Electronic Supplementary Material (ESI) for Lab on a Chip

Electronic Supplementary Information

Magnetically-actuated blood filter unit attachable to premade biochips

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1. Geometrical design of the plastic container

Fig. S1 shows geometrical designs of the plastic container. Diameters are different for three designs but lengths are the same (10 *mm*). One magnet (thickness of 3 *mm*) and a few (3~8) punched membranes (each of 0.6-*mm* thickness) of the same diameters (3, 4, & 5 *mm*) are inserted into a cylindrical container. The inner diameter of the container is 0.2 *mm* larger than the diameter of components inserted into the container. The gap between the membranes and the container is maximally 0.2 *mm*. Because the membranes are randomly stacked in the container without alignment, an open passage to the bottom of filter is not easily built by the gap. Moreover, because the lowest membrane is tightly bonded to a double sided tape, any blood cells that are occasionally leaked can be caught by the lowest membrane. In this way, direct leakage of blood particles through the gap around the edges of membranes is prohibited in the design. The plastic container can be fabricated by machining an acrylic plate or injection molding technique.

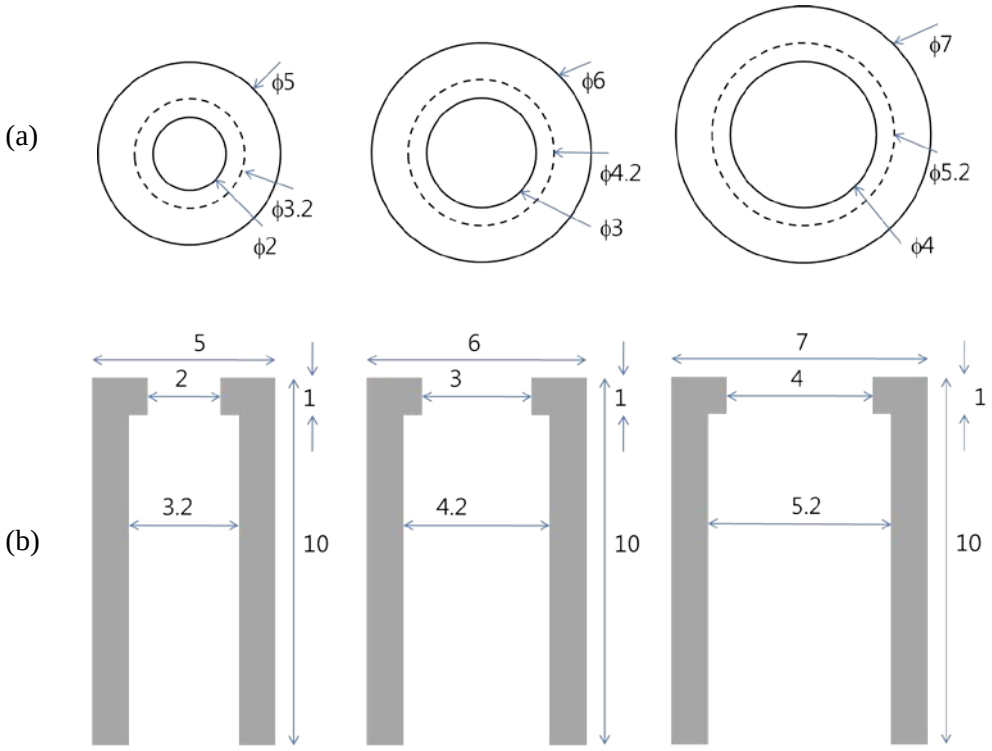


Fig. S1 Geometrical designs of the plastic container. The numbers in the figure are in *mm* scale. (a) A horizontal cross-sectional diagram, and (b) a vertical cross-sectional diagram.

