LIQUID MIXING STUDIES WITH AN INTEGRATED MIXER/VALVE

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Abstract

This work presents the design, fabrication, and testing of an integrated mixer/valve and a method for determining its mixing performance. The method correlates the mixing time to a quantitatively measurable observable. We present modeling and experimental results using this method.

1. Introduction

Microfabricated systems for chemical and biological analysis often include mixers for sample preparation. A key issue for all mixing subsystems is the measurement of their mixing performance - the mixing time.

We have designed and fabricated a microfabricated liquid mixer/valve as a test vehicle with which to conduct mixing studies. In addition, we have developed a method using the pH dependence of fluorescent dyes to correlate mixing length with a quantitatively measurable observable.

2. Device Structure

The structure of the integrated liquid mixer/valve is shown in Figure 1. The liquid mixer/valve consists of a two wafers: 1) a lower silicon wafer with a cantilever-plate flapper valve and fluid ports, and 2) an upper glass wafer which contains the fluidic channel. The inset of Figure 1 reveals a blow-up of the reagent-inlet port area. The cantilever-plate flapper valve is shown atop the reagent inlet port. Typical device dimensions are shown in Figure 2.

The schematic operation of the liquid mixer/valve is shown in Figure 3. At time zero, sample flows down the channel (Fig. 3a). When it is time to mix a reagent with the sample,

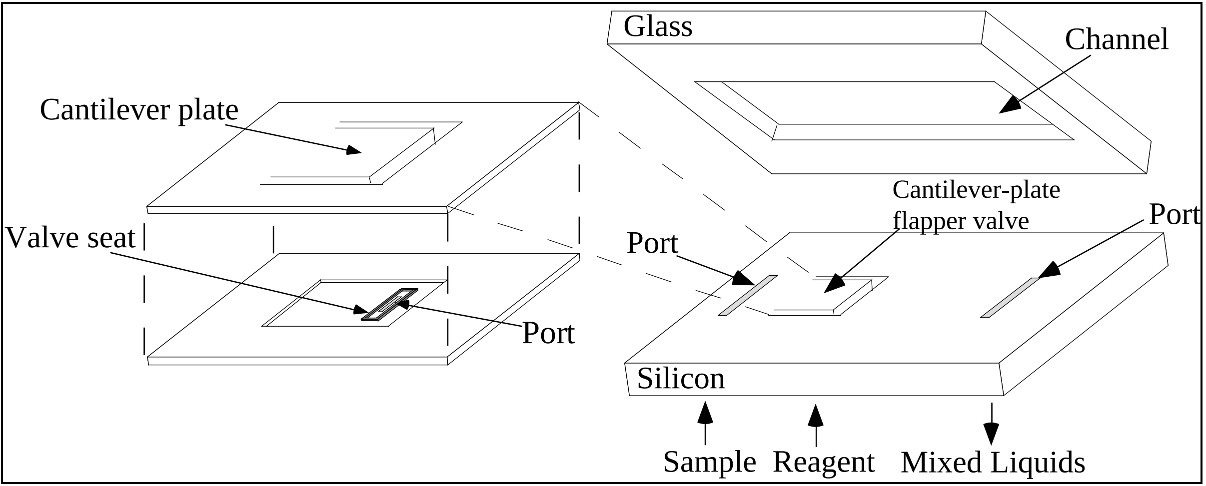
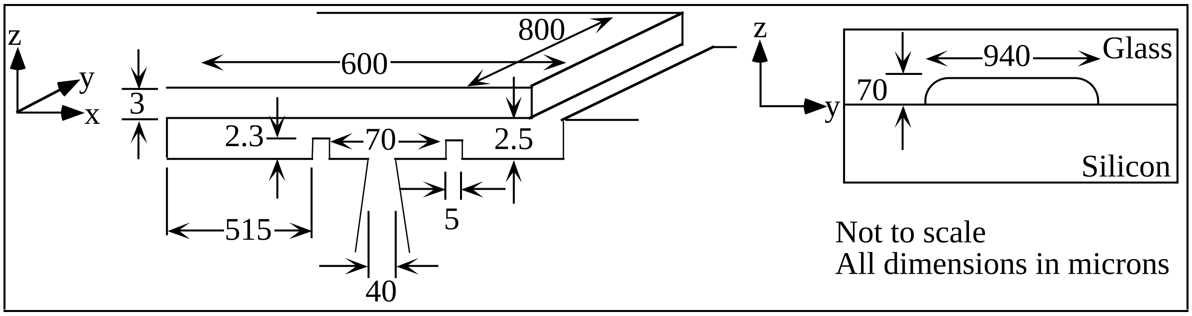


Figure 1: Schematic of integrated liquid mixer/valve.



Not to scale
All dimensions in microns

Figure 2: Dimensions of the cantilever-plate flapper valve and glass channel.

