SIZE- AND DEFORMABILITY-BASED SORTING OF PARTICLES USING ASYNCHRONOUS LOGIC CIRCUITS

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ABSTRACT

Separation of particles, droplets, and cells based on physical properties finds numerous applications in science and technology, ranging from biomaterials synthesis [1], medical diagnostics [2], photonics [3], drug delivery [4], and droplet microfluidics. Here we present microfluidic circuits capable of automatically sorting deformable particles based on hydrodynamic resistance [5], the extra resistance to fluid flow that a particle induces as it flows through a microfluidic channel. Prior to this paper we showed size-based sorting of gelatin particles, here we extend the work by demonstrating sorting of red blood cells (RBCs) by size and deformability-based sorting of cured and uncured photocurable droplets. Additionally, sorting of photocurable droplets illustrates the concepts of light-triggering of microfluidic circuits, which can be used to turn ON and OFF microfluidic circuit modes.

KEYWORDS
Sorting, deformability, microfluidic logic, cell, droplet.

INTRODUCTION

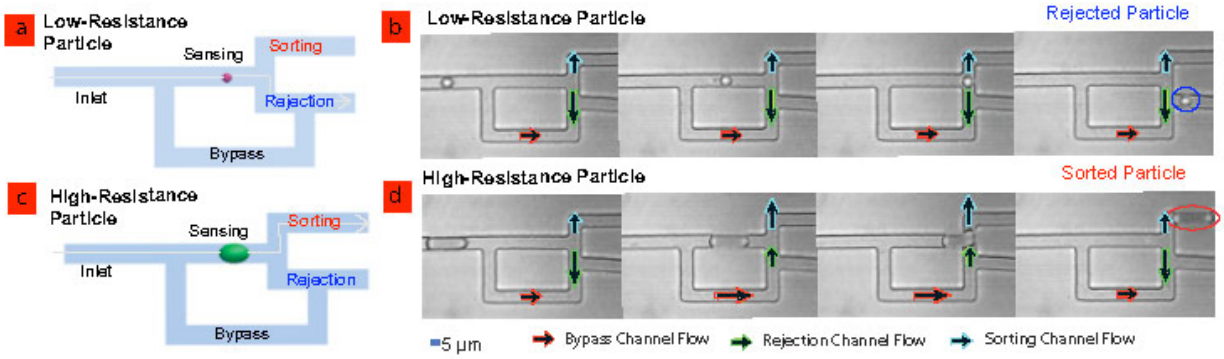

Figure 1. Hydrodynamic-Resistance Microfluidic Sorter. a) & c) Schematic diagram showing basic function for low and high hydrodynamic resistance gelatin particles, respectively. b) & d) Micrograph illustrating flow rate modulations that result in sorting of low and high resistance particles, respectively.

The sorting circuit, Figure 1, accepts a single deformable particle and switches it to either a sorting channel or a rejection channel depending on the relative magnitude of the increment in hydrodynamic resistance induced by the particle. Low resistance particles are rejected (Figure 1a and 1b), and high resistance particles are sorted (Figure 1c and 1d). The difference in resistance between different particles can be a result of either by size, as shown in Figure 1 for gelatin particles, or by differences in mechanical properties or adhesion. In the sorting circuit, the ratio of the flow rates in the sorting and rejection channels coming from the sensing channel are modulated by the presence of a particle in the sensing channel. By default, i.e. by appropriate choice of channel geometries, a higher fraction of the sensing channel flow is directed towards the rejection channel. When a high resistance particle flows through the sensing channel, part of the flow originally going to the sensing channel is redirected through the bypass channel into the second part of the rejection channel, decreasing the flow through the first part of the rejection channel, and changing the flow ratio exiting the sorting junction (junction formed by the sensing, sorting and first part of rejection channel). Since the particle trajectories at the junction are determined by the relative flow rates at the junction bifurcation, this modulation of the flow rates results in sorting of the particles.

