MetaBoFlux

A method to analyse flux distributions in metabolic networks

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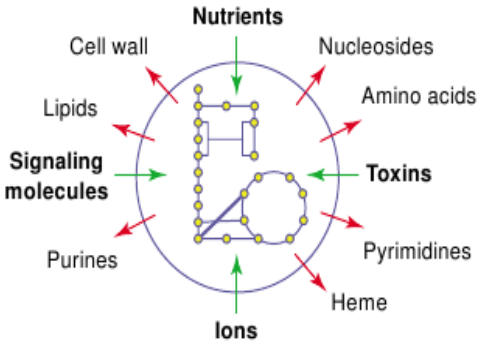
MetaBoFlux : Principle and method

Flux prediction :

Traffic patterns



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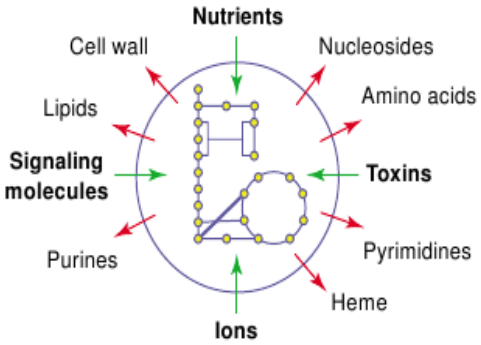

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   - Structure of the network
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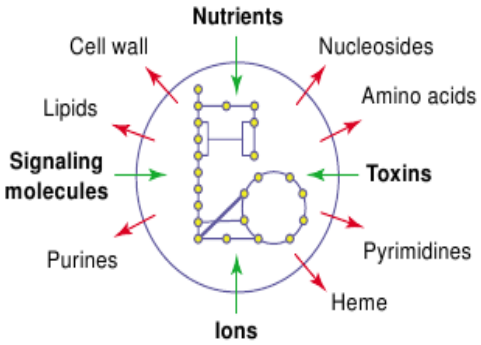

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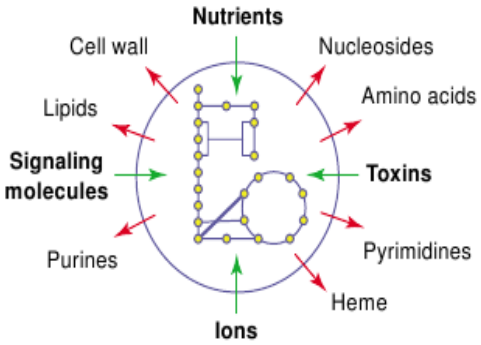

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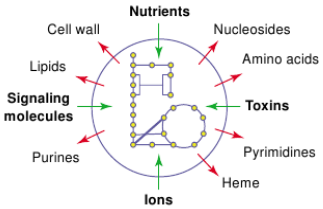

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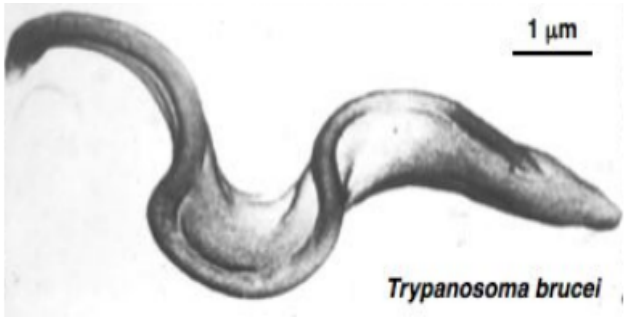
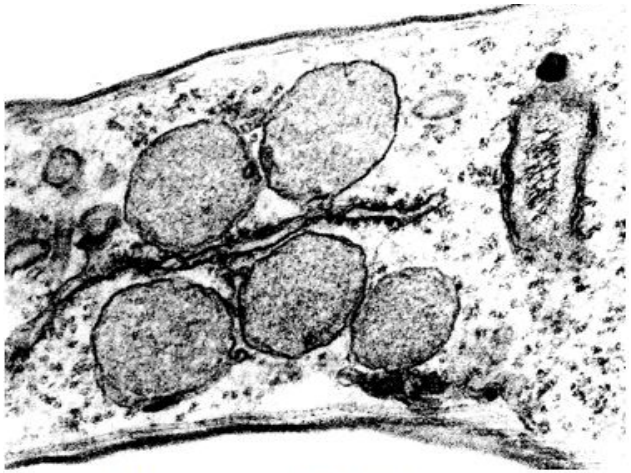
4. To predict the flux distribution
   - To obtain models of metabolic networks validated by experiments

   More information : Poster 10

Application to Trypanosoma brucei





- Glucose metabolism
  - Three compartments : Glycosome - Cytosol - Mitochondrion

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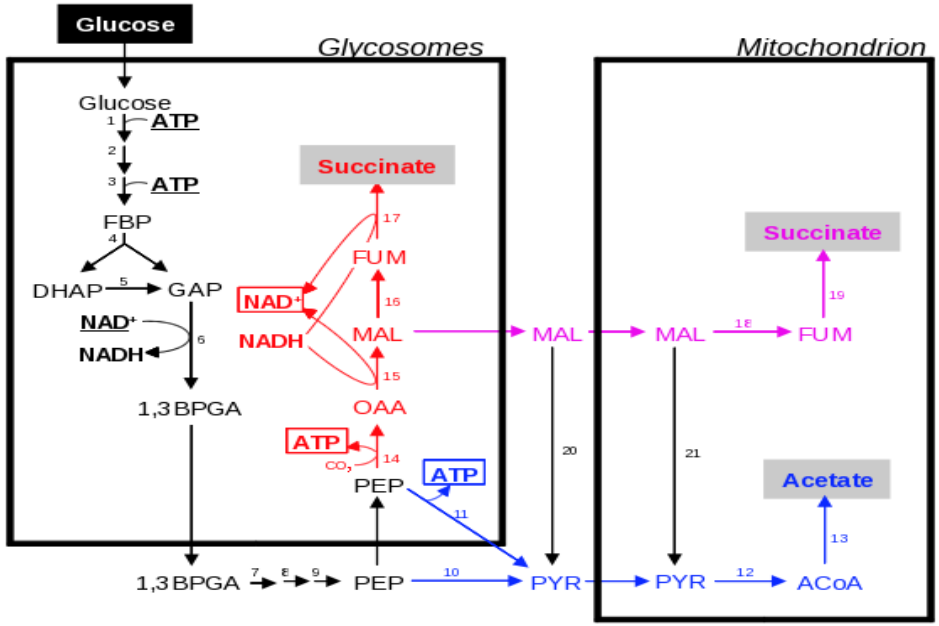

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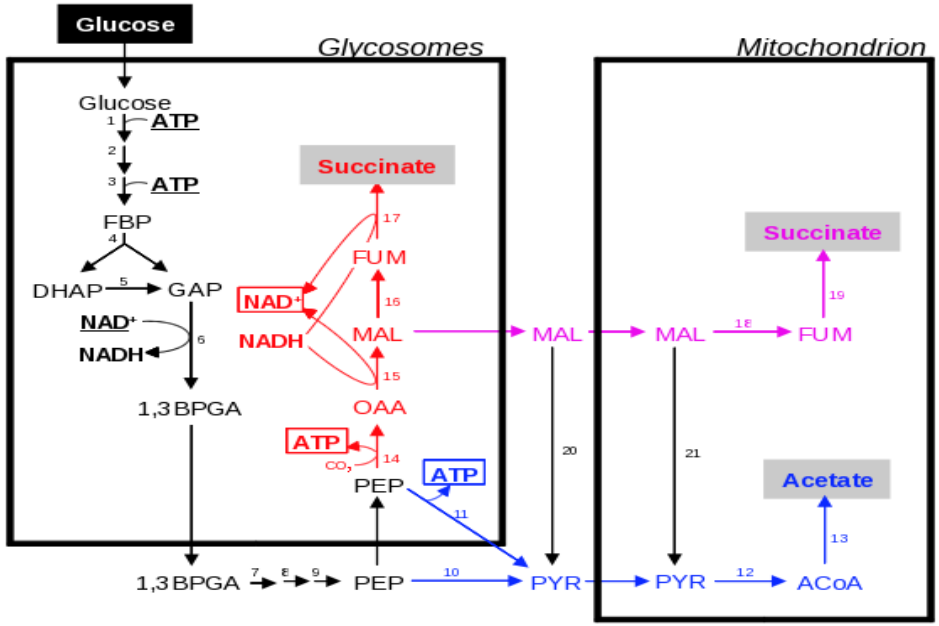
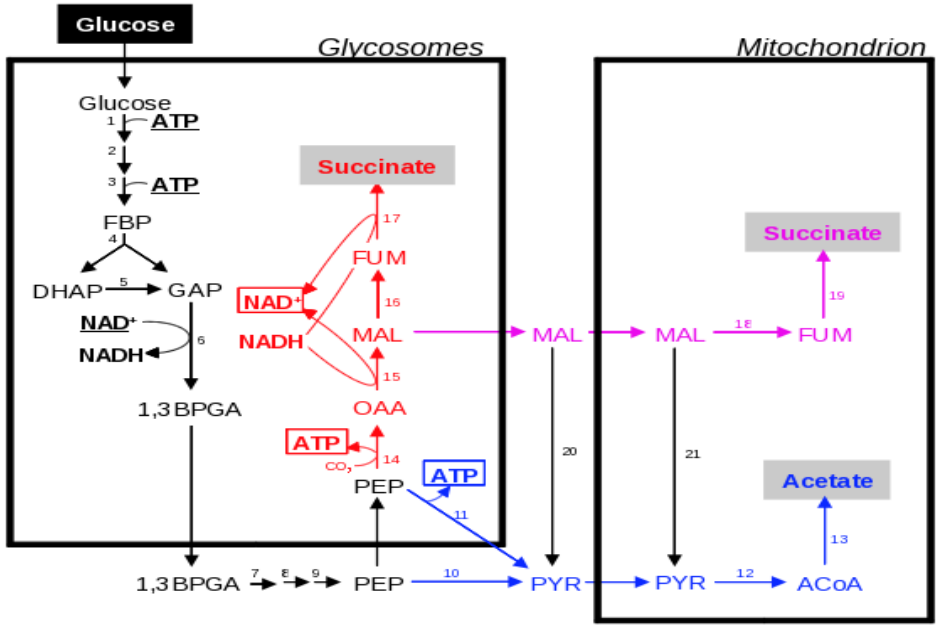


