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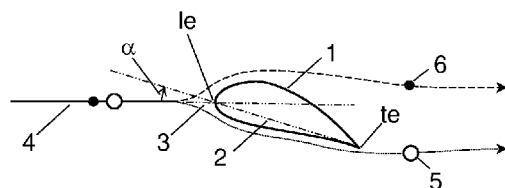


Figure 1

(57) **Abstract:** This invention describes a method and a device for microfluidic separation enhancement according to size. An asymmetric obstacle in the shape of cambered hydrofoil, placed at the downstream of the microfluidic channel increases the distance between particles of different sizes, which have been partially separated at the upstream of the microfluidic channel, resulting an enhancement in the separation efficiency. Thus, microchannel length is decreased, resulting a decrease in hydraulic resistance and footprint of the microchannel.

A METHOD OF MICROFLUIDIC PARTICLE SEPARATION ENHANCEMENT AND THE DEVICE THEREOF

Technical Field

The present invention generally relates to microfluidics and particularly to a separation enhancement method for particles suspended in a fluid according to size. Specific application may be the separation of circulating tumor cells (CTCs) from the blood samples.

Background

Manipulating microparticles have a great potential for identification and analysis of specific particles in many bio-chemical and clinical applications (Yoon, SciRep, 2016). The key parameter in terms of particle detection and analysis is precise manipulation of fluids and microparticles such as focusing, separation and fractionation (Zhang, LabChip, 2016). With processing or manipulating small amounts of fluids (10^{-3} to 10^{-12} milliliters) inside channels with dimensions of tens to hundreds of micrometers (Whitesides, Nature, 2006) microfluidic techniques leap forward as powerful approaches by carrying out precise separations and detections with low fluid samples, low cost, high sensitivity, and fast sample processing (Shen, LabChip, 2017).

Enabling label-free, rapid, high-throughput and efficient particle separation is essential in microfluidic platforms (Shen, LabChip, 2017). Without applying an external field, hydrodynamic separation techniques have a significant advantage over active techniques (such as electrophoresis, dielectrophoresis, magnetic, optical, and acoustic) in terms of equipment cost and experimental set-up complexity (Sajeeth, MicrofluidNanofluid, 2014). Hydrodynamic separation basically utilizes dimensional and/or elastic properties of particles. Among these, size-based separation is the most common technique. Different theories have been developed to separate particles with two different sizes in the microchannels, but pioneering studies have been carried out by Segre and Silberberg, who first noticed the presence of equilibrium positions of particles within the flow by examining the movements of them in a channel (Segre and Silberberg, Nature, 1962).

Hydrodynamic separation is highly dependent on the interaction between the particle and the wall or the fluid, such as inertial microfluidics. In particular, inertial microfluidics provides rapid, high-throughput, label-free and efficient particle separation by manipulating the microparticles without applying any external forces and using only forces arising from the system's fluid dynamics (Schaap, MicrofluidNanofluid, 2016). The idea behind that technique is creating inertial forces without affecting laminar flow conditions in the microfluidic channels. In general, it is possible to apply inertial forces with different microchannel geometries. Examples of different microchannel geometries can be listed as straight microchannels (Zhou, LabChip, 2013; Dudani, AnalChem, 2014), curved microchannels (Yoon, LabChip, 2009), smooth microchannels with vortex-forming cavities (Sollier, LabChip, 2014), serpentine microchannels (Zhang, SciRep, 2014; Jiang, RSCAdv, 2016), and spiral microchannels (Gregoratto, Proc of SPIE, 2007; Bhagat, LabChip, 2008; Nivedita, BioMicrofluid, 2013).

In a straight channel, two forces act on the particles and cause them to cross the fluid streamlines; shear gradient lift force and the wall lift force. Because of having a Poiseuille flow profile (parabolic flow profile) shear gradient lift force drives the particles towards the channel walls while wall lift force push them away from the wall because of asymmetric wake of the particles. This competition between these two forces create a net force named as the net lift force (F_L) and defines equilibrium positions for the particles in the cross-section of the channel. Cross section shape/type determines the equilibrium position amounts. A circular channel cross-section creates an annulus of equilibrium positions with a fixed distance from the center of the channel, four equilibrium positions along the four walls occur with a square cross-section, and a rectangular cross-section causes only two equilibrium positions near top and bottom walls in the middle of the channel. Net lift force is expressed as:

$$F_L = \frac{\rho 2U_{avg}^2 a^4}{D_H^2} c_L \quad (E1)$$

where, ρ is the fluid density, U_{avg} is the average fluid velocity in the channel, a is the particle diameter, c_L is the lift coefficient, D_H is the hydraulic diameter. Hydraulic diameter is expressed as:

$$D_H = \frac{2hw}{(h+w)} \quad (E2)$$

where, h is height, and w is width of the microchannel cross-section. According to Equation 1, particle diameter is substantial on the net lift force, thus different sized particles have various equilibrium positions in the channel cross-section.

On the other hand, the necessity to focus the particles to only one equilibrium position according to their size is met with creating a biasing force which can be created via curved channels. Therefore, multiple equilibrium positions overlap at a single focusing position. Because of the mismatch on the momentum of the fluid in the center and near-wall region of the curved channel, two counter-rotating secondary flows named as Dean flows occur. Dean flow is characterized by dimensionless Dean number:

$$De = Re \sqrt{\frac{D_H}{2R}} = \frac{\rho U_{avg} D_H}{\mu} \sqrt{\frac{D_H}{2R}} \quad (E3)$$

and here, R is the radius of curvature of the channel and Re is Reynolds number of the channel where μ is the fluid viscosity. In the spiral channels, Dean flow brings the Dean force on particles with a formula given by:

$$F_D = 3\pi\mu U_D a = 5.4 \times 10^{-4} De^{1.63} a \quad (E4)$$

where (Saffman, 1965, JFluidMech), is the transverse velocity by Dean flow. According to Equation 4, particle size (a) is a deterministic parameter on the Dean force. Focusing positions of particles depend on both F_L and F_D , and it varies significantly with the particle size ($F_L/F_D \propto a^3$). This means, different sized particles are located at different lateral positions along channel cross-section. Although main force on particle equilibrium positions is F_L , F_D modifies these equilibrium positions, reduces the number of them and facilitates single-stream focusing in curved microchannels (Gosset, AnalChem, 2009; Warkiani, NatProtoc, 2016).

For an efficient size-based particle separation, average flow speed of the liquid (U_{avg}), aspect ratio of the channel (a) and the confinement ratio (λ) of the channel should be determined in parallel. Confinement ratio can be calculated by dividing the particle diameter with the hydraulic diameter (D_H) of the channel:

$$\lambda = \frac{a}{D_H} \quad (E5)$$

5 According to Martel and Toner (Martel, SciRep, 2013), particles cannot be focused at any streamline in a spiral microchannel and scattered on the lateral plane under Dean forces, if confinement ratio is much less than 0.07. If it is about 0.07 or greater than it can be possible to separate the particles based on their sizes.

10 EP 1 585 583 B1 discloses a method and apparatus for separating the particles according to their size. For this purpose, obstacles which provide asymmetric flow are used. It is disclosed that obstacle arrays are aligned into a microfluidic channel and array of obstacles is positioned asymmetrical with respect to the applied flow direction. However, the obstacle is not in the form of hydrofoil and an array of obstacles is essential for separation.

15 The use of obstacle as a form of hydrofoil was disclosed in U.S. Pat. No. 9 433 880 B2. In this patent document, separation method of suspended particles including biological material was described and booster, which might be in the form of a hydrofoil, is positioned in the channel such that a trailing edge of the boosters disposed closer to the inner wall than the outer wall of the channel, while the leading edge is disposed closer to the outer wall to create an attack angle such that it shortens the flow path and transit time of the particles. The function of hydrofoil is to narrow the separation band to boost the particles, but not to separate the particles.

