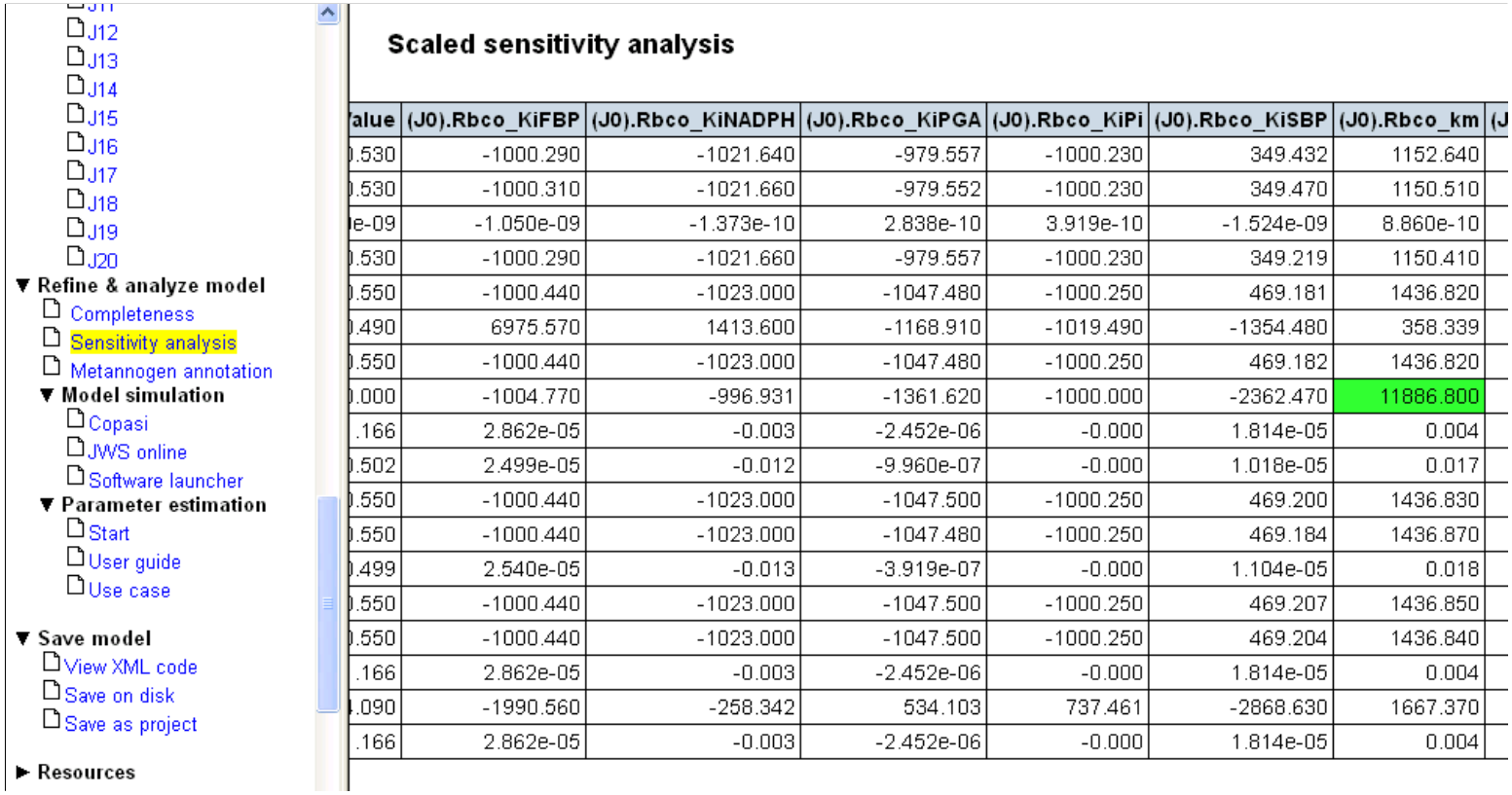
JWS online integration

(J. Snoep http://jjj.biochem.sun.ac.za/)



