

A Generic Multi-Criterion Approach for Mutant Strain Optimization

Paulo Maia^{1,2,*}, Isabel Rocha¹ and Miguel Rocha²

¹ IBB-Institute for Biotechnology and Bioengineering / Centre of Biological Engineering, Universidade do Minho, 4710-057 Campus de Gualtar, Braga, Portugal

² Department of Informatics / CCTC, University of Minho, Campus de Gualtar, 4710-057 Braga, Portugal

* contact: paulo.maia@deb.uminho.pt

Abstract

Motivation: The identification of genetic modifications that can lead to mutant strains that overproduce compounds of industrial interest is a challenging task in Metabolic Engineering. Evolutionary Algorithms and other metaheuristics have provided successful methods for solving the underlying *in silico* bi-level optimization problems (e.g. to find the best set of gene knockouts) [1]. Although these algorithms perform well in some criteria, they lose sense of the inner multi-objective nature of these problems.

Results: In this work, these tasks are viewed as multi-objective optimization problems and algorithms based on multi-objective EAs are proposed. The objectives include maximizing the production of the compound of interest, maximizing biomass and minimizing the number of knockouts. Furthermore, a generalization to integrate multiple-criterion capabilities into single-objective algorithms is proposed and implemented as an ensemble method. This new approach allows taking advantage of the solution space sampling capabilities of some algorithms (e.g. Simulated Annealing), while generating the set of solutions (Pareto-front) according to the multiobjective premises. The algorithms are validated with two case studies, where *E. coli* is used to produce succinate and lactate. Results show that this option provides an efficient alternative to the previous approaches, returning not a single solution, but rather sets of solutions that are trade-offs among the distinct objective functions.

Availability: Algorithms are implemented as a plug-in for the open-source OptFlux [2] platform available in the site <http://www.optflux.org>.

References

1. Rocha,M., Maia,P., Mendes,R., Pinto,J.P., Ferreira,E.C., Nielsen,J., Patil,K.R. and Rocha,I. Natural computation metaheuristics for the *in silico* optimization of microbial strains. *BMC Bioinformatics*, **9**, 499, 2008.
2. Isabel Rocha , Paulo Maia , Pedro Evangelista , Paulo Vilaça , Simão Soares , José P Pinto , Jens Nielsen , Kiran R Patil , Eugénio C Ferreira and Miguel Rocha. OptFlux: an open-source software platform for *in silico* metabolic engineering. *BMC Systems Biology* 2010, **4**:45, 2010

BIOINFORMATICS
OPEN DAYS

Detailed Program

Braga
1st and 2nd March, 2012



Universidade do Minho