Protein Dynamics Observations of Lambda Phage by Hybrid Petri Net

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1 Introduction

We will demonstrate how we can effectively observe the dynamics of concentrations of proteins of λ phage by using a hybrid Petri net (HPN) tool called Visual Object Net ++ [2].

The HPN has continuous and discrete elements. It is an extension of Petri nets which have been used to represent many kinds of systems including stochastic ones in the field of computer sciences and engineerings [1]. Then, it is possible to translate biological facts into HPNs and to observe continuous factors behavior such as mRNA or protein concentrations in a natural manner.

We show some computational results of the protein dynamics of the λ phage mechanism that is simulated and observed by implementing the HPN on Visual Object Net ++.

2 HPN Representation of Early Stage Gene Expression of λ Phage

We only give the outline of the early state gene expression of λ phage. Please refer to [6] for the details. Fig. 1 shows the gene regulation that determines the growth path of λ phage by the HPN. In the square surrounded by dotted line in the figure, the feedback mechanism of CI and Cro should be inserted [5]. P_L operon has the genes N, $cIII$, xis, and int. P_R operon has the genes cro, cII, O, P, and Q. $P_{R'}$ operon has the gene S and downstream genes that encode cell lysis proteins and head and tail coat proteins.

N protein regulates early gene expression by acting at three terminators: one between itself and the neighbor gene $cIII$, one between genes cro and cII, and one between genes P and Q. CII turns on cI and int. It encourages RNA polymerase to bind and begin transcription at two promoters that would remain silent: P_{RE} and P_I. CIII protein helps to establish lysogeny, that is, its role is to protect CII from degradation. Int protein helps to integrate the chromosome of λ phage into the host chromosome. In the case of reverse reaction, excision, the protein Xis is needed in addition with Int. Protein O and P proteins are required for DNA replication. Q protein turns on the late genes–those for lysis and for production of heads and tails. It anti-terminates specifically a small RNA begun at a promoter $P_{R'}$, located just to the neighbor of Q.

The bi-direction arcs between the place labeled N and three discrete transitions indicate that N anti-terminates the terminators to allow transcriptions of genes followed by the three transitions. The bi-direction arc between the place labeled Q and the discrete transition has the same meaning as

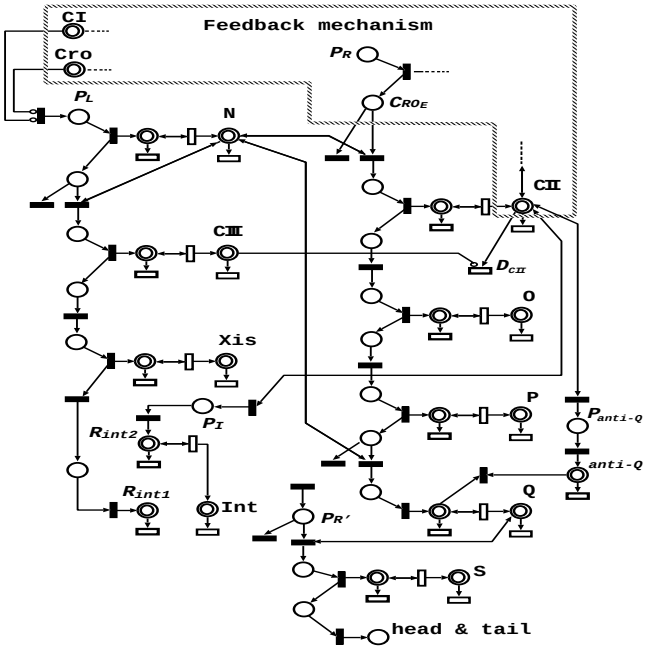

Figure 1: Expression of the growth pathway control of λ phage.

above. These bi-direction arcs have the weights representing the thresholds of concentration enough for the anti-terminations, although these are not represented explicitly in the figure.

The dynamics of protein concentrations expressed by Fig. 1 [5] are consistent with the biological facts well [6]. The files which we made can be downloaded from the website [3].

3 Discussion

McAdams and Shapiro [4] proposed a hybrid modeling approach that integrates conventional biochemical kinetic modeling within the framework of a electrical circuit simulation. However, basically, their model consists of two different kinds of parts, circuit diagrams and differential equations. We will show that HPN can integrate such different kinds of parts and perform the direct simulation on the HPN representing a gene regulatory network by using Visual Object Net ++.

References

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