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# The manufacture and Preliminary testing of a Novel Bio-MEMS Filtration Chip

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## ABSTRACT

In the clinical/microbiological laboratory there are currently several ways of separating specific cells from a fluid suspension. Conventionally cells can be separated based on size, density, electrical charge, light-scattering properties, and antigenic surface properties. Separating cells using these parameters can require complex technologies and specialist equipment which may damage sensitive cells. The pumping mechanism described here leaves samples undamaged either mechanically or chemically unlike many other current filtration techniques. This paper proposes new Bio-MEMS filtration chips manufactured using micro systems technology (MST) that, when used in conjunction with an optical microscope and a syringe, can filter and grade cells for size without the requirement for additional expensive equipment. These chips also offer great versatility in terms of design and their low cost allows them to be disposable, eliminating sample contamination.

***Keywords***: Bio MEMS, DRIE, Filters,

## 1 INTRODUCTION

The new proposed Bio-MEMS particulate and cell filter provides a purely mechanical separation technique of separating cell types from a suspension based on size and morphology. Since no chemical markers or contaminants are deliberately added the cells may still be used after separation. Further to this there is little additional equipment required to the standard laboratory apparatus: just the filter device and a microscope.

MEMS materials have been found to be biocompatible and readily accepted by tissues for the application of medical implants **[1]** for even prolonged exposures. Furthermore, the hydrophilic nature of the native oxide deposits within the capillaries of the device means that they are virtually harmless to the cells and their proteins[**2,3**]. The self-powered surface tension pumping techniques used to manipulate the fluid further reduces the need for external equipment, enhances reliability through avoiding mechanical moving components, minimises damage to cells that can be caused through mechanical pumping **[4]**, or thermal damage through marangoni **[5]** effect pumping.

The small scale of the device, the low unit cost, and disposability add further advantages to these bio-mems filters. In medical applications the risk of disease

communication and sample contamination, and the cost of sterilisation are driving the industry towards the use of disposable single-use technologies[6]. For these reasons these filters are particularly suitable for the medical and drug house research industries. Furthermore, with the advent of ART (Assisted Reproductive Technology), and further studies in immunology, the need for sorting mixed cell populations from one another and so the need for cell sorting continues to grow[7]. As practical applications for sorted cells continues to grow – so will the need for microscale mechanical cell filters. The principles of operation how the device was manufactured along with preliminary results from using the device will be given in the following sections. The paper will conclude with conclusions drawn from this work.

## 2 DESIGN

The Bio-Mems filter takes the form of a passive planar microfabricated fluidic filter which employs head pressure and surface tension of the working fluid in order to drive the sample through the device.

The principle of operation of the device is a very simple, a central reservoir is linked to a number of collection chambers via small micro machined channels containing the micro filter's elements. Prior to use the whole device is flooded with deionised water. The use of the hydrophilic surfaces through out the channels insures that wetting is easily achieved. At this point the system will be at equilibrium with the shape of the reservoirs adjusting themselves to balance surface tension and gravimetric pressures (see figure 1)

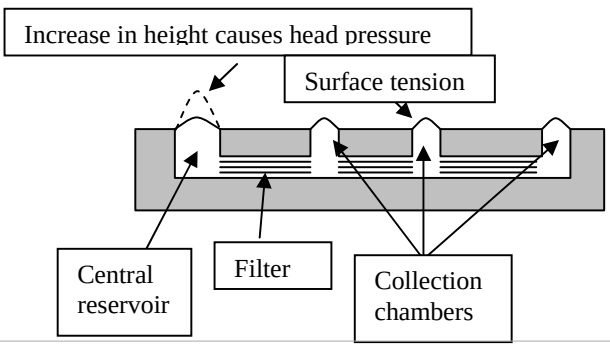

**Figure 1 Schematic of Pumping mechanism**

Next the sample containing material to be filtered can be injected into the central reservoir. This disturbs the equilibrium conditions causing the water to flow from this reservoir to the collection chambers being filtered as it flows. The height of the water in the central reservoir will rise generating a small head pressure. Surface tension may play a greater role in the pumping mechanism than suggested here however, the flow rate appears to be adequately accounted for by the head pressure of injected fluid. The calculation of a suitable head pressure to give the flow rates witnessed when the device was used is given in the analysis section of this paper.

