

# Searching for Limited Connectivity in Genetic Network Models

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## ABSTRACT

The inference of regulatory interactions between genes from time-course micro-array data is one of the most challenging tasks in the field of functional genomics. The multitude of genes that can now be measured using micro-array technology requires analysis tools that can easily scale-up with respect to the number of genes. This scalability is especially important when inferring genetic interactions, because this task is complicated by the combinatorial nature of gene interaction [2] and because the high cost of micro-arrays still limits the number of measured time-points severely. Because of this limitation of the data, it is essential to incorporate as much additional information as possible. This can be achieved by applying constraints based on general biological knowledge and by including specific knowledge about known interactions. In previous work [3], we have successfully improved the performance of genetic network models by applying constraints on the robustness of genetic networks. Because gene expression is known to be regulated by a limited number of gene products [1], we propose, in this paper, to limit the connectivity of genetic network models and to search for the most likely connections. We present a general approach in which we separate the task of finding the structure of the networks from the task of finding the best parameters. The first task amounts to a search problem and, through experimental investigation of several search strategies, it was found that this was most efficiently solved by an approach in which connections are sequentially added in a greedy manner. Further experimental investigations determined the best choice of the evaluation function. All experiments were done using GENLAB, a gene expression analysis toolbox developed by the authors and available at <http://www.genlab.tudelft.nl>. The strength of the proposed approach lies in the fact that it can be employed to virtually *all* genetic network models and allows genetic network models to scale up to large networks. This work was funded by the IMDS program of the Delft University of Technology.

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