Development of a Microfluidic pH control system using LTCC technology integrated with an ISFET sensor

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Abstract

Measurement and control of pH has many applications in chemical analysis and processes. Nowadays many efforts are done to make the analysis not only in static process, but also in dynamics systems where the flows are in movement. The integration of pH sensors in a microfluidic system offers advantages such as low reagents consume and high chemical reactions control and could be a great tool to control some processes such as encapsulating particles for drug delivery. In this work we present the preliminary studies of a pH control system integrated in a microfluidic device. The microfluidic systems were fabricated in LTCC co-fired ceramics with a square-wave 3D micromixer design with the purpose to mix different fluids. The 3D micromixer have cross-sections with 500 x 500 µm, an aperture to ISFET sensor and Ag/PdCl pseudo - electrode reference integrated at the same device. Besides were developed an electrical interface to measure and change the pH of the fluids mixed, composed by valves, electrical circuits and software to allow the fluids entrance. With this system were possible to modify the pH substance from 6 to 4, and the results show the viability of microfluidic system with ISFET integration and will help us in the next studies to produce particle with controlled pH.

Key words: micromixer, microchannel, pH control, Ag/PdCl reference electrode, ISFET

Introduction

Microfluidic micromixers offer many advantages such as portability, reduction of energy consumption and material (1). Besides they offer great stability in emulsion production and are useful to obtain mixtures with rapid time response. Different materials are well established to produce microfluidic devices, however LTCC (Low Temperture Co-fired Ceramic) technology offers advantages such as the possibility to manufacture 3D geometries, compatibility with thick film technology and others microfabrication process (2,3).

The integration of microfluidic devices with different sensors are reported in the literature and has interesting applications in miniaturized chemical analysis and chemical processes. The use of selective membranes or electrical sensors are reported allowing fast analysis in situ detecting dangerous species in drain water, in medical and cosmetic products, etc (4,5,6).

The ISFET, ion selective field effect transistor, are used to determine the pH of a solution through electrical measurements. With this kind of sensor it was possible to detect potassium, calcium and chlorine ions in blood samples, detection of urea and pH measures of rain water, important to pollution control (6,7, 8,9).

The integration of ion selective field effect transistors (ISFET) for pH measurement with microfluidic devices has been done in polymeric devices with Ag/AgCl reference electrode, with the purpose to detect the presence of dangerous species such as anionic and cationic surfactant in dental rinses and water environment (10,11). In that work, the authors compared the measures obtained in a batch system with the measures obtained in the microfluidic flow. The ISFET sensor in the microfluidic flow offer the same results obtained in batch analysis, with stability of potential response.

In this work we present preliminary results on the development of a microfluidic system that will be able to measure and control in flow conditions the pH of a desired solution. Initially, the pH control of a fluid was implemented in an open loop system that was constituted by a micromixer, a commercial pH sensor, valves and an electrical interface for PWM control. The PWM circuit controls the opening and closing valve by modifying the duty cycle, Acid or base is introduced into micromixer in different portions depending on the duty cycle value. The next step was the introduction of the ISFET sensor in the micromixer to have real time pH measurement.

These preliminary results are addressed to evaluate the feasibility of such combination and the encapsulation requirements for the final goal which is the integration of a single ISFET in the LTCC micromixer chip. The proposed application of this system is to be applied for particles production using complex coacervation, where droplets are coated by a polymer in special conditions that includes pH control.

Materials and Experimental

Firstly the study of pH control was made using an open loop system, without ISFET. This system was constituted by a micromixer patterned using a CO_2 laser (Versalaser – Universal Laser) and typical LTCC 951 (DuPont) sintering process.

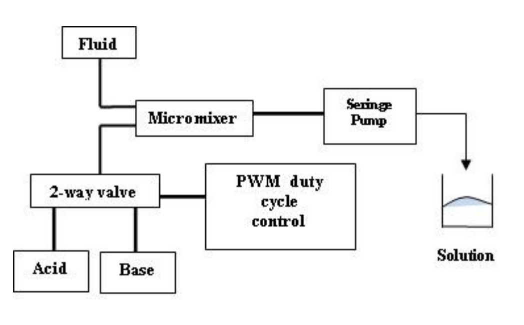


Figure 1a. PWM duty cycle control

The micromixer has 3D serpentine shape, with cross sections of 500µm x 500 µm using a laser velocity of 5% and density potency of 10%. Control of the entrance of fluids into the micromixer was made using a 2-way valve (BIO-CHEM) with PWM duty cycle control. The complete system scheme is shown in Figure 1a and 1b. Measurements were done using different concentrations of HCl solution with the purpose to modify solution pH. The fluids are withdrawed by suction via syringe pumps.

