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(54) **Apparatus and method for moving a micro-object**

(57) An apparatus for moving a micro-object (20) comprises a base (30) covered by a fluid layer (40), a magnetic, flow-inducing agent (10) provided within the fluid layer (40) on the base (30), a magnetic field generating device adapted to generate a magnetic field within the fluid layer (40), and a control unit adapted to control the magnetic field generating device to change the created magnetic field to move the flow-inducing agent (10).

The fluid layer (40) has a thickness sufficiently large to accommodate and cover the micro-object (20) to be moved as well as the flow-inducing agent (10), which is a rod (10) having an aspect ratio of at least 2 to 1 between its length and the next smaller dimension and wherein the rod (10) is magnetized perpendicular to his longest axis.

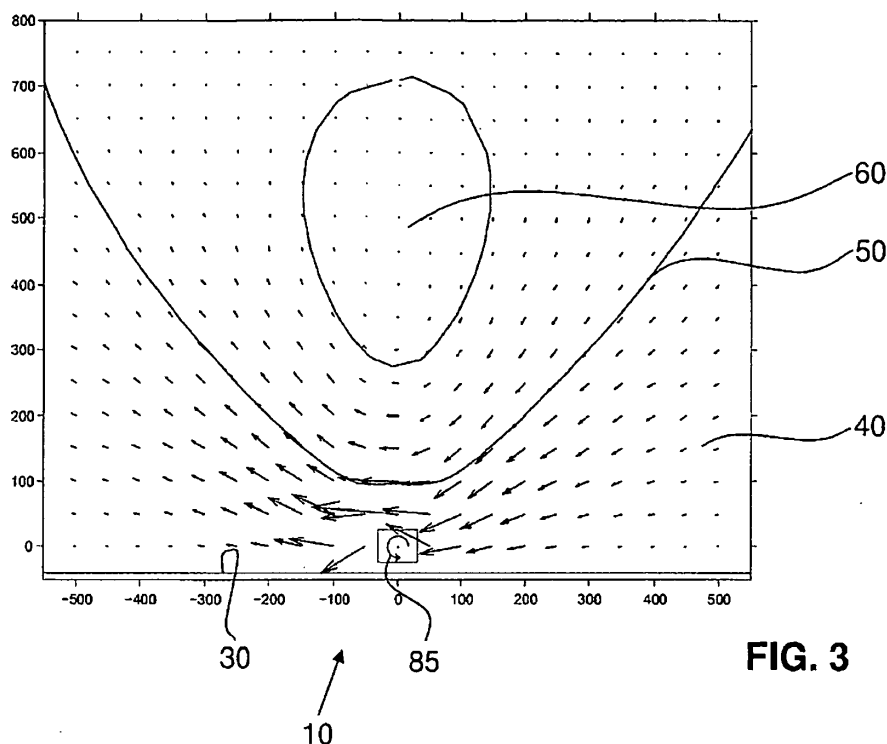


FIG. 3

Description

TECHNICAL FIELD

[0001] The present invention relates to an apparatus and a method for moving a micro-object in a low Reynolds number environment that can be used in the fields of biotechnology, medicine and crystal structure analysis, as well as other industrial applications requiring micro-operation.

PRIOR ART

[0002] Such an apparatus is known from US 2004/0209382 being used to trap and grip micro-objects and especially small crystal structures from a droplet. Such crystals have to be trapped and gripped for further analysis, i.e. in the field of biotechnology using crystal structure analysis.

[0003] The understanding of biological function requires the elucidation of the chemical mechanisms involved and this, in turn, requires the detailed knowledge of the structures of the reacting components. X-ray crystallography is the most successful method so far used to determine molecular structure at atomic resolution (almost 85% of all macromolecular structures have been determined by X-ray crystallography). The knowledge gained in such studies is of both academic and industrial interest and of critical importance for further advances in biology, medicine, and healthcare.

[0004] To date, this process step is still predominantly conducted manually by a trained expert moving e.g. the devices as mentioned in US 2004/0209382. Due to dexterity and precision challenges as well as operator fatigue, the late-stage failure rate is estimated to be around 50%.

[0005] Many approaches have been presented in the literature, involving some form of direct, mechanical contact (Hiraki et al. (2005), Acta Cryst. A61:C149-C150; Khajepour M., et al. (2013), Acta Cryst. D69, 381-387); ultrasonic wave pressure and microfluidics (Stefano Oberti et al., (2009) J. Appl. Cryst.. 42, 636-641), optical tweezers (Wagner et al., (2013) Acta Cryst. D69, 1297-1302), adhesives (Kitatani et al, (2008) Appl. Phys. Express 1 037002), laser-induced photoablation of a specialized crystallization substrate (Cipriani et al., (2012) Acta Cryst. D68, 1393-1399), a combination of suction with a capillary and subsequent transfer to a loop (Chen et al., Proc. 5th World Congress on Intelligent Control, 2004, 4651 - 4655) and use of a 6-axis industrial robot to mimic human manipulations (Viola et al., (2007). J. Appl. Cryst. 40, 539-545).

[0006] All of the methods mentioned above have major disadvantages in one area or another, and none of them have been developed to functional maturity or been commercialized.

[0007] Max T. Hou et al. have published in Appl Phys. Letts 96, 024102 (2010) on the self-propulsion of a plate-like magnetic microrobot in a rotating magnetic field. The microrobot mentioned in that article "A rolling locomotion method for untethered magnetic microrobots" is shown in different media and also in water.

[0008] L. O. Mair et al. have reported in the article "Highly controllable near-surface swimming of magnetic janus nanorods: application to payload capture and manipulation" in J. Phys. D: Appl. Phys. 44, 125001 (2011) on micro-fabricated nanorods driven by rotating magnetic fields. These nanorods can be made to translate over a surface when rotated in a fluid in a plane nearly parallel with a surface. Objects to be translated are chemically linked to the nanorod.

[0009] A further approach can be found in the article "Selective trapping and manipulation of micro scale objects using mobile micro vortexes" of the present inventors Tristan Petit et al. in Nanoletters 12(1), pages 156 to 160 (2012). There, the use of vortexes to transport micro objects is presented, wherein a twirling nanowire is used in a solution, wherein the nanowire is driven by a rotating magnetic field to generate a spiral vortex perpendicular to the long axis of the agent. This vortex can be used to transport micro objects close to a surface.

SUMMARY OF THE INVENTION

[0010] Based on this prior art it is an aim of the present invention to describe an apparatus and a controlling system to move delicate micro objects from a random starting position to a desired final position in a fluid environment in the low Reynolds number regime.

