# A MICROFLUIDIC AUTOSAMPLER WITH TRUE TEFLON VALVES: DESIGN AND APPLICATION TO SUSPENDED MICROCHANNEL RESONATOR MASS SENSORS

**William H. Grover[1], Yao-Chung Weng[2], and Scott R. Manalis[1,3]**

*[1]Biological Engineering Division, Massachusetts Institute of Technology, USA*
*[2]Computational and Systems Biology Initiative, Massachusetts Institute of Technology, USA*
*[3]Department of Mechanical Engineering, Massachusetts Institute of Technology, USA*

## ABSTRACT

We present an "autosampler chip," a microfluidic replacement for a conventional autosampler instrument. By actuating on-chip valves, nanoliter-scale volumes can be routed or pumped between any of the on-chip fluid connections. The valves utilize an inexpensive Teflon film that is impervious to virtually all chemicals. We also interface the autosampler chip to a suspended microchannel resonator (SMR) mass sensor. The autosampler chip performs all fluidic operations involved in building a complex multilayer inside the SMR, detecting protein binding, and stripping away the multilayer using "piranha" in preparation for the next measurement. This is one of many applications in which the autosampler chip could replace bulky and costly sample handling hardware.

**Keywords: Autosampler, Teflon, valves, suspended microchannel resonator**

## 1. INTRODUCTION

The conventional autosampler instrument is a ubiquitous "front end" in many biological and chemical assays. Benchtop autosamplers and other robotic sample handlers typically include multiple sample vials or microtiter well plates, machinery for choosing samples, pumps for dispensing known amounts of solution, and mechanisms for rinsing their internal volumes. While useful as generic tools for fluid manipulation in many different contexts, autosamplers are too large, expensive, and delicate for many point-of-care and field applications.

We present here a complete microfluidic replacement for a conventional autosampler. For maximum compatibility with a variety of chemical and biological systems, our autosampler chip is fabricated in glass and uses a chemically-inert Teflon valve membrane. These valves are modeled after previously-demonstrated monolithic membrane valves that utilize commercially-available PDMS membranes bonded between etched glass wafers [1]. Since these valve membranes are featureless (not molded as in soft lithography), many off-the-shelf materials can be substituted for PDMS in these valves. Alternative membranes for monolithic membrane valves were first investigated by scientists in the In Situ Instrument Systems Section at the NASA Jet Propulsion Laboratory [2].

## 2. RESULTS AND DISCUSSION

In this work, a 25 μm thick perfluoroalkoxy (PFA) Teflon membrane (DuPont) is thermally bonded between glass wafers containing etched fluidic and pneumatic features (Figure 1). The valves are normally closed; applying vacuum to an etched displacement chamber in the pneumatic wafer pulls the Teflon membrane away from a discontinuity in the fluid channel and opens the valve (Figure 2). These Teflon monolithic membrane valves control fluid flow as well as their PDMS-based counterparts (Figure 3).

To select from different samples and reagents, the microfluidic autosampler chip shown in Figure 1 includes two fluidic bus channels [3], each containing six bus valves with associated fluid connections. By opening selected bus valves, fluid from any of the six connections can flow to any other connection (Figure 4). In addition, by actuating the valves according to a pumping pattern, the autosampler chip can actively pump or recirculate fluid between any of the connections. Finally, the entire internal volume of the autosampler chip can be automatically rinsed to eliminate cross-contamination between samples. Taken together, these operations replace and expand upon the capabilities of a traditional autosampler.



