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# Continuous sorting of submicron particles in a pre-analytical device based on acousto-fluidic microsystem

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**Summary:** In this work, we present a pre-analytical module based on the combination of microfluidic and electroacoustic technologies to intercept and sort submicron biological particles. It is composed by assembling a lithium niobate (LN) substrate for acoustic function and a micromachined glass substrate for microfluidic channel. The interference between the two surface acoustic waves (SAWs) generated by inter digital transducers (IDTs) create a distribution of an acoustic radiation force (ARF). This force affects differently particles depending on their physical proprieties. The device is powered by an electronic circuit with a phase shifter to move the node of the standing surface acoustic wave (SSAW) along the channel width. When the device is powered at resonance frequency, experience has shown a submicron particles alignement at a fixed position along the channel. By shifting the SSAW phase, the particles are driven to one of the three channel outlets.

**Keywords:** Acoustic particle manipulation, continuous sorting system, microfluidic MEMS, standing surface acoustic wave, acoustic radiation force, extracellular vesicles.

## 1. Introduction

Manipulating micro and nano-biological particles like extracellular vesicles (EVs), without extracting them from their media, presents a big challenge for the biological, clinical and pharmaceutical communities. The goal behind EVs manipulation is to better detect and qualify them for diagnosis purposes. Multiple technics have been used in literature to improve the efficacy of sorting particles devices. In acoustic microfluidic devices, either bulk acoustic waves (BAWs) [1] or surface acoustic waves (SAWs) [2] can be used to generate acoustic standing wave fields to trap particles realizing meso-scale particle patterning. This concept has become possible by integration, in the same chip, of acoustic and microfluidic systems. It allows to control the interaction between the acoustic wave and the submicron particles at such small scale.

In this work, we will present the design, microfabrication and characterization of a particle separation device based on the combination of microfluidic and electroacoustic systems. Our objective is to intercept and sort EVs, which represent highly important mediators in cell-to-cell communication [3] [4]. Tracking those EVs "messengers" represents an attractive way to convey fundamental information between cells.

## 2. Methodology and principals

Based on the interference of two identical SAW in the microchannel, a standing surface acoustic wave (SSAW) is accured. It generates an acoustic radiation force (ARF) that affects differently particles in fluid depending on their properties. The heavy and dense particles tend to tighten towards the nodes while the light and compressible particles remain on the antinodes [5] [6]. This allow to align the large particles in the nodes and the small ones in the anti-nodes. By shifting the nodes position, we can drive the particles to the desired channel output.

## 3. Experimentation

### 3.1. Design and fabrication process

In Fig. 1, we draw a schematic of the design of submicron particles separation micro-device. It is composed of two inter digital transducers (IDTs) deposited on a lithium niobate (LN) substrate. A microfluidic channel with six outlets is fabricated by dry etching of the glass substrate. Both LN and glass substrates are then bonded to ensure the tightness of the fluidic circuit. The two IDTs generate SSAW that create ARF inside the microchannel. The width of the

acoustic channel (50µm) was designed to match the acoustic half-wavelength. Based on the speed of sound in LN and the acoustic wavelength, the frequency of 40 MHz is used to activate the SAW transducer. In these conditions, the acoustic chip has one pressure node located at the center and two pressure antinodes located at both channel walls.

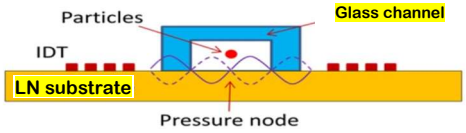


**Fig. 1.** Schematic of the acousto-fluidic device : it is composed of two IDTs patterned on LN substrate, the microchannel is realised by dry etching of a glass substrate.

### 3.2. Experimental setup

In order to characterize the microsystem we have manufactured a mechanical support (Fig. 2) allowing (i) to host the chip, (ii) ensure the six fluidic connections to a controlled injection system and (iii) electrical connection of the power supply. In Fig. 3 we represent a schematic view of the experimental setup. The device is powered by an AC sinusoidal signal generated by a, Anritsu 68147C synthesized signal generator. A power splitter divides the signal in two ways (0° and 180°) to power the two IDTs. The second one contains a continuously variable attenuator to balance the signal amplitute at the inputs of the IDTs. The first way contains an analog phase shifter to move the signal node and thus the SSAW pressure node along the channel width.

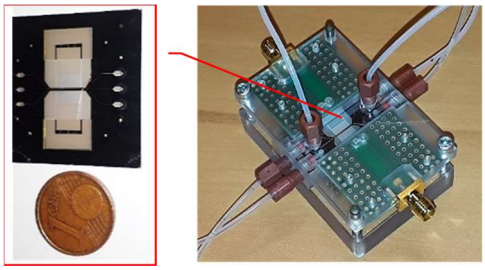

**Fig. 2.** The realized acousto-fluidic device (left) with electric and microfluidic connections (right).

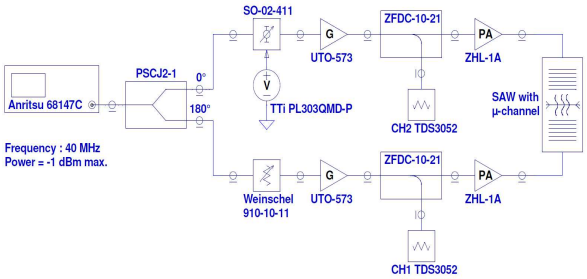


**Fig. 3.** Electronic circuit power supply.

## 4. Results and discussion

We used two sizes of synthetic fluorescent spherical particles of 480 nm and 920 nm in diameter in a circulating buffer. Initially, the 480 nm in diameter particles are randomly dispersed along the channel in both static and dynamic fluidic mode. When the power radiation is switched on, the randomly dispersed particles are aligned along the channel. By shifting the SSAW phase, we realize sorting by driving 480 nm in diameter particles to one of the three channel outlet (Fig. 4).

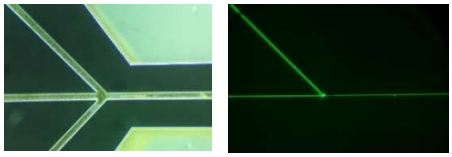

**Fig. 4.** Some results of the 480 nm in diameter particles sorting using SAW in 50 µm width microfluidic channel : fluorescence microscopy presents the capability of the device to modify the particles trajectory along the channel.

## 5. Conclusion

The main idea of this project is to be able to manipulate the nanoscale vesicles by acoustic waves. In this work, we experimentally validate the submicron particles alignment and sorting using SSAW microsystem. Experience has shown a submicron particles alignement at a fixed position along the channel. By shifting the SSAW phase, we can drive particles to one of the three channel outlet.

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