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A microfluidic system with integrated inkjet-printed capacitive sensors for biosensing applications

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Summary:
This paper presents a novel microfluidic system integrating an inkjet-printed interdigitated capacitive biosensor, specifically targeting Tumor Necrosis Factor alpha. The system exploits an aptamer-based functional layer whose dielectric permittivity is affected by the target analyte. Low-cost, rapid prototyping technologies have been exploited for the device fabrication. Experimental results demonstrate good sensor performances, especially within the low detection range of TNFα. In particular, a sensor responsivity of 15.291 fF/pM in the range [0-1] pM has been estimated.

Keywords: biosensing, IDC sensor, microfluidic, InkJet Printing, optimal design.

Background, Motivation and Objective

Advanced biochemical sensing techniques are crucial in many fields, such as food, environment and healthcare [1]. The quantification of biomarkers for the diagnosis of many diseases, typically requires expensive equipment and trained personnel. Thus, there is an increasing interest in the development of low-cost Point of Care system for the rapid detection of biomarkers [2]. To this aim, rapid prototyping technologies, such as InkJet Printing (IJP), exploiting suitable functional materials, inks and substrates, represent viable solutions to the affordable development of disposable biosensors [3] and chemical sensors [4].

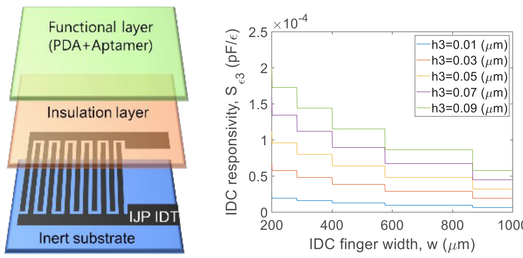
In this work a microfluidic biosensing system, for the detection of Tumor Necrosis Factor alpha (TNFα) is investigated. In particular, the design, the realization (by IJP technology) and the experimental behavior of the InterDigitated Capacitive (IDC) sensing element is addressed. Main novelties and advantages of the proposed approach are: i) the implemented architecture, exploiting a dedicated multi-layer stack for the realization of the IDC based readout sensing strategy; ii) the integration of the multi-layer IDC sensor within the microfluidic system, thanks to the thin film technology adopted for the realization of the sensor; iii) features offered by the sensor, especially at low target concentrations, including fast and reliable detection; iv) the low-cost of the sensing architecture, mainly supported by the adopted rapid prototyping technology; v) the use of transparent layers allowing for future potential development of electrical/optical multi-sensing approach.

Description of the New Method and System

The adopted measurement principle is based on the variations in the dielectric permittivity of a functional material, due to the trapping mechanism fixing the target analyte over the sensing surface. The fabricated IDC sensor has a multi-layer dielectric structure: i) an inert, 140 µm-thick, Polyethylene terephthalate (PET) substrate supporting the IDC structure; ii) a 46 µm-thick, polypropylene insulation layer bonded over the IDC sensor; iii) a Polydopamine (PDA) film realized by chemical deposition: a 50 mM Dopamine solution in 0.5 M Phosphate Buffer Solution (PBS) was casted on the insulation layer, up to full coverage of the support. The PDA film was left to deposit for 5 h in air and then left to dry up; iv) an aptamer-based functional layer: after washing with water, the PDA-coated sensor was left in contact overnight with a solution 1 microM of the aptamer specific for Tumor Necrosis Factor alpha (TNFa); the sensor was then washed with PBS and the surface was passivated with ethanolamine (1 mM in PBS, 15 minutes).

The sensor, whose structure is schematized in Fig. 1a, is embedded in a sealed microfluidic cell to convey the target analyte. The microfluidic cell, shown in Fig. 2a, is composed of a rigid plastic substrate and a soft Polydimethylsiloxane sealing layer.

To optimize the design of the IDC, a dedicated approach aimed at maximizing the device response against the analyte concentration has been adopted, by applying both the partial capacitance method and the conformal mapping transformation [5,6]. Given a sensing area of $7.0 \times 6.9\ mm^2$, fingers spacing has been fixed to 300 µm (constrained by the technology), fingers length to 7.0 mm (compliant with the device dimension). The adopted analytical model has been used to simulate the responsivity of the sensor to the dielectric permittivity of the functional layer, ϵ_3, as a function of the finger width, w, and functional layer thickness, h_3. Simulation results are shown in Fig. 1b, which demonstrates that the maximum responsivity is achieved for $w = 300\ \mu m$, regardless to h_3. The IDC is realized by InkJet printing a Metalon® JS-A102A silver nanoparticle ink on a Novele™ IJ-220 substrate, through a Dimatix® Printer DMP-2850. Developed electronic exploits the capacitance to digital converter AD7746, handled by a microcontroller (Arduino UNO) to perform data acquisition with a sampling frequency of 1 Hz. A peristaltic pump has been used to convey solutions to the sensing chamber.



a) b)

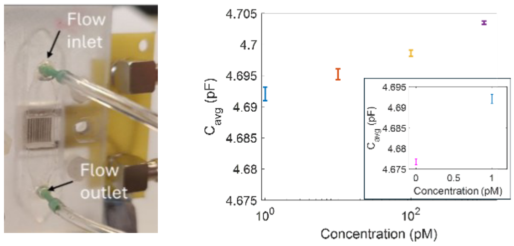
Fig. 1. a) Multilayer IDC structure; b) Simulated sensor responsivity vs track width, for different values of the functional layer thickness.

Results

To assess the behavior of the sensor, a dedicated measurement protocol has been adopted. The sensor output has been recorded during the following steps:(a) as first the microfluidic chamber has been filled with 40 mM of PBS (zero-target condition);(b) a solution of TNFα and 40 mM of PBS has been then injected in the microfluidic chamber for 10 min; (c) a flushing cycle of the functional layer with PBS, aimed at removing any exogenous compound, has been performed for 2.5 min; (d) successively, the sensor output has been acquired for at least 120 s; (e) above steps have been repeated for different analyte concentrations (1, 10, 100 and 1000 pM).

After the flushing cycle, followed by an idle 15 s time window, the average capacitance value, C_{av}, over an observation time window of 15 s has been estimated. The observation time interval has been selected as the minimum duration providing a stable averaged output.

The system response, reported in Fig. 2b, shows the mean values of the sensor output estimated through 5 consecutive observation intervals and their distribution (standard deviation), as a function of different target concentrations. The sensor responsivity estimated at [0, 1, 10, 100] pM are [15.291, 0.345, 0.038, 0.005] fF/pM, which offers suitable values, especially in the low detection range.



a) b)

Fig. 2. a) Real view of the microfluidic chamber b) Transduction diagram (the point at 0 pM is not shown due to the adopted scale). The inset shows the sensor behavior in the range [0, 1] pM.

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