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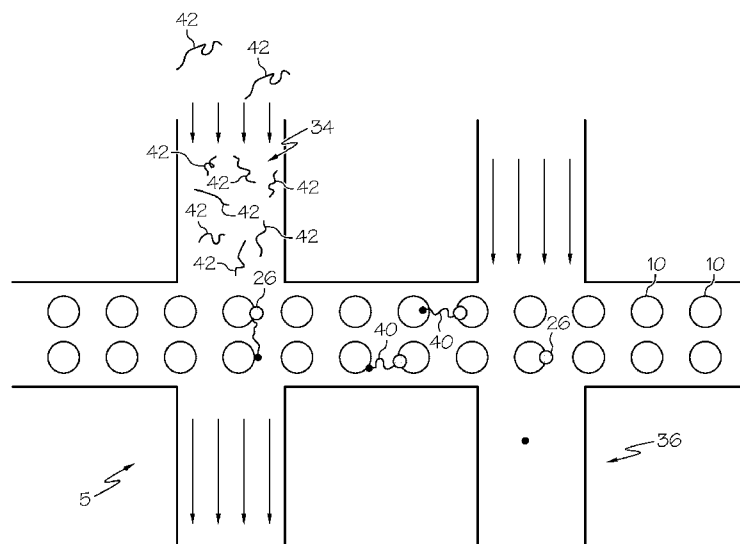


FIG. 8

(57) Abstract: A magnetic platform is provided and includes a patterned array of discrete magnetic elements positioned on a substrate, a plurality of first electromagnets for creating a first magnetic field substantially in the plane of the substrate, an electromagnetic coil for creating a second magnetic field substantially perpendicular to the plane of the substrate, and a control device for controlling the application of the magnetic fields. Processes for manipulating, transporting, separating and sorting micro- or nano-scale particles and biomolecules are also described.

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MAGNETIC PLATFORMS FOR BIOMOLECULE TRAPPINGS, MANIPULATIONS, AND SORTING

This disclosure relates to magnetic array platforms that provide trapping,
5 manipulation, and transport of individual micro- or nano-scale particles such as cells, viruses, DNA, proteins, and other biomolecules.

Historically, sorting technologies have focused on gross physical characteristics, such as particle size or density, or utilized some affinity interaction, such as receptor-ligand interactions or reactions with immunologic targets.

10 Electromagnetic response properties have also been utilized for particle sorting and characterization. For example, dielectrophoretic separators utilize non-uniform DC or AC electric fields for separation of particles. See, e.g., U.S. Pat. No. 5,814,200, Pethig et al., entitled "Apparatus for Separating By Dielectrophoresis."

Coherent light has been used to trap and manipulate particles. One of the
15 earliest workers in the field was Ashkin, U.S. Pat. No. 3,808,550 entitled "Apparatuses for Trapping and Accelerating Neutral Particles" which disclosed systems for trapping and containing particles through radiation pressure. Lasers generating coherent optical radiation were the preferred source of optical pressure.

Other particle manipulation techniques include the use of atomic force
20 microscopy (AFM) or magnetic force microscopy (MFM). An AFM uses a cantilever, sometimes with a receptor attached to the cantilever tip, to identify and manipulate a single cell or protein on a surface by stretching the cell in an out-of-plane direction. Similarly, an MFM utilizes a magnetic field to manipulate and stretch a cell or protein with a magnetic bead attached thereto in an out-of-plane direction.

25 The sorting of individual cells or micro- or nano-scale particles is an old problem, whether attempting to isolate a single cell or particle, or identifying a specific sub-population of cells or particles that behave differently or have different properties than the rest of the population. While instruments and techniques exist to enable cells or

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particles to be seen, manipulation of single cells or particles, or groups of them within a larger population, has been problematic.

As noted above, one traditional method of cell manipulation involves laser capture in which cells can be trapped using a laser beam. However, such systems are slow,
5 laser power intensive, and the process cannot be automated to isolate and manipulate large cell populations. Another traditional method, atomic force microscopy, can be used to identify and manipulate a single cell. However, it cannot be used to isolate and manipulate a population of cells.

Accordingly, the need still exists for a technique which can isolate, sort, and
10 manipulate individual biomolecules, including cells, proteins, and peptides and then can readily manipulate the biomolecules for testing, or to separate them from a heterogeneous population. Desirably, such a technique would be able to manipulate thousands or tens of thousands of biomolecules within a short period of time.

The present disclosure relates to magnetic array platforms that provide trapping,
15 manipulation, and transport of individual micro- or nano-scale particles such as cells, viruses, DNA, proteins, and other biomolecules. The term "biomolecules" as used herein encompasses all of these micro- or nano- scale particles including, but not limited to, cells, viruses, DNA, proteins, and peptides. Although the processes of the present disclosure are not limited to particular platforms or the context in which they are used, for the purposes
20 of illustration, the process steps are illustrated herein with reference to specific magnetic platforms.

In accordance with one embodiment of the present disclosure, a magnetic platform is provided and includes a patterned array of discrete magnetic elements positioned on a substrate, a plurality of first electromagnets positioned adjacent to the
25 substrate for creating a first magnetic field substantially in the plane of the substrate, and an electromagnetic coil positioned adjacent to the substrate for creating a second magnetic field substantially perpendicular to the plane of the substrate. The magnetic platform may

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also comprise a control device for controlling the application of the first and second magnetic fields.

In accordance with another embodiment, a process for manipulating a biomolecule in substantially one plane that includes providing a patterned array of discrete magnetic elements positioned on a substrate and a biomolecule having magnetic particles attached thereto. The biomolecule is trapped on the patterned array, and then manipulated by controlling the magnetic field.

In accordance with another embodiment of the present disclosure, a process for sorting biomolecules is provided and includes providing a suspension of mixed biomolecules and a magnetic platform including a patterned array of discrete magnetic elements positioned on a substrate, a plurality of first electromagnets positioned adjacent to the substrate for creating a first magnetic field substantially in the plane of the substrate, an electromagnetic coil positioned adjacent to the substrate for creating a second magnetic field substantially perpendicular to the plane of the substrate, and a control device for controlling the application of the first and second magnetic fields. Antibody-magnetic particle conjugates for a first biomolecule type are added to the suspension to couple with a first biomolecule type, and the magnetic fields are selectively controlled to cause the coupled first biomolecule type to be sorted from the cell suspension.