An alternative way to understand the operation of the proposed sorting circuit is depicted in Figure 2, where the equivalent resistance circuit is shown. The circuit can be understood based on the circuit topology and magnitude and direction of three flow rates: sensing channel flow (I_{sens}), sorting channel flow (I_{sort}), and the first part of the rejection channel ($I_{reject1}$). When a particle flows through the sensing channel inducing a certain hydrodynamic resistance, ΔR, the resulting flow can be understood as a linear combination of flows in the circuit under two different conditions: the original circuit with no induced hydrodynamic resistance (i.e. no particle), and a circuit with infinite induced resistance. In the circuit with infinite induced resistance, the flow through the first part of the rejection channel is reversed with respect to the former case, while the flow trough the sensing channel is zero. Hence, when a particle induces a finite hydrodynamic resistance, the flow through the first part of the rejection

978-0-9798064-5-2/µTAS 2012/$20©12CBMS-0001

channel decreases faster than the flow through the sorting channel. Beyond a certain threshold of induced hydrodynamic resistance, it causes majority of the fluid from the sensing channel to flow into the sorting channel, thereby directing the particle into the sorting channel. This kind of circuit relies on self interactions to modulate flows and produce sorting, as opposed to previously developed logic circuits that use particle-particle interactions to flow modulation; hence it is asynchronous since does not require particle-particle synchronization.

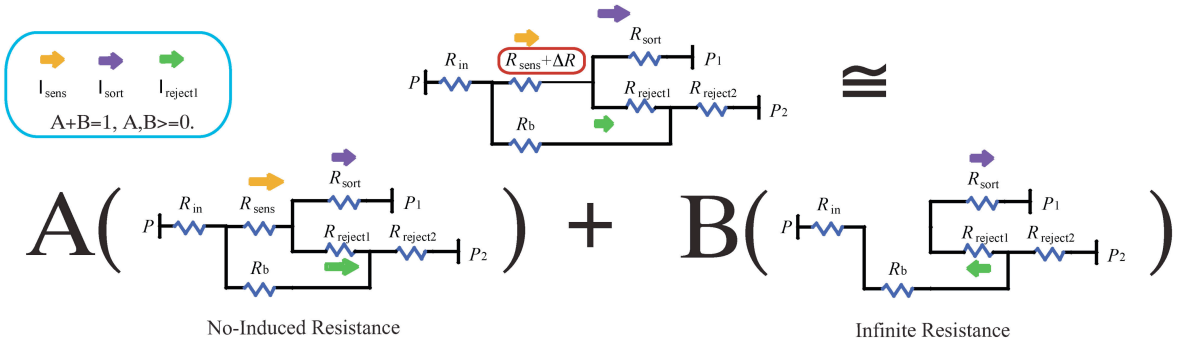

Figure 2. Sorter equivalent circuit and graphical explanation of device function. When a particle flowing through the sensing channel induces a large hydrodynamic resistance, the circuit can be considered as a weighted sum of two circuits: a circuit with no-induced resistance and a circuit with infinite resistance. The induced resistance generates a reduction and eventual inversion of the flow through the first part of the rejection channel, producing particle switching.

METHODS AND MATERIALS

Red blood cells. Cells were washed first with a solution of PBS. Then, media was replaced with the High Viscosity Media; a solution made of 9.1 mL PBS, 9 g dextran (MW=2x10^6), 0.1 g BSA, and 0.04 g Pluronic. At the same time, PDMS devices were incubated with High Viscosity Media for 30-60 minutes at 20 ºC (Room Temperature).

Photocurable Droplets: Two solutions were used to produce droplets: an oil phase, carrier mix, and a water-soluble phase, droplet mix. The oil phase was a mix of white light mineral oil with Span 80 (1% v/v). The droplet mix comprised poly-ethylene glycol diacrylate (67.5% v/v), hydroxy-2-methylpropiophenone (30% v/v), tween 20 (1.5% v/v), FITC BSA solution (10 µg/mL), and a solution of fluorospeheres (1% v/v). A Nikon Eclipse TE2000-U inverted microscope with a Nikon Plan Fluor 10x/0.3 objective was used to acquire images.

RESULTS AND DISCUSSION

We exemplify the potential of this technique to sort based on size and deformability by demonstrating two new applications of the sorting circuit: a) size-based sorting of red blood cells (Figure 3) and b) micro droplet switching induced by light polymerization (Figure 4).

Sorting of cells in constrained microfluidic channels is challenging because they tend to adhere to the channel surfaces and clog the channels. Here we show sorting of red blood cells (RBCs), by using modified media with pluronic, BSA, and high molecular weight sugars to reduce adhesion. In the experiments, cells were flown for more than 3 h without clogging, despite the narrow channels used. Since RBCs have a discoid shape, we used rectangular microchannels as depicted in Figure 3a. Since larger cells exert a higher resistance to flow, size can be used as a sorting criterion. After the cells are injected into the circuit, the cell population splits into two streams: sorted and rejected (Figure 2b). A histogram showing size distribution was obtained after analyzing samples coming from the rejected and sorting streams, Figure 3c and 3d. As expected, large particles are preferentially sorted with a resolution of ~2 µm, depicted by the transition zone in Figure 3d.

