Induction Mechanism Description of λ Phage by Hybrid Petri Net

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1 Introduction

It is well known that just after the chromosome of λ phage is injected into an *E. coli* cell, it may enter either lytic or lysogenic pathways depending on the environment in the *E. coli* cell [3]. In [2], we provided a strategy for describing gene regulatory network and succeeded in simulating a part of gene regulatory network of λ phage concerning to these pathway mechanisms by using the currently available tool called Visual Object Net ++ [1]. However, an important mechanism "induction" of λ phage did not realize in the gene regulatory network described in the paper [2]. In this paper, we firstly present a complete hybrid Petri net describing lytic and lysogenic pathways of λ phage by adding the induction mechanism including a well known biological phenomenon "retroregulation". Furthermore, we observe the dynamics of related protein concentrations by using Visual Object Net ++.

2 Induction Mechanism and Dynamics of Related Proteins

The concentration of CII protein is a key factor deciding the lysogen and lysis pathways. If CII is highly active then the infecting phage lysogenizes. That is, CII protein helps to increase CI proteins which represses all of other genes and also helps to increase Int proteins which is necessary to integrate λ phage chromosome into *E. coli* chromosome. Otherwise the λ phage grows lytically by keeping the concentration of Cro protein at some adequate level. When the ultraviolet light (UV) irradiates an *E. coli* in the lysogenic growth stage, the concentration of Cro protein grows, then the λ phage chromosome is escaped from the *E. coli* chromosome. In this situation, it is needed for λ phage chromosome that the concentration of Int and Xis proteins become high enough in order to begin to escape from *E. coli* chromosome. The Int protein concentration level is controlled by a sophisticated mechanism called "retroregulation" [3], but we omit the detail of it in this paper.

Figure 1(1) describes the induction mechanism of λ phage hierarchically. The discrete places in the upper layer of the figure indicate the states of the λ phage. If Z_1 has a token, λ phage is in the state just after its chromosome is injected to *E. coli* chromosome. Similarly, Z_2 and Z_3 indicate that λ phages are in the states of lysogeny and lysis, respectively. Although Z_4 and Z_5 imply the intermediate states between the two states among Z_1, Z_2, and Z_3 as shown in the figure, the meanings of these states are omitted here (see [3]). The discrete transitions have parameters which reflect the times required for changes of the states.

Figure 1(2) shows the dynamics of concentration of proteins which relate to the induction mechanism. This simulation is performed on the Visual Object Net ++. Int_A (Int_B) is the concentrations of protein Int produced by the P_{Int}-initiated transcript (P_L-initiated transcript), where P_{Int} and P_L are promoters (see [3] for details).

When the ultraviolet light (UV) irradiates the *E. coli* host at the time around 250, CI protein concentration begins to decrease and then the concentrations of Cro, Xis, and Int proteins are getting higher. Recall that Int and Xis proteins help to escape λ phage chromosome from *E. coli* chromosome. As soon as the Cro protein concentration reaches to some fixed level, the transcription of *xis* and *int* genes are stopped.

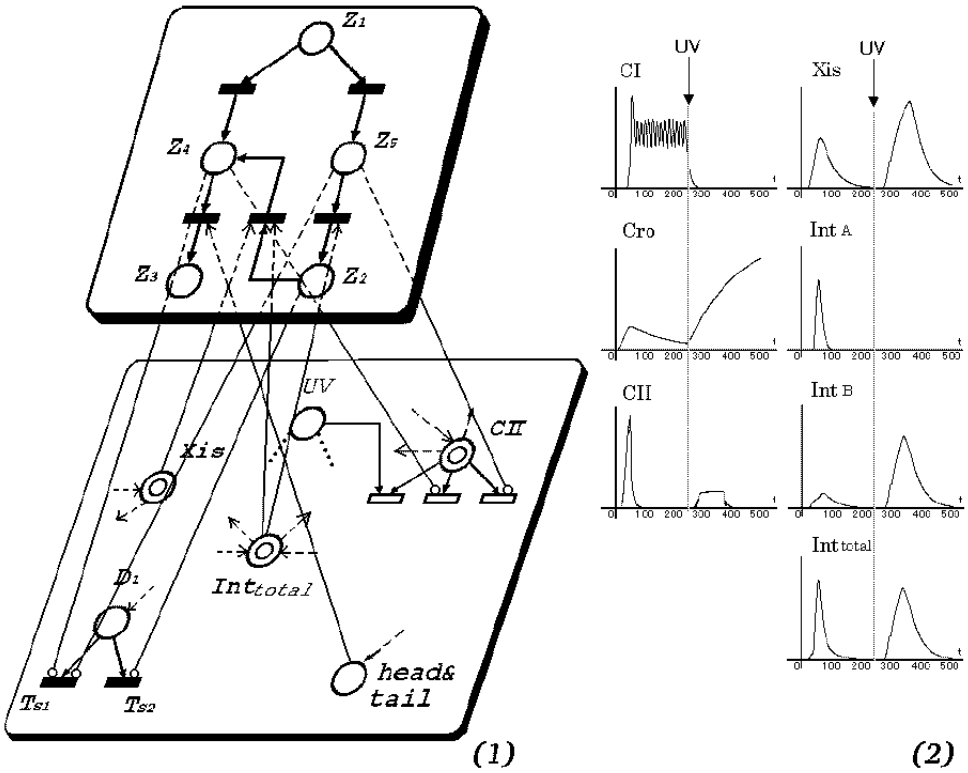

Figure 1: Induction mechanism and behavior: (1) Lysogenic and lytic pathways and the underlying biological mechanism, (2) Dynamics of concentrations of the related proteins

References

[1] Drath, R., Hybrid object nets: an object oriented concept for modeling complex hybrid systems, *Proc. Hybrid Dynamical Systems, 3rd International Confernce on Automation of Mixed Processes, ADPM'98*, 437–442, 1998

[2] Matsuno, H., Doi, A., Nagasaki, M., and Miyano, S., Hybrid Petri net representation of gene regulatory network, *Pacific Symp. Biocomputing*, 5:338–349, 2000.

[3] Ptashne, M., *A Genetic Switch Phage λ and Higher Organisms – Second Edition –*, Cell Press & Blackwell Science, 1992.