Theoretical Computer Science ••• (••••) •••–•••

Contents lists available at ScienceDirect

Theoretical Computer Science

www.elsevier.com/locate/tcs

Molecular computers for molecular robots as hybrid systems

Masami Hagiya *, Nathanael Aubert-Kato, Shaoyu Wang, Satoshi Kobayashi

ARTICLE INFO

Article history:
Received 28 September 2014
Received in revised form 10 October 2015
Accepted 2 November 2015
Available online xxxx

Keywords:
Molecular computing
DNA computing
Hybrid system
Molecular robotics

ABSTRACT

Various artificial molecular devices, including some made of DNA or RNA, have been developed to date. The next step in this area of research is to develop an integrated system from such molecular devices. A molecular robot consists of sensors, computers, and actuators, all made of molecular devices, and reacts autonomously to its environment by observing the environment, making decisions with its computers, and performing actions upon the environment. Molecular computers should thus be the intelligent controllers of such molecular robots. Such controllers can naturally be regarded as hybrid systems because the environment, the robot, and the controller are all state transition systems having discrete and continuous states and transitions. For modeling and designing hybrid systems, formal frameworks, such as hybrid automata, are commonly used. In this perspective paper, we examine how molecular controllers can be modeled as hybrid automata and how they can be realized in a molecular robot. We first summarize the requirements for such molecular controllers and examine existing frameworks of DNA computing with respect to these requirements. We then show the possibility of combining existing frameworks of DNA computing to implement a sample hybrid controller for a molecular robot.

1. Introduction

Many of the biomolecules whose behaviors have been understood so far act as molecular devices with modular functionalities, including sensing and actuation. Typical examples of molecular devices are membrane receptors and protein motors. In addition to those derived from living cells, various artificial molecular devices have been developed to date. Many of them are made of nucleic acid strands: DNA and RNA (refer to reviews such as [1] and [2], or journal issues such as [3]). The next research step is to develop an integrated system from such molecular devices [4]. We are interested in autonomous molecular systems that respond to their environment by observing the environment, making a decision based on the observation, and performing an appropriate action without explicit external control. We call such a molecular system a molecular robot. To repeat, a molecular robot reacts autonomously to its environment by observing the environment (and itself) with its sensors, making decisions with its computers, and performing actions to the environment. Therefore, such molecular robots need intelligent controllers which can be implemented with general-purpose molecular computers.

In addition, if a molecular robot consists of multiple molecular devices, it needs to have a structure that integrates them and separates them from their environment. According to current molecular technologies, we can imagine molecular robots enclosed by a vesicle or a gel. We are currently organizing the research project "Molecular Robotics" funded by MEXT, Japan,

* Corresponding author.
E-mail address: hagiya@is.s.u-tokyo.ac.jp (M. Hagiya).

http://dx.doi.org/10.1016/j.tcs.2015.11.002

and have proposed to develop two kinds of molecular robot prototypes [4,5]. One has been called the "amoeba robot" and the other, the "slime mold robot".

An amoeba robot, which we aim to create, is a vesicle enclosed by an artificial membrane made of lipids, called a liposome, and contains molecular devices, including chemical reaction circuits on the surface of, and inside, the membrane. Actuators of the robot (e.g., protein motors) are expected to change the shape of the liposome and eventually lead to locomotive actions. The robot may contain internal liposomes, which can 'explode' and emit molecules into the body. The robot itself can eventually 'explode' too.

While the body of an amoeba robot is made of a liposome, that of a slime mold robot is made of a gel (typically, a hydrogel), which can also work as an actuator of the robot because crosslinks in a gel can be made of DNA and such a gel can shrink or swell. Molecular devices are immobilized within the gel and DNA circuits can work inside the gel. The gel is expected to shrink or swell according to signals emitted from the devices. In relation to slime mold robots, Hagiya et al. formulated a computational model, called "gellular automata", in which cellular space is created by walls of gels [6]. Each cell is surrounded by gel walls and contains a solution in which chemical reactions take place. They may produce molecules called decomposers and composers, which dissolve or (re)construct a gel wall of the corresponding type.

