LAB-ON-A-CHIP WITH β-PVDF BASED ACOUSTIC MICROAGITATION

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Abstract: A fully-integrated lab-on-a-chip device for testing and monitoring biochemical parameters is described. The major innovation of this microdevice is the application of acoustic microagitation based on a β-PVDF piezoelectric polymer. The system parameters were optimized for an effective and rapid mixing.
Keywords: lab-on-a-chip, acoustic microagitation, PVDF.

INTRODUCTION

Microfluidic technology has become an important tool for chemical and biochemical analysis. The great interest in this technology stems from the inherent performance gains that include: reduced sample size, higher degree of integration, enhanced potential for automation and control of submicroliter volume fluids, shortened response time, potential for improved analytical performance, reduced chemicals storage, safety and reduced cost [1]. Drawbacks include resistance to flow at smaller dimensions and difficulties of mixing in the laminar flow regime [2].

In this way, various micromixing systems have been developed to overcome the limitation of mixing in microfluidic devices. The MEMS (Micro Electro Mechanical Systems) technology, such as micropumps and microvalves, is an example [3]. However, this solution increases the cost and the control system and it is also difficult to integrate in a single chip. Other approaches rely in long and complex channel topologies, that can be difficult to microfabricate and usually involve long transit and mixing times, especially when the diffusion coefficients of the fluids are small [4]. Other mechanism that has received limited attention but seems to be able to overcome this limitation is the use of acoustic streaming. This phenomenon relay on a steady flow generated by the propagation of acoustic waves in fluids. It arises from the transfer of momentum and energy of the acoustic field to the medium [5]. One possible way to achieve this effect is the use of a piezoelectric material.

In the last years, polymers have replaced traditional materials in various applications. One material that has received increased attention is the poly(vinylidene fluoride) – PVDF. It is still the polymeric material with the best electroactive properties. Moreover, it shares the piro- and piezoelectric characteristics, with an excellent combination of processability, mechanical strength, lightness, moldability and low production cost. PVDF presents an unusual polymorphism, showing four different crystalline phases. From the technological point of view, the β-phase is the one which shows better properties to be applied in sensors, actuators and transducers, due to its higher piezo-, pyro- and ferroelectric properties [6, 7].

In this way, the incorporation of a piezoelectric film, like the β-PVDF, would be an advantage in a lab-on-a-chip device, leading to an improvement in the mixing process of fluids.

DEVICE DESCRIPTION

This paper describes a fully-integrated disposable lab-on-a-chip device for biochemical analysis of biological fluids, with fluidic acoustic microagitation based on the piezoelectric β-PVDF polymer deposited underneath the microfluidic die (Figure 1). It is a point-of-care system with interesting features such as portability, low cost, disposability and automatic operation. It uses optical absorption spectrophotometry as the analytical measurement technique, which implies the use of transparent conductive oxide as the electrodes, deposited on both sides of the β-PVDF film. The enhancement of mixing and reaction time was studied for different amplitude and frequency signals applied to the electrical contacts of the β-PVDF film.
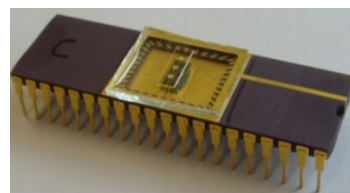

Figure 1. Picture of the device with the microfluidic die on top of the CMOS detection die.

Biodevice Operation

The lab-on-a-chip device can be divided into two main parts: the microfluidic die fabricated using a photoplastic material, like the SU-8, and the detection die fabricated in CMOS technology.

The first die is composed by three cuvettes: one for the chemical reagent, in order to obtain the baseline reference; other for the mixture of the sample with the reagent, to perform the analysis of the colored mixed solution; and a third one with the standard sample with a well-know concentration of the biochemical parameter that is being analyzed, for the calibration of the biochemical parameter concentration. The piezoelectric β-PVDF and the respective electrodes are deposited underneath the reaction chamber to produce the needed acoustic vibration, when activated by an electrical alternating signal.

On the other hand, the detection die includes the photodetectors, the readout electronics and the electronics for controlling the microagitation generated by the piezoelectric film. Moreover, above the photodetectors, several high-selective band-pass optical filters are deposited by Ion Beam Deposition. They select the wavelength according to the maximum absorption of the several biomolecules to be analyzed. The system detects simultaneously the three optical signals of the three microfluidic cuvettes.

