

## EVOLUTIONARY MULTIOBJECTIVE ALGORITHMS FOR *IN SILICO* METABOLIC ENGINEERING

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In Metabolic Engineering, the identification of genetic manipulations that lead to mutant strains able to produce a given compound of interest is a promising, while still complex process. Several different algorithms have been proposed to address this problem, namely mixed integer linear programming (MILP) [1] and more recently stochastic meta-heuristics, such as Evolutionary Algorithms (EAs) [2] and Simulated Annealing (SA) [3].

The most common approach consists in solving a bi-level optimization problem, where the strain that maximizes the production of some compound is sought, while keeping the biological objective of maximizing biomass. Although these approaches have provided good results, they give only one single optimal (or near optimal) solution to the problem. In many situations, a set of solutions with different trade-offs between the production of the desired compound and the biomass production would be desirable.

In this work, an approach based on Multi-Objective Evolutionary Algorithms (MOEAs) is proposed to this problem. In fact, since the mid-1980's, MOEAs are being used to solve all kinds of multiple-criterion problems in distinct scenarios and the multiobjective nature of the *in silico* Metabolic Engineering problem suggests that this is a good candidate for MOEAs. The MOEAs chosen for this task are two of the most popular algorithms, namely the SPEA2 and the NSGA-II, widely accepted as two of the algorithms with best overall performance.

The MOEAs are validated using a case study that considers the production of succinic acid with *E. coli*, using the available genome scale metabolic model [4]. The results are compared to previous work [2][3] regarding the same case study, where single objective EAs and SA approaches have been proposed. The results obtained are quite promising, since the MOEAs were able to find in a single run, a set of trade-offs between the two optimization aims that could only be reached by single-objective algorithms with several runs varying a threshold parameter.

1 - A.P. Burgard et al.. *Biotechnol Bioeng*, 84:647–657, 2003

2 - K. Patil, et al. *BMC Bioinformatics*, 6(308), 2005.

3- M. Rocha et al. In *Proceedings of the IEEE Symposium on Computational Intelligence in Bioinformatics and Computational Biology*, pages 331–337, Honolulu, USA, 2007. IEEE Press.

4- J.L. Reed, et al. *Genome Biology*, 4(9):R54.1–R54.12, 2003.