[0011] This objective is achieved by an apparatus for moving a micro-object comprising a base covered by a fluid layer, a magnetic, flow-inducing agent provided within the fluid layer on the base, a magnetic field generating device adapted to generate a magnetic field within the fluid layer, and a control unit adapted to control the magnetic field generating device to change the created magnetic field to move the flow-inducing agent. The fluid layer has a thickness sufficiently large to accommodate and cover the micro-object to be moved as well as the flow-inducing agent, which is a rod having an aspect ratio of at least 2 to 1 between its length and the next smaller dimension and wherein the rod is magnetized perpendicular to its longest axis.

[0012] The device is a rod of regular or irregular cross-section. The length of the device is preferably by far greater than or equal to the next smaller dimension and lies in the range between 1 micron and 1 millimeter. In other words, it

is a rod having an aspect ratio of at least 2 to 1, better 4 to 1, preferably 5 to 1, 7 to 1 or up to 10 to 1, between its length and the next smaller dimension. The device is magnetized roughly perpendicular to its longest axis. The transverse magnetization can be achieved either by appropriate orientation of the magnetic axis of a bulk material having a permanent magnetization (including but not limited to iron or neodymium compounds) or by the use of appropriately shaped inclusions of either soft or hard magnetic materials in a non-magnetic matrix.

[0013] With the device according to the present invention protein crystals can be selectively isolated out of a larger group of crystals of different sizes and shapes that are immersed in a growth solution. The selected crystal is brought to and placed on a dedicated extraction device for further handling. The extraction and subsequent flash-cooling is a crucial step in macromolecular crystallography worldwide.

[0014] It is mentioned, that the operation occurs in a fluid system in the low Reynolds number regime within a viscosity range of between 1 to 100 centipoise. The device is caused to rotate around its longitudinal axis, i.e. parallel to the supporting surface and is driven by rotating or oscillating magnetic fields thereby inducing a rolling motion of the agent across the surface. The control of the device is effected either manually by an operator or by a system involving automatic recognition of the agent and the object to be transported and the generation of the appropriate magnetic fields to achieve the desired effect.

[0015] The method of propulsion of micro objects using this device involves a fluid flow rather than direct contact by the agent. The method uses the device according to the invention rolling on a surface in the environment described above to create a roughly cylindrical vortex parallel to the long axis of the agent. The vortex is generated above the entire length of the agent and extends somewhat beyond the ends of the agent and moves and re-orientates with the agent. The fluid flow associated with a vortex can lift small objects off the surface in front of the agent and trap them in the vortex allowing them to be picked up, transported to a pre-specified position, and then released.

[0016] A method for moving such a micro-object in a fluid layer on a base by means of the magnetic, flow-inducing rod with an apparatus as mentioned above comprises the steps of: positioning the rod on the base in the fluid layer near the micro-object to be moved, wherein the orientation of the rod is essentially parallel to the base and roughly perpendicular to the smallest distance between the object to be moved and the rod, displacing the rod in direction of the object to be moved through application of a varying magnetic field, creating a fluid flow generating a vortex above the rod, and displacing the object through movement of the rod while retaining the object in the vortex.

[0017] Typical dimensions are $300 \times 60 \times 50$ micrometer, whereas the device/agent is transversely magnetized and rolls around its long axis on a surface in a rotating external magnetic field. In a liquid environment the device creates a rising flow in front of it (in the direction of its movement) and a vortex above its body. The flow and vortex are efficient for picking-up and trapping micro-objects of sizes ranging from microns to e.g. one millimeter depending on the size of the device/agent. In viscous solutions such a device can transport objects many times its own size and weight.

[0018] Further embodiments of the invention are laid down in the dependent claims.

[0019] In one embodiment the rod comprises a bulk material, having a permanent magnetization with its magnetic axis oriented perpendicular to the longitudinal axis of rod. Then it is also possible to have additional non-magnetic material giving the outer shape of the rod. However, the torque which can be executed is growing with the amount of magnetic material. In such a case it is preferred to have the magnetic material especially at and near the free ends of the rod, so that it is easier to navigate.

[0020] In another embodiment the rod comprises a non-magnetic bulk material providing its outer shape and including a plurality of hard magnetic particles having a permanent magnetization with their magnetic axes oriented perpendicular to the longitudinal axis of the rod. The distribution of the plurality of hard magnetic particles can be equal over the entire rod or more particles can be provided near the free ends so that there is a gradient of concentration of these particles.

[0021] A further embodiment of the rod comprises at least one soft magnetic post oriented perpendicular to the longitudinal axis of the rod and being included in a non-magnetic bulk material of the rod providing its outer shape. An increasing number of posts increases the possible maximum torque and improves the navigational possibilities.

[0022] The magnetized parts of the rod usually comprise iron and/or neodymium compounds or cobalt and/or nickel alloys.

[0023] The fluid layer comprises a fluid system within a viscosity range of between 1 to 100 centipoise, especially in a low Reynolds number regime. This can be e.g. a fluid based on or being water or a PEG solution. Then the fluid flow induced by the rotating rod creates a vortex area above the rotating rod within the fluid layer opposite to the base. The vortex area can be a roughly cylindrical vortex parallel to the long axis of the rod and generated above essentially the entire length of the rod.

[0024] The essential feature of the invention is the use of rods with transverse magnetization, allowing these rods to roll along their long axis on the surface of a container and enabling them to generate an extended, horizontal, cylindrical vortex that gently and controllably move other micro-objects - such as protein crystals - to the desired location. Other methods proposed for the transportation of micro-objects through the use of magnetically controlled agents have used longitudinally magnetized (or magnetizable) agents which have unfavorable geometries for transporting micro-objects.

[0025] A further advantage of the present rod device is the moderate overall system price being at about 10% - 20%

of complete systems mentioned above (Viola, et al, 2007; Khajepour et al, 2013), and is also less expensive than a trained expert. In comparison with human operators the proposed system achieves a higher success rate due to better repeatability, smoothness of operation, and lack of operator fatigue. Use of hydrodynamic forces results in more gentle handling compared with mechanical grippers. The system using such a micro rod can handle crystals from micron to millimeter size, in contrast to systems based on nanowires or optical tweezers. It is possible to work in native crystallization plates (in contrast to microfluidic/ultrasonic devices or the CrystalDirect system), thereby reducing system complexity and allowing smaller overall system size. The system can be driven by a small magnetic field generator (as the MiniMag from Aeon Scientific AG, Switzerland) and controlled by a simple personal computer system.

BRIEF DESCRIPTION OF THE DRAWINGS

[0026] Preferred embodiments of the invention are described in the following with reference to the drawings, which are for the purpose of illustrating the present preferred embodiments of the invention and not for the purpose of limiting the same. In the drawings,

- Fig. 1A to 1D show a sequence of side views in a wet environment with a micro-rod device and an object to be manipulated;
- Fig. 2A to 2G show side views and perspective views on three embodiments of micro-rod devices according to the invention;
- Fig. 3 a schematic and/or calculated side view on the environment to move an object to be manipulated with a micro-rod device according to the invention; and
- Fig. 4 a view from above on the micro-rod device with an object to be moved similar to Fig. 1.

