Bio-calculus: Its Concept, and an Application for Molecular Interaction

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1 Concept of *Bio-calculus*

There is a big gap between biology and computer science when they communicate to investigate biological phenomena. One of the problems is the difference between their expression systems. The expressions of biology clarify the components (e.g. gene, protein, and cells). Their transition and interaction (e.g. gene activation, protein phosphorylation and cell division) are diagramed. In many cases, mathematical models for these processes are not defined in biology. Thus, expressions of biology lack information essential for simulation analysis (e.g. the velocity of a process, the quantity of a component) and do not have background of essential for simulation since simulation is one of the main analytical methods in this field. The expressions also have mathematical background (e.g. calculus and probabilistic arguments).

Expressions of computer science are designed to include information since system analysis is another important method. Several expression systems have been proposed for expressing biological phenomena (e.g. differential equation [1, 2], stochastic method [3], and stochastic differential equation method [4]). In these systems, components of biological systems are mingled with mathematical symbolism. Transition and interaction of the components are far less visualized than in the diagramed expressions of biology. This is a critical weak point for biology since the components and their transition/communication are the main targets of biology. To bridge the gap between biology and computer science we have started to develop *bio-calculus* [5].

We reported the concept of *bio-calculus* [5]. *Bio-calculus* is an expression system that fulfills the following four requirements, which we think are necessary for the intended expression systems. 1) the description of bio-calculus clarifies the components of biological systems. 2) the description diagrams transition and communication of the components. 3) the description includes information essential for simulation analysis. 4) the description possesses background of mathematics.

The distinguished feature of *bio-calculus* is *multi-semantics*, where a syntax corresponds to several different semantics. *Bio-calculus* consists of *bio-syntax* and *bio-semantics-set*. *Bio-syntax* is the syntax of this calculus. The arrangement of *bio-syntax* is specifically designed to fulfill the requirements 1 and 2. *Bio-semantics-set* is a set of various kinds of *bio-semantics*. One of these *bio-semantics* is selected and applied to a *bio-syntax*. Thus, the semantics of a *bio-syntax* varies depending on the selected *bio-semantics*. This *syntax-semantics* relationship is necessary to fulfill the requirement 3 -

since almost all biological phenomena are far from completely understood, any phenomena will be explained by several simulation models and we cannot establish the single absolute model for any phenomenon. Each *bio-syntax* contains a special term *Semantics-ID*, which specifies a *bio-semantics* to the *bio-syntax*. To fulfill the requirement 4, *bio-calculus* is defined in the form of *bio-calculus*.

For the first step of the development of *bio-calculus*, we defined *bio-calculus* for molecular interaction [5]. Several important advantages of *bio-calculus* were discussed with simple examples [5].

2 Application for *Bio-calculus*

Based on the definition of *bio-calculus* for molecular interaction, we made an application for *bio-calculus*. This simulator has two graphic user interface, *Definition Window* and *Analysis Window*. In Definition Window (see Fig. 1(a)), users write a description of *bio-calculus*. In Analysis Window (see Fig. 1(b)-(c)), the value of each molecule is visualized at each time point. The syntax-semantics relationship of *bio-calculus* is faithfully realized in this simulator. In brief, a description of *bio-calculus* can be executed under several *bio-semantics* only by exchanging *semantics-IDs*. If some information is required for the exchange, the simulator notifies the required information. A model of *Xenopus* cell cycle [2] was translated into a description of *bio-calculus* and executed in this simulator.

(a) (b) (c)

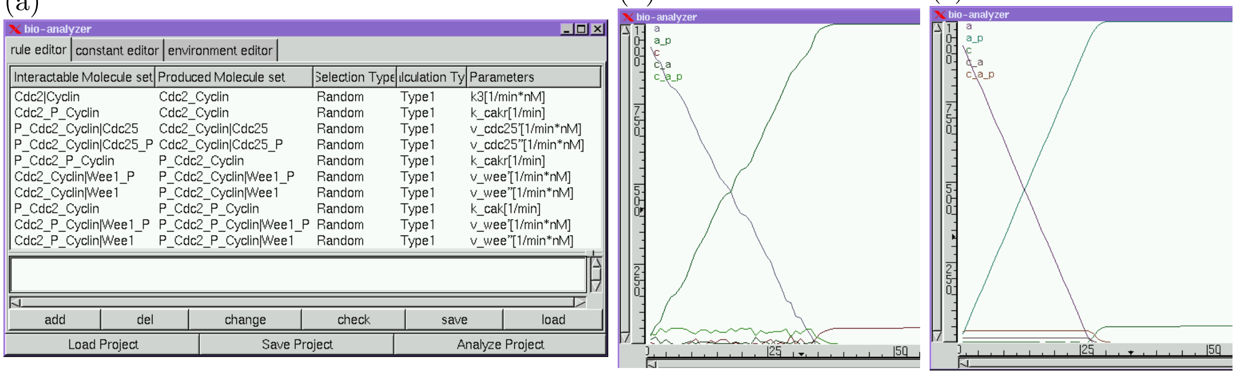

Figure 1: (a) Definition Window. Interaction rules in the window are translated from differential equations that are used in Marlovits et al. [2] for modeling the cell-cycle in *Xenopus* embryo. Some rules are shown for saving the space. (b)-(c) Analysis Window. In (b), *bio-calculus* description of Micaelis-Mentens equations are executed under Semantics1 - differential equation based semantics. In (c), the same *bio-calculus* description as (b) is executed under Semantics2 - stochastic equation based semantics.

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