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# A FLUIDICALLY CONTROLLED BI-MATERIAL ACTUATOR FOR AUTOMATION OF PAPER-BASED ASSAYS

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## KEY WORDS

Microfluidic, Diagnostic, Capillarity, Hygro-expansion, Cantilever, Small sample volume

## INTRODUCTION

Precise timing and sequential loading of multiple reagents is required to perform complex multistep immunoassays. Current paper-based lateral flow devices (LFDs) lack the crucial components, such as valves and actuators, for manipulation of reagents. Martinez et al. [1] reported a multilayer paper-based device that mechanically bridged discrete channels to promote wicking. Moreover, Li et al. [2] reported a method to stop and to promote wicking by manually separating and re-joining two paper channels. Both methods required external actuation. Chen et al. [3] and Gerbers et al. [4] developed novel autonomous two- and three-dimensional microfluidic valves involving no external actuation based on altering the hydrophobicity of a multilayered structure by means of a surfactant. With this technique they were able to control the order and mixing time of the sample and multiple reagents autonomously. These valves required long response times and large volumes of actuation fluids, however. To remedy this, Kong et al. [5] reported actuators based on selective wetting of folded paper strips. These strips reduced the actuator's response time to within two seconds from wetting while utilizing a very small volume of actuation fluid in the order of four microliters.

In this article, we describe the development of a novel paper-based autonomously-activated bi-material actuator constructed in the shape of a cantilever that is exploited in a fluidic circuit to sequentially load several reagents to the analyte detection area.

## MATERIALS AND METHODS

In this study, as stated earlier, a simple-to-manufacture, low-cost, autonomous, paper-based bi-material cantilever (B-MaC) is developed to provide fluids management for microfluidic circuits. The cantilever actuator is made from a strip of filter paper partially laminated with Scotch tape on one side. When the filter paper is exposed to fluid, the cellulose fibers experience hygro-expansion and the paper undergoes dimensional changes, whereas the adjoining tape layer remains constant in length. Due to this difference in behavior of the paper and tape components, the free end of the cantilever bends toward the side having the tape layer and thus,

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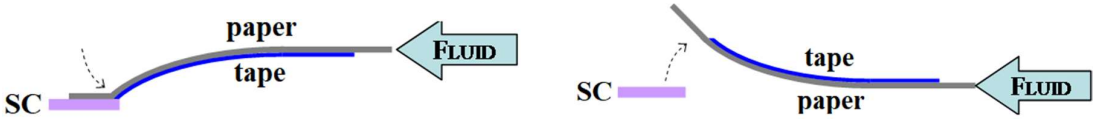
opens or closes a fluidic path provided at the stationary component (SC). The two orientations of the bi-material cantilever are shown in Fig. 1. As seen in Fig. 1A, when the tape layer is on the bottom side, the B-MaC bends downward as it becomes wet. If the tape layer is on top, then the B-MaC bends upward as shown in Fig. 1B.




A. Flow allowed at SC B. Flow prevented at SC

**Figure 1**: Schematic diagram of bi-material cantilever actuator operational in two configurations

In order to conduct a complex immunoassay and to sequentially load two or more reagents, in addition to sample fluid, one needs to construct a fluidic circuit. An example of a lateral flow device involving a B-MaC and additional components is illustrated in Fig. 2. The B-MaC, as stated earlier, is a narrow strip of filter paper, GE Whatman Grade 41, partially laminated by Scotch tape on one side. On the other side is an appropriately sized sample inlet to allow for controlled fluid deposition. The inlet is not shown in Fig. 2, but a view of it can be seen in Fig. 6. The other components of the device are as follows: 1) the reagent pad, made out of a glass fiber conjugate pad, EMD Millipore; 2) the stationary component (SC) underneath the reagent pad, made out of the same filter paper as the cantilever; 3) the nitrocellulose membrane detection area; 4) the waste pad, made from blotting paper, GE Whatman Grade GB003, and 5) a plastic support structure.

