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Inertial focusing of microparticles and its limitations

FJ Cruz¹, S Hooshmand Zadeh¹, ZG Wu^{1,2} and K Hjort¹

¹Engineering Sciences, Uppsala University, Ångström Laboratoriet, Uppsala, Sweden

²State Key Laboratory of Digital Manufacturing Equipment and Technology, Huazhong University of Science and Technology, Wuhan, China

javier.cruz@angstrom.uu.se

Abstract. Microfluidic devices are useful tools for healthcare, biological and chemical analysis and materials synthesis amongst fields that can benefit from the unique physics of these systems.

In this paper we studied inertial focusing as a tool for hydrodynamic sorting of particles by size. Theory and experimental results are provided as a background for a discussion on how to extend the technology to submicron particles. Different geometries and dimensions of microchannels were designed and simulation data was compared to the experimental results.

Keywords. Particle sorting, Inertial focusing, Micro-fluidic channel, PDMS.

1. Introduction

The field of microfluidics has experienced massive growth in the past two decades towards solving problems in healthcare, biological and chemical analysis, materials synthesis, and other emerging areas that can benefit from the scale, automation, or the unique physics of these systems. Microfluidic chips that focus, concentrate, order, separate, transfer, and mix particles and fluids have been demonstrated.

However, regarding sorting particles, not much progress has been made as we leave behind the microscale to approach the nano realm.

Inertial focusing is a phenomenon where suspended particles migrate across streamlines and focus at well-defined equilibrium points of the cross section. There is a necessity of large velocity gradients to influence particles and fluids while a laminar flow is maintained. Such combination of facts is only possible in micro scale, which is the reason for the lack of observation of similar behaviors in larger scales. Briefly, inertial focusing in straight channels is caused by the balance of two forces, figure 1.

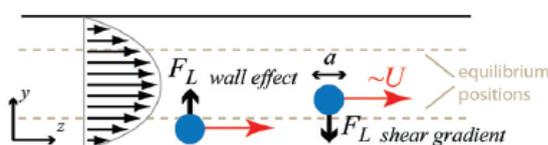


Figure 1. Main forces in a straight microchannel [1].

- a shear lifting force directed towards the walls of a channel due to the parabolic shape of the velocity profile.

$$F_{L, shear\ gradient} = \frac{2\rho U_f^2 a_p^4}{D_h^2} \quad \text{Eq. 1}$$

where ρ is the fluid density, U_f is the average flow velocity, a_p is the particle diameter and D_h the hydraulic diameter of the channel.

- a lifting force directed away from the wall due to interactions with the wall and a drag effect.

$$F_{L, wall\ effect} = 3\pi\mu a_p U_f \quad \text{Eq. 2}$$

where μ is the dynamic viscosity of the fluid. Also, these forces need to be strong enough to achieve focusing, which will set the focus length. To keep the lifting forces balanced as we scale down the size of the particle, we must compensate by scaling up the fluid velocity and scaling down the hydraulic diameter to the same factor. If we keep a constant aspect ratio, the flow rate should be linearly decreased as well.

The addition of curvature to the channel induces an uneven centrifugal force (since such force is proportional to the square of the velocity) and enables the development of a secondary flow called Dean flow, which redistributes the velocity profile, enhancing the lateral motion of particles and modifying the equilibrium positions [2], figure 2.

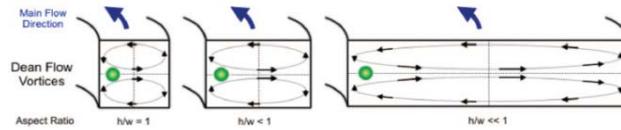


Figure 2. Secondary flow due to centrifugal forces [2].

Only one position remains stable and the enhancement of the lateral migration makes the particles reach such point within a shorter time than in straight systems.

A modification of the cross section with obstacles can also induce secondary flows that may be of advantage [3].

The aim of this paper is to provide experimental demonstrations on inertial focusing and a theoretical approach for the design of the channels and its limitations.

2. Experimental details

Microfluidic chips were fabricated with polydimethylsiloxane (PDMS, RT601, Wacker Chemie) and bonded to a glass slide.

PDMS was poured onto a SU-8 mold that was fabricated by UV lithography on a silicon wafer. It was cured for 1h at 70 °C, peeled off the mold and inlets and outlets were pierced with a biopsy punch.

