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(54) **MICROFLUIDIC DEVICE, APPARATUS AND METHOD FOR ENRICHMENT AND DILUTION OF MAGNETIC MOLECULAR ENTITIES**

(57) A microfluidic device (500) includes a substrate (100) with a fluid channel (250) extending from an inlet opening (210) to a channel branch (270). The fluid channel (250) includes a planar spiral portion (255) and at the channel branch (270) the fluid channel (250) branches in at least two outlet channels (280). A ferromagnetic auxiliary structure (300) is formed in a plane parallel to the planar spiral portion (255).

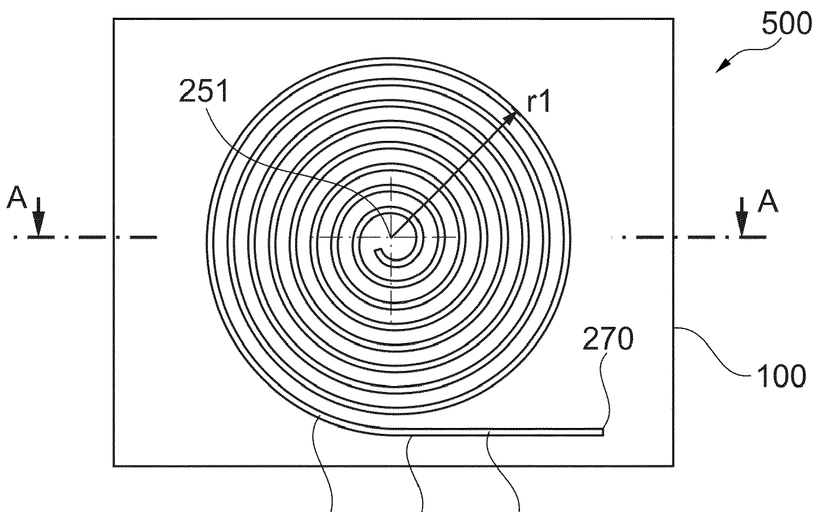

Fig. 1B

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Description

TECHNICAL FIELD

[0001] The present embodiments relate to a method of enrichment and/or dilution of magnetic molecular entities such as ions and molecules in a liquid, to an apparatus for enrichment of and for dilution of magnetic molecular entities and for a microfluidic device that may be used for separating magnetic molecular entities.

BACKGROUND

[0002] The difference in the magnitude of magnetic moments of different fractions in a fluid can be used to separate the different fractions. For example, under the influence of the magnetic field gradient in an inhomogeneous magnetic field, paramagnetic and ferromagnetic particles move into the direction of higher field strength and diamagnetic particles move into the direction of lower field strength.

[0003] M. Puchivari et al., Separation of Transition Metal Ions in an Inhomogeneous magnetic field; Journal of Physical Chemistry B; 2001. 105(17): p. 3343-3345 describe the separation of Fe^{3+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Ag^{+} and Cd2+, wherein ions of iron, cobalt, nickel and copper are pulled towards the field centre.

[0004] J.H. Kang and J.-K. Park, Magnetophoric Continuous Purification of Single-Walled Carbon Nanotubes from Catalytic Impurities in a Microfluidic Device. Small, 2007,3(10):p. 1784-1791 describe a micro reactor with a nickel structure that drives by magnetic force the mass transport of impurity-containing single-walled carbon nanotubes in a microfluidic channel

[0005] An object of the present embodiments is providing a method and an apparatus facilitating separation of magnetic molecular entities like molecules, ions and atoms in a cost-efficient way.

BRIEF DESCRIPTION OF THE DRAWINGS

[0006] The object is achieved with subject-matter of the independent claims. The dependent claims relate to further embodiments.

[0007] The accompanying drawings are included to provide a further understanding of the embodiments and are incorporated in and constitute a part of this specification. The drawings illustrate the embodiments of the microfluidic device, a separation apparatus and a method of enriching/diluting magnetic particles and together with the description serve to explain principles of the embodiments. Further embodiments are described in the following detailed description and the claims.

FIGS. 1A-1C show two horizontal and a vertical cross-sectional view of a microfluidic device with a fluid channel including a planar spiral portion and a ferromagnetic auxiliary structure formed in a plane parallel to the planar spiral section.

FIGS. 2A-2B show details of schematic vertical cross-sectional views of microfluidic devices arranged in an external magnetic field according to embodiments.

FIG. 3A is a diagram showing the magnetic field in and in a vicinity of the fluid channel of the microfluidic device of FIG.2A in a plane orthogonal to the flow direction for discussing effects of the embodiments.

FIG. 3B is a diagram showing the magnetic field in and in a vicinity of the fluid channel of the microfluidic device of FIG.2B in a plane orthogonal to the flow direction for discussing effects of the embodiments.

FIG. 4 is a diagram showing the magnetic field strength along a vertical diameter of the fluid channels of FIG. 2A and FIG. 2B as a function of a distance to the auxiliary structure for discussing effects of the embodiments.

FIGS. 5A-5C show schematic vertical cross-sectional views of microfluidic devices with auxiliary structures according to other embodiments.

FIGS. 6A-6B show a schematic plan view and a schematic cross-sectional view of another microfluidic device according to an embodiment with the auxiliary structure including a spiral part with windings laterally interleaved with windings of a planar spiral portion of a fluid channel.

FIGS. 7A-7C show a plan view and two cross-sectional views of a microfluidic device according to a further embodiment.

FIG. 8 is a schematic block diagram of a separation apparatus according to a further embodiment.

DETAILED DESCRIPTION

[0008] In the following detailed description, reference is made to the accompanying drawings, which form a part hereof and in which are shown by way of illustrations specific embodiments in which the embodiments may be practiced. It is to be understood that other embodiments may be utilized and structural or logical changes may be made without departing from the scope of the present disclosure. For example, features illustrated or described for one embodiment can be used on or in conjunction with other embodiments to yield yet a further embodiment. It is intended that the present disclosure includes such modifications and variations. The examples are described using specific language, which should not be construed as limiting the scope of the appending claims. The drawings are not scaled and are for illustrative purposes only. Corresponding elements are designated by the same reference signs in the different drawings if not stated otherwise.

[0009] The terms "having", "containing", "including", "comprising" and the like are open and indicate the presence of stated structures, elements or features but do not preclude the presence of additional elements or features. The articles "a", "an" and "the" include both the plural and the singular unless the context clearly indicates otherwise.

[0010] The term "on" is not to be construed as meaning only "directly on". Rather, if a first element is positioned "on" a second element, a third element may be positioned between the first and second elements.

[0011] A molecular entity is any constitutionally or isotopically distinct atom, molecule, ion, radical, complex, etc., identifiable as a separately distinguishable entity.

[0012] According to an embodiment a microfluidic device includes a substrate and a ferromagnetic auxiliary structure. The substrate may be or may include a thin plate with two parallel main surfaces, wherein the plate may include or consist of silicon, glass, LTCC (low-temperature cofired ceramics), or polymers, e.g., PDMS (polydimethylsiloxane), TPE (thermoset polyester or thermoplastic polymers. The substrate may be based on a one-piece plate or may be formed by stacking and bonding two or more plate-like parts.

[0013] The substrate includes a fluid channel that extends from an inlet opening to a channel branch, wherein at the channel branch the fluid channel branches into two or more outlet channels. The fluid channel includes a planar spiral portion that winds at continuously increasing distance around a centre point. In other words, a flow axis of a process liquid, which enters the fluid channel through the inlet opening and which flows through the fluid channel, winds around the centre point of the spiral portion in a horizontal plane. The horizontal plane may be parallel to at least one main surface of the substrate. The inlet opening may be closer to a centre of the spiral portion than the channel branch such that the process liquid may flow outwardly into the direction of lower curvature of the spiral portion.

[0014] The cross-sectional area of the spiral portion orthogonal to the flow axis may be uniform or may deviate from a mean cross-sectional area by not more than 10% of the mean cross-sectional area. The cross-sectional area may be rectangular with rounded corners or oval, wherein a longer axis of the cross-sectional area may be orthogonal or parallel to the horizontal plane. The cross-sectional area of the fluid channel is such that a flow of a process liquid containing magnetic molecular entities is predominantly laminar. In other words, the total flow through the fluid channel includes a plurality of partial flows that mix at most to a negligible degree.

