MICROFLUIDIC PARTICLE SIZE SORTER FOR BIOMEDICAL APPLICATIONS

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Nowadays microfluidics are an important part of micromachining engineering and are used to control and manipulate a broad range of fluids such as blood samples, bacterial cell suspensions, protein or antibody solutions. This versatility has promoted a very fast development of different microfluidic devices and their use in such diverse techniques as capillary electrophoresis [1], sample injection of proteins for analysis via mass spectrometry [2], PCR amplification [3], DNA analysis [4], cell manipulation, separation and pattering [5] and chemical gradient formation [6]. They also can be used to obtain a variety of interesting measurements including molecular diffusion coefficients [7], pH [8] or enzyme reaction kinetics [9]. Many of these applications are already being used for clinical diagnostics [10].

Here we present a new design of particle size sorter, made with a combination of SU-8 based UV-Lithography and poly(dimethylsiloxane) (PDMS) soft lithography technologies, for the separation of microparticles from solution depending on their diameters. The UV-Lithography technique is employed for the construction of the negative master. This technique provides a low-cost technology for the construction of tall microstructures with high aspect ratios for MEMS applications [11]. The master is then coated, in an evaporator, with a flourosilane monolayer which acts as a hydrophobic layer and eliminates adhesion of the polymer to the master during the replication.

The master is replicated in elastomeric PDMS, whose properties make it a suitable support material for miniaturized biological studies. PDMS has the advantages of being inexpensive, flexible, optically transparent and biologically compatible. Designs can be easily realised and the structures bonded to other surfaces (e.g. glass). The device and a PDMS top piece are then introduced into an O_2 plasma. The plasma causes both surfaces to be activated and their union gives rise to a very strong bond, that when complete allows high pressures to be utilised in the system. The immersion of the (initially hydrophobic) PDMS in the oxygen plasma makes it hydrophilic, which assists in the introduction of water based solutions through the device. The introduction and management of the liquid flow is made using syringes controlled by micromanipulators.

The device developed here allows a fast, low cost and effective separation of elements depending on diameter. The biological compatibility of the device means it will be useful for the differentiation of the different kinds of cells in a suspension. For example, its application to blood analysis could allow the separation of red blood cells depending on mean corpuscular volume (MCV), an indice is commonly used in medical diagnostics and employed for the classification of anemias. Similarly, the calculation of red blood cell distribution width (RDW) permits the detection of the significant variation in cell size that certain disorders cause. Finally, recent studies [12] point the reduction of neuronal cell size as an indicator of a possible case of schizophrenia or bipolar disorder (BPD).

The scalability of the design, the improvement of the characteristics of the filter and the modification of the negative master using Focused Ion Beam (FIB) lithography suggests that we could reach nanometric dimensions with the filter, opening the door to a number of new applications.

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Figures:

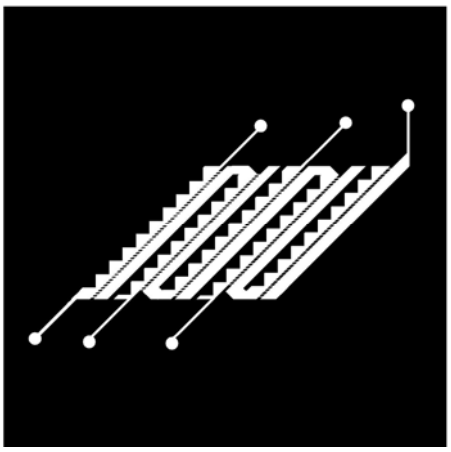

Figure 1. General overview of the filter design. The hole at the bottom left hand corner is the sample input. The other five are outputs of the different sizes particles.

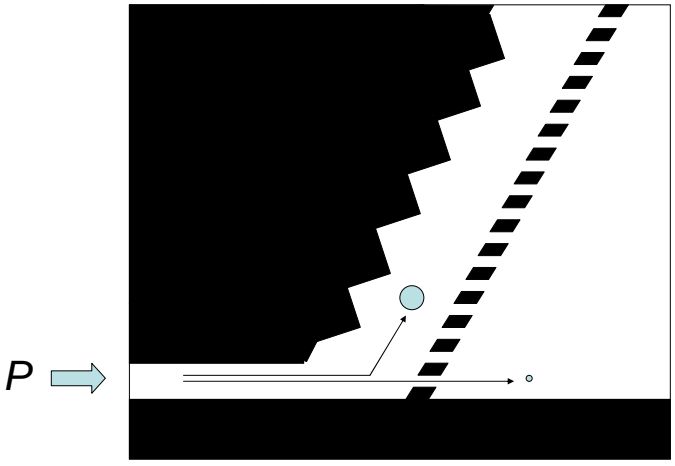

Figure 2. Principle of operation of the filter. The small particle enters to the secondary cavity and continues to smaller filters however the big one is forced to continue to the correspondent output.