In accordance with another embodiment of the present disclosure, a process for separating biomolecules is provided and includes a magnetic platform that includes a patterned array of discrete magnetic elements positioned on a substrate, a plurality of first electromagnets for creating a first magnetic field, an electromagnetic coil for creating a second magnetic field and a control device for controlling the application of the first and second magnetic fields. A mixture of magnetically labeled and unlabeled biomolecules is flowed through a first fluid channel, trapping the magnetically labeled biomolecules on the magnetic platform. The magnetic fields produced by the platform to cause the magnetically labeled biomolecules to be transported from the first fluid channel to a second fluid channel. The magnetically labeled biomolecules are then detached from the platform in the second fluid channel.

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The following detailed description of specific embodiments of the present disclosure can be best understood when read in conjunction with the following drawings, where like structure is indicated with like reference numerals and in which:

Fig. 1 shows a perspective view of a magnetic platform in accordance with one
5 embodiment;

Fig. 2 is a plain view of several stages in the transport of a biomolecule on a magnetic platform as depicted in Fig. 1 in accordance with one embodiment;

Fig. 3 schematically illustrates the use of in-plane and perpendicular magnetic fields to move a magnetic particle on the magnetic platform depicted in Fig. 1 in
10 accordance with another embodiment;

Figs. 4 schematically illustrates the changing magnetic fields of the magnetic platform as depicted in Fig. 1 in accordance with one embodiment;

Fig. 5 schematically illustrates the transport of a biomolecule in conjunction with the magnetic platform of Fig. 1 in accordance with another embodiment;

Fig. 6 illustrates a process of manipulating a biomolecule in conjunction with
15 the magnetic platform depicted in Fig. 1 in accordance with yet another embodiment;

Fig. 7 illustrates a suspension disposed on the magnetic platform depicted in Fig. 1 in accordance with one embodiment; and

Fig. 8 is a plain view of a magnetic platform in conjunction with a micro fluidic
20 device in accordance with another embodiment.

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Referring to Figs. 1 and 2, a magnetic platform 5 comprises a patterned array of discrete magnetic elements positioned on a substrate 12, a plurality of first electromagnets 14 positioned adjacent to the substrate 12 for creating a first magnetic field substantially in the plane of the substrate 12, and an electromagnetic coil 16 positioned adjacent to the substrate 12 for creating a second magnetic field substantially perpendicular to the plane of the substrate 12. The magnetic platform 5 may also comprise a control device 18 for controlling the application of the first and second magnetic fields.

Magnetic fields originating from discrete micron-scale magnetic elements such as circular or elliptical disks are provided on the magnetic platform to trap and manipulate biomolecules such as cells, viruses, DNA, proteins, and other micro- or nano-scale biological material. Further details regarding the magnetic elements will be provided later in the description. As used herein, the term "biomolecule" is meant to encompass all of these micro- and macro-scale biological materials. However, it is also contemplated that the platform may be used to sort other materials and particles in addition to biomolecules.

Referring to Fig. 2, a magnetic particle 22 may be attached to a biomolecule 20 at one, or both ends of the biomolecule 20. As explained in detail below, the array of magnetic elements 10 may carry the magnetic particle 22, along with the attached biomolecule 20 towards a disk 24 for further transport and processing. Alternatively, the array of magnetic elements 10 may be arranged to transport and sort biomolecules according to a signal communicated by a control device.

Once attached, the magnetic particles 22 function as handles to transmit magnetic forces to manipulate and maneuver the biomolecules 20. The biomolecules may be attached to the magnetic particles using known chemical techniques. After attachment to the magnetic particle 22, the biomolecule 20 may be indirectly manipulated by the application of a magnetic field to cause the magnetic particle 22 to move from one magnetic element 10 to another magnetic element 10, thereby transporting the biomolecule 20 along a path defined by the array of magnetic elements 10 on the platform 5.

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Because movement of a domain wall involves reorienting the magnetization vector, a domain wall traveling in narrow channels is accompanied by the emanating magnetic field that tracks along with the wall. The associated field gradients exert magnetic forces that are sufficient to trap particles as small as 5 nm, and exert forces
5 exceeding 300 pN. Each trap therefore acts as a three-dimensional potential energy well for micro- or nano- sized objects. However, it is also contemplated that other particle sizes and forces may be utilized to capture and manipulate the particles. Domain walls and the operation of domain wall generated forces either through magnetic fields or electric currents are described in PCT Application WO 2009/143444.

10 The fabrication of an entire array of these magnetic elements provides an extended potential energy landscape. Such arrays and landscapes may be useful in manipulating microscopic objects, including but not limited to biomolecules, and organizing them into useful and interesting configurations. The use of continuous magnetic wires with spin polarized currents that are placed on the same platform as the
15 array of magnetic elements provides another framework to not only study how different particles can be maneuvered along predetermined paths, but also how they move through the landscape when driven by other forces. It is also contemplated that these arrays may be useful in studying other characteristics of materials provided in these arrays.

The design, architecture, material parameters, and structural dimensions of the
20 magnetic elements determine the specific trapping sites, domain wall profile, widths, and field gradients. Magnetic particles, with and without tethered biological entities, can be trapped at domain walls. The architecture of the magnetic elements promotes coupling of adjacent trapped particles through specific molecular links.

The magnetic elements may comprise any suitable magnetic material including,
25 but not limited to, iron oxide, cobalt, iron, nickel and other magnetic material, and combinations thereof. In one configuration, the magnetic elements comprise FeCo. Alternatively, it is also contemplated that the magnetic elements may comprise other magnetic materials suitable to transport magnetic particles across a platform.

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The magnetic particles may comprise any suitable magnetic material including, but not limited to, iron oxide, cobalt, iron, nickel and other magnetic material, and combinations thereof. In one configuration, the magnetic particles comprise FeCo.

