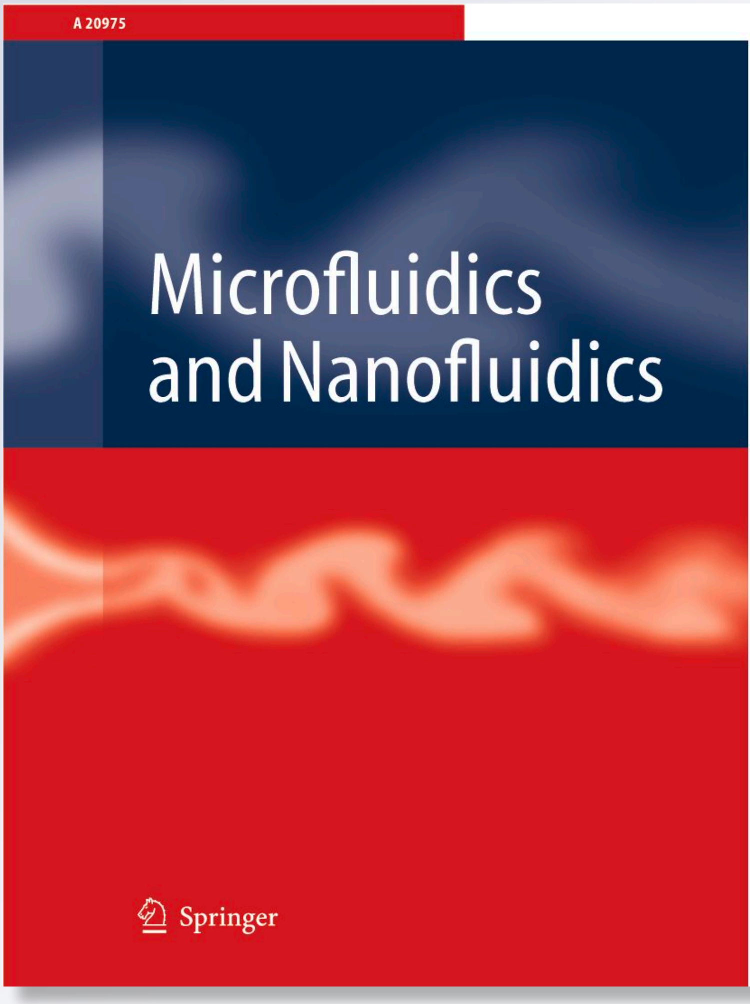
Efficiency of size-dependent particle separation by pinched flow fractionation

Aparna Srivastav, Thomas Podgorski & Gwennou Coupier

Microfluidics and Nanofluidics

ISSN 1613-4982

Microfluid Nanofluid
DOI 10.1007/s10404-012-0985-8



Microfluid Nanofluid
DOI 10.1007/s10404-012-0985-8

RESEARCH PAPER

Efficiency of size-dependent particle separation by pinched flow fractionation

Aparna Srivastav · Thomas Podgorski · Gwennou Coupier

Received: 6 January 2012 / Accepted: 1 April 2012

Abstract Pinched flow fractionation is shown to be an efficient and selective way to quickly separate particles by size in a very polydisperse semi-concentrated suspension. In an effort to optimize the method, we discuss the quantitative influence of the pinching intensity in the balance between the requirements of selectivity and minimal dilution.

Keywords Particle separation · Pinched-flow fractionation

1 Introduction

Sorting micro-particles of different sizes for analytic and preparative purposes has become a great challenge in the fields of chemical or biology research, or even industrial production. The development of microfluidic techniques has enabled control of flows at a scale similar to the size of the particles together with the use of small amounts of fluid, a target in the process of improving efficiency and reducing costs and dilution of samples.

