2008－MPS－68 (37)
2008／3／6

A Note on a Mathematical Model for Computational Moleware Communications Based on Molecular Motors

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分子モーターに基づく計算的なモレウェア・コミュニケーションのための数学モデルについて

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Abstract A mathematical model for moleware communications is proposed in terms of theories of computer science to formulate the information processing mechanism of signaling pathways related to kinases and molecular motors.

概要 モレウェア・コミュニケーションのための数学モデルを提案するし、計算機科学の方法によってキナーゼ・シグナリング・パスウェイと分子モーターにおける情報処理メカニズムを定式化される。

***1. Introduction**: Molecular Motors as Moleware Engines*

With its biological functions on filament movement, cytoskeleton, microtubule and chromosome dynamics, the molecular mechanism of motor proteins may also provide us some hint of explanation on the movement phenomena of biological systems at the molecular level. Research and development on molecular motors cover analysis, simulation, synthesis and applications in biosensor and actuator.

Motor proteins are classified into three major categories: dynein, kinesin and myosin [1]. To understand the mechanics features of molecular motors, we need the biochemistry knowledge on motor proteins. The building block of motor protein in architecture are heavy chain, intermediate chain and light chain – three kinds of molecular structure found in motor proteins. Here "heavy", "intermediate" and "light" come from that the corresponding chains with different number of molecules correspond to different weights. On its molecular structure in a form of molecular complex, a motor protein consists of three parts called head, arm, and tail, in which the head is for generating force. The microtubule and actin (actin filament) are the rails for molecular motors. Actin filaments and microtubules are protein polymers. On an intuitive concept, a microtubule is a tube constructed by tubulins. The biophysics and biochemistry features of molecular motors are the basis for analyzing the biological functions of

(1) cell division, chromosome dynamics, and centrosome movement;
(2) cytoskeleton and cytokinesis;
(3) the processes of transporting cargo molecule and vesicular transportation in cells.

The motor-proteins and "rails" are two major aspects of the movement of molecular motors. Kinesin and dynein "walk" on microtubule; myosin "walks" on actin. The energy feeding process is made by the ATP hydrolysis process.

The motor protein has two directions where the trail is regarded as the reference. The microtubule dynamics is reflected on the polymerization and depolymerization process. The molecular movement is influenced by the two states of polymerization and depolymerization process. The tubulin also has two states. A molecular motor "running" on a surface is a vivid "image" for us to understand its mechanics behavior [1]. One of the promising applications of molecular motors is expected in nano-medicine, e.g., molecular drug

delivery systems.

In biomolecular information processing, molecules can be used to represent information. It is necessary to design the operators to update the states of the biomolecular information processing systems. Among nanomachines, the molecular motor is one of the most important medium considering its feasibility in engineering. Communications are expected to be realized by the molecular motors that carry the cargo molecules. Some cargo molecules can be used to encode the messages. Here, moleware communication refers to the computational study on the communication processes in terms of information theory where the signaling molecules in cells such as kinases, phosphates, the proteins with the state of phosphorylation or dephosphorylation are used for designing codes and the phosphorylation/dephosphorylation pathways are the tools for the corresponding encoding/decoding processes. The model of moleware communication derived here is called *Computational Moleware Communication based on Molecular Motors* (CMCMM for short), which will be formalized in next section.

2. The Mathematics Model

According to the informatics characteristics of the molecular signaling process of CMCMM model presented in section 1, we adopt the automata [2] form – a deterministic finite automaton or automata -- to formulate it. The notations are defined as follows:

- Q – a finite set of states. The state of the molecular information processing system we will discuss here is denoted as $Q = \{q(t)\}$ where $q(t)$ refers to the string made by the molecules at the time t in this system.
- Σ– a finite set of input symbols. The symbols denote the molecules.
- δ – a transition function that is described as the rule

  IF ((input symbol in Σ) AND
  (current state in Q))
  THEN {next state in Σ}.

- q_0 – the starting state that belongs to the set Q.
- F – the set of the final states that is a subset of Q.

The automata model is denoted by

$$A = (Q, \Sigma, \delta, q_0, F).$$

The corresponding information processing mechanisms formulated by automata here are limited to molecular motors and kinase pathways.

The "primitive" form is defined to describe the logical process of the CMCMM model. In terms of logical description of the information processing, an abstract model designed in terms of mathematics is proposed as follows.

At first, let the logical operator for the movement of a molecular motor be

$$move\ (x, y, m) \tag{1}$$

where x and y refer to the starting point and destination while m refers to the index of the molecular motor. The signaling pathways located at location x and y are defined as $F(x)$ and $G(y)$, respectively. The concentrations of the "effector" of these two pathways are denoted as $f(x)$ and $g(y)$, respectively. Assumed that the output of the pathway $F(x)$ activates the molecular motor m and the molecular motor m activates $G(y)$ as well. Then we have that

$$\begin{aligned} & F(x) \text{ -}>^{s} f(x) \\ \Rightarrow\ & move(x, y, m) \\ \Rightarrow\ & G(y) \text{-}>^{s} g(y) \end{aligned} \tag{2}$$

where "->^{s}" and "=>" denote the pathway signaling process and casual relation between a pathway and a molecular motor, respectively. Equivalently, we have that