DESCRIPTION OF PREFERRED EMBODIMENTS

[0027] Fig. 1 shows a sequence of side views in a wet environment 40 with a micro-rod device 10 and an object 20 to be manipulated in a wet environment 40 on a bottom surface 30. Fig. 2 shows side views and perspective views on three different embodiments of micro-rod devices according to the invention. Similar features receive similar or identical numerals. In other words; Fig. 2A to 2G show different embodiments of transversely magnetized devices as fabricated by (but not limited to) the methods described in the following paragraphs.

[0028] The micro-rod device 10 according to an embodiment of the invention has a length of 300 micrometer, a width of 60 micrometer and a height of 50 micrometer. It has therefore the form of a parallelepiped-shaped body with a length which is at least 5 times longer than height or width. The length is measured between the two opposing end surfaces 71 and 72 along the longitudinal axis, which end surfaces 71 and 72 have side edges of 50 and 60 micrometer length. The outer dimensions are predetermined by the polymer capsule 70, within which three soft magnetic cylinders 11, 12 and 13 are provided. The cylinders 11, 12 and 13 are oriented one parallel to another in view of their longitudinal axis. They are embedded in a non-magnetic polymer matrix perpendicular to the overall longitudinal axis of the device 10. The overall length between the end surfaces 71 and 72 as well as the number of embedded cylinders 11, 12, 13 is chosen at the fabrication stage. Therefore the number of embedded cylinders can be one, two, three as shown here, or more; especially 4, 5, 7 or 10. It is an arbitrary number. If the device is longer a higher number of cylinders is preferred to have a higher portion of magnetized material with the device 10.

[0029] The present device is therefore a rod of a rectangular cross-section. The rod 10 is magnetized perpendicular to its longest axis. In the present embodiment the transverse magnetization is achieved by the use of cylindrically shaped inclusions 11, 12 and 13 of either soft or hard magnetic materials (including but not limited to iron or neodymium compounds) in a non-magnetic polymer matrix providing the outer form of said parallelepiped.

[0030] Although the form of the device 10 according to this embodiment of Fig. 1 and 2A to 2G is a parallelepiped, it is possible that the large side surfaces 73, 74, 75 and 76 are rounded to provide a cylinder having its longitudinal axis perpendicular to the longitudinal axis of the cylinders 11, 12 and 13.

[0031] Fig. 2A and 2B comprise plain cylinders 11, 12 and 13 being terminated with the upper or lower surface 74 or 75 of the resin environment or more generally within the polymer matrix 70.

[0032] Fig. 2C shows a slightly different approach of the embodiment of Fig. 1, wherein the posts 11, 12 and 13 are covered by an isolating layer 77. The posts 11, 12 and 13 are made of 30 micrometer diameter and 50 micrometer long posts and consist of a cobalt nickel alloy (Co-Ni). The volume fraction of CoNi in the rod can reach up to 20 percent. When SU-8, an epoxy based photosensitive polymer, is used as filler 70, then the volume fraction of CoNi reaches 65 % by weight. This allows a high magnetization of the rod and sufficient torques are generated to drive agents in a liquid environment 40, especially in a high viscosity fluid.

[0033] The magnetic field is varied to allow the device 10 to rotate in direction 85, whereas the movement direction follows arrow 80. Thus object 20 is pushed along bottom 30 in the liquid environment 40. The flow of the induced

movement raises the object to be manipulated above the device 10, as can be seen in Fig. 3, and traps it in a vortex area 60. Then, with the adapted speed the device 10 displaces the trapped object 20 within vortex area 60. An extraction device 90 is shown in Fig. 1C to capture the object 20 to be handled. Therefore, extraction device 90 comprises a handle 92 and in internal opening 91 around a ring shaped basic form. Extraction device 90 could also be tweezers or other appropriate devices or places. In the end, the aim of the use of the device 10 is to move an object 20 to a specific delivery point, whereas it is an advantage, that the object is moved above the ground 30 and within a fluid 40 so that it can easily deposited on said extraction device 90 positioned at the level of the device 10 and thus below the object 20, so that it can move by impetus and gravity into the correct extraction position.

[0034] Fig. 2A to 2C also show the result of possible fabrication processes comprising a photosensitive photopolymer and electroplated magnetic metals with good adhesion between the two materials. A silicon wafer covered with a silicon dioxide sacrificial layer is used as a substrate, followed by an evaporated titanium and gold bilayer that is patterned by a lift-off process. A thin layer of adhesion promoter and a 50 micrometer thick layer of a SU-8 epoxy based photosensitive polymer are spin-coated on the wafer (not shown) and patterned into tethered structures and rod shapes with cylindrical holes within the rod bodies. The holes are then filled with CoNi alloy by an electroplating process, followed, as shown in Fig. 2C by another thin layer of electroplated gold, i.e. protection layer 77, being segmented into three portions with intermediate openings 78.

[0035] The wafer can then be diced into small chips and immersed into buffered Hydrofluoric (BHF) acid solution to etch away the sacrificial SiO₂ substrate and release structures from the substrate. Finally, a micro-laser milling machine can be used to cut the devices 10 from their tethers.

[0036] In the embodiments according to Fig. 2A to 2C the device is made by patterning of non-magnetic material into a rod-shape with one or several cavities in the rod. The cavities are filled with soft- or hard-magnetic material such that the preferred magnetization direction of the entire structure is roughly perpendicular to the long axis of the rod. The non-magnetic material can be (but is not limited to) photopatternable or thermal-cured polymers such as SU-8 (MicroChem Corp) or polydimethylsiloxane (PDMS; Dow Corning Corp.), or other materials, such as silicon or silicon oxide, and is patterned by photolithography, molding, screen-printing, etching, etc. The magnetic material can be (but is not limited to) iron, cobalt, nickel, or neodymium compounds and is filled in the cavities by electroplating. Electrolytes of metallic compounds are commercially available.

[0037] Fig. 2D and 2E show a side view and a perspective view onto a micro-rod device 110 according to a further embodiment of the invention. The dimensions of such a micro-rod device 110 are similar or identical to the embodiment according to Fig. 2A to 2C and it develops a similar vortex 60. The difference is that the polymer matrix 70 comprises a mix of composites consisting of a non-magnetic matrix 70 and magnetic particles 111 into a rod-shape. The non-magnetic material can be (but is not limited to) photopatternable or thermal-cured polymers such as SU-8, polydimethylsiloxane (PDMS), or polyurethane (BJB enterprises). The magnetic material 111 can be (but is not limited to) iron or neodymium compounds with particle size from tens of nanometer to a few microns. The composite can be patterned by photolithography, molding, or screen-printing. Magnetic particles are magnetized by application of external magnetic fields during the fabrication processes in a direction roughly perpendicular to the long axis of the rod structure. Iron oxide particles are available from Alfa Aesar; Neodymium-iron-boron particles are available from Magnequench International, Inc.