- Glucose metabolism
  - Three compartments : Glycosome - Cytosol - Mitochondrion
  - Model proposed by [Bringaud et al., 2006]
  - No information on flux distributions and compliance to the constraints

Application to Trypanosoma brucei



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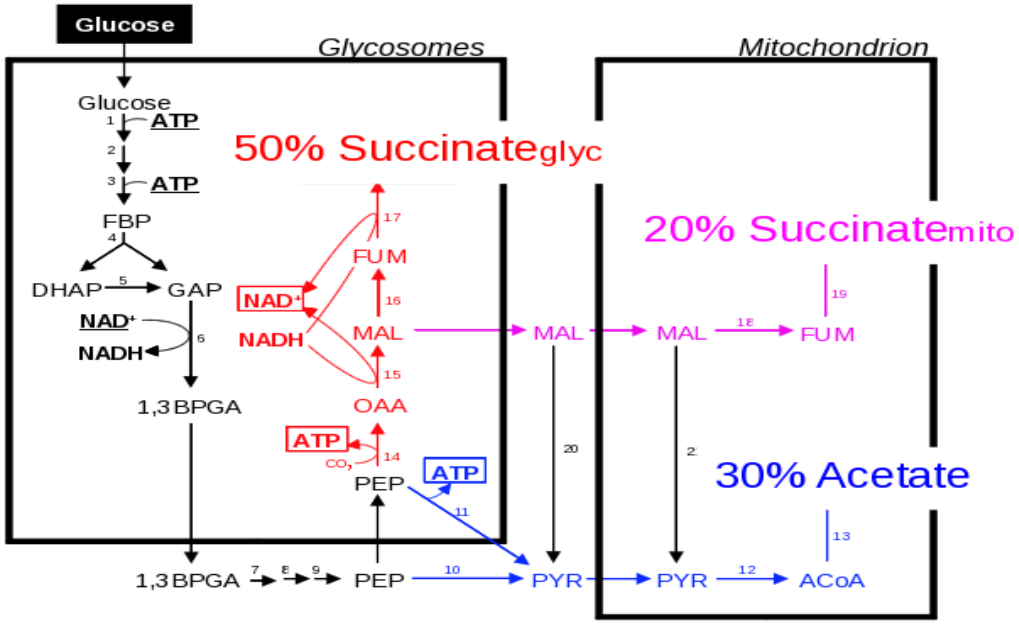

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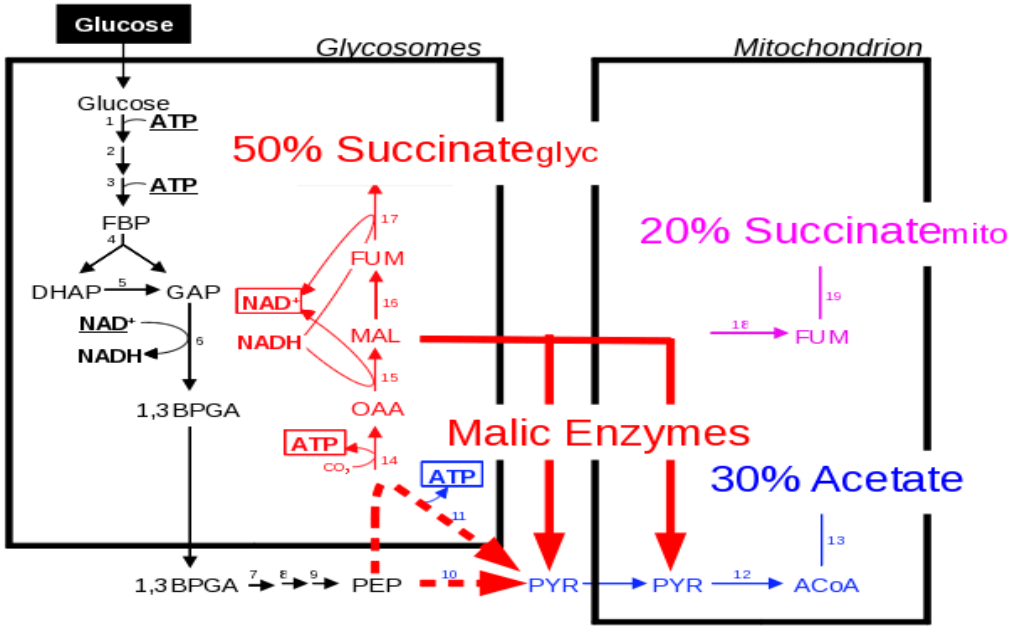

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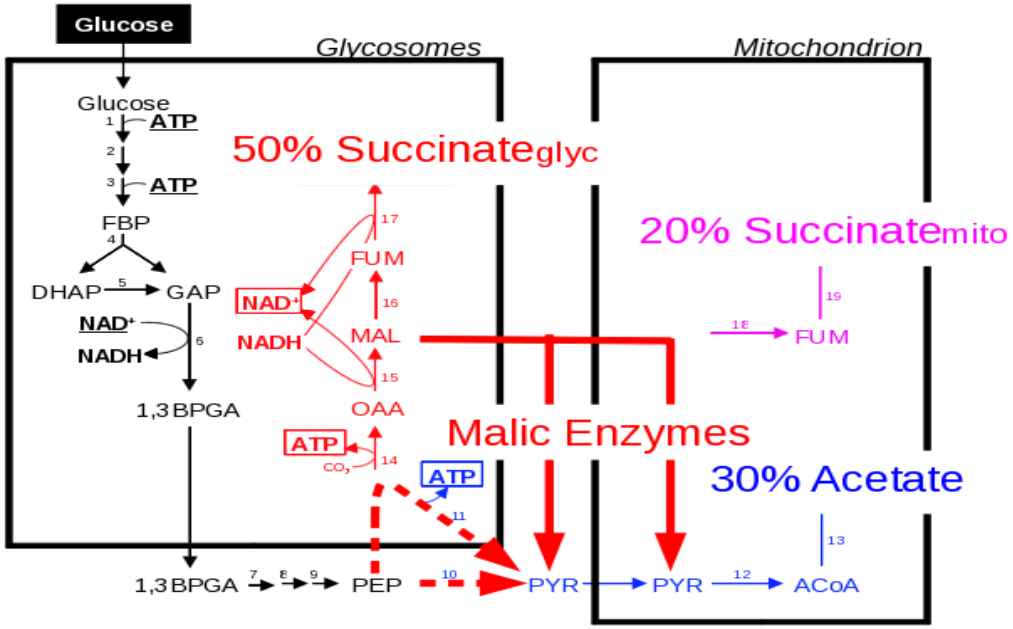