As reviewed in Pamme (2007) and Kersaudy-Kerhoas et al. (2008), several systems were recently developed in that purpose. In general, one expects a quick and precise separation of large quantities of particles, together with low cost and human intervention. In addition, the ability to handle highly concentrated suspensions can also be considered as a requisite. Among these systems, pinched flow fractionation (PFF), which was initially proposed in Yamada et al. (2004), has the advantage of being a continuous process based only on hard-core interaction between particles and walls (Luo et al. 2011) which is optimized by dedicated flow control. In particular, no use of an external field such as gravity or pressure waves is needed, so that no specific particle property is required.

The principle of PFF is extremely simple (see Fig. 1): the suspension of (spherical) particles to be sorted is pushed against a wall by a particle-free pinching fluid. Due to their finite size, the centers of the particles are then located on the flow streamline one particle radius distant from the wall. In principle, collecting each of these streamlines leads to collecting each sub-population of the sample. In practice, two geometrical improvements are necessary. As most of the pinching fluid will remain particle-free, it is convenient to limit its volume. The pinching is thus realized in a channel (the pinched segment) whose width $2d$ should be similar to the diameter $2R_{\max}$ of the largest particle to be sorted. Secondly, collecting sub-samples with narrow size distributions requires that the lateral distance between the different populations is increased. This is achieved through a broadening of the pinched segment, allowing to add downstream collecting channels (Andersen et al. 2009).

As at least the top half of the fluid will remain particle-free, it is convenient to drain it through a single outlet, to maximize the space available for the expansion of particle-charged streamlines (Takagi et al. 2005; Vig and Kristensen 2008; Maenaka et al. 2008). Alternatively, Sai et al. (2006) added microvalves to close some collecting outlets to better control the final destination of the particles. At low Reynolds number, which generally applies to such systems, the final destinations in the collecting set-up of the fluid streamlines created after pinching should theoretically not depend on the geometry of the pinched segment and its expansion. Some works, however, explored the possible

A. Srivastav · T. Podgorski · G. Coupier (✉)
Laboratoire Interdisciplinaire de Physique,
CNRS et Université J. Fourier-Grenoble I,
BP 87, 38402 Saint-Martin d'Hères, France
e-mail: gwennou.coupier@ujf-grenoble.fr

Published online: 27 April 2012

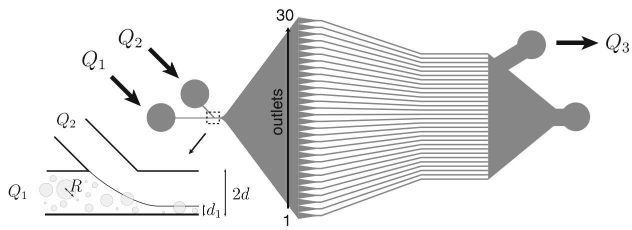


Fig. 1 Scheme of the sorting device. The particles suspension is injected with flow rate Q_1 and is pinched by a particle-free fluid with flow rate Q_2 in a segment of width $2d$. The suspension then enters a broad segment and splits into 30 outlets. In our experiment, $2d = 70$ μm and the thickness of the channels is 99 μm. Drainage with flow rate Q_3 was also added, but its effect is not discussed here

geometrical variations and their consequences on separation efficiency as compared to the expected one (Yamada et al. 2004; Zhang et al. 2006; Maenaka et al. 2008). Anyhow, it is likely that the small variations observed are mainly due to channel imperfections, 3D effects or optical errors (Jain and Posner 2008).

In most of the above cited papers, the proposed set-up is validated by injecting a very dilute mixture of a small number (between 2 and 4) of sub-populations of spherical particles with very different radii. Noting λ the ratio between the radii of a large particle and a smaller one, the following papers include such a validation: Yamada et al. (2004), $\lambda = 2$; Takagi et al. (2005), $\lambda \geq 1.4$; Zhang et al. (2006), $\lambda = 2.5$; Sai et al. (2006), $\lambda \geq 1.4$; Jain and Posner (2008), $\lambda = 1.5$; Morijiri et al. (2011), $\lambda = 1.7$. Vig and Kristensen (2008) considered seven sub-populations which are mixed and sorted, but their concentration is very low (0.05 %). As a result, those studies do not fully validate all expected performances of a sorting device, namely the possibility to separate efficiently particles out of a continuum of sizes in a concentrated sample while avoiding excessive dilution in the process. As concentration may lead to increased interactions between particles and possibly decrease the selectivity of the system, the influence of this parameter needs to be explored.