20 In U.S. Pat. No. 9 427 688 B2, use of obstacles for dispersion of particles was disclosed. In this patent document, a field of obstacles, which can also be in the form of a hydrofoil, is utilized to disperse the particles based on the interaction of the particles and the obstacles. It was claimed that due to asymmetrical interaction of the particles with the obstacles, particles can be shifted to one side of the obstacles. However, particular use of a hydrofoil for separation of particles was not addressed.

25 Size-based separation can be realized on spiral shaped microfluidic channels without the need of a hydrofoil. The use of spiral channels for particle separation was disclosed in U.S. Pat. No. 8 208 138 B2. In this patent document, a spiral microchannel with plurality of loops is utilized to separate the particles of different sizes by benefiting from the Dean drag forces and lift forces on the particles. In U.S. Pat. No. 9 458 489 B2 spiral channels are utilized similarly to separate the blood cells based on their sizes. However, use of spiral channels without a hydrofoil requires

several number of turns of the spiral channel to obtain significant particle separation at desired flow rate.

Such methods and devices can be utilized in liquid biopsy applications for CTC (Circulating tumor cells) separation. CTCs are the cells that disseminate into blood from primary or metastatic tumors and play a crucial role in metastatic cascade. CTCs are scarce cells present in the blood of cancer patients. Prognostic value of CTCs has been proven and approved by FDA for breast, prostate and colorectal cancer, where the higher number CTCs (>5 CTCs/7.5 ml blood) is correlated with lower overall survival rate (OSR). Other potential clinical utilities of CTCs include disease monitoring, therapy guidance, patient stratification for precision medicine and personalized therapy, screening for early diagnostics, cancer research, and drug development.

However, detection of CTCs is not easy task due to their low amount in the blood samples, as low as one CTC in a billion blood cells. None of the current CTC isolation technologies can provide necessary sensitivity, reliability, robustness, ease of use and cost efficiency, which are the most important user needs in terms of clinical and economic perspectives.

Summary

A first aspect of the present disclosure provides a method for separating particles according to their sizes via an asymmetrical hydrofoil, the method comprising:

forwarding particles to a microfluidic size-based particle separation system composed of an upstream part and a downstream part and the asymmetrical hydrofoil which is positioned inside the microfluidic size-based particle separation system,

wherein said asymmetrical hydrofoil is positioned on a streamline coincident with a main axis passing through a leading edge having an attack angle with the chord line, and

wherein said asymmetrical hydrofoil is asymmetric about the chord line connecting the leading edge and the trailing edge of the asymmetrical hydrofoil making a non-zero attack angle with the main axis which is the axis parallel to the stream and passing through the leading edge of the asymmetrical hydrofoil.

Yet another aspect of an embodiment of the present disclosure provides a device for performing the above method, the device comprising:

one upstream channel;
two downstream channels;

an asymmetrical hydrofoil located at the near upstream of the intersection of the downstream channels on a streamline coincident with a main axis passing through a leading edge having an attack angle with a chord line and wherein said asymmetrical hydrofoil is asymmetric about the chord line connecting the leading edge and the trailing edge of the asymmetrical hydrofoil making non-zero attack angle with the main axis which is the axis parallel to the stream and passing through the leading edge of the asymmetrical hydrofoil; and a separation wall between the two downstream channels, such that the separation wall tip is located right at the downstream end of the vortex region formed at the downstream of the flow separation point on the asymmetrical hydrofoil, wherein streamlines carrying different sized particles at the upstream channel with distance in between, such that one streamline is above and the other is below the main axis, are separated at the asymmetrical hydrofoil and directed to the said two downstream channels, such that different sized particles can be collected separately.

Some, but not necessarily all, embodiments of the present disclosure may provide enhanced separation of particles via asymmetric obstacle in the shape of cambered hydrofoil and a microfluidic size-based particle separation system composed of an upstream part that is in spiral form and a downstream part that is in straight form. As particles flow inside the upstream part of the microchannel, inertial effects cause the particles to flow in different focused pathways, which results a size-based separation. Cambered hydrofoil increases the lateral distance between particles, which results in enhancement in the separation efficiency. Thus, better separation may be achieved in a shorter spiral channel, reducing the hydraulic resistance and footprint. Being able to reduce the required number of spiral turns accompanies with other several advantages:

- **Lower-pressure operation:** The hydrodynamic resistance of the channel is significantly decreased if the number of turns of the spiral channel decreases. This enables working with the same fluid flow rates while applying much smaller pressure values at the inlet. This gives an advantage to the device on the

regulatory side and reduces the facility requirements of the laboratory that the system will be operated.

- **Throughput:** As the pressure requirement is reduced, the device may be operated with higher flow rates, increasing the throughput. This brings advantage for downstream analysis as the viability of the cells drastically reduced with increased test duration.
- **Smaller footprint:** Reduced number of turns decreases the footprint of the device, which potentially decreases the production costs (both for MEMS and polymer fabrication techniques).

Incorporation of the hydrofoil may enhance the separation efficiency. This may translate to an analysis that has higher purity and recovery rate values, overriding the performance of the state-of-the-art systems.

One application of an embodiment of the disclosure is on biomedical microsystems for in vitro diagnostic purposes, while another application is related to sample preparation before any downstream analyses, such as molecular, genetic, or mutation analysis. Embodiments of the present disclosure may be used in microfluidic platforms for enriching/separating circulating tumor cells (CTCs) from the blood samples of cancer patients benefiting from the size differences between the CTCs and other peripheral blood cells: the CTCs are typically larger than the other blood cells. Due to their larger sizes, CTCs are focused on a pathway closer to the inner wall of a spiral microchannel than the other blood cells, and therefore they can be separated from the rest of the sample by dividing the channel into two outlets (sample and waste outlets). Employing a cambered hydrofoil at the upstream of the junction of the outlet channels may enhance the separation efficiency as well reducing the necessary channel length, associated footprint, and pressure requirement to reach the required sample flow rate.

Brief Description of the Figures

FIG. 1 is a representative view of particle separation around a cambered hydrofoil with non-zero attack angle;

FIG. **2** is a representative view of particle separation around a cambered hydrofoil with non-zero attack angle and the vortex region at the downstream of the hydrofoil;

FIG. **3** is a simulation result of particle separation around a hydrofoil, where larger size particles flow below the hydrofoil.

FIG. **4** is a simulation result of particle separation around a hydrofoil, where larger size particles flow above the hydrofoil.

FIG. **5** is a simulation result of distribution of different sized particles around a hydrofoil, where larger size particles flow above the hydrofoil.

FIG. **6** is a simulation result of distribution of different sized particles around a hydrofoil, where larger size particles flow below the hydrofoil.

FIG. **7** is a representative view of particle separation around a hydrofoil and flow of the particles around a separation wall located at the downstream of the hydrofoil;

FIG. **8** is a representative view of separation of distribution of particles around a hydrofoil and flow of the distribution of particles around a separation wall located at the downstream of the hydrofoil;

FIG. **9** is a representative view of an embodiment, where different sized particles are separated by a hydrofoil and flow through two different downstream channels.

FIG. **10** is a representative view of an embodiment, where distributions of different sized particles are separated by a hydrofoil and flow through two different downstream channels.

FIG. **11** is a representative view of an embodiment, which is composed of a spiral upstream channel, a hydrofoil and a separation wall at the downstream, and two downstream channels.

FIG. **12** is an experiment result showing focusing of different sized particles along a spiral channel.

FIG. **13** is an experiment result showing the distribution of different sized particles at a cross section along a spiral channel.

FIG. **14** is a simulation results showing separation of distribution of particles around a hydrofoil and flow around a separation wall.

FIG. **15** is SEM image of an embodiment showing an upstream spiral channel, a hydrofoil and a separation wall at the downstream, and two downstream channels.

Description of The Components And Parts Of The Invention

The components shown in the figures prepared for a better explanation of the

microfluidic particle separation enhancement device is numbered separately and explanation of each number is given below.