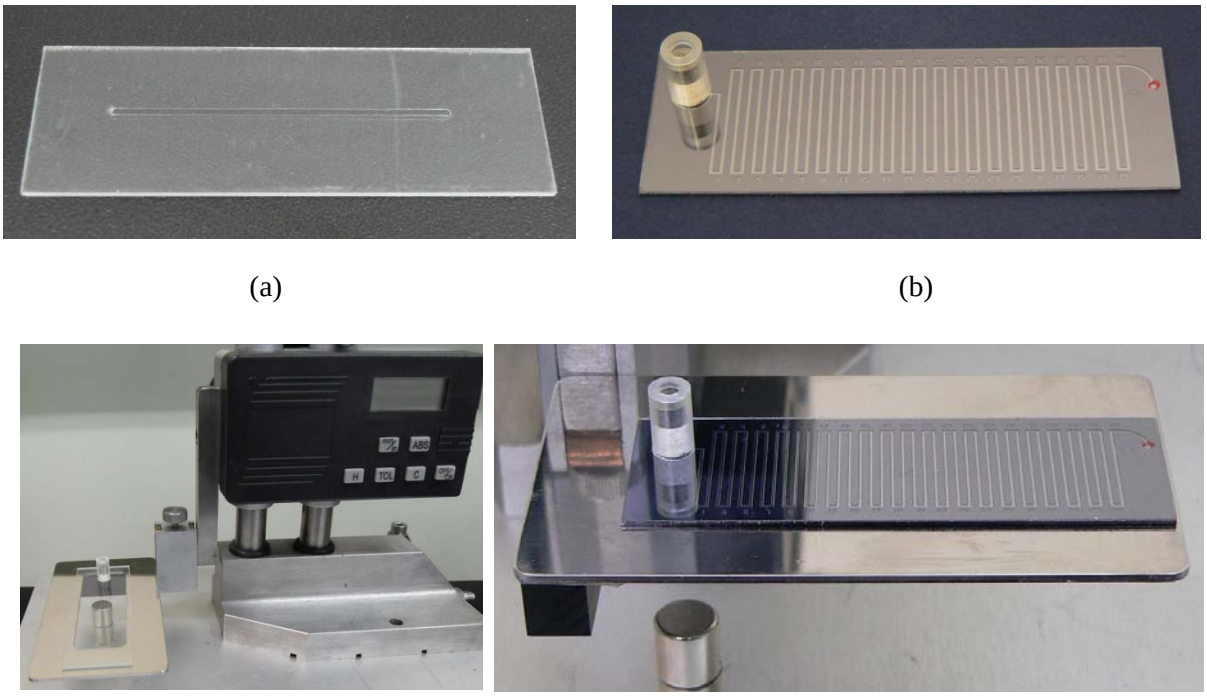
2. Microfluidic metering chips and an experimental setup

A simple microfluidic chip was fabricated as a model of a biochip to measure the volume of plasma extracted from the filter unit. Two adhesive-coated PET films (Crystalex®, Gmp) (area 25 × 75 mm^2, thickness of 100 μm) were punched to form a straight hole (width of 1 *mm*, length of 50 *mm*) and bonded with a glass slide (area 25 × 75 mm^2) as a bottom substrate. Then, a PET film, with 2 punched holes of 1-*mm* diameter, was bonded to the chip as a lid to form a straight rectangular channel of 50 × 1 × 0.2 mm^3 in the glass-PET chip (Fig. S2a).

A microfluidic metering chip made of different materials was also fabricated in order to check the dependency of the plasma recovery on biochips. A long serpentine rectangular channel was etched in a silicon wafer with an etched depth of 100±5 μm and width of 500 μm. Also, numbers are etched at each corner of the serpentine channel in order to read the liquid volume filling the channel from the inlet in μl scale. The silicon plate with the channel was sealed by an adhesive-coated polyester (PET) film (Crystalex®, Gmp, area 25 × 75 mm^2, thickness of 100 μm), which has punched inlet/outlet holes. A roller was used during the lamination step for bubble-free sealing. Finally, the Si-PET microfluidic metering chip with the size of 25 × 75 × 0.75 mm^3 was fabricated (Fig. S2a). The cross-sectional area of the rectangular channel is 0.5 × 0.1 mm^2 (1/4 of the cross section of the glass-PET chip). The smaller cross-section gives higher viscous flow resistance to the plasma flow in the microchannel[S1]. The contact angle of blood on Si surface is larger than that on glass surface, which means that the capillary pressure for flow into the microchannel is lower for Si-PET chip. Because the viscous resistance and the capillary pressure affect the plasma flow in the channel, they should be simultaneously considered in the design of a microfluidic chip.

An experimental setup was constructed to test the performance of the filter (Fig. S2c). An Nd-Fe-B magnet (10-*mm* diameter and 10-*mm* length with 5030 Gauss, LG magnet) was positioned below the microfluidic metering chip to apply external magnetic force. The blood filter unit, inlet of the metering chip, and external magnet were aligned vertically. The distance between the filter and the external magnet was modulated by a linear translation system constructed with a digital height gauge

(Bluebird®, NA192-300s). Initially, the external magnet was positioned 30 mm below the filter unit (exactly, the distance between the lower surface of the microfluidic chip and the upper surface of the external magnet). After the introduction of the blood sample into the filter unit and the waiting time, the external magnet was slowly moved during 6 seconds from initial position close to the filter unit with the constant approaching speed of 5 *mm/s*. Then, the external magnet was contacted on the bottom of the microfluidic chip. Under this situation, we additionally waited 30 seconds and measured the volume of extracted plasma. The magnet-moving time and the additional waiting time were given sufficiently long in order to obtain reproducible and stable experimental results, thus these times could be further reduced for faster operation. In this regards, although the overall operation time should include the initial waiting time, the magnet-moving time, and the additional waiting time, the initial waiting time was considered as the operation time of the filter unit in this paper.



