# *Xenopus* Cell Cycle Pathway for Simulating Cell Division Processes by Genomic Object Net

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## 1 Introduction

To establish methods for modeling multicellular systems is the current important issues in biopathway simulations. This paper proposed a new method for modeling cell division processes with using a famous multicellular phenomenon "the changes in cell division cycles from synchronous to asynchronous in *Xenopus*" and succeeded in simulating this phenomenon with GON.

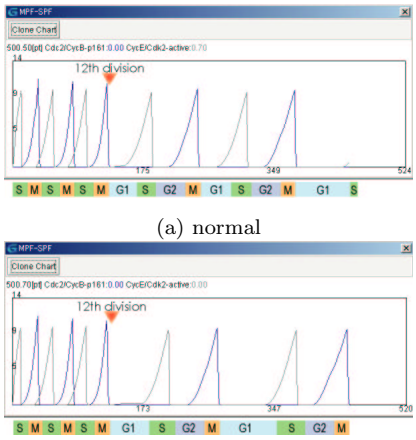
Matsuno *et al.* [3] modeled and simulated a *Drosophila* multicellular patterning by Delta-Notch signaling pathway by using a software "Genomic Object Net" which is developed based on hybrid functional Petri net (HFPN) architecture. However, in this model, cellular formation is fixed throughout the simulation. Then, we construct an HFPN model of *Xenopus* cell cycle pathway which includes the mechanism for cell division control as well as checkpoint processes. With this model, dynamic cell division processes of *Xenopus* early embryo including the changes in cell division cycles from synchronous to asynchronous [1] are simulated.

## 2 *Xenopus* Cell Cycle Model by Hybrid Functional Petri Net

We first modeled a HFPN pathway of *Xenopus* cell cycle which consists of MPF activity, SPF activity, and two checkpoint mechanisms. M-phase promoting factor (MPF) [2] , which is a dimer of cyclin-dependent protein kinase (Cdc2) and cyclin B (CycB), is essential to initiate mitosis. S-phase promoting factor (SPF) was firstly defined by Strausfeld *et al.* [4] as analogy to the MPF. The details of the HFPN pathway are shown in the URL [5].

In the mechanism for dividing a cell in the constructed *Xenopus* cell cycle pathway, "universal place" and "universal transition" are used. With these elements, changes in the cell volume due to cell divisions are realized. Several numbers of data with different types such as integer, real, and Boolean can be assigned to the universal place.

Figure 1 shows two types of MPF and SPF concentration behaviors from the 10th to 14th mitotic division. (Note that MBT is the 12th mitotic division.). From the following observations, it can be said that our HFPN cell cycle model succeeds in simulating the influences of cell volume on MPF and SPF oscillations. The MPF and SPF oscillation cycles of small cell are lengthened compared to normal size cell (b). Behavior of the simulation results are animated GON Visualizer (Figure 2) [6].




(a) normal

(b) small

Figure 1: Simulation results of MPF and SPF concentration behaviors. (a) Normal cell. Both of oscillation cycles of MPF and SPF concentrations change after the 12th division (G1 and G2 phases are inserted). (b) Small cell. The volume of the small cell is half of the normal cell. The period of oscillation is longer than the normal cell.

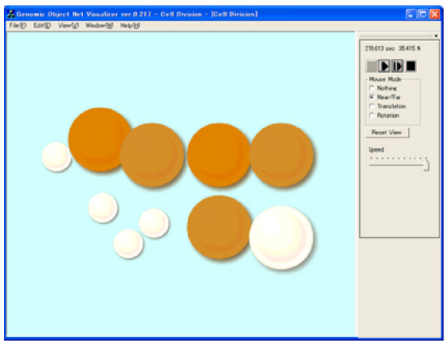


Figure 2: Screenshot of GON Visualizer. The diameter and the color of each cell change according to two series of values for the cell volume and the MPF concentration in the CSV file, respectively.

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[5] `http://genome.ib.sci.yamaguchi-u.ac.jp/~fujita/CellCycle/`

[6] `http://www.GenomicObject.Net/`