- (1) hydrofoil
- (le) leading edge
- (te) trailing edge
- (2) chord line
- (3) main axis
- (4) streamline coincident with the main axis
- (5) larger particles
- (6) smaller particles
- (7) flow separation point
- (8) vortex region
- (9) streamline above the main axis of the hydrofoil
- (10) streamline below the main axis of the hydrofoil
- (11) 14 μm diameter particles
- (12) 10 μm diameter particles
- (13) Separation wall
- (T) Separation wall tip
- (14) distribution of larger particles
- (15) distribution of smaller particles
- (16) Upstream channel
- (17) a, b Downstream channels
- (18) a, b Different sized particles
- (19) a, b Distribution of different sized particles
- (20) Inlet
- (21) Spiral channel
- (22) a, b Outlets
- (23) Streamline carrying 20 μm diameter fluorescent particles
- (24) Streamline carrying 10 μm diameter fluorescent particles
- (a) attack angle
- (a) distance between the streamline at the upstream of the hydrofoil

- (h) projected height of the hydrofoil
- (d) distance between the streamlines at the close proximity at the downstream of the vortex region

Detailed Description of The Invention

The present invention utilizes hydrofoils to enable and enhance the separation of different sized particles with same densities. A cambered hydrofoil (1), which is asymmetric about the chord line (2) connecting the leading edge (le) and the trailing edge (te) of the foil, located in a stream at a non-zero attack angle (α), which is the angle between the chord line and the main axis (3) measured from the main axis such that the attack angle (α) is positive as shown in Figure 1, generates a pressure gradient along the foil accompanied with a velocity gradient, according to conservation of momentum. Hence, average velocity on one side of the foil will be higher in comparison to that on the opposite site. In this case, when a streamline coincident with the main axis (4) and carrying particles with two different sizes meets the leading edge of the foil, larger particles (5) in the stream tend to flow through one side of the foil with smaller average velocity due to their relatively high inertia. On the other hand, smaller particles (6) flow along the faster stream since they can be accelerated easier due to their smaller inertia. Therefore, the hydrofoil can be used to separate the particles in a stream, based on their sizes.

Another aspect with utilizing hydrofoils with non-zero attack angle is the flow separation and the downstream vortices, as presented in Figure 2. When the flow speed is sufficiently high, viscous effects become relatively less effective and the inertia of the fluid becomes dominant. Hence, the flow cannot follow the hydrofoil surface and gets separated. The point where this occurs is termed as the flow separation point (7). At the downstream of the flow separation point, vortices are formed to satisfy the conservation of angular momentum of the fluid. If a flow carrying particles gets separated from the surface of the hydrofoil, particles in the stream tend not to drift towards the vortex region (8). Therefore, particles separated according to their sizes at the leading edge of the hydrofoil do not meet at the downstream of the hydrofoil within the vortex region. Consequently, when two particle-carrying parallel streamlines meet the hydrofoil, such that one streamline (9) is above the main axis (3) of the hydrofoil and the other streamline (10) being below the main axis (3) of the hydrofoil and there is a distance (a) between the

streamlines at the upstream of the hydrofoil, which is less than the projected height of the hydrofoil (h), then since the particles past the hydrofoil cannot drift into the vortex-region (8), the distance between the streamlines (d) at the close proximity at the downstream of the vortex region will be greater than (a) as illustrated in Figure 2, enhancing the separation of the particles. This result is irrespective of whether streamline (9) or streamline (10) carries the larger or smaller particles, since the streamlines cannot cross the main axis (3) passing through the leading edge of the hydrofoil at the upstream. Figure 3 presents the results of the simulation showing the trajectories of 14 μm diameter particles (11) and 10 μm diameter particles (12) carried by streamlines below and above the main axis, respectively. Figure 4 represents the case in which 14 μm diameter particles (11) and 10 μm diameter particles (12) carried by streamlines above and below the main axis, respectively.

In case when different sized particles are not focused on single streamlines but distributed over several streamlines, wherein these two particle distributions coincide at the main axis (3), either particle separation or enhancement of particle separation occurs at the downstream of the hydrofoil. Here, the efficiency of the particle separation can be characterized by referring to the definition of resolution commonly used in chromatography applications (T. Hanai, 1999):

$$R = 1.18 \frac{d_{p,2} - d_{p,1}}{w_{0.5h,1} - w_{0.5h,2}} \quad (\text{E6})$$

where, R is the resolution, $d_{p,2}$ is the location of the peak of smaller (or larger) particles along the channel width, $d_{p,1}$ is the location of the peak of larger (or smaller) particles along the channel width, $w_{0.5h,1}$ is the width of the distribution of larger (or smaller) particles at half height of its distribution peak, and $w_{0.5h,2}$ is the width of the distribution of smaller (or larger) particles at half height of its distribution peak. Practically, $R > 1$ indicates that the distribution of the particles does not overlap. Referring to this definition, in case where the attack angle (α) is positive, the result will be the enhancement in the efficiency of the particle separation when larger sized particles are distributed about a streamline passing through the low pressure side of the hydrofoil (such as streamline (9) in Figure 2); otherwise, the result will be complete particle separation with $R > 1$. Accordingly, Figure 5 shows the results of the simulation in which a hydrofoil with a positive attack angle (α) is located in the stream and 14 μm diameter particles (11) are distributed about a streamline which passes through the lower pressure side of the hydrofoil above the main axis, while 10 μm diameter particles (12) are distributed about a

streamline which passes through the higher pressure side of the hydrofoil below the main axis. It is seen that some of the 14 μm diameter particles (11) flow with the streamlines carrying 10 μm diameter particles (12). However, the distance between the peak points of the distributed particles is increased at the downstream of the hydrofoil, which indicates improved R value hence separation efficiency. On the other hand, Figure 6 shows the results of the simulation in which the same hydrofoil in Figure 5 is used and 14 μm diameter particles (11) are distributed about a streamline which passes through the higher pressure side of the hydrofoil below the main axis, while 10 μm diameter particles (12) are distributed about a streamline which passes through the lower pressure side of the hydrofoil above the main axis. The results show that none of the 14 μm diameter particles (11) flow with the streamlines carrying 10 μm diameter particles (12) and the distance between the distributions of the particles is increased at the downstream of the hydrofoil.

Another aspect with utilizing hydrofoils is related to the vortex region (8) at the downstream of the hydrofoil. Since particles past the hydrofoil do not tend to drift into the vortex region (8), a separation wall (13), which divides the stream into two distinct streams (3) and the tip (T) of which is located right at the downstream end of the vortex region, prevents mixing of different sized particles, which are already separated by the hydrofoil, along the separation wall (13). Figure 7 represents this case in which larger particles (5) and smaller particles (4) carried by parallel streams, one of which is above and the other is below the main axis (3), are separated by a hydrofoil and a separation wall (13) located at the downstream. Similarly, Figure 8 represents the case in which distribution of larger particles (14) and distribution of smaller particles (15) are separated by a hydrofoil and a separation wall (13) is located at the downstream.

Methods illustrated in Figures 2 and 7 can be utilized in an embodiment utilizing hydrofoils to separate particles of similar density based on their sizes, as shown in Figure 9. The embodiment includes one upstream channel (16), two downstream channels (17a, 17b), and a hydrofoil (1) located at the near upstream of the intersection of the downstream channels. Particle carrying streamlines with distance (a) in between, such that one streamline is above and the other is below the main axis (3), in the upstream channel (16) will be separated at the hydrofoil (1) and

5 directed to downstream channels (17a, 17b). Thus, different sized particles (18a, 18b) can be collected at different downstream channels (17a, 17b).

Another embodiment shown in Figure 10 utilizes the methods illustrated in Figures 5, 6, and 7. This embodiment again includes one upstream channel (16), two downstream channels (17a, 17b), and a hydrofoil (1) located at the near upstream of the intersection of the downstream channels. Streams carrying distribution of different sized particles (19a, 19b) with a distance (a) in between their peak positions, such that the peak positions are located at two sides of the main axis (3), in the upstream channel will be separated at the hydrofoil (1) and directed to different downstream channels. When larger sized particles are distributed about a streamline which passes through the lower pressure side of the hydrofoil, such as streamline (9) in Figure 2, the result is the enhancement of the particle separation and collection of separated particles at downstream channels (17a, 17b). Otherwise, the result is a complete particle separation and collection of separated particles at downstream channels (17a, 17b).

