Extended Abstracts of the 2015 International Conference on Solid State Devices and Materials, Sapporo, 2015, pp826-827

Molecular Analysis in Biological Samples by Actuator-Integrated Microfluidic Chips

Yuzuru Takamura [1,2]

[1] Japan Advanced Institute of Science and Technology.
1-1 Asahidai, Nomi, Ishikawa, 923-1211, Japan.
Phone: +81-761-51-1661 E-mail: takamura@jaist.ac.jp
[2] CREST, Japan Science and Technology Agency, Kawaguchi, Japan.

Abstract

BioMEMS technology using microfluidic platform integrated with actuators on chip is one of the attractive approach for a high performance and innovative devices in bio-medical application. In this paper, a high sensitive point of care devices, and a molecular analysis in single cell chip keeping with special information for single cell on 2D plane were reported and discussed.

1. Introduction

In these decades, many microfluidic devices have been developed and placed on the market. Some of them, such as DNA chip, capillary electrophoresis and next-generation sequencer, have achieved great successes as life-science tools, and have made big impact not only on the market, but also on the academic side by leading successive medical knowledge and technologies. Beside that, many collaboration works between electronics and biotechnology have been discussed and studied. We also have been developed high sensitive measurement devices using microfluidic technology for bio-medical and environmental application [1-4]. There are much potential techniques left still in this field, and one of the attractive candidate, we think, is actuator-integrated microfluidic chip.

In this paper, we would like to introduce two topics of high performance microfluidic chip integrated with actuator as a key factor. One is the high sensitive point of care devices, and the other is molecular analysis chip keeping with special information for single cell on 2D plane.

2. High sensitive point of care device

The amounts of glucose and insulin are important indices for life style diseases such as metabolic syndrome. The measurement of insulin in blood requires high sensitive detection in order of a few ng/mL. In most of the cases for such measurements in raw samples, blood, urine or saliva, require the immunoassay with bind/free separation. The bind/free separation needs washing step by trained operator or robot, and makes total system larger and more expensive. If the washing step is completed by disposable and low cost integrated actuator, it enables the POCT devices with low-cost and easy operation as well as self-monitoring of blood glucose.

We developed automated and compact (W115 x D150 x H105 mm) assay system of insulin and glucose (Fig.1). It consists of electrochemical analyzer, micropump driver. A plastic disposable microchip consists of screen-printed electrode and multilayer PDMS including pneumatic controlled micro pump. When the process is started via touch panel, diaphragm pump is operated to deliver the whole blood to the electrode and immunoreaction between immobilized antibody and insulin is incubated under continuous flow. Then series of reagent injections are automatically implemented for the washing of electrode and electrochemical measurement. Whole process is operated within 15-20 min.

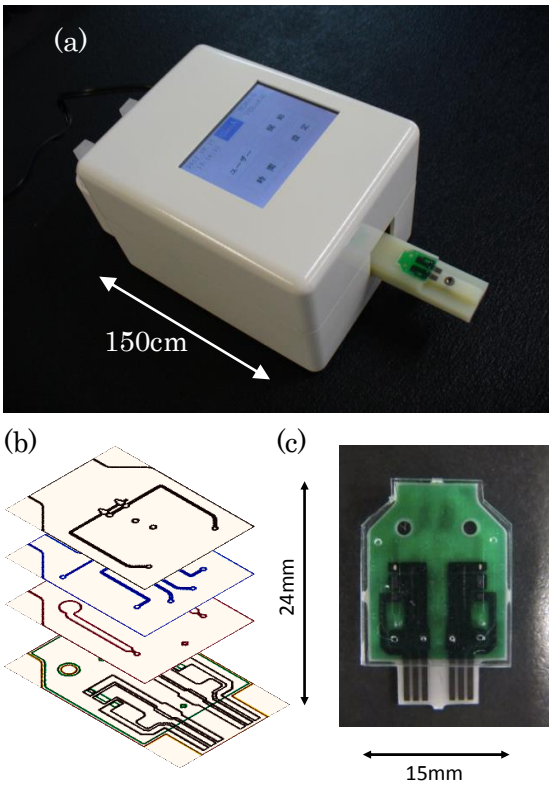

Fig. 1 (a) Photograph of measurement devices for insulin and glucose measurement. (b) Schematic illustration of a microchip. (c) The fabricated chip [5].

3. PZT actuator array and its application to research on neurological diseases.

We are also developing a technical base for single cells analysis on 2D plane, such as cell array, tissue surfaces, sections, and cultured cell networks, by developing the array of cell-analysis-units constructed with micro actuators. The cell-analysis-units will have the function to monitor the each living cell on the unit, to know the type of cell, its function, and its stage in disease in long term. The units will also be able to extract the contents of cells, from selected cells or from all cells on the units in any timing on demand, to hand out the contents to a next generation sequencer or a mass spectrometer for further analysis at the single molecule level with positional information. This research is expected to contribute not only to the study for various intractable diseases, such as the cancer and arteriosclerosis, but also for treatments and drug discovery.

For this purpose, we are developing on-chip lead zirconium titanate (PZT) actuators by solution process, which are expected to enable low-cost large-area fabrication of active devices by printing and annealing of functional Ink. We already made PZT actuator by solution process with temperature less than 450 degree C, which is advantageous for integration with active matrix FET array.

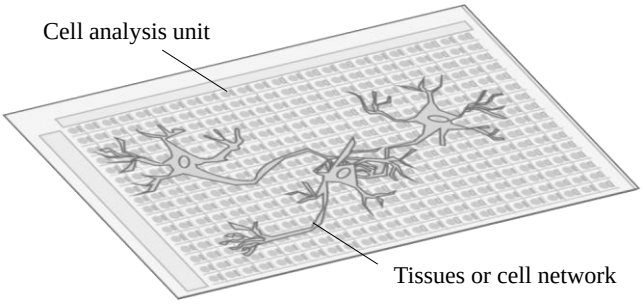

Fig. 2 Concept of single cell analysis chip on 2D plane with spatial information. Cell-analysis-units of each position constructed with micro actuators will extract the molecules from the cell.

References

[1] K. Sugiyama Pulse-heating ionization for protein on-chip mass spectrometry,Analytical Chemistry, 86(15) (2014) :7593-7.

[2] A.Apilux et al., Dvelopment of Automated Paper-Based Devices for Sequential Multistep Sandwich Enzyme-Linked Immunosorbent Assays Using Inkjet Printing, Lab Chip,13(1) (2013) 126-135.

[3] A. Kitano et al., High sensitive elemental analysis for Cd and Pb by liquid electrode plasma atomic emission spectrometry with quartz glass chip and sample flow, Analytical Chemistry 83(24) (2011) 9424-9430.

[4] K. Maehashi et al., Label-free protein biosensor based on aptamer-modified carbon nanotube field-effect transistors, Analytical Chemistry, 79 (2007) 782-787.

[5] S. Shiohara et al., Microsystem Technologies, 20 (2013) 273-279.