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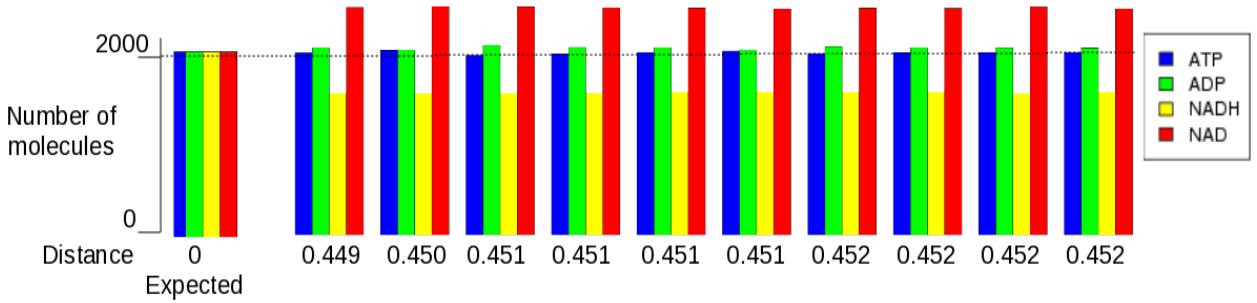
- Model validation and flux flexibility analysis

Metaboflux : Model validation

- Balance scale of ATP/ADP and $NADH/NAD^{+}$



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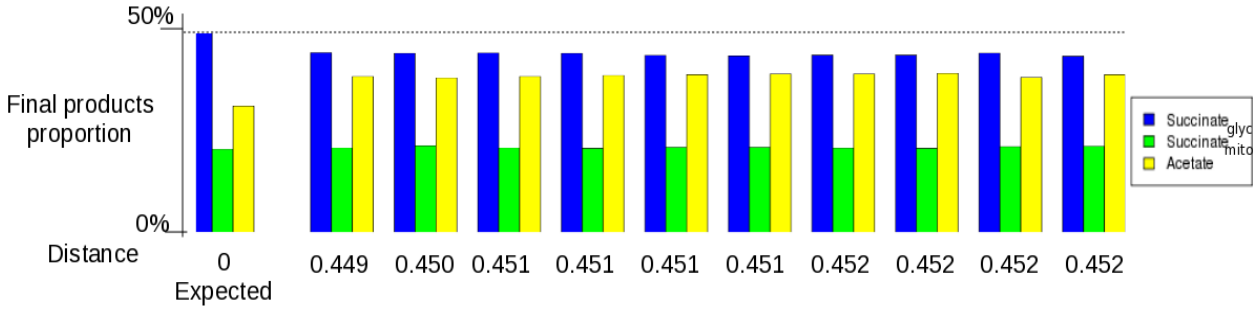

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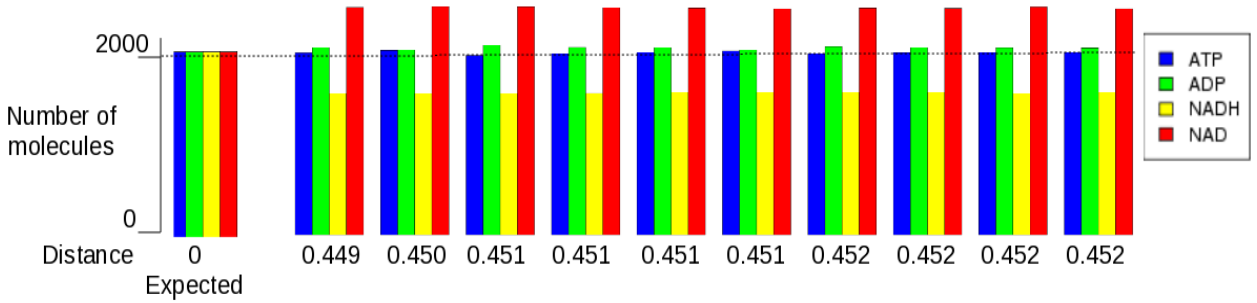

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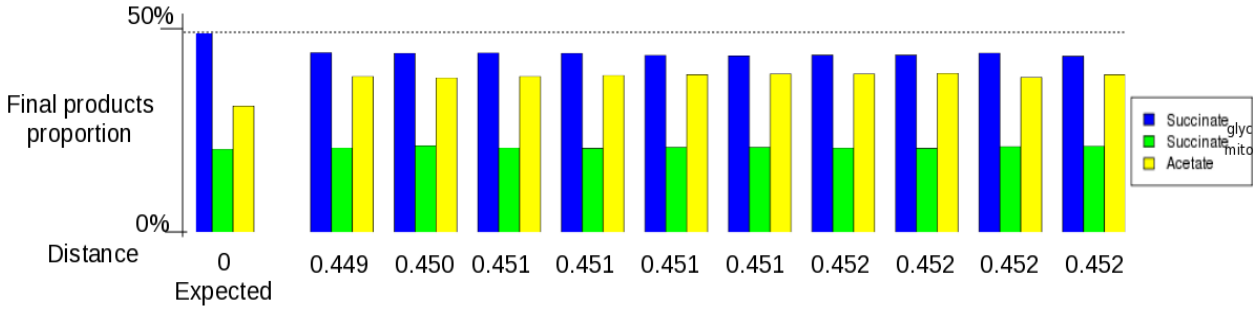
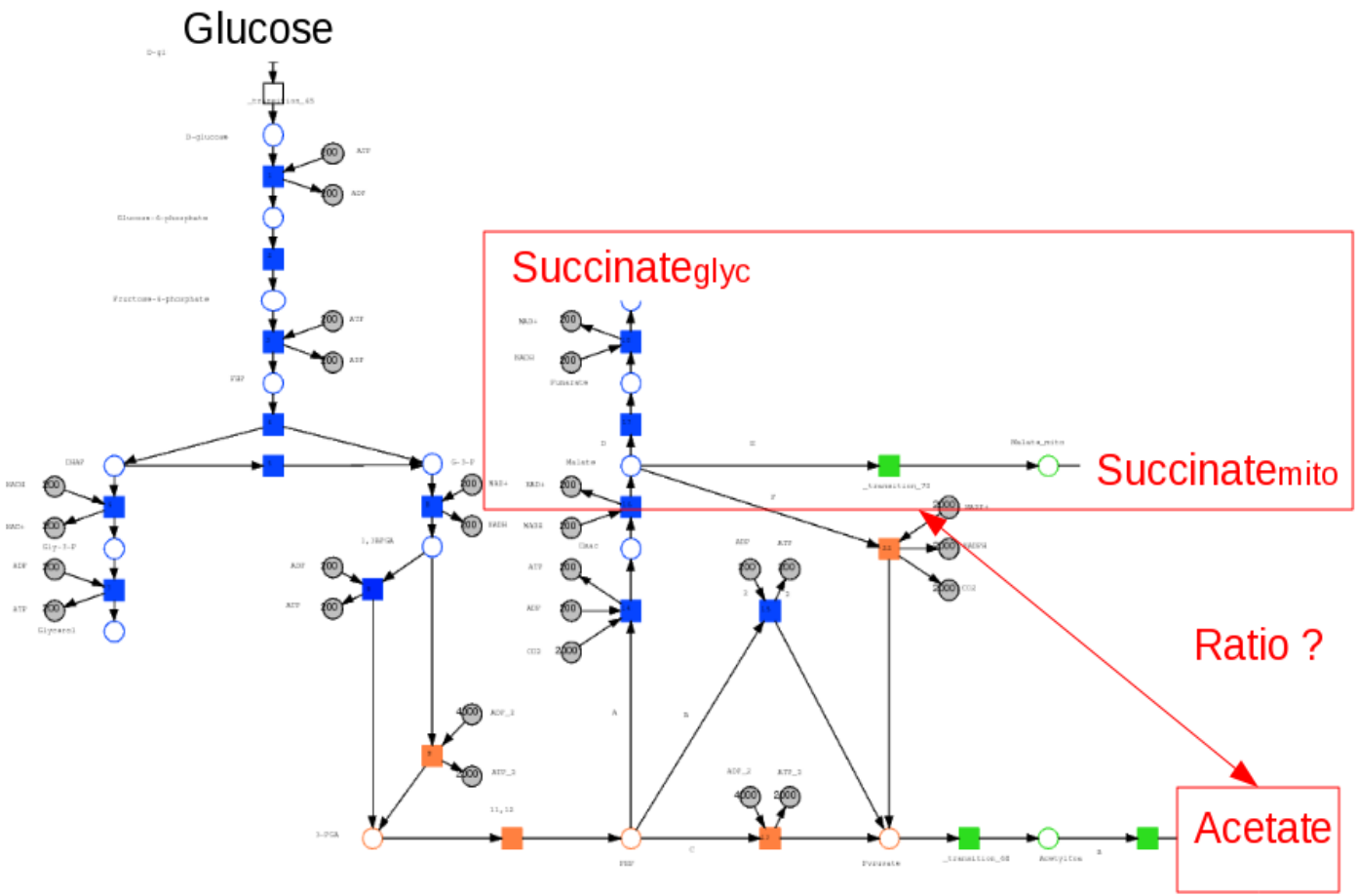