10 The upstream channel (16) in Figures 9 and 10 can be in the form of a spiral (Figure 11). In this embodiment, when a mixture of different sized particles is dispensed through the inlet (20), Dean vortices formed across the spiral channel (21) cause different sized particles focus on or distribute about two distinct streamlines. The particles carried by these streamlines can be separated by a hydrofoil (1) and separated particles can be directed to different outlets (22a, 22b) through downstream channels (17a, 17b) divided by a separation wall (13).

In case of a spiral channel, particles typically tend to get distributed about a streamline at the inner loops of the spiral and get focused on the streamline at the outer loops as they flow in the spiral (Gregoratto, Proc of SPIE, 2007; Bhagat, LabChip, 2008; Nivedita, BioMicrofluid, 2013).

30 Figure 12 shows the focusing of fluorescent particles with nominal diameters of 10 μm and 18 μm at distinct streamlines (23, 24), where streamline (23) is visualized by the fluorescence of 18 μm diameter particles and streamline (24) is formed by the fluorescence of 10 μm diameter particles. As shown in Figure 12, although larger particles are focused at earlier loops, focusing of both small and large particles is observed only after the 6th loop of the spiral. By utilizing hydrofoils, it is possible to separate the particles at earlier loops, which eliminates the need for long spiral channels thus decreasing the overall hydrodynamic resistance. Figure 13 shows the

distribution of the particles with nominal diameters of 10 μm ($9.45 \pm 0.87 \mu\text{m}$) and 18 μm ($17.59 \pm 3.89 \mu\text{m}$) based on their fluorescent intensities across the 3rd loop of the 300 μm wide spiral channel. Nominally 10 μm diameter particles are distributed between 80 μm and 220 μm of the width of the channel while nominally 18 μm diameter particles are distributed narrowly about a streamline located at 95 μm . Simulations based on this experimental data shows that particles with nominal diameters of 10 μm and 18 μm can be separated by utilizing a hydrofoil with 30 degrees attack angle and a separation wall located right at the downstream end of the vortex region (Figure 14). Therefore, another embodiment, whose scanning electrode micrograph presented in Figures 15, can be used to separate particles that are distributed over several streamlines. The embodiment comprises of a upstream spiral channel (21), hydrofoil (1), a separation wall (13), and two downstream channels (17a, 17b).

In one embodiment of the invention a method for separating particles according to their sizes via a cambered hydrofoil is disclosed, where forwarding particles to the cambered hydrofoil, on a streamline coincident with the main axis (4) passing through the leading edge (le) having an attack angle of α with the chord line. Said cambered hydrofoil is asymmetric about the chordline connecting the leading edge (le) and the trailing edge (te) of the hydrofoil making non-zero attack angle with the main axis which is the axis parallel to the stream and passing through the leading edge of the hydrofoil.

In another embodiment of the invention, a method for enhancing the separation of two particle-carrying parallel streamlines is disclosed, where one streamline is above the main axis of the hydrofoil and the other streamline being below the main axis of cambered hydrofoil and there is a distance (a) between the streamlines at the upstream of the cambered hydrofoil, which is less than the projected height (h) of the cambered hydrofoil, characterized in that forwarding two particle-carrying parallel streamlines to meet the cambered hydrofoil, then since the particles past the cambered hydrofoil cannot drift into the vortex-region (8) formed at the downstream of the flow separation point (7) on the cambered hydrofoil, distance between streamlines (d) at the close proximity at the downstream of the vortex region will be greater than (a).

In other embodiment of the invention a method for increasing the resolution of separation (R)

$$R = 1.18 \frac{d_{p,2} - d_{p,1}}{W_{0.5h,1} - W_{0.5h,2}}$$

according to below formula of two distributions of two different sized particles coinciding at the main axis is disclosed, where one distribution peak is above the main

axis of the hydrofoil and the other distribution peak is below the main axis of cambered hydrofoil, characterized in that forwarding said two particle distributions to cambered hydrofoil then since the particles in the distributions past the cambered hydrofoil cannot drift into the vortex-region (8) formed at the downstream of the flow separation point (7) on the cambered hydrofoil, the particles on the streamlines above the main axis follow a path through the upper side of the hydrofoil, the particles on the streamlines below the main axis follow a path through the lower side of the hydrofoil, and particles on the streamline coincident with the main axis follow a path such that larger particles on the streamline tend to flow through side of the hydrofoil with smaller average velocity and smaller particles flow through the side of the hydrofoil with larger average velocity.

In another embodiment, a method for preventing mixing of different sized particles, which are already separated or enhanced or resolution is increased by a hydrofoil via a separation wall (13) which divides the stream into two distinct streams, where, the separation wall (13) tip (T) is located right at the downstream end of vortex region (8) formed at the downstream of the flow separation point (7) on a cambered hydrofoil

A device using all methods given above is also presented by the invention comprising one upstream channel, two downstream channels, separation wall (13) between these two downstream channels, and the separation wall tip (T) is located right at the downstream end of the vortex region formed at the downstream of the flow separation point on a cambered hydrofoil, wherein streamlines carrying different sized particles at the upstream channel with distance (a) in between, such that one streamline is above and the other is below the main axis, are separated at the hydrofoil and directed to the downstream channels such that different sized particles can be collected separately. The device further comprises one inlet (20) operative to receive fluid containing particles and two outlets (22) operative to deliver fluid containing particles, wherein the upstream channel is in form of a spiral (21).

Throughout the specification and the claims that follow, unless the context requires otherwise, the words "comprise" and "include" and variations such as "comprising" and "including" will be understood to imply the inclusion of a stated integer or group of integers, but not the exclusion of any other integer or group of integers.

Throughout the specification and the claims that follow, unless the context requires otherwise, the words "comprise" and "include" and variations such as "comprising" and "including" will be

understood to imply the inclusion of a stated integer or group of integers, but not the exclusion of any other integer or group of integers.

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CLAIMS

1. A method for separating particles according to their sizes via an asymmetrical hydrofoil, the method comprising:
 - forwarding particles to a microfluidic size-based particle separation system composed of an upstream part and a downstream part and the asymmetrical hydrofoil which is positioned inside the microfluidic size-based particle separation system,
 - wherein said asymmetrical hydrofoil is positioned on a streamline coincident with a main axis passing through a leading edge having an attack angle with the chord line, and
 - wherein said asymmetrical hydrofoil is asymmetric about the chord line connecting the leading edge and the trailing edge of the asymmetrical hydrofoil making a non-zero attack angle with the main axis which is the axis parallel to the stream and passing through the leading edge of the asymmetrical hydrofoil.

2. A method according to claim 1 further comprising:
 - forwarding two particle-carrying parallel streamlines,
 - wherein one of the two particle-carrying parallel streamlines is above the main axis of the asymmetrical hydrofoil and the other of the two particle-carrying parallel streamlines is below the main axis of asymmetrical hydrofoil, to meet the asymmetrical hydrofoil, then since the particles past the asymmetrical hydrofoil cannot drift into the vortex-region formed at the downstream of the flow separation point on the asymmetrical hydrofoil, a distance between streamlines at the close proximity at the downstream of the vortex region will be greater than a distance between the streamlines at the upstream of the asymmetrical hydrofoil and less than the projected height of the asymmetrical hydrofoil.