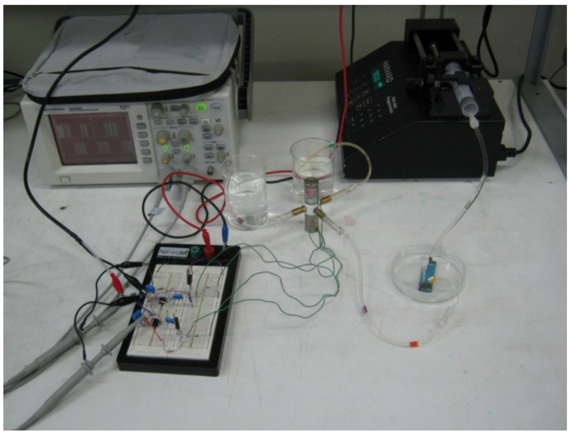


Figure 1b. PWM duty cycle control experimental arrangement

In the second phase an ISFET sensor fabricated in IMB-Spain was introduced to obtain pH signal. An initial attempt to integrate ISFET to a micromixer presented problems, like bubble generation, so we decided to use a separated ISFET. The micromixer geometry was modified with an aperture for the fluid contact with the ISFET sensor. also, in the same device was introduced an Ag/Pd (DuPont-9061) reference electrode fabricated by screen printing. A chloride electrodeposition was done using a galvanostat circuit (LSI-POLI). In this process we used a potential of 0,375 mV and a current of 100 mA cm^{-2} in HCl solution (0.1 mol). In Figure 2 is shown the galvanostat circuit used for this process ([12],[13].

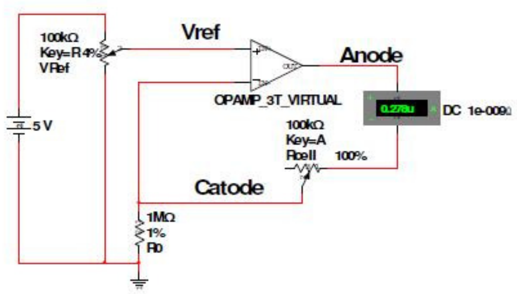


Figure 2. Galvanostat circuit

A PMMA base is designed in a CNC machine (Roland MDX- 40) to support the pre-encapsulated ISFET. The complete arrangement of the micromixer with the integrated ISFET is shown in Figure 3.

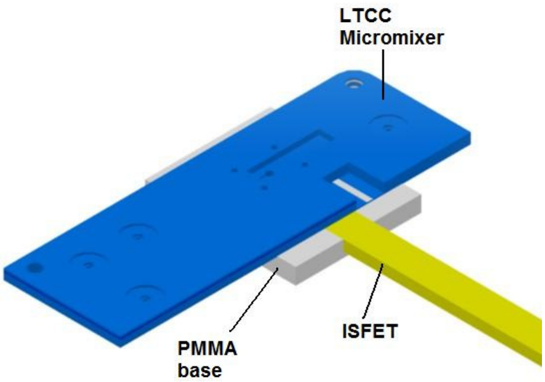


Figure 3. LTCC micromixer with the ISFET

The Figure 4 is shown the micromixer geometry design which was made in different layers to form a 3D device, and we can see the correct position of ISFET and Ag/PdCl reference electrode.

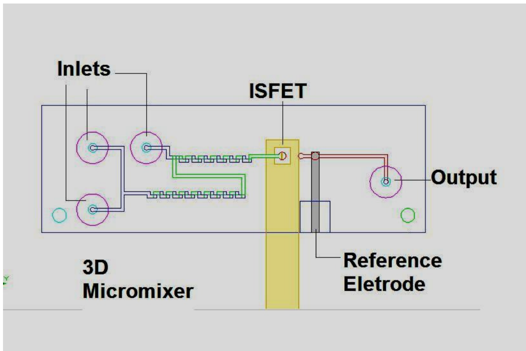


Figure 4 – 3D micromixer internal design

The 2-Way (BIOLAB) valve works with software developed with LabView. A square wave with 2Hz was applied in each valve and the software changes the duty cycle depending on the pH measurement. To modify the duty cycle the VI operate with the equation 1:

$$Duty_f = Duty_{inicial} \pm (pH_{measured} - pH_{desired}) * 0,5 * 10 \qquad [1]$$

In our case, the $pH_{desired}$ is in the range of 4 – 4,5 and $Duty_{inicial}$ was 50%. The VI frontal panel and diagram block with the control in detail are presented in Figure 5 a and 5b.

