A theoretical analysis of the resolution due to diffusion and size dispersion of particles in deterministic lateral displacement devices

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Abstract
We present a model including diffusion and particle-size dispersion for the separation of particles in deterministic lateral displacement devices also known as bumper arrays. We determine the upper critical diameter for diffusion-dominated motion and the lower critical diameter for pure convection-induced displacement. Application of our model to data suggests that the systematic deviation, observed for small particles in several experiments, from the critical diameter for separation given by simple laminar flow considerations may be explained by diffusion and size dispersion.

1. Introduction
In 2004, Huang et al [1] developed the elegant method of particle separation by deterministic lateral displacement in so-called microfluidic bumper arrays. The method, which relies on the laminar flow properties characteristic of microfluidics, shows a great potential for fast and accurate separation of particles on the micrometer scale [1–4]. Among the key assets of the deterministic lateral displacement separation principle are that clogging can be avoided because particles much smaller than the feature size of the devices can be separated, that the devices are passive, i.e. the particles bump into solid obstacles or bumpers, and that the separation process is continuous.

More precisely, particle transport in microfluidic bumper arrays is primarily governed by convection due to the fluid flow and by displacement due to interaction with the bumpers in the array [1]. These processes are deterministic and the critical diameter for separation of relatively large particles in these devices is well understood in terms of the width of flow lanes bifurcating around the bumpers in the periodic arrays [3]. However, if bumper arrays and particles are scaled down, diffusion will influence the separation process and affect the critical particle size significantly. Previously reported data on separation of particles in bumper arrays all show a bias toward larger critical particle size than that given by the width of the flow lanes nearest to the bumpers of the array [1–3]. In this work we extend existing models by adding diffusion and taking particle-diameter dispersion into account, and thereby explain the observed discrepancy.

In bumper arrays particles are convected by the fluid flow through an array of bumpers placed in columns separated by the distance $\lambda$ in the flow direction, see figure 1(a). For a given integer $N$, the array is made $N$-periodic in the flow direction by displacing the bumpers in a given column a distance $\lambda/N$ perpendicular to the flow direction with respect to the bumper positions in the previous column. Due to this periodicity of the array and the laminarity of the flow, the stream can naturally be divided into $N$ lanes, each carrying the same amount of fluid flux, and each having a specific path through the device, see [1].

For a given steady pressure drop, the fluid in the device moves with an average velocity $u_0$. Assuming a parabolic velocity profile $u(x)$ in the gap of width $w_g$ between two neighboring bumpers, see figure 1(b),

$$u(x) = 6u_0 \frac{x}{w_g} \left(1 - \frac{x}{w_g}\right),$$

(1)
becomes truly zigzag-shaped [1]. Large particles with the array [1]. This is illustrated by the almost horizontal trajectory of a small particle in the upper flow lane (small illuminated sphere).

In figure 1, the total flow rate \( Q_{\text{tot}} \) is given by

\[
Q_{\text{tot}} = \int_0^{w_g} u(x) \, dx = w_g u_0. \tag{2}
\]

By numerical simulations at low Reynolds numbers relevant for the actual devices, \( Re \approx 10^{-3} - 10^{-2} \), we find the assumption of a parabolic flow profile in the gap region well justified. This also agrees with the usual estimate for the entrance length \( l_{\text{entr}} = 0.06 Re \, w \), which is here of the order of 1 nm.

For an \( N \)-periodic array, the \( N \) flow lanes in a given gap carry the same flow rate \( Q_{\text{tot}}/N \). The width \( w_l^{(i)} \) of lane \( l \) is found by solving

\[
\frac{Q_{\text{tot}}}{N} = \int_{x^{(0)}}^{x^{(0)}+w_l^{(i)}} u(x) \, dx,
\]

where \( x^{(0)} = \sum_{j=0}^l w_l^{(j)} \) is the starting position of lane \( l \). In the simple bifurcating flow-lane model [1, 3] the critical diameter \( d_c \) is given as \( d_c/2 = w_1^{(1)} \). A small particle with \( d < d_c \) will never leave its initial flow lane and will thus be convected in the general flow direction following a so-called zigzag path. The conventionally used name zigzag path refers to the case where the bumpers are large compared to their center-to-center distance. In this case the path, which appears almost straight in figure 1 given the smallness of the bumpers, becomes truly zigzag-shaped [1]. Large particles with \( d > d_c \) will quickly bump against a bumper and from then on be forced by consecutive bumping to follow the skew direction of the array geometry, the so-called displacement path. When a particle gets bumped by a bumper in the array it will be displaced perpendicular to the flow direction until its center is located one particle radius \( d/2 \) from the surface of the bumper. This corresponds to \( n_l \) lanes of displacement,

\[
n_l = \frac{N}{w_k u_0} \int_0^{d/2} u(x) \, dx = N \frac{d^2}{4 w_k^2} \left( 3 - \frac{d}{w} \right). \tag{4}
\]

