Design and Implementation of a web-based knowledgebase and modelling software for prokaryotes

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Motivation

We are offering a web based modelling software called "CyanoDesign". It offers an easy to understand interface and allows quicky modifying and reevaluating the model based on previous simulation results. CyanoDesign uses common formats to store the model, therefore interoperability with other, more complex modelling tools like COBRA [1] is guaranteed.
This tool is part of CyanoFactory KB, a knowledge base that has been developed and further extended on the basis of WholeCell KB [2]. Model data can be annotated and cross referenced to other components of the warehouse or to external biological databases.

Metabolic modelling

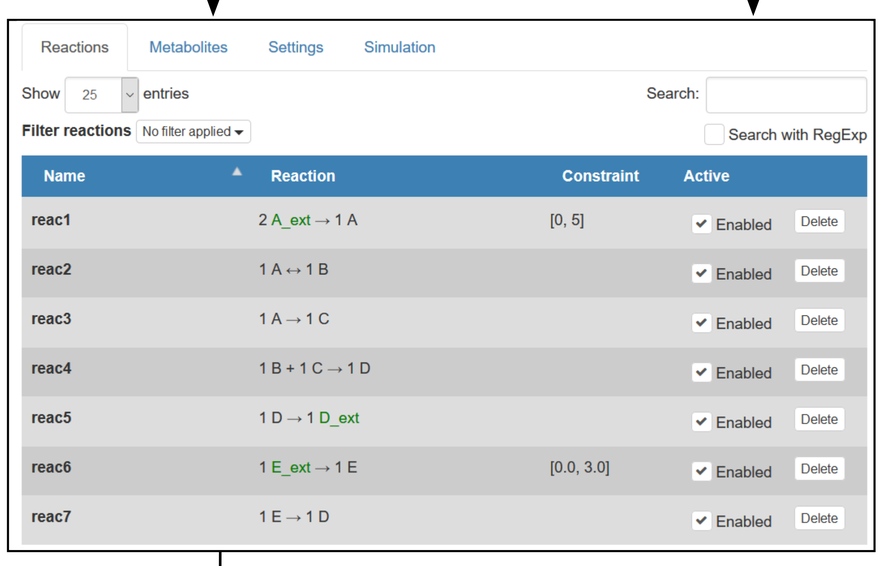
Metabolic modelling allows experimenting with organisms *in silico*. This works by creating a model which contains all relevant metabolic reactions of the organism. At first the model is automatically annotated from biological databases and then manually curated based on experimental data and expertise of the modeller. This list of chemical reactions is converted to a computational model and algorithms like Flux Balance Analysis [3] are able to predict parameters like biomass and growth. The simulation result is provided back to experimentalist and in an iterative process the model becomes more precise over time.

CyanoDesign Modelling Workflow

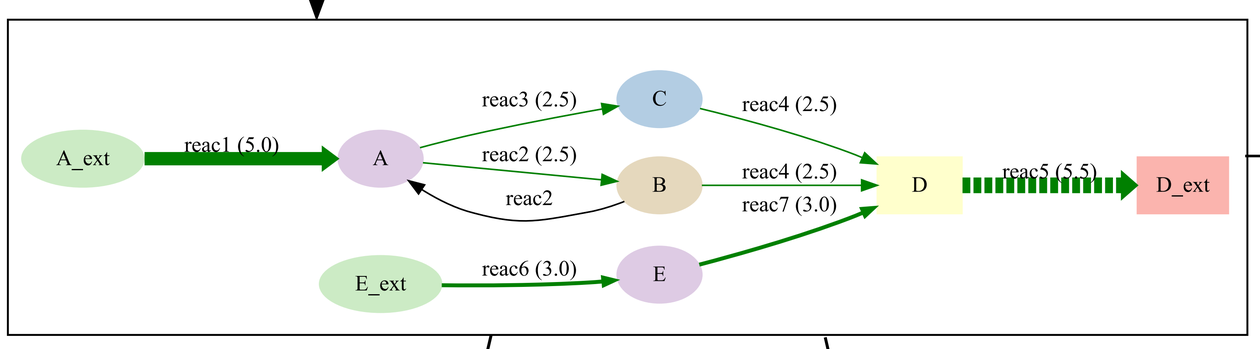
Create metabolic model

```
reac1: 2 A_ext  -> A
reac2:   A     <-> B
reac3:   A      -> C
reac4:   B + C  -> D
```