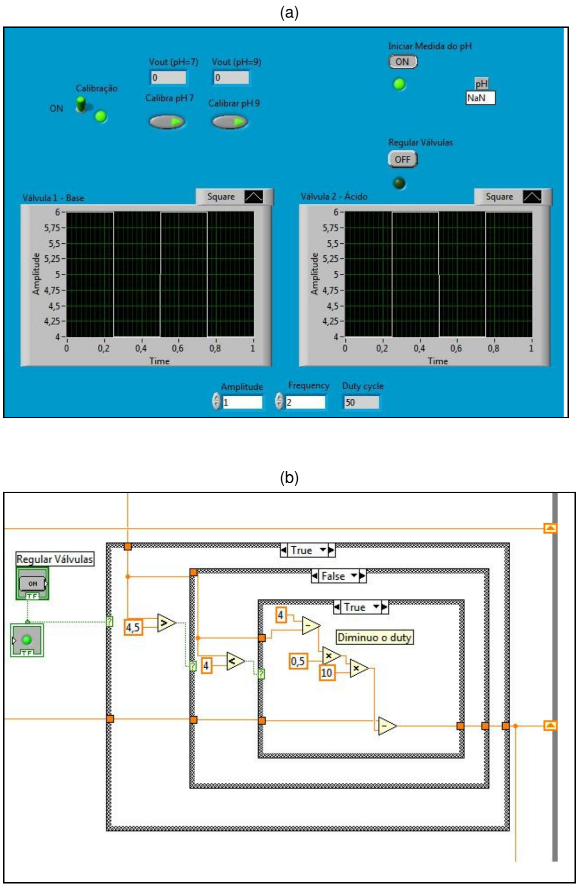


Figure 5. Valve control VI.

Results

PWM tests

The first test was done with the purpose to study the control of the pH using valves to introduce more acid or basic fluids in an ordinary solution. The pH was measured in a batch way. It was introduced deionized water with pH of 6,75 and by changing the valves duty cycle we could change the solution ph as depicted in figure 6.

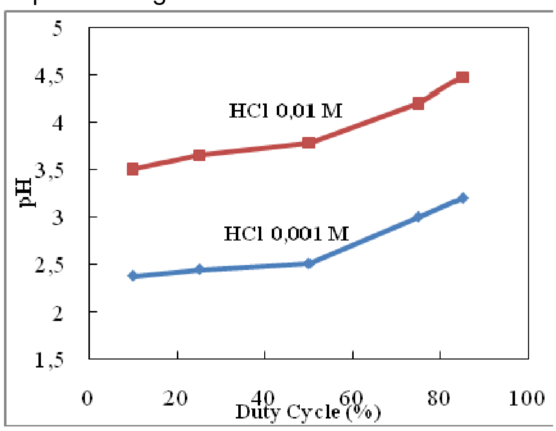


Figure 6. Graphic of pH versus duty cycle variation which indicates the activation period of 2-way valve.

For example, when the duty cycle is 50%, the 2-way valve maintain acid and base entering with the same proportion or, for a value of 80%, the base valve was active in a more time than the acid valve. In this case the purpose was to modify the pH solution (pH 6,75) to a pH range of 4-4,5 introducing different concentrations of HCl (0,01 – 0,001 M). By regulating the duty cycle it was possible to reduce the solution's pH and with a less concentrated solution (HCl 0,001M) it was possible to obtain a better control in a desired range. With this result we switch to the other step, where the measurement of pH was done in microfluidic system channels.

ISFET integration in microfluidic device

The initial integration of ISFET chip within the microfluidic device is shown in Figure 7.