Two explanations :

1. Bad topology
2. Inconvenient constraints

Metaboflux : Flux flexibility analysis

- Acetate/Succinate profile



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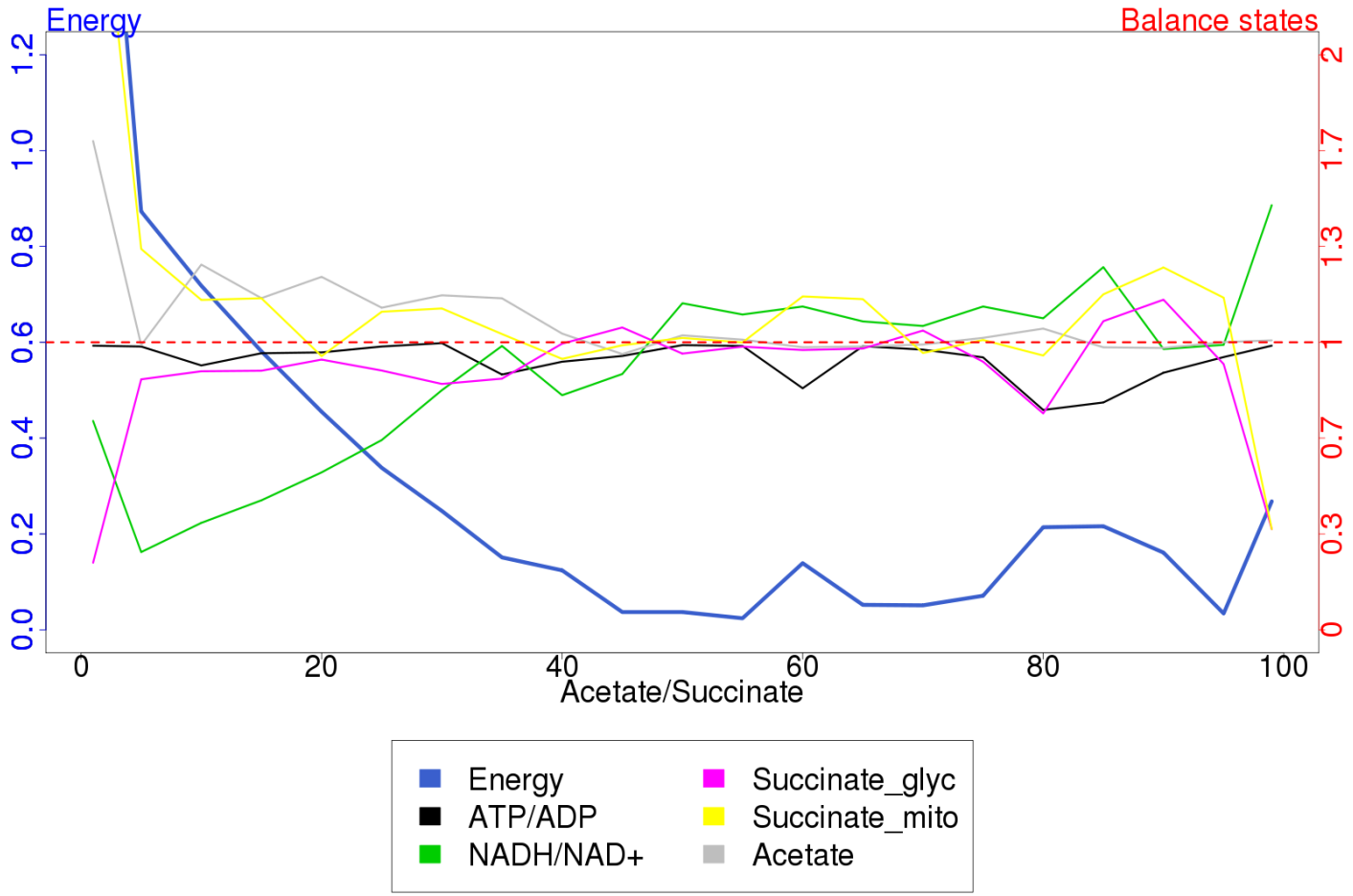

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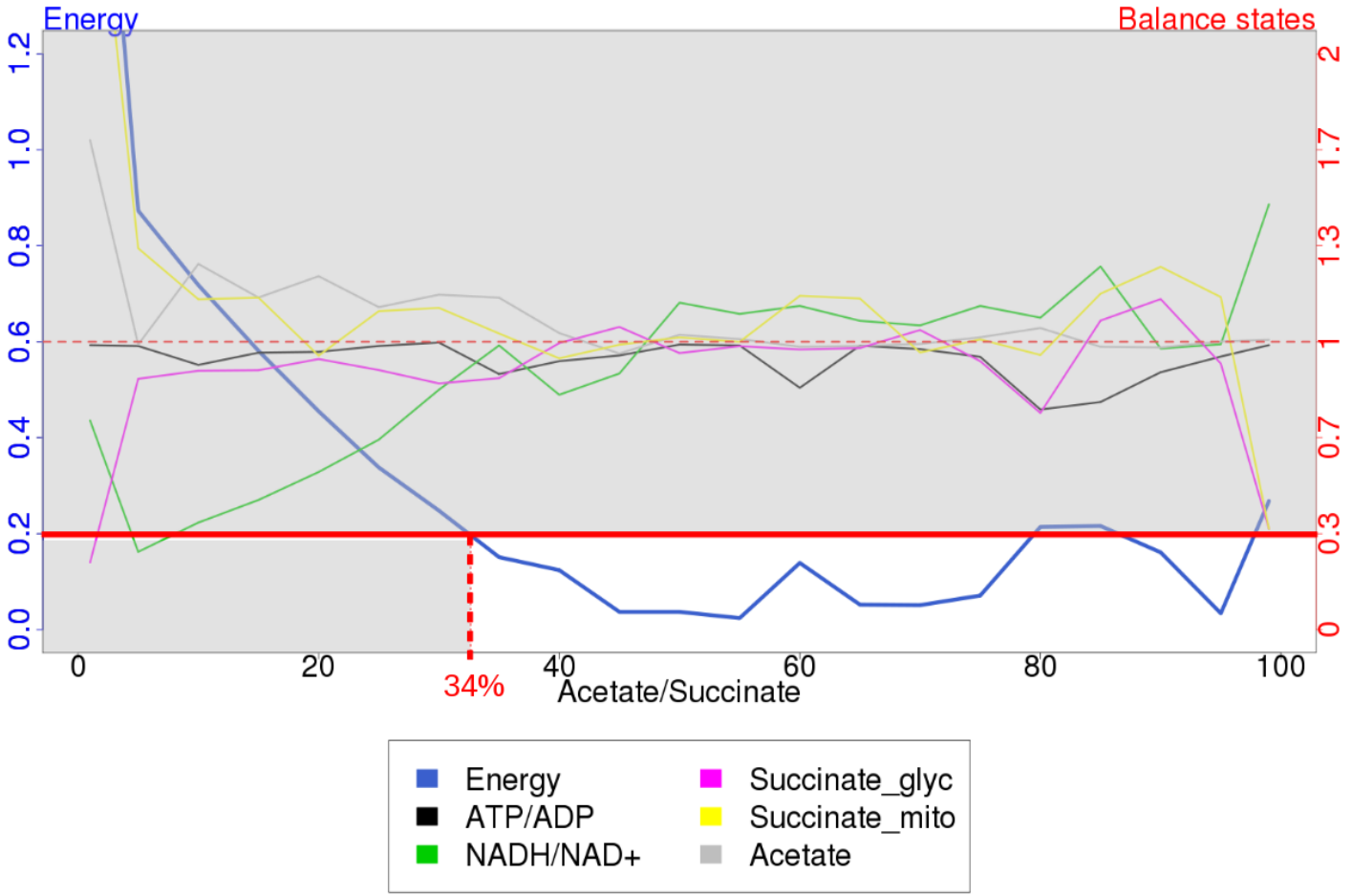

