Utilizing bifurcations to separate particles in spiral inertial microfluidics

Rahil N. Valani,¹,²,† Brendan Harding,²,† and Yvonne M. Stokes¹,‡
¹School of Mathematical Sciences, University of Adelaide, South Australia 5005, Australia
²School of Mathematics and Statistics, Victoria University of Wellington, Wellington 6012, New Zealand

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Particles suspended in fluid flow through a closed duct can focus to specific stable locations in the duct cross-section due to hydrodynamic forces arising from the inertia of the disturbed fluid. Such particle focusing is exploited in biomedical and industrial technologies to separate particles by size. In curved ducts, the particle focusing is a result of balance between two dominant forces on the particle: (i) inertial lift arising from small inertia of the fluid, and (ii) drag arising from cross-sectional vortices induced by the centrifugal force on the fluid. Bifurcations of particle equilibria take place as the bend radius of the curved duct varies. By using the mathematical model of Harding, Stokes, and Bertozzi¹ we illustrate via numerical simulations that these bifurcations can be leveraged in a spiral duct to achieve large separation between different sized particles by transiently focusing smaller particles near saddle-points. We demonstrate this by separating similar-sized particles, as well as particles that have a large difference in size, using spiral ducts with square cross-section. The formalism of using bifurcations to manipulate particle focusing can be applied more broadly to different geometries in inertial microfluidics which may open new avenues in particle separation techniques.

The ability to separate particles of different sizes suspended in a fluid is important in many biomedical and industrial technologies. For example, efficient isolation of rare circulating tumor cells from a large concentration of red blood cells and white blood cells in a blood sample can revolutionize cancer diagnostics and help in determining a likely prognosis. Another example is the detection and separation of waterborne pathogens in drinking water. Microfluidics has become an important tool for particle separation due to small sample consumption, fast processing time, high spatial resolution and high portability. Amongst the different possible microfluidic technologies aimed at particle separation, inertial microfluidics has been used widely because of its ease of operation and high separation resolution.

Segré and Silberberg first reported that particles suspended in fluid flow through a straight pipe with a circular cross-section can migrate across streamlines and accumulate to an annular region at approximately 60% of the pipe radius. This deviation of particles from fluid streamlines is due to the inertial lift force acting on the particle that arises from small but non-negligible inertia of the disturbed fluid flow at low to moderate Reynolds numbers. This results in the phenomenon of inertial migration and subsequent focusing of particles. In straight ducts, the locations where no net force acts on the particle in the duct cross-section, henceforth referred to as particle equilibria, vary with the geometry of the duct cross-section, particle size, and the flow Reynolds number. Adding curvature to the duct also influences particle equilibria via the introduction of cross-sectional vortices to the flow, known as Dean vortices. Curved microchannels with circular and spiral geometries are commonly used in inertial microfluidic devices aimed at particle separation by size. In these channels, the interplay between (i) the inertial lift force arising from fluid inertia, and (ii) the secondary drag force arising from Dean vortices, determines the number, nature and location of particle equilibria. By tuning the relative strength of these forces via changes in the bend radius, the particle equilibria can be manipulated to achieve particle separation for different sized particles.

Spiral channels with rectangular and trapezoidal cross-sections have shown promise for efficient size-based particle separation. In these geometries, the various parameters are chosen such that one obtains a horizontal separation between the particle equilibria of the chosen particle sizes to be separated. The particles focus to their respective stable equilibrium points or a stable limit cycle towards the end of the spiral channel after which the channel is split into multiple channels to collect the separated particles. Another separation method commonly used with circular and spiral channels having rectangular cross-section is known as Dean Flow Fractionation (DFF). In this method, the spiral channel has two inlets, one consisting of the sample containing particles typically a mix of two distinct sizes) and the other through which a sheath flow is introduced. As the particles flow through the curved channel, the Dean vortices transport the smaller particles towards the outer wall, while a balance of inertial lift and secondary drag equilibrates the larger particles near the inner wall, thus achieving separation between the two particle sizes. Note that with this method, the smaller particles do not reach a stable equilibrium position, rather, their well-controlled migration due to Dean vortices drives their separation from the larger particles. A variant of DFF has also been developed to separate several different smaller (sub-micron) sized particles and is called High-Resolution Dean Flow Fractionation (HiDFF).

