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SURFACE ACOUSTIC WAVE-INDUCED MICROSTREAMING IN DROPLETS FOR THE ENHANCEMENT OF BIOSENSING PERFORMANCES

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ABSTRACT

A droplet-based micro-total analysis system (microTAS) based on digital microfluidics, involving surface acoustic wave (SAW) microstreaming dedicated to the enhancement of the performance of biosensors was designed and studied. We first present the characterization of the flow induced in the droplet during SAW stirring. We then present the evaluation of the biosensor performance enhancement obtained using SAW, evaluated by finite element simulation. We finally stress on the importance of the Damköher and Peclet numbers in the design of stirring-based microTAS systems.

INTRODUCTION

Flows in microTAS are often characterized by a very low Reynolds number, and happen to be laminar. In the case of biosensors associated to microTAS, it has been pointed out that mass transport is often limited by diffusion of the analytes from the convection laminar flow to the biosensing surface, limiting time scales and sensitivity. To overcome this issue, the enhancement of biosensor performance by electrothermal stirring within microchannels was first reported by Meinhart et al. [1]. Other studies focus on analyte transport simulation near biosensors, stressing on the fact that the real challenge of microTAS-associated biosensors is not the biosensor itself but the microfluidics used for analyte transportation [2].

SAW-based microTAS are currently becoming popular for they allow contactless stirring in fluids, and are particularly adapted to digital (droplet-based) microfluidics. However, the main problems that need to be addressed when using SAW are the complexity of the induced flow and its poor reproducibility. Yeoh et al. [3] proposed a SAW-based centrifugation system permitting flow rotation in a reproducible way by playing on the configuration of transducers and reflectors.

SAW STREAMING

A microliter droplet is placed between a hydrophobic piezoelectric substrate and a hydrophobic glass cover. Both the substrate and the cover are covered with a Octadecyltrichlorosilane (OTS) hydrophobic layer. SAWs are radiated towards one half of the droplet using interdigitated transducers. A vortex is then induced in the droplet in a reproducible manner, due to momentum transfer between the solid piezoelectric substrate and the liquid. A general view of the system is shown in Fig.1.

Speed cartographies of the flow induced in the droplet are realized using the Particle Image Tracking technique for different SAW generation powers. Instantaneous images of the flow are realized using a high-speed video camera at 200 frames per second and an aperture time of 500! s on a 0.25! l droplet containing 1! m diameter fluorescent particles. Figure 1 shows the mean speed measured in the droplet as a function of the inlet power. The great dependence of the induced mean speed enables a large range of flow speeds in the stirred droplet. Moreover, the flow was visualized with a low depth of field objective (20! m) and found to be circular and 2D in a large thickness range of the droplet.

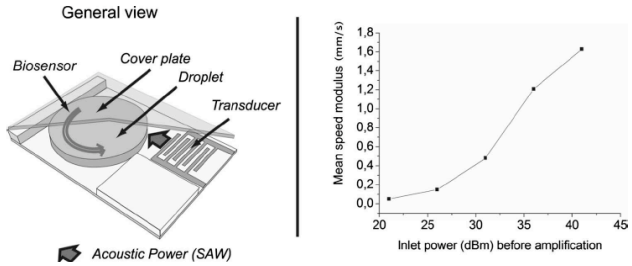


Figure 1. General layout of the device (left), mean speed of the induced circular flow as a function of the SAW power (right).

BIOSENSING PERFORMANCE ENHANCEMENT

At the biosensor surface, the reaction kinetics consumes analytes but their transport is limited by diffusive effects. In this case, the Damköhler number (D_a) brings valuable information, by comparing these two effects. Calling respectively the characteristic reaction time and diffusion time "$_c$ and "$_M$, D the diffusion coefficient and h a characteristic length of the microchannel, "$_M$#h^2/D. Calling R_T the ligand concentration on the surface in mole/m$ and k_a the reaction constant of the analyte consumption reaction, the Damköhler number can be written:

$$D_a = \frac{\tau_M}{\tau_C} = \frac{k_a R_T h}{D} \qquad (1)$$

Depending on the type of reaction, the calculation of D_a helps to determine if a specific bio-interaction will benefit from mass SAW-based microstreaming. For example, the binding of biotin to immobilized streptavidin is characterized by a D_a number of approximately 10^4. In this case, stirring will significantly improve the reaction rate.