[0015] The microfluidic device further includes a ferromagnetic auxiliary structure that may be formed in a plane parallel to the planar spiral portion. A distance between the spiral portion and the auxiliary structure may be at most 2mm, at most 1mm or at most 0.6mm. For example, the auxiliary structure may be in direct contact with the fluid channel and may form a portion of the inner surface of the fluid channel.

[0016] The ferromagnetic auxiliary structure may laterally extend across at least a main portion of the outline of the spiral portion, or across the complete outline of the spiral portion, wherein the outline of the spiral portion is the area within the outer edge of the outermost winding.

[0017] Ferromagnetic materials show a permanent magnetic moment in the absence of an external magnetic field. The auxiliary structure may include an elementary ferromagnetic material such as cobalt (Co), iron (Fe) and nickel (Ni), may contain or consist of a Heusler alloy or another ferromagnetic compound.

[0018] A process liquid containing magnetic molecular entities may be fed through the inlet opening into the fluid channel and flows outwardly into direction of the channel branch. The magnetic molecular entities may include, e.g. magnetic molecules, atoms and/or ions of rare earth elements, e.g., metals form the lanthanides group such as holmium(III) ions and ferrous metals.

[0019] With the microfluidic device arranged in an external magnetic field, the ferromagnetic auxiliary structure locally distorts the external magnetic field in close vicinity to the fluid channel. The resulting field distortion is a positive gradient which exerts a force on the magnetic molecular entities in the process liquid flowing through the fluid channel. In the fluid channel, the comparatively strong magnetic field gradient is oriented perpendicular to the fluid flow axis along at least 80% or along the complete spiral portion.

[0020] With the auxiliary structure locally distorting the external magnetic field, the field gradient in the fluid channel may be comparatively strong even if the externally applied magnetic field is highly uniform. For example, a change of the magnetic field strength along a vertical extension of the fluid channel may be at least 30%, e.g., at least 50% of the field strength of the external magnetic field. Within the fluid channel, in particular, within the planar spiral portion paramagnetic molecules, ions, and/or atoms move into direction of the higher magnetic field strength, whereas diamagnetic ions move into direction of the lower magnetic field strength.

[0021] The strongly laminar flow along the flow axis effects that after a magnetic ion has moved along the magnetic field gradient, the ion does not or only to a negligible degree move in the opposite direction as a result of turbulences. In other words, co-flowing portions of the total flow through the fluid channel do not mix. The microfluidic device is further designed such that the effect of magnetic separation is maximized despite the persisting effect of molecular diffusion in the directions orthogonal and parallel to the flow.

[0022] Paramagnetic ions enrich in a partial flow in the half of the fluid channel oriented to the ferromagnetic auxiliary structure and dilute in a partial flow in the half of the fluid channel averted from the ferromagnetic auxiliary structure. Diamagnetic ions enrich in the partial flow in the half of the fluid channel averted from the ferromagnetic auxiliary structure and dilute in a partial flow in the half of the fluid channel oriented to the ferromagnetic auxiliary structure.

[0023] The outlet channels are arranged such that one of the outlet channels collects a partial flow enriched with molecular entities attracted by the stronger magnetic field and/or diluted from molecular entities attracted by the weaker magnetic field and such that the other one of the outlet channels collects a partial flow diluted from molecular entities attracted by the stronger magnetic field and/or enriched with molecular entities attracted by the weaker magnetic field.

[0024] The spiral portion of the fluid channel provides a comparatively long fluid channel in a given area and uses an external magnetic field with high area efficiency. The spiral portion facilitates a highly efficient application of the microfluidic device in combination with an electromagnet or permanent magnet whose size is relatively small. Other than meandering fluid channels, the spiral portion lacks of sharp bends that may induce some turbulence in the fluid channel, wherein the turbulence may re-mix to some degree previously enriched and/or diluted partial flows of the process liquid. The spiral portion is designed such that in conjunction with a proper flow rate re-mixing by curvature-induced vortices is avoided over a maximum length.

[0025] The flow axis in the planar spiral portion may be formed with equally and uniformly spaced spiral windings, wherein, starting from the spiral centre and after one full turn of the spiral, along each complete spiral winding a distance between neighbouring spiral windings remains constant or at least to a high degree constant with deviations of at most 10%, 5%, or 1% from a mean distance between neighbouring windings. For example, the planar spiral portion may be or may be approximated to a high degree by an Archimedean spiral, wherein the spiral of the fluid flow axis can be described in a polar coordinate system by equation (1).:

$$r = a + b \cdot \theta \qquad (1)$$

wherein r and θ are the polar coordinates, r=0 defines the location of the spiral centre, a and b are real numbers. A spiral with uniform distance between all neighbouring windings, e.g., an Archimedean spiral may provide high area efficiency at uniform distortion of the magnetic field along the flow axis.

[0026] A distance between the outlet channels may continuously increase with increasing distance to the channel branch, wherein partial flows can be separated from each other with high efficiency.

[0027] The auxiliary structure may be arranged such that the direction of increasing magnetic field is parallel to the planar spiral portion. Then, beginning from the channel branch, the distance between the outlet channels may increase along the horizontal direction and the outlet channels may be formed in the plane of the planar spiral portion. Alternatively, the auxiliary structure may be arranged such that the direction of increasing magnetic field is orthogonal to the planar spiral portion. Then, beginning from the channel branch, the distance between the outlet channels increases along the vertical direction and the outlet channels may be formed in a plane orthogonal to the planar spiral portion.

[0028] The outlet channels may include straight channel portions that directly adjoin the channel branch, wherein an angle between neighbouring outlet channels is in a range from 20 degree to 40 degree, e.g., about 30 degree to effectively separate two partial flows. The channel branch 270 may have the shape of the letter Y.

[0029] The distance between the planar spiral portion and the auxiliary structure may be at most 2 mm, for example, at most 1 mm or at most 0.6 mm such that the field distortion caused by the auxiliary structure generates a comparatively strong magnetic field gradient within the fluid channel. A stronger magnetic field gradient in the fluid channel increases the efficiency of magnetic separation.

[0030] The auxiliary structure may be formed in a direction vertical to the spiral portion, in other words "above" or "below" the spiral portion. In particular, the auxiliary structure is completely formed "above" or "below" the spiral portion.

An auxiliary structure formed above or below the spiral portion facilitates a small distance between neighbouring windings of the spiral portion such that the total length of the spiral portion in a given substrate area can be increased. In addition, the auxiliary structure may be provided in a cost-efficient way, by bonding or adhering the auxiliary structure on one of the main surfaces of the substrate.

[0031] Alternatively, a portion of or the complete auxiliary structure may be formed in the plane of the spiral portion. For example, the auxiliary structure may include a planar spiral part with the windings of the spiral part interleaved with the windings of the spiral portion of the fluid channel. For example, the auxiliary structure may be a flat plate attached, e.g., bonded to a planar main surface of the substrate.

[0032] The auxiliary structure may include a planar spiral part, wherein a radius of the planar spiral part of the auxiliary structure and a radius of the planar spiral portion of the fluid channel show the same angle dependency. In other words, the same mathematic equation with the same coefficients describes the flow axis of the fluid channel and the curved longitudinal axis of spiral part of the auxiliary structure.

[0033] The auxiliary structure may exclusively include the spiral part or may further include a main body, wherein the spiral part is formed or mounted on a flat surface of the main body. The spiral part of the auxiliary structure may be formed directly above or below the spiral portion of the fluid channel, wherein the spiral part may increase the magnetic field in the fluid channel at least along the complete spiral portion in an efficient way.

[0034] A radius of curvature of the spiral part pointing to the fluid channel may be equal to or smaller than the radius of curvature of the spiral portion at the side pointing to the auxiliary structure.

[0035] The spiral part may be a continuous structure with uniform cross-sectional area along the curved longitudinal axis of the spiral part. The continuous spiral part may be formed in a cost-efficient way, for example, by bending a wire or by moulding and may provide a uniform magnetic field gradient along the complete length of the spiral portion of the fluid channel. In case of an auxiliary structure formed by bending a wire, the diameter of the wire may be equal to or smaller than a diameter of the fluid channel.

[0036] Alternatively, the spiral part may include a plurality of protrusions arranged along a spiral line.

