Multiplexed cell sensing using a hybrid microfluidic, nanomechanical and dielectrophoretic device

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Developing new analysis and detection techniques is a key point for maintaining the relentless advances in the scope of nanotechnology, which eventually can provide innovative solutions to many other fields like, medicine, industry or biology. In this sense, biomedical applications are probably the most challenging since they demand working under physiological conditions, which may differ completely from the optimal working conditions employed in many nanotechnological techniques (e.g. high vacuum). In this scope, microfluidics has emerged as a promising technique since it allows working with liquid samples obtaining a high throughput. Nonetheless, despite the advantages obtained, microfluidics itself provides limited information about the sample under analysis, so it needs to be combined with other approaches so as to obtain more versatile techniques. For this reason, in this work we develop a new sensing scheme which merges inside the same device three different techniques: microfluidics, nanomechanical sensing and dielectrophoresis.

The developed device consists on a microfluidic channel free-standing for a certain length so it can mechanically oscillate in flexural modes (Suspended microchannel resonator, SMR, Fig. 1). By means of a laser doppler vibrometer and a piezoelectric actuator, the mechanical resonance frequency of the SMR can be tracked in real time [1], therefore a frequency shift is registered when a cell crosses the suspended region as a consequence of the mass variation. Previous works have demonstrated mass is not only an adequate parameter for cell sensing but also it provides information of high biological relevance [2]. We checked the validity of this device as cell sensor by flowing through it different samples containing *saccharomyces cerevisiae* with different concentrations down to 10^2 cells/mL, detecting the presence of these microorganisms in any case while characterizing their mass distribution (Fig. 2).

Nevertheless, despite their biophysical relevance and usefulness for cell detection, mass measurements present some limitations when it comes to discern between different types of microorganisms [3]. To overcome this problem, we have integrated gold electrodes on the SMR device (Fig. 1), so we can combine simultaneously measurements of the mechanical and electrical properties of the samples under test, obtaining a multiplexed analysis. When a voltage is applied on the electrodes, two different physical phenomena happen. On one hand, the electric field inside the microchannel produces electrophoretic forces which can immobilize the passing particles at a specific point (Fig. 1). This trapping opens the door to optimize mass measurements as well as filtering particles by immobilizing those with specific electrical properties. On the other hand, the applied voltage produces a stress on the electrode-microchannel interface, giving as a result a resonance frequency shift whose value depends directly on the electrical permittivity of the sample (Fig. 3). When combined with the mechanical measurements, this electrical characterization enhances the cell detection as well as provides information of high biophysical relevance.

References

[1] Calmo, R. *et al*., Sensors and Actuators B: Chemical, 283 (2019) 298.
[2] Cetin A. E., *et al*, Nature Communications, 8 (2017) 1613.
[3] Martín-Pérez, A. *et al*., ACS Sensors, 4(12) (2019) 3325.

Figures

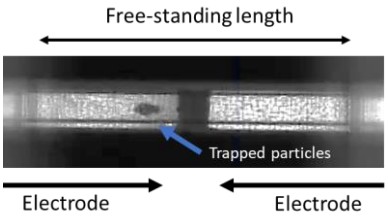

Figure 1. Microscope image of the developed device containing a cluster of immobilized particles by dielectrophoretic forces.

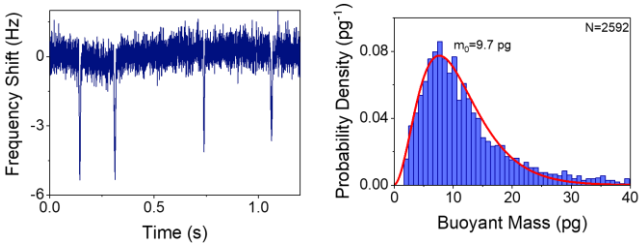

Figure 2. (left) Resonance frequency shift produced by the pass of 4 *s. cerevisiae* cells and (right) cell mass distribution obtained for a whole sample.

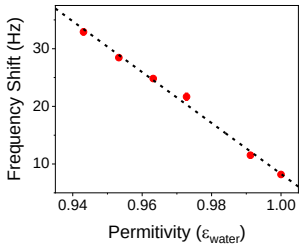

Figure 3. Mechanical resonance frequency shift produced when 200 V at 100 kHz voltage is applied on the electrodes for samples of different electric permittivity.