ABSTRACT
We demonstrate a microfluidic circuit that enables passive sorting of deformable particles based on the hydrodynamic resistance induced as they pass through a microchannel. Deformable gelatin particles with diameters in the range of 12-26 µm were sorted with a resolution of 1 µm in a single step, while viscous glycerol droplets were sorted from water droplets of similar size. This technique may find use in cell sorting and analysis and in two-phase microfluidics.

KEYWORDS: Deformability, Hydrodynamic Resistance, Sorting, Cells, Droplets.

INTRODUCTION
Sorting of cells, droplets, and particles based on physical characteristics including size and deformability is important for bioseparation, diagnostics, and two phase microfluidics. For example, red blood cell deformability is altered during malaria and sepsis [1,2]. While several methods have been developed to sort particles based on size, few techniques exist for sorting based on deformability; and these methods are usually associated with high cost (e.g., optical tweezers) or limited resolution (e.g., filtration-based techniques).

We present here a simple microfluidic circuit that enables continuous self-sorting of deformable particles based on the hydrodynamic resistance that the particle induces in a microchannel. The hydrodynamic resistance directly relates to the particle’s physical properties, such as size and deformability, and therefore enables sorting based on these parameters. We used gelatin particles dispersed in oil to demonstrate size-based sorting, and water and glycerol droplets of similar size suspended in oil to demonstrate deformability-based sorting.

THEORY
When a particle or droplet of dimensions comparable to that of the channel encounters a symmetric junction in a microchannel at low capillary number, it follows the branch with the higher instantaneous flow rate if it does not split [3,4]. Our sorting technique leverages this effect by employing a feed-forward circuit that biases a microfluidic Y-junction based on the hydrodynamic resistance induced by a particle as it enters a ‘sensing’ channel. The resulting modulation of flow at the junction switches the particle into one of two output channels depending on the resistance it induces, which correlates with the physical properties of the particle in question (e.g., size, viscosity, deformability, etc.).

Figure 1 shows an image of the device showing its main components: an input channel splits into two output channels (upper and lower) at a locally symmetric sorting junction. The input channel is connected to one of the output channels via a ‘bypass channel’, and the channel immediately preceding the sorting junction is the ‘sensing channel’.

Figure 1: Sorting device (left) and equivalent electric circuit (right) – black arrows show flow directions.

To design the device, we modeled it as an electric circuit, also shown in Figure 1, where flow rates (Q), applied pressures (P), and hydrodynamic resistances (R) were substituted by analogous currents (I), voltages (V), and electrical resistances (R), respectively. Using this model, we chose channel dimensions and inlet/outlet pressures that would result in the desired sorting behavior. Specifically, the bypass channel flow rate was maintained lower than that in the unobstructed sensing channel. Secondly, the baseline flow rate in the upper channel was maintained lower than the lower channel so that the Y-junction is biased towards the lower channel. The design was such that an increase in resistance in the sensing channel results in increase of the flow rate in the upper channel, thereby changing the junction bias at a threshold resistance induced in the sensing channel. Thus, a particle that induces a resistance higher than the threshold is sorted into the upper channel, while other particles are sorted into the lower channel. The threshold resistance at which switching occurs is determined by channel geometry and applied pressures, and can therefore be tuned by changing the pressures at the outlets. Figure 2 shows the effect of sensing channel resistance on flow rates, together with a schematic of the expected sorting behavior for a low-resistance particle and a high-resistance particle, respectively.
EXPERIMENTAL

The devices were fabricated by molding in PDMS using SU-8. The channels have a square cross section 20 µm x 20 µm.

Light mineral oil (Mallinckrodt Chemicals) was used as the continuous phase; Span 80 (Sigma-Aldrich) was added to the oil at a concentration of 1% (v/v) to stabilize the droplets against coalescence. Glycerol (BDH) was obtained from VWR, and DI water was supplied by a Millipore Direct-Q 3 UV water purification unit. The water and glycerol droplets were generated on the chip using two T-junctions upstream of the sorting junction.