Sensitivity analysis

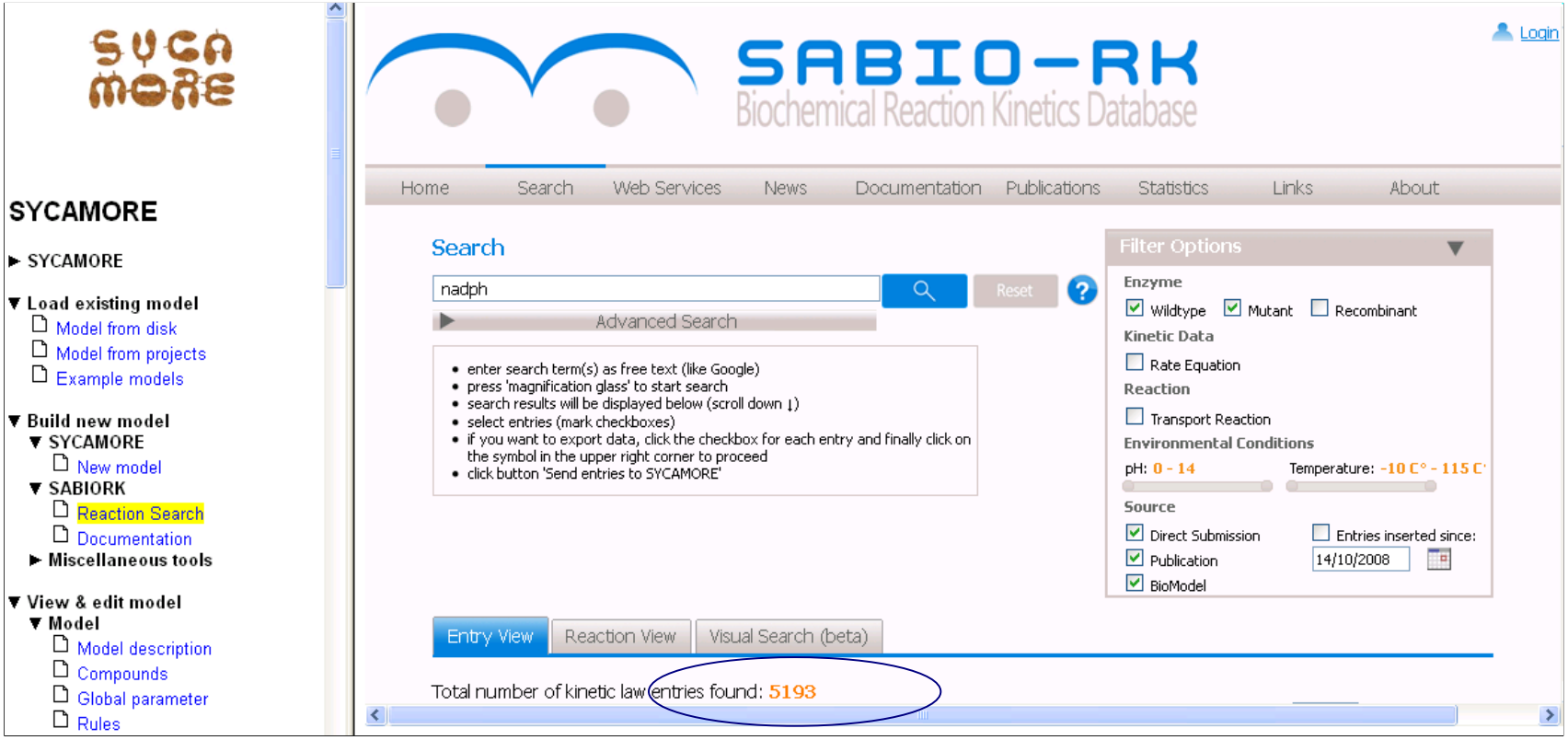
Find those parameters to which the concentrations of interest are most sensitive. These parameters are expected to be crucial for the models behaviour. (COPASI backend)