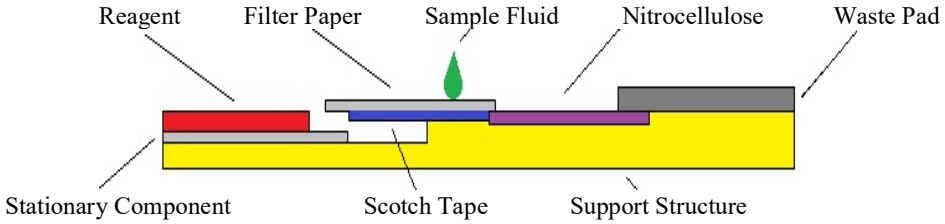



**Figure 2**: Schematic diagram of a bi-material cantilever actuator in a 1-D lateral flow device

An assay (biological test) using a device of the same structure as the one in Fig. 2 has been carried out. A series of photos of the actual device and the state of the fluids is shown in Fig. 3. First, about 75 microliters (μL) of the reagent fluid is applied to the reagent pad. When the reagent pad is fully soaked, a reservoir becomes available in front of it at the SC. A small volume of sample fluid (12 μL) is then pipetted in the sample area (see the green food-dye colored water in the top photo of Fig. 3). As the sample is delivered, it flows in both directions, toward the test area and also the cantilever valve. Due to the hygro-expansion of cellulose fibers, the cantilever starts to bend downward and within a few seconds contacts the stationary component. As seen in the center photo of Fig. 3, the cantilever touches the SC and begins wicking the reagent fluid towards the test zone. After a few minutes, a strong signal begins forming at the line in the nitrocellulose membrane. The signal at 180 seconds can be seen to the left of the purple tape in the bottom photo of Fig. 3.

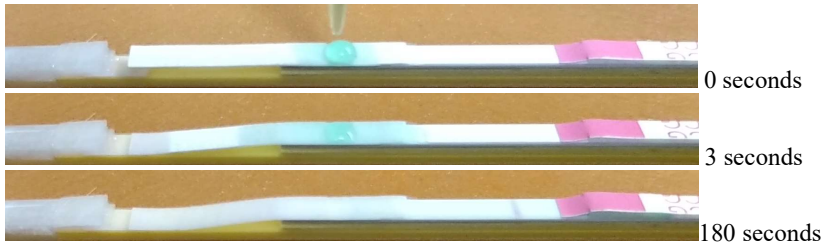



**Figure 3**: Actual 1-D single B-MaC lateral flow device

Although the results of a flow-through single-valve B-MaC were shown above, the use of this microfluidic automation device is not limited to simple applications only. The bi-material actuator can be extended to complex systems as well, where several reagent fluids are involved and sequential loading or timing delays are required, such as is in an ELISA protocol. Fig. 4 demonstrates the use of a partitioned B-MaC to stop fluid flow through a stationary component after a given time has elapsed. That time is determined by the duration of the timing-fluid flow through the π structure shown in Fig. 4 and actuation of the B-MaC. The white arrows in the figure indicate the fluid flow direction.

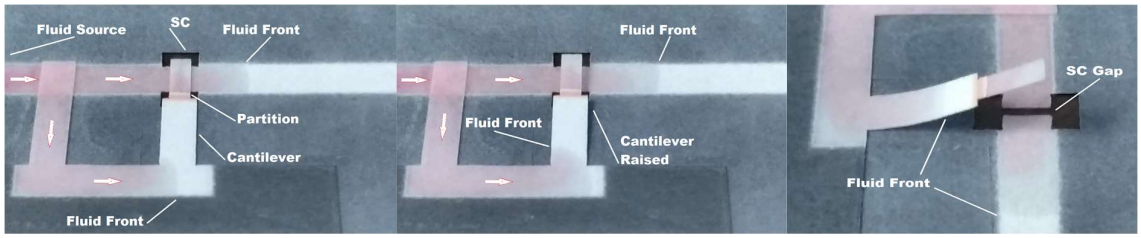



**Figure 4**: Demonstration of the B-MaC in a time delay circuit: A. The B-MaC is engaged with SC and allows flow; B. Timing fluid raises the B-MaC and stops flow through the SC; C. Improved view of the fluidic disconnect.