To form the bond, the PDMS and glass surfaces were activated by plasma exposure with a corona discharger for 30 s prior to coming in contact. A hydrogen bond was formed, which turned covalent after the samples were put into the oven at 70 °C for 30 min.

Fluorescent polystyrene particles (Thermoscientific TM) with diameters of 10, 3 and 1 μm were suspended in deionized water at a concentration of 10^5 particles/ml.

A precision syringe pump (Harvard Instruments) was used to control the flow through the channels. The experiments were carried out under an inverted microscope.

3. Results and discussion

Inertial focusing relies on the equilibrium of forces acting on the particles. Such forces are strongly dependent on the geometry of the channel, on its dimensions and on the shape and size of particles. This means that the channel should be tuned specifically for the targeted particle size and it will focus only a certain bandwidth of particles.

3.1. Experimental work

The phenomenon was first studied in straight microchannels with 10 μm particles, figure 3. Equilibrium lines were achieved after a few millimeters from the inlet, in agreement to Dino Di Carlo [1], figure 4.

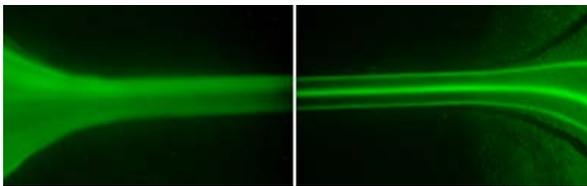


Figure 3. Equilibrium positions for 10 μm particles in a straight microchannel, 60x100 μm ($h \times w$) at 200 $\mu\text{l}/\text{min}$.

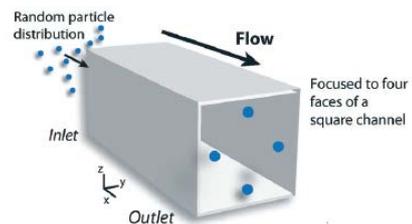


Figure 4. Theoretical equilibrium positions in a microchannel with rectangular cross section [1].

Adding curvature to the channels (spiral shape, growing radius from 0.7 mm up to 4.5 mm) not only led to a single equilibrium position but also faster alignment was achieved (after 1 loop, ~ 10 mm), figure 5. Changing the height of the channel, 3 μm particles were focused close to the inner wall while those of 10 μm were displaced to the center, figure 6.

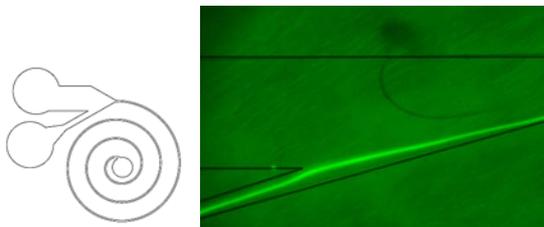


Figure 5. Equilibrium position for 10 μm particles in a curved microchannel, 80x100 μm ($h \times w$) at 200 $\mu\text{l}/\text{min}$.

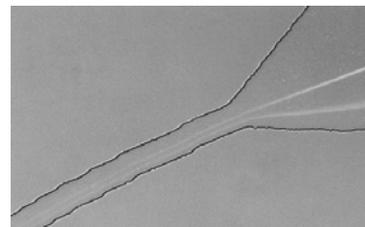


Figure 6. Equilibrium position for 10 μm and 3 μm particles (middle line and lateral line respectively) in a curved microchannel 30x100 μm ($h \times w$) at 200 $\mu\text{l}/\text{min}$.

Finally, obstacles along the inner wall of a curved channel were studied to find if that would improve the performance [3]. In this case, 10 μm particles quickly focused close to the wall while 3 μm particles did not reach a line but gathered in a band, closer to the center, figure 7.

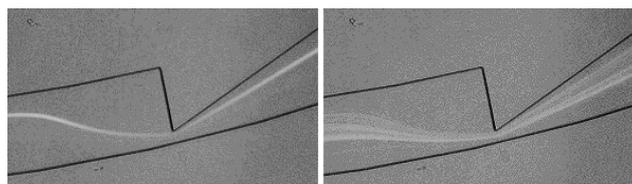


Figure 7. Equilibrium position for 10 μm and 3 μm particles (left and right respectively) in a curved microchannel with obstacles at the inner wall 40x100 μm ($h \times w$) at 200 $\mu\text{l}/\text{min}$.

