Design and Fabrication of a Lab-on-a-Chip incorporating µPCR and a Label-Free Micromechanical Capacitive Biosensor into a flexible PCB platform

Despina Moschou [a], Nikolaos Vourdas [a], George Kokkoris [a], George Tsekenis [b], Vasiliki Tsouti [a], Ioanna Zergioti [c], Angeliki Tserepi [a], Stavros Chatzandroulis [a]

[a] NCSR "Demokritos", Ag.Paraskevi, 15310, Greece
[b] FBRAA, Athens, 115 27, Greece
[c] NTUA/Physics, Athens, 15780, Greece
e-mail: stavros@imel.demokritos.gr

Keywords: Lab-on-Chip, µPCR, capacitive biosensors, microfluidics, µTAS

Abstract Text

In order for any biosensor to be successful in reliable DNA detection, it is necessary to multiply beforehand the DNA in the sample under examination, so as to bring the concentration within the limits of detection of the device. This task is routinely achieved using the polymerase chain reaction (PCR) in order to replicate DNA and is widely used in bio-analysis such as microbial detection and medical diagnosis. In this work, we present the integration of a µPCR with a 64 element micromechanical capacitive biosensor array [1] into a PCB platform (Fig. 1). The sensor (Fig. 2) takes advantage of surface stress changes during biological interactions and is able to translate them into a capacitive signal. Each sensing element consists of an ultrathin silicon membrane on which receptor molecules are immobilized. During bio-molecular interactions, the stress exerted on the membrane surface changes, forcing it to deflect, which in turn results in a change in device capacitance. Use of a PCB as an integration platform allows for the implementation of both the microfluidic and electrical circuit necessary for sensor connections as well as for a continuous flow µPCR device on the same chip. When the DNA-containing sample enters the system, it first goes through the µPCR part, where the DNA is to be multiplied. Next, the sample is carried through microfluidic channels to the biosensors silicon chip, where detection takes place. The complete design of the LoC including the integrated µPCR and biosensor system is shown in Fig. 1 and is compatible with an instrument which is responsible for flow and temperature control of the LoC, where necessary. The µPCR microfluidic channels are placed directly over the heaters (depicted in red) which are designed to form three heating zones [2], so that by means of cycling the sample through them, in continuous flow, DNA multiplication can be achieved. Heat transfer computations for one thermal cycle of the whole µPCR [3] indicate good temperature uniformity within each thermal zone and are in agreement with the experimentally determined small power consumption for the device operation. The sensor itself sits in a chamber (for hybridization) in the right hand side of the chip which accommodates two microfluidic inputs and two outputs to ensure even transfer of the sample and complete coverage of the chamber area. Finally, the chip is completed with a pre-concentration chamber placed before the sensor, where the PCR product is converted to ssDNA ready for detection on the biosensors, and a waste chamber at the end of the microfluidic circuit, where pumping is implemented. First evaluation results of the individual components of the integrated system indicate that DNA multiplication is possible (Fig. 3) and that the biosensor array is able to detect single mutations of the KRAS gene, which is responsible for colon cancer (Fig. 4).

[1] V. Tsouti, M.K. Filippidou, C. Boutopoulos, P. Broutas, I. Zergioti, S. Chatzandroulis, Sens. Act. B , Vol. 166–167, pp. 815-818 (2012)

[2] E. Mavraki, D. C. Moschou, G. Kokkoris, E. Kouris, N. Vourdas, S. Chatzandroulis, A. Tserepi, Eurosensors XXV, Athens, Greece, 4-7 September 2011.

[3] G. Kokkoris, D. Moschou, E. Mavraki, S. Chatzandroulis, A. Tserepi, 3rd Micro & Nano Flows Conference, Thessaloniki, Greece, 22-24 August 2011.

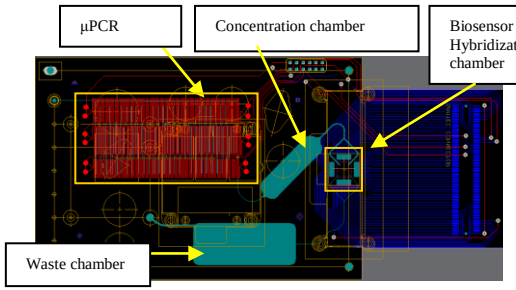

Figure 1. Complete design of all LoC layers

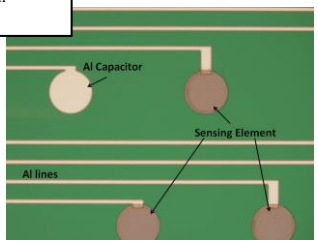

Figure 2. Image of part of the sensor array consisting of membranes and an Al capacitor.

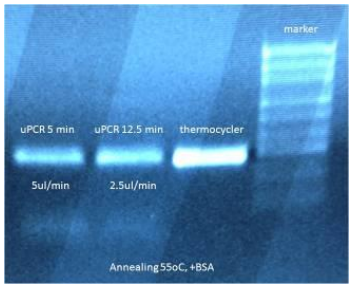

Figure 3. Comparison of µPCR products with that of conventional thermocycler

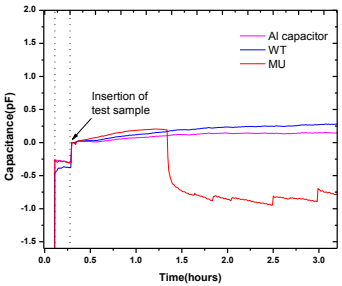

Figure 4. Response of sensing elements in the sensor array to mutated K-ras genes

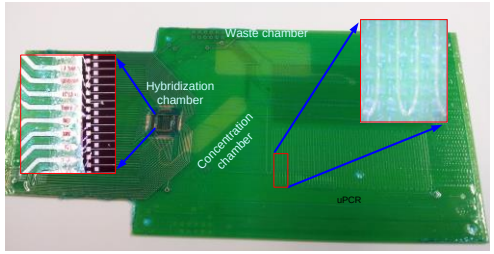

Figure 5. Fabricated LoC. Bioensor chip is wire bonded to Cu pads on the PCB.