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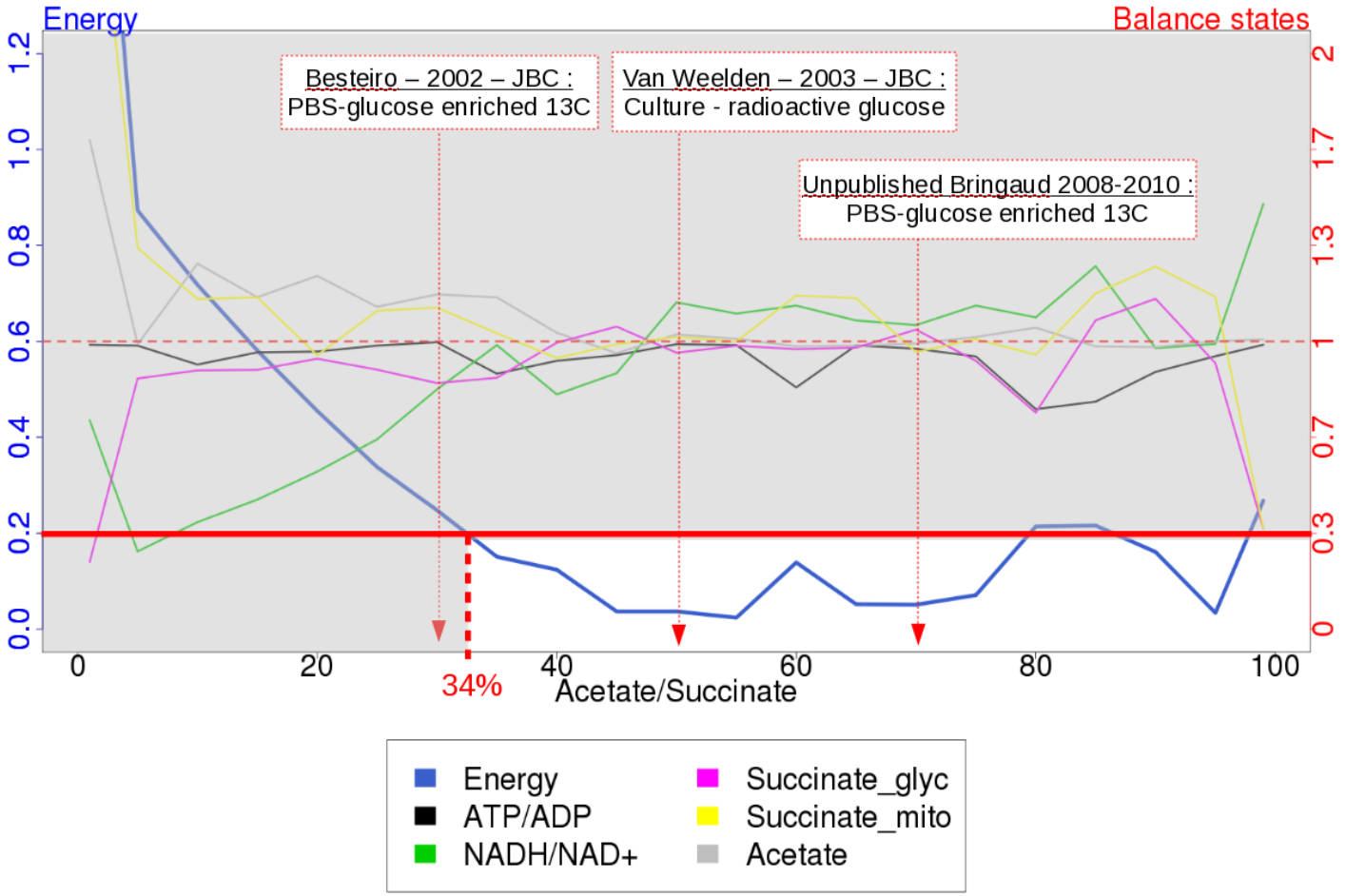

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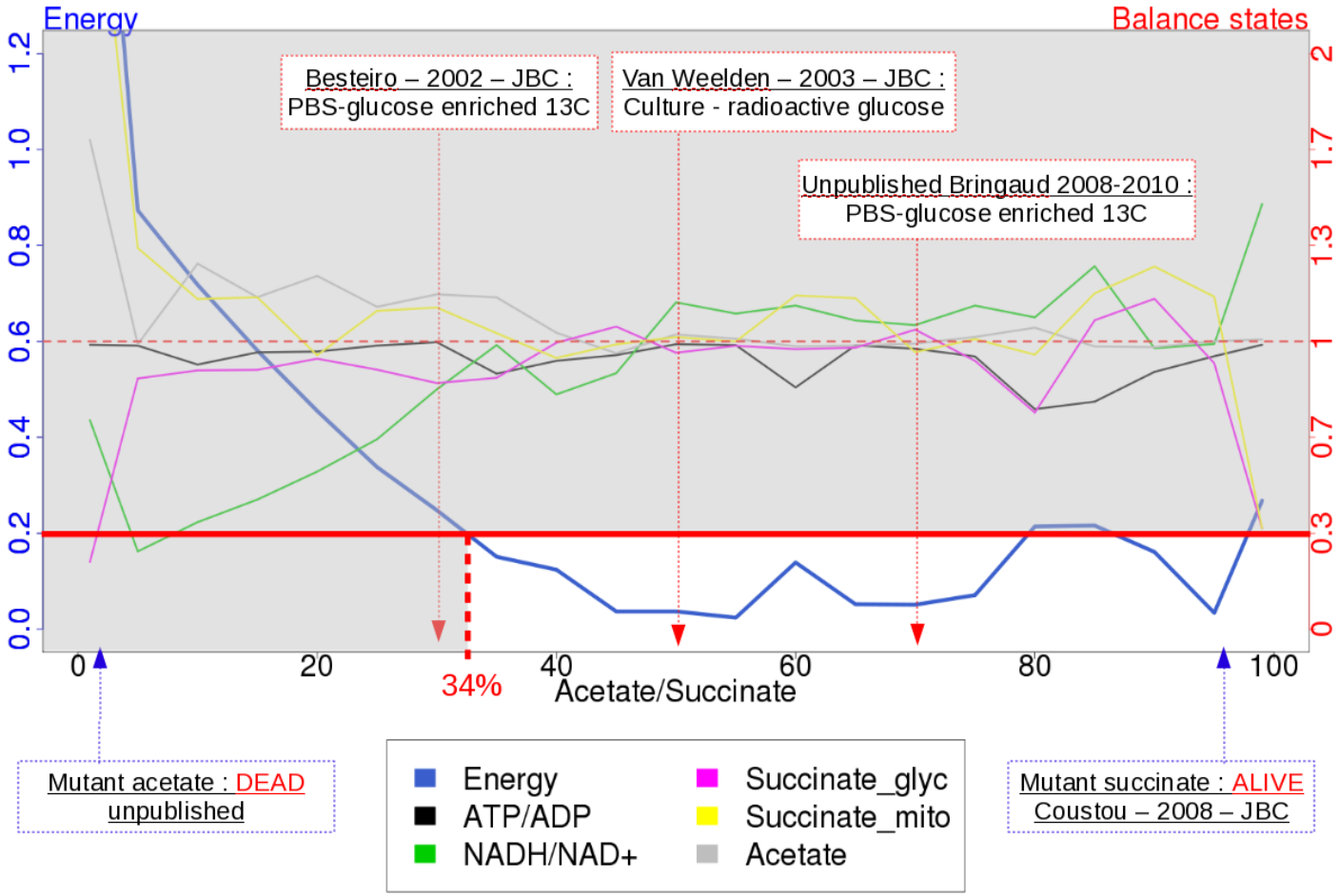

