2017 International Symposium on Nonlinear Theory and Its Applications,
NOLTA2017, Cancun, Mexico, December 4-7, 2017

Bifurcations in an Asynchronous Cellular Automaton Model of Gene Network

Takuya Yoshimoto and Hiroyuki Torikai†

†Department of Computer Science, Kyoto Sangyo University
Motoyama, Kamigamo, Kita-Ku, Kyoto 603-8555, Japan
Email:i1788296@cse.kyoto-su.ac.jp,torikai@cse.kyoto-su.ac.jp

The cancer may be caused when a mutation occurs in a gene network. In order to clarify occurrence mechanisms of the cancer, many mathematical models of gene network have been investigated [1]-[2]. For example [2] investigates a mathematical model the mutation of p53 gene, which causes the cancer. Fig. 1 shows time waveforms of the p53 gene network. The black graph shows the concentration x of protein generated by the p53 gene and the gray graph shows the ratio dmg of damaged DNA in the cell. These graphs show that the large DNA damage (i.e., $dmg = 100$) triggers oscillation of the p53 protein x and the p53 protein x decreases the DNA damage dmg. That is, the p53 protein plays an important role to inhibit generation of the gene.

In this paper, we investigate a p53 gene network model the dynamics of which is described by an asynchronous cellular automaton [3]-[4]. The model has four registers storing the following four discrete state variables.

$$\begin{array}{rl} \text{DNA damage ratio} & Dmg \in A_N, \\ \text{p53 protein concentration} & X \in A_N, \\ \text{Mdm2 protein concentration} & Y \in A_N, \\ \text{ATM kinase concentration} & Z \in A_N, \end{array} \tag{1}$$

where $A_N = \{0, \ldots, N-1\}$. The model has four uncoupled clocks that trigger transitions of the discrete states variables as follows.

$$\begin{array}{lll} \text{If } C_{Dmg}(t) = 1, & \text{then} & Dmg(t_+) \\ & & := f_{Dmg}(Dmg(t), X(t), Z(t)), \\ \text{If } C_X(t) = 1, & \text{then} & X(t_+) := f_X(X(t), Z(t), Y(t)), \\ \text{If } C_Y(t) = 1, & \text{then} & Y(t_+) := f_Y(X(t), Y(t)), \\ \text{If } C_Z(t) = 1, & \text{then} & Z(t_+) := f_Z(Dmg(t), Z(t)), \end{array} \tag{2}$$

where $f_{Dmg} \in \{-1, 0, 1\}$, $f_X \in \{-1, 0, 1\}$, $f_Y \in \{-1, 0, 1\}$, and $f_Z \in \{-1, 0, 1\}$. These functions are implemented by logic gates and reconfigurable wires, which determine the smooth vector field of the model. Fig. 2 shows time waveforms of the cell automaton model of the p53 gene network. The black graph shows the concentration X of protein generated by the p53 gene and the gray graph shows the ratio Dmg of damaged DNA in the cell. Comparing Figs. 2 and 1, we can confirm that our model can reproduce the inhibition of the DNA damage dmg by the p53 protein x.

In the presentation, we will compare hardware costs of an FPGA-implemented our model consumes and an FPGA-implemented p53 gene network model [2].

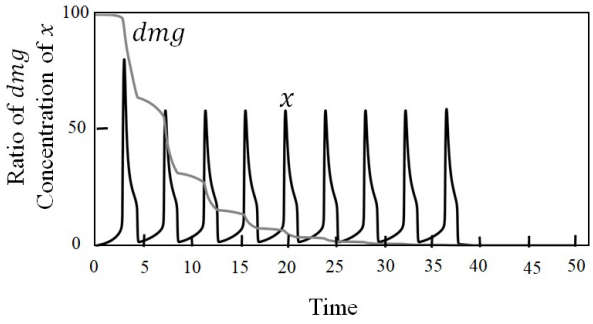

Figure 1: Time waveforms of the p53 gene network model [2].

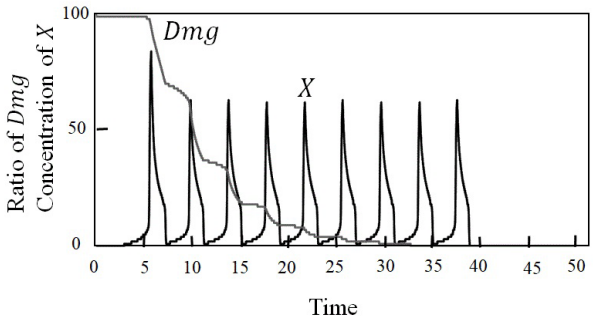

Figure 2: Time waveforms of our gene network model.

References

[1] E. Barillot, et. al., Computational Systems Biology of Cancer, CRC Press, 2013.

[2] V. Chickarmane, et al., A Model for p53 Dynamics Triggered by DNA Damage, SIAM Journal on Applied Dynamical Systems, vol. 6, no. 1, pp. 61-78, 2007.

[3] T. Yoshimoto and H. Torikai, A Novel Hardware-Efficient Gene Network Model based on Asynchronous Cellular Automaton Dynamics, NOLTA, IEICE (accepted).

[4] K. Takeda and H. Torikai, A Novel Hardware-Efficient Cochlea Model based on Asynchronous Cellular Automaton Dynamics: Theoretical Analysis and FPGA Implementation, IEEE Trans. CAS-II (accepted).