

Gene Toggle Switches Only with Positive Feedback Loops

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1 Introduction

Construction of synthetic gene-regulatory networks and designing of them have been drawing much attention these days. Some simple synthetic gene-regulatory networks such as a genetic toggle switch and a gene oscillator have already been constructed in *E.coli* [1, 2]. In these studies, mathematical models are used to predict the behaviors of the gene networks and compared with experimental data.

However, the mathematical models of these gene networks were very simple, obtained by ignoring a lot of components and elements, i.e. time delays, transportation factors which could significantly change the dynamical properties of model for large or complicated networks.

Although these simple models predicted the behaviors of the simple gene networks very well in these works, it is still an open problem to explore whether such simple models are also useful for analyzing and designing more complicated and high dimensional artificial gene networks. Furthermore, when a gene network has a lot of components and includes some factors like time delays, it is quite difficult to analyze a gene network mathematically.

2 A Reduction Method of a Gene Network Only With Positive Feedback Loops

In this paper, by using the theory of dynamical systems, especially monotone dynamical systems [3, 4], we prove that a gene network model can be reduced to a simpler version if the gene network is composed of only positive feedback loops (Fig. 1). Moreover, we show that a gene network with only positive feedback loops has the following desirable properties as a gene switch:

1. It is automatically guaranteed that almost all orbits of a gene network model with only positive feedback loops converge to stable equilibrium points. Thus, it is unnecessary to check if or not a gene switch has only equilibrium points as attractors.

2. Even if all the time delays of the model are ignored by replacing all the delays with 0, the equilibrium points and their stabilities are invariant. Thus, it is no problem for designing a gene switch to use ordinary differential equations rather than functional differential equations that are more troublesome to analyze.
3. The dimension of the model can be reduced by changing some differential equations (ODEs) into algebraic equations, keeping the equilibrium points and their stabilities invariant.

3 Designing of a Gene Switch

When we design a gene switch with a mathematical model and implement it in *E.coli*, the gene switch model should have not only necessary switching properties but also biologically realistic parameters and configuration. We also show that the reverse of the previous reduction method holds, that is, we can make a gene switch model more complicated but biologically more realistic by adding some components to a gene switch (Fig. 2).

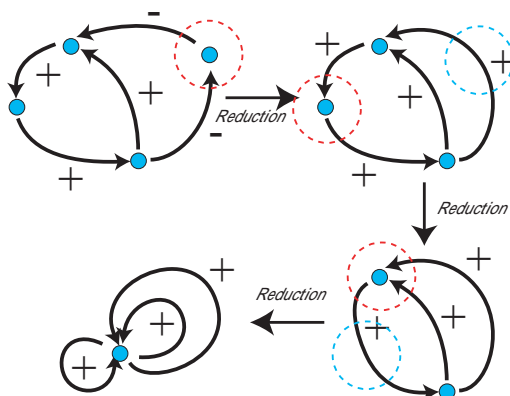


Figure 1: Reduction of a gene switch only with positive feedback loops.

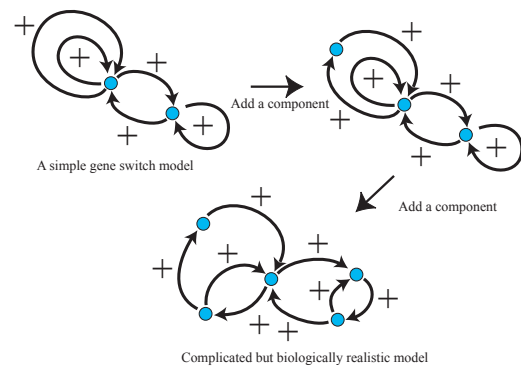


Figure 2: Design process of a gene switch only with positive feedback loops.

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