In the bulk fluid, where the lanes are assumed to have equal width \( \lambda/N \), see figure 1(a), the displaced distance \( \ell_{\text{disp}} \) is therefore

\[
\ell_{\text{disp}}(d) = n_l \frac{\lambda}{N} = \frac{d^2}{4 w_k^2} \left( 3 - \frac{d}{w} \right). \tag{5}
\]

In this work we extend the simple bifurcating flow-lane model by including diffusion and particle-diameter dispersion.

2. Model including diffusion

During the average time \( \tau = \lambda/u_0 \) it takes a particle to move by convection from one column to the next, it also diffuses. We assume that the diffusion process perpendicular to the flow direction is normally distributed with mean value zero and variance

\[
\sigma^2 = 2 D \tau, \tag{6}
\]

where the diffusivity \( D \) is given by the Stokes–Einstein expression

\[
D = \frac{k_B T}{3 \pi \eta d}. \tag{7}
\]

Here \( k_B \) is Boltzmann’s constant, \( T \) is the temperature and \( \eta \) is the viscosity of the fluid. Throughout the paper we use this expression to calculate \( D \) for any given particle size.

In figure 2 are sketched the two limits of (a) a small strongly diffusing particle, for which the interaction with the bumpers as well as the role of the flow lanes is negligible, and (b) a large particle, for which diffusion rarely brings the particle out of its given lane, and where each bumping event resets the position of the particle.

Note that we do not model Taylor–Aris dispersion explicitly. The reason is that this convection–diffusion phenomenon mainly affects the particle distribution along the flow direction [5]. However, we are not interested in the detailed arrival times of the particles in the outlet, only in their transverse distribution.
The probability of bulk displacement and the shift in position of the next bumper. The time interval $\tau$ is the difference $\tau_{disp} = \lambda / N$ between the bulk displacement and the shift in position of the next bumper. The probability $p_{esc}$ for this to happen is given by the integral of the Gaussian tails (see figure 2) in the neighboring lanes, i.e., by the error function

$$p_{esc}(d) = \frac{1}{2} \left( 1 - \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{(d - \frac{\lambda}{2\sigma(d)})} e^{-\frac{u^2}{2}} du \right),$$

(8)

where we have introduced the $d$-dependence explicitly. When a particle is transported through a bumper array it must bump at every bumper within one period of the array in order to be displaced one gap at the outlet. Thus, if the particle escapes at least one time in $N$ attempts, it will not be displaced. We define the critical particle size $d_c$ to be the size for which half of the particles escape bumping as they pass one period of the array. Thus $d_c$ can be found by solving

$$\sum_{k=0}^{N} \binom{N}{k} p_{esc}(d_c)^k [1 - p_{esc}(d_c)]^{N-k} = \frac{1}{2},$$

(9)

In figure 3 we have plotted the result of our model calculation for the critical particle sizes as a function of the bumper period for parameter values corresponding to the bumper arrays used by Inglis et al [3] (full line), Huang et al [1] (dashed line) and Larsen [6] (dotted line). The corresponding measured data points from these papers are plotted as circular, square and triangular points, respectively.

It must be emphasized that although the authors of [3] in their text only describe bumper arrays with a relative column displacement $\varepsilon = 1/N$, they do plot, without comments, data points with other displacements, e.g., $\varepsilon = 0.3$. These non-$1/N$ bumper arrays lead to more complicated displacement characteristics. This interesting topic, which we are currently studying, goes beyond the scope of the present work, where we focus on the influence of diffusion and particle-size distribution on the more simple and most widely used $1/N$-bumper arrays.

In figure 3, we have therefore only plotted data points from [3] with $\varepsilon = 1/N$.

