FREELY SELECTABLE DIRECTION OF SEPARATION FOR DIFFERENT PARTICLE SPECIES WITH A NEW MICROFLUIDIC SEPARATION DEVICE

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ABSTRACT
We present a simple microfluidic device, that is capable of separating three colloidal bead species from each other by forcing one freely selectable particle type to migrate into the opposite direction of the other types. Our principle is based on the coupling of the beads to an electric field, generated by suitably designed electrical pulses and microstructures and can in theory be extended to a large number of different particle species.

KEYWORDS: Separation, Microparticles, Electrophoresis, Dielelectrophoresis

INTRODUCTION
Standard biotechnological separation techniques hold the disadvantage, that the separation criterion is often unchangeably implemented during fabrication. Gel electrophoresis is such a technique, where the predefined and therefore fixed gel density dictates the size range of the analyte molecules. A major improvement would be a fast dynamic and versatile adaptation of the selection criterion to the current separation task. Therefore we designed, fabricated and characterized a new microfluidic device which allows such dynamic and selective adaption of the separation criterion *and* migration direction during operation. As a proof-of-concept, we demonstrate the separation of one arbitrary micro bead species out of three different kinds with freely selectable migration direction. In contrast to our previous work, where absolute negative particle mobility (ANM) [1,2] was exploited to separate two particle species in a geometric obstacle field [3], our new concept is based on electrodeless dielectrophoresis (DEP) and is operated and controlled with specifically shaped electrical pulses.

EXPERIMENTAL
The device is made of poly(dimethylsiloxane) and consists of a standard cross injector and a 20 mm long analysis channel structured with a 10 mm triangle array (see Fig. 1). These triangles have a height and a baseline of 10 micrometers. All channels are 10 micrometers high and have a width of 300 micrometers. Between the triangles, DEP traps are created by an alternating voltage U_{AC} while a superimposed constant voltage U_{DC} drives the negatively charged particles with diameters d_1=1.1 µm, d_2=1.9 µm and d_3=2.9 µm through the channel by electrophoresis (EP).

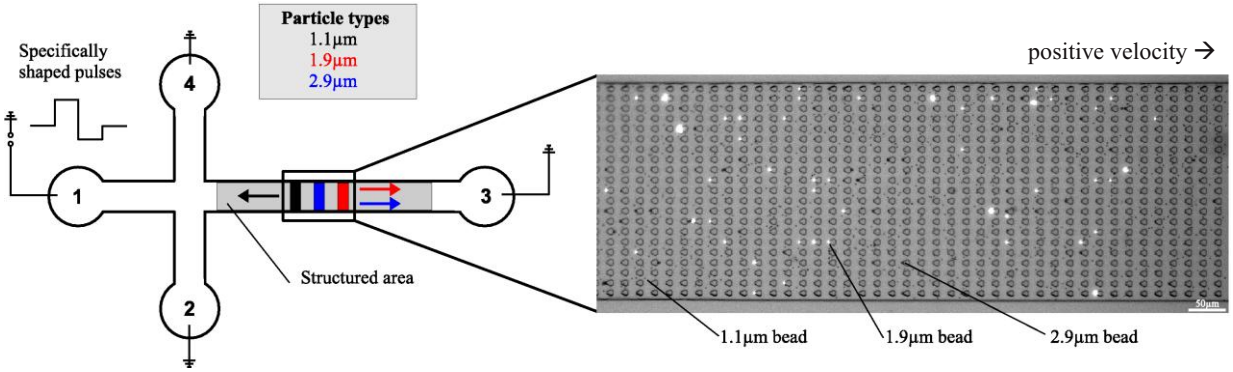

Figure 1: Schematic drawing of the microfluidic device (left) and a micrograph of the structured area during the experiment (right). When a voltage U_{AC} is applied between 1 and 3, the non-conducting obstacles create an inhomogeneous electric field distribution, which results in DEP traps. The obstacles have a triangle form with a height and a baseline of 10µm length.

Depending on the relative strengths of EP and DEP forces induced by U_{DC} and U_{AC}, respectively, selection of the particle types which are trapped and which are still transported is readily possible by setting the system to four major force regimes A-D (see Fig. 2d). With these four regimes one can design specific voltage sequences as done in Tab. 1. First, regime A is addressed to set the system to a known state where all particles are trapped by DEP. Then the particles are separated within B and/or C by consequently holding back a certain particle species. At the end, regime D terminates the sequence, so that effective migration of certain beads into opposite directions is possible. This idea can in principle be extended to a larger number of different particle types by adding more force-regimes and sequence steps.