COMSOL numerical simulations were carried out to study the efficiency of the SAW stirring in the case of a droplet based microbioreactor of diameter 1mm. Assuming a 2D flow, the simulated model takes into account the convective and diffusive effects in the analyte carrying fluid and the binding kinetics on the biosensor surface. This approach was thoroughly developed by Meinhart et al [1].

On the biosensor surface, equation (2) is solved:

$$\frac{\partial B}{\partial t} = k_a c_s (R_T - B) - k_d B \quad , \quad \frac{\partial B}{\partial t} = D \frac{\partial c}{\partial y}\bigg|_{y=0} \qquad (2)$$

With *c* the local concentration of analytes in the droplet, and *B* the surface concentration of bound analytes on the biosensor surface, corresponding to the condition y=0. k_a and k_d are respectively the association and dissociation reaction constants of the analyte on the biosensor surface. The boundary condition set to slip on the outer surface of the droplet. Simulation results show that a depleted zone of low analyte concentration is formed near the biosensor in the case of an interaction without stirring. As shown in Fig.2, the geometry of the depleted zone is modified when stirring is applied, as it is pushed in the direction of the flow. In our case, which is assimilated to a simple circular flow, the depleted zone reaches a permanent state consisting of an analyte-poor layer situated in the outer perimeter of the stirred droplet.

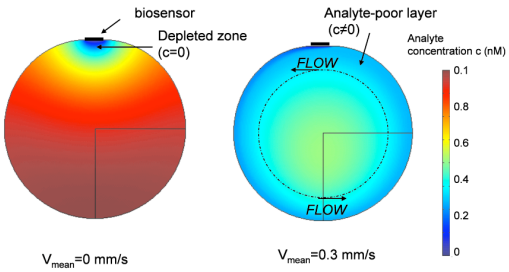
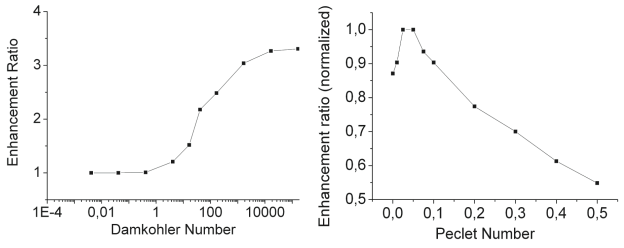


Figure 2. Simulated concentration profiles with (right) and without SAW stirring (left), t=10 000s.

To evaluate the benefits of in-situ microstreaming with SAW, the same simulations were conducted for D_a numbers ranging from 10^4 to 10^8 M^{-1}/s, by ranging the diffusion coefficient from 4.10^{-12} to 4.10^{-9} m$/s, and the association coefficient ka from 10^4 to 10^8 M^{-1}/s. The enhancement factor of analyte capture, defined as the ratio of the binding rate with streaming B and the binding rate without streaming B_0, is plotted in Fig. 3 for different values of Da. Calculations are completed in the case of a mean flow speed of 0.5mm/s.



(a) (b)

Fig.3. Calculated enhancement factor as a function of the Damköhler (a) and Peclet (b) numbers.

Our calculations show that the enhancement ratio reaches a plateau value at high Da numbers. In the case of our specific flow configuration, the enhancement factor reaches 3.2 for the interaction of streptavidin on immobilized biotin ($Da=10^3$).

The reported simulation results can be compared to an experimental values obtained using the droplet-based Surface Plasmon Resonance (SPR) sensor streamed in-situ using SAW reported by Galopin et al. [4]. By monitoring the streptavidin - biotin binding interaction on an activated gold slide, they showed that SAW stirring brings an improvement factor of more than 2. This difference can be accounted to the high complexity of the induced 3D flow, which was modeled in a simple manner in our calculations. Finally, the calculation of the enhancement factor as a function of the Peclet number shows that for each Da, an optimum Peclet number can be can be calculated, corresponding to an optimum stirring speed.

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