alue	(J0).Rbco_KiFBP	(J0).Rbco_KiNADPH	(J0).Rbco_KiPGA	(J0).Rbco_KiPi	(J0).Rbco_KiSBP	(J0).Rbco_km	(J
.530	-1000.290	-1021.640	-979.557	-1000.230	349.432	1152.640	
.530	-1000.310	-1021.660	-979.552	-1000.230	349.470	1150.510	
e-09	-1.050e-09	-1.373e-10	2.838e-10	3.919e-10	-1.524e-09	8.860e-10	
.530	-1000.290	-1021.660	-979.557	-1000.230	349.219	1150.410	
.550	-1000.440	-1023.000	-1047.480	-1000.250	469.181	1436.820	
.490	6975.570	1413.600	-1168.910	-1019.490	-1354.480	358.339	
.550	-1000.440	-1023.000	-1047.480	-1000.250	469.182	1436.820	
.000	-1004.770	-996.931	-1361.620	-1000.000	-2362.470	11886.800	
.166	2.862e-05	-0.003	-2.452e-06	-0.000	1.814e-05	0.004	
.502	2.499e-05	-0.012	-9.960e-07	-0.000	1.018e-05	0.017	
.550	-1000.440	-1023.000	-1047.500	-1000.250	469.200	1436.830	
.550	-1000.440	-1023.000	-1047.480	-1000.250	469.184	1436.870	
.499	2.540e-05	-0.013	-3.919e-07	-0.000	1.104e-05	0.018	
.550	-1000.440	-1023.000	-1047.500	-1000.250	469.207	1436.850	
.550	-1000.440	-1023.000	-1047.500	-1000.250	469.204	1436.840	
.166	2.862e-05	-0.003	-2.452e-06	-0.000	1.814e-05	0.004	
.090	-1990.560	-258.342	534.103	737.461	-2868.630	1667.370	
.166	2.862e-05	-0.003	-2.452e-06	-0.000	1.814e-05	0.004	