3. A method according to claim 1 further comprising:
 - forwarding two particle distributions, which are two distributions of two different sized particles coinciding at the main axis, where one distribution has a

peak above the main axis of the asymmetrical hydrofoil and the other distribution has a peak below the main axis of the asymmetrical hydrofoil and a resolution of separation is according to below formula:

$$R = 1.18 \frac{d_{p,2} - d_{p,1}}{w_{0.5h,1} - w_{0.5h,2}}$$

wherein:

$d_{p,2}$ is the location of the peak of smaller (or larger) particles along a channel width,

$d_{p,1}$ is the location of the peak of larger or smaller particles along the channel width,

$w_{0.5h,1}$ is the width of the distribution of larger or smaller particles at half height of its distribution peak, and

$w_{0.5h,2}$ is the width of the distribution of smaller (or larger) particles at half height of its distribution peak,

then since the particles in the distributions past the asymmetrical hydrofoil cannot drift into the vortex-region formed at the downstream of the flow separation point on the asymmetrical hydrofoil, the particles on the streamlines above the main axis follow a path through the upper side of the asymmetrical hydrofoil, the particles on the streamlines below the main axis follow a path through the lower side of the asymmetrical hydrofoil, and particles on the streamline coincident with the main axis follow a path such that larger particles on the streamline tend to flow through a side of the asymmetrical hydrofoil with smaller average velocity and smaller particles flow through the side of the hydrofoil with larger average velocity.

4. A method according to claim 2 or 3 further comprising positioning a separation wall, which divides the stream into two distinct streams, in a such a way that a tip of the separation wall is located right at the downstream end of vortex region formed at the downstream of the flow separation point on the asymmetrical hydrofoil.
5. A device using method according to claim 4, comprising:
 - one upstream channel;
 - two downstream channels;

an asymmetrical hydrofoil located at the near upstream of the intersection of the downstream channels on a streamline coincident with a main axis passing through a leading edge having an attack angle with a chord line and wherein said asymmetrical hydrofoil is asymmetric about the chord line connecting the leading edge and the trailing edge of the asymmetrical hydrofoil making non-zero attack angle with the main axis which is the axis parallel to the stream and passing through the leading edge of the asymmetrical hydrofoil; and

a separation wall between the two downstream channels, such that the separation wall tip is located right at the downstream end of the vortex region formed at the downstream of the flow separation point on the asymmetrical hydrofoil,

wherein streamlines carrying different sized particles at the upstream channel with distance in between, such that one streamline is above and the other is below the main axis, are separated at the asymmetrical hydrofoil and directed to the said two downstream channels, such that different sized particles can be collected separately.

6. The device of claim 5 further comprising one inlet operative to receive fluid containing particles and two outlets operative to deliver fluid containing particles, wherein the upstream channel is in form of a spiral.

Figure 1

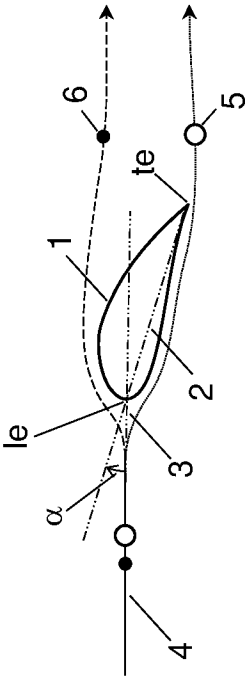


Figure 2

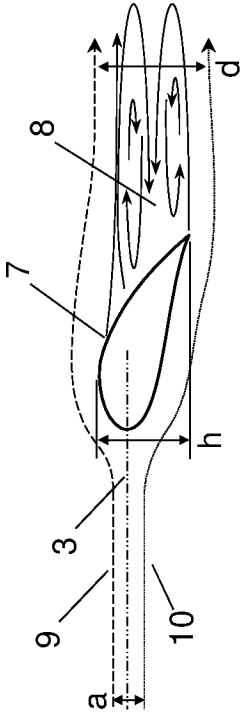


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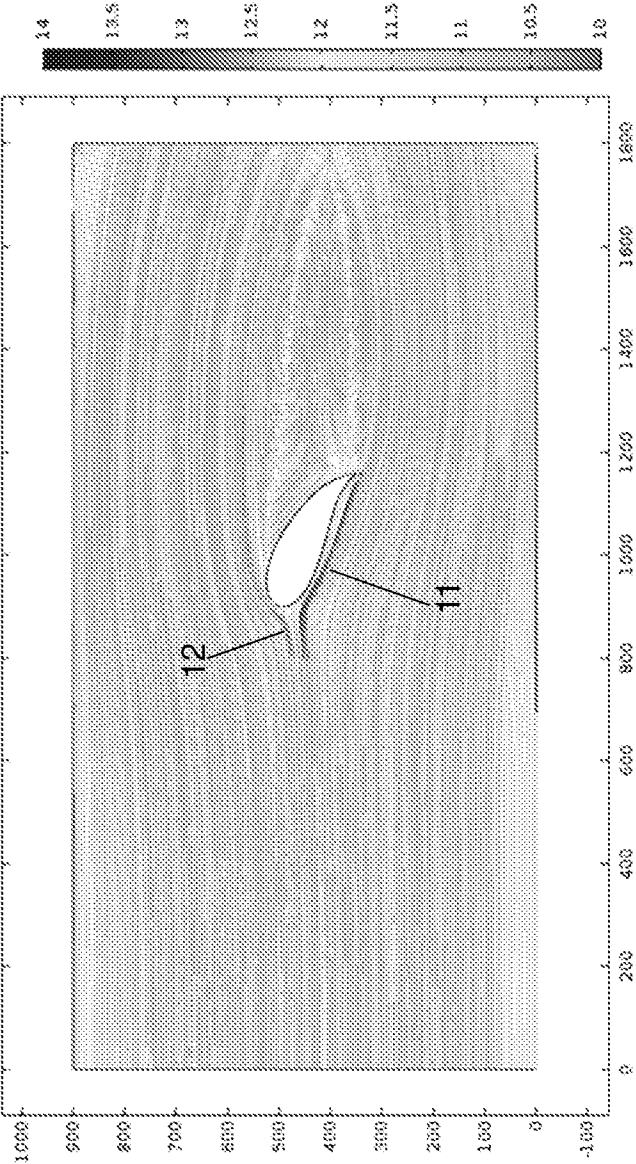


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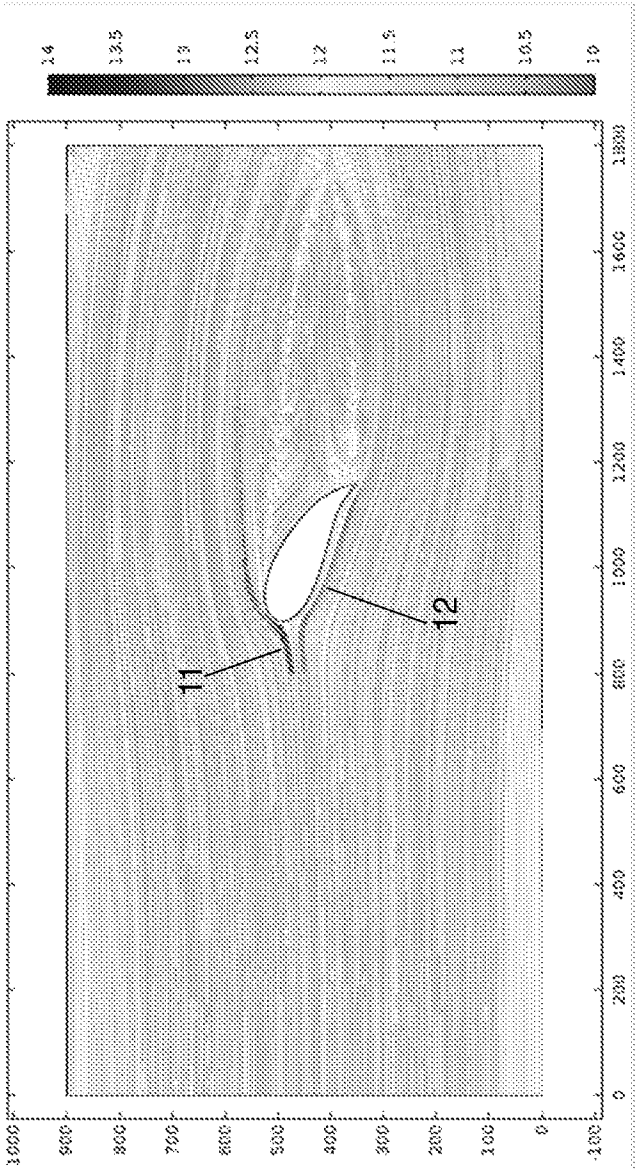