Maenaka et al. (2008) have considered an emulsion with continuous droplet radius distribution between 0 and 30 μm, with a concentration of 5 %. The sample is injected at a flow rate $Q_1 = 300$ μL/h, with a confining flow $Q_2 = 9$ Q_1 (see Fig. 1), and three collecting channels are used. The size distributions in these three channels are quite well separated, although overlappings of around 5 μm seem to occur. As the initial population is only split into three sub-populations, the monodispersity, that is, the existence of a narrow size distribution relatively to the mean size, remains weak in each of them.

In this paper, we wish to go further and optimize the flow rate ratio Q_1/Q_2 between the suspension and the pinching fluid, to find the good balance between the requirements of selectivity and minimal dilution. In the meantime, we show that sub-samples with good monodispersity can be quickly obtained.

2 Experimental set-up

As test particles, we use lipid vesicles obtained through the standard electroformation technique (Angelova et al. 1992), which straightforwardly produces polydisperse samples with a continuous size distribution. To ensure spherical shapes and prevent lateral migration in the pinched segment due to viscous forces (Coupier et al. 2008), a sucrose solution is encapsulated and vesicles are immersed in a slightly hypo-osmotic glucose solution. Being spherical, the vesicles can only deform if their membrane is stretched. The ability of the flow to stretch the membrane is given by the capillary number $C_a = \eta U/\kappa_s$, where η is the fluid viscosity, U its typical velocity, and κ the membrane stretching modulus, of order 0.3 N/m for DOPC membranes (Rawicz et al. 2000). The maximum flow rate considered here will be 20 mL/h, in a channel of typical size 100 × 100 μm^2, therefore, C_a will be of order 10^{-3} at the maximum, and vesicle deformation can be neglected. The use of different fluids inside and outside the vesicles also allows particle visualization through a phase contrast microscope coupled to a fast camera. The sorting device is a standard PDMS microfluidic chip bounded to a glass plate (Fig. 1). The pinched segment has width $2d = 70$ μm and thickness 99 μm. From now on, we set d as the length scale of the problem. The sorted sub-samples are observed in 30 collecting channels located at the end of the broadened segment. In this proof of concept device with no sample collection, they all converge to a unique outlet at atmospheric pressure. Additional drainage through a sucking with flow rate $Q_3 = 0.9$ $(Q_1 + Q_2)$ was added to increase the number of channels with particles. Note that the best location of this drainage is a complex issue as an infinity of geometrical variations are possible (Yamada et al. 2004; Takagi et al. 2005; Vig and Kristensen 2008; Maenaka et al. 2008). We shall not explore this in this work.

The particles have radii lying between 0 and 0.97 (in d unit), and split into the 16 first channels (which indicates that our drainage is not optimal). In each outlet channel, the mean radius $\langle R \rangle_i$ of the particles and the standard deviation is measured. The flow rate Q_2 was kept constant to 10 mL/h, and Q_1 was varied between 0.2 and 10 mL/h. We wish to find the optimum ratio Q_1/Q_2 but this parameter would depend on the chosen width $2d$ (larger d would require larger Q_2 for the same pinching efficiency), which depends itself on the maximum size of the particles to be sorted. A more appropriate parameter is, therefore, the width d_1 occupied in the pinched-segment by the fluid coming from channel 1. Roughly, d_1 should be of the order of the radius of the smallest particles to be sorted.

Finally, initial volume concentrations of 0.8 and 4.8 % are considered.

3 Results

Figure 2a, b shows the mean sizes of the particles in the different channels for different values of d_1 between 0.16 ($Q_1 = 0.2$ mL/h) and 1 ($Q_1 = 10$ mL/h). For $d_1 \leq 0.51$, good separation is achieved, with standard deviations of the order of the half distance between two neighboring mean values.