Obstacles were put also along the outer wall of a curved channel. The flow created by the obstacles dominated over the curvature and the particles were dragged to the outer wall.

No focusing was observed for 1 μm particles in any design. A channel with dimensions suitable for such particle size was tested - 10x30 μm ($h \times w$). No result was obtained since the high pressure drop led to leakage of the system.

3.2. Theoretical discussion

As shown in eq. 1, the shear lifting force is strongly dependent to the size of the particle (to the power of four), to the flow velocity and to the dimensions of the channels (both to the power of two). On the other hand, the required channel length to achieve focus is proportional to the cube of the particle size (eq. 6). If nothing else is changed, alignment for a 10 times smaller particle requires a microchannel 1,000 times longer. To avoid such long channels, the cross section and the flow rate need to be tailored in order to focus a target particle size. It has the limitation that as particles decrease in size, higher velocities and smaller channels are needed, which turns into a large drop of pressure.

At the same time, such tailored conditions are valid for the target but not for a wide span around it; much larger particles will not fit in the channel and much smaller ones will not feel the lift force.

According to Di Carlo, the dimensions of the channel should be such that $a_p/h > 0.1$. The width should also be matched to the height in a relation of $h < w < 6h$ [1].

This agrees with our obtained results, where in a 30x100 μm channel the smallest particles we could focus were those of 3 μm since 1 μm particles do not suffice the condition..

Following the formula recommended by Fuerstman et al. for the pressure drop in rectangular cross section channels [5], fulfillment of the conditions above mentioned will mean a growth of the pressure drop to the power of 3 with a linear shrinkage of the targeted particle size (if the same length was used).

$$\Delta P \approx \frac{Q \ 12 \ \mu \ L}{h^3 \ w \ [1 - 0.630 \frac{h}{w}]} \quad \text{Eq. 3}$$

However, as we decrease the width of the channel, particles need to migrate less transversal distance. The required focus length depends on the slowest of the two velocities of lateral migration and Dean velocity. In our case, it will be the lateral migration velocity.

The required focus length (L_I):

$$L_I = \frac{U_f}{U_L} \ w \quad \text{Eq. 4}$$

where U_L is the lateral migration velocity:

$$U_L = \frac{\rho C_L U_{max}^2 (a_p)^3}{3\pi\mu D_h^2} \quad \text{Eq. 5}$$

and then:

$$L_I = \frac{24\pi\mu D_h^2}{\rho U_f (a_p)^3} w \quad \text{Eq. 6}$$

Hence, the required focus length will scale linearly with the size of the particle, allowing for shorter channels and thus relieving some pressure drop.

Putting all together, the pressure drop needed to achieve focus of particles increases with the square of the decrease of particle size.

Some exemplifying conditions that will suffice the conditions to achieve focus of a targeted particle size are summarized in table 1. In the three last examples, the height is at its upper limit of ten times the size of the particle. A decrease in height would make the focusing easier but the pressure drop would increase.

Table 1. Example of conditions to achieve focus depending on the targeted particle size. With decreased particle size, the channel length can be decreased.

Particle Size (μm)	Channel length (mm)	Height (μm)	Width (μm)	Flow rate (μl/min)	Average speed (m/s)	ΔP (bar)
10	20	80	100	200	0.4	0.3
3	20	30	100	200	1.1	3.6
1	7	10	30	65	3.7	38
0.3	2	3	10	20	11	360

As stated earlier, when scaling the system with the aim of sorting 1 μm particles, the pressure drop was too high in our case of using PDMS bonded to a glass. The chips started to leak. For further studies aiming at sub-micron particles, the microchannels must be fabricated with more robust materials. A proper material would be glass, in which microfluidics have shown to stand pressures up to 690 bar [4] and which allows for observation of the channels thanks to its transparency.

4. Conclusions

Microfluidic designs, using inertial focusing for separation, offer a solution for sorting particles in the micro scale at high through-put ($Q > 60 \mu\text{l}/\text{min}$).

Focusing particles of 10 and 3 μm was achieved with PDMS microchannels, while there was no success for those of 1 μm. This is due to the high pressure drop necessary to reach inertial focusing, which requires more durable microfluidics, e.g., made of glass. Alas, to separate particles far smaller than 1 μm in size will require too high pressure drops also for more durable microfluidic systems.

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