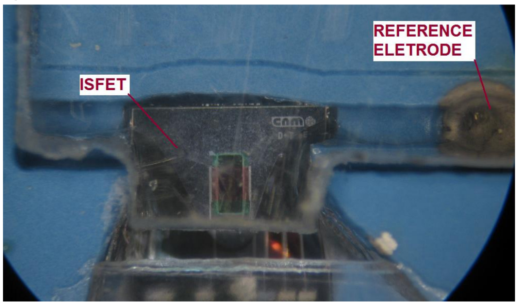


Figure 7. First ISFET integration in microfluidic device

However, generation of bubbles in microchannels causes Vg instabilities. Besides, this arrangement causes difficulties to clean the ISFET inside the micromixer.

To solve this problem a new arrangement (Fig 3) was proposed. The Figure 9 presents the actual arrangement for testing of 3D micromixer with ISFET sensor.

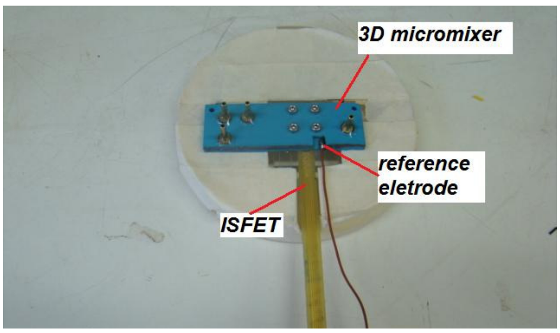
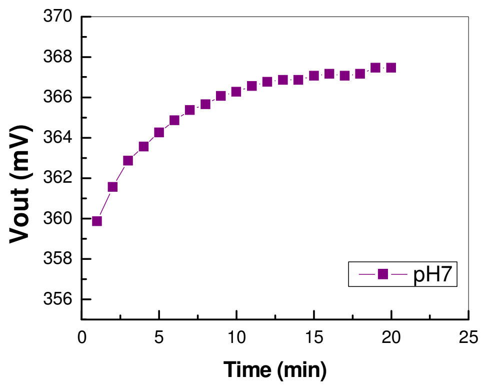


Figure 9. Arrangement used for testing 3D micromixer with ISFET sensor

The Figure 10 presents the Vg in contiuous flow (4 mL/min) response along the time for buffers solution with pH 7 and 9 . The results presents a drift of (0,71 mV/h), but after 10 min the system was stabilized.

(a)



(b)

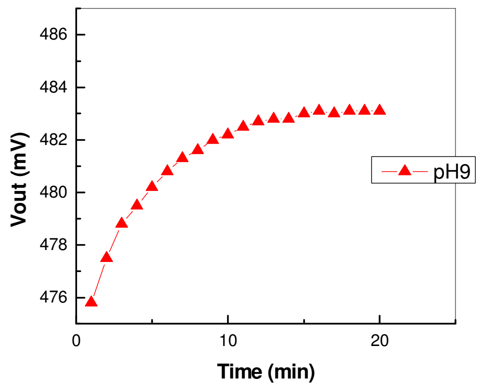


Figure 10. ISFET Vg variation along the time for a buffer solution pH 7

In the table I is presented the results for ph control with the microfluidic system using deionized water as basic solution and an HCl solution in low concentration (0,001 mol – pH 3,35) as control solution.

Table I – pH measured values for duty cycle variation

Duty Cycle (%)	Vout (mV)	pH
50	64,82 ± 2	3,8
51	73,49 ± 2	3,96
52,7	82,16 ± 2	4,12
51,9	79,99 ± 2	4,08
51,35	76,74 ± 2	4,02

The results show that the VI measures and compares the pH values, and by changing the duty cycle it possible to set the pH to a desired value.

For better results we should work with acid or base solutions in low concentrations to modify the pH of a solution.

A PID controller must be introduced in VI in order to allow management of Vg response along the time. Besides, the microfluidic system must be improved also with the purpose to integrate the ISFET chip to the LTCC substrate. These steps are in development and will be publish in future works.

Conclusion

In the present work we develop a continuous flow pH measurement and control of a liquid solution in a micromixer. It was evaluated the possibility to modify the pH of a desired solution by opening and closing valves with acid and basic control solutions. The complete integration of ISFET sensor in a microfluidic device is complex and present some instabilities and difficulties to prevent leakages. In despite of these difficulties we conclude that is possible to measure and modify the pH of a solution in a system in continuous flow. This work are still in progress and new results will be published in the future.

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