Piezoelectric β-PVDF polymer

In addition to the excellent characteristics referred previously, PVDF has a set of properties very attractive when incorporated in microfluidic devices. It has low acoustic and mechanical impedance, important for the propagation of acoustic waves in fluids, as it is the purpose of this study. Despite ceramic materials have usually higher electromechanical coupling coefficients, comparatively to polymeric materials, if the sound waves are propagated through fluids or plastic, most of the acoustic energy is reflected in the boundary layer between the piezoelectric material and the propagation medium. Due to the high acoustic impedance of the ceramic comparatively to fluids or plastics, the reflection coefficient on the boundary layer is above 90%. In this way, only a fraction of the acoustic energy generated by the piezoelectric element is transferred to the propagation medium [8].

Other notable feature of the PVDF is its transparency, essential as the film is deposited in the reaction chamber in which the analytical measurement is performed by spectrophotometry. So, both PVDF and the corresponding electrodes must be transparent to the visible light. Therefore, transparent conductive oxides such as ITO (Indium Tin Oxide) or AZO (Aluminium doped Zinc Oxide) must be used [9].

Also, PVDF is highly resistant to chemical agent and aging. While ceramic materials break easily and have hard and dense structures, PVDF is flexible, has low density and can be easily produced into thin films [6].

Acoustic Microagitation

The phenomenon of acoustic streaming was first analyzed in detail by Eckart in 1948 [10] and overviewed by Nyborg in 1965 [11]. The acoustic streaming can be used in various applications [5]. In this work, it is applied for chemical or pharmaceutical purpose as liquid mixing. In this way, acoustic streaming is generated by the acoustic waves produced when an electrical signal is applied to the contacts of a piezoelectric film. Thus, the absorption of the acoustic waves by the fluid results in a radiation pressure in the fluid itself along the direction of the acoustic attenuation and propagation (Figure 2) [2, 5]. This absorption and the consequently originated motion cause the acoustic microagitation, improving the mixture and reaction of fluids.
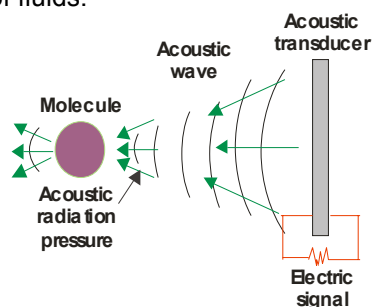

Figure 2. Generation of acoustic waves for fluids microagitation.

Mathematically, the acoustic intensity I decay exponentially, generating a force/pressure F on the fluid within a reservoir or channel,

$$F = \frac{I}{c \times l_{\mu}} e^{-x/l_{\mu}} \quad , \qquad (1)$$

Where c is the sound velocity in the fluid, l_{μ} is the absorption length in the fluid and x is the distance from the acoustic film [2].

EXPERIMENTAL PROCEDURES AND RESULTS

The study of the acoustic microagitation technique efficiency in the mixture of fluids was carried out using a Diagnostic kit containing a proper reagent and a standard of urine with 5 mg/dL of uric acid concentration [12]. The reaction produces a pink color with a maximum absorption at 550 nm, monitored by optical absorption spectrophotometry (Shimadzu UV-3101PC). Microagitation was studied for various frequencies and amplitudes of the electrical signal applied to the aluminium electrical contacts of a 110 μm thick β-PVDF.

The system was calibrated for an absorbance of 0 a.u. filling the cuvette with deionized water. The evolution of the reaction was studied up to a maximum time of 20 minutes, which is the time value of the complete mixture without oscillation.

The results obtained for the several frequencies are shown in Figure 3. The signal applied to the electrical contacts of the β-PVDF film is sinusoidal and has an amplitude of 10 V.
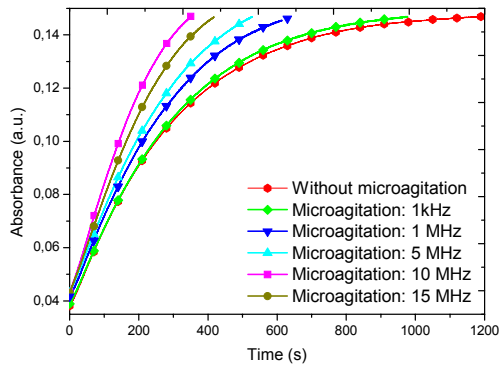

Figure 3. Absorbance as function of time for a signal of 10 V at several frequencies.

All the curves show similar behavior, being the main difference the time at which the complete mixture is completed. This time is related directly with the reaction velocity presented by the curves slop, superior at the beginning of the reaction, and decreasing up to the absorbance of 0.148 a.u., which corresponds to the absorbance value at 20 minutes without microagitation.