The considerations for the manufacture of the filter were to offer the designer of the filters as much flexibility as possible in their designs. At the same time the processing route had to be as simple as possible as one of the main benefits of these devices is to be their low cost.

The filters were manufactured from two wafers; one of silicon and the other glass. The actual filter is etched in the silicon wafer using DRIE etching (deep reactive ion etching) and the glass wafer provides a 'lid' to seal the filtering chambers. Figure 2 contains a schematic to aid the reader before going on to describe the manufacture of the filter.

The main body of the filter is manufactured from a bulk silicon wafer and completed in two distinct steps. The first is the etch cycle carried out to etch the large holes through the wafer where the sample to be deposited is placed prior to being filtered and the others where it is subsequently collected. These holes are etched to within 60 microns of the bottom surface of the wafer. The second step involves removing the wafer from the chamber and etching the cavities and the filtration components of the design into the other side of the wafer. To ensure alignment between the holes and the filter channels the wafer has to be patterned at the same time using a double sided mask aligner. In addition to this it is not currently possible to etch all the way through a wafer using a DRIE without bonding it to a second wafer referred to as a handle wafer, prior to the second etch step being carried out.

Once these two etching steps have been completed, the wafer is removed from the handle wafer and the glass wafer is bonded to the filtration side of the wafer creating a lid. This is done by anodically bonding the two wafers together. Under clean room conditions the devices are sealed using a self-adhesive polythene layer: keeping them free from contamination whilst the wafer is diced into chips, and until the device is used.