The magnetic particles may comprise a structure selected from a group
5 consisting of a polymer particle containing a magnetic material, a non-polymeric particle containing magnetic material, and combinations thereof. In one embodiment, the magnetic particles may be in the form of polymer particles having magnetic material embedded therein. One example of such a magnetic particle is commercially available under the
10 trademark Dynabead. Alternatively, the magnetic particles may take other forms, such as having the magnetic material dispersed throughout the magnetic particle, or having the magnetic material make up a distinct portion of the magnetic particle. Non-polymeric particles are also contemplated where the magnetic material is surrounded by other compositions. Alternatively, the magnetic particle may also contain no coating material, and may comprise magnetic material. However, other configurations of magnetic particles
15 are also contemplated for use in the system and methods as disclosed herein.

Generally, external magnetic fields are provided that can continuously tune the magnetic energy landscape to enable biomolecules and other objects, on a scale as small ranging from about 5 to about 10000 nanometers in size, to be maneuvered along desired trajectories. In one aspect, the associated field gradients may exert magnetic forces
20 exceeding 100 pN. However, other field gradients are also contemplated.

Referring again to Fig. 1, in one embodiment, the external in-plane first magnetic field may be created by four orthogonally spaced electromagnets 14. Alternatively, the external in-plane magnetic field may be produced with other arrangements and orientations of magnets. A perpendicular second magnetic field may be
25 produced by an electromagnetic coil 16. However, the perpendicular magnetic field may also be provided in other fashions. The electromagnets and electromagnetic coil may be of any type suitable to create a magnetic field operable to transport a biomolecule on the platform.

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Referring to Fig. 3, by remotely switching the direction of the perpendicular second field between out-of-plane and into-plane orientations, as well as rotating the in-plane first magnetic field, the magnetic particles 22 can be moved to a specific location on the planar array. The orientation of the in-plane magnetic field is shown by arrows, while
5 the perpendicular fields are represented by circle with enclosed dot (out-of-plane) or cross (into-plane). Furthermore, it is also contemplated that other magnetic field arrangements may be useful in conjunction with the systems and methods disclosed herein.

In one configuration, the first magnetic field may have a strength ranging from about 1 to about 500 Gauss, and the second magnetic field may have a strength ranging
10 from about 1 to about 500 Gauss. The fields may also have other strengths suitable to enable the platform to sort, manipulate, and trap particles as described herein.

The magnetic elements may be provided in a variety of sizes suitable to provide the sorting and trapping functionality described herein. In one embodiment, the magnetic elements may have a length ranging from about 100 to about 10000 nanometers, and a
15 height ranging from about 10 to about 500 nanometers. The magnetic elements may also have a length ranging from about 100 to about 1000 nanometers, and height ranging from about 20 to about 200 nanometers. However, other lengths and widths of the magnetic elements are also contemplated for use with the magnetic platform disclosed herein.

The magnetic elements may have a shape selected from the group consisting of
20 circular disks, elliptical disks, oval disks, and wires. Alternatively, it is also contemplated that the magnetic elements may take other forms and shapes suitable to transport and orient biomolecules on a magnetic platform. In one configuration, the magnetic elements may be elliptically shaped disks having an aspect ratio of about 3:1. However, other aspect ratios and shapes are also contemplated. Depending on the shape of the magnetic
25 elements, their magnetization will align such that they act like tiny bar magnets or develop regions of different magnetizations that are separated by magnetic domain walls. By manipulating the external magnetic fields, the configuration of the array and shapes of the magnetic elements, biomolecules can be trapped and transported to a desired location.

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Referring to Fig. 4, in addition to ellipses, the magnetic elements 10 may have a circular shape. The circularly shaped elements 10 may trap magnetic particles 22, and then transport them around their edge by rotating the magnetic field. At desired locations on the circumference of the magnetic element, the magnetic particles 22 with attached
5 biomolecule can be induced to jump to the next magnetic element 10 by manipulating the magnetic fields.

Referring again to Fig. 2, by "patterned array," we mean an interconnected system of at least two such magnetic elements 10 positioned adjacent to one another. An example would be an array of elliptical disks such that the spacing between the adjacent
10 disks in the array varies. Using lithography techniques, arrays of magnetic elements 10 are created with nano-scale precision that enable well-defined planar assemblies of micron- or nano-scale magnetic elements 10 to be created such that biomolecules 20 attached to magnetic particles 22 may be trapped and manipulated on and along the surface of such arrays. In one embodiment, the long axis of each magnetic element is oriented at a right
15 angle to the adjacent magnetic element's long axis. Alternatively, the magnetic elements 10 may be oriented in other ways, such as at a substantially right angles to one another, or even in an orientation roughly 45° in respect to the adjacent magnetic element 10. It is also contemplated that the patterned array of magnetic elements may be arranged in other patterns suitable to sort and transport biomolecules and other particles across the platform
20 5.

The distance between the magnetic elements in the patterned array may vary depending on the size of the biomolecules, the strength of the magnetic fields, and many other factors. In one configuration, the distance between the magnetic elements ranges from about 100 to about 10000 nanometers. However, it is also contemplated that the
25 distance between the magnetic elements may be any distance suitable to provide transport to the biomolecules across the substrate.

As will be understood, the design and architecture of the patterned arrays enable different trapping site configurations to be fabricated. This permits the fabrication of two-dimensional magnetic platforms having different layouts for trapping micro- and nano-

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sized magnetic particles at specific locations. Such magnetic platforms enable the study of individual molecules, the interactions between large molecules, and the response of such molecules to external stimuli.

Referring to Fig. 2, the magnetic elements 10 may be provided on the substrate 12 using photolithography techniques that involve coating a substrate 12 with a layer of electron beam resistive material, writing the desired pattern using electron beam lithography, and sputtering a thin film of magnetic material onto a substrate 12. The lithography, in conjunction with known developing processes, can also remove the resistive material thus enabling the magnetic elements 10 to be sputtered on to the substrate 12 to create the desired pattern or array. The patterns may be chosen based on results from a simulation program which models the magnetic domains in thin films in the presence of external magnetic fields. The substrate may comprise silicon, silica oxide-based glass, metal oxide, polymer, or combinations thereof. The film may have a thickness ranging from about 10 to about 1000 nm. The lithographic creation of the arrays allows the architecture of the magnetic platform to be designed and fabricated with spatial resolutions determined by present nano-scale fabrication techniques. One example of a suitable simulation program is provided by Donahue, M. J., and D. G. Porter. See 1999 OOMMF User's Guide, Version 1.0, Interagency Report NISTIR 6376, National Institute of Standards and Technology, Gaithersburg, MD. This public code can be found at the URL <http://math.nist.gov/oommf/>.

