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Journal of Advances in Artificial Life Robotics
Vol. 1(2); September (2020), pp. 56–59
ON LINE ISSN 2435-8061; ISSN-L 2435-8061
https://alife-robotics.org/jallr.html

Research Article

Modeling and Simulation of Molecular Artificial Intelligence with DNA computing by using Abstract Rewriting System on Multisets

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ARTICLE INFO

Article History
Received 25 November 2019
Accepted 19 July 2020

Keywords
Molecular artificial intelligence
DNA computing
Bio-chemical logic gate
The seesaw gate reaction

ABSTRACT
We have bio-chemically realized Artificial Intelligence by using DNA reactions, which is composed of a well-known as oscillating DNA reactions, the seesaw gate reaction. Through biochemical experiments, we confirm that mismatched interact-able DNA sequences can adapt to perturbations of environmental change, which is caused by making point mutation in an input sequence. Based on this result, we model this reaction by using abstract chemistry and confirm that the model exhibits the same behavior as biochemical experiments. Through computational simulations show that this DNA reaction can compose the logic gate bio-chemically.

1. Introduction

Research on DNA computing has evolved into research on Molecular Robots[1]. Recent vast advances in computing power, artificial intelligence, AI researches are progressing and expanding rapidly. Shortly, AI research will develop into molecular AI and merge with molecular robots. From various challenges in AI researches, we aim to compose an adaptive system. An adaptive system is a system, which can change behaviors in response to the change of environment; adaptiveness has been an essential subject Robotics in general [2].

In this paper, we model an adaptive system by using the Toehold Strand Displacement Reaction, which has commonly used in DNA computing [3]; simulate the model by using the Abstract Rewriting System on Multisets, ARMS [4],[5],[7],[8]. ARMS is a physiochemically strict hybrid computational model, which integrates the discrete and continuous mathematical model

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1.1 *Self-sustained Chemical Reaction Networks, CRN*

In this research, we use a simple self-sustaining Chemical Reaction Network, CRN [6];

$$A + B \rightarrow C + D, \quad (1)$$
$$C + E \rightarrow A + F. \quad (2)$$

CRN and its dynamics have studied in Chemistry and Physics since innovation of the low of mass action[6]. In this CRN, we assume that the concentrations of B and E are sufficient and D and E flow out immediately, so the concentration of A to be sustained.

This CRN describes the seesaw gate reaction by using Toehold mediated Strand Displacement Reaction, TMSD, which has commonly used in DNA computing.

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1.2. *Seesaw gate reaction by Toehold mediated Strand Displacement Reaction, TMSD*

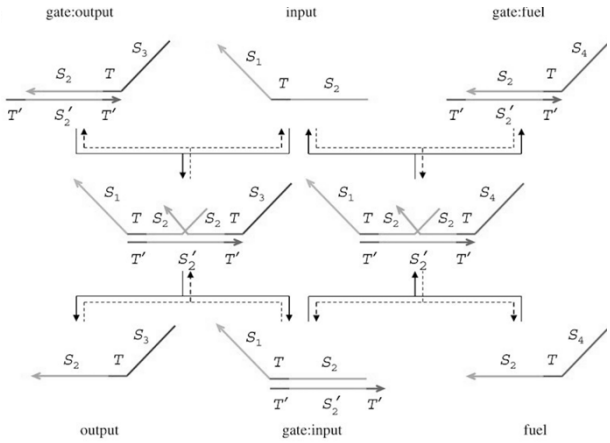

Fig. 1. Seesaw Gate Reaction; from the Journal of the Royal Society Interface, 2011[3] (distributed under the terms of the Creative Commons Attribution License)

Toehold mediated Strand Displacement Reaction, TMSD is a reaction between a double-strand DNA and single-strand DNA (Fig.1), in which a strand in a double-stranded DNA is replaced with the same or nearly identical single-strand DNA. DNA strand displacement reaction is composed of the three single strands named the 'invader','incumbent' and the 'substrate'; this reaction is a swapping reaction between the invader and the incumbent strands on the substrate strand. The invader corresponds to an input signal, while the incumbent corresponds to an output signal. Toehold Exchange Reaction TER, which is known as a class of strand displacements, since this reaction allows sequence-dependent control, it is peculiarly useful. In TMSD, the shorter incumbent forms a partial duplex with the more extended, complementary substrate; then, the invader hybridizes with the toehold, which is the unbound region of the partially duplexed complement.