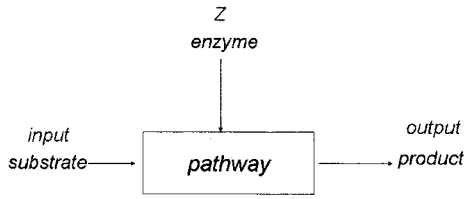
$$f(x) \text{ --> } g(x)$$

i.e.,

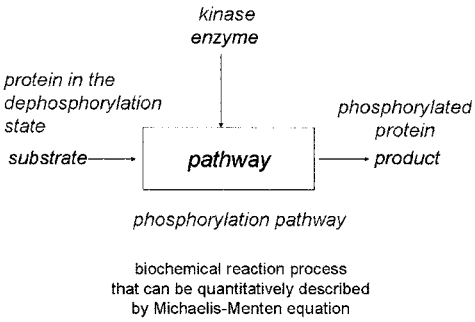
$$f(x, t_1) \rightarrow g(y, t_2) \tag{3}$$

where t_1 and t_2 denotes the time before and after the movement of the molecular motor. The notations "-->" and "→" in (3) refer to the equivalent process in (2). It is a promising idea to study the possibility of integrating the cellular pathways and molecular motors [3, 4]. The informatics aspect of cellular signaling pathways (signal transduction [5]), provides hints on innovating a new information processing paradigm, inspired by signaling pathways in cells [6-8], especially on an abstract model in mathematics for

information processing inspired by cellular pathways.



(a) Abstract concept of a pathway



(b) Comparison of an abstract concept and the biochemistry terms

Figure 1 Representation of a pathway

In Fig. 1, let the input be the substrate and the output be the product of the pathway. The data structure of the related information processing unit is a directed graph. In order to study the performance of the information processing model, the corresponding quantitative calculation is necessary. When we apply the Michaelis-Menten equation [9] in the phosphorylation process, we have that

$$product(n+1)\text{-}product(n) = k_3 * enzyme * substrate(n)/(substrate(n)+k_m) \quad (4)$$

$$substrate(n+1)\text{-}substrate(n) = k_3 * enzyme * substrate(n)/(substrate(n)+k_m) \quad (5)$$

Through the states of phosphorylation and dephosphorylation, the binary codes can be designed for a mathematics model for describing the information in the kinase/phosphatase pathways.

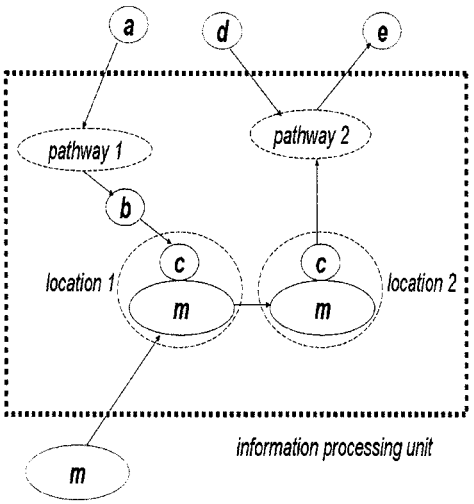


Figure 2 Example of CMCMM

On the formulation of the transition process of the automata model, an example is given as follows:

state (0)
a (the input to pathway 1)
d (the input to pathway 2)

state (1)
b (the output of pathway 1)
d (the input to pathway 2)

state (2)
c (location 1), *m* (location 1)
d (the input to pathway 2)

state (3)
c (location 2) *m* (location 2)
d (the input to pathway 2)

state (4)
e (the output of pathway 2)

The input *m* in state (2) is also the input to the entire unit

$$\{a, d\} \times m \rightarrow e, \quad \text{i.e., } a\ \theta\ d \rightarrow e, \quad (6)$$

where θ refers to an operator. The notation "->" refers to the corresponding signaling process.
The pathways involved in the above processes are denoted as follows:
(i) pathway 1 (a, b),
(ii) pathway 2 ($\{c, d\}$, e),
(iii) molecular motor m.
The information processing unit is shown in Figure 2.

A generalized rule is defined as follows:

$$z_1 z_2 \rightarrow^{r} z_3$$

in a deterministic finite automaton *DFA(i)* defined above, *(7)*

where $i = 0, 1, \ldots, n\text{-}1 (n \in N)$; "$\rightarrow^{r}$" refers to the string-rewriting operator.

If molecular motors $m_0, m_1, \ldots, m_{n-1}$ are used to activate the pathways indexed as 0, 1, ..., n-1 in *DFA(0)*, *DFA(1)*, ..., *DFA(n-1)*, the following string rewriting process can be derived as

$$S_0 S_1 \ldots S_{n-1} \rightarrow^{r} S'_0 S'_1 \ldots S'_{n-1} \quad (8)$$

where the set of $\{S_0, S_1, \ldots, S_{n-1}\}$ and $\{S'_0, S'_1, \ldots, S'_{n-1}\}$ refer to the states of the system before and after the operations of the molecular motors; If the state of S'_0 consists two symbols a and b (molecules), we can get that

$$S_0 S_1 \ldots S_{n-1} \rightarrow^{r} ab S'_1 \ldots S'_{n-1}, \quad (9)$$

Let $A = S_0 S_1 \ldots S_n$, $B = bS'_1 \ldots S'_n$, then it is inferred that

$$A \rightarrow^{g} a B \quad (10)$$

where $\rightarrow^{g}$ refers to the operation "$\rightarrow$" in the definition of formal languages.
If $S'_0, S'_1, \ldots$, and S'_n are the same and denoted as a, it is inferred that

$$A \rightarrow^{g} a. \quad (11)$$

According to the definition of regular language

$$A \rightarrow^{g} a B \text{ or } A \rightarrow^{g} a. \quad (12)$$

where A and B are string and a is a letter in the alphabet set, it is possible to generate the set of a regular language by the above-mentioned model.

3. Conclusion

We have formulated the molecular information processing mechanism by a mathematics model and inferred that it is possible to generate the regular language set by the proposed mathematics model.

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