Influence of Different Types of Delay and Instability Induced by Stochastic Fluctuations in the Expression of a Self-Repressed Gene

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Most biological functions in cells depend on networks of interacting genes and proteins. These networks can display complex dynamical behavior such as self-sustained oscillations. To understand which ingredients are essential for triggering oscillatory behavior, we study a simple model where the expression of a single gene is repressed by his own protein. An analytic oscillation threshold can be written for this model, which allows one to show rigourously that a non-trivial transcriptional dynamics with a finite gene response time is equivalent to a time delay, and favors oscillations [1].

However, other forms of delay exist, in particular due to transport, transcription, or translation. We have therefore extended the model of Ref. [1] to take into account reversible or irreversible transport of protein between cytoplasm and nucleus, both as an explicit delay and as a reactional delay, and we have studied how these two types of delay affect the dynamics of the self-repressed gene when they are combined with a finite gene response time. In particular, this allows one to understand how the interaction of two time delays can repress or enhance oscillations. To understand the role of fluctuations, we have also constructed a modified version of the model of Ref. [1], where both the average values and variances of gene activity and molecule concentrations are dynamical variables. This allows us to study how nonlinearities and stochastic fluctuations interact, and to show that the latter can induce oscillatory behavior in this system without requiring nonlinear degradation.

[1] Morant et al., Phys. Rev. Lett. 102, 068104 (2009).