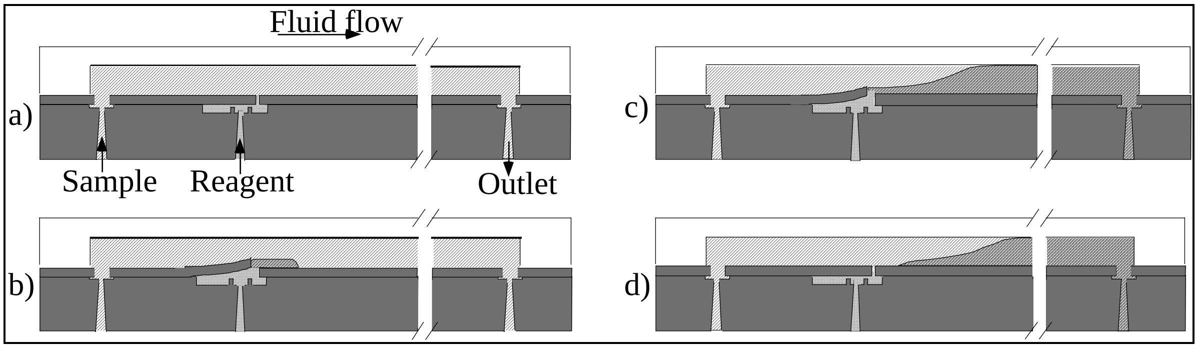


Figure 3: Operation of the liquid mixer/valve

the reagent is injected into the sample stream (Fig. 3b), and the two mix diffusively in a few seconds (Fig. 3c). After the desired section of sample is prepared, the reagent is shut off (Fig. 3d) and the mixed sample and reagent flow down the channel and out of the mixer/valve.

The liquid mixer/valve is controlled by varying the reagent and sample flow rates. The relative flow rates in turn determine the mixing ratio and the pressures at the reagent and sample ports; the cantilever plate aligns itself accordingly. Thus, the device is passively pressure-actuated.

3. Device Fabrication

A simplified fabrication process flow is shown in Figure 4. Starting with 4” silicon wafers, a thin oxide is grown and the valve seat is defined and etched through the oxide (Fig. 4a) and 2.5 μm into the silicon (Fig. 4b). Following this, the fluidic ports are patterned and etched through the wafer using a deep reactive-ion etching system (Fig. 4c). Next, the wafers are cleaned and fusion bonded to SOI (silicon-on-insulator) wafers with a 3 μm silicon overlayer (Fig. 4d). The cantilever-plate will be formed from this overlayer. Next, the bulk silicon from the top side of the bonded pair is removed in KOH (Fig. 4e). After the buried oxide is removed, the cantilever plate is patterned and etched (Fig. 4f). It is released from the

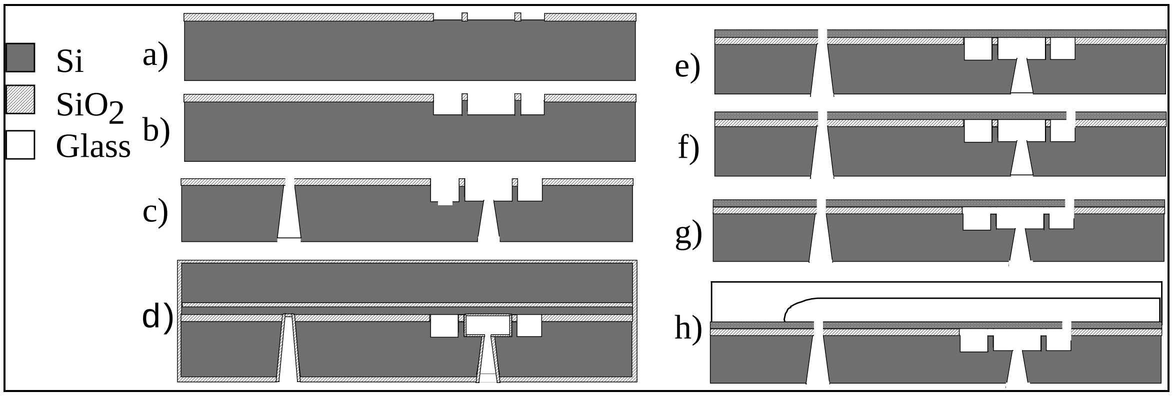


Figure 4: Fabrication process flow.

substrate by removing the thin holding oxide with BOE (buffered oxide etch) (Fig. 4g). Concurrently, channels are patterned in glass wafers using a three-part masking scheme (see for example [1]). Finally, the two wafers are anodically bonded together and diced (Fig. 4h).

4. Mixing Length Measurements

The impetus for developing a method for measuring the mixing length becomes apparent when one considers that the lamination in this device occurs in the vertical direction. Thus, the demarcation between two mixing liquids will not be easily observable from the top of the device. To this end, we have adapted work done on measuring mixing in turbulent flows [2,3]. This method uses the fact that the fluorescence quantum yield of the fluorescent dye fluorescein is pH-dependent. In a basic medium (pH>10), the fluorescence quantum yield of fluorescein approaches 1.0 - the fluorescence is on. In acidic media (pH<3), the fluorescence quantum yield of fluorescein approaches ~0.3 - the fluorescence is off.