Referring again to Fig. 1, a control device 18 may be provided for controlling the application of the first and second magnetic fields. In one embodiment, the control device 18 comprises a voltage controller and a current controller, electrically connected to the plurality of first electromagnets 14 and the electromagnetic coil 16. The voltage controller may regulate the voltage transmitted to the magnets and coil to ensure that the desired voltage is provided to each of the magnets and coil. In addition, the current controller may regulate the amount of current supplied to the electromagnets and coil to ensure the desired transport and movement on the platform 5. The control device 18 may be a joystick, where manipulation of the joystick corresponds to movement of the

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magnetic particles, achieved through programming of a software application.

Alternatively, the control device 18 may be a range of other devices suitable to direct the magnetic fields on the platform 5 to effect the transport and sorting of a biomolecule, such as voice-activated controls. The control device may be programmed using software such as LabView, or other software systems.

In one embodiment, digital signals from the joystick are transmitted to the digital inputs on a data acquisition card of a computer. The signals from the data acquisition card may be read by LabVIEW routines which then interpret what magnetic field should be transmitted based on the signals from the control device to effect the desired movement or sorting. The signals may operate at a range of voltages, ranging from about 0 to about 5 volts. However, other voltages are also contemplated for use. A LabVIEW routine may also calculate the necessary voltage required to control the movement of the particle based on input from the control device. The voltage signals may be amplified before driving current through the electromagnets and the coil. Alternatively, other systems may be used to control the interaction between the control device and the current and voltage supplied to the plurality of electromagnets and coils.

The in-plane electromagnets may be operated at a voltage range from about 0 to about 20 volts. The current supplied to the in-plane electromagnets may range from about 0 to about 500 mA. The power supplied to the in-plane electromagnets ranges from about 0 to about 10 Watts. However, other power and current ranges are also contemplated for use with the methods disclosed herein.

The out-of-plane electromagnets may be operated at a range of voltages ranging from about 0 to about 3.6 volts. The current supplied to the out-of-plane electromagnets may range from about 0 to about 5 A. The power supplied to the out-of-plane electromagnets ranges from about 0 to about 18 Watts. However, other power and current ranges are also contemplated for use with the methods disclosed herein.

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Referring to Fig. 4, in one embodiment, magnetic particles 22 are attracted to the magnetic elements 10 through the magnetic field associated with each magnetic element 10. In response to the rotating in-plane magnetic field, the magnetization of each magnetic element 10 changes the orientation of the field, causing the magnetic particle 22 with biomolecule attached to become trapped and transported along the circumference of the magnetic element 10. Upon reaching the vicinity of a neighboring magnetic element 10, the magnetic particles 22 “jump” from one magnetic element 10 to the neighboring magnetic element 10. The direction of rotation of the external magnetic field may be reversed to change the direction of magnetic particle 22 movement. Eventually, as shown in Fig. 2, a magnetic particle 22 may be loaded onto a desired circular disk 24 that is at the end of the patterned array for further transport and processing. The magnetic particles 22 may be attached to a biomolecule in a variety of manners, including attaching at the end of the biomolecule, attaching at a median point on the biomolecule, and at other portions of the biomolecule as well.

Referring to Fig. 5, in one example, a biomolecule 20 may be a single human T-lymphocyte cell. The cell may be attached to a magnetic particle 22. In this example, the magnetic elements were 5 μ m diameter disks spaced apart at 5 μ m intervals. Previously separated T cells (CD3 positive) from human blood cells were attached to magnetic particles 22 using known chemical techniques. The magnetic particles 22 and attached biomolecules 20 were transported across the platform 5 via the magnetic elements 10. The molecules were then transported to the continuous wire on which it could be maneuvered by a magnetic field or electric current.

Referring to Fig. 6, in another embodiment, the magnetic platform may be used as a device resembling a pair of magnetic tweezers. In one configuration, two circular disks 24 of different diameters may be provided on the platform 5 adjacent to one another. Magnetic particles 22 may be attached to opposite sides of a biomolecule 20 in the manner described above. The loaded magnetic particles 22 may be attached to the disks 24 through magnetic attraction. The biomolecule 20 may be stretched by rotating the disks 24 in opposite directions by applying the magnetic fields. The trapped biomolecule 20

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may then be transformed back to its original shape by reversing the current flow, thereby compressing the biomolecule 20. More generally, the magnetic particles 22 may act as handles for the biomolecule 20, allowing the object to be compressed, twisted, and manipulated in other ways. It is also contemplated that the magnetic particles may be
5 attached to other objects to provide a platform for manipulation of the objects. The magnetic platform configuration described permits real-time observations of single or multiple molecules or other small objects trapped and controllably manipulated in a two-dimensional environment.

Referring to Fig. 7, in yet another embodiment, the magnetic platform 5 allows
10 magnetically labeled cells to be separated and sorted from unlabeled cells. In one configuration, a suspension 30 of a cell mixture may be provided on the magnetic platform 5. The suspension 30 may comprise a wide range of compositions and consistencies, containing numerous cell types. An appropriate amount of first anti-body magnetic particle conjugates 26 may be introduced to the suspension 30 of cells that target a first
15 cell type of interest. These conjugates may selectively bond to the first cell type by known bonding techniques in order to provide a magnetic component to the target cells. The magnetic elements 10 may be activated using magnetic fields to transport the magnetically labeled particles to one side of the magnetic platform 5, and a plurality the zigzag shaped wires 32 in the manner described above. The wires 32 may then be magnetically activated
20 to transport the cells along the wires 32 and away from the suspension 30 for further transport and processing.

Once all of the first antibody-magnetic particle conjugates 26 are removed, a second anti-body magnetic particle conjugate (not shown) may be provided targeting the next cell type of interest. The process may be repeated as many times as desired to
25 separate cell types of interest from the cell suspension 30.