Table 1. Characterization of the applied voltage sequences that induce the three separations. a) Separation of the 1.1µm beads from the 1.9µm and the 2.9µm beads. b) Separation of the 1.9µm beads from the other two types. c) Separation of the 2.9µm beads from the other two types. The voltages set the system to one of the four regimes from Fig. 2d) and are supplied over the time range Δt.

a)			b)			c)		
Δt [s]	**U_{DC} [V]**	**U_{AC} [V]**	**Δt [s]**	**U_{DC} [V]**	**U_{AC} [V]**	**Δt [s]**	**U_{DC} [V]**	**U_{AC} [V]**
10	0	400	10	0	400	10	0	400
40	15	360	90	15	400	50	-15	320
12	-10	0	25	-16	330	12	10	0
			10	10	0			

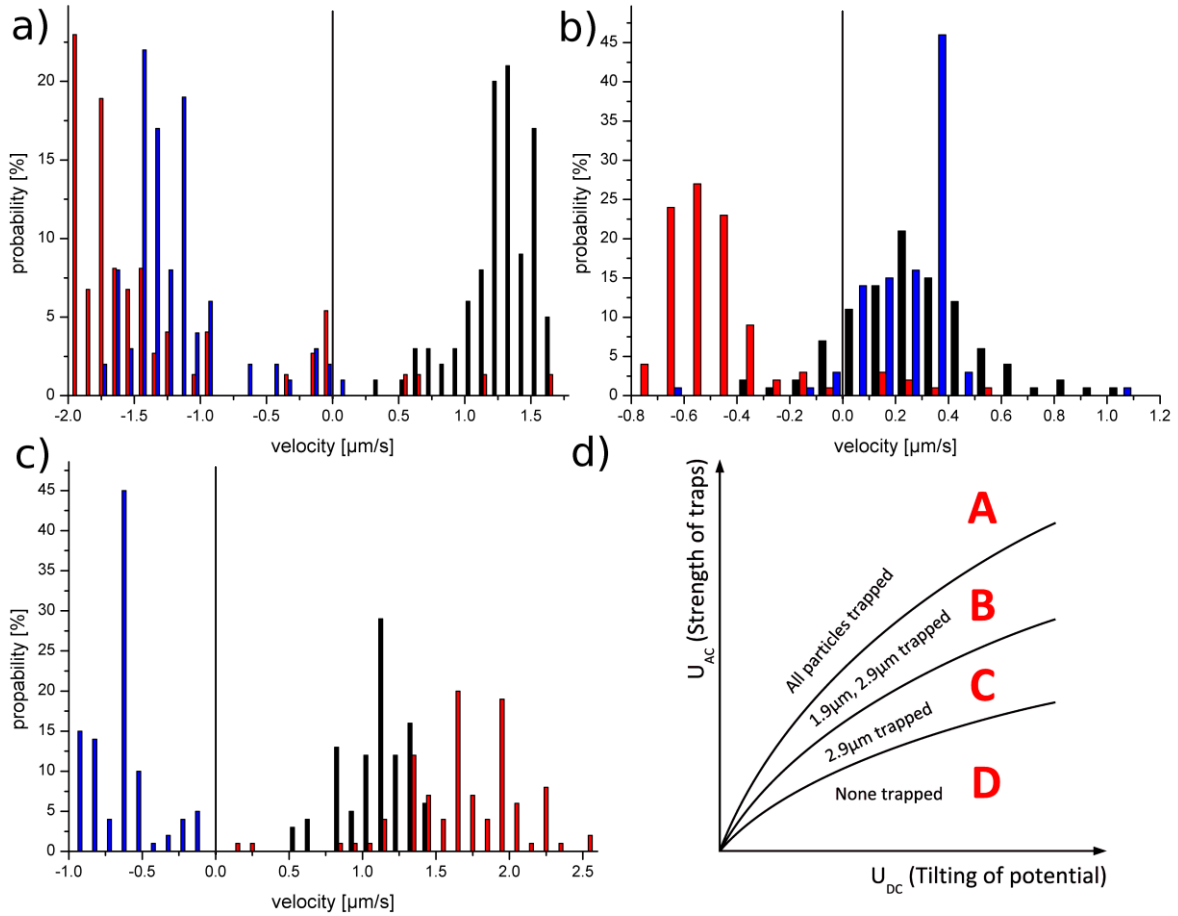

Figure 2: a)-c): Analysis of a mixture of micro beads (d_1=1.1µm, d_2=1.9µm, d_3=2.9µm). In a) and c) the smallest and the largest particles have been separated (with the protocols in Tab 1a,c) from the other two types. It is even possible to separate the middle sized 1.9µm beads from the smaller and larger particles as shown in b) with the protocol from Tab 1b). 100 particles of each species were analyzed. d): Different DEP trapping regimes that result from a combination of an alternating voltage U_{AC} and a direct voltage $U_{DC} > 0$. An analogous situation is present for $U_{DC} < 0$.

RESULTS AND DISCUSSION

Fig. 2 a)-c) shows the experimental separation of the three micro bead species where in a) the 1.1µm particles move into the opposite direction of the 1.9µm and the 2.9µm particles. In b) the voltage schemes were changed such that the 1.9 µm beads are extracted from the mixture of 1.1µm and 2.9µm beads. In c) the largest particles of 2.9µm diameter move into the opposite direction of the 1.1µm and the 1.9µm particles. Consecutive repetitions of this voltage scheme leads to further separation of the different species.

We can therefore show that our microfluidic device is capable of extracting a freely selectable bead species out of other types by effectively moving it into the opposite direction with quite effective separation speeds.

CONCLUSION

Within a novel microfluidic device, three microparticle species have been separated from each other by letting one of them effectively migrate into the opposite direction of the other ones. Possible applications range from single molecule DNA or protein separation to single cell analysis, which is highly relevant for the new field of systems biology [4]. The device can also be adapted to non-biologically motivated separation problems like the dynamic separation of nanoparticles or carbon nanotubes or any other polarizable objects and can in principle be extended to an arbitrary number of different species sizes.

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