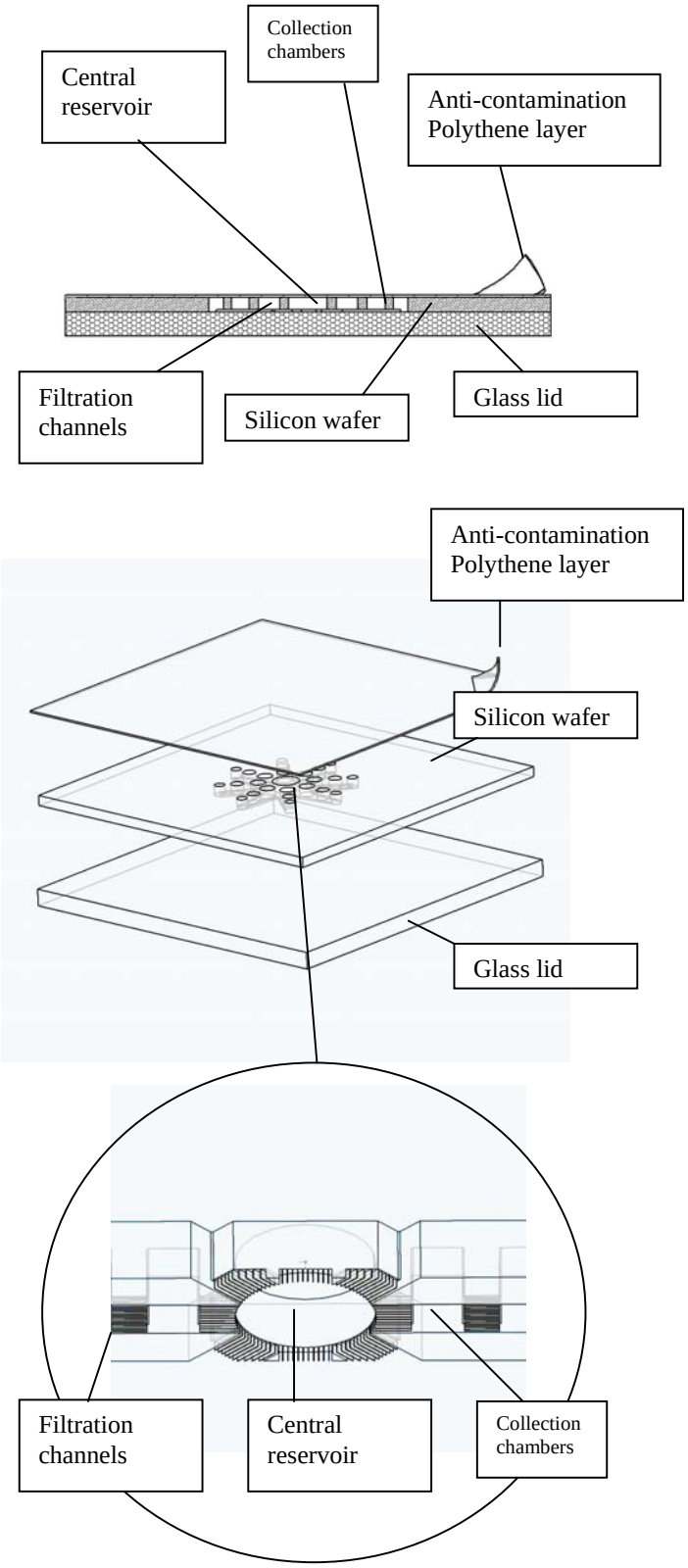


**Figure 2 Schematic of new Bio-MEMS Chip**

Below are micrographs of the silicon layer after the holes and filtration cavities had been micro machined and prior to the glass layer being anodically bonded on.

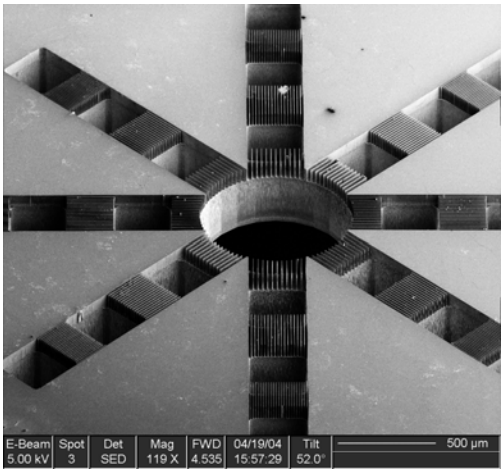


**Figure 3 A micrograph of the filtration side of the silicon wafer**

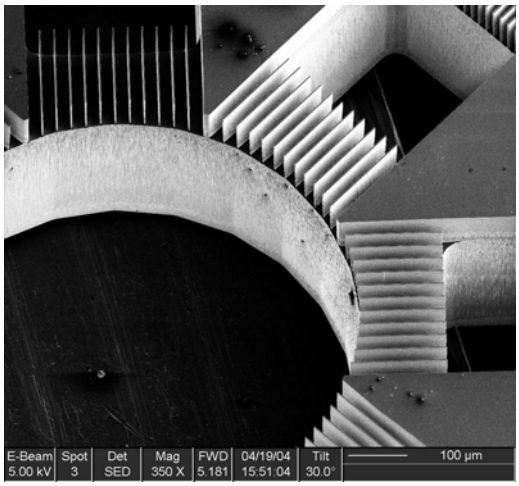


**Figure 4 A micrograph showing the quality of the etched features, the alignment between the filters and the reservoir and collection chambers**

## Preliminary Results

The capillary action of the device is used to wet the device. The fluid was pippeted into the central reservoir and observed through an optical microscope. Figure 5 shows a micrograph of one of the test devices being wetted which was observed from underneath through the glass slide. The first collection chamber has filled and the fluid is making its way through the second part of the filter and starting to fill the second chamber. It was found that the flow from the central reservoir to fill all the surrounding chambers took seconds.

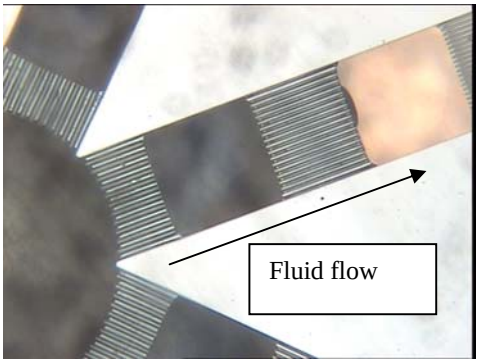


**Figure 5 bio-mems chip being tested**

Once the device was wetted a bubble of fluid containing ragweed pollen and john smut spores was placed in the central reservoir. The surface tension of this bubble is believed to be the primary pumping mechanism of the filter. The former was graded to be 19-23 microns diameter and the later to be 3-4 microns in diameter. The following micrographs show the different samples being filtered within a device.