Fig. 5 shows a lateral flow device where an immunosorbent assay is performed. The three-dimensional fluidic circuit contains both flow-through and partitioned B-MaCs. Two reagents are previously loaded into their respective pads prior to the sample being deposited at time zero (Fig. 5A). The sample then flows in both directions and B-MaC 1 is activated (Fig. 5B). Once B-MaC 1 is engaged with SC 1, the reagent 1 (green) flows through the test area as well as in the delay channel under B-Mac 2 (see Fig. 5C). As seen in Fig. 5C, the green reagent is visible in the last leg of the delay channel, as it activates B-Mac 2 at about 3 minutes. The engagement of B-MaC 2 causes reagent 2 (red) to start flowing toward the test area. Reagent 2 arrives at the test area at about 8 minutes. The test is allowed to run and a strong signal develops as shown in Fig. 5D.

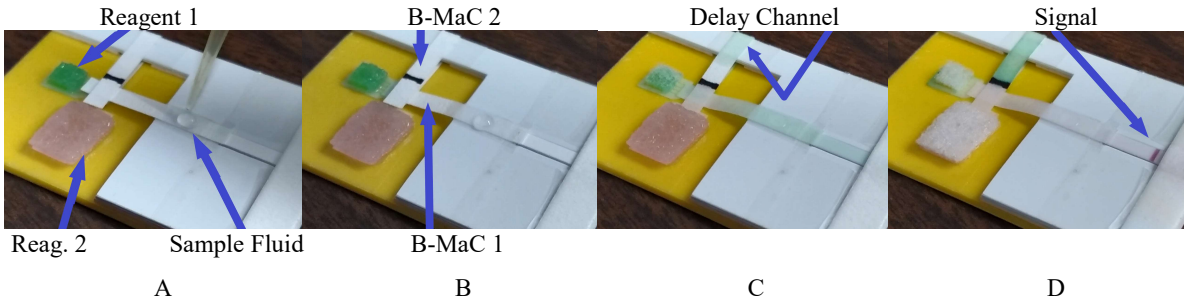



**Figure 5**: Two-valve, two-reagent, three-dimensional fluidic circuit

Fluid actuated valves, like the bi-material cantilever, make it possible to construct lateral flow paper-based devices that are as easy to use and low cost as conventional test strips, yet capable of conducting more complex assays. To make them even simpler to use and more autonomous, we have developed a cartridge, within which the paper-based device including the valves, is housed and where the reagents are stored in cavities. At the time a test is to be run, the operator, by a simple action, releases the reagents to their respective pads. The operator then proceeds with the loading of the sample fluid and reading the assay results 10 to 20 minutes later. An example of such housing is shown in Fig. 6. A top view of the cartridge is shown in Fig. 6A where the test site is visible through the rectangular hole on the right side. The sample port where the sample is deposited on B-MaC is also visible. On the left side of the photo is shown a tape layer, which releases the reagents held in cavities when pulled. The B-MaC valves then prevent the reagents from flowing until the sample fluid is loaded. As described in Fig. 2 above, the sample fluid activates the cantilever valve that provides a path for the reagent to flow to the test site and along with the sample fluid generate a signal. Fig. 6B shows the bottom

side of the top cover where the reagent cavity is located. In the figure the cavity is covered by inkjet tape to prevent the fluid from flowing out until the tape is pulled. Fig. 6C is the same as Fig. 6B but shows the cavity partially exposed as the tape has been pulled back partially.


A. Top view of housing B. Bottom view of cover C. Reagent chamber partially exposed

**Figure 6**: Reagent storage and delivery by tape sealed chamber within housing

## CONCLUSION

This study focused on the development and application of a new bi-material paper-based cantilever actuator. This actuator operates on the hygro-expansion of cellulose fibers which leads to dimensional change of paper when exposed to water. The bi-material actuator of this study lends itself to a wide range of microfluidic diagnostic systems, including, ELISA protocols, which requires several reagents, their sequential loading, and time delays.

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