ANALYTE CAPTURE IN AN ARRAY OF FUNCTIONALIZED DROPLETS FOR A REGENERABLE BIOSENSOR

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ABSTRACT

We are proposing a new architecture of biosensor based on droplets, not as reaction chambers, but as regenerable detection interface. We focus here on the microfluidic aspects and show the design, realization and characterization of a biochip for the production of functionalized droplet and their arrangement in a dense array. We then demonstrate the capacity of the array to capture analyte from a cross-flowing liquid, using a biotin/streptavidin model.

KEYWORDS: biosensor, regenerable, microfluidics, microemulsion, functionalization, analyte capture

INTRODUCTION

Marker-less biosensors are aimed at protein quantification or antibody detection without the need for attaching fluorescent or magnetic markers. Their principle of operation rests on three functions. Firstly, they require functionalization of a surface with bioreceptor for the bioanalyte of interest. Usually capture with high specificity is targeted, like antibody/antigen or ligand/protein bindings. Then the bioanalyte circulates close to the functionalized surface for capture. Finally, a transducer (opto-electro-electrochemico-acousto…) is used to measure surface change reveling the presence of bound bioanalyte. In general the functionalization is performed on a flat surface outside the biochip and it cannot be reused. This forces to use disposable biochips, making it expensive to integrate the most sensitive acoustic detection scheme [1].

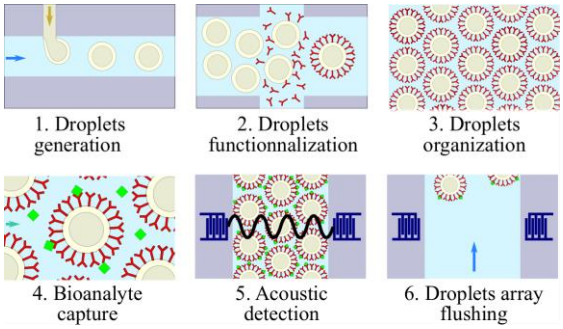

Figure 1: Functions required for a droplet based biosensor with bioanalyte capture and regeneration.

Our new sensing approach (Fig.1) is, as far as we can tell, the first time that a biosensor using the surface of a dense array of droplet for bioanalyte capture is proposed. The closest work existing is based on functionalized solid particles [2] that does not work with acoustic sensing and cannot benefit from its high sensitivity.

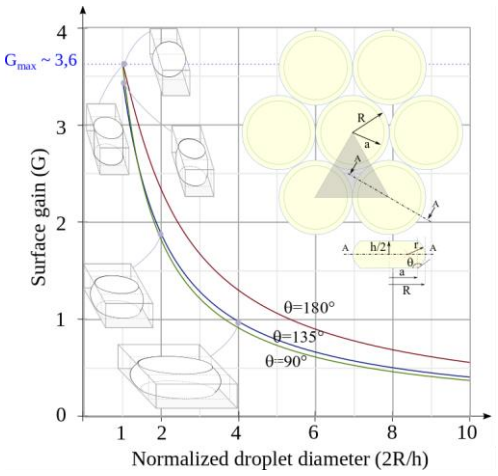

Figure 2: Gain of capture surface w.r.t. flat sensor as a function of squeezed droplets diameter and contact angle.

THEORY AND SIMULATION

We have first found (Fig.2) that the squeezed droplet array has a much larger (up to 3.6) capture area compared to a "flat" sensor of the same chamber surface and presents more efficient capture (25 times shorter capture distance), suggesting more complete capture of rare bionalyte.

We have also conducted numerical flow simulation to guaranty regular filling of the analysis chamber, where the droplets can be retained by the forked channels of the droplets sieve (Fig.3).

EXPERIMENTAL AND RESULTS

We have established a protocol for generating and functionalizing directly the soja oil droplets inside the biochip, resulting currently in biotin terminated droplet surfaces. We have developed a complete microfluidic chip, using Si/glass process, with provision for acoustic sensing integration below the analysis chamber (Fig.3). A computer-controlled system manages the 7 input/output ports to arrange the droplets in a dense array. The array is easily evacuated and replaced for regenerating the functionalized surface without dismounting the device.

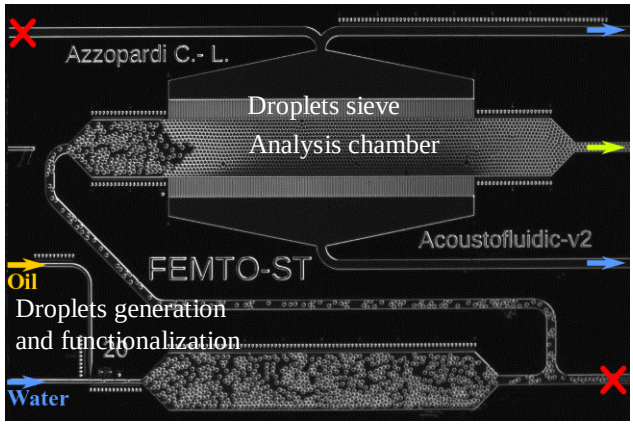

Figure 3: View of the chip during droplets generation and array organization in the analysis chamber

We have then studied the flow of bioanalyte inside the droplet array in the analysis chamber and shown it is similar to flow in a porous medium. Finally, we have observed the formation of biotin-streptavidin-biotin bridge in the array, proving the efficiency of our proposed capture architecture.

CONCLUSION

This project is the first step toward a high sensitivity regenerable biosensor using oil droplet surface as capture area and with integrated high sensitivity acoustic detection. We are currently working on the integration with a silicon/AlN process of the acoustic transducer below the analysis chamber.

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