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Microfluidic-nanophotonic label-free biosensors for Lab-on-a-chip applications

Tesis Doctoral

D. Francisco J. Blanco Barro.

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CNM I.M.M.

CSIC

ikerlan
ik4 research alliance

Directores:

Dña. Laura M. Lechuga.

Dr. Ciencias Químicas

D. Jorge Elizalde García.

Dr. Ingeniería Industrial

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Tribunal nombrado por el Mgfco. y Excmo. Sr. Rector de la Universidad Politécnica de Madrid, el día de de .

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Abstract

The advance of the microfluidic devices has opened a wide possibility to improve the sensitivity and selectivity of label-free biosensor devices and to reduce the cost of the manufacturing processes. These strategies have been developed into the concept of Lab-on-a-chip (LOC). The miniaturization of LOC devices allows the improvement of the overall performance of the analytical devices by minimizing the scale on which the analysis is performed. In addition, the possibility to integrate microelectronics, optoelectronic, micromechanical, and microfluidic components in the same manufacturing cycle opens the possibility to reduce the cost of the final device.

Existing microfluidic technologies are based on fabrication process and materials which are not compatible with label-free biosensor devices. There is no microfluidic technology which allows the integration of biosensor devices in a truly portable LOC device. Furthermore, there is not investigation of label-free biosensing protocols inside microfluidic channels.

In this thesis the research leading towards a Microfluidic-optical label-free biosensor as the first step to obtain a Lab-on-a-chip have been presented. Various aspects of such integrated devices have been addressed, starting with the development of a novel low temperature CMOS compatible wafer-bonding technology based on the SU-8 polymer. The research includes a detailed material and fabrication characterization studies. Using this novel bonding technology 3-D interconnected straight walls microchannels has been achieved. The microfluidic technology allows the hybrid integration and packaging of three-dimensional interconnected microchannels with different MEMS and CMOS substrates.

The microfluidic technology has been integrated with silicon Mach-Zehnder Interferometer label-free biosensor devices. This technology allow us to obtain high quality 3D microfluidic interconnected networks aligned on top the biosensor devices. The development of fluidic interconnects is another challenge. A novel method to connect and packaged them easily is developed. Flow experiments were conducted in order to known the fluid flow behaviour though these novel microfluidic devices. The results obtained improve the performance with respect to standard polymer microfluidic devices

These highly integrated devices have been developed to perform biosensing measurements. Novel biosensing protocols have been developed to be used in a microfluidic channel. The integrated microfluidic devices have been validated to be use as biosensor, for detecting the biomolecular reaction between a receptor module and its complementary analyte. Two types of biomolecular interactions were tested to study the suitability of our device for biosensing applications:

(i) An environmental application: the detection of the metabolite of the Chlorpyrifos pesticide was performed.

(ii) A biomedical application: the immunoreaction between human Growth hormone (hGH) and the anti-hGH monoclonal antibody have been monitored.

In addition, the microfluidic technology developed in this Thesis has been integrated in polymer (PMMA) low cost substrates and tested for Capillary Electrophoresis applications with excellent results compared to standard microfluidic commercial devices; these developments open the possibility to integrate different biosensor and lab-on-a-chip devices in a single low cost polymer platform.