Conclusion - Perspective

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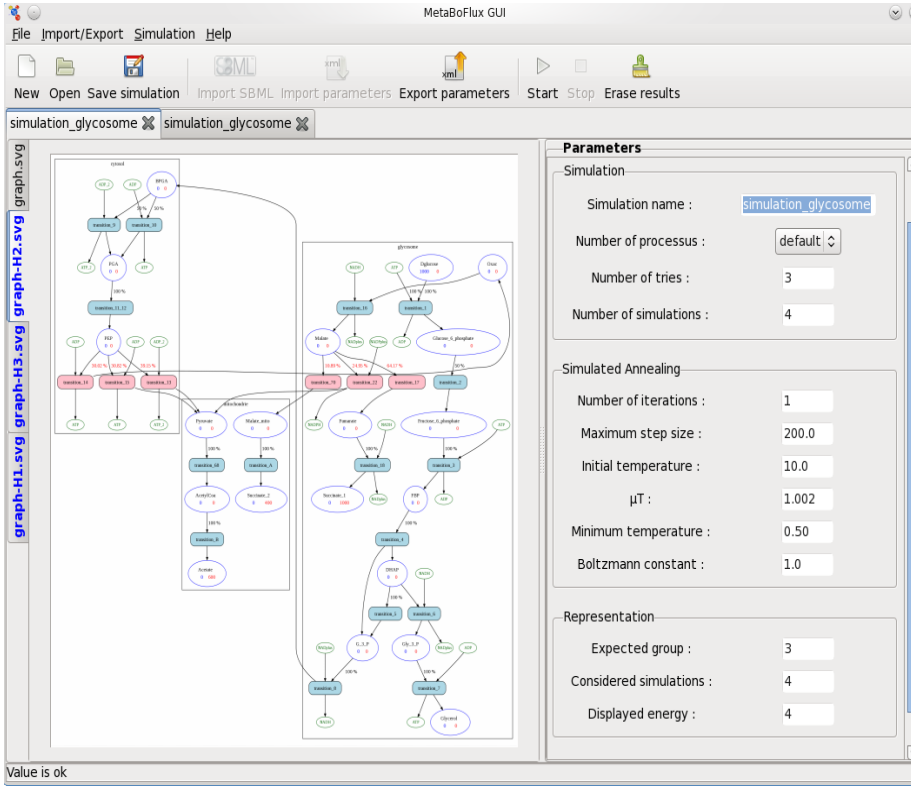
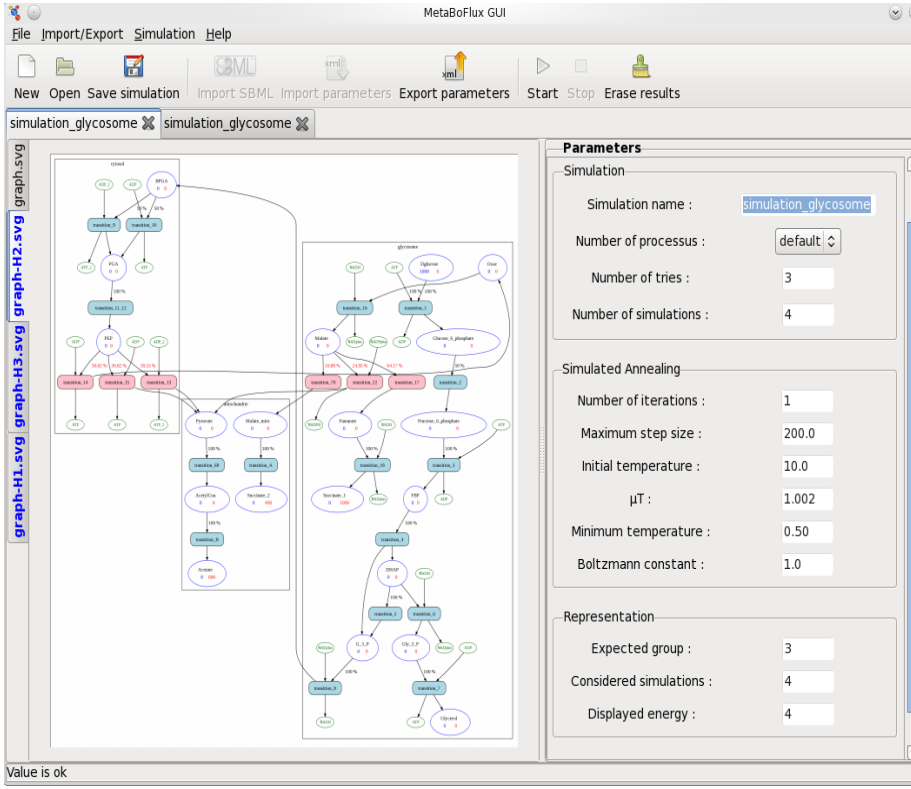
  - New tool for model validation and flux analysis
  - Standalone application under GPL licence



Download :
www.cbib.u-bordeaux2.fr/metaboflux
(soon available)

Conclusion - Perspective

- Metaboflux
  - New tool for model validation and flux analysis
  - Standalone application under GPL licence
- Trypanosoma brucei
  - No relevant malic enzymes constraint
  - Biological model compatible with other constraints
  - Flexibility consistent with experimental data
  - Further analysis on the flexibility will be proceed and validated by experiments



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Acknowledgments

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- Dr. Patricia Thébault, Bordeaux University
- Pr. Frédéric Bringaud, CNRS
- Dr. Fabien Jourdan, INRA

Contributors :

- Laurent Gil
- Daniel Jacob

And :

- Dr. Claire Lemaitre

LaBRI, CBiB
Metabotryp ANR

Thanks !

Extended Flux Balance Analysis

Extended FBA are dedicated to specific applications :

- Energy balance analysis (EBA) eliminates thermodynamically wrong solutions [Beard et al., 2002]
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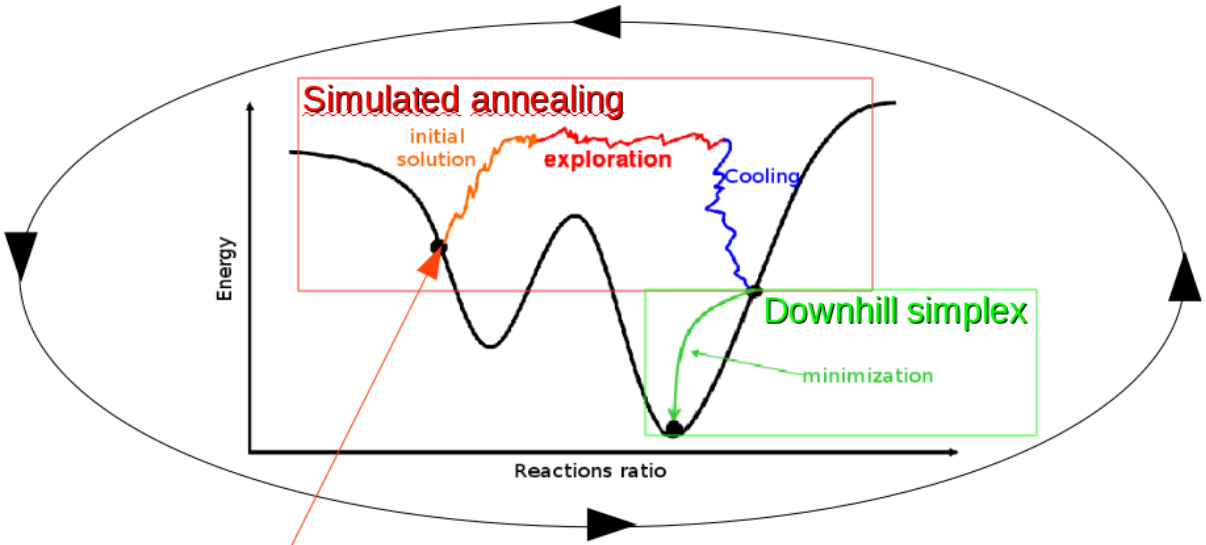
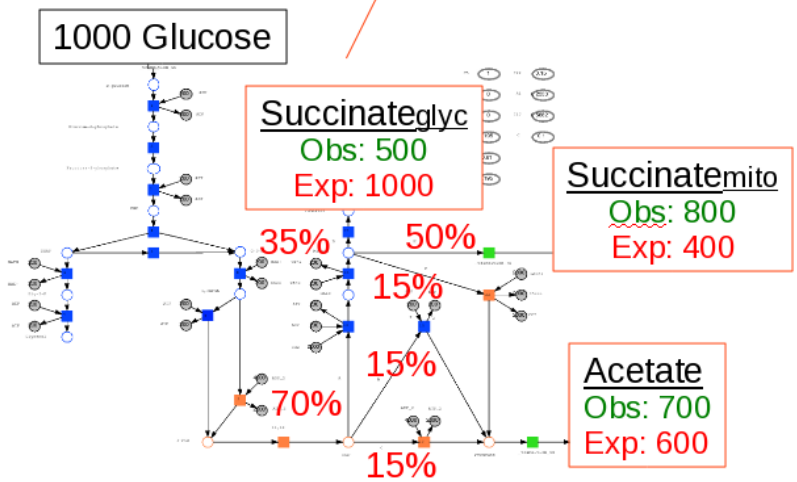
Limited Validation :

- Structure of the metabolic network
- Limited for experimental data integration
- No validation or flux analysis from biological constraints