Referring to Fig. 8, in another embodiment, the magnetic platform 5 may be used in conjunction with a micro fluidic device. The micro fluidic device may comprise an array of discrete magnetic elements 10. In one aspect, a mixture of magnetically labeled biomolecules 40 and unlabeled biomolecules 42 are flowed through a first fluid channel

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34. Alternatively, any number of biomolecule types may be provided in the first fluid channel. The magnetically labeled biomolecules 40 are attached to the magnetic particles 22 and are trapped on magnetic elements 10.

The magnetic fields produced by the magnetic platform may be selectively
5 controlled by a control device to cause the magnetically labeled biomolecules to be transported from the first fluid channel 34 to the second fluid channel 36 along the array of magnetic elements 10. In one configuration, selectively controlling the magnetic field may include switching the direction of the second magnetic field between out of plane and in-plane orientations, and rotating the first magnetic field. However, it is also contemplated
10 that there are other means of selectively controlling the magnetic fields that may be used in order to transport a magnetic particle 22 or a biomolecule 20 across a micro fluidic device.

After relocation to the second fluid channel 36, the magnetically labeled biomolecules 40 are detached from the magnetic elements 10 on the platform 5 in the
15 second fluid channel 36 by for example, chemical means, such as use of suitable enzymes. It is contemplated that the process may be repeated in multiple iterations in order to sort a mixture of biomolecules 20 comprising more than two biomolecule types, by magnetically labeling one group of biomolecules 20 and sorting them into a fluid channel, and then labeling an additional group of biomolecules 20, and sorting them into an additional fluid
20 channel, until all types of biomolecules 20 are sorted as desired. Although two fluid channels are shown, it is understood that a plurality of fluid channels may be used to suit the requirements of the sorting process, and sort larger or more diverse groups of biomolecules.

The availability of mobile magnetic traps as described herein offers new control
25 that is needed for rapid progress in several branches of science and engineering. In particular, the femto- to pico-Newton scale forces linked to the methods and devices described herein are ideally suited for probing single microparticles and biomolecules 20 ranging from the about 10 to about 10000 nm length scales. In physics and chemistry, the methods and devices described herein can provide an understanding of nanoclusters in the

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transition region between single molecule and microscopic structures where puzzling challenges remain. In biology, the methods and devices described herein can be used to study many vital inter- and intra-cellular processes. Nanoscale engineering will benefit from the options provided by the described methods and devices for organizing,
5 manipulating, and analyzing individual tiny objects. The tunable magnetic trap arrays and methods of use as described herein meet these needs.

Industrial applications which rely on transporting magnetic nanoparticles cover a broad spectrum. The methods and devices described herein have utility in micro fluidic devices to manipulate fluid-borne entities inside a network of microscopic channels for
10 clinical diagnosis, forensic applications, and environmental analysis. Specifically, the mobile magnetic traps, used in conjunction with micro fluidics channels can be used to separate cells and/or particles of interest from a variety of fluids including blood, plasma, or other body fluids as well as water or other fluid samples. Embodiments of the present invention may also find use in portable devices for environmental and medical analysis.

15 It is also noted that recitations herein of “at least one” component, element, etc., should not be used to create an inference that the alternative use of the articles “a” or “an” should be limited to a single component, element, etc.

It is noted that recitations herein of a component of the present disclosure being “programmed” in a particular way, “configured” or “programmed” to embody a particular
20 property, or function in a particular manner, are structural recitations, as opposed to recitations of intended use. More specifically, the references herein to the manner in which a component is “programmed” or “configured” denotes an existing physical condition of the component and, as such, is to be taken as a definite recitation of the structural characteristics of the component.

25 For the purposes of describing and defining the present invention it is noted that the terms “substantially” and “approximately” are utilized herein to represent the inherent degree of uncertainty that may be attributed to any quantitative comparison, value, measurement, or other representation. The terms “substantially” and “approximately” are

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also utilized herein to represent the degree by which a quantitative representation may vary from a stated reference without resulting in a change in the basic function of the subject matter at issue.

Having described the subject matter of the present disclosure in detail and by
5 reference to specific embodiments thereof, it is noted that the various details disclosed herein should not be taken to imply that these details relate to elements that are essential components of the various embodiments described herein, even in cases where a particular element is illustrated in each of the drawings that accompany the present description. Rather, the claims appended hereto should be taken as the sole representation of the
10 breadth of the present disclosure and the corresponding scope of the various inventions described herein. Further, it will be apparent that modifications and variations are possible without departing from the scope of the invention defined in the appended claims. More specifically, although some aspects of the present disclosure are identified herein as preferred or particularly advantageous, it is contemplated that the present disclosure is not
15 necessarily limited to these aspects.

It is noted that one or more of the following claims utilize the term “wherein” as a transitional phrase. For the purposes of defining the present invention, it is noted that this term is introduced in the claims as an open-ended transitional phrase that is used to introduce a recitation of a series of characteristics of the structure and should be
20 interpreted in like manner as the more commonly used open-ended preamble term “comprising.”

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CLAIMS

1. A magnetic platform comprising:
 - a patterned array of discrete magnetic elements positioned on a substrate;
 - 5 a plurality of first electromagnets positioned adjacent to the substrate for creating a first magnetic field substantially in the plane of said substrate;
 - an electromagnetic coil positioned adjacent to the substrate for creating a second magnetic field substantially perpendicular to the plane of said substrate; and
 - a control device for controlling the application of said first and second magnetic
 - 10 fields.
2. The magnetic platform of claim 1, wherein the magnetic elements have a length ranging from about 100 to about 10000 nanometers, and a height ranging from about 10 to about 500 nanometers.
- 15 3. The magnetic platform of claim 1, wherein the distance between the magnetic elements ranges from about 100 to about 10000 nanometers.
4. The magnetic platform of claim 1, wherein the magnetic elements are oriented at
- 20 substantially 90° angles to the long axis of the adjacent magnetic element.
5. The magnetic platform of claim 1, wherein the magnetic elements are selected from the group consisting of circular disks, elliptical disks, and oval disks.
- 25 6. The magnetic platform of claim 1, wherein the magnetic elements comprise elliptically-shaped disks having an aspect ratio of about 3:1.
7. The magnetic platform of claim 1, wherein the substrate comprises silicon, silica oxide-based glass, metal oxide, polymers, or combinations thereof.

