436m Population Distribution Patterns in Cells with Oscillatory Genetic Network Dynamics

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The ability to create synthetic regulatory networks offers new opportunities for dynamic control of gene expression. Understanding the expression patterns of simple, synthetic gene regulatory networks will not only shed light into the complexity of naturally occurring networks but it will also provide a platform for expression control that can be valuable in biotechnological applications. The behavior of synthetic regulatory networks depends on specific properties of the regulatory elements chosen, as well as the architectural framework in which they are connected. In addition, their expression dynamics is vastly influenced by the fact that the intracellular environment varies among the cells of a population. Therefore, understanding the relationship between the architecture of synthetic regulatory networks and cell population heterogeneity is of fundamental importance.

The model regulatory network studied here is termed the "repressilator" [1]. It is composed of three coupled promoter-repressor pairs. The components of the network are arranged in a cyclic formation of negative feedback loops, which either can lead to oscillatory behavior or stable expression of the system. In this study, existing plasmids encoding this network and a green fluorescent protein (GFP) reporter gene were inserted into an E. coli host. A series of shake flask experiments was performed under different extracellular conditions and the GFP levels were monitored over time using flow cytometry, thus providing information about the distribution of fluorescence among the cells of the population as well as the mean expression dynamics. Additional insights into the single-cell behavior of the network were gained using fluorescence microscopy. These measurements were used to characterize the fluorescence distribution patterns obtained for different extracellular inducer concentrations and their association to oscillations in the mean expression dynamics. Therefore, these studies contribute towards the elucidation of the complex interplay between oscillatory behavior at the single cell level and the distribution of phenotypes at the cell population level as a function of extracellular conditions.

1. Elowitz, M.B. and S. Leibler, A synthetic oscillatory network of transcriptional regulators. Nature, 2000. 403: p. 335-338.