On-chip Robotics for Biomedical Innovation

Fumihito Arai

Abstract We defined Robot-on-a-Chip(Robochip) as a microfluidic chip in which micro-nano robots are installed, and which is targeting the single-cell based measurement, analysis, cloning and anatomical manipulation to contribute to the on-chip manipulation such as cell sorting. On-chip Robotics is needed to systematize the methods for micro-nano manipulation on a chip. Here we introduce our recent works on Robot-on-a-Chip driven by laser trapping force and by magnetic force for biomedical innovation.

1 Introduction of On-chip Robotics

Micro-nano Robotics plays an important role to supply advanced devices and equipments and to achieve technological innovation in biomedical science and engineering. In the past, there are a lot of research works on micro-nano manipulation. The actuation method of the manipulator is classified into the contact type and non-contact type. Miniaturization of the manipulation tools is the key issue to improve performance. A micro-nano technology is indispensable for miniaturization as well as functionalization. We have studied on non-contact type manipulation to improve performance of the manipulation system to contribute biomedical science and engineering. The targets of manipulation are micro-nano scale biological objects, such as oocyte, cell, microbe, virus, DNAs and so on, which are kept in water. If the manipulation tools are miniaturized and put in the closed space with the objects, we can eliminate unwanted disturbances, and therefore manipulation performance is stabilized.

We have studied on Robot-on-a-Chip(Robochip). We defined Robochip as a microfluidic chip in which micro-nano robots are installed, and which is targeting the

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single-cell based measurement, analysis, cloning and anatomical manipulation to contribute to the on-chip manipulation such as cell sorting. On-chip Robotics is needed to systematize the methods for micro-nano manipulation on a chip. Merit of Robochip technology is summarized as follows.

(1) Miniaturization
(2) High speed actuation
(3) Low disturbances
(4) Repeatability
(5) Disposable structure
(6) Easy to integrate with μ-TAS (High expandability)

For non-contact actuation of the miniaturized tools, we can apply laser trapping force, magnetic force, electrostatic force, and ultrasonic force. Here we introduce our recent works on On-chip Robotics for biomedical innovation.

2 Robot-on-a-Chip Driven by Laser Trapping Force

On-chip single cell analysis is an important approach for research and development in life science, pharmaceutical industry, livestock agriculture, and so on. Optical tweezers are well known as one of the noncontact manipulation methods used in a closed space and much has been reported. Optical tweezers are suitable to manipulate a single micro to nano scaled particle. Direct laser manipulation is not recommended for cell manipulation and advantage of using microtools was shown by the author (Arai et al. 2000). We achieved three-dimensional 6 DOF manipulation of the laser trapped object (Arai et al. 2006). Recent research attention has been focused on functionalization of the tools and their dexterous manipulation.

We proposed novel manipulation method using multiple laser beams. We named it Integrated Optical Tweezers(IOT)(Arai et al. 2008) which is made by integrating Time-Shared Scanning method(TSS)(Arai et al. 2004) and Generalized Phase Contrast method(GPC)(Eriksen et al. 2002). We made polymer microtools by photolithography (Fig. 1)(Arai et al. 2008) and by self-assembly(Fig. 2), and functional gel microtools by salting-out which can measure local environment information

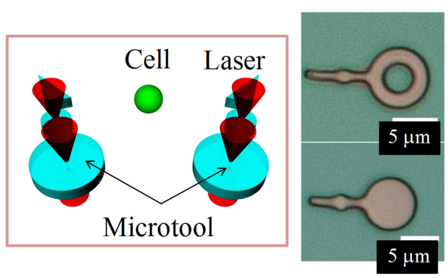

Fig. 1 Microtools made by photolithography

such as pH and temperature(Maruyama et al. 2008). We developed bilateral control system and succeeded in manipulation of these microtools.

We applied IOT and microtools for measurement of mechanical property of cells and functional analysis of cell membrane. TSS is suitable to manipulate a single virus on a chip(Arai et al. 2009).