With these two facts, the following experiment can be envisioned. If fluorescein in a basic solution is mixed with an acidic solution, such that the final solution is acidic, then the fluorescein will go from being ON to being OFF. Locating the point where this transition occurs will locate the point where the pH is approximately neutral. The length from the onset of mixing to this point is dubbed the fluorescence turn-off length (FTOL). If a model is formed that can correlate the FTOL with a simulated mixing length, then we can infer the mixing length by measuring the fluorescence turn-off length.

It is necessary to point out and to emphasize that the FTOL is NOT the same as the mixing length. The fluorescence turn-off length is a measure of the pH of the solution. The pH is not linearly related to the proton concentration - rather, it is the logarithm of the proton concentration. In addition, the diffusivities of the acid, base, and fluorescein are different, and thus the acid/base will not mix in the same amount of time as the fluorescein.

In order to match experimental data with a model, simulations from two slightly different models were run using Matlab. The simulations model three-component time-dependent diffusion with reaction. The simulations start with the initial concentration profiles for the hydrogen ions (H^+), hydroxyl groups (OH^-), and fluorescein. They model the time evolution of the H^+ and OH^- including reaction. From the concentration profiles of the H^+ and OH^-, the pH of the solution is calculated for all time. Next, the fluorescence quantum yield of fluorescein is calculated from the pH using data from the literature [4]. Finally, the fluorescein concentration for all time is calculated using an analytical formula. It is integrated along the height of the channel along with its fluorescence quantum yield to give the simulated intensity profile, from which the FTOL can be extracted.

The first model (Model1) calculates the initial sample and reagent heights in the channel from the mixing ratio, and uses an overall average flow velocity to compute the distance traveled versus time. The second model (Model2) uses the plate deflection derived from simulations to predict the sample and reagent heights in the channel, and calculates the reagent flowrate from the geometry of the valve-opening. These two models can be seen as extremes of the actual situation, and thus, the experimental data should fit in between them.

Experimentally derived and simulated turn-off lengths are shown in Figure 5, along with extracted mixing times and lengths for some representative flow conditions in Figure 6. The pressures necessary to actuate these flowrates vary up to 0.5 psi, depending on flow conditions. As can be seen, the fluorescence turn-off lengths for the data lie in-between the two extreme simulations. Some of the difference (but not all) between the data and models is due to imprecision in the diffusivities of the analytes.

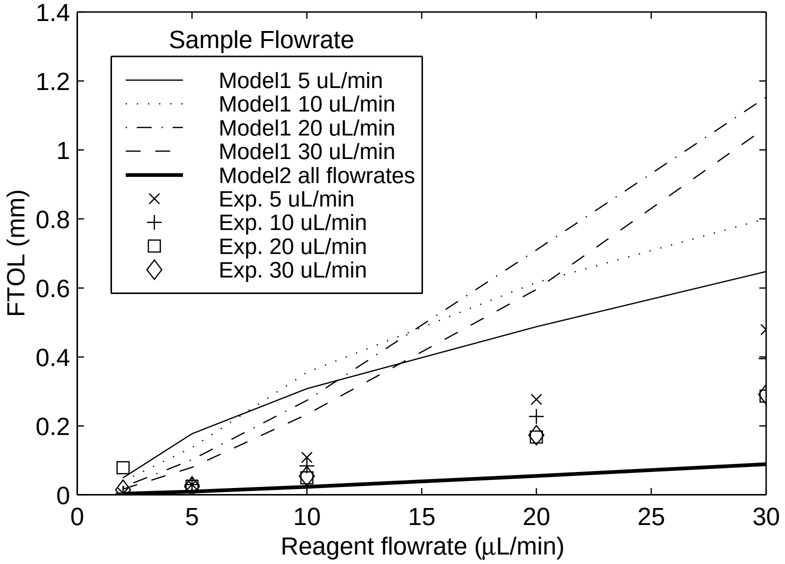


Figure 5: Comparison of simulated and experimental FTOLs.

Flowrates		Extracted Quantities	
Sample (μL/ min)	Reagent (μL/ min)	Mixing Time (s)	Mixing Length (mm)
5	5	3.7	9.4
5	30	2.1	18.6
30	5	4.1	36.3
30	30	3.7	55.5

Figure 6: Representative extracted mixing lengths and mixing times.

What the simulations and experiments show is that the actual mixing situation in the liquid mixer/valve may be better than pure diffusional mixing. This would be expected, since the flap creates a free-shear layer which can be unstable and can shed vortices, enhancing mixing. The results also show that diffusion is the predominant mixing effect. Lastly, the results emphasize that the fluorescence-turn off length is not the same as the mixing length.

5. Conclusions

This work has three important results. First, we have designed and fabricated an integrated mixer/valve which allows for non-continuous mixing of two liquids. Second, we have shown that the FTOL, which is a measure of where the acid and base neutralize each other, is different from the mixing length; it can be much longer or shorter than the mixing length, depending on the flow conditions. Third, we have provided experiments and simulations as a step towards correlating this observable with the mixing time, which cannot be directly measured in many situations.

Acknowledgments

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