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Pathway Assistant: a web portal for metabolic modelling

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Metabolic modelling

The metabolism of an organism consists of a complex network of biochemical reactions transforming small molecules (*i.e.*, metabolites) into others

n Metabolic modelling is a study of metabolism

- n the discovery of the topology of the metabolic network
- n the estimation of the pathway velocities
- n the modelling of regulation of metabolism
- n Computational metabolic modelling is
 - n about automating above examples
 - n a relatively new and strongly progressing discipline





Automated generation of metabolic networks



alucose





Pathway Assistant: a web portal for metabolic modelling

- n Pathway Assistant portal is a collection of related metabolic modelling tools supporting multiple workflows.
- The design of Pathway Assistant is based on two main principles:
 - n We want to deploy and update tools rapidly and iteratively based on the feedback given by the domain experts.
 - n We want to present all modelling tools as an integrated user interface for end users.
- N We aim to attain these goals with using SaaS software delivery model and a portal environment.
- n We use web techniques like Java portlets and AJAX.





Pathway Assistant tools and supported workflows







Metabolic Engineering Phase 1 importing network with ReMatch

University of Helsinki Department of Computer Science	FAI HWAY	ASSISTATI Edit
Topology Generator ReM	Itch Flux Estimator	
ReMatch		1 1
Load another network		L-Arginine => ArgBM
Name:	Nettab Network	Search from: VARM VKEGG Ligand VUser-added (w/o mappings) VUser-add mappings)
Description:	Imported from Nettab_network.txt	Change
Is network public? Change	⊖Yes	2 reactions ARM
Show identifications — Add reaction		cyt]: L-Arginine => D-Arginine 5.1.1.9; (act): D braining = A braining
D-Xylulose 5-phosphate => D-Ribulose 5-phosphate		Cyt] : D-Arginine => L-Arginine 5 1 1 0: edit
1 Isocitric acid => Succinic acid + Glyoxylic acid		Confirm
1 Succinic acid + Glyoxylic acid => Isocitric acid		Add new reaction
CO2 + Oxaloacetic acid	=> L-Methionine	
D-Glycerate 3-phosphat	e => D-Glycerate 2-phosphate	
FAD + Succinic acid => Fumaric acid + FADH2		L-Arginine Picture of molecule Known synonyms: (S)-2-Amino-5-guanidinovaleric acid 2-amino-5-guanidinovaleric acid ARG Arginine D-2-Amino-5-guanidinovaleric acid D-Arginine L-Arginine
1 ADP + Phosphoenol-pyruvic acid => ATP + Pyruvic acid		
1 D-Glyceraldehyde 3-phosphate => Dihydroxy-acetone phosphate		
1 ATP + D-Glycerate 3-phosphate => ADP + 1,3-Bisphospho-D-glyceric acid		
8 L-Aspartic acid + ? => Oxaloacetic acid + ?		
0 Oxaloacetic acid => L-Aspartic acid		
1 D-Ribose 5-phosphate + D-Xylulose 5-phosphate => D-Glyceraldehyde 3-phosphate +		
0 CO2 + Glycine => Pyruvic acid		
Oxaloacetic acid => CO2 + Phosphoenol-pyruvic acid		
2 L-Arginine => ArgBM		
1 D-Giveeraldehvde 3-phosphate + D-Sedoheptulose 7-phosphate => D-Fructose 6-phos		L-arginine R
CO3 + 2 Over elutoria said => 1 Areisine		arg

Pathway Assistant Portal - Version 0.2 © University of Helsinki 2004







Phase 2 Open the network in Topology Generator







Phase 3 set up basic parameters for Yield maximisation



Seathway Assistant Portal - Mozilla Firefox	
Ele Edit View Go Bookmarks Iools Help	
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Set Search Task Parameters	
Type of task	
Random scoring No evaluation Yield maximisation	
Metabolites in database Nr. of molecules in view Show metabolites by name	Coeff
1000 Refresh Search L-Histidine	1.0
C00209 Oxalic acid () C2H204 Show	
C07083 Styrene () C0H8 Show	
C00697 N2 () N2 Show	
C00024 Acetyl-CoA () C23H38N7O17P3S Show Save OLinear function	n
C00010 CoA () C21H36N7016P3S Show CAggregate	e function
Externals	Min Max
Reactions in database Number of reactions in view Show reactions containing	-1.0 1.0
4001-5000 5001-6000 6001-7000 7001-8000	0.0 1.0
All Naringenin + 2-Oxo-olutaric acid + O2 = Dihydro-kaemoferol + Succinic acid + CO2	
□ D-Glutamine + H20 => D-Glutamic acid + NH3	
H20+H20+C00125+C00125+C00125+C00125+C00125+C00126+C	
the first construction of the second se	
NADP+ + L-Malic acid => NADPH + CO2 + Pyruvic acid Constrained reactions	Min Max
Protoporphyrin IX + Magnesium = Magnesium protoporphyrin IX + 2 H+	
adu selected leactions lo consulaired leactions	
Save Demove	
Reaction constraints - Advanced parameters	
1-1000 1001-2000 2001-2836 Nr. of molecules in view Show metabolites by name Cofactor lists: The usual set of cofactors Minimal set of en	ergy and redox cofactors No cofactors
Show only constrained metabolites	Default cofactor constraints
C00001 H20 () H20	
http://mit.127.can/can/indout/jc.cape.co/indout/C000K/jSp110-1	





Phase 4 start the search of alternative metabolic networks





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Phase 5 browse alternative networks







Last phase: visualization of modifications in a candidate network







Preliminary results of Pathway Assistant project

- n SaaS model suits well for productisation of bioinformatics methods
- n Portal environment and portlets offers certain benefits:
 - n Rapid distribution of new tools for portal users
 - n Eases expandability of the system
 - n Eases integration of the tools inside the portal
- n AJAX is a good way to improve usability of user interface
- n Combining of portlet and AJAX techniques has challenges
- n Pathway Assistant is available in Internet:
 - http://www.cs.helsinki.fi/group/sysfys/software/pa/