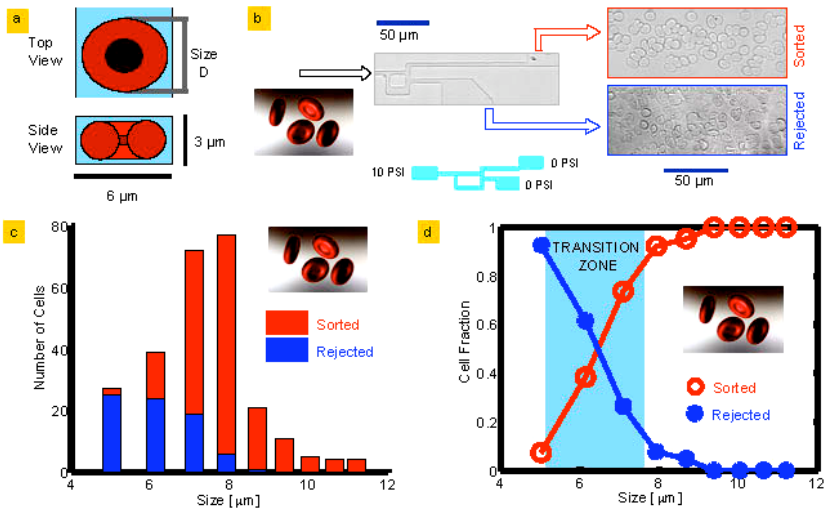

Figure 3. Size-based sorting of RBCs. a) Schematic diagram showing cell and channel dimensions. b) Micrograph showing device geometry, operation conditions, and sorted & rejected cells. c) Size distribution of the rejected and sorted cells. d) Fraction of sorted and rejected cells as a function of cell size.

Finally, we demonstrated particle separation based on deformability by sorting of otherwise identical droplets of uncured and cured photocurable liquid immersed in mineral oil solution. Droplets were generated upstream of the sorting circuit using a T-junction in which the photo curable mix was injected into the oil carrier. Before arriving at the sorting circuit, the droplets could be illuminated by a UV-light from a mercury lamp (Figure 4). By tuning the outlet pressures, the switching threshold could be tuned so that uncured droplets were rejected while cured droplets were switched (Figure 4b and 4d). This experiment demonstrates switching of particles based on deformability, and also illustrates a new concept enabled by the use of hydrodynamic resistance: switching of particles induced by light.

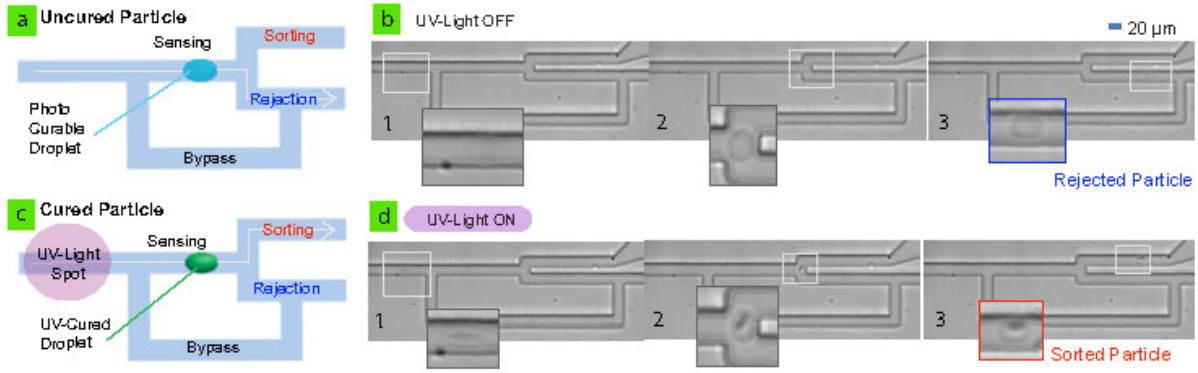

Figure 4. Deformability sorting of photocurable particles. a) & c) Schematic diagram showing setup for photo-curing droplets and resistance sorter circuit; UV-light OFF and ON respectively. b) Micrograph showing rejection of a low-resistance uncured particle. d) Micrograph showing curing and sorting of a UV-cured droplet.

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