[0037] A groove may extend from one of the main surfaces of the substrate into the substrate. The groove may include a planar spiral section parallel to the spiral portion of the fluid channel. At least a portion of the auxiliary structure may be arranged in the groove. The groove may be formed in the same way as the fluid channel, e.g., by etching, moulding or milling. The groove facilitates a simply alignment of the spiral part of the auxiliary structure and the spiral portion of the fluid channel and facilitates a small distance between auxiliary structure and fluid channel of less than 2mm, e.g. less than 1mm with only low adverse impact on the mechanical stability of the substrate.

[0038] According to an embodiment the groove may expose the fluid channel and the auxiliary structure may form a part of the inner surface of the fluid channel.

[0039] The substrate may include one single groove with a spiral section in one of the main surfaces or may include grooves on both main surfaces of the substrate.

[0040] A cross-sectional area of the fluid channel orthogonal to the fluid flow axis may be a circle.

[0041] Alternatively, the cross-sectional area may be rectangular with rounded corners or may be oval, wherein the greater one of two orthogonal extensions of the cross-sectional area may be parallel or orthogonal to the planar spiral portion.

[0042] A diameter of a circular cross-sectional area of the fluid channel may be in a range from 100 μm to 1 mm. For diameters below 100 μm, a significant fall of pressure may occur along the flow direction for a process liquid that includes an aqueous solution containing ions of rare earth elements and that passes the fluid channel at a flow rate of 3ml/h. For diameters greater than 1 mm, at the same flow velocity the flow may get more turbulent. Turbulences remix previously enriched and diluted partial flows and deteriorate magnetic separation efficiency.

[0043] In fluid channels with noncircular cross-sectional area, the cross-sectional area may be in a range from π x 2500 μm^2 to π x 0.25 mm^2, wherein an aqueous solution containing magnetic ions may pass through the fluid channel at high rate, highly laminar flow and at high magnetic separation efficiency.

[0044] According to another embodiment, a magnetic separation apparatus for separating magnetic molecular entities may include a magnetic field unit that is capable of generating a magnetic field in a field space, e.g., an electromagnet or a permanent magnet. The magnetic separation apparatus further includes a microfluidic device with a fluid channel including a planar spiral portion and with a ferromagnetic auxiliary structure formed in a plane parallel to the planar spiral portion at a distance of at most 2 mm. The auxiliary structure locally distorts the comparatively uniform magnetic field in the field space such that even in a comparatively small field space with small lateral dimensions a strong magnetic field gradient can be generated that is effective across a comparatively long fluid channel.

[0045] The area efficient microfluidic device facilitates cost-efficient cascading for higher yield and cost-efficient parallelizing for higher throughput.

[0046] A method of separating magnetic ions may include arranging a microfluidic device as described above in a field space of a magnetic field unit. A process liquid, e.g. an aqueous solution containing ions of rare earth elements, is fed into the inlet opening of the microfluidic device. At least two different partial flows of the aqueous solution can be separated from the process liquid through two or more outlet openings, wherein in at least one partial flow at least one magnetic molecular entity is enriched and in the other the magnetic molecular entity is diluted.

[0047] FIGS. 1A shows a vertical cross-sectional view and FIGS. 1B-1C show parallel horizontal cross-sectional views of a microfluidic device 500 with a substrate 100 with two parallel main surfaces 101, 102 at opposite sides. In the substrate 100, a fluid channel 250 extends from an inlet opening 210 to a channel branch 270, where the fluid channel 250 branches into two outlet channels 281, 282 that end at outlet openings 291, 292. Apart from the inlet opening 210 and the outlet openings 291, 292 at the end of the outlet channels 281, 282, the fluid channel 250 is spaced from both main surfaces 101, 102 and may be completely closed.

[0048] The inlet opening 210 may be formed close to the centre of a first main surface 101 at the front side of the microfluidic device 500. A first outlet opening 291 may be formed in a peripheral portion of the first main surface 101. A second outlet opening 292 may be formed directly opposite to the first outlet opening 291 in the opposite second main surface 102.

[0049] The fluid channel 250 includes a planar spiral portion 255 that may directly adjoin the inlet opening 210. A straight portion 258 may connect the spiral portion 255 and the two outlet channels 281, 282. A curved longitudinal axis of the spiral portion 255 forms or approximates to a high degree an Archimedean spiral, wherein a distance between neighbouring windings is in a range of 0.5 to 5 mm. A cross-sectional area of the fluid channel 250 orthogonal to the curved longitudinal axis may be a circle with a diameter of at most 1mm, e.g., at most 0.6mm.

[0050] A groove 150 is formed in the second main surface 102. Alternatively, the groove 150 may be formed in the first main surface 101 or in both the first and the second main surface 101, 102 grooves 150 may be formed.

[0051] The groove 150 may include a planar spiral section 155. The spiral section centre point 151 and the spiral portion centre point 251 of are on the same vertical axis. The radius r2 of the planar spiral section 155 of the groove 150 and a radius r1 of a planar spiral portion 255 of the fluid channel 250 have equal angle dependency. In other words, both planar spirals are defined by the same equation. For example, in terms of polar coordinates related to the centre points 151, 251, both spirals may be defined by $r = a + b \cdot \theta$, wherein the coefficients a and b are the same for both spirals.

[0052] A ferromagnetic auxiliary structure 300 includes a spiral part 355 formed in the groove 150. The auxiliary structure 300 may be formed in a lower portion of the groove 150, may fill the groove 150 completely, or may extend beyond the groove 150. FIGS. 2A-2B show cross-sections of a portion of a microfluidic device 500 with four windings of the spiral portion 255. The cross-sectional area of the spiral portion 255 orthogonal to the flow direction may be a circle with a diameter d0 in a range from 100μm to 2mm, for example, about 1mm.

[0053] A centre-to-centre distance d2 between neighbouring windings of the spiral portion 255 may be in a range from 2 mm to 4 mm. A groove 150 extends from a second main surface 102 into the substrate 100. The groove 150 forms a planar spiral with the same angular relationship of the radius as the spiral portion 255 and with the same centre point such that the groove 150 is vertically aligned to the spiral portion 155. In other words, a vertical projection of a spiral section 155 of the groove and of the spiral portion 255 of the fluid channel 250 into the same plane may fully overlap.

[0054] In FIG. 2A the microfluidic device 500 is positioned in an external magnetic field B with a magnetic field vector orthogonal to the spiral plane.

[0055] In FIG. 2B the microfluidic device 500 is positioned in an external magnetic field B with a magnetic field vector parallel to the spiral plane.

[0056] FIG. 3A shows lines of equal magnetic field strength in an area close to the auxiliary structure 300 and in the adjoining fluid channel 250 in case the magnetic field vector is parallel to the spiral plane as depicted in FIG. 2A.

[0057] FIG. 3B shows lines of equal magnetic field strength in an area close to the auxiliary structure 300 and in the adjoining fluid channel 250 in case the magnetic field vector is orthogonal to the spiral plane as depicted in FIG. 2A.

[0058] In FIG. 4 line 501 shows the magnetic field strength along the vertical diameter of the fluid channel 255 of FIG. 3A and line 502 shows the magnetic field strength along the vertical diameter of the fluid channel 255 of FIG. 3B as a function of a distance x to the auxiliary structure 330. The external magnetic field is a uniform magnetic field with a magnetic field strength of 0.5 T. The minimum distance between the fluid channel and the auxiliary structure is 0.6mm.

[0059] For the orthogonal magnetic field, the highest magnetic field strength and the highest magnetic field strength gradient occur at the side of the fluid channel oriented to the auxiliary structure. For the parallel magnetic field, the lowest magnetic field strength and the highest magnetic field strength gradient occur at the side of the fluid channel oriented to the auxiliary structure.

[0060] In both cases, the magnetic field strength in the fluid channel asymptotically approximates the magnetic field strength of the external magnetic field at the side averted from the auxiliary structure and in both cases a significant magnet field gradient can be observed in the complete cross-sectional area of the fluid channel such that magnetic separation occurs in the complete fluid channel.

[0061] The separating force effective on magnetic molecular entities is a function of the vector product of magnetic induction (magnetic flux density) B and the gradient grad (B) of the magnetic induction B. As indicated by lines 501, 502, in case the magnetic field vector is orthogonal to the spiral plane, the effective magnetic induction B in the fluid channel 250 is greater than in case the magnetic field vector is parallel to the spiral plane and consequently the arrangement as illustrated in FIG. 2A may show higher separation efficiency than the arrangement in FIG. 2B.

