COMBINED DENSITY AND SIZE-BASED SORTING IN DETERMINISTIC LATERAL DISPLACEMENT DEVICES
Stefan H. Holm1*, Jason P. Beech1 and Jonas O. Tegenfeldt1
1Solid State Physics and Nanometer Structure Consortium (nmC@LU), Lund University, Sweden

ABSTRACT
We present a deterministic-lateral-displacement (DLD) device that extends the capabilities of this traditionally size-based particle separation technique to also be sensitive to density. By the use of T-shaped posts instead of the normally cylindrical posts the particle trajectory through the device will be a function of its vertical position which in turn is determined by the buoyancy of the particles. The potential lies in fast sorting of complex biological samples together with diagnosis and treatment-monitoring of diseases affecting cell-density, eg. cancer, sickle-cell anemia and malaria. We demonstrate proof-of-principle of combined size-and-density-based sorting, specifically particles of identical size but different density.

KEYWORDS: Deterministic Lateral Displacement, Density, Fractionation

INTRODUCTION
DLD is a powerful microfluidic technique first shown capable of separating particles based on size[1] and recently shown by our group to have the potential to discriminate cells based on shape[2] and deformability[3].

In this work we implement separation based on density in a DLD device by the use of T-shaped posts instead of the traditionally cylindrical posts, (Fig 1C). As the critical size above which particles are laterally displaced is a function of the distance between the posts (the gap, G) we achieve a device with two separate critical sizes. As the vertical position of a particle depends on the buoyancy force the trajectory through the device will be a function of both the particle size and density.

It has been shown that cell density is a highly specific biomarker with an intrinsic cell-to-cell variation a 100-fold lower than that of volume or mass variation[4]. Further, the cell density is known to vary over the course of the cell-cycle[5], due to apoptosis[6] and diseases such as malaria, sickle cell anemia and cancer[7]. With these characteristics, cell density is a highly interesting biomarker which combined with the power of DLD have the potential to open up for new separation schemes.

THEORY
In DLD the sample flows through a symmetric array of micrometer-sized posts under laminar flow conditions. Hydrodynamic and steric interactions between posts and particles give rise to a separation where larger particles are deflected at a specific angle with respect to the flow. However, small particles are not affected by these interactions and travel through the device without being laterally displaced, Fig 1A, thus achieving a separation of the particles. The specific size above which particles are deflected is known as the critical size. This value, $D_c$, is a function of the periodicity of the array, $N$, and more important for this work the distance between two posts, the gap (G), see the unit cell in Fig 1B.

Traditionally the posts of a DLD device have been cylindrical with a single gap, and a single critical size as a result. However, by the use of T-shaped posts we obtain a device with two distinct gaps and consequently two separate critical sizes. The particles trajectory through the device will thus be a function of both its size and also its lateral position.

Figure 1. (A) Schematic illustration showing a section of a DLD device, with posts colored blue. The hydrodynamic center of the small yellow particle is able to fit within the black flow stream while the larger red particle is laterally displaced to the adjacent flow stream for each row. (B) A unit cell in the DLD array together with definitions of the period and the critical size. (C) Illustration showing the normal cylindrical posts and the T-shaped posts used in this work. With T-shaped posts two different gaps, and consequently two separate critical diameters are present, where the particles' vertical positions determine their behavior in the device.
EXPERIMENTAL

Flow simulations of the device was carried out using COMSOL Multiphysics 4.3 (COMSOL AB, Sweden). The result for the flow through a unit cell is shown in Fig 2A together with horizontal slices of the unit cell showing the flow profiles at the center height of the small and large gap section respectively. The flow profile between two posts, which determines the critical diameter in the DLD device was then plotted (gap size normalized). From here the critical particle sizes, $D_c$, can readily be determined. (B) SEM-micrograph showing an overview of the device with the inlets and outlets and the separation array. (C) SEM-micrographs of the device inlet followed by higher magnified micrographs of the center section of the device showing the T-shaped posts.

RESULT AND DISCUSSION

As expected the heavy silicon microspheres (negative buoyancy) sediment to the bottom and depending on the orientation of the device they experience the low or the high critical size (Fig 3A). In this case they are only separated for the small gap with an expected critical size of 3.50 µm and not in the large gap with an expected critical size of 7.00 µm.
More interestingly, mixing particles of different density we demonstrate that we can separate particles that have similar size and that differ in density only (Fig. 3C). Here, the buoyance on the PS particles forces them to flow into the upper section of the device with a critical size above the particle sizes while, again the silicon particles sediment into lower level with a lower critical size which is between the size of the particles, and consequently only the large Si particles are displaced towards outlet 2.

CONCLUSION

We have successfully demonstrated a proof-of-principle device where separation is sensitive not only to size but also density of the particles. In contrast to other alternative single-cell techniques for density characterization[4], this approach is entirely passive.

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REFERENCES


CONTACT *S.H. Holm, tel: +46 (0)70-4099380; Stefan.Holm@fft.lth.se