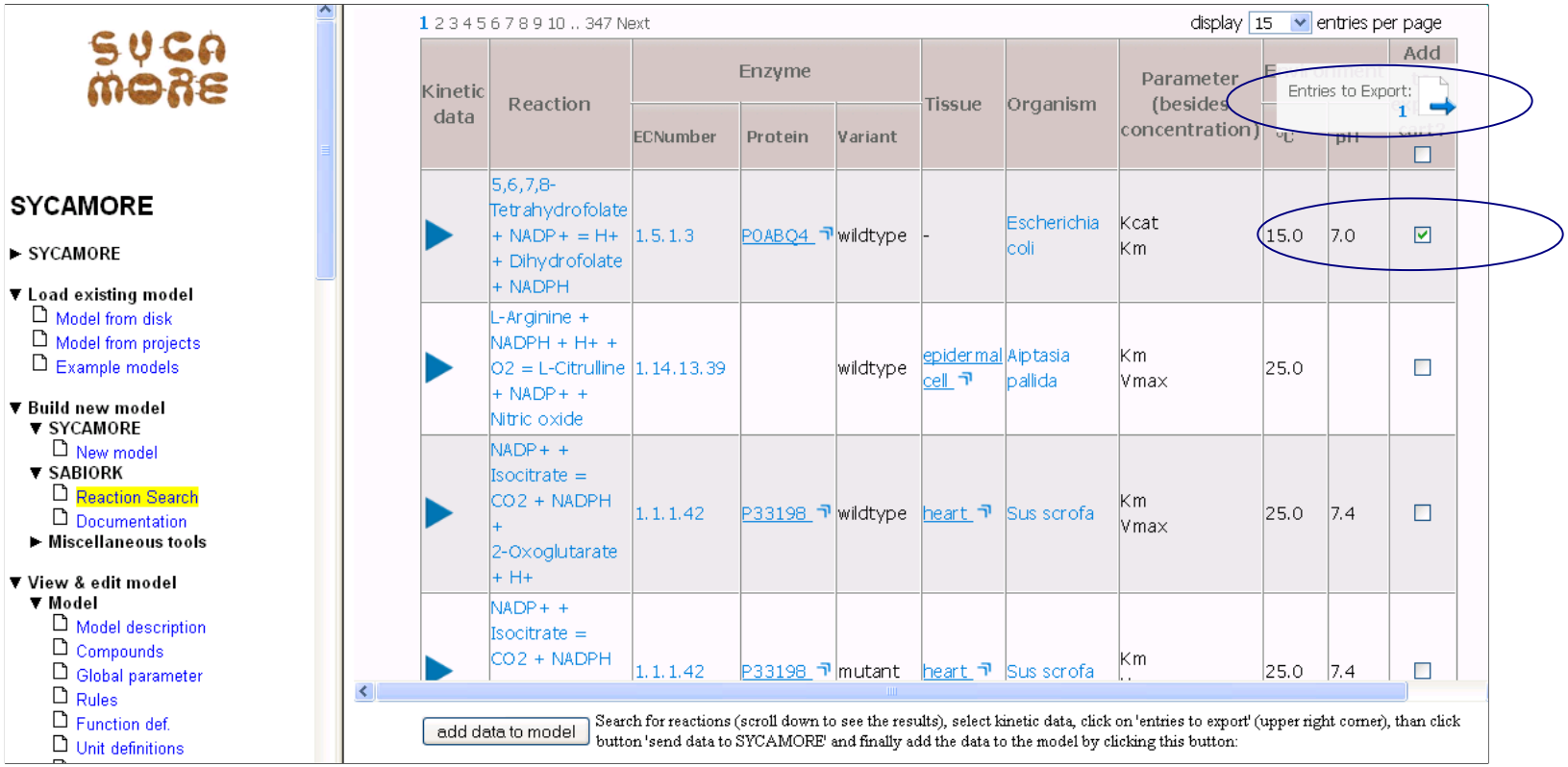
Database supported modelling I

SABIO-RK: search for data



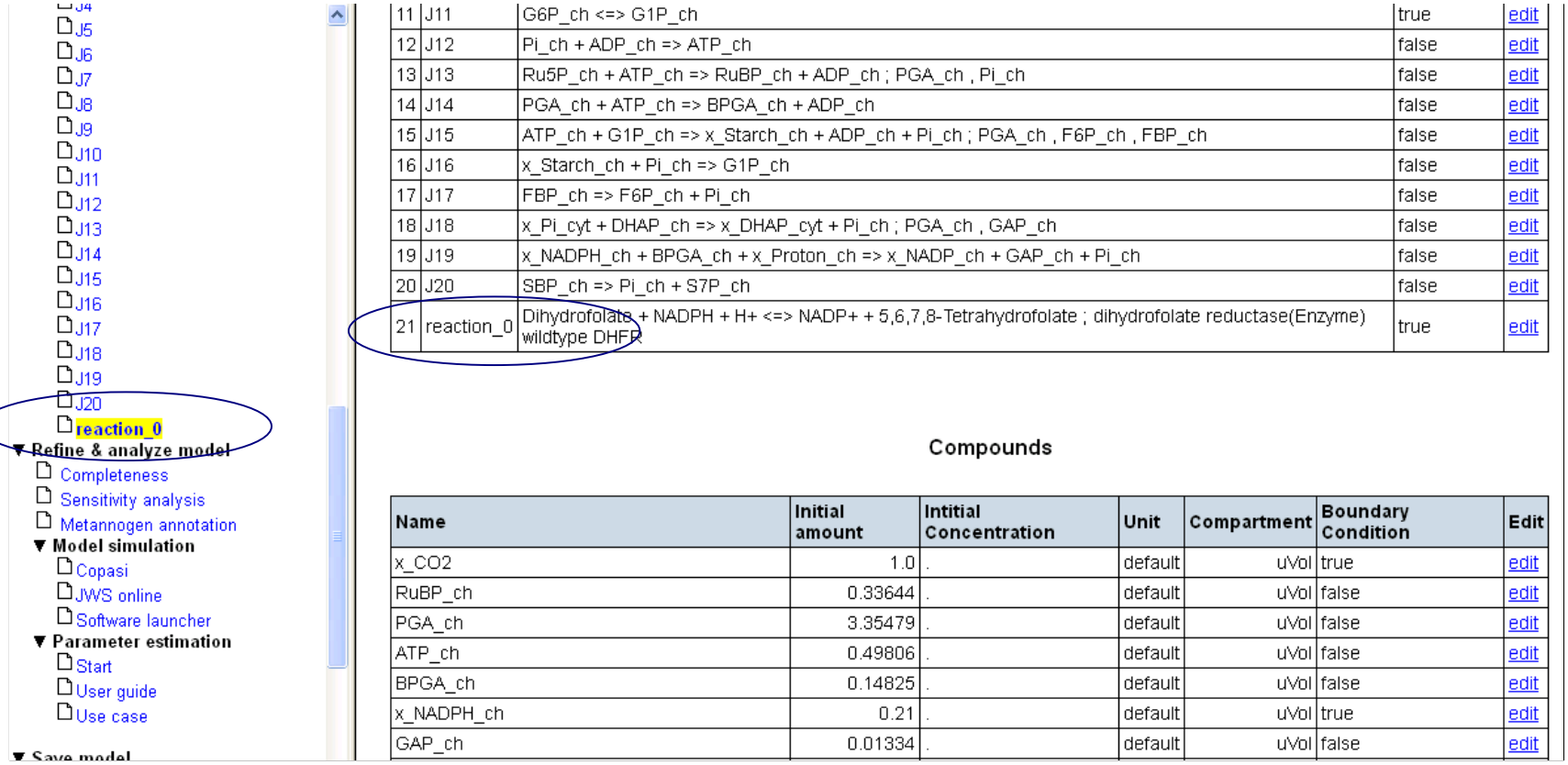
Database supported modelling I

SABIO-RK: data export



Database supported modelling II

SABIO-RK: data import into SYCAMORE



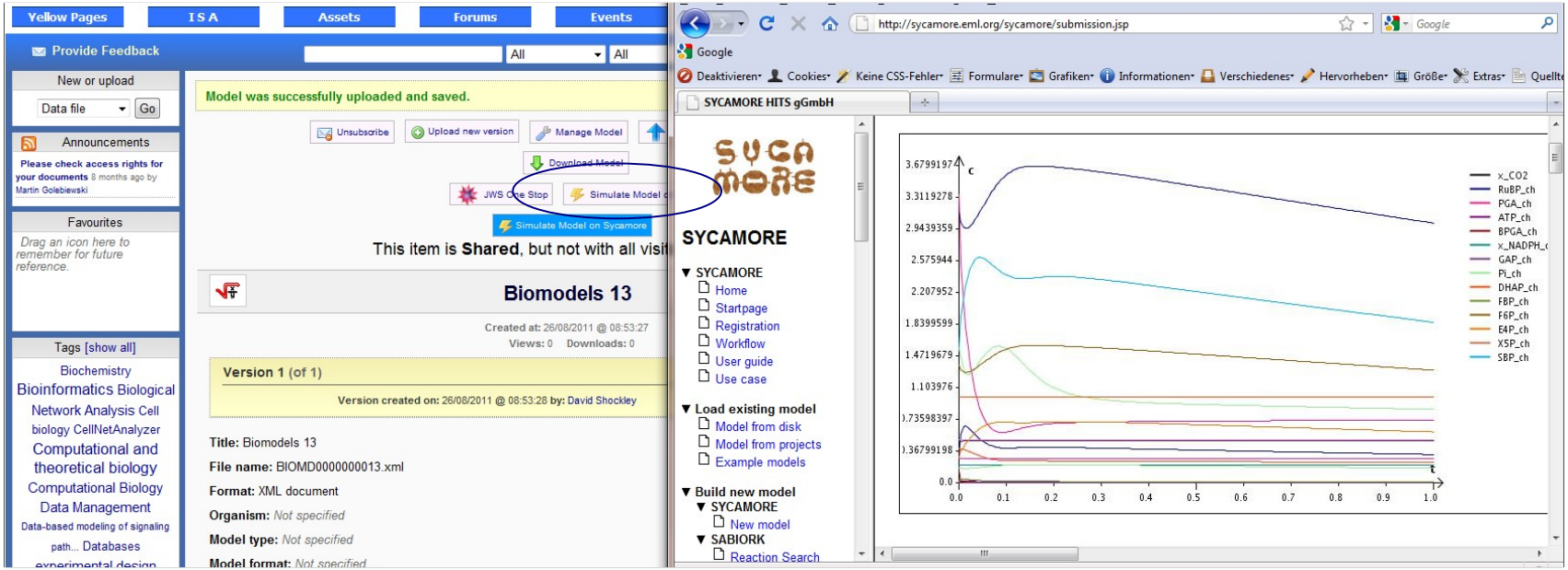
11	J11	G6P_ch <=> G1P_ch	true	edit
12	J12	Pi_ch + ADP_ch => ATP_ch	false	edit
13	J13	Ru5P_ch + ATP_ch => RuBP_ch + ADP_ch ; PGA_ch , Pi_ch	false	edit
14	J14	PGA_ch + ATP_ch => BPGA_ch + ADP_ch	false	edit
15	J15	ATP_ch + G1P_ch => x_Starch_ch + ADP_ch + Pi_ch ; PGA_ch , F6P_ch , FBP_ch	false	edit
16	J16	x_Starch_ch + Pi_ch => G1P_ch	false	edit