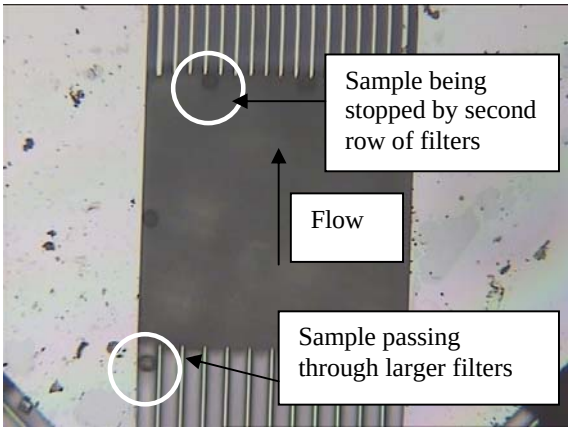


**Figure 1 Ragweed pollen spores passing through the first filter but unable ot pass through into the next chamber**

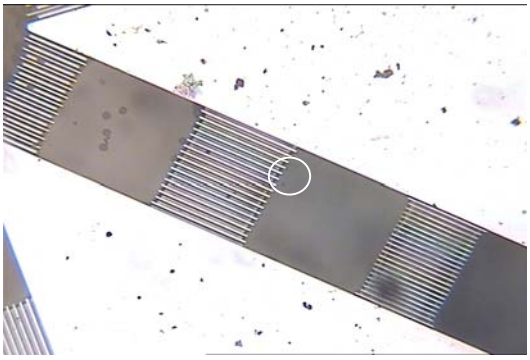

**Figure 2 Filtering a sample containing both spores. John smut spores can be seen to pass through the second filter**

## ANALYSIS

After capillary action had been used to wet the device, the sample was pumped through the filter by using the head pressure in the central reservoir and assuming the surface tension pressures in the central reservoir and collection chambers balanced. The head pressure may be approximated to :

$$\Delta p = \rho g h \qquad (1)$$

where ρ density of water

g 9.81

h height of fluid

And laminar flow can be determined by using

$$Q = \frac{2Ad^2\Delta P}{\mu f RE \Delta L} \qquad (2)$$

Where A Area of the channel

D Hydraulic diameter of the channel

ΔP Pumping pressure

μ Viscosity (for water 1.003x $10^{-3}$)

fRE Friction constant for a rectangular micro-channel

ΔL Length of channel

By determining the velocity of the spores in the system from video footage (0.015mm/sec) and rearranging the above standard equations we were able to work out what pressure was propelling the spores through the filters. The pressure was found to be 0.5pascals and by using equation 1 we were able to determine the required height of fluid to generate an appropriate head pressure. This was found to be 50μm a height consistent with those experienced when carry out physical testing

## Conclusions

These new and novel filters offer great promise as an emerging technology to a variety of applications. Although at this point the pumping phenomena is not fully characterised, working filters have been demonstrated, validating their potential.

The versatility in their design, low cost and ease of manufacture all add to the fact that these chips can be utilised with only the need for a pipette and an optical microscope. There is no requirement for additional typically expensive and bulky equipment and the samples are not contaminated after filtration – opening new opportunities for field-based cell analysis.

The process simplicity leads to a marked reduction in processing time. This speed and ease of use means devices such as these could be used for applications such as on the spot diagnostics for hospitals, lab-on-a-chip pre-processing, drug house research and field applications.

Through further development of channel and filter element geometries it will be possible for cells to be further disseminated by morphology. The incorporation of electrodes could introduce potential gradients for ion separation, and the deposition of antigenic compounds on the capillary walls could offer potential for separation based on chemical as well as mechanical properties.

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