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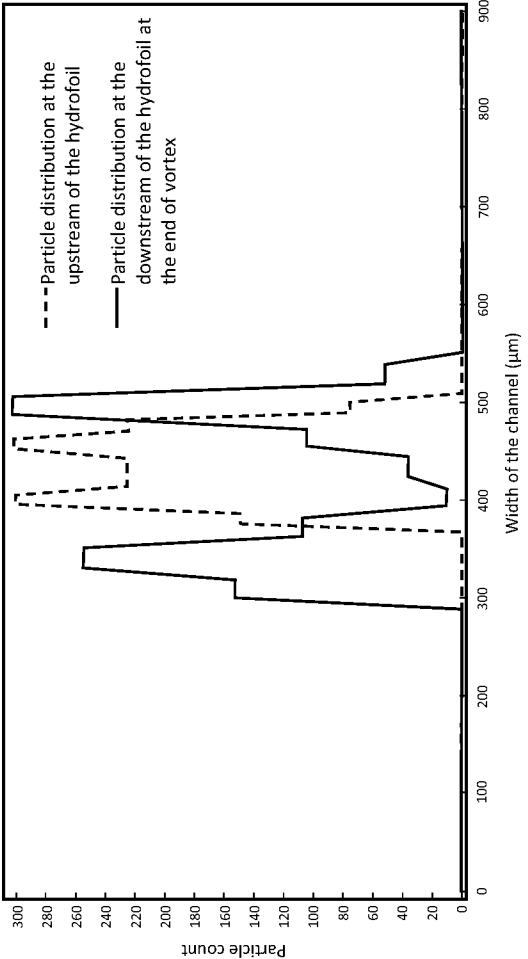
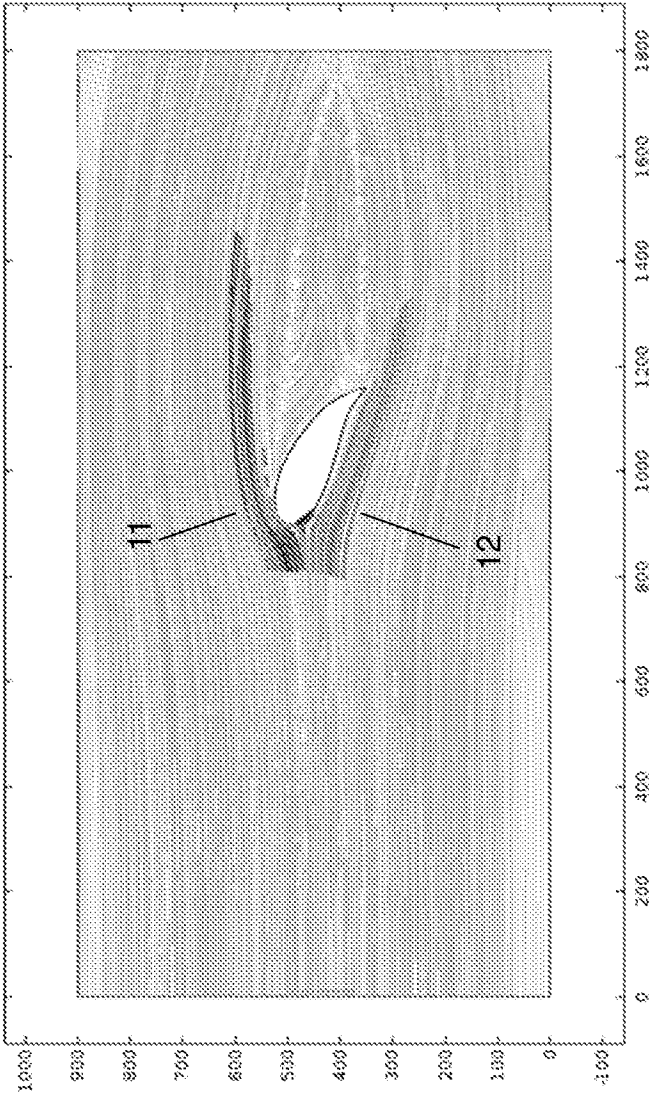


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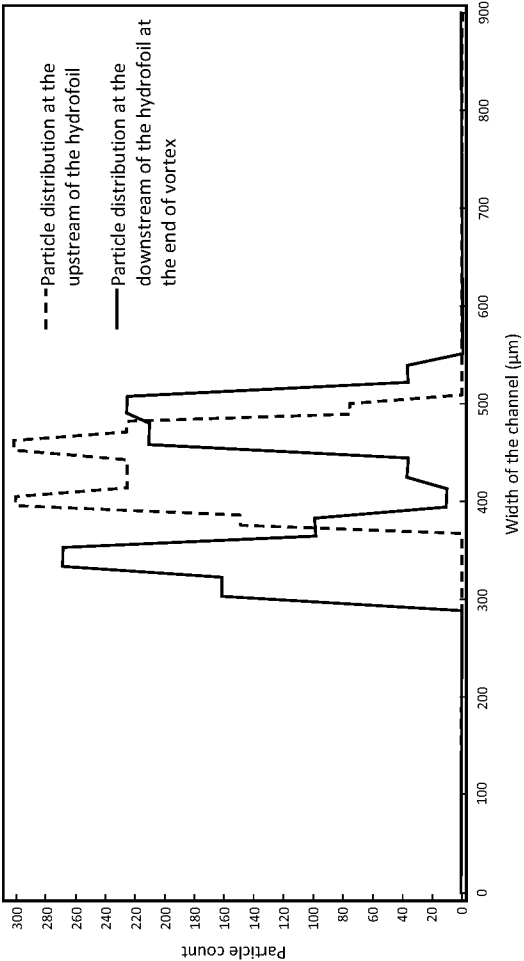
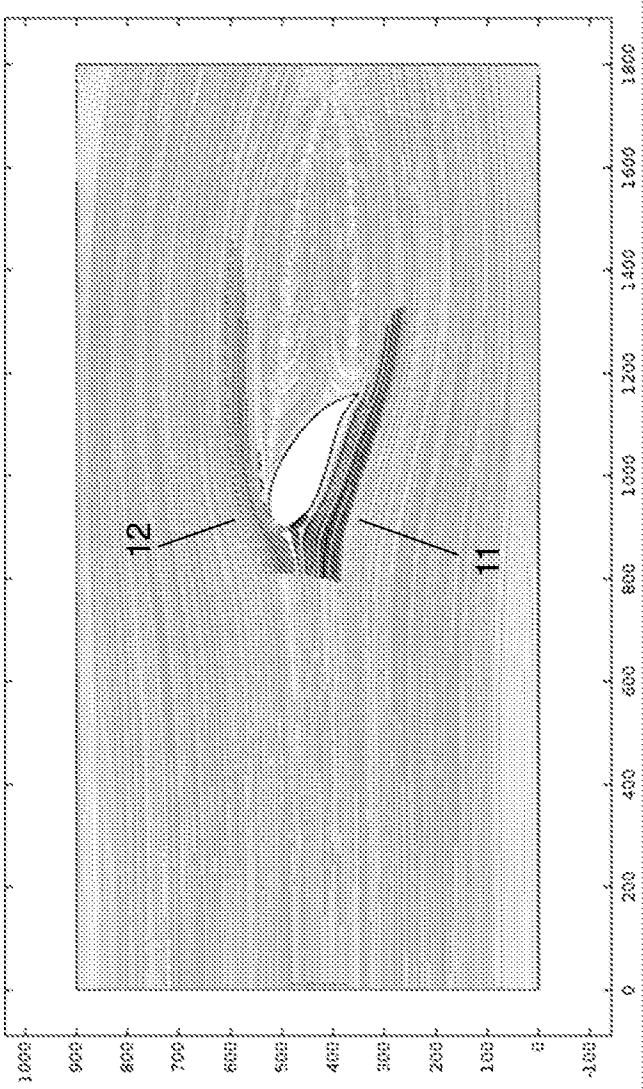