1.3. *Multiset Rewriting System on Multisets, ARMS*

We have proposed a CRN, based on Abstract Rewriting Systems, ARS; the ARS is a theoretical model of computation; we expand ARS on the multiset as Abstract Rewriting system on Multisets. A multiset is defined as a simple set and a map, which returns the duplication of an element. A denotes for the set of alphabets, and every element of ARMS is an element of A. We denote duplication (multiplicity) the element as M(a), $a \in A$. For example, M (a) and M (b) of {a, a, b, b} are 2, and M (c) = 0. In this paper we describe a multiset explicitly or a vector $w = (M(a_1), M(a_2) \ldots M(a_n))$. The union of two multisets M_1, M_2 is the addition of vectors w_1 and w_2; the inclusion of M_1, M_2 is $M_1(a_i) \leq M_2(a_i)$ for all $a_i \in A$. We denote A# as a set of all combinations of multisets over A including an empty multiset.

A reaction rule $l \rightarrow r$, $l, r \in A\#$ is a pair of a multiset and a reaction vector $w_r = -l + r$. A reaction (rewriting) calculation is defined as $w_{i+1} = r + w_i$, where i denotes the step time of the multiset. For example, an ARMS with a reaction rule a, b → a, c; since $l = (1, 1, 0)$ and $r = (1, 0, 1)$, $w_r = -(1, 1, 0) + (1, 0, 1) = (0, -1, 1)$ and in case $w_i = (1,1,1)$, $w_{i+1} = (1,1,1) + (0, -1, 1) = (1, 0, 2)$; which denote the reaction calculation of from {a, b, c} to {a, c, c} by a, b → a, c.

2. Model

In the seesaw gate reaction, first, TMSD occurs between the single-strand DNA named 'input', and the double-strand DNA named 'gate:output' then single-strand DNA named the 'output' strand and the double-strand DNA named "input:gate" are produced. In the CRN, it is described as A + B → C + D, where A stands for input, B, gate:output, C, input:gate and D, output. Since input:gate reveals a scaffold (T) for interaction with the single-stranded DNA named 'fuel ', SDR occurs next between fuel and input:gate, then the input and gate:fuel are produced, it is described as C + E → A + F ; where C stands for input:gate, E, fuel strand, and F, gate:fuel. In this reaction these two reactions occur like a seesaw, while input strand consumed in the first reaction and supplied in the second reaction.

2.1. *Environment Change by giving a point mutation in the input strand*

To change the environment of CRN, we give a point mutation in the input strand; input' stands for mutated input strand. We confirmed that even if a point mutation occurred in input strand, several mutated input strands can bind and form mismatched pair with gate:output through biochemical experiments [9]. The self-sustaining CRN with non-mutated input strand is described as;

input + gate:output ↔ input:gate + output (1),

input:gate + fuel ↔ input + gate:fuel (2).

While, the CRN with the mutated input strand, input':

input' + gate:output ↔ input':gate + output (3),

input':gate + fuel ↔ input' + gate:fuel (4).

Since the binding force of mismatch strands pair is weaker than non-mismatch one; we express it by changing reaction speed to the reaction speed of the mismatched pair is slower than non-mismatched one.

3. Method

In the CRN, the rate constants for the forward and reverse reactions are the same; the rate constant for the mutated input strand is 100 times slower than the non-mutated input strand.

4. Result

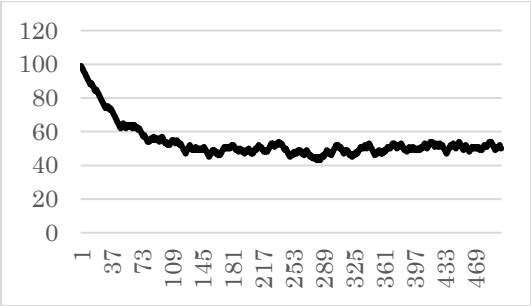

Fig. 2. Time change of the number of input strands. The horizontal axis of the graph is the number of steps (one reaction is one step), and the vertical axis is the number of input strands; because of the structure of reaction rule is the same, the time change of the amount of input's strands are equivalent.