In addition to this separation, the obtained sub-samples have a good monodispersity: the particles of radii ranging from 0.05 to 0.97 split into 16 sub-samples where the mean radius increases quasi linearly and the standard deviation is roughly constant in the different channels and equal to 0.017 for $d_1 = 0.16$, 0.021 for $d_1 = 0.36$ and to a still reasonable 0.036 for $d_1 = 0.51$. Note that if particles of radii between 0 and 1 are perfectly separated into 16 sub-populations, the size difference between the smallest and the largest particle in each sub-population is 0.063, which gives a standard deviation of around 0.016, so with $d_1 = 0.16$ we reach the best possible monodispersity with our choice of outlet channels.

The monodispersity quality can be estimated by the ratio between the standard deviation and the mean radius, and from channel 1 to channel 16 we find that it goes from 17 to 2 % when $d_1 = 0.16$ and from 36 to 4 % when $d_1 = 0.51$. The low quality for small particles is related to the choice of outlet channels with equal widths, but the good quality obtained for larger particles show that this is just a scale issue that would be solved by local refinements at the level of the outlets receiving the smallest particles.

As d_1 is increased even more, the standard deviations increase drastically while the mean radius varies less between the outlets, in particular for high radii, so separation is not achieved. Note that for $d_1 = 0.62$, outlets 14–16 have narrow standard deviations, as well as outlet 16 for $d_1 = 0.77$: the pinching is still strong enough to prevent smaller particles from being at the same level as the large particles that enter these outlets. For intermediate channels (around channel 10) or for $d_1 = 1$, the population is roughly bidisperse. This can be seen in Fig. 3a: the narrow distribution of outlet 3 becomes wider in outlets 7 and 10 and two distinct populations appear in outlets 12 and 15. A possible explanation of this phenomenon can be reached through purely geometrical considerations if one takes into account the effects of walls in inlet 1, before pinching. In this area, the distribution of small particles extends to closer distances

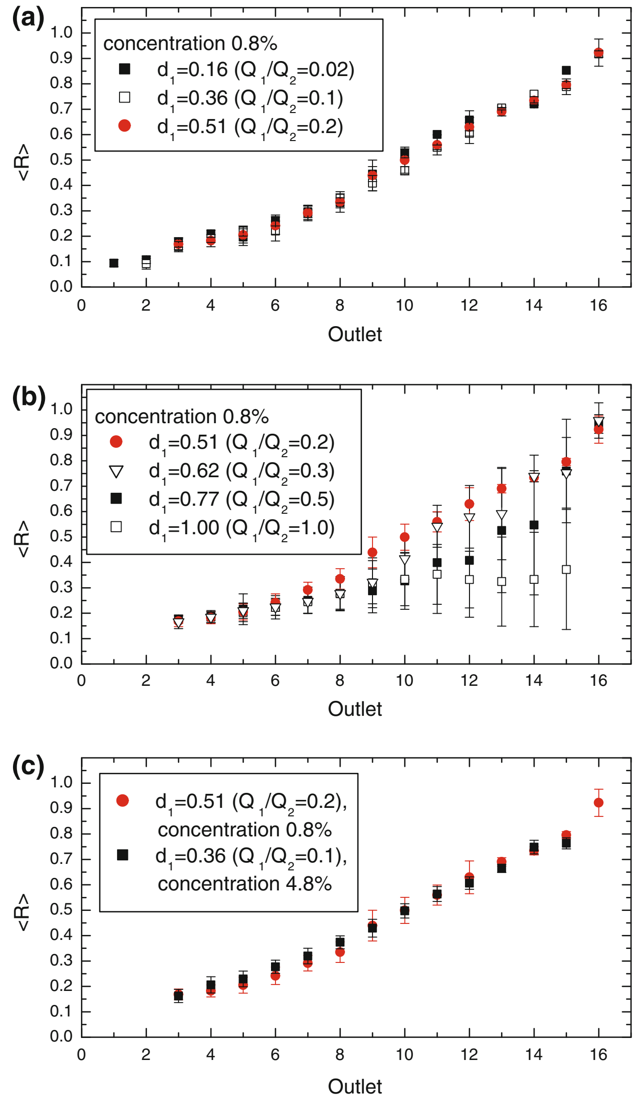


Fig. 2 Size distributions in the outlet channels. **a**, **b** results for initial concentration of 0.8 % and varying pinched width *d1* (that is, varying *Q1/Q2*). **c** Results for initial concentration of 4.8 % compared with previous ones (color online)