The deformable gelatin particles were synthesized by suspending a water-based gelatin solution in the oil phase, prepared by adding 0.05 g/mL gelatin from bovine skin (G9382, Sigma-Aldrich) to water (with 0.1 mg/mL Rhodamine Chloride or Patent Blue V Calcium Salt to facilitate imaging), followed by sonication, heating to 85ºC, and stirring, to ensure complete mixing. 0.4% by volume of the solution was added to the oil with surfactant, vortexed for 10 min, and stored at 4°C until used.

The flows were controlled by manually adjusting the supply pressures for the different fluid streams using a pressure monitoring and control unit built in-house. The device was mounted on a Nikon TE-2000U microscope equipped with an Andor iXon camera. Sizing of the particles was done by measuring – on the acquired image – the apparent diameter of the undeformed particles after they exit the narrow (20 µm) output channels into the much wider reservoirs. Our imaging setup allowed for a resolution of 1.1 µm.

RESULTS AND DISCUSSION

A suspension of gelatin particles was introduced through the input channel with a pressure of 8 psi applied to the input stream, while the pressures at the outlets were kept at zero. This yielded average flow velocities on the order of 1 mm/s.

The particle size distribution at the 2 outlets is shown in Figure 3(a). We notice that particles less than 12.2 µm were almost evenly distributed among the 2 outlets, without any observed sorting effect. For the larger particles, we find that 22 out of the 23 particles ranging in size between 12.2 µm and 17.8 µm exited from the lower channel, while all particles larger than 17.8 µm (17 particles of diameters between 17.8 µm and 28.9 µm) exited through the upper channel. This behavior was repeatable.

The small particles (<12.2 µm) do not exhibit any sorting behavior due to their small size compared to the channel which allows them to follow the streamlines into either outlet channel. Particles in the intermediate size range (12.2 µm – 17.8 µm), however, are centered in the sensing channel, but the induced resistance is not sufficient to reverse the junction bias. Therefore, as they reach the junction, they follow the lower channel which has the highest instantaneous flow rate. Finally, the largest particles (> 17.8 µm) induce a resistance high enough to bias the flow towards the upper output channel and follow that route.

Next, we increased the pressure at the upper output channel to 3 psi, we would expect this to increase the threshold switching resistance, hence size cutoff, since a larger resistance would be required to divert the flow towards the upper channel. Indeed, we found that the threshold particle size increased from around 17.8 µm to around 22 µm: particles of 23.3 µm or larger exited through the upper channel, while particles ranging in size between 13.3 µm and 21.1 µm exited through the lower channel, and those smaller than 10 µm exited at either outlet. The size distribution of the particles at the outlets for this case is shown in Figure 3(b).
To demonstrate sorting based on deformability, we sorted droplets of equal size, but different viscosities: water droplets and glycerol droplets dispersed in oil. A glycerol droplet, approximately 1000 times more viscous than a water droplet, is expected to exhibit a much higher resistance to flow and a lower deformability than the water droplet. Flowing them in the sorting device, we found that the water droplets exited the device through the lower channel, while the glycerol droplets exited through the upper channel, as shown in Figure 4. The same results were obtained when using a dilute glycerol solution of viscosity equal to approximately 100 times that of the water. That demonstrates that the change in droplet viscosity gets translated into a change in the hydrodynamic resistance, and can therefore be detected using this device.

CONCLUSION

We have shown a microfluidic device for sorting deformable particles based on the hydrodynamic resistance they induce in a microchannel, which can be related to various physical properties, and can be influenced by particle-wall interactions. This could find application in cell sorting and bioseparation for therapeutics and point-of-care diagnostics, as well as in the industrial applications of two-phase microfluidics, e.g., pharmaceutics, food industry, etc.

The main strength of our device over existing methods lies in its simplicity: no sensing or detection add-ons are required to perform the sorting. Moreover, the device can be easily customized to change the sorting parameter or the sorting threshold, and multiple devices can be combined in parallel (to increase throughput) or in series (to increase resolution).

REFERENCES


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