Upload to CyanoDesign

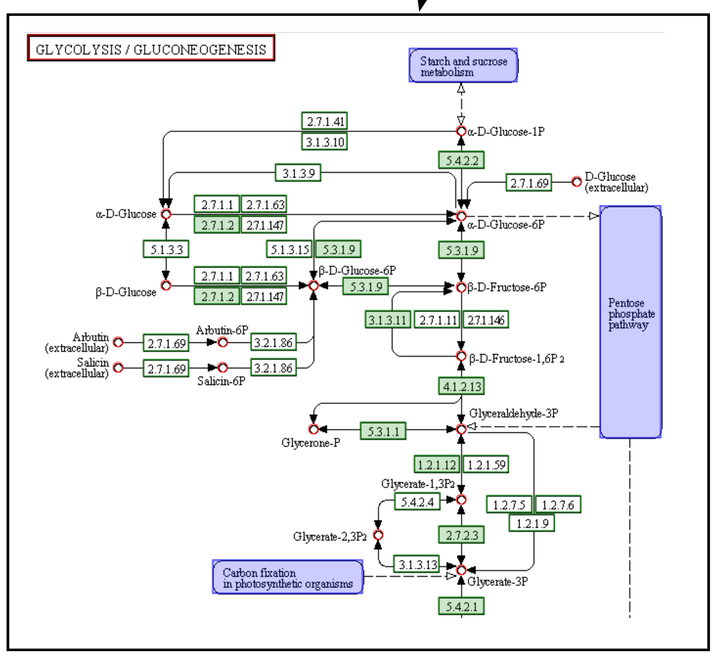


Simulate

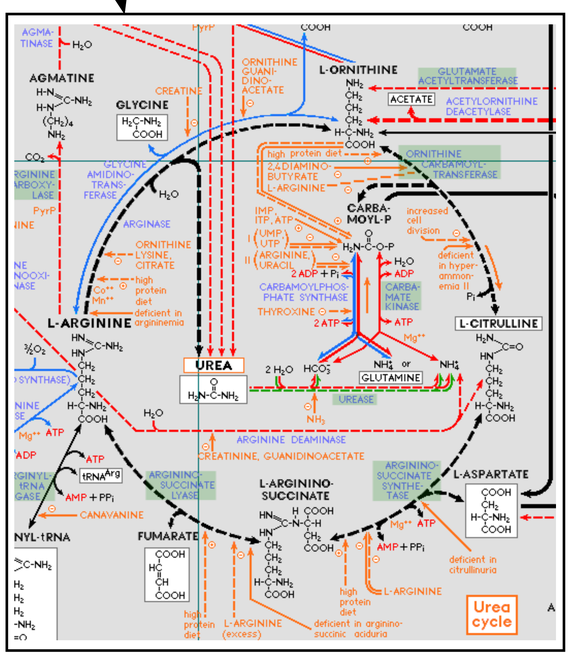


Access cross references

KEGG Pathways

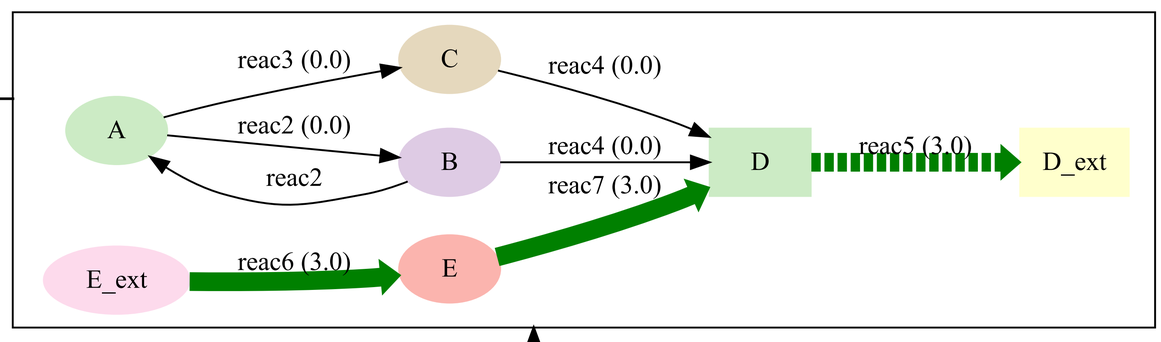


Biochemical Pathways



Simulate again

Modify model
e.g. knockout reactions



Iterative improvement

At first the user uploads his model or uses a predefined one from the CyanoDesign website. Then he is presented with an interface which shows all reactions and metabolites that exist in the provided model of the organism. Here he can select the reaction to optimize for (here: reac5) and CyanoDesign returns a graphical representation of the model with all fluxes attached. The flux is the flow of metabolites through the model. This model can be cross referenced with other components of the warehouse.
By knocking out a reaction and simulating again we can see that the flux of the top path goes down to zero which means this reaction was essential.

References

[1] Schellenberger J., Que R. et al. "Quantitative prediction of cellular metabolism with constraint-based models: the COBRA toolbox v2.0." In: Nat Protoc 2011, 6:1290–1307.
[2] Karr J. R., Sanghvi J. C. et al. "WholeCellKB: model organism databases for comprehensive whole-cell models." In: Nucleic Acids Res. 2013 Jan;41:D787-92.
[3] Orth J. D., Thiele I., and Palsson B. Ø. "What is flux balance analysis?" In: Nat Biotechnol. 2010 Mar; 28(3): 245–248.

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