2.1. Diffusion model

In order to escape bumping, a particle must diffuse more in the time interval $\tau$ than the difference $\ell_{disp} = \lambda / N$ between the bulk displacement and the shift in position of the next bumper. The probability $p_{esc}$ for this to happen is given by the integral of the Gaussian tails (see figure 2) in the neighboring lanes, i.e., by the error function

$$p_{esc}(d) = \frac{1}{2} \left( 1 - \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{(d - \frac{\lambda}{2\sigma(d)})} e^{-\frac{u^2}{2}} du \right),$$

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where we have introduced the $d$-dependence explicitly. When a particle is transported through a bumper array it must bump at every bumper within one period of the array in order to be displaced one gap at the outlet. Thus, if the particle escapes at least one time in $N$ attempts, it will not be displaced. We define the critical particle size $d_c$ to be the size for which half of the particles escape bumping as they pass one period of the array. Thus $d_c$ can be found by solving

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2.2. Comparison with experiments

The observation that the critical particle size in a $1/N$ bumper device is larger than the width of the first flow lane is also supported by the experimental data in figure 2 of [3]. Our model suggests that the deviation of the critical particle size from the width of the first flow lane can be explained by diffusion of the particles. In figure 3 it is seen how well the theoretical lines predict the transition between zigzag paths and displacement paths: the full line divides open and closed circles, the dashed line divides open and closed squares, and the dotted line divides open and closed triangles.

Using parameter values corresponding to the bumper device presented by Huang et al [1] our model predicts a critical particle diameter of 0.45 times the width of the gap for the particles traveling through the device with an average velocity of 400 $\mu$m s$^{-1}$. This is in good agreement with figure 2(a) in [1].

3. A discrete model including diffusion and dispersion

Particles typically used in experiments on particle separation are not mono-disperse. Their average diameters are distributed around a certain mean value with a relative standard deviation $\Delta d / d$, which typically is 20%, 10% and 5% for particles with $d = 25$ nm, $d = 100$ nm and $d = 500$ nm, respectively.

Faced with such a size dispersion it is very useful to have a simple method for predicting its effect. In the following
Figure 4. Relative numbers $r_0$, $r_1$ and $r_d$ of particles following the zigzag path, the displacement path and neither of these two paths, respectively, plotted as a function of the normalized, average particle diameter $d/d_c$, where $d_c = 118$ nm. The parameters of the bumper array are taken from [6]: $N = 100$, $\lambda = 8 \mu$m, $w_g = 1 \mu$m, $L = 20N\lambda = 16$ mm and $u_0 = 250 \mu$m s$^{-1}$. The buffer liquid is water at room temperature. Neglecting diffusion (solid symbols), the particles follow the zigzag path if $d < d_c$ and the displacement path if $d > d_c$. Including diffusion (open symbols), with $D$ given by equation (7), the small particles are not influenced by the bumpers. For $d > 2.1d_c$ the influence of the bumpers sets in, and for $d > 3.4d_c$ the particles follow the displacement path. The full black curves are the predictions using the results in sections 3.4.1 and 3.4.2, while the thick black vertical lines indicate the particle size when small particles stop behaving purely diffusive (left-most lines) and when large particles begin a purely deterministic displacement (right-most lines).

we therefore introduce a discrete model of the transport of particles with different diameters $d$ in an $N$-periodic bumper array taking convection, diffusion and size dispersion into account. The model allows us to study the relative influence of all three phenomena on the separation efficiency in a fast and simple manner. We illustrate our model by using the specific parameters from the bumper device presented in [6], see figure 4. In particular our results suggest that the critical size for separation or displacement, studied above, must be supplemented by a smaller critical size below which pure diffusion governs the motion of the particles in the bumper array. This prediction has not yet been tested experimentally.

3.1. Definition of the discrete model

At any instant, a particle is assumed to be positioned in the center of a flow lane $l$ of gap $g$ in some column $c$ of the array. For simplicity we further assume that the size distribution of any given set of particles is a normal distribution with a mean value given by the size quoted by the manufacturer and a relative standard deviation of 10%.

By convection any given particle moves from one column to the next. If it ends up in the last lane ($l = N - 1$) in one gap, it will be shifted to the first lane ($l = 0$) in the subsequent gap. Otherwise it will stay in the current gap and move up one lane. In our model pure convection is therefore described by the discrete map

$$ (c, g, l) \mapsto \begin{cases} (c + 1, g + 1, 0), & \text{if } l = N - 1, \\ (c + 1, g, l + 1), & \text{otherwise}. \end{cases} \quad (10) $$