[0062] In FIG. 5A the auxiliary structure 350 is a flat plate that may be formed or bonded onto at least that main surface 101, 102 of the substrate 100 that shows the smaller distance to the spiral portion 255 of the fluid channel 250.

[0063] In FIG. 5B the auxiliary structure 350 includes a main body 352 and protrusions 353 extending from the main body 352 into the direction of the substrate 100. The protrusions 353 may be laterally separated pillars or cones formed along a spiral line aligned to the spiral portion 255. Alignment fittings 359 of the auxiliary structure 359 and corresponding alignment grooves 160 in the main surface 101, 102 may facilitate the alignment between the protrusions 353 of the auxiliary structure 350 and the spiral portion 255 of the fluid channel 250.

[0064] In FIG. 5C the auxiliary structure 350 includes a spiral part 355 formed on at least one of the first and second main surfaces 101, 102 of the substrate 100, wherein a distance between auxiliary structure 350 and the spiral portion 255 of the fluid channel 250 is less than 2 mm, for example less than 1mm or at most 0.6 mm. One or more alignment grooves and one or more alignment fittings of the auxiliary structure may facilitate sufficient alignment between the spiral part 355 and the spiral portion 255.

[0065] FIGS. 6A-6B show a microfluidic device 500 with the auxiliary structure 350 including a spiral part 355 that is formed in a groove 150, wherein a spiral section 155 of the groove 150 is formed between the windings of the spiral portion 255 of the fluid channel 250. In particular, the windings of the spiral section 155 may be in the centre between two neighbouring windings of the spiral portion 255. The magnetic field distortion induced by the auxiliary structure 350 effects a decrease of the magnetic field along a horizontal direction parallel to the spiral plane. The outlet channels 280 may be formed in the plane of the fluid channel 250 and may end in vertical channel openings 290. The outlet channels 280 may be straight, the branch 270 may have the shape of the letter Y, and an angle α between the two outlet channels 280 may be about 30°.

[0066] FIGS. 7A-7C show a further microfluidic device 500 in greater detail. The microfluidic device 500 may include fittings 370. Each fitting 370 is formed on one of the main surfaces 101, 102 of the substrate 100. The fittings 370 may allow the connection of the inlet opening 210 and/or the outlet openings 291, 292 to a microfluidic pump or to the outlet opening of another microfluidic device of the same or similar type. The fittings 370 facilitate the integration of the microfluidic device 500 in a microfluidic system that cascades a plurality of the microfluidic devices 500.

[0067] The spiral portion 255 as well as the spiral part 355 may be described by variable t in equations (2) and (3):

$$X(t) = 0.0006 * (\cos(t)+t*\sin(t)) \quad (2)$$

$$Y(t) = 0.0006 * (\sin(t)-t*\cos(t)) \quad (3)$$

t=0 describes the centre point of the spiral. The spirals may be defined in a range for t from -1.8640688 to 18*π. Equations (2) and (3) give the values for X(t) and Y(t) in meters.

[0068] The microfluidic device 500 may be based on a one-piece substrate 100 formed, for example, by 3D printing or may be a two-piece device, wherein the upper half and the lower half of the fluid channel 250 are formed in the surfaces of two separated plates which are then bonded together such that two half channels complete each other to the fluid channel 250. Alternatively or in addition, a portion of the substrate including the outlet channels 281, 282 may be formed in the same way as two-piece part and then attached to the portion with the fluid channel 250. For further details, reference is made to the description of the previous FIGS.

[0069] FIG. 8 shows a magnetic separation apparatus 900 for separating magnetic molecular entities such as ions, atoms, and molecules. A magnetic field unit 400 generates a magnetic field in a field space 450. The magnetic field in the field space 450 may be highly uniform. A microfluidic device 500 with a fluid channel, an auxiliary structure and two outlet openings as described above is arranged in the field space 450.

[0070] The diameter of the fluid channel may be 1mm. A pump may drive an aqueous solution containing a 0.1M concentration of holmium (III) ions through the fluid channel at a flow rate of 3ml/h. With a magnetic field strength of 0.5T in the field space 450, a significant enrichment of holmium (III) ions can be observed in an output flow through one of the outlet openings and a significant dilution of holmium (III) ions can be observed in an output flow through the other outlet opening.

Claims

1. A microfluidic device, comprising:

a substrate (100) comprising a fluid channel (250) extending from an inlet opening (210) to a channel branch (270), wherein the fluid channel (250) comprises a planar spiral portion (255) and wherein at the channel branch (270) the fluid channel (250) branches in at least two outlet channels (280); and
a ferromagnetic auxiliary structure (300) formed in a plane parallel to the planar spiral portion (255).

2. The microfluidic device according to the preceding claim, wherein
a distance between neighbouring windings of the planar spiral portion (255) deviates by not more than 5% from a mean distance between the neighbouring windings.

3. The microfluidic device according to any of the preceding claims, wherein
with increasing distance to the channel branch (270) a distance between the outlet channels (280) continuously increases with increasing distance to the channel branch (270).

4. The microfluidic device according the preceding claim, wherein
the outlet channels (280) comprise straight channel portions directly adjoining the channel branch (270), and wherein an angle between neighbouring outlet channels (280) is in a range from 20 degree to 40 degree.

5. The microfluidic device according to any of the preceding claims, wherein
a distance (d1) between the planar spiral portion (255) and the auxiliary structure (300) is at most 1 mm.

6. The microfluidic device according to any of the preceding claims, wherein
the auxiliary structure (300) is arranged in a direction vertical to the planar spiral portion (255).

7. The microfluidic device according to any of the preceding claims, wherein
the auxiliary structure (300) comprises a planar spiral part (355) and a radius (r2) of the spiral part (355) of the auxiliary structure (300) and a radius (r1) of the planar spiral portion (255) of the fluid channel (250) have equal angle dependency.

8. The microfluidic device according to the preceding claim, wherein
the spiral part (355) is a continuous structure with uniform cross-sectional area along a curved longitudinal axis of the spiral part (355).

9. The microfluidic device according to any of the preceding claims, wherein
the substrate (100) comprises a groove (150) formed in a main surface (101, 102) of the substrate (100), the groove (150) comprises a planar spiral section (155) parallel to the spiral portion (255), and wherein at least a portion of the auxiliary structure (300) is formed in the groove (150).

10. The microfluidic device according to any of the preceding claims, wherein
the planar spiral portion (255) has a circular cross-sectional area orthogonal to a fluid flow axis.

11. The microfluidic device according to the preceding claim, wherein
a diameter of the cross-sectional area of the planar spiral portion (255) is in a range from 100 μm to 1 mm.

12. A magnetic separation apparatus for separating magnetic molecular entities, the magnetic separation apparatus comprising:

a magnetic field unit (400) capable of generating a magnetic field (405) in a field space (450); and
a microfluidic device (500) according to any of the preceding claims in the field space (450).

13. A method of separating magnetic ions, the method comprising:

arranging a microfluidic device (500) as claimed in any of claims 1 to 12 in a field space (450) of a magnetic field unit (400); and
feeding an aqueous solution (550) comprising magnetic ions (555) into the inlet opening (210) of the microfluidic device (500).

