

Identifying stress-related functional modules and extracting regulatory relationship in gene expression patterns

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When a cell grows in optimal conditions it develops and expresses its genetic material so that it provides the necessary means for survival. Every perturbation in this environment causes alterations in the genetic program as an attempt to sustain the cell's internal homeostasis and survival, a response of vital importance, since growth conditions of living cells are not static but undergo continuous and often drastic changes [1]. The best way to characterize a procedure such as the stress response is to build a model that describes the events that take place during the procedure and the links between them.

The regulation of gene transcription and translation, which determines the situation of a cell in any particular time, is controlled with high accuracy during a cell's life. This is achieved through certain transcription factors that bind DNA in specific regulatory regions and repress or induce the transcription of respective genes. A group of genes that is controlled by the same transcription factor(s) and exhibits a similar expression profile under the same conditions can form a group or a *module* of genes [2]. Quantifying the connection between the regulators and the genes that they regulate inside a module will further reveal the influence of each component in the cellular machinery.

In this work we used a sophisticated algorithm, called GRAM [3] to identify functional modules in yeast using gene expression data [4] combined with protein-DNA binding data [5]. In a second step we used Artificial Neural Networks (ANNs) to build a structurally constrained model of the stress response in yeast establishing the interconnections between the transcriptional regulators and the regulatory genes predicted by GRAM. We managed to accurately predict the expression response of a particular gene given the expression profiles of the transcriptional regulators in the upstream pathway.

References

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