

Computational Analysis of SOS Response in Ultraviolet-Irradiated *Escherichia coli*

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Keywords: computational modeling and simulation, SOS response, protein interaction

1 Introduction

The SOS response is a complex mechanism that is induced following DNA damage caused by UV irradiation. This system includes protein interactions and coordinated activation of a large number of diverse unlinked genes involved in DNA repair, error-prone DNA replication, etc. In this study, we demonstrate the mathematical modeling for the early stage of the SOS regulatory system taking account of protein and mRNA levels. The simulation results show that the behavior of the system changes according to the severity of DNA damages, the basal level of expressions and the binding properties of the repressor protein. This provides some elemental principles of gene regulatory systems controlled by protein interactions together with operators [5].

2 Method

The regulatory mechanism of the SOS system is diagrammed schematically in Fig. 1. In the uninduced state, LexA repressor protein expressed in small amount binds to the *lexA* operator and to the operators of the *recA* gene and other genes (Fig. 1A). Following DNA damage, the coprotease activity of existing RecA protein is activated by binding to the single-stranded DNA (ssDNA) created by discontinuous DNA synthesis past the pyrimidine dimers. Activated RecA (RecA^{*}) causes LexA to cleave itself.

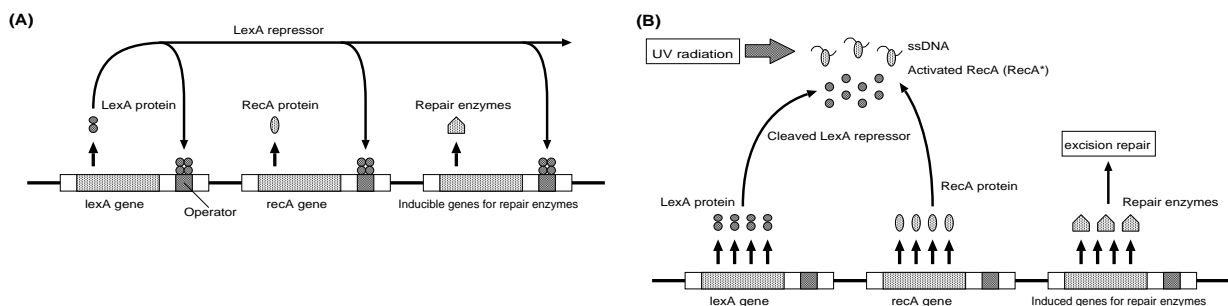


Figure 1: Diagrammatic representation of the mechanism of SOS response [2].

In the induced state, *lexA* dissociating from the promoter regions allows transcription of all of the SOS genes to occur in a coordinated manner (Fig. 1B). When the DNA damage signal disappears by the repair of the pyrimidine dimers or the ssDNA, RecA reverses to the inactivated conformation. LexA repressor accumulates, and genes under LexA control are once again repressed.

We described the protein and mRNA concentrations in the LexA-RecA regulation mechanism with deterministic differential equations using parameters found in literatures.

3 Results and Discussions

Our simulated time courses of proteins and mRNA shown in Fig. 2 quantitatively agree with biological experimental results [4]. We have shown that the behavior of the SOS system changes according to the severity of DNA damages caused by UV irradiation. This probably derives from the capacity of the excision repair and leads to the error free repair mechanism induced by different kinds of SOS genes as a last resort in order to survive.

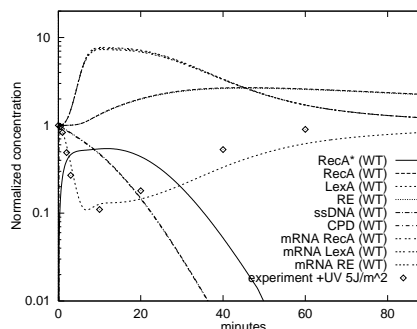


Figure 2: The simulation results of time courses.

We also have demonstrated how mutations in each gene have effects on the total behavior. It has been reported that the various SOS genes differ with respect to the basal level of expression and the degree to which they are induced [3]. Our simulation results have supported the idea that mutations in promoter regions change the basal level of each protein, which reflects the role of the protein in the system. The higher basal expression level of RecA is certainly required for the protein to cleave LexA efficiently and that of SOS genes is required for repairing DNA damages.

The SOS regulation is a well-designed system composed of protein interactions and repressor binding. A large amount of biological study has been done [1], but it is hard to elucidate the mechanism of SOS system from expression data alone. This study could contribute to the understanding of transcriptome and proteome system.

References

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