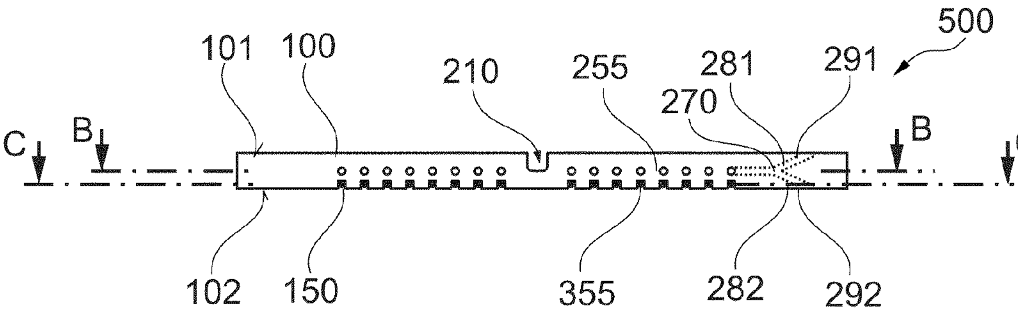

Fig. 1A

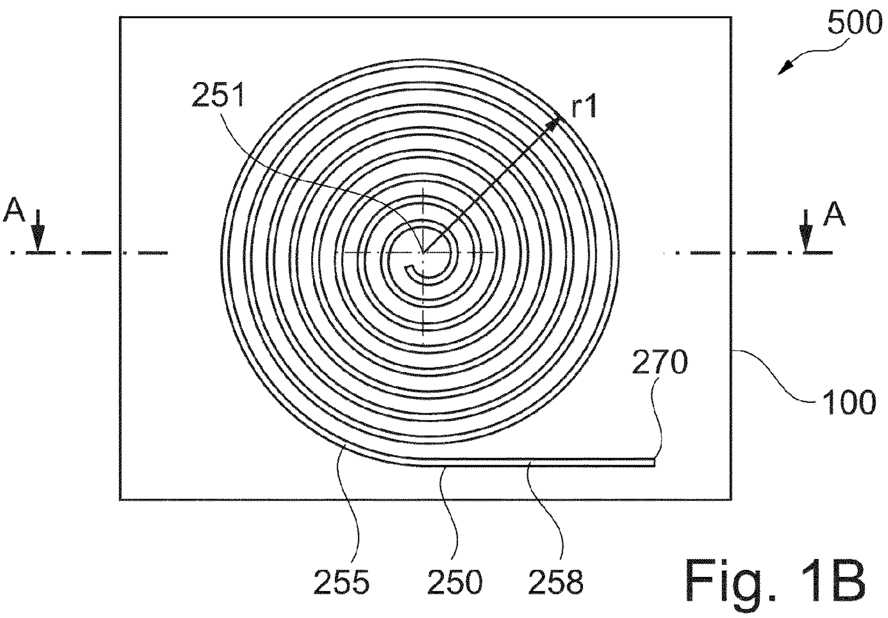

Fig. 1B

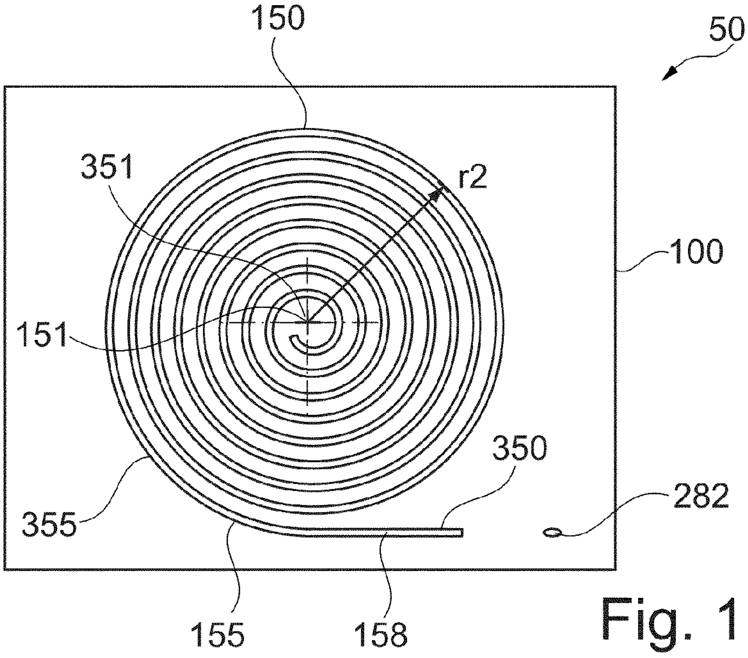

Fig. 1C

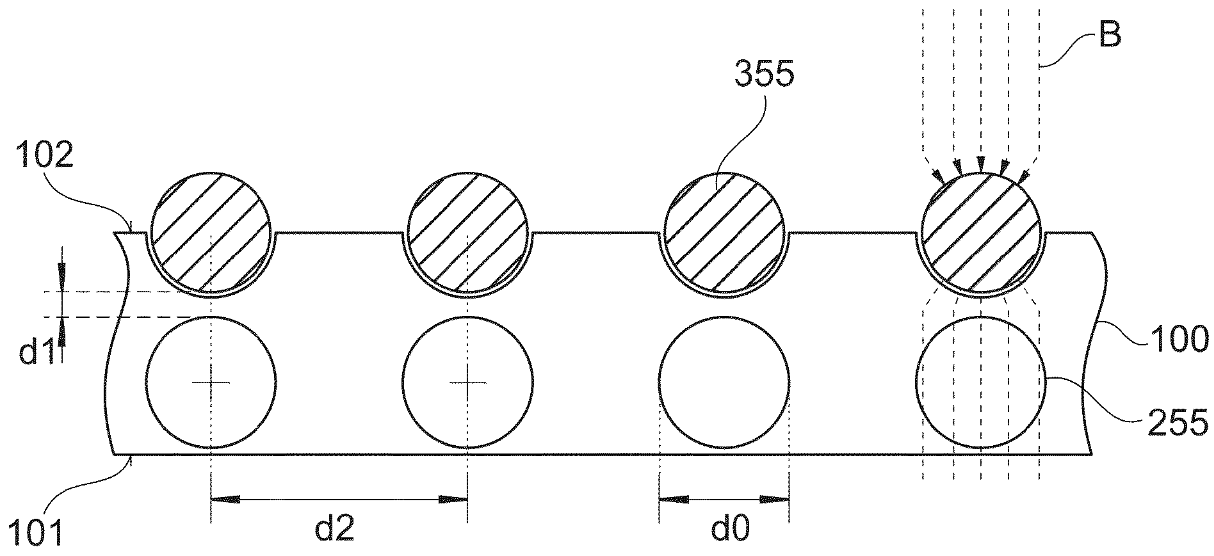
B
355
102
100
d1
255
101
d2
d0

Fig. 2A

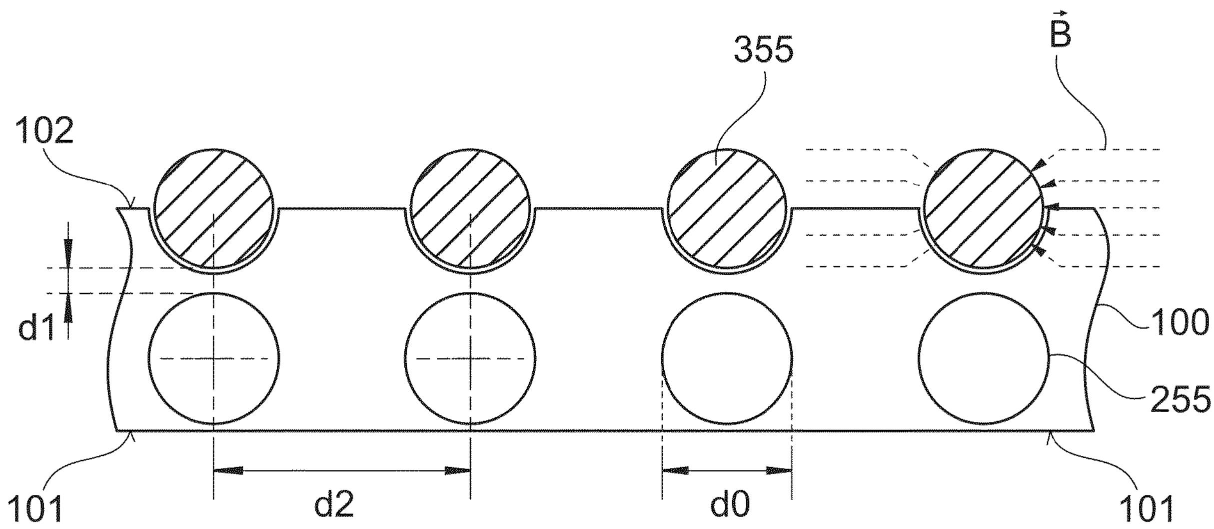
$\vec{B}$
355
102
100
d1
255
101
d2
d0
101

