Metabolic pathways design guided by bioinspired metaheuristics

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Background

Nowadays, biotechnological advances provide an easy way to manipulate microorganisms in order to transform them into perfect industrial plants. A variety of methods have been developed for the design of novel pathways. However, current proposals do not take into account the availability of substrates for each reaction within the pathway and are mainly based on classical search strategies, sharing their limitations when the search space is large. Thus, design of new methods for pathway design is a challenging task due to the huge number of potential solutions to explore, and the feasibility considerations that must be taken into account to design and guarantee novel pathways.

Results

We propose a novel bioinspired algorithm for pathways design, that guarantees feasibility and minimize the number of exogenous reactions needed to introduce into a microorganism. The proposal is based on ant-colony optimization, a known metaheuristic for search in large solution spaces. Solutions found are evaluated in terms of size, number of exogenous reactions and feasibility, among other aspects. The algorithm was tested on many artificial design problems, achieving always 100% of feasibility. Fig 1 shows an artificial pathway to produce Succinate from alpha-D-glucose-1P, when considering Glycolysis as base metabolism. The algorithm used 155 seconds to identify the 2 exogenous reactions required, from among 1580 available in *E. coli*. Another test was performed on a real problem, with a search space with 17,000 reactions in order to modify *E. coli* to produce Isopropanol. Solution found was 100% feasible and identical to the one obtained in (Atsumi *et al.*, 2010)[1], whose pathway was manually designed, and tested in a wet-lab experiment.

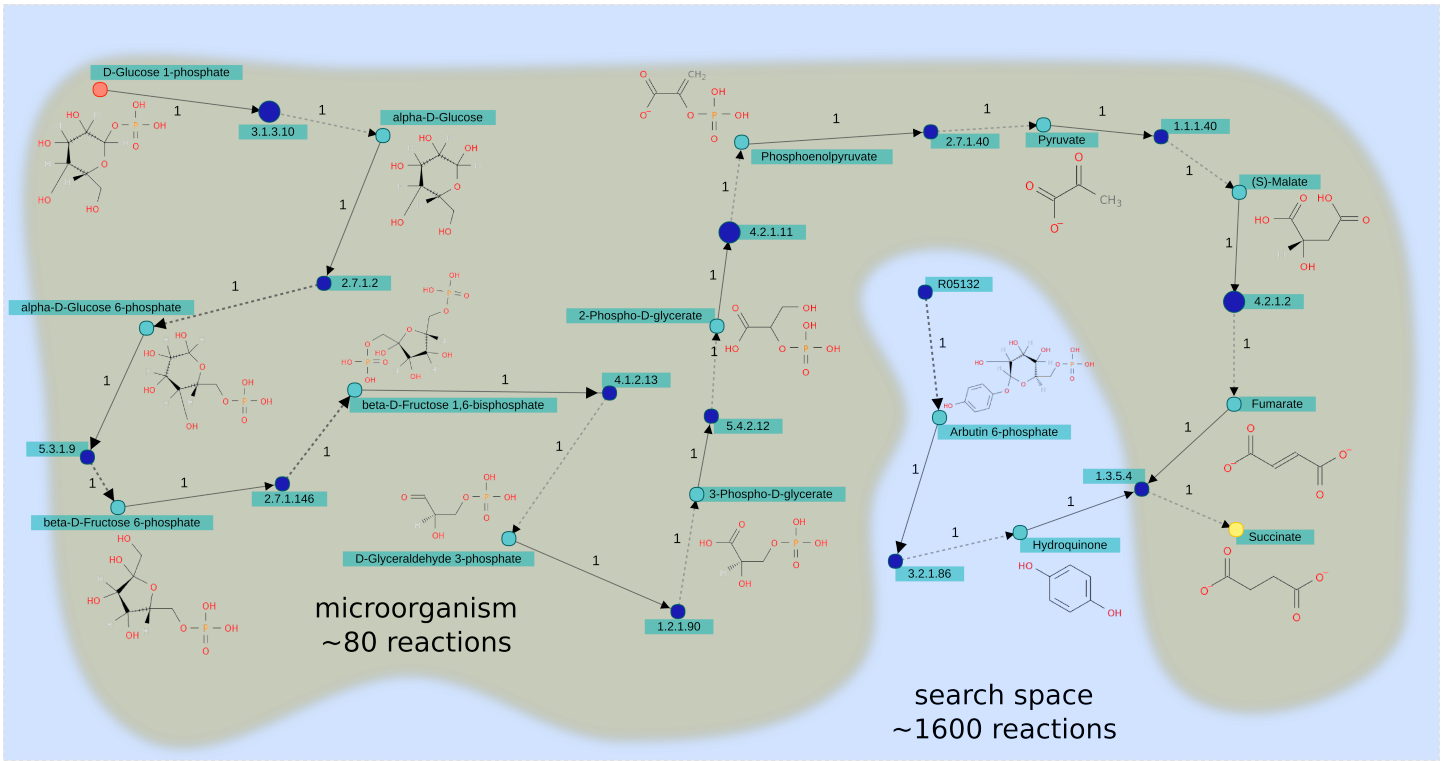

Figure 1. Novel metabolic pathway designed to produce Succinate from alpha-D-glucose-1P within the glycolysis. Only the backbone compounds involved in the synthesis of Succinate are shown. Reactions belonging to the standard glycolysis pathway are shaded in gray. Source and target compounds are in red and yellow, respectively. Blue circles indicate reactions.

[1] DOI: 10.1007/s00253-009-2085-6

Conclusions

We proposed a bioinspired algorithm for designing novel metabolic pathways. It helps to identify clue reactions that could be incorporated into an organism, in order to produce commercially interesting compounds, with as few modifications as possible. Furthermore, designed pathways always respect the availability of substrates for each reaction. Preliminary experimental results show that this algorithm produces solutions which could be useful from a practical point of view. Clearly, this algorithm could be useful for metabolic engineering, helping to design new biochemical mechanisms to produce valuable compounds.

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