E-CELL: Software Environment for Whole Cell Simulation and Analysis

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1 Introduction

E-CELL is a generic software package we have developed for whole cell modeling and simulation. Given a set of substance definitions and reaction rules, the E-CELL System (Fig. 1) simulates those reactions by pseudo-parallel computation of each reaction rule. The user can then observe dynamic changes in quantities of the substances and activities of the reactions through graphical user interfaces. The user can also alter these quantities interactively, making it possible to conduct "virtual experiments".

The system is based on Structured Substance-Reactor model, which consists of three classes of objects, Substances, Reactors, and Systems, which represent molecular species, reactions, and functional and/or physical compartments, respectively.

The E-CELL simulation environment consists of several software Components; the E-CELL Core System, E-CELL Manager, rule file compilers, and various data converters/processors. The E-CELL simulation environment can also be utilized as a framework for parameter estimation, and for other methods of mathematical analysis such as time series analys is and metabolic control analysis.

2 Parameter Estimation Mechanism

Parameter estimation can be viewed as the searching minimum of a certain evaluation function, which we define as the square sum of the difference between the experimental value and the calculated value. The Modified Powell method and the Genetic Algorithm are provided as software modules of the E-CELL simulation environment.

3 Mathematical Analysis

3.1 Time series analysis

Impulse-response is employed to analyze the cell system constructed in the E-CELL simulation environment. Information about (a) difference in time between reactions in a metabolic pathway, (b)

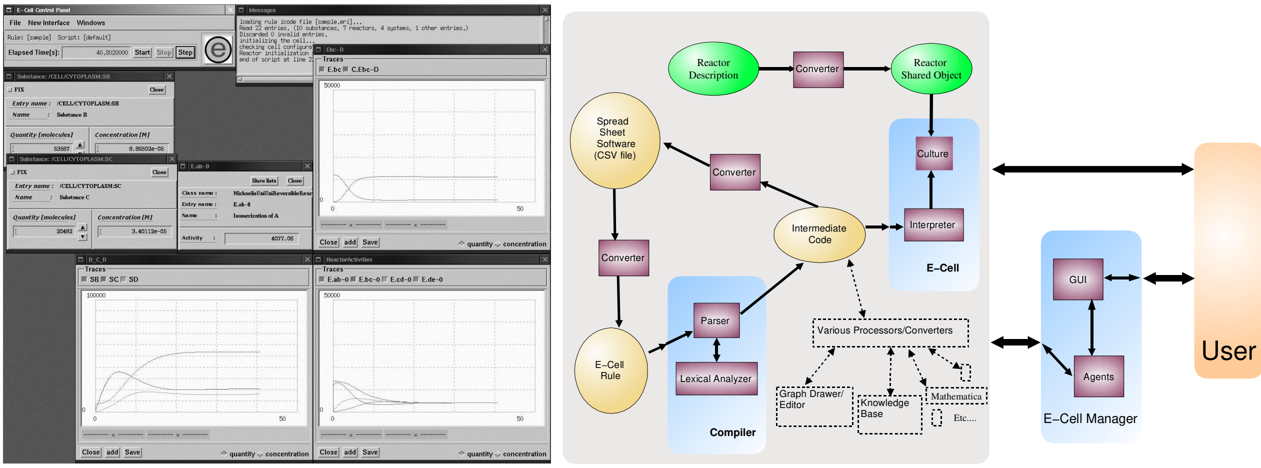

Figure 1: E-Cell Simulation Environment

dependencies among the reactions, and (c) other characteristics of the transfer function between the reactions, can be obtained from an impulse response.

The multivariate auto regressive (AR) model is applied to analyze the oscillating time series. In particular, we employed the power contribution ratio, which is an index of how fluctuation of one variable depends on the other variables at each frequency.

3.2 Metabolic control analysis

Among many approaches to Metabolic Control Theory, the structural approach, which utilizes linear algebra, was selected for its convenience in obtaining elasticity, the control coefficient, and additional characteristic properties.

The goal of this analysis is to describe the inter-dependency among simulation objects as a matrix; a Jacobian, control coefficient matrix.

Connectivity of the system and the condition of the steady state can be obtained from the elasticities and the control coefficients.

4 Software Availability

As of December, 1999 the second beta package of E-CELL , version 0.9b, is available on http://www.e-cell.org. Version 1.0 of the package, which is distributed with a source code, will be made available in early 2000.

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