[0038] Fig. 2F and 2G show a side view and a perspective view onto a micro-rod device 210 according to a further embodiment of the invention. The dimensions of such a micro-rod device 210 are similar or identical to the embodiment according to Fig. 2A to 2E and it develops a similar vortex 60. This procedure uses a patterning of hard-magnetic material into a rod-shape 211 which is magnetized in a direction roughly perpendicular to the long axis of the rod structure. This can be achieved by either cutting bulk magnetized magnetic material 211, such as a neodymium-iron-boron sheet, using laser machining or wire electrodischarge machining, or depositing hard-magnetic material on a substrate using electroplating, sputtering, etc. and patterning the material into a rod-shape. External magnetic fields are applied during the deposition process to magnetize the material in the required direction.

[0039] All aforementioned non-magnetic and magnetic materials for the production of the devices 10, 110 and 210 should be insoluble in water, chemically stable, non-corrosive, and compatible with micro-objects 20 to be moved. Exception can be made if additional materials are applied on the outer-surface of the device such that the device fits the aforementioned properties.

[0040] Fig. 3 shows a schematic and/or calculated side view on the environment to move an object 20 to be manipulated with a micro-rod device 10 according to the invention; therefore it comprises a side view on the fluid environment 40 to move the object 20 to be manipulated (not shown in Fig. 3) with a micro-rod device 10 similar to the device shown in Fig. 1. Device 10 can also be the device 110 and 210 from the other embodiments mentioned here.

[0041] Fig. 3 shows the fluid environment as e.g. a petri dish like recipient/container having a bottom wall 30, side walls (not shown) and which recipient is filled with a fluid such as water or other fluids having a wide range of viscosities, e.g. from distilled water to highly viscous solutions. The rods 10 can e.g. operate in solutions having a viscosity of up to at least 100 centipoise. An electromagnet arrangement is provided in the vicinity of the recipient as well as a control unit (both not shown in Fig. 3). The electromagnet arrangement is adapted to create a magnetic field within the fluid 40 to

induce a rotation of the rod 10 in fluid 40. Rod 10 initially and before application of the magnetic field remains through gravity at the bottom 30 of the recipient.

[0042] The control unit for the electromagnet arrangement is adapted to create a magnetic field changing over time to interact with the rod 10 causing the rotation of the rod. Such control units are known in the prior art and can be obtained e.g. through Aeon Scientific AG, Switzerland (S. Schuerle, S. Erni, M. Flink, B.E. Kratochvil, and B.J. Nelson, IEEE T Magn 49 (1), 321 (2013)).

[0043] The rotating movement 85 of the rod 10 through the fluid 40 is represented by a number of vector arrows. A streamline 50 is drawn within the field of flow vectors above the device 10 being on the bottom surface 30 of the fluid environment 40. The streamline 50 defines a well-defined vortex region 60 above the rod device 10. Therefore, if the rod 10 is rotated through actuation of the electromagnets in the created magnetic field, e.g. in the direction from the right to the left in Fig. 3, an object (not shown) in front of it will be elevated through the fluid movement and propelled into the area 60 above the rod 10. Then the fluid flow maintains the object in the area 60 above the rod 10 including through a reorientation of the rod 10 imposed by the control system. Especially, it is possible to effect a rotation of rod 10 around an axis perpendicular to the bottom wall 30, i.e. that rod 10 effects a movement over ground 30 following a curved arc.

[0044] The device 10 can rotate around its longitudinal axis, i.e. parallel to the supporting surface 30 and is driven by rotating or oscillating magnetic fields thereby inducing a rolling motion of the device 10 across the surface 30. The control of the device 10 is effected either manual by an operator controlling the control unit acting on the electromagnet arrangement or by a system involving automatic recognition of the device, especially optical recognition, and the object to be transported and the generation of the appropriate magnetic fields to achieve the desired effect.

[0045] The method of propulsion of micro objects using this device involves a fluid flow rather than direct contact by the rod 10. The method uses the device 10 according to the invention rolling on a surface 30 in the wet environment 40 to create a roughly cylindrical vortex parallel to the long axis of the rod 10. The vortex is generated above the entire length of the rod 10 and extends somewhat beyond the ends (beyond surfaces 71 and 72 of the rod 10 and moves and re-orient with the rod 10. The fluid flow associated with the vortex can lift small objects 20 off the surface in front of the rod 10 and trap them in the vortex 60 allowing them to be picked up transported to a pre-specified position and then released.

[0046] Fig. 4 shows a further image of a view from above on the micro-rod device 10 with an object 20 to be moved. The object 20 is in front of the rod 10 which is here on covered by a capsule 70. Therefore the three cylinders 11, 12 and 13 are shown and the longitudinal dimension of the device 10 ends by the end surfaces 71, 72 extending beyond the external cylinders 11 and 13. It is noted that the object 20 has almost the longitudinal dimension of the rod device 10. This is possible since the vortex area 60 extends over the entire length of the rod 10.

[0047] The micro-rod 10 rolling along its long axis on a flat or slightly curved surface 30 uses contact-free fluid flow 50 generated by the rotation of the rod 10 to lift, capture and transport a micro-object 20, adapted to move the micro-object 20 from an initial position to a target location where it is positioned on a dedicated extraction device according to prior art. This method can then be used for the manipulation of micro-objects 20 such as for crystal harvesting in the field of high-throughput crystallography.

[0048] The device 10 enables application of a method of propulsion which is non-contact in appropriate fluids 40 (flow drag induced by an individual end-effector). The actuation is a wireless, magnetic drive to induce rolling motion of the rod 10 across a surface 30. The control can be effected for open-top magnetic fields. Rod 10 can be a polyhedral right prism with magnetization normal to the long axis and can be used in fluids having a wide range of viscosities, from distilled water to highly viscous solutions. The system is adapted to manipulate any kind of micro-objects 20, including (but not limited to) delicate protein crystals and biological cells, having a greatest dimension being similar to the length of the rod 10.

[0049] The motion of the devices 10 was evaluated in solutions of different viscosities. Three orthogonally nested Helmholtz coil pairs were used to generate uniform rotating magnetic fields at the center of the coils. The devices 10 were tested in DI water (viscosity of 1 mPa·s) and 20% PEG 3350 solution (polyethylene glycol, molecular weight: 3350) (viscosity of 9.28 mPa·s). The translational speed of the devices 10 were determined in different solutions when driven by rotating magnetic Fields of different frequencies. The speed of the device 10 was dominated by the rotation frequency and the viscosity of the solutions. If a device 10 rolls on a surface without slip, the speed of the device equals the rod perimeter times the rotation frequency. A deviation between this ideal speed and the experimental data indicates slippage of the device 10 when rotating, and the slippage increases at higher viscosity and higher speed, where the device 10 faces higher fluidic drag forces.

