Molecular Artificial Intelligence by using DNA reactions

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Abstract

We have developed molecular Artificial Intelligence system by using DNA molecules, where "intelligence" means that the reaction system can "select" DNA molecules to sustain their reactions. We have bio-chemically implemented the reaction system by using the DNA strand-displacement reaction and have obtained several mutated DNA sequences that can sustain the reactions. We confirmed that when we give non-mutated input and mutated input sequences (the system can also use them as input), the system is able to select higher concentration one, regardless of it having mutation or not. And we confirmed that reaction behaviors in the time series of concentration of non-mutated input and mutated input show oscillations; it would show that the system selects higher concentration one in between non-mutated and mutated one according to its concentration. Since the system exhibits adaptive autonomous behaviors, this DNA reaction networks system realize molecular Artificial Intelligence.

Keywords: Molecular Robotics, Molecular Artificial Intelligence, DNA computing, Seesaw gate

1. Introduction

The aim of this contribution is composing *molecular artificial intelligence, molecular AI* for molecular robots that are made by organic materials such as DNA or proteins.

It has been developed *bio-computers*; various bio-computers with natural media such as DNA, slime molds have been realized; and many kinds of *parts* to synthesize a bio-computer, by using mainly DNA, such as logic gates or circuits have been produced. Based on these progresses, molecular robots have been created.

On the definition of intelligence has been discussed not only in AI but also in philosophy and there have proposed many standpoints and definitions from each of them. We will take the standpoint proposed by *Kazuhisa Todayama* [1] and *Ruth Millican* [2]; in order let *systems* to be *autonomous* likewise a living systems, (there are several requirements that they proposed but) one main requirement is having problems to take care of themselves; such problems are affordable from its environment including us; for example, an electric robot needs electric power supply, in the most of cases, users of the robot (environment) take care of and recharge it or pre-programmed in the robot to go to recharge place themselves, such as a *clean robot* [3].

Their claim is that in order let the robot to be autonomous, we should give only minimal *settings* to adapt its environment; it almost impossible to give such a perfect minimal setting so Millican claims that evolution mechanisms are irreducible to refine the minimal settings by evolutional searching with *mutations* and *natural selections* [2].

On this standpoint, we reconsider *what is intelligence of living systems?*; living systems in wild life must select appropriate food sources from the environment; even if *parents* do not teach appropriate and not *toxic* foods, even if they have *instructors* or not, must select appropriate one and avoid harmful ones, otherwise will go extinct. Hence *select-ability, ability to make appropriate selections* must be one factor of the minimal settings.

We prepare DNA reaction networks that keep on maintaining the start sequence, where the start sequence interacts with an input (*food*) sequence and they transformed into intermediate sequences and from the interactions in the intermediate sequences, start sequence is re-produced. Hence the reaction system can maintain start sequence.

Firstly, we modified a well-known DNA reaction systems, the *seesaw gate* and constructed the self-maintaining reaction system, experimentally and confirmed it works (it is notice that it is not simulation by PC).

Next, we mutated an input sequence randomly and examined if the reaction behaviors were changed. We confirmed that, in 6 cases in 38 trials, even if it has mutation in the input sequences, the system still works correctly and reproduces the start sequences. We examined efficiency of such reactions by comparing reaction speed and quantity changes of input sequences and it has shown that they are not significant different in efficiency between no-mutation and mutated input cases.

Finally, we gave not mutated (normal) input sequences and mutated sequences to the system and observed if the system is able to select *appropriate* one, where *appropriate* means to select the input sequences in the higher concentration regardless of it has mutation or not. We confirmed that the system can select higher concentration irrespective of having mutation or not. And we also confirmed behaviors in the time series of concentration of normal input and mutated input sequences showed oscillations; we conjecture that the because of system select higher concentration one, selected input sequences are switched among non-mutated and mutated input sequences.

These results illustrate that the system made of DNA reaction networks are able to select input sequences in higher concentration so it will able to adapt the environmental change. Therefore, from Biological and philosophical points of views, this system realizes molecular Artificial Intelligence.

2. Methods

Since simple hybridization reactions cannot be cascaded, other reaction mechanism such as strand displacement reactions [4] have been used. Strand displacement is the process which two strands partially or fully hybridize to each other, displacing one or more pre-hybridized strands in the process. Strand displacement can be initiated at complementary single-stranded domains (referred to as toeholds) and progresses through a random walk-like branch migration process. Strand displacement reactions can be cascaded to eliminate this need for external triggers at every step;

this enables the engineering of complex autonomous systems.

Strand displacement releases at least one single stranded nucleic acid product, such as the output. In a DNA strand displacement cascade, this output serves as the input to the downstream reaction. Unlike electric or biological circuits that are powered by a standardized energy source (electrical voltages or ATP concentrations), strand displacement-based circuits cannot be easily recharged because the reactant species for each strand displacement reaction are different.