One can also imagine combinations of amoeba and slime mold robots. For example, one can introduce internal liposomes into a solution surrounded by gel walls. If an internal liposome explodes, the molecules emitted from the liposome may dissolve a gel wall, or shrink or swell it. Beyond amoeba and slime mold robots and their combinations, we can foresee future generations of molecular robots including multi-cellular robots and robots that are hybrids of molecular and electronic devices [4]. Applications of such molecular robots are expected to include intelligent drug delivery (emitting a drug only at the right place), artificial internal organs (e.g., sensing the blood sugar level and emitting insulin at the right time), intelligent stents (exploring the blood stream and expanding the blood vessel at the right place), contaminated soil cleaners, brain–machine interfaces, and eventually an artificial brain.

For both the amoeba and slime mold robots, we are implementing molecular computers based on chemical reactions that process information from sensors and control actuators.

In this paper, we examine possible approaches to making such intelligent molecular controllers for the amoeba and slime mold robots. In particular, we regard such controllers as hybrid systems [7] because the environment, the robot, and the controller are all state transition systems, having both discrete and continuous aspects (i.e., they have both discrete and continuous states and make both discrete and continuous state transitions). For modeling and designing hybrid systems, formal frameworks such as hybrid automata are commonly used [8]. In this paper, we examine how molecular controllers can be modeled as hybrid automata and how they can be realized in molecular robots. As an example, we examine how a timed automaton can be realized as a molecular controller.

2. Requirements for molecular computers for molecular robots

In this section, we examine the requirements for a molecular computer that controls a molecular robot. Such a computer receives inputs from the sensors of the molecular robot and is expected to send orders to the actuators of the robot. It controls the system, consisting of the robot and its environment, to preserve certain conditions.

Reactiveness Just like an electronic computer that controls a mechanical robot, a molecular computer that controls a molecular robot should respond to external signals or changes in the environment by sending orders to the actuators of the robot. In short, a molecular computer should be a real-time reactive system. In particular, a molecular computer for a molecular robot should handle changes of inputs from the environment. We say that a molecular computer is time-responsive if, when inputs to the computer change after its initial computation, outputs are re-computed to reflect the new inputs [9,10]. Molecular computers for molecular robots should thus be time-responsive.

Statefulness Generally, outputs from a molecular computer may depend on the history of its inputs. If so, it should have states that store part of the history that is necessary for computing outputs, and change them in response to new inputs. As discussed below, there may be both discrete and continuous states.

Hybridness Inputs from the sensors may be instantaneous signals from the external environment or may be continuous measurements of the environment. The former kind of input is called a discrete event. Photo-irradiation for a short period of time is a typical example. Another example is pouring a solution into the environment that leads to a discrete change in concentrations of some molecular species.

A molecular robot may sometimes be required to invoke a discrete event. For example, to make a fast conformational change of an amoeba robot by protein motors, the concentration of ATP should change instantaneously to start the motors in a coordinated fashion. To invoke such discrete events, the computer should also be able to make discrete state transitions. The explosion of an internal liposome is a possible discrete state transition because it is a type of phase transition and occurs instantaneously when certain conditions of the membrane are satisfied [11].

In short, the system consisting of the robot and the environment, including the computer controlling the robot, is a typical hybrid system in the sense that it may have both discrete and continuous states and make both discrete and continuous state transitions. Discrete transitions may change the differential equations governing the continuous temporal evolution of the system, and continuous changes of the system may accumulate to cause discrete transitions. The computer controls

Please cite this article in press as: M. Hagiya et al., Molecular computers for molecular robots as hybrid systems, Theoret. Comput. Sci. (2016), http://dx.doi.org/10.1016/j.tcs.2015.11.002