Because of the finite diameter $d$ of the particle there is a minimum and a maximum lane number that it can occupy. The minimum lane number is the smallest integer $l_{\text{min}}$ that satisfies

$$ \sum_{l=0}^{l_{\text{min}}} w_1(l) > \frac{d}{2}, \quad (11a) $$

Similarly, the maximum lane number $l_{\text{max}}$ is the largest integer that satisfies

$$ \sum_{l=l_{\text{max}}}^{N-1} w_1(l) > \frac{d}{2}, \quad (11b) $$

Consequently, the simple convection mapping from equation (10) needs to be modified to account for the finite size of the particles

$$ (c, g, l) \mapsto \begin{cases} (c + 1, g + 1, l_{\text{min}}), & \text{if } l = N - 1, \\ (c + 1, g, l + 1), & \text{if } l < l_{\text{max}} - 1, \\ (c + 1, g, l_{\text{max}}), & \text{otherwise}. \end{cases} \quad (12) $$

The above convection scheme accounts for the separation of particles in deterministic lateral displacement devices
according to size. The critical particle diameter predicted by this model is
\[ d_c = 2u_1^{(0)} \]
in accordance with the geometric arguments of [3]. To characterize the separation quantitatively, we define the relative particle numbers \( r_0, r_1 \) and \( r_d \) as

\[ r_0 = \text{relative number of particles following the zigzag path,} \]
\[ r_1 = \text{relative number of particles following the displacement path,} \]
\[ r_d = \text{relative number of all other particles.} \]

With these definitions the sum \( r_0 + r_1 + r_d \) is always unity. If \( r_0 = 1 \) all particles follow the zigzag path and if \( r_1 = 1 \) all particles follow the displacement path. If \( r_d \neq 0 \) some of the particles end up at positions not explained by the deterministic analysis of the separation process. In figure 4 we have plotted the relative particle numbers \( r_0, r_1 \) and \( r_d \) as a function of the average particle diameter.

3.2. Pure mono-disperse convection

For mono-disperse and non-diffusing particles, the model results, as expected, in two modes: the zigzag mode and the displacement mode, see the closed circles in figure 4. For \( d < d_c \) we have \( r_0 = 1 \), and for \( d \geq d_c \) we have \( r_1 = 1 \), while we always have \( r_d = 0 \). The relative particle numbers can therefore be written as

\[ (r_0, r_d, r_1) = \begin{cases} (1, 0, 0) & \text{for } d < d_c, \\ (0, 0, 1) & \text{for } d \geq d_c. \end{cases} \] (15)

3.3. Influence of size dispersion

If we assume that the particles are not mono-disperse, but are distributed around a mean size \( d \) with standard deviation \( \Delta d \), the shift as a function of \( d \) from the zigzag mode to the displacement mode happens gradually instead of abruptly at a certain critical size \( d_c \) (figure 4, closed squares). The relative number of particles following the zigzag path \( r_0 \) can be found by integrating over all particle sizes smaller than the critical diameter given by the array geometry

\[ r_0 = \int_{-\infty}^{d_c} \frac{1}{\sqrt{2\pi(\Delta d)^2}} \exp\left(-\frac{(s-d)^2}{2(\Delta d)^2}\right) ds. \] (16a)

Similarly, the relative number of particles following the displacement path \( r_1 \) can be found by integrating over all particle sizes larger than \( d_c \):

\[ r_1 = \int_{d_c}^{\infty} \frac{1}{\sqrt{2\pi(\Delta d)^2}} \exp\left(-\frac{(s-d)^2}{2(\Delta d)^2}\right) ds. \] (16b)

The system is still a bi-modal system because \( r_d = 0 \) for all particle sizes.

3.4. Influence of diffusion

In 1D during the time step \( \tau \) a particle diffuses the distance \( \ell \), the average of which is the size-dependent diffusion length \( \sigma(d) \) given by

\[ \sigma(d) = \langle \ell \rangle = \sqrt{2D\tau} = \sqrt{\frac{2k_BT}{3\pi\eta d u_0}}. \] (17)

In our model we discretize the transverse diffusion as the properly rounded number \( n_{jump} \) of flow lanes crossed by the particle during diffusion,

\[ n_{jump} = \frac{N}{\lambda} \ell. \] (18)

The addition of diffusion smears out the displacement of the particles and causes the critical diameter to be larger than in the diffusion-less case (figure 4, open symbols).

3.4.1. Bumping criterion for small particles. Very small particles are completely dominated by diffusion, and the particle distribution at the end of the array is simply given by the transverse diffusion of the particles during the time \( L/u_0 \) it takes for the particle to be convected all the way through the array, see figure 2(a). For small particles we therefore have

\[ r_0 = \int_{1/2}^{1/2} \frac{1}{\sqrt{2\pi\sigma^2}} \exp\left(-\frac{x^2}{2\sigma^2}\right) dx. \] (19)

where \( \sigma^2 = 2DL/u_0 \). In figure 4 we have plotted \( r_0 \) versus \( d/d_c \), and \( r_1 = 1 - r_0 \) as the thick black curves in the interval \( 0 < d/d_c < 2.1 \).