Fig. 2B

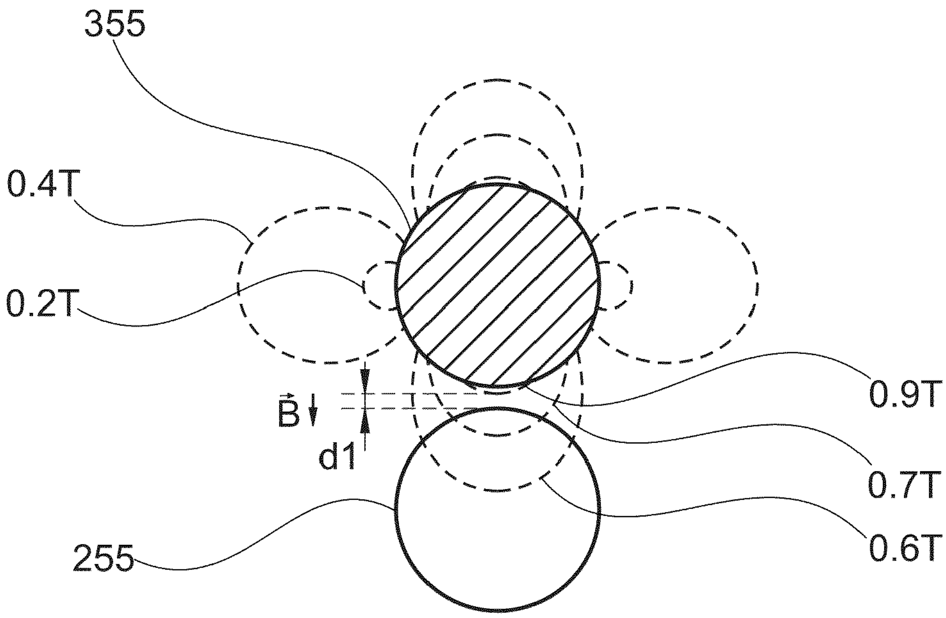
355
0.4T
0.2T
B
d1
255
0.9T
0.7T
0.6T

Fig. 3A

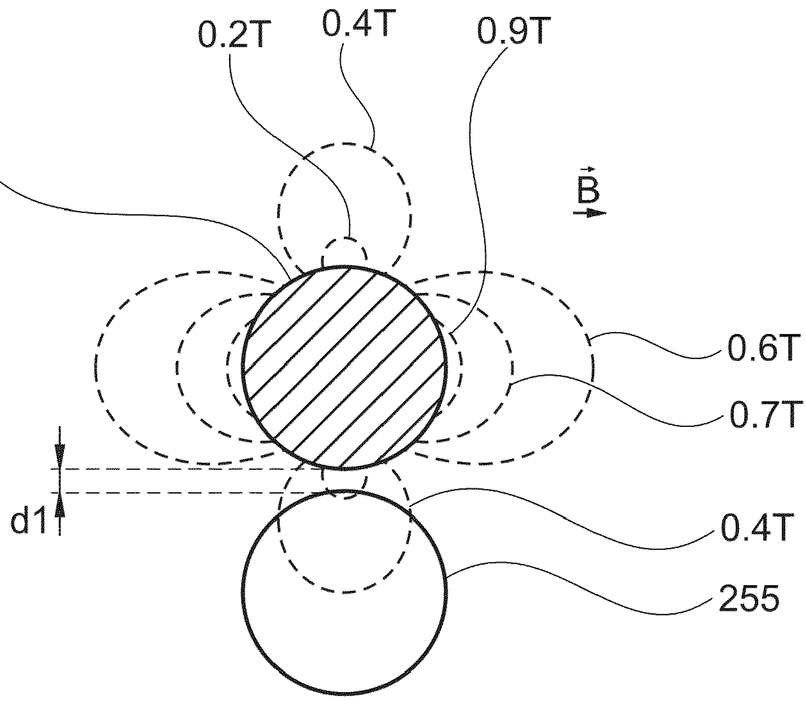
0.2T
0.4T
0.9T
355
B
0.6T
0.7T
d1
0.4T
255

Fig. 3B

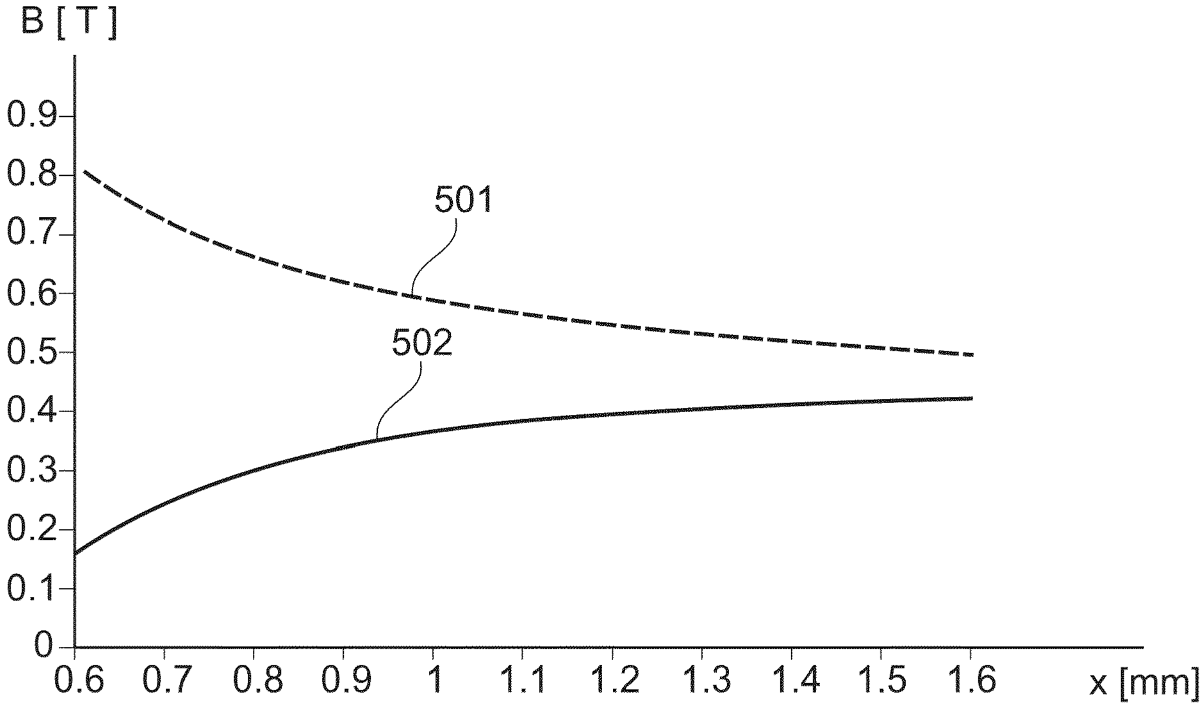
B [T]
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
501
502
0.6
0.7
0.8
0.9
1
1.1
1.2
1.3
1.4
1.5
1.6
x [mm]