[0050] The flow field around a rolling device 10 on a surface was investigated using a finite element analysis package (COMSOL Multiphysics). The single-phase laminar flow module, which solves the Navier-Stokes equations in a rotating coordinate system, was applied since the motion occurs in the low Reynolds number region (Re is on the order of 10^{-3}). Modeling a rolling rectangular rod 10 had to take into account that the contact points with the ground 30 and the height of the rotation axis vary with rotation angle. To simplify the calculations the device was modeled as rotating around an axis fixed at 41 micrometer above the surface. To mimic the real situation the surface was set as a moving boundary,

and the boundary speed and inlet flow velocity corresponded to the translational speed of the device 10 determined in the experiments. Only a half-length (150 micrometer) of the device 10 was modeled due to the symmetry of the system. A cylinder surrounding the rod and a large block were built to represent the rotating frame and the fixed frame of fluid, respectively. The half-rod, the cylinder, and the large block were aligned on the plane where the central cross section of the device 10 is situated, and all sides on this plane were set to be symmetrical. The simulation for the device 10 used a rotation at 2 Hz, a translational speed of 155 micrometer/s, and a fluid viscosity of 9.28 mPa·s. The arrows in Fig. 3 indicate the direction and the relative magnitude of the flow velocity $U(x, y, z) = (U_x, U_y - Vt, U_z)$, where U_x, U_y, U_z indicate the velocity of flow from the simulation results at position (x, y, z) in the X, Y, Z directions, and Vt is the inlet flow speed. At a certain distance ahead of the device 10 the flow above the supporting surface rises, thereby initiating the process of picking up objects 20 from a substrate. The plot of streamlines 50 in Fig. 3 indicate the formation of a vortex above the device 10, which is ideal for a gentle trapping of objects 20 to be transported.

[0051] The flow around the device 10 was confirmed experimentally by observing the motion of small particles suspended in the surrounding solution (in addition or at the place of an object 20). An eight-core magnetic field control system was utilized to generate magnetic fields in these experiments, and a side-view camera was applied to observe the particles around the device 10. Polystyrene particles (10 micrometer in diameter) were dispersed in the PEG solution to indicate the direction and speed of flow around a rolling agent. The device 10 was driven at a frequency of 2 Hz. The tracks of the particles confirmed the calculated flow patterns.

[0052] The fluid flow generated by a device 10, 110 or 210 according to embodiments of the invention can also lift, trap and transport larger objects, e.g. a 130 micrometer polystyrene sphere as object 20 being raised up and trapped by the vortex generated by a rolling device 10. The sphere initially sat on the bottom 30 of a plastic container filled with PEG solution. As the device 10 approached (rotation rate 2 Hz), fluid flow ahead of the device 10 overcame gravity and the stiction between the sphere and the substrate. The rising flow ahead of the device 10 lifted the sphere up to a position higher than the agent, allowing it to pass underneath the sphere as object 20. As the sphere lagged behind the device 10, the sinking flow behind the agent 10 pulled the sphere downward and in toward the device 10. After the sphere as object 20 and the device 10 were in close proximity, the sphere was soon brought to the top of the agent by the flow over the surface of the agent and was trapped in the vortex 60 generated by the agent 10. The sphere could be stably transported to any predefined location.

[0053] Higher rotation frequencies produce stronger vortices above the device 10. e.g. transporting objects 20 at 10 Hz. A polystyrene bead was trapped above the device 10 moving at approximately 575 micrometer/s, confirming that objects are reliably trapped in the vortex 60 even when transported at higher speeds. The viscous drag force experienced by a sphere moving with respect to the surrounding fluid at low Reynolds number is given by Stokes' law: $F_{\text{drag}} \sim 6\pi\mu RV$, where μ is the dynamic viscosity of the fluid, R is the radius of the sphere, and V is the velocity of the sphere relative to the fluid. For example, a 100 μm sphere exposed to a fluid flow velocity of 155 $\mu\text{m/s}$ in the PEG solution = 9.28 mPa·s experiences a drag force of 1.36 nN, and larger objects correspondingly more. If the sphere is in water the drag force is approximately ten times smaller, but this can be compensated to some extent by driving the device at a higher frequency. The drag force is relevant for both the initial, lifting phase, where the force must be sufficient to overcome stiction and gravity in order to raise the object off the bottom, and the transport phase, where the drag force from the flow induced by the device 10 must be sufficient to keep it trapped. The force required to overcome gravity in the lifting phase will scale with the volume of the object (R^3), while the drag force scales with R , showing that there will be an upper limit to the size of an object that can be lifted. By the same logic, smaller objects will not present a problem, but a limit will be reached when the size of the object is similar to the thickness of the unstirred layer, at which point a small object sitting on the bottom of a container is shielded from the flow. This restriction will apply to any very thin object, but a flat plate will have the additional disadvantage that stiction forces will play a larger role than, for example, for a small sphere of the same height.

[0054] Due to the transverse magnetization, the device 10 rolls around its long axis on a surface 30, generating a vortex 60 parallel to and above the rod 10 in low Reynolds number fluidic environments. The vortex 60 and the rising flow ahead of a rolling device 10 are ideal for the non-contact picking-up and trapping of objects ranging in size from a few microns up to about 1 mm. The extended horizontal dimension of the device 10, made possible by a fabrication that uniquely defines the transverse magnetization direction, results in an extended trapping vortex 60 and, thus, enhances the transport properties compared with geometries such as spinning spheres or relatively compact rocking plates. In particular, the transported object 20 will tend to follow the device even during relatively tight turns. The rod 10 needs no special substrate or surface characteristics of the bottom surface 30, or subsurface guidance or orientation schemes, and is suitable for the manipulation of delicate specimens such as cells, micro-organisms, or fragile protein crystals. Trapped micro-objects 20 can dynamically re-align within the flow field 50, further minimizing any stress resulting from the gentle flow experienced. The geometry of the device 10 with the aspect ratio of at least 2:1 (transverse length to height/width) results in a combination of surface mobility and gentle, stable trapping of micro-objects 20 for directed transport, making the device 10 suitable for applications in fields as diverse as biological research, biomedical applications, and micro-assembly.

