Modular Front-End Sample Preparation Microdevice for Integrated Hydrophobic Protein Separation System

Environmental and clinical sample preparation is one of the most critical steps in biological and chemical detection. Although biological and chemical assays are becoming increasingly more sensitive, absolute detection limitations are often a function of sample background contaminant concentrations. Purifying sample streams prior to detection will greatly improve the sensitivity and performance of the assays. Separating the various components present in the sample, such as molecules, lysed cell matter, and solutes, into hydrophilic and hydrophobic fractions will provide a first order purification. A device capable of separating constituents based on hydrophobicity must be able to mix and separate immiscible fluids as well as interface with subsequent assay/detection devices. This project addresses these technical challenges.

Figure 1. Wafer-level photograph of completed devices.

Project Goals

The goal of this project is to improve microscale-mixing capabilities of immiscible fluids. To achieve this, a novel microelectromechanical system (MEMS) vertical mixer is fabricated and demonstrated. The system includes a multiplexed fluid inlet system, MEMS vertical vortex mixer, and fluidic I/O packaging.

Relevance to LLNL Mission

Work on this device advances several processing techniques and packaging to extend LLNL capabilities in areas such as silicon/glass anodic bonding, non-conventional glass etching, immiscible fluid mixing and integrated vertical microfluidic systems. The project will have a significant technological impact on the instrumentation community and will enhance the state of the art in biological and chemical detection, part of LLNL's national security mission.

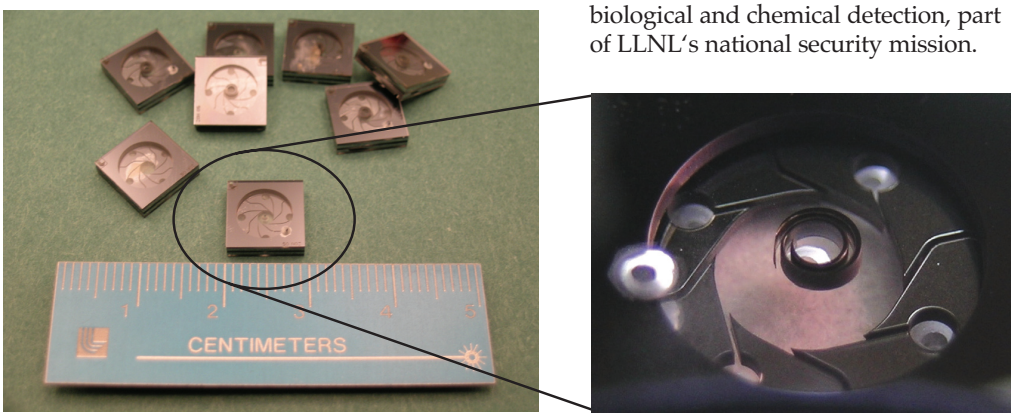

Figure 2. Final five-layer device with close up of final out-of plane 5-layer mixer.

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FY2005 Accomplishments and Results

During FY2005, we reached milestones that include novel five-/seven-layer silicon/glass anodic bonding, specialized glass etching, and immiscible-fluid mixing. An overarching technical challenge was to construct a multilayer (> 4) glass/silicon structure.

Demonstration of novel processing approaches allowed for the bonding of multiple multilayered sets, such as bonding a three-layered bonded set (glass/silicon/glass) to a two-layered bonded set (Fig. 1). Fracture testing of the bond demonstrated that the glass/silicon interface was stronger than the Pyrex glass, confirming the reliability of the novel anodic bond process.

A five-layer prototype was built using acetate overlay masks for photolithography as an attempt to reduce fabrication costs and prototyping time. The devices suffered from inadequate photolithographic resolution due to UV masking limitations, causing irregular silicon structures and fluid flow. Shifting to laser-cut polymer masking materials for glass etching and conventional glass/chrome masks for silicon etching eliminated these problems (see Figs. 2 and 3).

It is now possible to fabricate an out-of-plane modularized, multilayered, glass/silicon microdevice. Each layer performs a distinct function; therefore, simply adding additional layers can extend the functionality of the device. The packaging uses O-ring compression fitting to introduce and extract fluids to/from the device, eliminating the necessity for glue or epoxy to connect off-chip fluidic I/O (Fig. 4).

A key element of the micromixer is the ability for direct visual diagnostics during mixing. The glass/silicon structure provides a glass-viewing window of the emulsion chamber and linear-mixing channel, which affords visual confirmation of mixing (in conjunction with fluorescent/colored dyes) prior to chemical analysis of solute concentrations.

A multilayer, modular, fluidic micromixer device was fabricated and tested as a first order sample preparation/purification bio-instrument. Preliminary results of the device demonstrate good mixing of aqueous solutions (aqueous color dye solution and plain DI water) for modest-pulsed inlet pressures (~30 psi).

Related References

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2. Kirner, T., *et al.*, "Static Micromixers for Modular Chip Reactor Arrangements in Two-Step Reactions and Photochemical Activated Processes," *Chemical Engineering Journal* **101**, pp. 65-74, 2004.
3. Lemenand, T., *et al.*, "Droplets Formation in Turbulent Mixing of Two Immiscible Fluids in a New Type of Mixer," *International Journal of Multiphase Flow* **29**, pp. 813-840, 2003.

(a) (b)

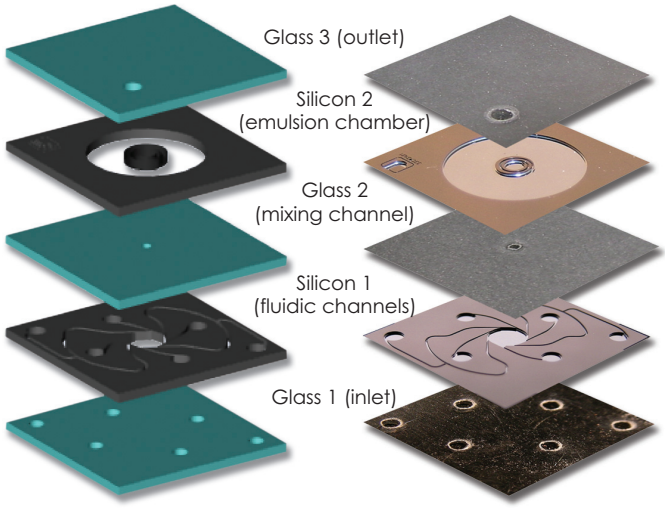

Figure 3. (a) Composite diagram and (b) photograph of five-layer mixer.

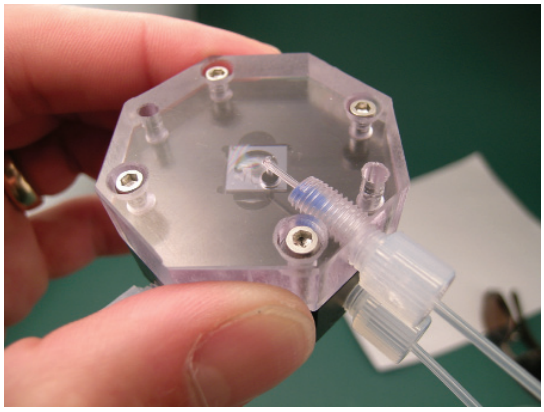

Figure 4. Photograph of custom fluidic I/O packaging with device at center.