Many advances in particle separation methods are primarily driven by experimental trial-and-error, with the potential of predicting and optimizing particle separation based on theoretical models and numerical simulations not yet being fully exploited. Although the use of theoretical and numerical methods has progressed our understanding of particle equilibria and their bifurcations in straight channel,
the three-dimensional spiral duct as follows: sectional co-ordinates are related to the global co-ordinates of a square cross section of side length $l$. The enlarged view of the cross-section illustrates the local cross-sectional $(r, z)$ co-ordinate system, and the secondary flow (gray closed curves) induced by the curvature of the duct. The edge labeled “inner wall” is the side closer to origin $(x, y, z) = (0, 0, 0)$ while the edge labeled “outer wall” is the side further away from the origin.

recently, progress has also been made to gain a systematic understanding of the particle equilibria in curved channels. This has improved the understanding of how various system parameters, such as particle size, bend radius and aspect ratio of the cross-section, can affect the location and nature of the particle equilibria. Subsequently, rich bifurcations in particle equilibria have been observed with respect to variations in the bend radius of the curved duct. Herein, we illustrate how these bifurcations can be utilized to design spiral microchannels that produce large separation between two sets of different sized particles. Although we restrict the present study to a square cross-section and certain particle sizes to illustrate the separation mechanism, the general formalism is applicable to a broad range of geometries in which similar bifurcations in the particle equilibria take place.

With reference to Fig. 1, consider a particle of density $\rho$ and radius $a$ suspended in an incompressible fluid flow of the same density $\rho$ and dynamic viscosity $\mu$ flowing through an Archimedean spiral duct. The instantaneous radius of the spiral varies with the azimuthal angle $\theta$ according to $R(\theta) = R_{\text{start}} + (\Delta R/2\pi N_{\text{turns}})\theta$ where $\Delta R = R_{\text{end}} - R_{\text{start}}$ is the change in radius from the start to the end of the spiral duct and $N_{\text{turns}}$ represents the number of turns of the spiral. The cross-section of the channel is uniform and has a square geometry with side length $l$. The horizontal and vertical co-ordinates within the square cross-section are denoted by $r$ and $z$, respectively, with the origin at the center of the square i.e. the domain is $-l/2 \leq r \leq l/2$, $-l/2 \leq z \leq l/2$. These cross-sectional co-ordinates are related to the global co-ordinates of the three-dimensional spiral duct as follows:

$$\mathbf{x}(\theta, r, z) = (R(\theta) + r)\mathbf{i} + (R(\theta) + r)\sin(\theta)\mathbf{j} + z\mathbf{k}.$$  

The location of the particle’s center is given by $\mathbf{x}_p = \mathbf{x}(\theta_p, r_p, z_p)$. In the absence of the particle, the incompressible steady fluid flow in a curved duct driven by a steady pressure gradient is referred to as Dean flow. The presence of a particle disturbs this background Dean flow and the particle responds to this disturbed flow. Harding et al. developed a general model for the leading order forces that govern the motion of such a particle in flow through a curved duct (constant $R(\theta)$) at sufficiently small flow rates. The forces on the particle from the fluid are calculated and used to construct a first order model for the trajectory of the particle giving the following dynamical equations of motion:

$$\frac{dr_p}{dt} = -Re \frac{F_{s,r}}{C_r}, \quad \frac{dz_p}{dt} = -Re \frac{F_{s,z}}{C_z} \quad \text{and} \quad \frac{d\theta_p}{dt} = \frac{\bar{u}_a}{R/a + r_p},$$  

where $\bar{u}_a$ is the axial component of the background fluid flow velocity, $F_{s,r} = F_s \cdot \mathbf{e}_r$ and $F_{s,z} = F_s \cdot \mathbf{e}_z$ are the radial and the vertical components of the cross-sectional force, respectively, with corresponding drag coefficients $C_r$ and $C_z$ that vary with the particle’s position in the cross-section. The particle Reynolds number is $Re_p = Re (a/l)^2$, where $Re = \rho U_m l / \mu$ is the channel Reynolds number with $U_m$ the characteristic axial velocity of the background fluid flow. Here, we use a quasistatic approximation for the background fluid flow and extend this particle dynamics model to investigate particle dynamics in spiral ducts. This approximation is reasonable for spiral ducts with slowly changing curvature where the flow locally does not differ significantly from Dean flow in a constant curvature duct with the same curvature.