to the top wall than larger ones. If the pinching is not strong enough, a reminiscence of this distribution will be found in the pinched fluid, with some small particles higher than larger ones. On the other hand, the bottom wall in the pinched segment prevents the largest particles from respecting this initial order and they must stay in upper position, where non-pinched small particles lie.

Finally, it is remarkable that separation with d_1 around 0.5 is almost as good as with the more intuitive choice of $d_1 = 0.16$, which is of the same order as the smallest particles considered here (even smaller ones, that enter channel 1, were barely distinguishable). If all the small particles present in the initial suspension were present in the whole pinched area of width $d_1 = 0.51$, they should be present until channel 10, where $\langle R \rangle = 0.50$, which is

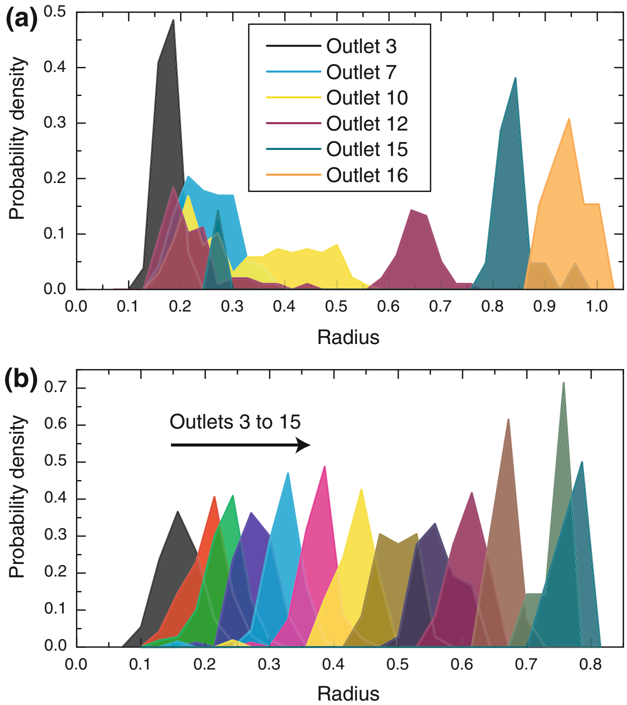


Fig. 3 Particle probability densities $n_i(R)$ in the outlets. $n_i(R)dR$ is the probability to get a vesicle of radius between R and $R + dR$ when picking up one in channel i. **a** For some selected outlets for a concentration of 0.8 % and $d_1 = 0.77$ (same data as in Fig. 2b). **b** In the 14 outlets analyzed for a concentration of 4.8 % and $d_1 = 0.36$ (same data as in Fig. 2c) (color online)

clearly not the case. One must, therefore, admit that collective effects take place, so that for instance, small particles could be pushed against the wall by larger particles.

Finally, as shown in Figs. 2c and 3b, good separation and monodispersity are also achieved for a concentration of 4.8 %: standard deviations are 0.027 with $d_1 = 0.36$, which is comparable with the more dilute case. The monodispersity quality reaches 3 % for the larger particles.