30

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8. The magnetic platform of claim 1, wherein the first magnetic field has a strength ranging from about 1 to about 500 Gauss, and the second magnetic field has a strength ranging from about 1 to about 500 Gauss.

5

9. The magnetic platform of claim 1, wherein the control device comprises a voltage controller and a current controller, wherein the voltage controller and the current controller are electrically connected to the plurality of first electromagnets, and the electromagnetic coil.

10

10. The magnetic platform of claim 1, wherein the control device is a joystick.

11. A process for manipulating a biomolecule in substantially one plane comprising:
providing a patterned array of discrete magnetic elements positioned on a substrate;
15 providing a biomolecule having magnetic particles attached thereto;
trapping said biomolecule on said patterned array; and
manipulating said biomolecule by controlling a magnetic field in the plane of said
patterned array.

20 12. The process of claim 11, wherein the magnetic particles comprise a structure selected from a group consisting of a polymer particle containing a magnetic material, a non-polymeric particle containing magnetic material, and combinations thereof.

13. The process of claim 11, wherein the magnetic particles have a diameter ranging from
25 about 10 to about 10000 nm.

14. The process of claim 11, wherein manipulating the biomolecule comprises stretching, compressing, or twisting.

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15. The process of claim 11, further wherein manipulating said biomolecule further comprises providing two disks;
attaching said magnetic particles to opposite ends of the biomolecule;
attaching said magnetic particles to each of said disks; and
5 manipulating the biomolecule by rotating said disks in opposite directions.

16. A process for sorting biomolecules comprising:
providing a suspension of mixed biomolecules;
providing a magnetic platform comprising:
10 a patterned array of discrete magnetic elements positioned on a substrate,
a plurality of first electromagnets positioned adjacent to the substrate for creating a first magnetic field substantially in the plane of said substrate,
an electromagnetic coil positioned adjacent to the substrate for creating a second magnetic field substantially perpendicular to the plane of said substrate, and
15 a control device for controlling the application of said first and second magnetic fields;

adding antibody-magnetic particle conjugates for a first biomolecule type to said suspension to couple with said first biomolecule type;
selectively controlling the magnetic fields produced by said platform to cause said coupled
20 first biomolecule type to be sorted from said cell suspension.

17. The process of claim 16, wherein selectively controlling the magnetic field comprises switching the direction of the second magnetic field between out of plane and in-plane orientations, and rotating the first magnetic field.
25

18. A process for separating biomolecules comprising:
providing a magnetic platform comprising:
a patterned array of discrete magnetic elements positioned on a substrate;
a plurality of first electromagnets for creating a first magnetic field substantially in
30 the plane of said substrate;

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an electromagnetic coil for creating a second magnetic field substantially perpendicular to the plane of said substrate; and
a control device for controlling the application of said first and second magnetic fields;

- 5 flowing a mixture of magnetically labeled and unlabeled biomolecules through a first fluid channel;
trapping said magnetically labeled biomolecules on said magnetic platform;
selectively controlling the magnetic fields produced by said platform to cause said magnetically labeled biomolecules to be transported from said first fluid channel to a
10 second fluid channel; and
detaching said magnetically labeled biomolecules from said platform in said second fluid channel.

19. The process of claim 18, wherein the control device comprises a joystick.
15

20. The process of claim 18, wherein selectively controlling the magnetic field comprises switching the direction of the second magnetic field between out of plane and in-plane orientations, and rotating the first magnetic field.

