Gene regulation in time and space: a model of the interdependence between genome structure and gene network dynamics

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***Short Abstract* — Gene regulatory networks (GRN) at transcription level represent a crucial step of cellular information processing. While data suggest a highly structured spatial organization of co-regulated genes, most GRN models completely neglect spatial effects. Here, we investigate the interdependence between genome structure, GRN topology and GRN dynamics in the framework of an artificial genome model. Our study suggests that local concentration effects, for example induced by positional regularities of co-regulated genes, considerably reduce noise and increase robustness of regulatory dynamics. Further, we investigate how these effects could be exploited by evolution, e.g. for efficient switching between cell phenotypes.**

***Keywords* — Gene regulatory networks, spatial organization, artificial genomes**

Data on the spatial organization of genomes, obtained both from experiments and bioinformatics, suggest strong positional regularities of co-regulated genes on chromosomes. For example, it has been shown that the genes which are regulated by a given transcription factor (TF) and the gene coding for this TF tend to be located periodically along the DNA [1]. It was suggested that a solenoidal organization of chromosome structure [2] can explain the periodic pattern by distance minimization in 3d space. Using a thermodynamic framework based on a polymer model of DNA with sparse, interacting transcription sites, it was further shown that periodic gene positions, for different topologies of chromosome structuring, can favor the formation of transcription factories [3]. These regularities suggest that cells exploit local concentration effects induced by spatial proximity of co-regulated genes to optimize the efficiency of gene regulation [4,5,6].

Here, we investigate the effects of spatial genome organization on the topology and dynamics of GRN within the framework of an artificial genome model [7]. Our study suggests that local concentration effects can considerably reduce noise and increase robustness of regulatory dynamics. Using evolutionary algorithms, we also show how evolution may exploit these effects for cellular information processing, e.g. for switching between different cell phenotypes in response to environmental signals.

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