4 Conclusion

We have shown that PFF is an efficient technique to separate a semi-concentrated polydisperse suspension of micrometric spherical particles into sub-samples with tiny overlappings. In addition, monodisperse suspensions with a few percent of variation in sizes can be obtained from that initial suspension where size variations reach 50 %. Moreover, broader initial size distribution would probably not increase the final monodispersity quality in each sub-sample since the main issue is to separate small to medium sized particles. According to the desired monodispersity quality of the final sub-samples, the location and width of the collecting outlets can be optimized. Here, we considered outlets of equal width, which resulted in constant standard deviation between sub-samples, and thus, low relative monodispersity quality in the small particles samples. Getting constant monodispersity quality requires to consider outlet of linearly increasing width. If one wishes to get concentrated samples at the outlet, a pinched suspension width four or five times larger than the radius of the smallest particles surprisingly appears to be a good compromise: confining more tightens the distributions a little bit, but dilutes the samples more, while a weaker confinement leads to bad sorting. These conclusions are valid for a semi-concentrated suspension (concentrations around 5 %) and for quite high flow rates (some mL/h, that is one order of magnitude higher than in Maenaka et al. 2008). Note that for $Q_1 + Q_2 = 11$ mL/h, the Reynolds number is of order 100 in the pinched segment, so lateral drift of inertial origin could have perturbed the sorting (Segre and Silberberg 1961). However, inertial lift or viscous lift (that can occur in the case of deformable particles) often increases with particle size, therefore they should preserve the sorting effect and only shift the location of collecting outlets.

In addition, we have shown that bidisperse suspensions can be easily obtained through weaker pinching.

References

Andersen KB, Levinsen S, Svendsen WE, Okkels F (2009) A generalized theoretical model for "continuous particle separation in a microchannel having asymmetrically arranged multiple branches". Lab Chip 9:1638–1639

Angelova MI, Soleau S, Meleard P, Faucon JF, Bothorel P (1992) Preparation of giant vesicles by external AC electric fields: kinetics and applications. Progr Colloid Polym Sci 89:127–131

Coupier G, Kaoui B, Podgorski T, Misbah C (2008) Noninertial lateral migration of vesicles in bounded Poiseuille flow. Phys Fluids 20:11702

Jain A, Posner JD (2008) Particle dispersion and separation resolution of pinched flow fractionation. Anal Chem 80:1641–1648

Kersaudy-Kerhoas M, Dhariwal R, Desmulliez MPY (2008) Recent advances in microparticle continuous separation. IET J Nanobiotechnol 2:1–13

Luo M, Sweeney F, Risbud SR, Drazer G, Frechette J (2011) Irreversibility and pinching in deterministic particle separation. Appl Phys Lett 99:064102

Maenaka H, Yamada M, Yasuda M, Seki M (2008) Continuous and size-dependent sorting of emulsion droplets using hydrodynamics in pinched microchannels. Langmuir 24:4405–4410

Morijiri T, Sunahiro S, Senaha M, Yamada M, Seki M (2011) Sedimentation pinched-flow fractionation for size- and density-based particle sorting in microchannels. Microfluid Nanofluid 11:105–110

Pamme N (2007) Continuous flow separations in microfluidic devices. Lab chip 7:1644–1659

Rawicz W, Olbrich KC, McIntosh T, Needham D, Evans E (2000) Effect of chain length and unsaturation on elasticity of lipid bilayers. Biophys J 79:328

Sai Y, Yamada M, Yasuda M, Seki M (2006) Continuous separation of particles using a microfluidic device equipped with flow rate control valves. J Chrom A 1127:214

Segre G, Silberberg A (1961) Radial particle displacements in Poiseuille flow of suspensions. Nature 189:209–210

Takagi J, Yamada M, Yasuda M, Seki M (2005) Continuous particle separation in a microchannel having asymmetrically arranged multiple branches. Lab Chip 5:778–784

Vig AL, Kristensen A (2008) Separation enhancement in pinched flow fractionation. Appl Phys Lett 93:203507

Yamada M, Nakashima M, Seki M (2004) Pinched flow fractionation: Continuous size separation of particles utilizing a laminar flow profile in a pinched microchannel. Anal Chem 76:5465

Zhang X, Cooper JM, Monaghan PB, Haswell SJ (2006) Continuous flow separation of particles within an asymmetric microfluidic device. Lab Chip 6:561–566