Fig. 4

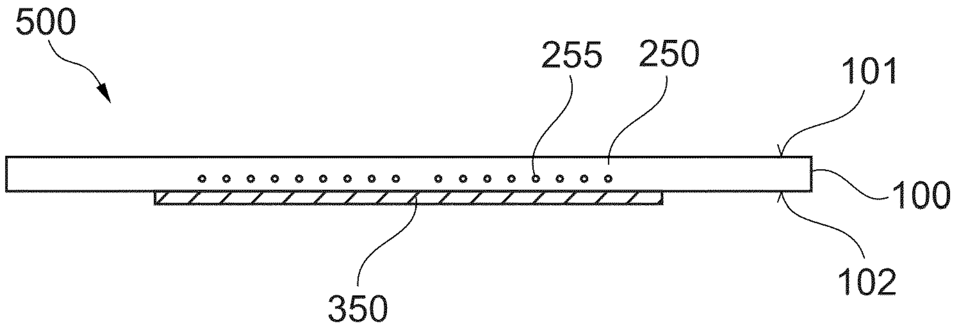

Fig. 5A

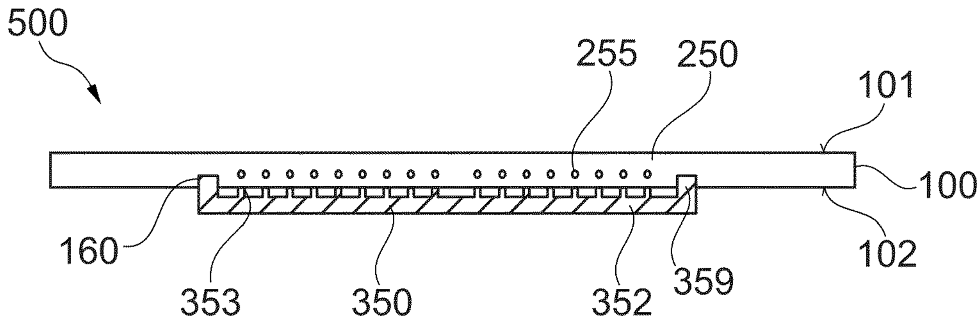

Fig. 5B

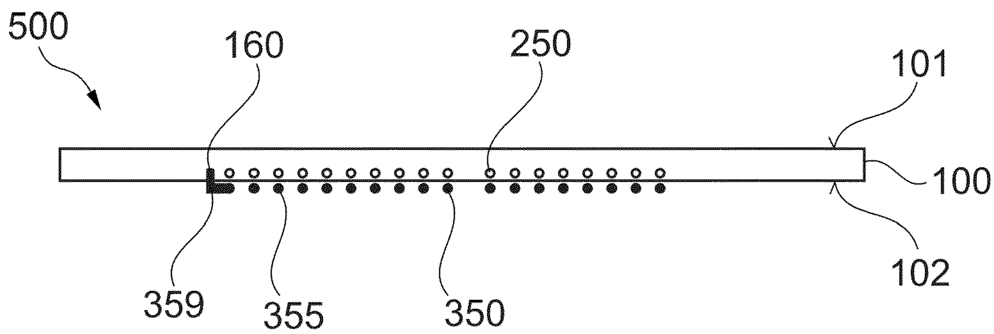

Fig. 5C

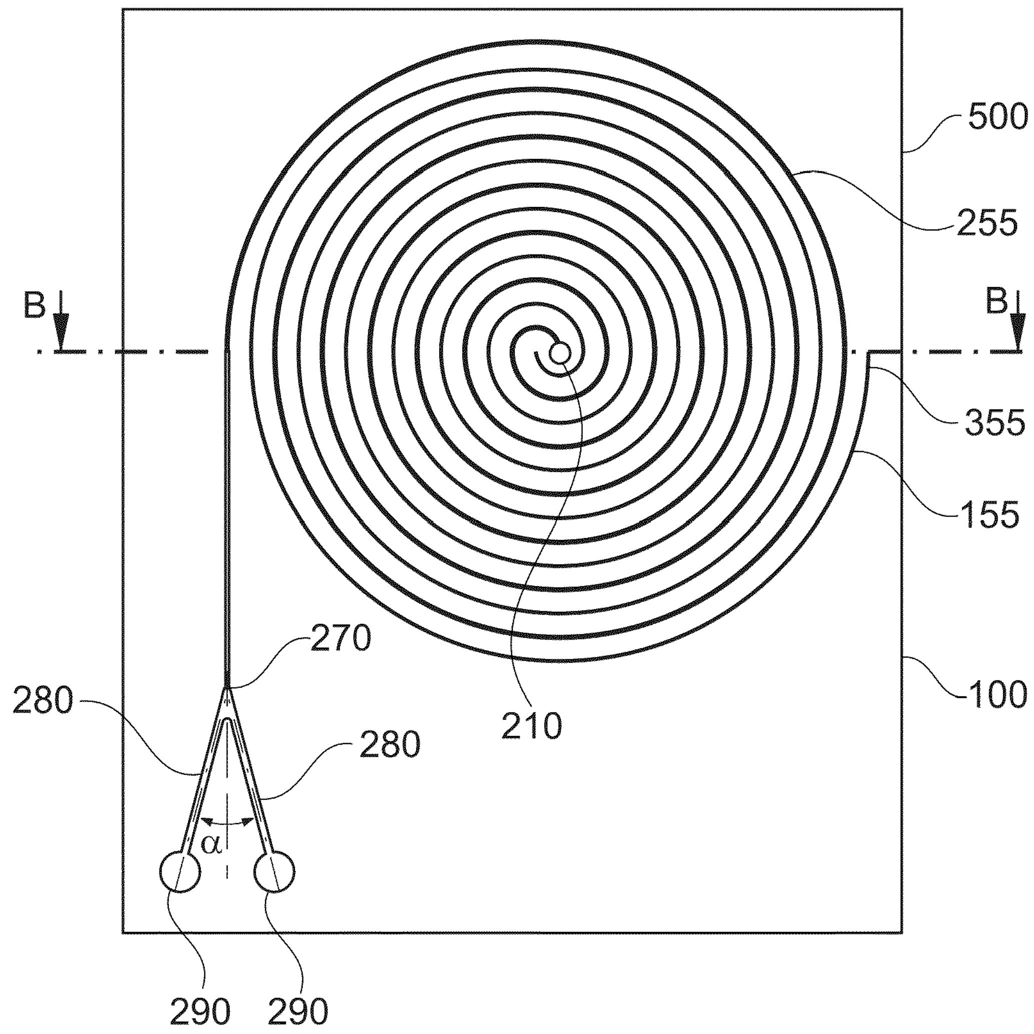
500
255
B
B
355
155
270
280
280
210
100
α
290
290

Fig. 6A

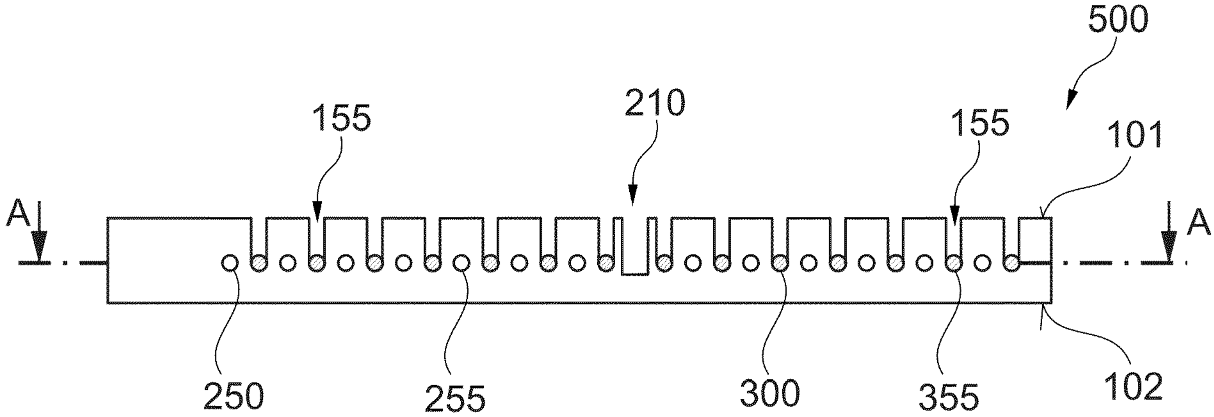
500
155
210
155
101
A
A
250
255
300
355
102