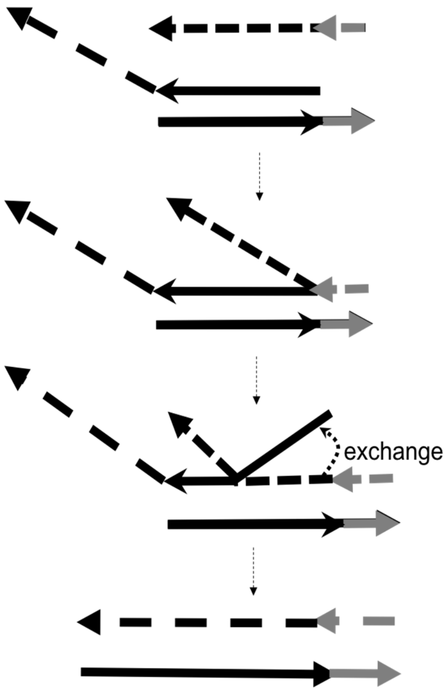

Fig.1. Strand displacement reaction; Strand Displacement Reaction; Dynamic DNA nanotechnology often makes use of toehold-mediated strand displacement reactions. In this example, the short arrow binds to the single stranded toehold region on the strand, and then in a branch migration process across region 2, the strand is displaced and freed from the complex. Reactions like these are used to dynamically reconfigure or assemble nucleic acid nanostructures. In addition, the strands can be used as signals in a molecular logic gate.

We modified the Seesaw gate reaction [4] by composed by the strand displacement reaction (Fig.2.); in order to confirm these reactions (1) and (2) circulate, we add the reaction; fuel + gate:marker → gate:fuel + marker (3);

input + gate:fuel ↔ gete:input + fuel (1),
gate:input + output ↔ gete:output + input (2),
fuel + gate:marker → gate:fuel + marker (3).

The reaction (3) examines the fuel sequence is produced and confirm the reaction (2) regenerate the input sequence. We confirm that the input sequence has been regenerated.

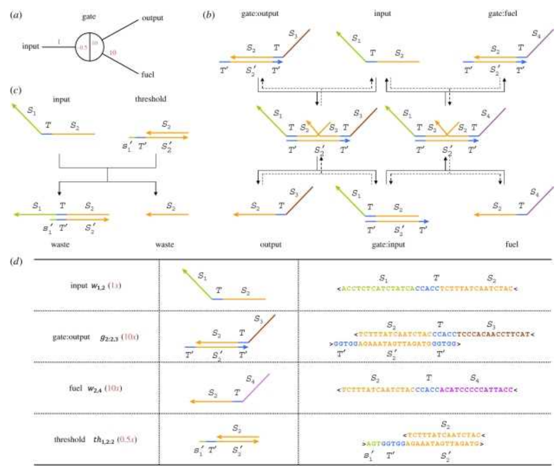

Fig. 2. Fig. 2. Seesaw gate reaction of DNA sequences: (a) Abstract gate diagram. Red numbers indicate initial concentrations. (b) The DNA gate motif and reaction mechanism. S1, S2, S3 and S4 are the recognition domains; T is the toehold domain; T0 is the Watson–Crick complement of T, etc. Arrowheads mark the 30 ends of strands. Signal strands are named by their domains from 30 to 50, All reactions are reversible and unbiased; solid lines indicate the dominant flows for the initial concentrations shown in (a), while the reverse reactions are dotted. (c)

3. Result

From biochemical experiments, we observed that when we added non-mutated input and mutated input, system select higher concentration one (Fig.3). And we also confirmed behaviors in the time series of concentration of normal input and mutated input sequences showed oscillations (Fig.3). And when the concentration decreases, the concentration of another input increases, hence we conjecture that the because of system select higher concentration one, selected input sequences are switched among non-mutated and mutated input sequences. These results illustrate that the system made of DNA reaction networks are able to select input sequences in higher concentration so it will able to adapt the environmental change. Therefore, from Biological and philosophical points of views, thie system realizes molecular Artificial Intelligence (Fig.3).

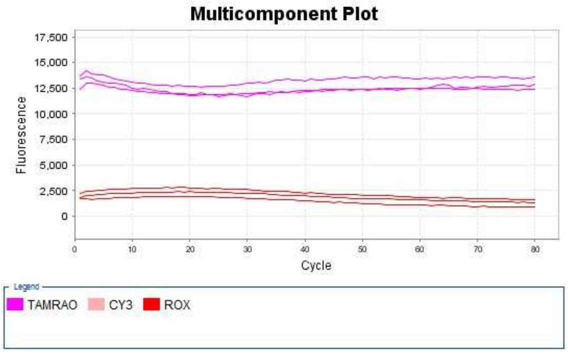

Fig. 3. Time series of concentration of normal input (below) and mutated input (upper); where mutated input was selected and concentration decreases.

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