978-0-9798064-0-7/μTAS2007/$20©2007CBMS

We demonstrate the capabilities of the autosampler chip by interfacing it to a suspended microchannel resonator (SMR) mass sensor [4,5] (Figure 5). When particles or solutions with different densities flow through the vibrating silicon microchannel, the resonance frequency of the channel changes by a measurable amount. In Figure 6, the autosampler chip is used to alternately flow two solutions of different densities through the SMR. The autosampler chip replaces the contents of the SMR in only 300 ms. The autosampler chip is also used to build up and then remove a complex multilayer on the inside surface of the SMR in Figure 7. Frequency changes following polylysine-polyethylene glycol-biotin and neutravidin solutions indicate that binding has occurred inside the SMR, and the return to baseline frequency following delivery of "piranha" to the SMR (concentrated sulfuric acid and hydrogen peroxide) confirms the removal of the multilayer. Preliminary results suggest that the Teflon valves remain unchanged and fully functional following piranha exposure. This is one of many applications in which the microfluidic autosampler could replace bulky and costly upstream fluidic hardware for cheaper and more portable analysis systems.

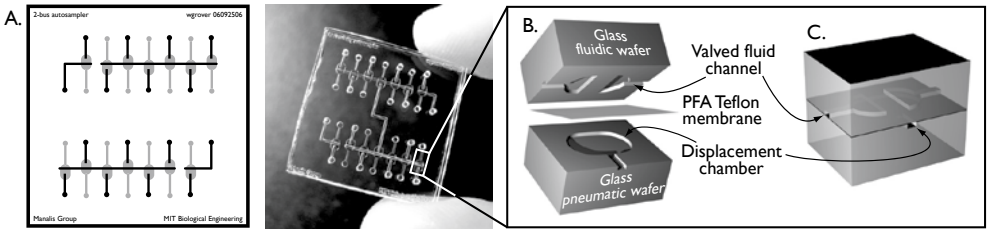


**Figure 1.** (A) The microfluidic autosampler chip. Black features are etched into the fluidic wafer and gray features are etched into the pneumatic wafer. Exploded (B) and assembled (C) detailed views of a single PFA Teflon valve.

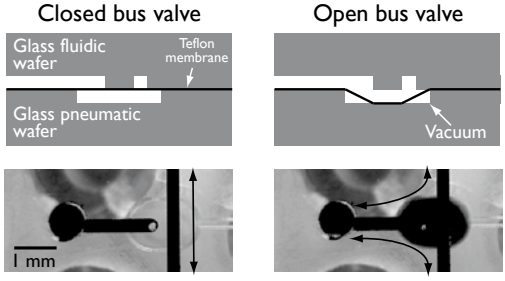


**Figure 2.** Cross-sectional diagrams and top-view photos of dye in closed and open Teflon bus valves. In the closed valve, fluid is still free to flow through the vertical bus channel. Opening the valve diverts flow through the valve.

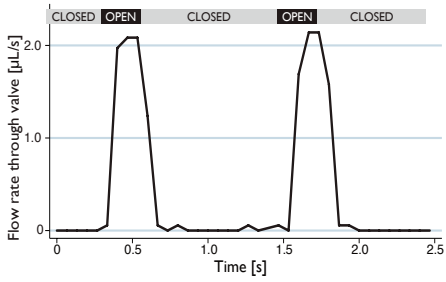


**Figure 3.** Pressure-driven flow of water through a Teflon monolithic membrane valve held alternately open for 300 ms and closed for 1 s.

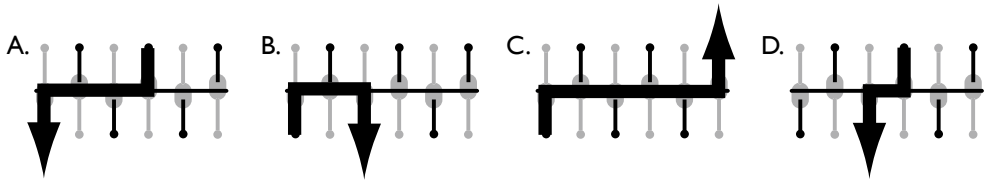


**Figure 4.** Illustrations of three of the 30 possible paths of fluid flow between the six fluidic connections on one of the two bus channels in the autosampler chip. Operation C rinses the internal fluid volume of the autosampler chip. Flow can be driven by external pressure or actively pumped by the autosampler chip if the valves are actuated in a pumping pattern [1].