3 Robot-on-a-Chip Driven by Magnetic Force

It is desired to have actuators which have the ability of enough actuation force to manipulate cells as well as the softness enough to be harmless to actuate cells. We proposed a magnetically driven microdevice for making a disposable microchip with simple control. We reported novel polymeric magnetically driven microtools (MMT) for non-intrusive and no contamination experiments on a chip (Yamanishi et al. 2007). The composites were formed by suspending magnetite nanoparticles(Ex: Fe_3O_4, average diameter $\phi 200nm$) in polydimethylsiloxane (PDMS). Young's modulus can be changed between KPa order and GPa order by selecting proper materials. We developed a hybrid MMT which has a metal part in it. We improved the system by using 3D fabrication of MMT (Fig. 3) (Yamanishi et al. 2008) and magnetic field concentration for powerful actuation(Arai et al. 2009). It can generate mN order force with low cost, which is quite different characteristics from that of the laser driven microtools. We applied it for several on-chip applications. Table 1

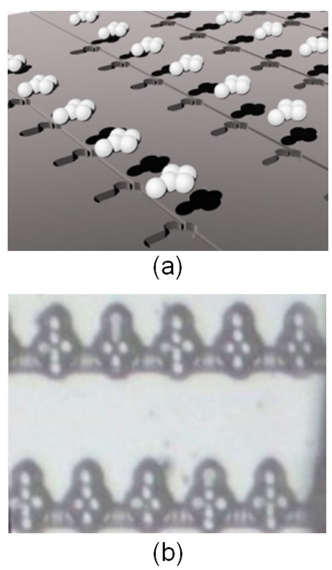

Fig. 2 Fabrication of the microtools using self-assembly (a) Concept (b) Self-assembly

summarized the classifications of the driving method of MMTs. Figure 4 shows an example of a hybrid type 2DOF-MMT. It can be applied for the cloning process. Concept of the on-chip enucleation is shown in Fig. 5. A swine oocyte is deformed by the narrow(shallow) microchannel as shown in Fig. 6 so that the nucleus in the oocyte is easily detected by the fluorescent microscope. On-chip robotics will contribute to improve the cloning process.

4 Summary

We introduced our Robot-on-a-Chip(Robochip) technology. On-chip Robotics plays an important role to supply advanced devices and equipments for biomedical science

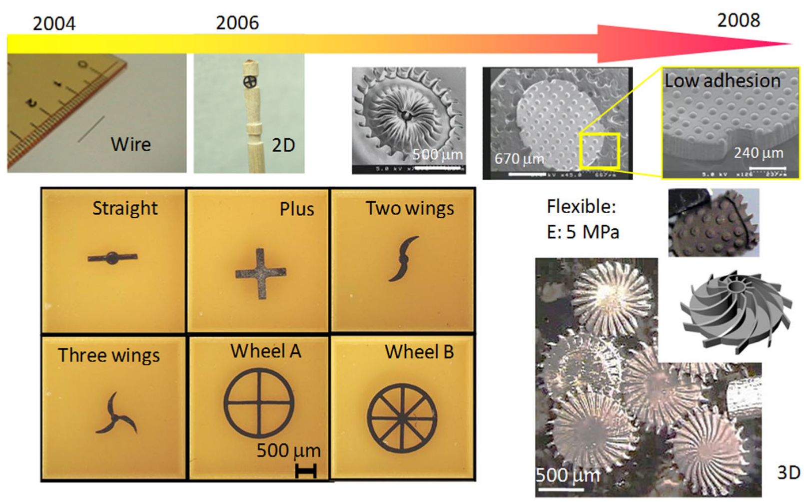

Fig. 3 Magnetically Driven Microtools: MMT

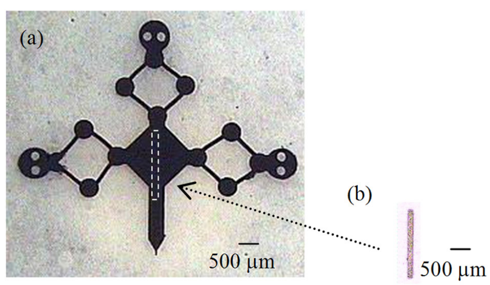

Fig. 4 Fabricated hybrid type 2DOF-MMT (a) Photo of 2DOF-MMT, (b) Ni plate fabricated by plating

and engineering. For future improvement, it is obvious that micro-nanotechnology plays an important role. Interdisciplinary education as well as research works between engineering, biological and medical fields are promoted.

