MULTIPURPOSE MICROCHIP SYSTEM FOR PHOTOMETRIC CHEMICAL ANALYSIS INTEGRATED WITH TEMPERATURE CONTROLLED SOLUTION MIXER

T. Noda[1], N. Hirokubo[1], Y. S. Shin[1], K. Miyamura[2], K. Matsumoto[2], H. Takao[1, 3], K. Sawada[1, 3] and M. Ishida[1, 3]

[1]Toyohashi University of Technology, JAPAN
[2]HORIBA, Ltd., JAPAN
[3]Japan Science and Technology Agency CREST, JAPAN

ABSTRACT

In this paper, practical useable microchip for chemical analysis is presented. The microchip can be performing photometric detection of solution, i.e. absorptiometry and turbidimetry, using integrated high performance long optical path length sensor. Moreover, high uniformity solution mixer is integrated as pre-treatment unit. Sample solution is not only mixed with reagent, but also controlled temperature by integrated micro-heater and feedback control circuit. Thanks to high performance mixer and temperature control mechanism, chemical reaction speed becomes constant, reproducibility and accuracy of measurement becomes higher. As one of demonstration of practical use for blood testing, C-reactive protein (CRP) was measured using the microchip by Latex Turbidimetric Immunity Assay (LTIA) method.

KEYWORDS: Photometric Sensor, On-Chip Mixing, Blood Testing, C-Reactive Protein

INTRODUCTION

Absorptiometry and turbidimetry is used widely for chemical analysis. Miniaturization of these analyses is demanded to realize handheld chemical analyzer, especially in medical application as point of care testing device. Highly sensitive absorptiometry microchip was succeeded in development by our group [1]. The microchip showed enough performance for blood hemoglobin amount measurement [2], however, pre-treatment of sample solution was external manual process. This is serious problem to prevent practical use. Some of micro-fluidic chips have same problem [3-4], not only our chip. In this paper, pretreatment unit of solution is integrated with photometric sensor, to realize not only convenient operation but also high reproducibility and accuracy. The microchip can be applicable for multipurpose measurement using photometric analysis, and contribute to realize ubiquitous chemical analysis.

THEORY

The microchip has 3 layer structure; Circuit layer, Fluidic channel layer and Cap glass (Fig. 1). Fig. 2 shows layout of integrated elements of the microchip. Sample solution and reagent are introduced into the microchip separately. Solutions are heated up by micro-heaters located on the bottom of the channel, and integrated

978-0-9798064-1-4/µTAS2008/$20©2008CBMS

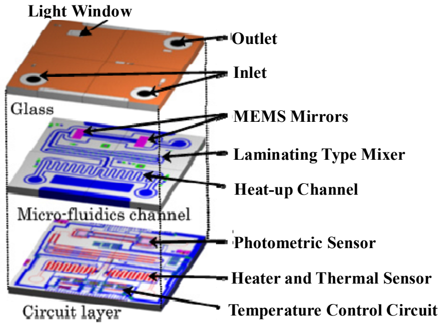

Figure 1. Schematic diagram of the microchip.

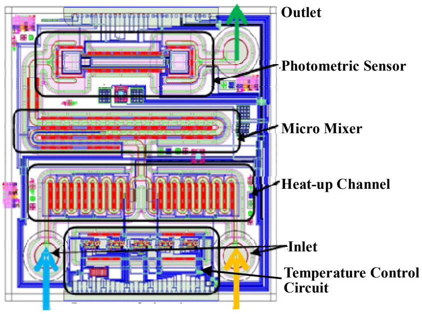

Figure 2. Layout of integrated elements in plane view.

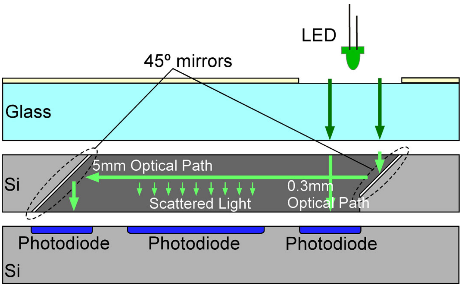

Figure 3. Cross sectional view of photometric sensor.

