E-CELL Project Overview: Towards Integrative Simulation of Cellular Processes

Masaru Tomita [12]
mt@sfc.keio.ac.jp
Kenta Hashimoto [13]
kem@sfc.keio.ac.jp
Kouichi Takahashi [13]
shafi@sfc.keio.ac.jp
Yuri Matsuzaki [13]
yuri@sfc.keio.ac.jp
Ryo Matsushima [13]
ryo@sfc.keio.ac.jp
Kanako Saito [13]
t95401ks@sfc.keio.ac.jp
Katsuyuki Yugi [12]
t95980ky@sfc.keio.ac.jp
Fumihiko Miyoshi [12]
t95894fm@sfc.keio.ac.jp
Hisako Nakano [14]
s96649hn@sfc.keio.ac.jp
Sakura Tanida [12]
t94613st@sfc.keio.ac.jp
Thomas S. Shimizu [15]
tss26@cus.cam.ac.uk

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

1 Introduction

The E-CELL project [1] was launched in 1996 at Keio University in order to model and simulate various cellular processes with the ultimate goal of simulating the cell as a whole. The first version of the E-CELL simulation system, which is a generic software package for cell modeling, was completed in 1997. The E-CELL system enables us to model not only metabolic pathways but also other higher-order cellular processes such as protein synthesis and membrane transport within the same framework. These various processes can then be integrated into a single simulation model.

Using the E-CELL system, we have successfully constructed a virtual cell with 127 genes sufficient for "self-support". The gene set was selected from the genome of *Mycoplasma genitalium*, the organism having the smallest known genome. The set includes genes for transcription, translation, the glycolysis pathway for energy production, membrane transport, and the phospholipid biosynthesis pathway for membrane structure.

2 Ongoing Research

We are now in the second phase of the project, in which the following cellular processes are being modeled using the E-CELL system:

- Other metabolic pathways, including the TCA cycle, the pentose-phosphate cycle, and biosynthesis pathways for nucleotides and amino acids (Fig. 1).
- DNA replication and procaryotic cell cycle [2].
- Lambda phage gene regulatory network.
- Signal transduction for bacterial chemotaxis [3].
- Kinetic model of human red blood cell [4].

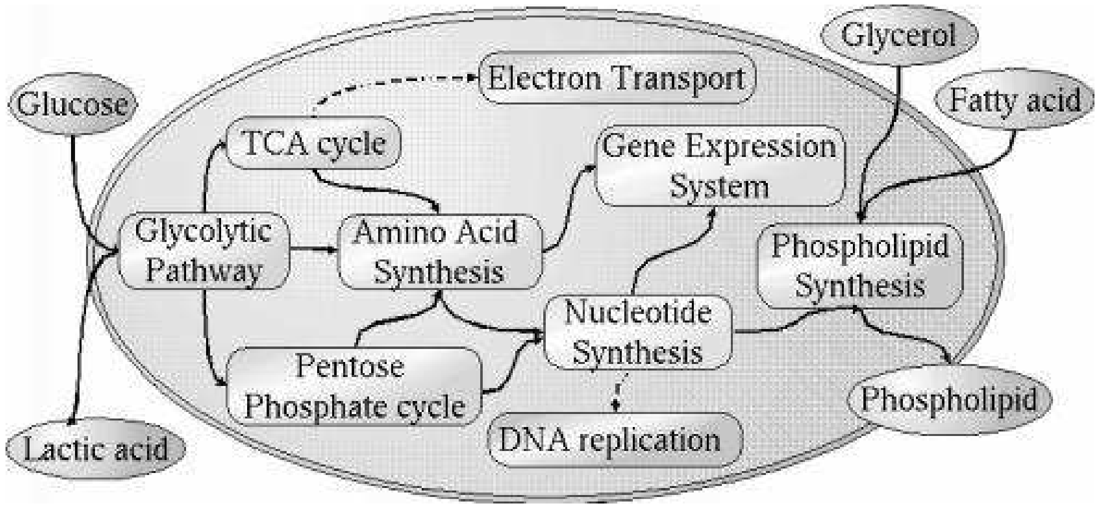

Figure 1: "Self-Supporting" Cell Model '98.

3 Concluding Remarks

Besides cell modeling work described above, the E-CELL simulation software itself is being improved in several important ways [5]. For example, reaction rules and substance definitions for simulation can now be written as a spread sheet table using any commercially or publicly available spread sheet software. Methodologies for time series analyses of metabolic network using the E-CELL system are also being developed [6]. The E-CELL system will be made available in early 1999 from our website.

Acknowledgements

We would like to thank Craig Venter and Clyde Hutchison for their support in an early stage of the E-CELL project. Doug Brutlag, Peter Karp and Nobuyoshi Shimizu also gave us useful comments at the beginning of the project. The E-CELL project is funded in part by a Grant-in-Aid for Scientific Research on Priority Areas from the Ministry of Education, Science, Sports and Culture of Japan.

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).

[2] Hashimoto, K. *et al.*, Modeling of transcription, translation and DNA replication using the E-CELL simulation system, *Genome Informatics 1998*, Universal Academy Press, 1998.

[3] Matsuzaki, Y. *et al.*, Modeling of the signal transduction for bacterial chemotaxis using the E-CELL simulation system, *Genome Informatics 1998*, Universal Academy Press, 1998.

[4] Matsushima, R. *et al.*, Modeling of human red blood cell using the E-CELL simulation system, *Genome Informatics 1998*, Universal Academy Press, 1998.

[5] Takahashi, K. *et al.*, Modeling theory and software architecture of the E-CELL simulation system, *Genome Informatics 1998*, Universal Academy Press, 1998.

[6] Saito, H. *et al.*, Multivariate time series analysis of metabolic network using the E-CELL simulation system, *Genome Informatics 1998*, Universal Academy Press, 1998.