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Table 1 Classification of driving method of MMT

Classifications	***Characteristics***
A. Control Method of Magnetic Field	
1. Fixed Electromagnet	Magnetic poles and magnetic field are controlled by the electric magnets
1.1 Switching the magnetic pole	ON/OFF type
1.2 Distribution of the magnetic field	Continuous type
2. Move of Electromagnet	Control the position of the electric magnet by an actuator and control the magnetic pole and magnetic field. (piezoelectric, AC/DC motor, etc..)
3. Move of Permanent Magnet	Control the position of the permanent magnet by an actuator and control the magnetic pole and magnetic field. (piezoelectric, electromagnet, AC/DC motor, etc….)
B. Magnetic Characteristics of MMT	
1. VR-type	Use materials with a high magnetic permeability
2. PM-type	Use a permanent magnet
C. Degree of Freedom	
1DOF x, (y, z) - lateral	Continuous, ON/OFF
1DOF rotation	Continuous, step
2DOF xy-lateral, lateral + rotation	Continuous, ON/OFF, step
Multi-degree of Freedom	Continuous, ON/OFF, step

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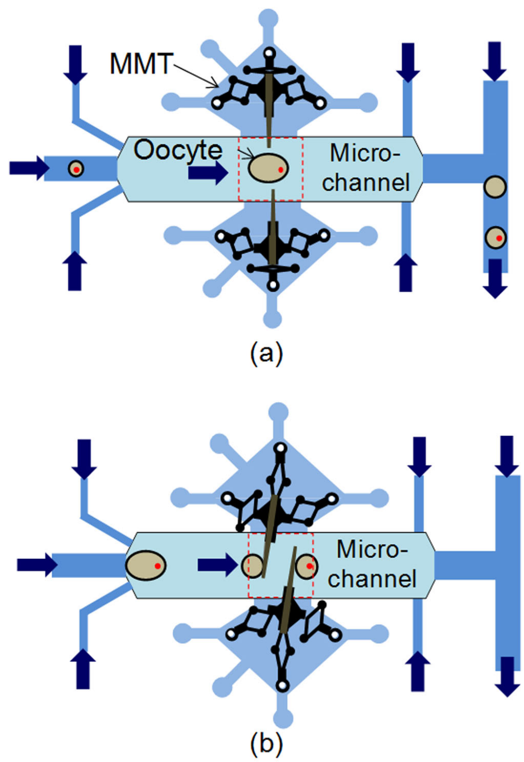

Fig. 5 Concept of the enucleation on a chip. The oocyte is deformed by the shallow microchannel. (a) Before cut, (b) Separation(after cut)

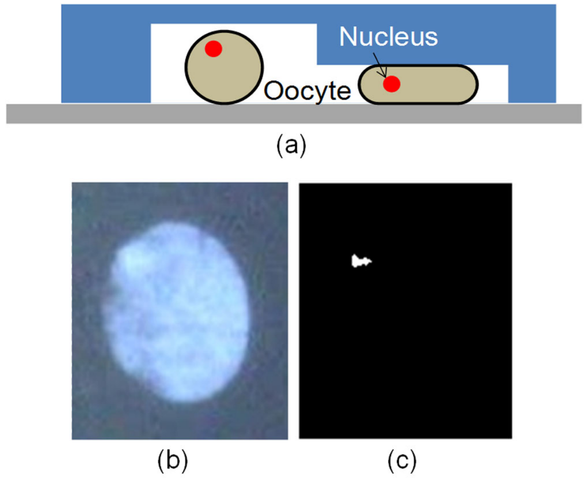

Fig. 6 Image of the oocyte deformed by the shallow microchannel. (a) Side view of the microchannel (b) Fluorescent image of deformed oocyte (c) Extraction of the nucleus by image processing(binalization)