20

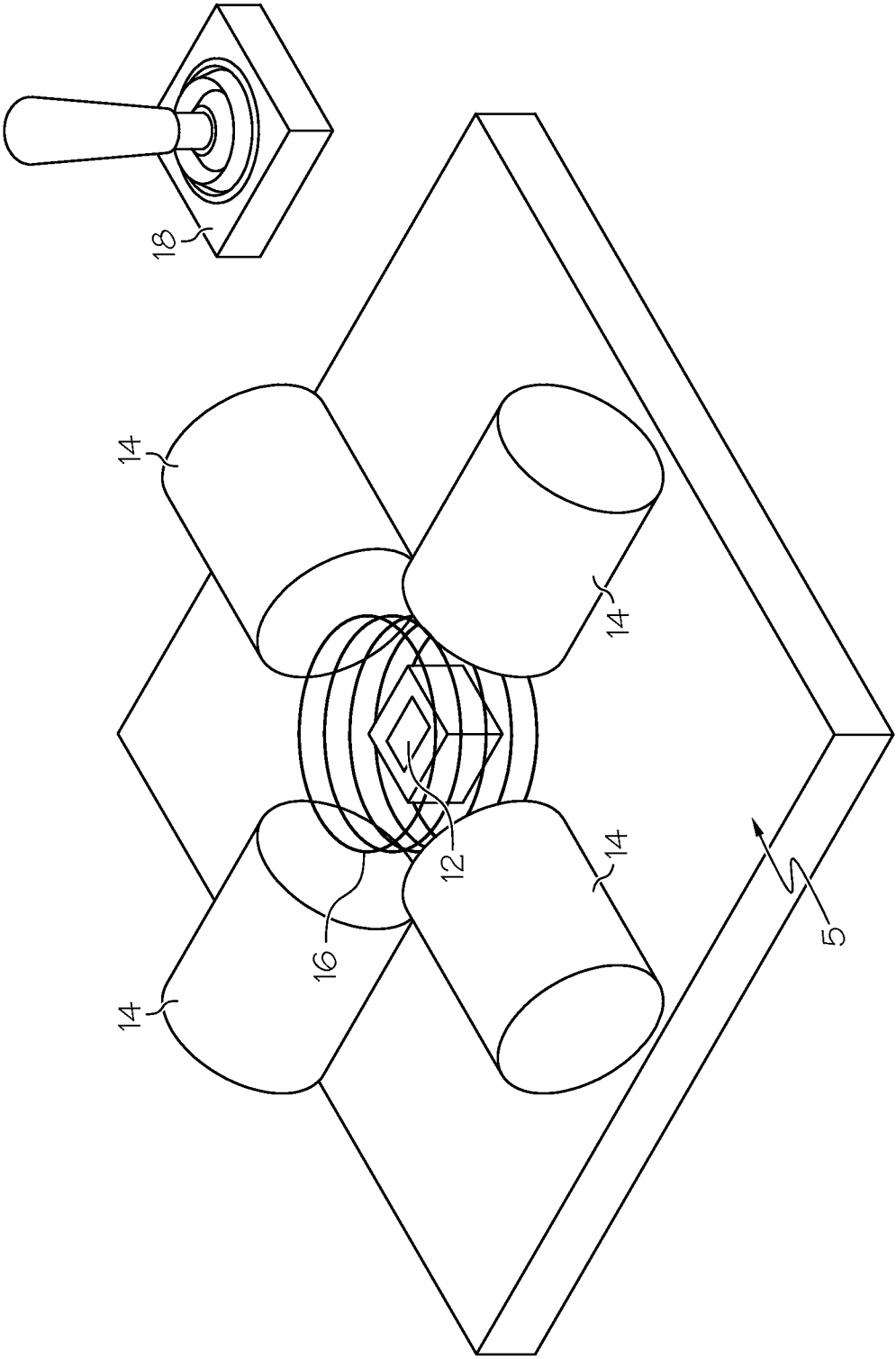


FIG. 1

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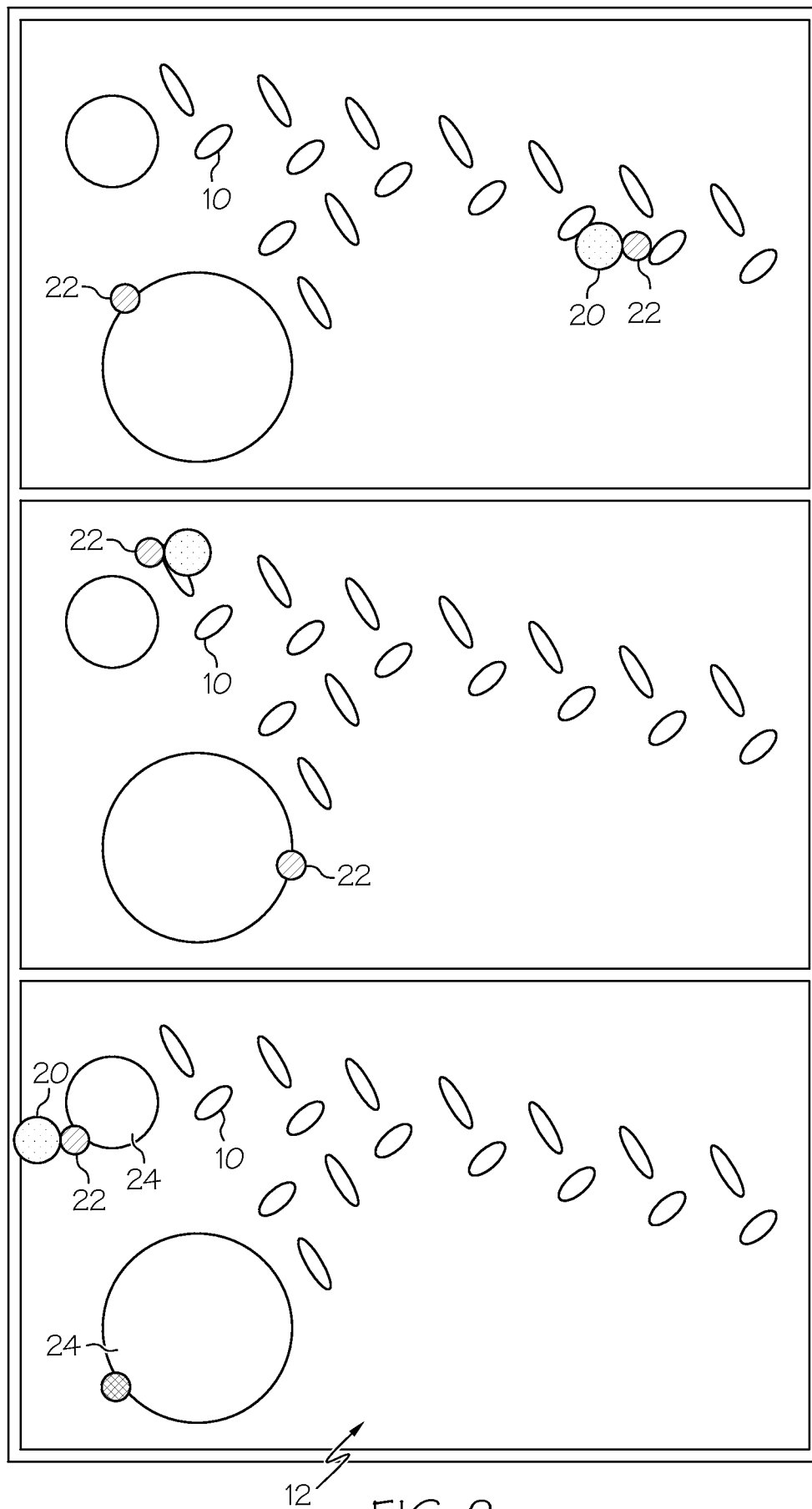