Figure 7

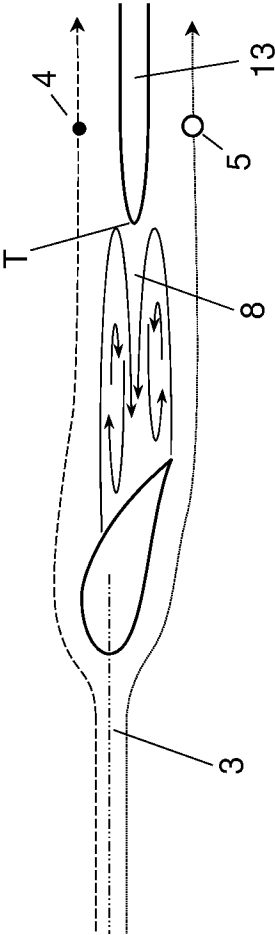


Figure 8

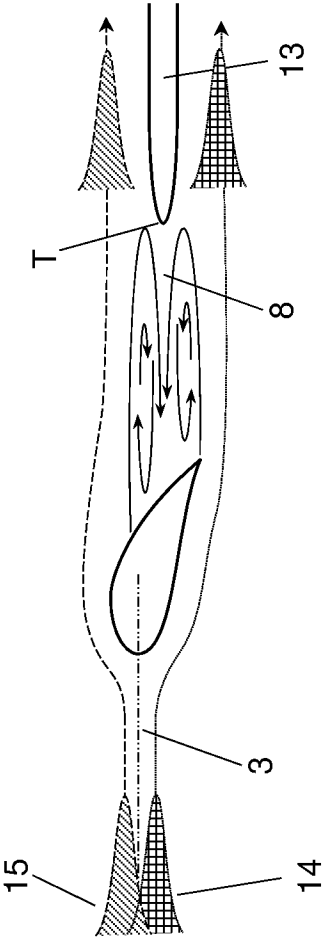


Figure 9

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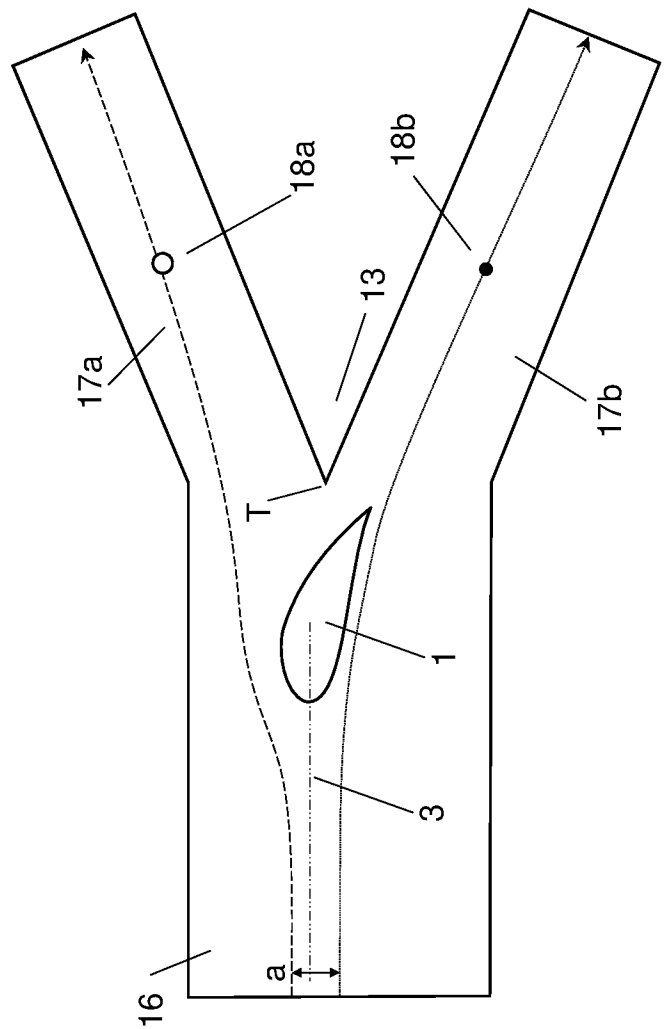