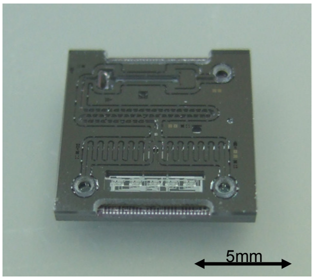

Figure 4. Photograph of the completed microchip.

thermal sensors detect temperatures. Solution temperatures are controlled by feed back control circuit. Heated up solutions are mixed together during flow through mixer channel. The mixer channel has 50 steps of "lamination mixer". Number of laminar flow layers in the channel is doubled by passing through the every step of the lamination mixer. 2^{N+1}layers can be made by N step mixer. High uniformity of solution is obtained, and achieves high reproducibility and accuracy. Integrated photometric sensor has two optical paths for absorptiometry (Fig. 3). One of that is 5 mm lateral optical path using 45º mirrors, and the other one is 0.3 mm straight optical path. Moreover, scattered light photodetector for turbidimetry is integrated at the bottom of lateral optical path.

RESULTS AND DISCUSSION

Designed microchip was fabricated successfully, and above elements were integrated into 11mm square microchip (Fig. 4). As one of demonstration of practical use of the microchip, CRP in blood was measured with LTIA method (Fig. 5). Blood sample and antibody sensitized latex reagent were mixed together, and turbidity was measured. Mixing and turbidity measurement were performed at 37 ºC, CRP concentration was obtained from reaction rate of mixture. Reaction rate was measured using fabricated microchip (Fig. 6). Solution mixing and photometric detection were succeeded on the "one" microchip.

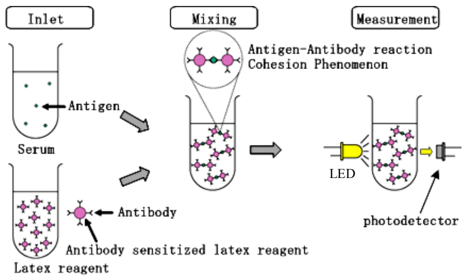

Figure 5. Principle of C-reactive protein (CRP) measurement with Latex Turbidimetric Immunity Assay (LTIA).

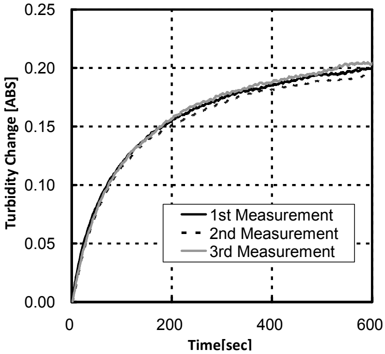

Figure 6. Measurement results of reaction rate using on-chip mixer and photometric sensor.

CONCLUSIONS

The microchip can be applicable to multi-purpose chemical measurement that includes medical application. Moreover, high reproducibility , high accuracy and easy operation without manual pre-treatment are achieved.

ACKNOWLEDGEMENTS

This work was supported by The Global COE Program "Frontiers of Intelligent Sensing" from the Ministry of Education, Culture, Sports, Science and Technology, Japan (MEXT).

REFERENCES

[1] T. Noda, H. Takao, M. Ashiki, H. Ebi, K. Sawada and M. Ishida, Characteristics of High-Resolution Hemoglobin Measurement Microchip Integrated with Signal Processing Circuit, Japanese Journal of Applied Physics, 43, pp. 2392-2396, (2004).

[2] T. Noda, H. Takao, K. Yoshioka, N. Oku, M. Ashiki, K. Sawada, K. Matsumoto and M. Ishida, Performance of absorption photometry microchip for blood hemoglobin measurement integrated with processing circuits and Si (110) 45° mirrors, Sensors and Actuators, B-119, pp. 245-250, (2006).

[3] A. Oki, H. Ogawa, M. Nagai, S. Shinbashi, M. Takai, A. Yokogawa and Y. Horiike, Development of Healthcare Chips Checking Life-Style-Related Diseases, Materials Science and Engineering, C-24, pp. 837-843, (2004).

[4] R. Kurita, N. Yabumoto and O. Niwa, Miniaturized One-Chip Electrochemical Sensing Device Integrated With a Dialysis Membrane and Double Thin-Layer Flow Channels for Measuring Blood Samples, Biosensors and Bioelectronics, 21, pp. 1649-1653, (2006).