Fig. 6B

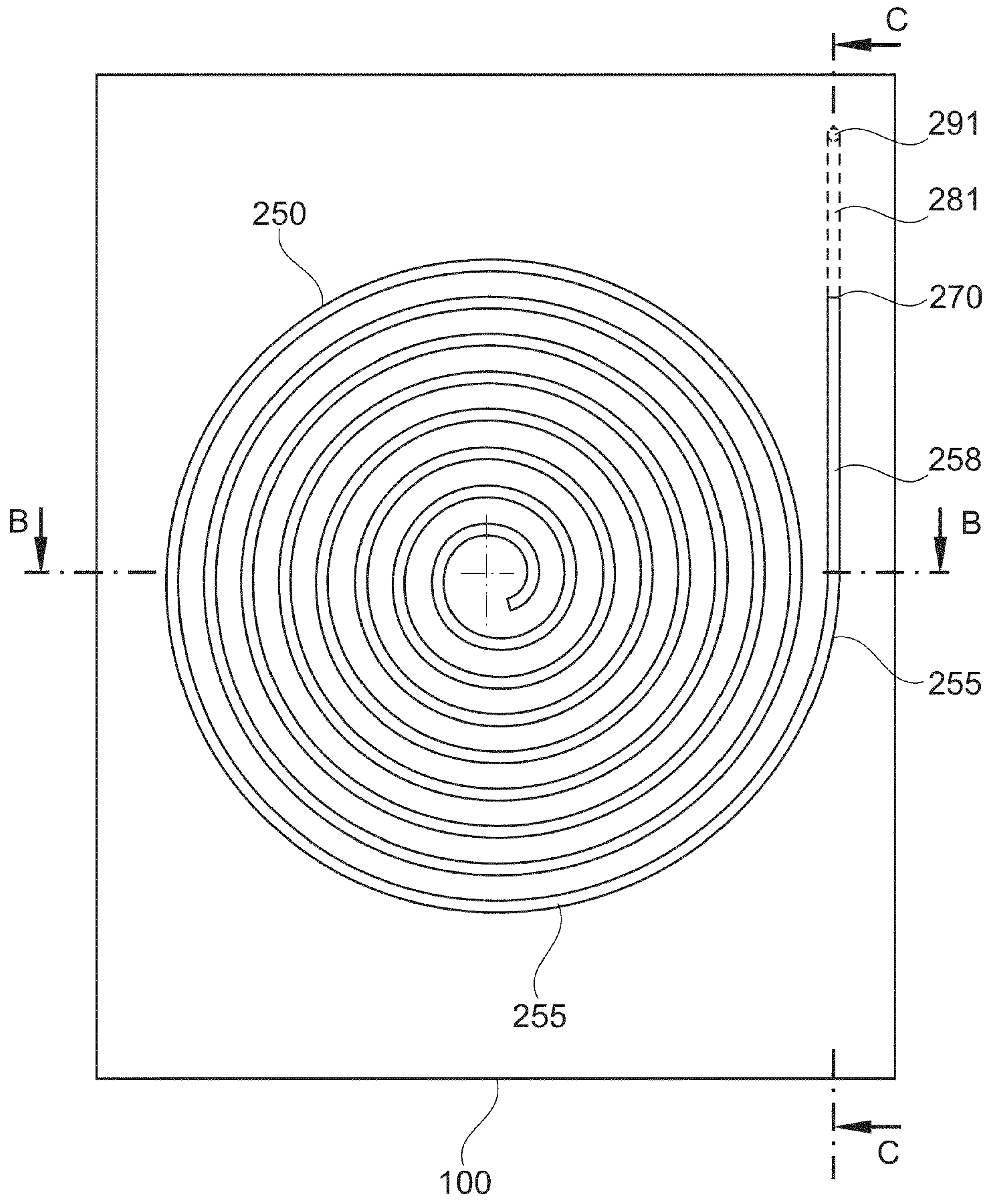

Fig. 7A

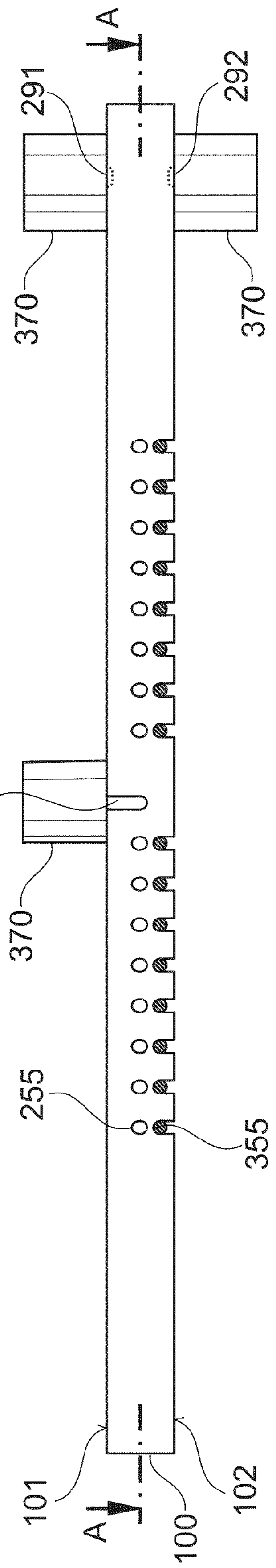

Fig. 7B

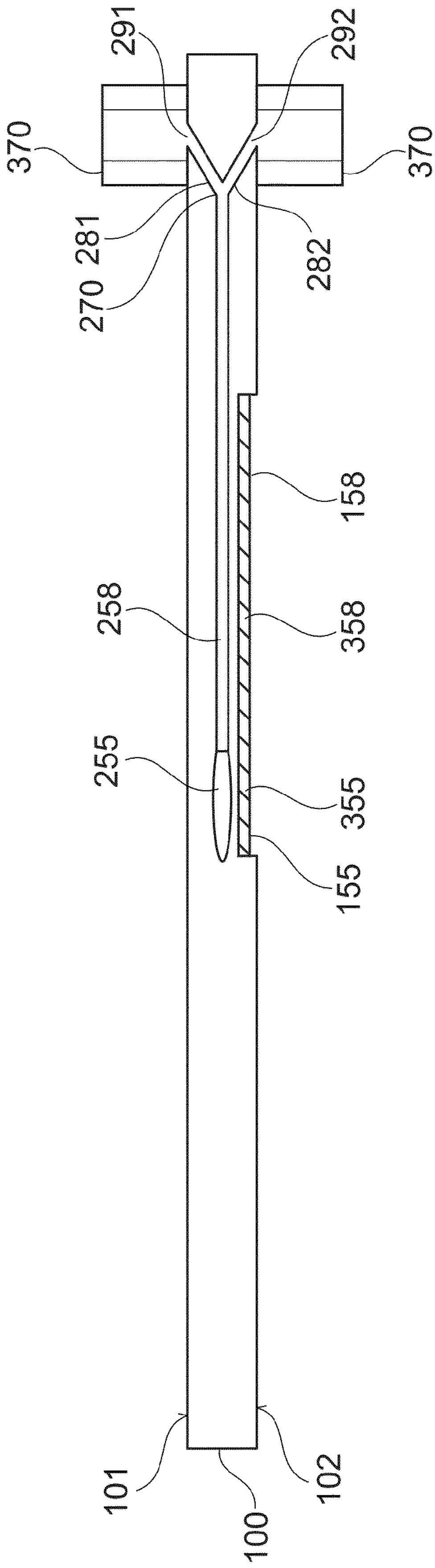

Fig. 7C

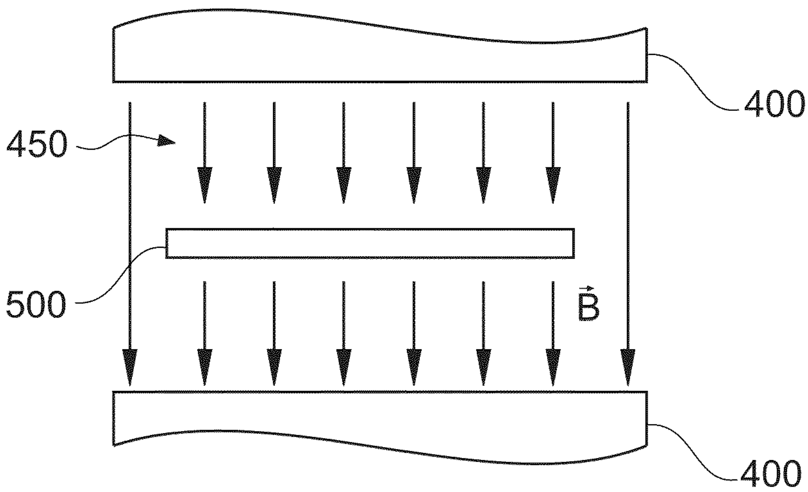

Fig. 8

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European Patent Office
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EUROPEAN SEARCH REPORT

Application Number
EP 18 21 5771

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
Y	WO 2015/057159 A1 (CLEARBRIDGE BIOMEDICS PTE LTD [SG]) 23 April 2015 (2015-04-23) * figure 1 *	1-13	INV. B01L3/00
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TECHNICAL FIELDS SEARCHED (IPC)

B01L

The present search report has been drawn up for all claims

1

Place of search	Date of completion of the search	Examiner
The Hague	17 May 2019	Campbell, Paul

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
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P : intermediate document

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E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C01)

ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO. EP 18 21 5771

17-05-2019

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For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

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- **J.H. KANG ; J.-K. PARK.** Magnetophoric Continuous Purification of Single-Walled Carbon Nanotubes from Catalytic Impurities in a Microfluidic Device. *Small,* 2007, vol. 3 (10), 1784-1791 **[0004]**