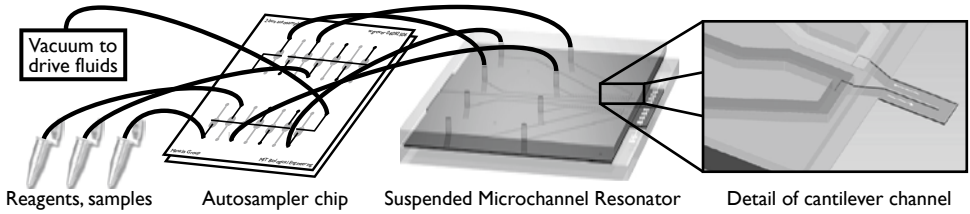


**Figure 5.** Diagram showing fluidic connections (capillary tubing) between the autosampler chip and the suspended microchannel resonator (SMR) sensor. Using on-chip valves and a single vacuum source, the autosampler chip controls all routing of samples and reagents to and from the cantilever channel.

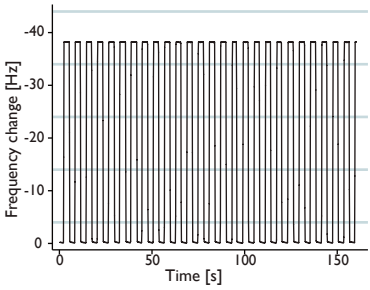


**Figure 6.** Frequency response of the SMR while the autosampler chip switches rapidly between flowing water (0 Hz relative frequency) and 0.5 x phosphate buffered saline (-38 Hz; mostly 70 mM NaCl) through the SMR. The autosampler chip replaces the 10 pL contents of the cantilever every 3 seconds, requiring only 300 ms per switch.

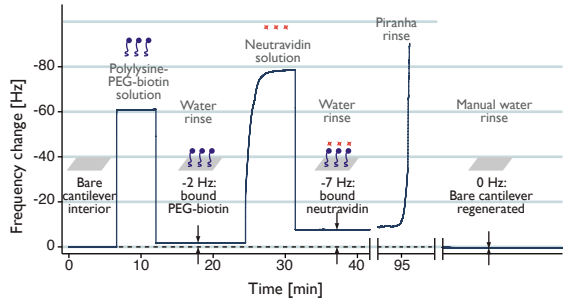


**Figure 7.** Using the autosampler chip to build and remove a complex polylysine-polyethylene glycol-biotin-neutravidin multilayer on the inside surface of the SMR. The -7 Hz change at 35 minutes confirms binding of polylysine-PEG-biotin and neutravidin to the inside walls of the cantilever channel. The autosampler chip then delivers piranha (concentrated sulfuric acid with hydrogen peroxide) to remove the multilayer. The return to baseline frequency after rinsing confirms that the SMR surface was regenerated. The Teflon valves appear to remain fully functional following piranha exposure.

1. W. H. Grover, A. M. Skelley, C. N. Liu, E. T. Lagally and R. A. Mathies. Monolithic membrane valves and diaphragm pumps for practical large-scale integration into glass microfluidic devices. *Sensors and Actuators B* **89** (3), 2003.

2. Peter A. Willis, In Situ Instrument Systems Section, NASA Jet Propulsion Laboratory, California Institute of Technology, personal communication.

3. W. H. Grover and R. A. Mathies, An integrated microfluidic processor for single nucleotide polymorphism-based DNA computing. *Lab on a Chip* **5**, 2005.

4. T. P. Burg and S. R. Manalis, Suspended microchannel resonators for biomolecular detection. *Applied Physics Letters* **83** (13), 2003.

5. T. P. Burg, M. Godin, S. M. Knudsen, W. Shen, G. Carlson, J. S. Foster, K. Babcock, S. R. Manalis. Weighing of biomolecules, single cells and single nanoparticles in fluid. *Nature* **446**, 2007.