LIST OF REFERENCE SIGNS

10	micro-robot device	76	large side surface
11	first side cylinder	77	protection layer
12	middle cylinder	78	intermediate opening
13	second side cylinder	80	movement direction
20	movable object	85	rotation direction
30	bottom surface	90	extraction device
40	fluid environment	91	reception
50	fluid field flow vector	92	handle
60	vortex area	110	micro-robot device
70	polymer capsule	111	magnetic particles
71	end surface	210	micro-robot device
72	end surface	211	bulk magnetized magnetic material
73	large side surface		
74	large side surface		
75	large side surface		

Claims

1. An apparatus for moving a micro-object (20), comprising:

- a base (30) covered by a fluid layer (40),
 - a magnetic, flow-inducing agent (10, 110, 210) provided within the fluid layer (40) on the base (30),
 - a magnetic field generating device adapted to generate a magnetic field within the fluid layer (40), and
 - a control unit adapted to control the magnetic field generating device to change the created magnetic field to move the flow-inducing agent (10, 110, 210),
 wherein the fluid layer (40) has a thickness sufficiently large to accommodate and cover the micro-object (20) to be moved and to accommodate and cover the flow-inducing agent (10, 110, 210),
characterized in that the flow-inducing agent (10, 110, 210) is a rod having an aspect ratio of at least 2 to 1 between its length and the next smaller dimension and **in that** the rod (10, 110, 210) is magnetized perpendicular to its longest axis.

2. The apparatus according to claim 1, wherein the rod (210) comprises a bulk material, having a permanent magnetization with its magnetic axis oriented perpendicular to the longitudinal axis of rod (210).

3. The apparatus according to claim 1, wherein the rod (110) comprises a non-magnetic bulk material (70) providing its outer shape (71, 72) and including a plurality of hard magnetic particles having a permanent magnetization with its magnetic axis oriented perpendicular to the longitudinal axis of the rod (110).

4. The apparatus according to claim 1, wherein the rod (10) comprises at least one hard or soft magnetic post (11, 12, 13) oriented perpendicular to the longitudinal axis of the rod (10) and being included in a non-magnetic bulk material (70) of the rod (10) providing its outer shape (71, 72).

5. The apparatus according to any one of claims 2 to 4, wherein the magnetized parts of the rod (10, 110, 210) comprise iron and/or neodymium and/or cobalt and/or nickel compounds.

6. The apparatus according to any one of claims 1 to 5, wherein the rod (10, 110, 210) is of regular or irregular cross-section and wherein the length of the rod (10, 110, 210) in the longest dimension is between 1 micron and 1 millimeter.

7. The apparatus according to any one of claims 1 to 6, wherein the fluid layer (40) comprises a fluid system within a viscosity range of between 1 to 100 centipoise, especially in a low Reynolds number regime.

8. The apparatus according to any one of claims 1 to 7, wherein the fluid flow of the rotating rod (10, 110, 210) creates a vortex area (60) above the rotating rod (10, 110, 210) within the fluid layer (40) opposite to the base (30).

9. The apparatus according to claim 8, wherein the vortex area (60) is a roughly cylindrical vortex parallel to the long axis of the rod (10, 110, 210) and generated above essentially the entire length of the rod (10, 110, 210).

5 10. A method for moving a micro-object (20) in a fluid layer (40) on a base (30) by means of a magnetic, flow-inducing rod (10), with an apparatus according to any one of claims 1 to 9, comprising the steps of

- 10
- positioning the rod (10, 110, 210) on the base (30) in the fluid layer (40) near the micro-object (20) to be moved, wherein the orientation of the rod (10, 110, 210) is essentially parallel to the base (30) and roughly perpendicular to the main direction of the smallest distance between the object (20) to be moved and the rod (10),
 - displacing the rod (10) in direction of the object (20) to be moved through application of a changing magnetic field, while creating a fluid flow (50) generating a vortex (60) above the rod (10), and
 - displacing the object (20) through movement of the rod (10) while retaining the object in the vortex (60).