Non-linear optimization





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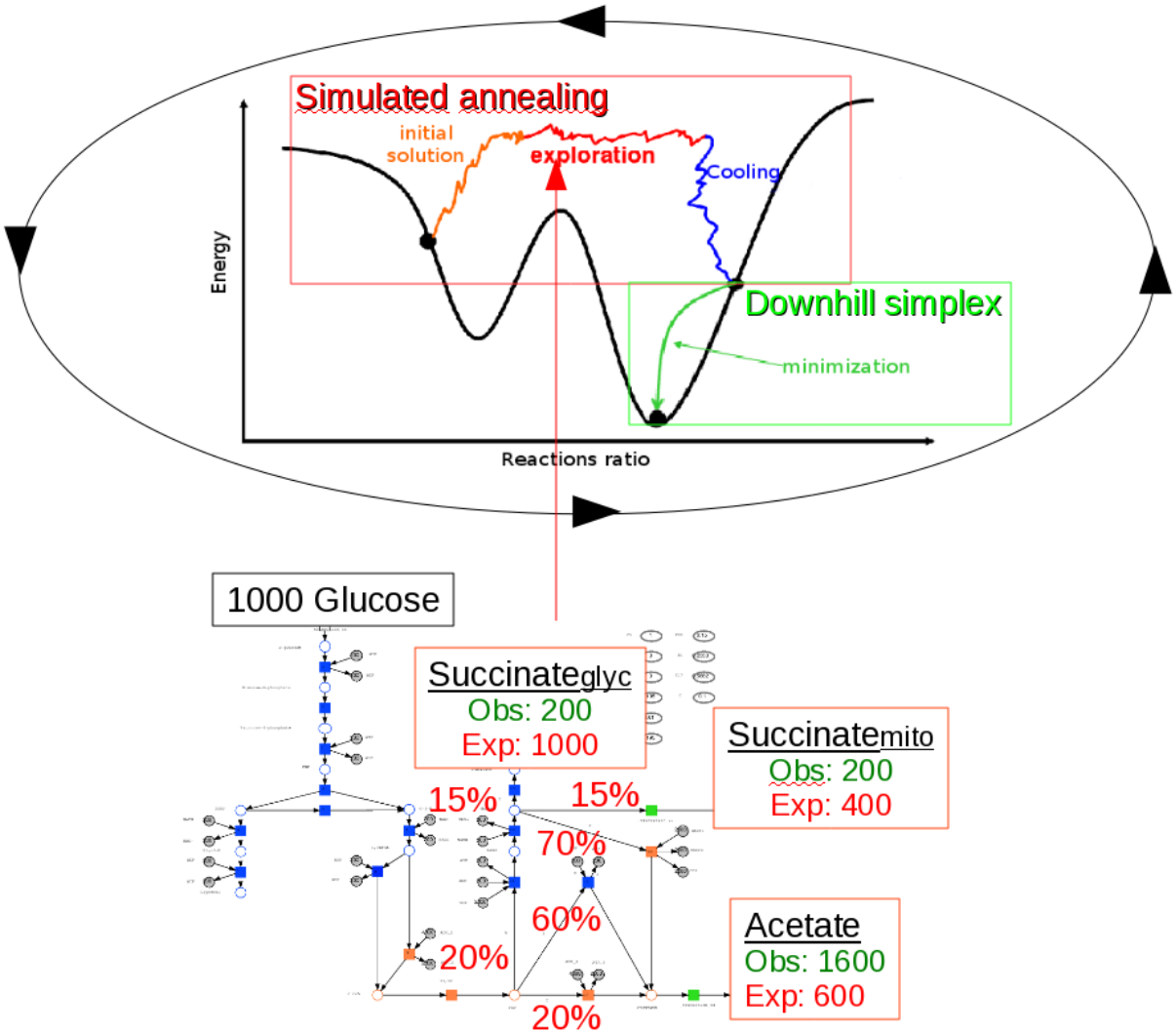

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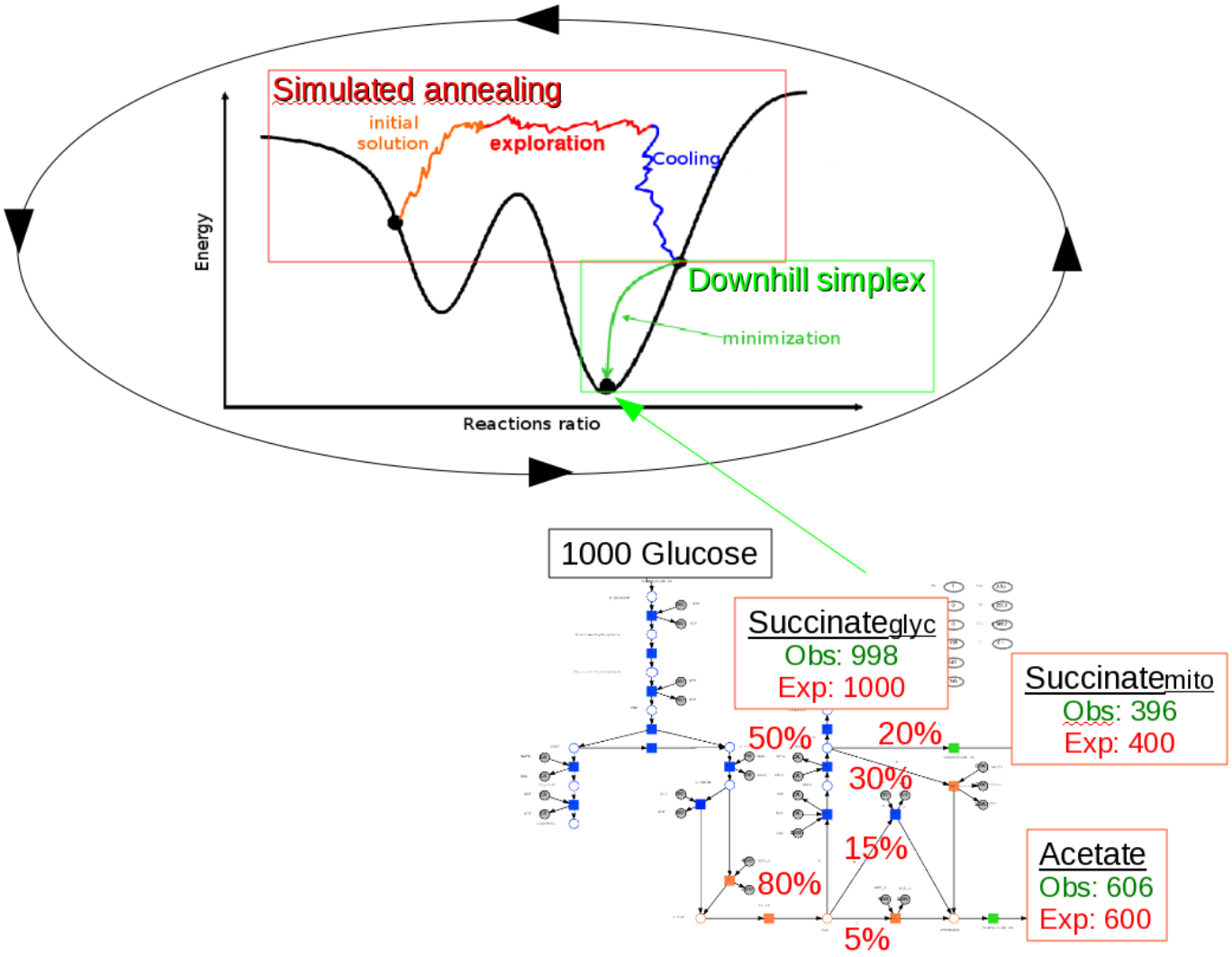

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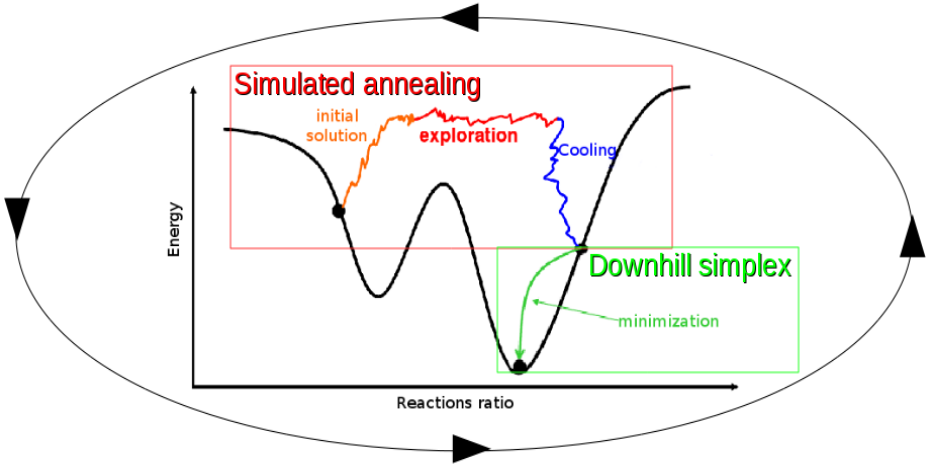

To achieve the global optimum :

- Estimate the complexity of each metabolic network to set the right temperature (complex operation)