Numerical implementation of this model involves using a finite element method to compute the forces acting on the particle (see Harding et al. for more details). Once the forces are pre-computed at numerous points in the cross-section and for numerous system parameter values, interpolants of $C_r, C_z, F_{s,r}, F_{s,z}$ are constructed and the particle dynamics are then simulated using the MATLAB solver ode45. For simulations of particle dynamics in a spiral duct, we fix the channel Reynolds number to $Re = 25$. All the results presented herein are in dimensionless units with the dimensionless variables denoted by an overhead tilde and the lengths scaled by $l/2$.

Consider particles of three different sizes $\tilde{a}_1 = 0.05$, $\tilde{a}_2 = 0.10$ and $\tilde{a}_3 = 0.15$. For these particle sizes in a curved duct of constant bend radius, nine different particle equilibria exist inside the square cross-section for large bend radius (see Fig. 2 and also Fig. 2(a,b) of Valani, Harding, and Stokes); four stable nodes (green) near the center of the four edges, four saddle points (yellow) near the corners and an unstable node (red) near the center of the square cross-section. A slow manifold is formed along a closed curve that connects all the stable nodes and saddle points due to a large disparity in the magnitude of the two eigenvalues for these equilibria. As the bend radius is decreased progressively, a number of bifurcations take place. Firstly, saddle-node bifurcations take place where the stable nodes near the center of the top and bottom walls of the square collide and annihilate with the saddle points located near the inner wall. Further decreasing the bend radius results in the stable node located near the outer wall undergoing a subcritical pitchfork bifurcation with the two saddle points located above and below, and the three equilibria merge into a single saddle point. As the bend radius is yet further reduced, the unstable node near the center of the duct migrates towards the stable node located near the inner wall and undergoes a series of bifurcations. Finally, at small bend radius, we get...
FIG. 2. Particle equilibria at different constant bend radii for three different particle sizes \( \tilde{a}_1 = 0.05 \), \( \tilde{a}_2 = 0.10 \), and \( \tilde{a}_3 = 0.15 \). The radial \( \tilde{r} \) and vertical \( \tilde{z} \) location of the equilibria are plotted as a function of the bend radius \( \tilde{R} \); note that \( \tilde{R} \) decreases from left to right. The panels towards the right show the location of equilibria in the square cross-section as filled circles. The size of the circle corresponds to particle size and the color of the circles denotes the type of equilibria: unstable node in red, stable node in green, saddle point in yellow, unstable spiral in purple and a stable spiral in cyan. The parameters \( \tilde{R}_{A1} \approx 3000, \tilde{R}_{B1} \approx 1250, \tilde{R}_{A2} \approx 700, \tilde{R}_{B2} \approx 210, \tilde{R}_{A3} \approx 470 \) and \( \tilde{R}_{B3} \approx 85 \). The gray curves in each of these images illustrate typical trajectories of particles within the cross-section while the dashed square shows locations of the center of the particle for which it will hit the walls of the duct. The gray shaded region in the left panels of (a), (b) and (c) corresponds to regions of a single stable node (SSN).

(i) unstable spirals with an encompassing limit cycle around them for a small particle of \( \tilde{a}_1 = 0.05 \), and (ii) stable spirals for \( \tilde{a}_2 = 0.10 \) and \( \tilde{a}_3 = 0.15 \).

We now demonstrate how these bifurcations can be utilized to separate two particles with small and large differences in size in an Archimedean spiral channel. We start by noting the bend radii corresponding to the existence of a single stable node (SSN) near the inner wall. This is shown by the gray shaded region in the left panels of Fig. 2. For each particle size \( \tilde{a}_i \), we denote the bend radius corresponding to start and end of the SSN region by \( \tilde{R}_{A_i} \) and \( \tilde{R}_{B_i} \) respectively, with \( \tilde{R}_{A_i} > \tilde{R}_{B_i} \). We notice that with \( \tilde{a}_3 > \tilde{a}_2 > \tilde{a}_1 \), we have \( \tilde{R}_{A3} < \tilde{R}_{A2} < \tilde{R}_{A1} \) and \( \tilde{R}_{B3} < \tilde{R}_{B2} < \tilde{R}_{B1} \). Now, we classify the particles to be separated into two classes based on their SSN regions: (i) particle sizes for which their SSN regions overlap and (ii) particle sizes for which their SSN regions do not overlap.

