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Synthetic analysis of the effect of parameter balance on phenotypic stabilities in a synthetic mutual inhibitory network

Ryoji Sekine[1]
green-dolphin@es.dis.titech.ac.jp

Daisuke Kiga[2]
kiga@dis.titech.ac.jp

Masayuki Yamamura[2]
my@dis.titech.ac.jp

[1] Department of Computational Intelligence and Systems Science, Tokyo Institute of Technology, Kanagawa 226-8503, Japan

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Mutual inhibitory network, in which two genes inhibit each other, appears in high frequency in various organisms from bacteria to mammalian: for example, Nanog and Gata6 in embryo [1]. Cells carrying the mutual inhibitory network are known to exhibit either of two distinct phenotypes where one gene is expressed a lot while the other is slightly when parameters such as the expression rate constants of the two genes are balanced [2]. However, quantitative knowledge about the effect of parameter balance on the stability of each phenotype is not experimentally investigated well. In this work, we analyzed the effect of the parameter balance to phenotypic stabilities in a synthetic mutual inhibitory network constituting of CIts and LacI, based on P_{luxlac} toggle [3]. The net rate constants of the CIts expression in our synthetic mutual inhibitory network can be tuned by the addition of an inducer N-acyl homoserine lactone (AHL). We measured the phenotypic ratios, determined by the switching rates and growth rates of each phenotype, at stationary state under various AHL concentrations, and analyzed the relationship between the switching rate corresponding to the phenotypic stabilities and the balance of the promoter strength. Our results and approach would be a basis of an experimental system to estimate and adjust switching rates and phenotypic ratios in mutual inhibitory networks of interest.

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