Modeling of Transcription and DNA Replication Using the E-CELL Simulation System

Kenta Hashimoto [12] **Fumihiko Miyoshi** [13] **Thomas S. Shimizu** [14]
kem@sfc.keio.ac.jp t95894fm@sfc.keio.ac.jp tss26@cus.cam.ac.uk
Takeshi Satoyoshi [13] **Masaru Tomita** [13]
t96457ts@sfc.keio.ac.jp mt@sfc.keio.ac.jp

[1] Laboratory for Bioinformatics
[2] Graduate School of Media and Governance
[3] Department of Environmental Information
Keio University, 5322 Endo, Fujisawa 252-8520, Japan
[4] Department of Zoology, Cambridge University, CB2 3EJ, UK

1 Introduction

We are currently constructing a "self-replicating" hypothetical cell by integrating models of DNA replication, transcription and translation, as well as other metabolic pathways, using the E-CELL simulation system, which is a generic software package for simulation of cellular processes [1]. We discuss a problem in designing such an integrative model with both transcription and replication; that is, the problem of DNA polymerase colliding with RNA polymerase when both of them simultaneously process the same part of chromosome.

2 Transcription

The model of transcription is presented in figure 1. To initiate transcription, RNA polymerase first binds to a polymerase binding site on chromosome. Various transcriptional factors promote or suppress this polymerase binding process. Nucleotides are consumed by the mRNA elongation process, and elongation of mRNA is completed by the transcription termination process. Molecules of mRNA are degraded spontaneously over time, releasing their nucleotides to the cytoplasm.

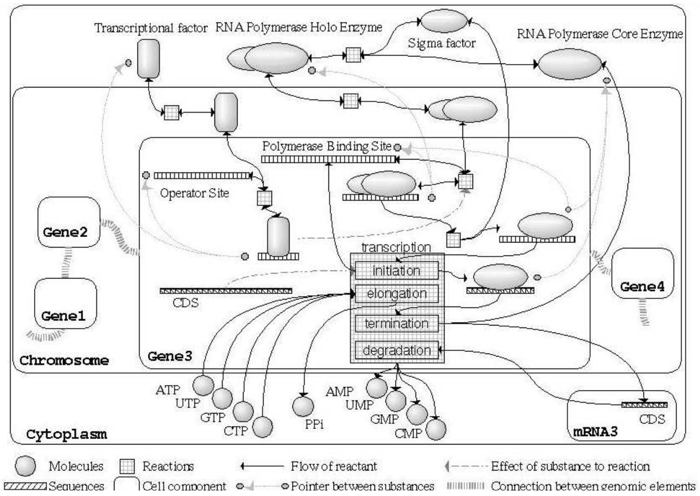
3 Replication

Fig. 2 illustrates our model of DNA replication. The process of replication initiation is shown in the left half of the figure. First, four dnaA proteins bind to dnaA boxes on oriC, forming a dnaA complex. Second, DNA polymerase and other replication machinery, such as helicase and gyrase, forms a complex.

Elongation process of replication is shown in the right half of the figure. Chromosome is modeled as an ordered list of genes and other genomic elements. The elongation process traces the gene list, and creates copies of the genes one by one. All substances bound to the genes being replicated are taken off and released into the cytoplasm.

4 Avoiding the Conflict between Transcription and Replication

When RNA polymerase and DNA polymerase are collided on chromosome, the RNA polymerase is taken off and released to the cytoplasm; In this way, we can cope with the "collision" problem. To implement this, pointers are maintained among substances such as RNA polymerase, transcriptional factors and binding sites. Grey dotted arrows in figure 1 and figure 2 show the pointers defined among substances.



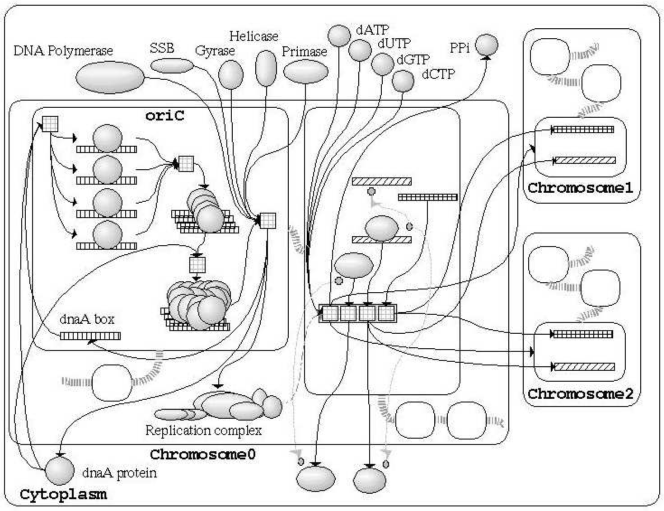


Figure 2: Model of replication.

5 Concluding Remarks

We have integrated models of transcription and DNA replication, and coped with the problem of polymerase collision by introducing additional book keeping mechanism. We now plan to apply our model discussed above to simulation of genetic network of bacterium phage λ.

References

[1] Tomita, M., Hashimoto, K., Takahashi, K., Shimizu, T., Matsuzaki, Y., Miyoshi, F., Saito, K., Tanida, S., Yugi, K., Venter, J.C., and Hutchison, C., E-CELL: Software environment for whole cell simulation, *Bioinformatics*, (to appear).