(a) (b)

(c)

Fig. S2 (a) The microfluidic metering chip made by glass-PET lamination, (b) the microfluidic metering chip made by Si-PET lamination, and (c) the experimental setup for magnetic actuation by controlling the distance between the filter unit and the external magnet.

3. An example of application of the filter unit

The filter unit was compatible to any kind of biochips regardless of their materials. We applied the filter unit to a CMOS FET-based nanowire biosensor to detect biomarkers in the blood sample. A microfluidic chip made of PDMS was bonded with Si-based CMOS FET biosensor, and the filter unit was attached to an inlet of the microfluidic chip. Under the reference actuating conditions, extracted blood plasma filled favorably the microchannel over CMOS-sensor array.

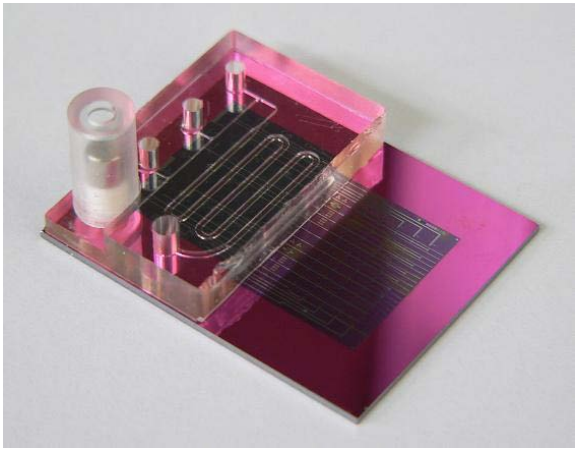
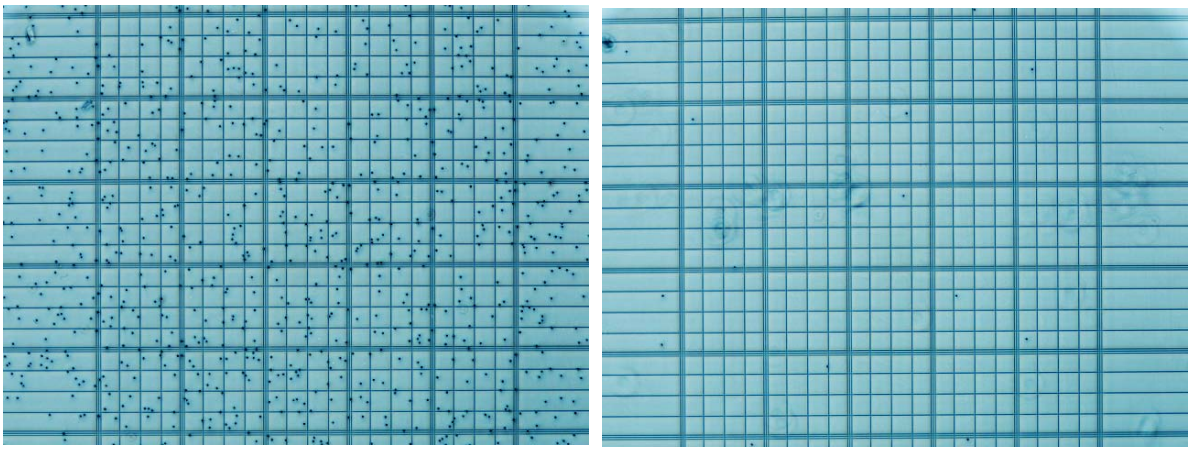


Fig. S3 Exemplary application of the filter unit to a biochip.

4. Blood cell count by a hemocytometer

To test how the present filter unit efficiently removes the blood particles, we counted the number of blood particles in the whole blood sample and the number of residual blood particles after the filteration using a hemocytometer. The whole blood sample was diluted a thousand-fold for expeditious cell counting.



(a) (b)

Fig. S4 Images of cell counting using an hemocytometer for (a) a thousand-fold diluted blood (~6.31 × 10^6 blood particles in 1 μl of whole blood), and (b) plasma obtained from the new filter device (~80 particles in 1 μl plasma).

Blood particle removal efficiency (%)

= (the number of removed particles) / (the number of blood particles per unit of sample volume) × 100

= {1- (the number of residual particles per unit of plasma volume) / (the number of blood particles per unit of sample volume) } × 100

= {1- 80 / (6.31×10^6)} × 100

= 99.99866 %

References:

S1. A. I. Rodriguez-Villarreal, M. Arundell, M. Carmona and J. Samitier, Lab Chip, 2010, 10, 211.