17	J17	FBP_ch => F6P_ch + Pi_ch	false	edit
18	J18	x_Pi_cyt + DHAP_ch => x_DHAP_cyt + Pi_ch ; PGA_ch , GAP_ch	false	edit
19	J19	x_NADPH_ch + BPGA_ch + x_Proton_ch => x_NADP_ch + GAP_ch + Pi_ch	false	edit
20	J20	SBP_ch => Pi_ch + S7P_ch	false	edit
21	reaction_0	Dihydrofolate + NADPH + H+ <=> NADP+ + 5,6,7,8-Tetrahydrofolate ; dihydrofolate reductase(Enzyme) wildtype DHFR	true	edit

Compounds

Name	Initial amount	Intitial Concentration	Unit	Compartment	Boundary Condition	Edit
x_CO2	1.0	.	default	uVol	true	edit
RuBP_ch	0.33644	.	default	uVol	false	edit
PGA_ch	3.35479	.	default	uVol	false	edit
ATP_ch	0.49806	.	default	uVol	false	edit
BPGA_ch	0.14825	.	default	uVol	false	edit
x_NADPH_ch	0.21	.	default	uVol	true	edit
GAP_ch	0.01334	.	default	uVol	false	edit

Integration into VLN SEEK

Analysis of models stored in SEEK



Parameter estimation: PIPSA

- Often, kinetic parameters for enzymes such as Km or kcat/Km are not available from the desired species but have been measured for enzymes from other species
- The electrostatic potential is one of the key determinants of enzymatic catalysis
- PIPSA, **P**rotein **I**nteraction **P**roperty **S**imilarity **A**nalysis, can be used to aid the estimation of kinetic parameters, based on known parameters of similar species