Consider particles of size \( \tilde{a}_2 = 0.10 \) and \( \tilde{a}_3 = 0.15 \) as an example of the first class of particles. If we choose a spiral duct with \( \tilde{R}_{\text{start}} \) near \( \tilde{R}_{A3} \) and \( \tilde{R}_{\text{end}} \in [\tilde{R}_{B3}, \tilde{R}_{B2}] \), then this selection will ensure that both particle sizes have a SSN near the inner wall at the start of the spiral. At the end of the spiral, particles of size \( \tilde{a}_2 \) will not have a SSN since \( \tilde{R}_{\text{end}} < \tilde{R}_{B2} \) while particles of size \( \tilde{a}_3 \) will still have a SSN. An example of particle dynamics with this selection of parameters is shown in Fig. 3(a) and supplemental video S1. Particles of both sizes initially snap onto the slow manifold and focus to their respective SSNs.

For the second class of particles having no overlap between their SSN regions, for example, particles of size \( \tilde{a}_1 = 0.05 \) and \( \tilde{a}_3 = 0.15 \), we cannot use the above described mechanism to separate the particles because multiple stable nodes exist for \( \tilde{a}_3 \) for the bend radii corresponding to the SSN region of \( \tilde{a}_1 \). However, if we inject particles only on half of the cross-section, rather than allowing particles to be anywhere in the cross-section, then we can focus the larger particles selectively to specific stable nodes leading to a clean separation between the two particle sizes. For example, we choose the start bend radius \( \tilde{R}_{\text{start}} \) of the spiral to be near \( \tilde{R}_{A1} \) and the ending radius to be such that \( \tilde{R}_{\text{end}} < \tilde{R}_{B1} \), and initiate the particles in the inner half of the cross-section, as is commonly done in DFF. With this choice of parameters the smaller particles initially focus to the SSN near the inner wall and then migrate...
FIG. 3. Novel particle separation mechanism by exploiting bifurcations. Particle trajectories and snapshots of the cross-section at five equally spaced points along the spiral $R_{\text{start}}, R_1, R_2, R_3$ and $R_{\text{end}}$, for a collection of non-interacting particles of two different sizes. (a) Particles of size $a_2 = 0.10$ (blue) and $a_3 = 0.15$ (green) with initial conditions randomly distributed over the entire cross-section and $R_{\text{start}} = 500$ and $R_{\text{end}} = 150$ with 6 turns, and particles of size $a_1 = 0.05$ (orange) and $a_3 = 0.15$ (green) with initial conditions randomly distributed over the inner half of the cross-section with spiral radii $R_{\text{end}}$. See also supplemental videos S1 to S3).

The findings of this study are based on the model developed by Harding, Stokes, and Bertozzi. Further data supporting the findings of this study is available at https://github.com/brendanharding/IILFHC.

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CONFLICT OF INTEREST

The authors have no conflicts to disclose.

DATA AVAILABILITY STATEMENT

The authors have no conflicts to disclose.
FIG. 4. Particle separation with variations in the number of turns \( N_{\text{turns}} \) and the radius \( R_{\text{end}} \) at the end of the spiral duct, with fixed \( R_{\text{curt}} = 500. \) (a) Horizontal position \( \tilde{r} \) of particles of size \( a_2 = 0.10 \) (green) and \( a_1 = 0.15 \) (blue) at the end of the duct as a function of the number of turns for an Archimedean spiral with \( R_{\text{end}} = 150. \) (b) Regions of particle separation (gray) in the parameter space formed by \( N_{\text{turns}} \) and \( R_{\text{end}}. \) The white region corresponds to particles either not focused in the horizontal direction (when the horizontal standard deviation of either cluster is more than the corresponding particle radius) or not well separated (when the horizontal separation between the cluster centers is less than \( 3(a_2 + a_1). \)) The horizontal dashed black line corresponds to the plot in panel (a) for \( R_{\text{end}} = 150. \)

available from the corresponding author upon reasonable request.

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