

Duplication of a self-repressed gene: an evolutive approach to loss of cross-links

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Study of genetic network is a field of current research interest owing to its importance in understanding the phenomenon of cell regulation. In this contest we focus on Escherichia Coli. Escherichia Coli has been studied experimentally fairly well and a lot of data pertaining to the information of its genetic network is available. Recent studies have shown interesting aspects of this network. The 76% of the genes of E. Coli transcriptional regulation network are self-repressed genes¹, and the 70% of the self-repressed genes are obtained by duplication². Moreover M.Cosentino-Lagomarsino et al.³ have shown that E.Coli transcriptional regulation network is essentially feedforward with no cross-links between duplicated self-repressed genes. This aspect is peculiar since we expect to find cross-links between duplicated self-repressed genes (see figure).

The aim of this work is study the loss of cross-links in a network composed of duplicated self-repressed genes. In particular we want to investigate if networks with no cross-links have some particular functionality for which they are positively selected by evolution.

The link between networks and functionality is the temporal behavior of the concentration of the proteins involved in the networks⁴. We model networks as a well stirred reactor with high copy number for each kind of reactant. In this way we can model networks by a set of ordinary differential equations whose variables are the concentrations of the reactants. The evolutionary pressure is modeled by a cost function⁵ (CF). The CF is defined like: $\int_0^T (A(t) - F(t))^2 dt$ where $A(t)$ and $F(t)$ are, respectively, the concentration of protein A and the value of the superimposed functionality at the time t .

We have used two different methods. In the first method we calculate the CF's landscape. Minima of the CF are the networks, composed by duplicated self-repressed genes, that are best suited to perform the superimposed functionality. In the second method we have realized, tested and used an evolutionary algorithm based on P.Francois and V.Hakim⁵ to explore the space of net-

works.

Both methods find the same minima in all the CFs that we have used. Depending on the CF we find that the networks that are best suited to perform the superimposed functionality are the networks without cross-links. In one particular case in which the CF present a continuous variety of minima the methods give different information. While landscape give only information about the variety, simulation with the evolutive algorithm give information about the probability to reach each minimum.

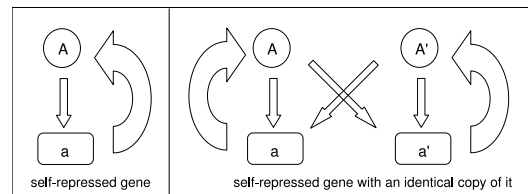


Figura 1. Left figure: self-repressed gene network. Right figure: duplicated self-repressed gene network.

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¹ D. Tieffry, A.M. Huerta, E. Perez-Rueda and J. Collado-Vides (1998) *BioEssays* 20 433-440

² S.A. Teichmann and M.M. Babu, Gene regulatory network growth by duplication, *Nat. Gen.* (2004) 36 492-496

³ M. Cosentino Lagomarsino, P. Iona, B. Bassetti and H. Isambert, Hierarchy and feedback in the evolution of E.coli transcriptional network, *PNAS* (2007) 104, 5516,5520

⁴ J.J.Tyson, K. C. Chen and B. Novak, Sniffers, buzzers, toggles and blinkers: dynamics of regulatory and signaling pathways network in the cell, *Current Opinion in Cell Biol.* (2003), 15 221-223

⁵ P.Francois and V.Hakim, Design of genetic networks with specified functions by evolution in silico, *PNAS* (2004)101, 580,585