

# Parameter Estimation Mechanism of E-CELL Simulation Environment

Yusuke Saito<sup>13</sup>

t96406ys@sfc.keio.ac.jp

Kouichi Takahashi<sup>12</sup>

shafi@sfc.keio.ac.jp

Tomoharu Iwata<sup>13</sup>

t97117ti@sfc.keio.ac.jp

Tomohiko Aikawa<sup>13</sup>

t97001ta@sfc.keio.ac.jp

Masaru Tomita<sup>13</sup>

mt@sfc.keio.ac.jp

<sup>1</sup> Laboratory for Bioinformatics

<sup>2</sup> Graduate School of Media and Governance

<sup>3</sup> Department of Environmental Information

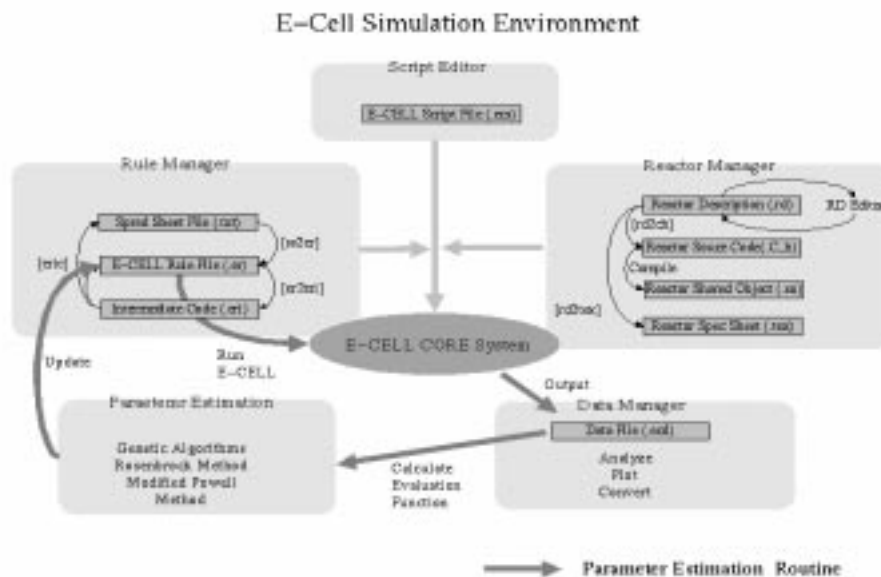
Keio University, 5322 Endo, Fujisawa 252-8520, Japan

## 1 Introduction

We have been developing the E-CELL simulation environment for whole cell scale modeling, simulation and analysis of biochemical reaction network [2]. The E-CELL simulation environment consists of several software components such as E-CELL Core System, E-CELL Manager, the rule file compilers, and various data converters/processors. The whole process of rule writing, simulation, and analysis is managed by E-CELL Manager.

In order to make it possible to conduct whole cell scale simulation in reasonable fidelity, a complete set of parameter values for kinetic equations would be required. In reality, however, not all the parameter values are usually known.

The E-CELL simulation environment can also be utilized as a framework of parameter estimation, time series analysis and other means of analysis of whole cell system.



## 2 Parameter estimation mechanism

Parameter estimation can be viewed as searching minimum of a certain evaluation function, which we define square sum of difference between experiment value and calculation value as the following formula:

$$F = \sum_{i=1}^N \sum_{j=1}^n \left( \frac{x_{cal,i,j} - x_{exp,i,j}}{x_{exp,i,j}} \right)^2$$

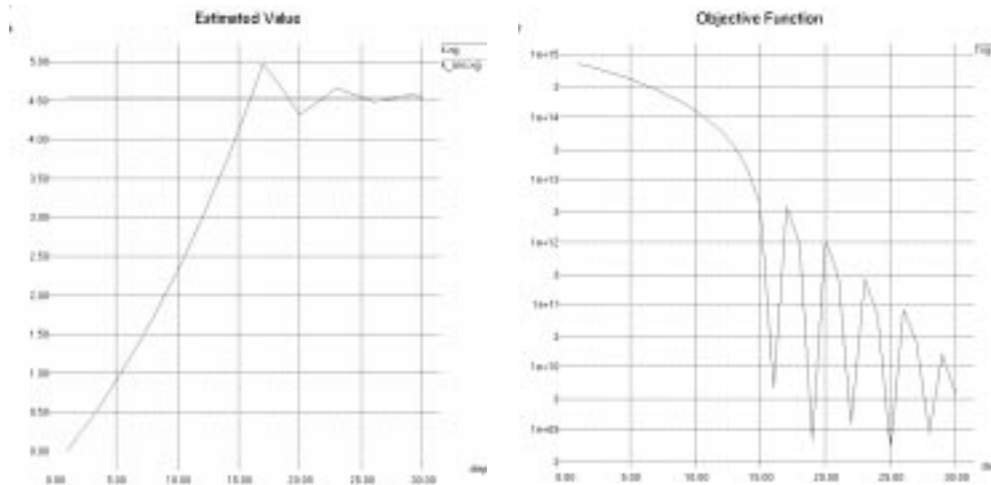
where  $N$  is the number of sampling points,  $n$  is the number of variables,  $X_{cal}$  is calculation value, and  $X_{exp}$  is experiment value.

The evaluation function can also be steadiness of the time series. In this way, a set of parameters which leads the cell model to a steady state can be obtained.

Three optimization methods (the Rosenbrock method, the Modified Powell method and Genetic Algorithm) are provided as software modules of E-CELL simulation environment and called by E-CELL Manager.

### 3 Sample Run

We adopted the erythrocyte model as a sample case of parameter estimation. This model has 41 enzymatic reactions and 60 intermediate metabolites (Nakayama *et al.* [1]). We masked the equilibrium constant (Keq) of the reaction catalyzed by Enolase, which is one of the enzymes in the glycolysis pathway. The following figures show successful convergence of estimated value of Keq and value of the evaluation function.



### 4 Concluding Remarks

This work is the first step towards large-scale parameter estimation, which we believe is one of the most important key technologies for cell simulation.

### Acknowledgments

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### References

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