The mixture is faster with the implementation of acoustic microagitation for all tested frequency, being the time necessary to obtain a complete mixture only two sevenths for a resonance frequency of 10 MHz (315 s), comparatively to the mixing time without microagitation (1200 s). These results are in agreement with the theoretical idea that a maximum transmission of the acoustic waves occur at the resonance frequency of the piezoelectric film [13].

With these results, it was created a polynomial fitting of the mixture time as a function of the signal frequency. This model is the most appropriate in this case, obtaining a correlation coefficient of approximately 0.97. This curve allows the determination of the mixing time for any frequency in the range from 0 to 15 MHz, according to the parameters presented in Table 1.
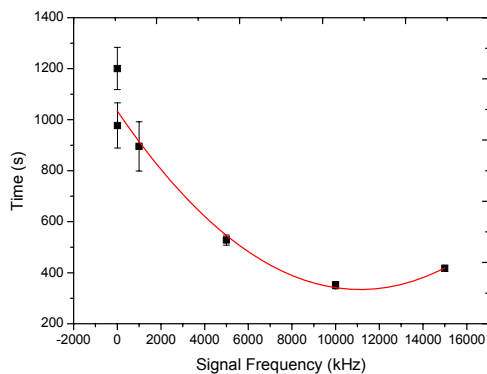

Figure 4. Mixing time as a function of frequency for a signal of 10 V.

Table 1. Variables of the polynomial fitting obtained from Figure 4.

Equation	$y = B_1 x^1 + B_2 x^2 + Intercept$		
Adj. R-Square	0,97417		
	Variables	Value	Standard Error
Time	Intercept	1076,755	43,795
	B_1	-0,142	0,001
	B_2	6,553E-6	4,893E-7

Then, the microagitation was studied for various amplitudes of the signal at the resonance frequency of 10 MHz. The results are shown in the Figure 5.
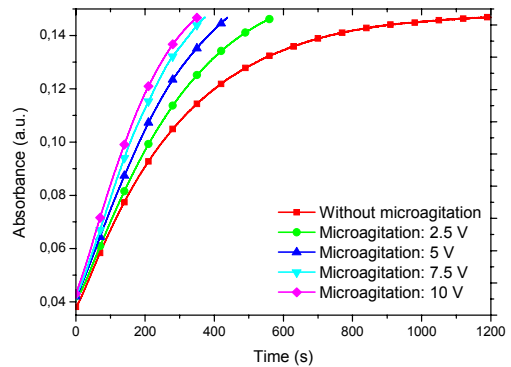

Figure 5. Absorbance as function of time for a 10 MHz frequency signal with various amplitudes.

In this case, the complete mixture is achieved faster with the higher amplitude: 351 s at 10 V vs 1200 s without oscillation. For this application in CMOS technology, an amplitude of 5 V is used. For this signal, the mixture time is achieved in approximately three eights (438 s) of the time without microagitation (1200 s).

Figure 6 represents the evolution of the mixing time as a function of the amplitude of the signal with a 10 MHz frequency applied to the contacts of the 110 µm thick β-PVDF. In this case, an exponential decay behavior was observed and fitted. The obtained correlation coefficient was approximately 0.96. The equation and fitting parameters are described in Table 2. In this way, for any amplitude in the range of 0-10 V, it is possible to determine the mixing time.
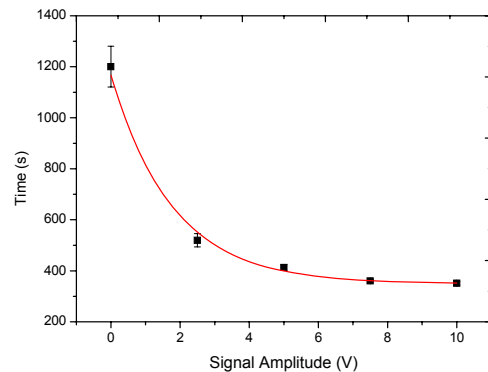

Figure 6. Mixing time as function of the signal amplitude at a frequency of 10 MHz.

Table 2. Variables of the exponential decay fitting obtained from Figure 6.

Equation	$y = A_1 e^{-(x/t_1)} + y_0$		
Adj. R-Square	0,96004		
	Variables	Value	Standard Error
Time	y_0	348,767	6,946
	A_1	817,285	98,585
	t_1	1,792	0,213

CONCLUSION

The application of acoustic microagitation improves mixing and reaction time making this technique suitable for improving microfuidic reaction times. Experimental results show best results with an electrical signal at the resonance frequency of the β-PVDF piezoelectric film. In the case of the amplitude signal, the higher the voltage, the shorter the time of mixture.

In this way, given the characteristics required for the type of application reported here, acoustic microagitation becomes a preferred technique for effective mixing, decreasing the size and complexity of microfluidic devices.

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