As the particle diameter is increased, the bumpers begin to become important as the diffusion length \( \sigma(d) \), equation (17), is decreased and becomes equal to the displacement length \( \ell_{disp} \), equation (5). Using the criterion \( \sigma(d_1) = \ell_{disp} \), with the parameter values used in figure 4, we find that particles stop behaving as small diffusion-dominated particles and start interacting with the bumpers when \( d_1 = 2.1d_c \). This cross-over value is indicated by the left-most vertical lines in figure 4, and it fits well with the simulation data. Note that the specific value of the pre-factor is determined for \( d_c = 118 \) nm.

3.4.2. Bumping criterion for large particles. Large particles will interact with the bumpers at every row in the array and their position is thus reset at every bump to be \( \ell_{disp} \), see figure 2(b). Diffusion can therefore be neglected for such particles, they all follow the displacement path, and \( r_1 = 1 \).

As the particle diameter is lowered, the probability \( p_{esc} \) that a particle escapes the displacement path can be estimated by the probability of diffusing from the displaced position to the last flow lane in the gap, i.e. the distance \( \ell_{disp} - \frac{d}{2} \). This probability \( p_{esc} \) is given by equation (8). In figure 4 we have plotted \( r_d = p_{esc} \) and \( r_1 = 1 - r_d \) as thick black curves in the interval \( 3.4 < d/d_c < 6 \).

In order to follow the displacement path, a particle must bump at each row in the array. If we consider an \( N \)-periodic array with \( m \) full periods, the particles will have \( mN \) bumping opportunities as they pass through the entire array. If a particle
evades bumping at a bumper, it will be convected by the flow through a full period of the array before bumping is possible again. Because of the escape, it will miss $N$ bumping opportunities and end up one gap from the displacement path, see figure 5. Consequently, if a particle escapes one time, it will only have $(m - 1)N$ bumping opportunities and has therefore escaped bumping with a probability of $1/(m - 1)N$. The upper critical particle size $d_2$ for convection-induced displacement is defined using equation (8) as

$$p_{\text{esc}}(d_2) = \frac{1}{(m - 1)N}. \quad (20)$$

For the device used in the experiments by Larsen [6] we find $d_2 = 3.4d_c$. The predicted upper limit for diffusion dominated motion and the lower limit for convection-induced displacement compares well with the experimental observation by Larsen [6] that some particles end up in a transition region between the displacement path and the zigzag path (figure 3, gray triangles). Based on the data for $1/N = 1/100$ in figure 3 the experimentally observed transition region begins at $d_1 = 0.16w_g = 1.4d_c$ (the highest lying gray triangle) and ends at $d_2 = 0.40w_q = 3.4d_c$ (the lowest lying white triangle). Considering the simplicity of the discrete model this is in fair agreement with our model predictions, $d_1 = 2.1d_c$ and $d_2 = 3.4d_c$.

4. Conclusion

Experimental data on separation of particles in bumper arrays all show a systematic deviation from predictions made from the bifurcating flow-lane model [1, 3, 6]. Application of the model presented in this paper to the available data suggests that this systematic deviation may be explained by diffusion. In addition, we have proposed a simple discrete model for quickly simulating particle separation in bumper arrays. In contrast to the single critical particle size found in earlier analyses based solely on the deterministic separation processes, our work including diffusion identifies two particle sizes characteristic for the separation in bumper arrays: a small particle size $d_1$ below which diffusion dominates and a larger particle size $d_2$ above which the deterministic processes govern the sorting. Particles of intermediate sizes will neither follow the average flow direction nor the direction set by the array geometry. If bumper devices are scaled down both $d_1$ and $d_2$ are larger than the critical size predicted in the existing literature.

The presented model takes particle diffusion and size dispersion into account and has been validated against experimental data for a bumper device with period $N = 100$. In this example the transition from zigzag paths to displacement paths happens at particle sizes in the interval from 2.1 to 3.4 times the critical particle size predicted from geometrical arguments. This transition interval is in qualitative correspondence with the experimental observations from Larsen [6]. Our discrete model and the estimates presented in this paper suggest that particles smaller than twice the geometrical critical size of the $N = 100$ bumper device behave diffusively and are not affected by the bumpers because the small diffusive particles rarely come into contact with the bumpers due to random Brownian motion. We believe that our discrete model will be useful for design and evaluation of bumper arrays with any given specification.

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