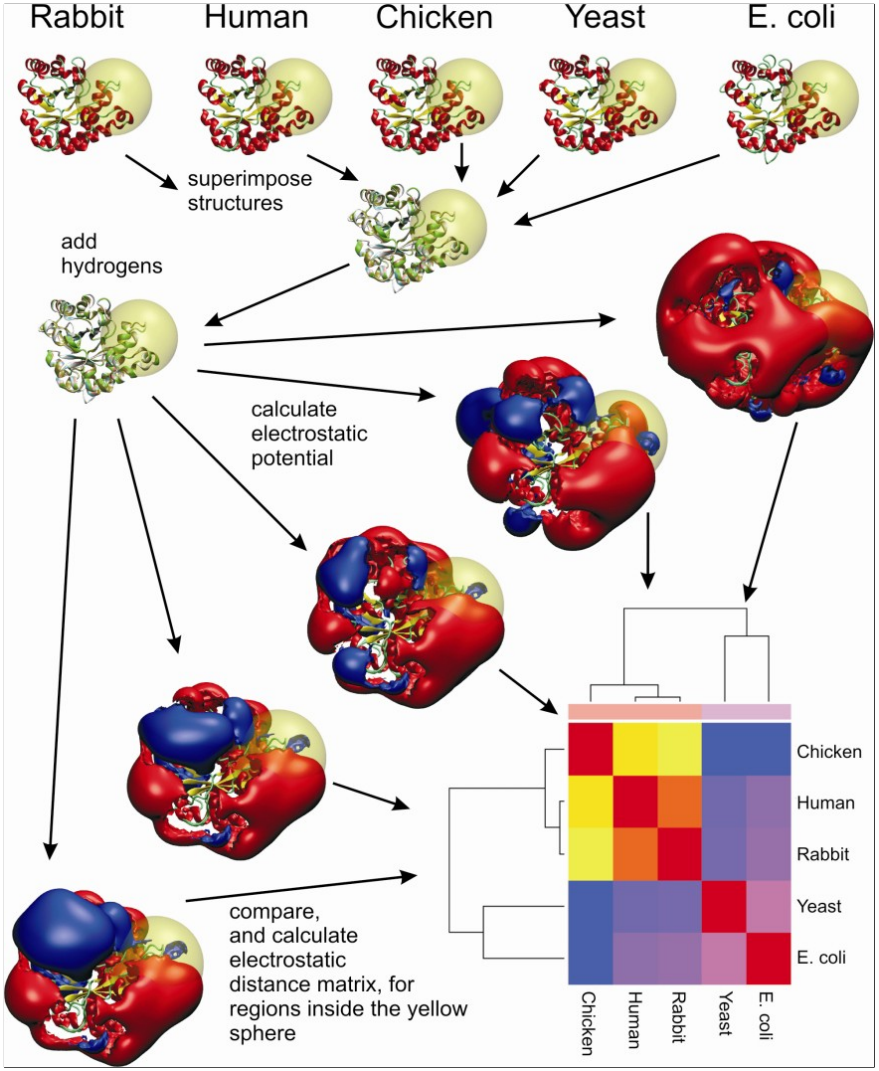
- qPIPSA: UniProt ID of enzyme as starting point (SYCAMORE)
- webPIPSA: PDB files as starting point (Protein Data Bank structure file; pipsa.eml.org/pipsa/)

- qPIPSA: BMC Bioinformatics 2007, 8: 373
- webPIPSA: Nucleic Acid Research, doi:10.1093/nar/gkn181