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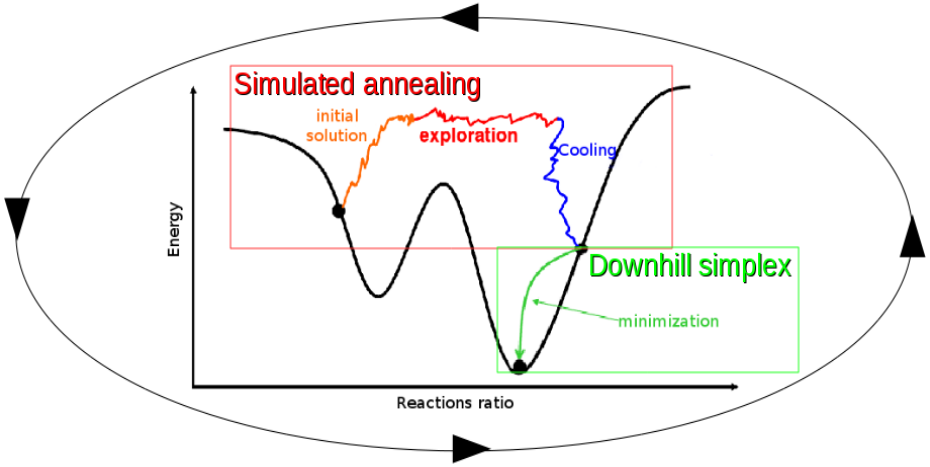
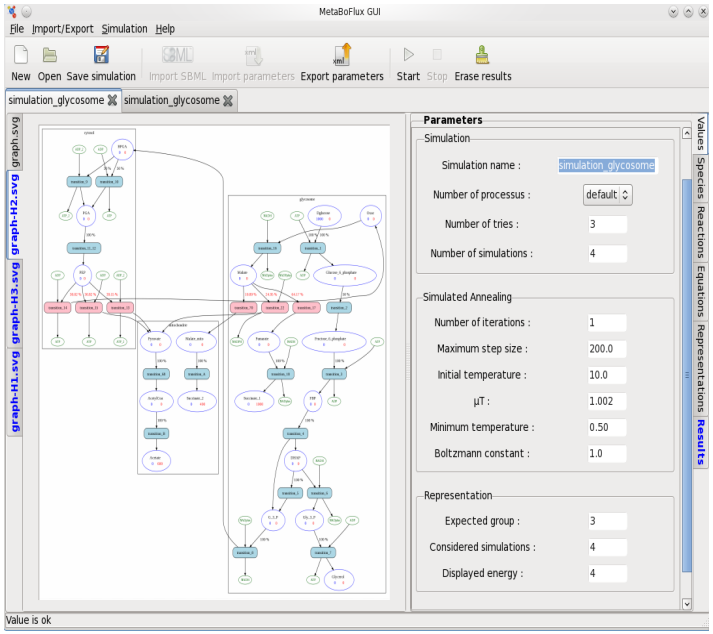
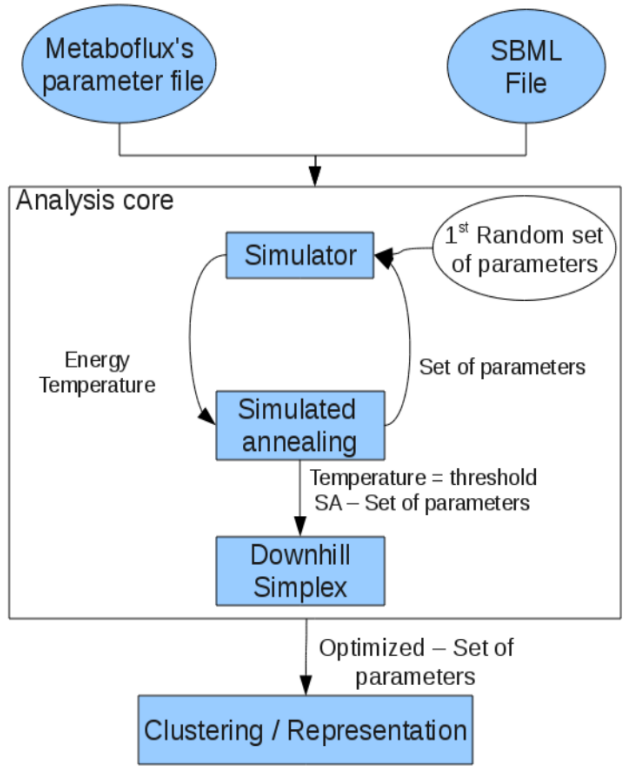


To achieve the global optimum :

- Estimate the complexity of each metabolic network to set the right temperature (complex operation)
- Perform N-parallel simulated annealing
- Increase our chances to find a global optimum and good local minimum

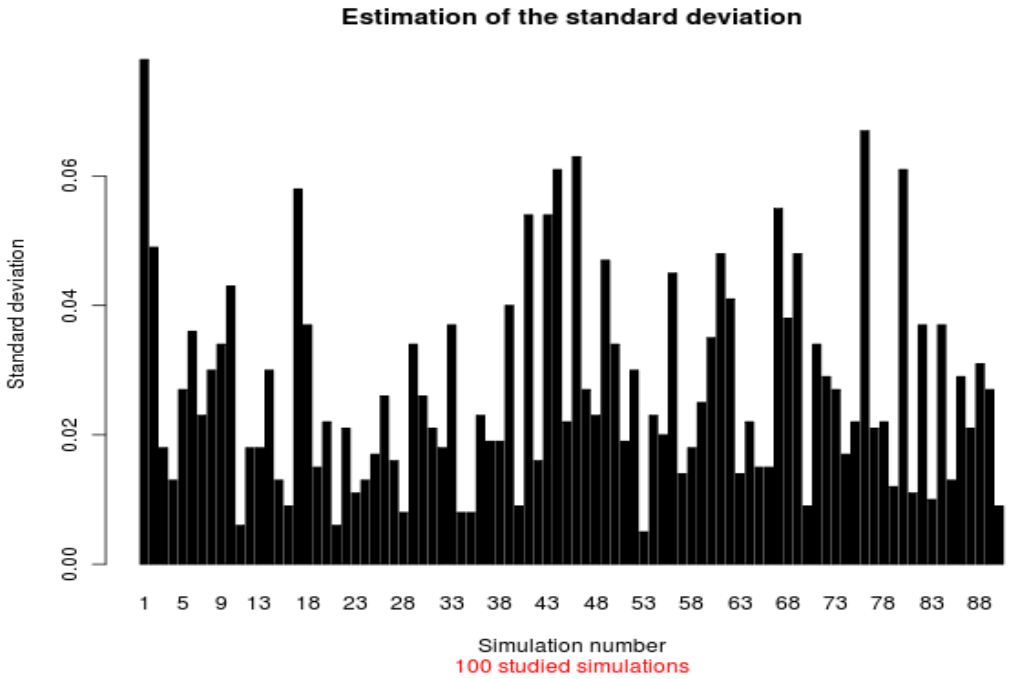

MetaBoFlux GUI
File Import/Export Simulation Help
New Open Save simulation Import SBML Import parameters Export parameters Start Stop Erase results
simulation_glycosome
simulation_glycosome
graph.svg
graph-H2.svg
graph-H3.svg
graph-H1.svg
Parameters
Simulation
Simulation name :
simulation_glycosome
Number of processus :
default
Number of tries :
3
Number of simulations :
4
Simulated Annealing
Number of iterations :
1
Maximum step size :
200.0
Initial temperature :
10.0
µT :
1.002
Minimum temperature :
0.50
Boltzmann constant :
1.0
Representation
Expected group :
3
Considered simulations :
4
Displayed energy :
4
Values
Species
Reactions
Equations
Representations
Results
Value is ok


Metaboflux's parameter file
SBML File
Analysis core
Simulator
1st Random set of parameters
Energy Temperature
Set of parameters
Simulated annealing
Temperature = threshold
SA – Set of parameters
Downhill Simplex
Optimized – Set of parameters
Clustering / Representation

Quality checking

Two ways to control the quality of results :

1. Simulation checking



- To check that the energy is well determined.
- If there is high variation, we should increase the number of simulation.

Quality checking

Two ways to control the quality of results :

1. Simulation checking
2. Optimization checking

Histograms | Log of best energies

	Energy	AcetylCoa	Malatemito	Acetate	NADH	Succinate2	NADPH	NADPplus	Pyruvate
1	1.393	0	0	1280	2829	391	2122	1878	0
2	1.458	0	0	1340	2750	176	2106	1894	0
3	1.459	0	0	1146	2773	510	2029	1971	0
4	2.237	0	0	1747	3501	174	2167	1833	0

- To check if every metabolite is consumed.
- Maybe the constraints are too high ?

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