

A two-phase partition method that simulates the dynamic behavior of the gene regulatory networks with high accuracy at a remarkably high speed

Hiroyuki Kurata

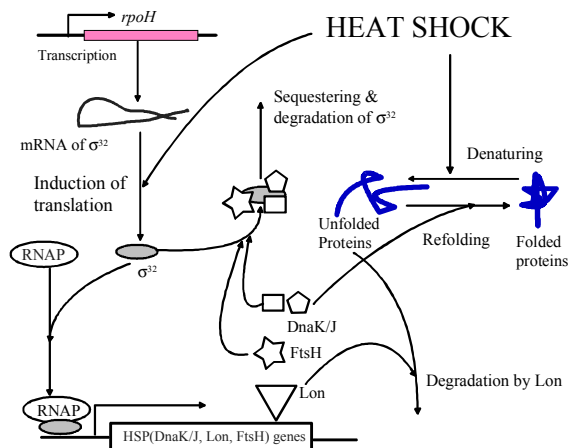
Department of Biochemical Engineering and Science, Kyushu Institute of Technology

Kawazu, Iizuka, Fukuoka 820-8502, Japan.

kurata@bse.kyutech.ac.jp

ABSTRACT

The general problem in mathematically simulating a biological system is that the differential equations with the rate parameters whose values were quite different in the time-scale of reactions were so stiff that the calculation time became quite large. Metabolic Control Analysis (MCA) and Biochemical Systems Theory (BST) have been demonstrated to be useful for simulating metabolic circuits. On the other hand, conventional mass action equations or the method for simplifying complicated networks into rate equations (Michaelis-Menten rate equations etc.) have been employed to simulate the molecular networks consisting of proteins and DNAs, such as stress responses, cell division, chemotaxis, and circadian clocks [1-3]. Needless to say, conventional mass action equations consume lots of time for calculation because they use ordinary differential equations. The simplified rate equation method depended on the structures of the network and on the values of the system parameters, because it neglects some reactions to simplify a complicated network. To overcome these problems, a two-phase partition method was developed that automatically divided all the biochemical reaction equations into two phases: the binding phase and the reaction phase. This method simulated all the reactions involving protein and DNA signal transduction, and calculated them at an extremely high speed. This method was newly developed for simulating a gene regulatory network without knowing the detailed values of biochemical parameters, based on the algorithm that had been proposed by Park [4] for metabolic analysis. Actually, the two-phase partition method accurately simulated the dynamic behavior of the heat shock response that contained the huge differences in the time-scale of reactions (Fig 1). The calculation speed was 4×10^4 -fold higher than the conventional mass action method. The heat shock response was an excellent model showing the dynamic behavior with a quick and sharp transient response of a regulatory protein.



REFERENCES

- [1] Bray, D., Bouret, R.B.&Simon, M.I. (1993).Computer simulation of the phosphorylation cascade controlling bacterial chemotaxis. *Mol. Biol. Cell* **4**, 469-482.
- [2] Goldbeter, A. (1995).A model for circadian oscillations in the *Drosophila* period protein (PER). *Proc. R. Soc. Lond. B* **261**, 319-324.
- [3]Tyson, J.J., Novak, B., Odell, G.M., Chen, K.&Thron, C.D. (1996).Chemical kinetic theory: understanding cell-cycle regulation. *TIBS* **21**, 89-95.
- [4] Park, D.J.M. (1974).The hierarchical structure of metabolic networks and the construction of efficient metabolite simulators. *J. Theor. Biol.* **46**, 31-74.