FIG. 1A

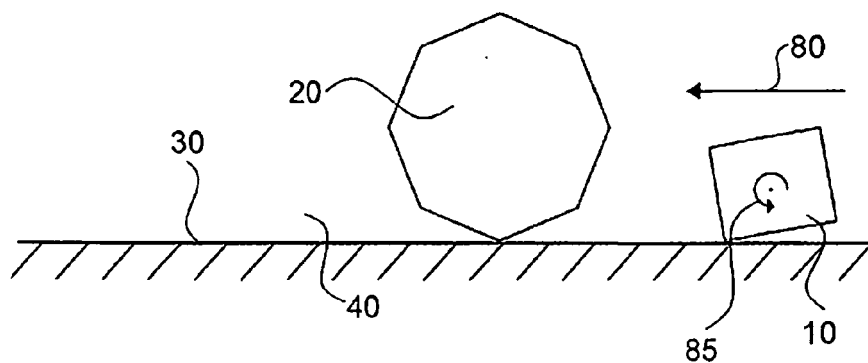


FIG. 1B

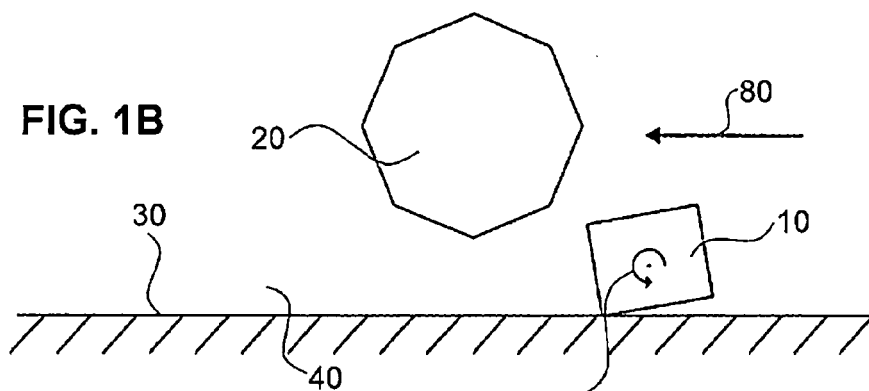


FIG. 1C

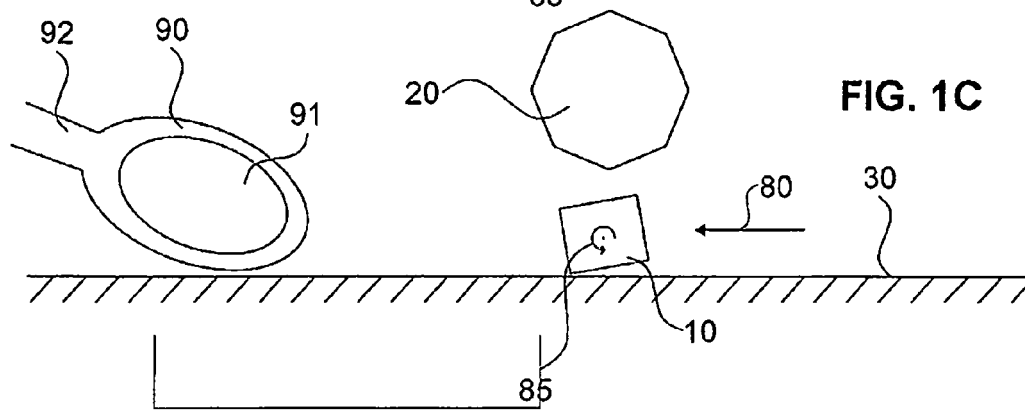
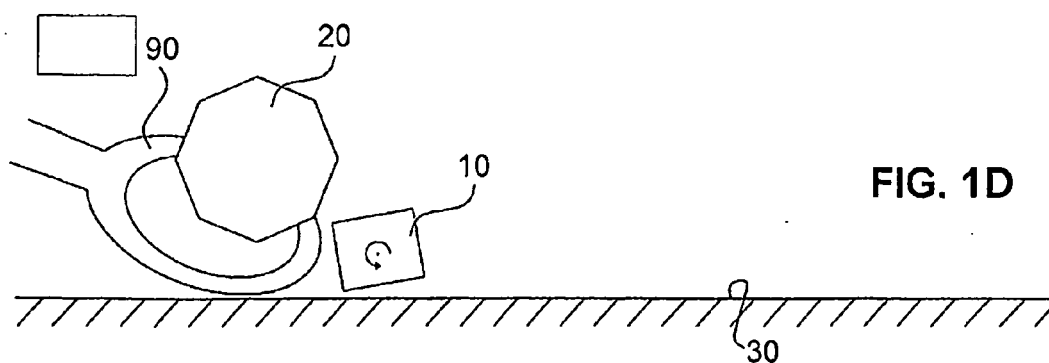
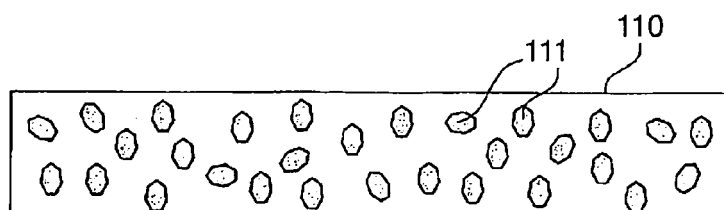
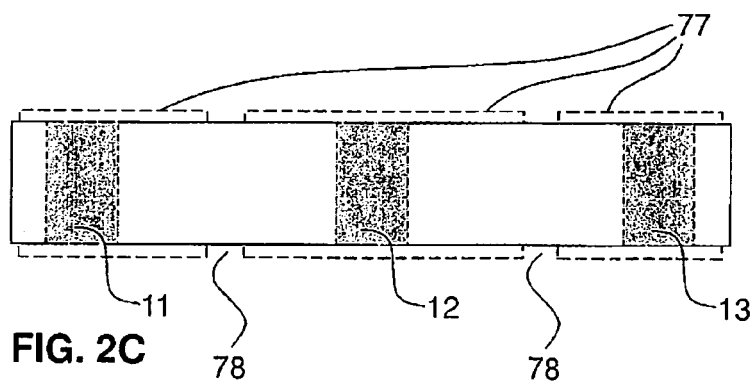
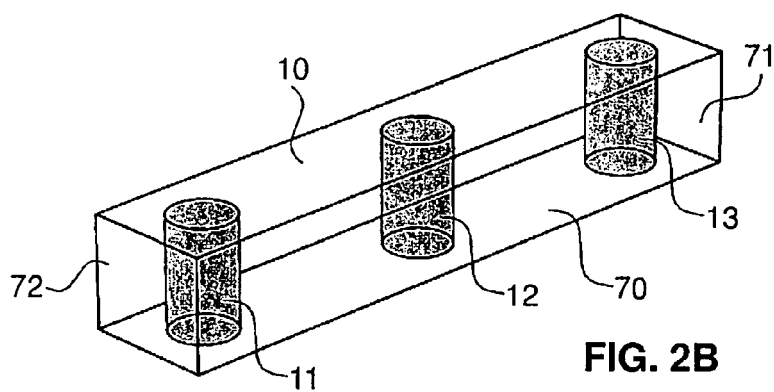
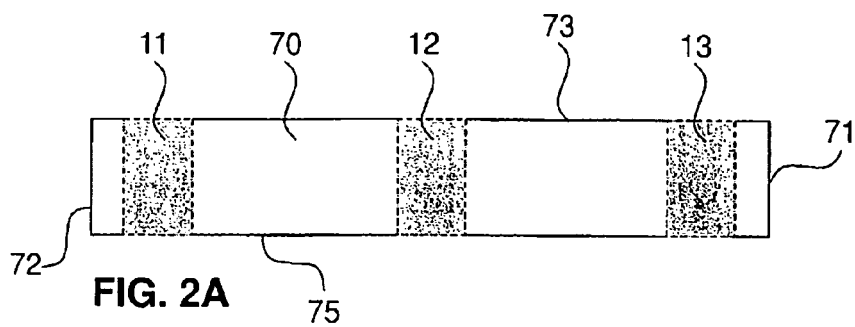


