Hydrodynamic Resistance and Sorting of Deformable Particles in Microfluidic Circuits

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Abstract:

Sorting of micro particles has numerous applications in science and technology, from cell analysis to sample purification for biomaterials, photonics, and drug delivery. Methods used for particles separation relied only on procedures that involved sedimentation, filtration through porous material or other physical procedures that could be performed macroscopically and in bulk; only recently has miniaturization of fluid systems enabled individual particle separation at the macroscopic level. In the 1980?s, as new fabrication techniques originally used to miniaturize circuits became available, they were used to miniaturize structures used for filtration, creating new membranes for filtration with sub millimeter thickness and new fluidic devices that enabled completely new functionalities.

Hydrodynamic resistance, the extra resistance induced by a particle as it flows through a microfluidic channel, has been recently proposed as a viable property for particle characterization. Particle-induced hydrodynamic resistance can be linked to relevant biological properties, e.g. deformability, which is an important parameter in diseases like sickle cell anemia, malaria, sepsis and some kinds of cancers In this work we propose the concept of “hydrodynamic resistance sorting”, which adds to the repertoire of current sorting technologies. We propose a microfluidic circuit capable of sorting particles according to the hydrodynamic resistance they induce in micro channel as they flow through. The circuit has two flow modes: rejection and sorting modes. The microfluidic circuit switches from rejection to sorting mode automatically when a particle induces an increment in hydrodynamic resistance larger than a designed threshold value. The circuit uses the concept of microfluidic logic, in which a microfluidic system has multiple discrete output modes, (sorting and rejecting particle modes), which are activated by an input variable, in this case the hydrodynamic resistance. As opposed to previous logic microfluidic circuits based on droplets, the sorting circuit uses particle self-interactions and does not require particle synchronization to enable microfluidic logic; hence the circuit is asynchronous. Further, we show the circuit’s ability to work with cells by sorting red blood cells and tested the circuit’s capacity to sort particles based on mechanical properties by sorting cured and uncured droplets made of a UV-curable solution.
Finally, in addition to development of circuits to sort particles based on hydrodynamic resistance, we investigated the link between hydrodynamic resistance and the change in mechanical properties experienced by cells. From first principles it is unclear exactly how and to what extent cell mechanical properties affect cell passage through constrained channels. Force opposing cell passage could be proportional to the cell velocity, as it occurs during lubrication of rigid objects, or proportional to normal forces, as it occurs in the case of many macroscopic objects sliding on surfaces. We used a microfluidic differential manometer, particle image velocimetry, high-speed imaging, confocal microscopy and non-dimensional analysis to investigate the relationship between cell mechanical properties, friction forces and hydrodynamic resistance. The results revealed that the transport of cells through constrained channels is a soft lubrication flow, where the driving force depends primarily on viscous dissipation and secondarily on the compressive forces acting on the cell.

This work advances our understanding of the flow of deformable particles through constrained channels and provides a method to sort single particles based on their hydrodynamic resistance. The devices developed here have potential applications in biomechanical analysis of cells, bio-separation, point-of-care diagnostics, as well as in two-phase microfluidics.