When there is either input or input' strand, the reaction reaches an equilibrium state (Fig.2). In the case when input and input' strands coexist, if both concentrations are the same since the reaction speed of the input strand is 100 times faster than the input' strand, the input' strand rarely to react. In the case when the concentration of the input' strand is 100 times larger than the input strand, the input' strand mainly to react. These results of simulations show the CRN can adapt to environmental change; if the concentration of non-mutated strand is smaller than the muted one, the reaction system selects it and can sustain reactions (Fig.3).

5. Discussion

The simulation results show that when the amount of input strands is half to the number of input' strands, the concentrations of both become the same in the equilibrium state, and the equilibrium state shifts by

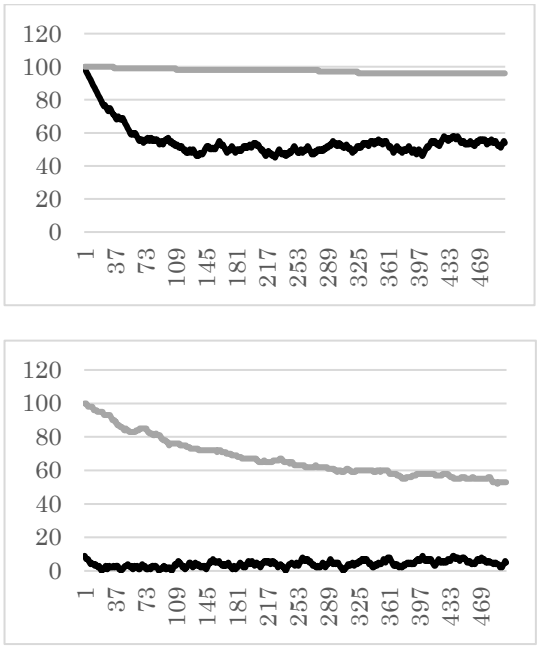

Fig.3. (Top) Time change of the number of the input and input' strands. When the same amount of the input and input' strand, the input' strand does not react. (Bottom) When the number of the input' strand is significant if the amount the input' strand is 100 times larger, the reaction system will use the input' strand.

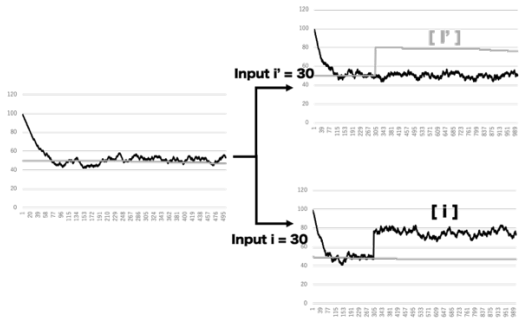

Fig. 4. The bit shift operation by adding the strands. by adding the 30 of the input strands [i] or input' strand the equilibrium state shifts from around 50 to 80.

adding input or input' strands. By using this characteristic, we can express a basic unit of information, a bit. We set the value of a bit to 0 when the number of the input or input strand is approximately 50, which is an equilibrium state. By adding input strands into the system, the equilibrium state shifts; in this simulation, we add 30 strands, then the equilibrium state shifts from 50 to around 80 (Fig.4). We define the value of a bit as 1 for this shifted equilibrium state. In the case when the bit of input is 1, if we remove 30 strands of input strands then