FIG. 1D





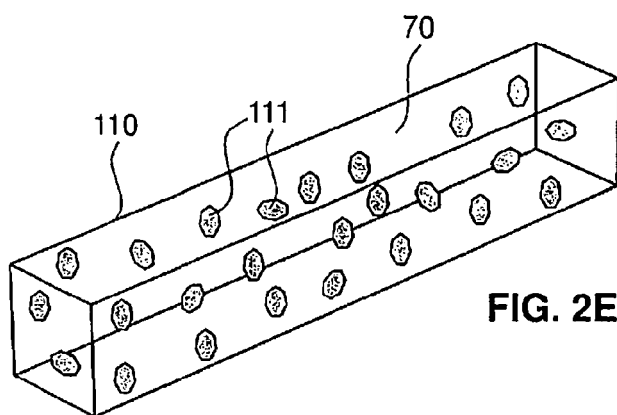


FIG. 2E

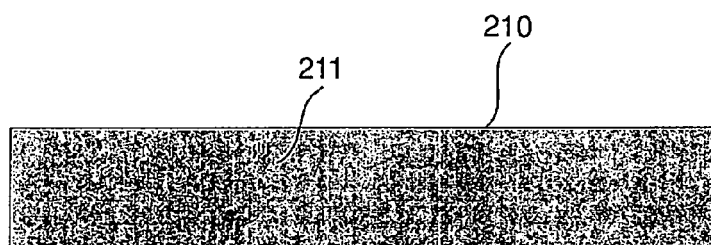


FIG. 2F

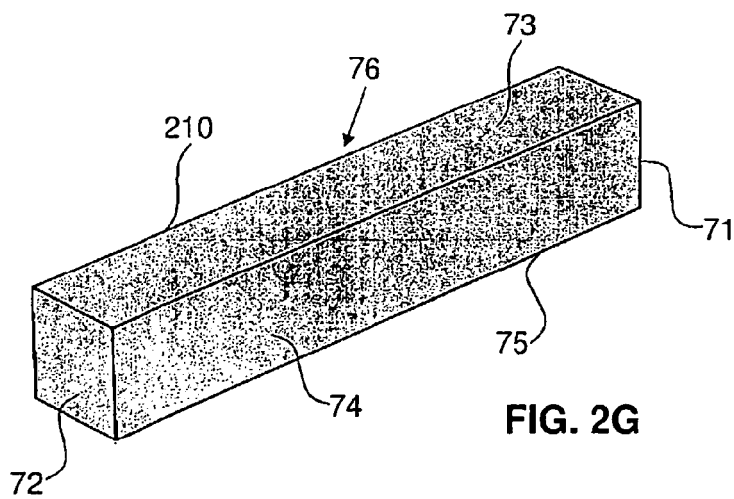
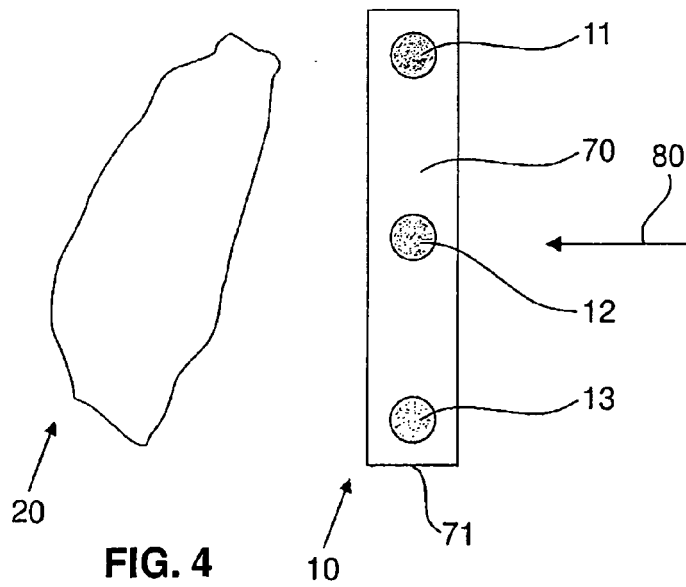
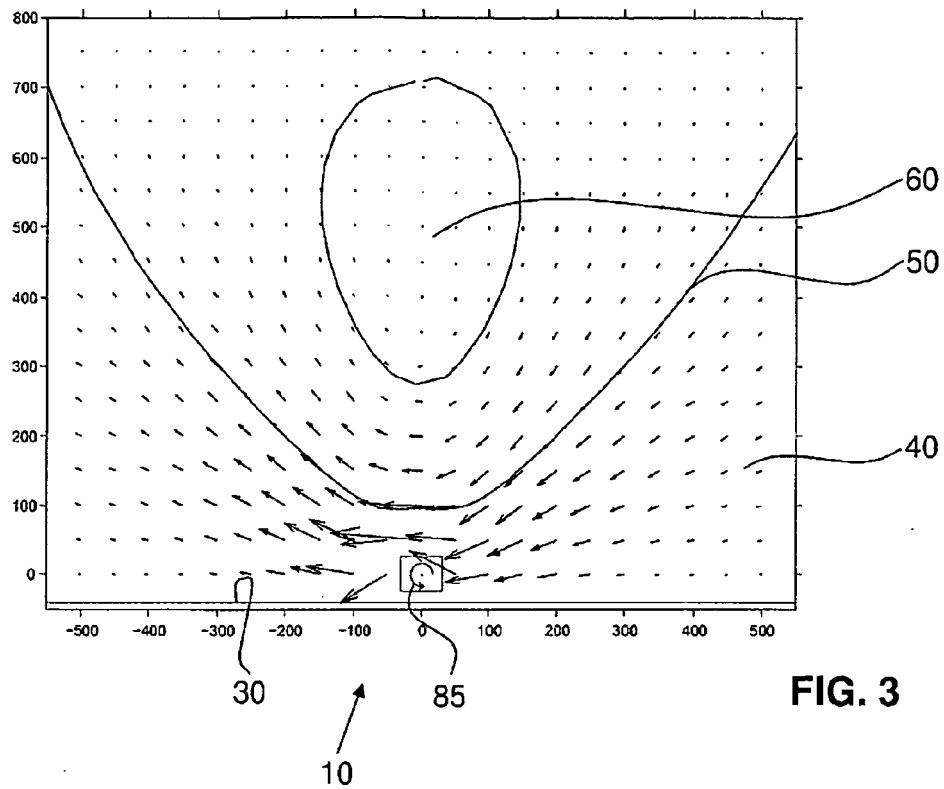


FIG. 2G





EUROPEAN SEARCH REPORT

Application Number
EP 13 00 3582

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Y	* page 1, column 1, line 3, paragraph 2 - column 2, line 15, paragraph 2 * * page 2, column 1, line 4, paragraph 1 - column 2, line 5, paragraph 2 * * page 3, column 1, line 6, paragraph 3 - line 7 *	9,10	
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Y	* paragraph [0038], [0041], [0044], [0047], [0048], [0050],; figures 10,17 *	4	
Y	TRISTAN PETIT ET AL: "Selective Trapping and Manipulation of Microscale Objects Using Mobile Microvortices", NANO LETTERS, vol. 12, no. 1, 11 January 2012 (2012-01-11), pages 156-160, XP055092021, ISSN: 1530-6984, DOI: 10.1021/nl2032487 * description of fig. 2; figure 2 *	9,10	TECHNICAL FIELDS SEARCHED (IPC) B01L
The present search report has been drawn up for all claims			
Place of search The Hague		Date of completion of the search 12 December 2013	Examiner Ueberfeld, Jörn
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention 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)



EUROPEAN SEARCH REPORT

Application Number
EP 13 00 3582

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	JIYUN KIM ET AL: "Programming magnetic anisotropy in polymeric microactuators", NATURE MATERIALS, vol. 10, no. 10, 7 August 2011 (2011-08-07), pages 747-752, XP055092653, ISSN: 1476-1122, DOI: 10.1038/nmat3090 * desription of fig. 1; figure 1 * -----	4	
			TECHNICAL FIELDS SEARCHED (IPC)
The present search report has been drawn up for all claims			
Place of search		Date of completion of the search	Examiner
The Hague		12 December 2013	Ueberfeld, Jörn
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention 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			

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12-12-2013

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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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