BioDrive: Simulator for Biochemical and Genetic Networks

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1 Introduction

Recent progresses of molecular biology enable us to obtain massive data on various aspects of living systems. In order to study a biological system as a system, it is desirable to use the dedicated simulator that can model essential features of the system. There has been several previous efforts to design simulators for kinetics such as GEPASI [1], E-CELL [2] and Virtual Cell [3]. These simulators allow quantitative simulations of biochemical reactions based on ordinary differential equations (ODEs). However, since these simulators are difficult to use for biologists, we develop a *biologist-friendly* simulator BioDrive which can simulate biochemical reactions and gene expressions.

2 System

BioDrive is a generalized biochemical simulator for single-cellular organisms. It can simulate *biochemical reactions* (e.g., protein-protein interactions) and *gene expressions* (e.g., transcription and translation). It gives you an environment that can easily compute and visualize biological systems, if they are described in simultaneous ODEs. BioDrive consists of a simulation kernel and a graphical user interface (GUI).

2.1 The BioDrive Kernel

The kernel of BioDrive consists of a parser and a solver. The parser reads a *rulefile* in which definitions of the target biological systems and simulation environment are described. It translates the description of the *rulefile* into a form that can be calculated by the solver. The solver computes the biochemical reactions and gene expressions. We can select either the Euler method or the fourth-order Runge-Kutta method for the numerical method in current version of BioDrive.

2.2 The BioDrive GUI

The BioDrive GUI consists of the Tracer Window and the Substance Window. The Tracer Window shows concentration level of substances over time series. The Substances shown in the Tracer Window are defined in the Substance Window.

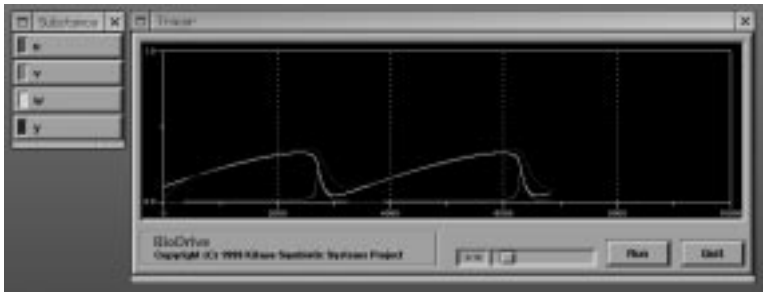

Figure 1: A snapshot of GUI. The right part is a Tracer Window and the left part is a Substance Window.

3 Results and Discussion

In order to demonstrate the usefulness of the simulator, we have tested Tyson's model [4] of cell cycle regulation resulting in the same issue (shown in Fig. 1).

We would like BioDrive to have a large number of features and facilities. The current version of BioDrive is able to simulate biochemical systems on deterministic modeling. However, since the stochastic modeling which can consider the kinetic reactions with small number of participating molecule is shown to be more reasonable than conventional deterministic modeling [5], BioDrive should allow several forms of stochastic simulations. In order to understand higher developmental processes such as morphogenesis, it is indispensable to develop a simulator for multi-cellular organisms which can describe not only biochemical reactions and gene expressions, but also protein diffusion, cell-cell interactions, and so forth. We are developing the extended version of BioDrive for multi-cellular organisms [6]. Besides, we are integrating parameter searching and optimization algorithms to avoid false data fits.

4 Conclusion

In this paper, we introduced a new simulator for single-cellular organisms, which satisfies the needs of serious biological investigations. BioDrive can compute biochemical reactions and gene expressions based on ODEs, and visualize the temporal patterning in a single cell. We are developing BioDrive to extend features and facilities to be more sophisticated version.

References

[1] Mendes, P., GEPASI: a software package for modelling the dynamics, steady states and control of biochemical and other systems, *Comput. Appl. Biosci.*, 9(5):563–571, 1993.

[2] 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*, 15(1):72–84, 1999.

[3] Schaff, J. and Loew, L.M., The virtual cell, *Pacific Symposium on Biocomputing 1999*, World Scientific, 228–239, 1999.

[4] Tyson, J.J., Modeling the cell division cycle: cdc2 and cyclin interactions, *Proc. Natl. Acad. Sci.*, 88:7328–7332, 1991.

[5] Arkin, A., Ross, J., and McAdams, H.H., Stochastic kinetic analysis of developmental pathway bifurcation in phage lambda-infeacted *Escherichia coli* cells, *Genetics*, 149(4):1633–1648, 1998.

[6] Kyoda, M. K., Muraki, M., and Kitano, H., Construction of a generalized simulator for multi-cellular organisms and its application to Smad signal transduction, *Pacific Symposium on Biocomputing 2000*, World Scientific, 2000, (to appear).