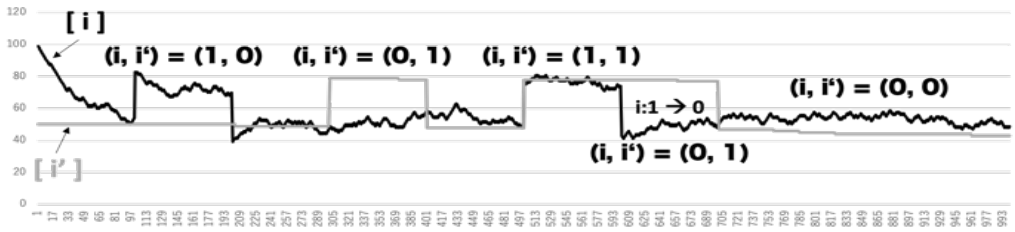

Fig. 5. 2-bit register using the CRN. The value of the bit is 0 when the number of the strand is around 50, while 1 for approximately 80. [i], [i] stands for the number of input, input' strand respectively.

the equilibrium state shift from 80 to 50 and the value of the bit return from 1 to 0; this operation of bit is the same when input' strands are used (Fig.4).

We confirmed that by adding or removing 30 strands, a two-bit register can realize by using this CRN (Fig.5). For Biochemical implementation, removing strands will be able to realize by adding double-strand DNA, which is named as 'threshold'[3] (Fig.6).

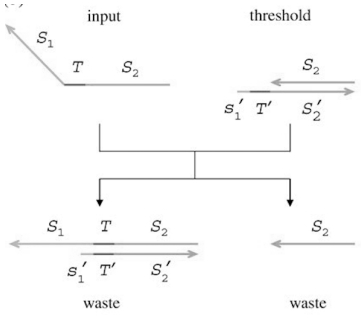

Fig. 6. The threshold; from the Journal of the Royal Society Interface, 20113 (distributed under the terms of the Creative Commons Attribution License)

Biochemical implementation of DNA circuits by using this two-bit register is our future work. The speed of computation of DNA logic circuits [5] often need hours to compute and complicated reactions, through our biochemical experiments of this model, transient time to equilibrium state is around half-hour [6] and reactions are simple compared with other models e.g. [6].

Since this his two-bit register holds information as dynamic equilibrium states, is suitable for constructing artificial intelligence of molecular robots because brain activities such as attention can be regarded as a dynamic equilibrium state[9].

References

1. S. Yusuke, Y. Hiratsuka, I. Kawamata, S. Murata and S. M. Nomura. "Micrometer-sized molecular robot changes its shape in response to signal molecules." *Science Robotics* 2 (2017).
2. Ziemke, T., & Sharkey, N. E. (2001). A stroll through the worlds of robots and animals: Applying Jakob von Uexkülls theory of meaning to adaptive robots and artificial life, *Semiotica*, *2001*(134), 701-746.
3. L. Qian, E. Winfree, A simple DNA gate motif for synthesizing large-scale circuits, Journal of the Royal Society Interface, Vol. 8, 2011.
4. M. Umeki and Y. Suzuki, A Simple Membrane Computing Method for Simulating Bio-Chemical Reactions, Computer and Informatics, 27, 529-550, 2008.
5. Wegscheider, R. (1901) Über simultane Gleichgewichte und die Beziehungen zwischen Thermodynamik und Reactionskinetik homogener Systeme, Monatshefte für Chemie / Chemical Monthly 32(8), 849--906.
6. Y. Suzuki, Emergence of Adaptive behavior in simulations by using Abstract Rewriting System on Multisets, ICAROB, 2020.
7. Song T, Eshra A, Shah S, et al. Fast and compact DNA logic circuits based on single-stranded gates using strand-displacing polymerase. Nat Nanotechnol. 2019;14(11):1075-1081. doi:10.1038/s41565-019-0544-5
8. Y. Suzuki and R. Taniguchi, Toward Artificial Intelligence by using DNA molecules, Journal of Networking and Artificial Life, 5(2), pp128-130, 2018, Atlantis Press
9. Lajoie Y, Teasdale N, Bard C, Fleury M. Attentional demands for static and dynamic equilibrium. Exp Brain Res. 1993;97(1):139-144. doi:10.1007/BF00228824

Authors Introduction

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He is an Associate Professor of Graduate School of Informatics, Nagoya University Japan. graduated from Japan Advanced Institute of Science and Technology in 1995, received Doctor degree of Informatics from Kyoto University in 2001.