Figure 10

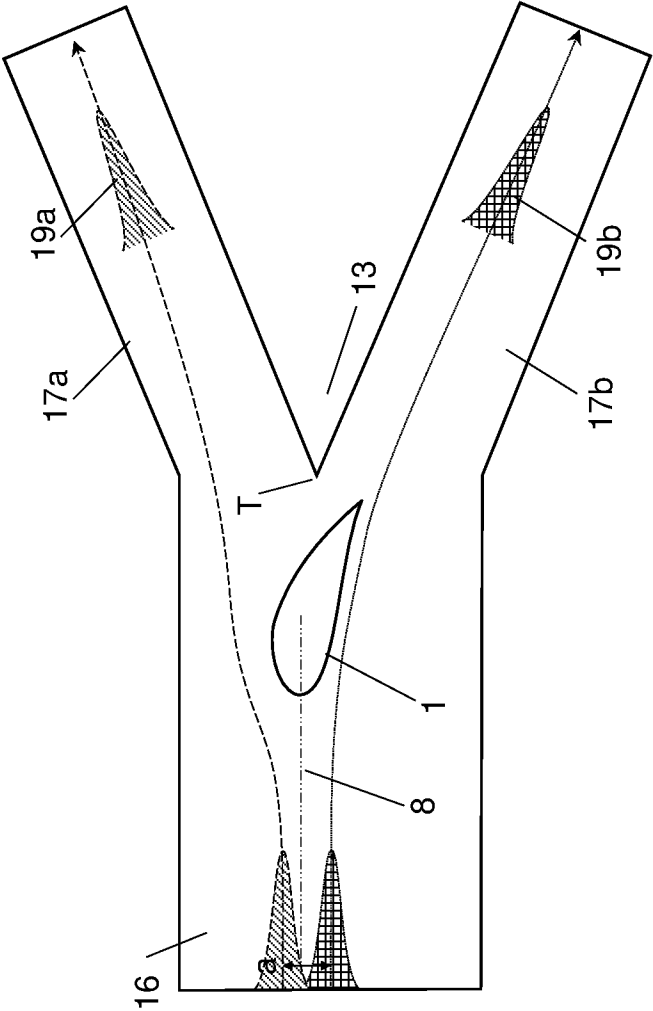


Figure 11

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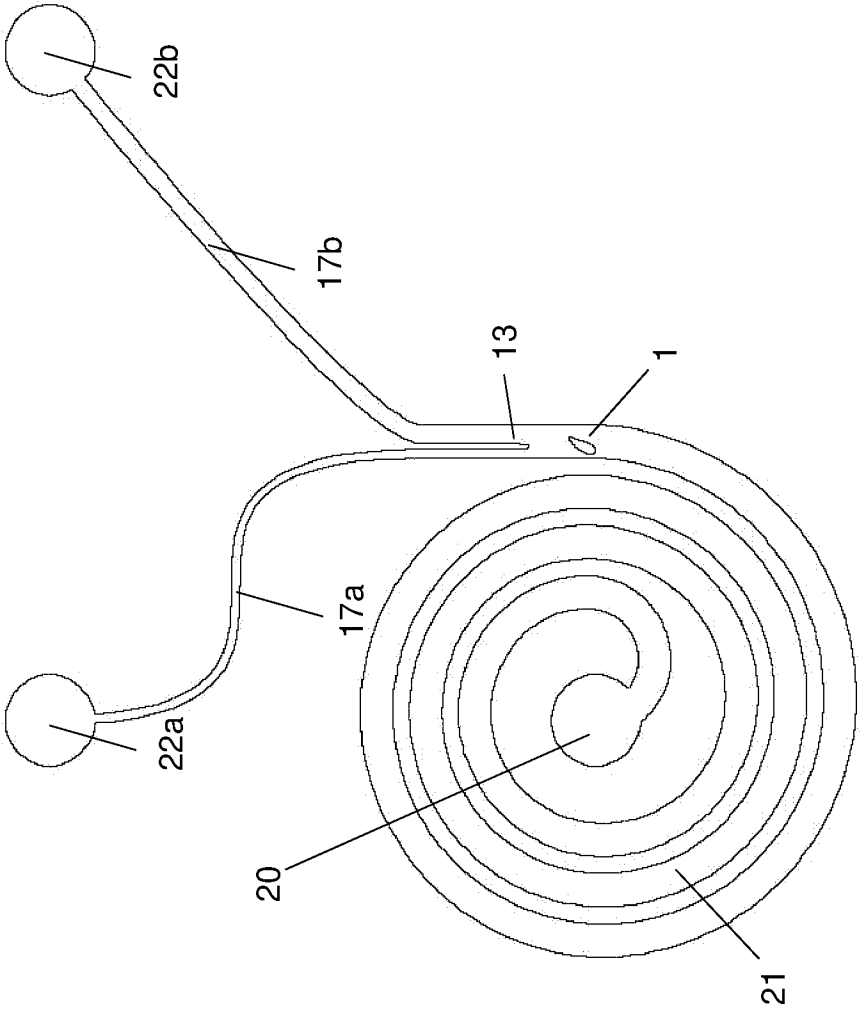


Figure 12

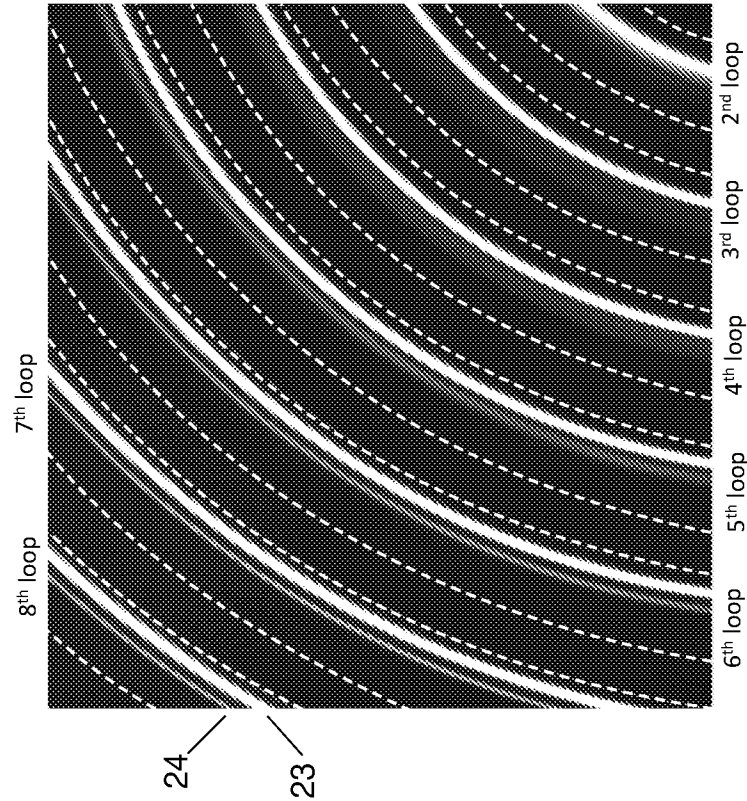


Figure 13

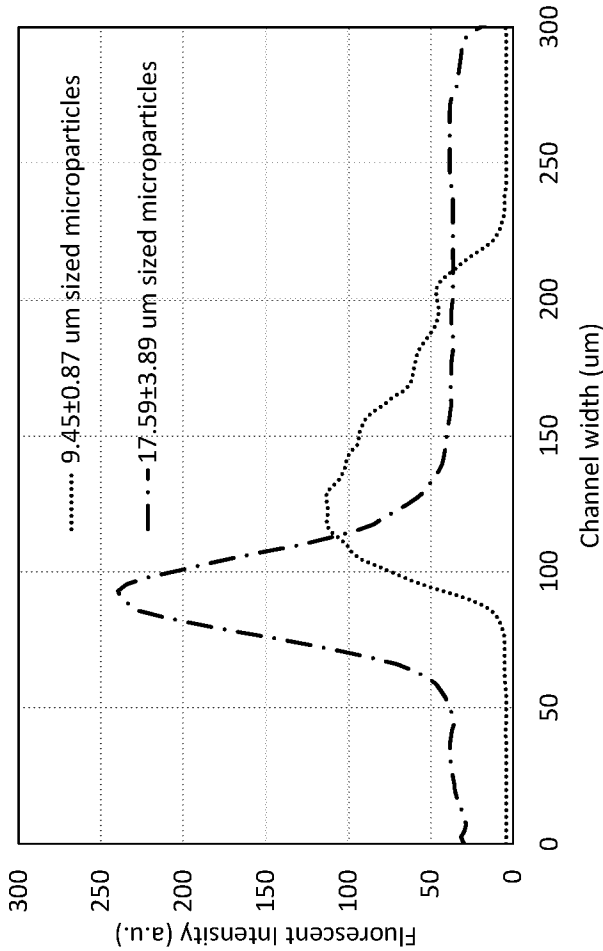


Figure 14

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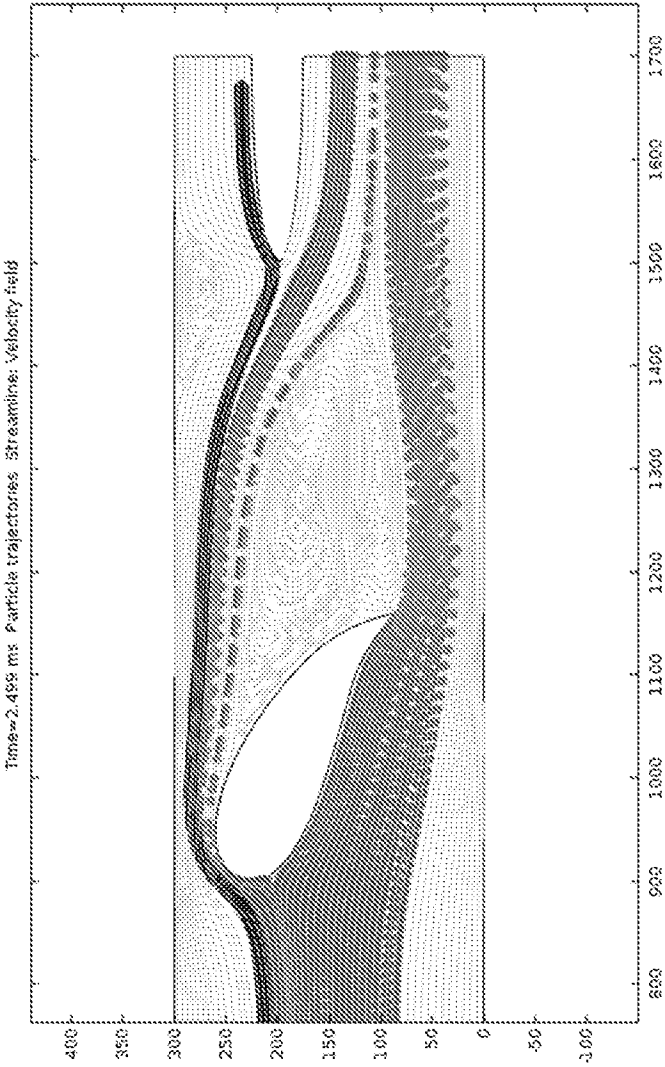


Figure 15

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