Parameter estimation: PIPSA

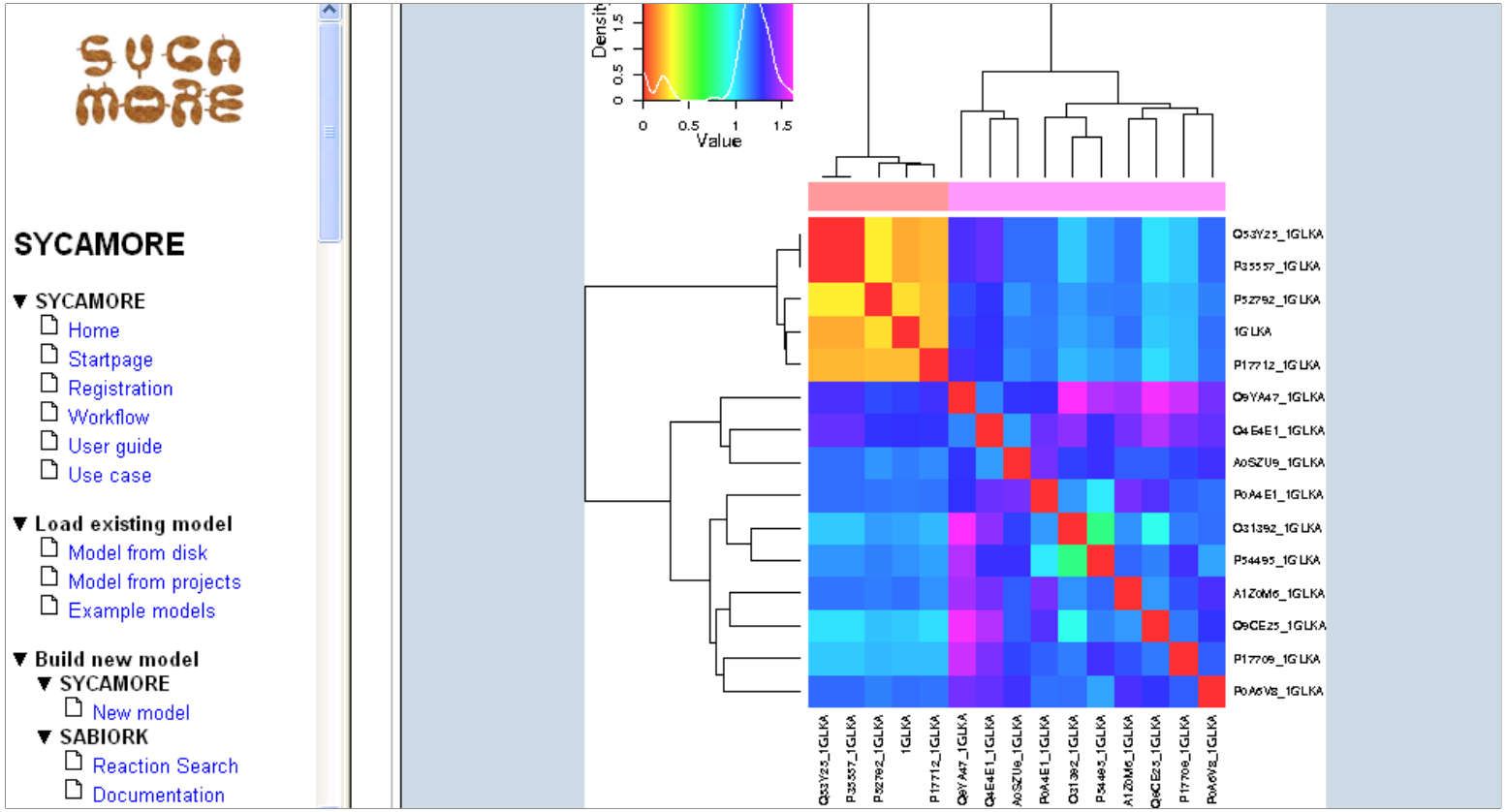
Schematic overview of the workflow employed in webPIPSA. The protein structures are a subset of the Triosephosphate Isomerase.

Output: heatmap, no numeric values



Parameter estimation: qPIPSA

Output: heatmap (no numerical values)



Summary features

- Model editing
- Loading, saving, storage of models
- Database supported modelling (SABIO-RK)
- Sensitivity analysis
- Pathway visualization
- Model simulation (COPASI, JWS online)
- Structure based parameter estimation (qPIPSA)

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