FIG. 2

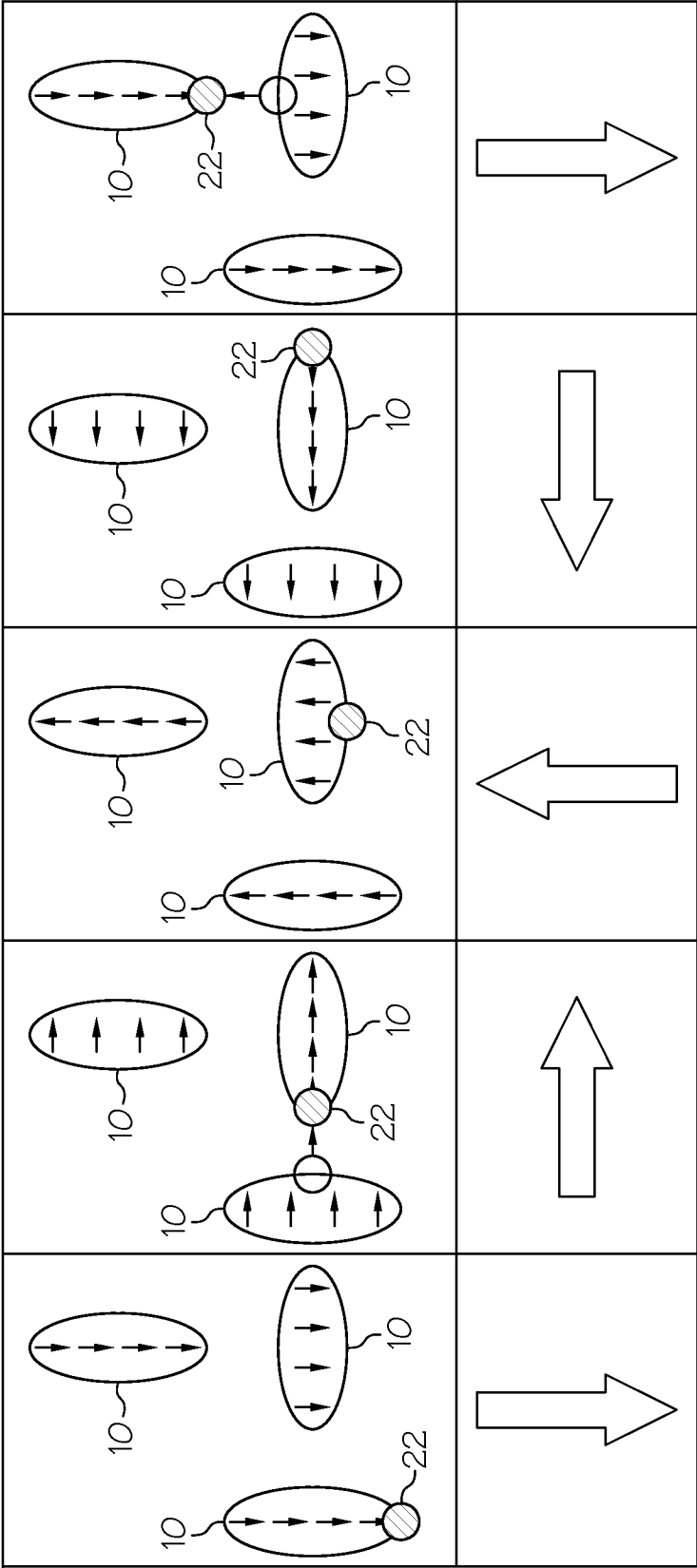


FIG. 3

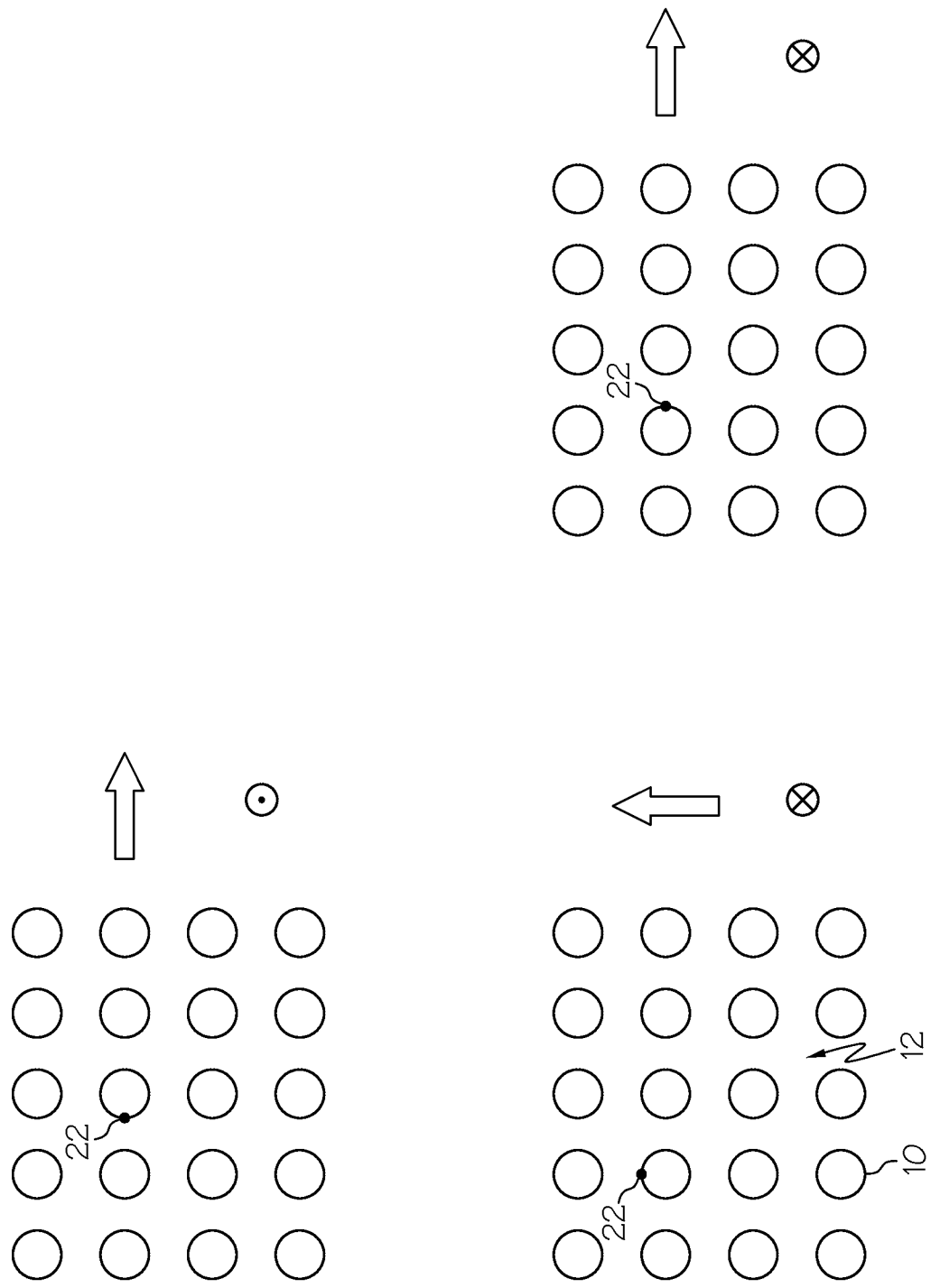
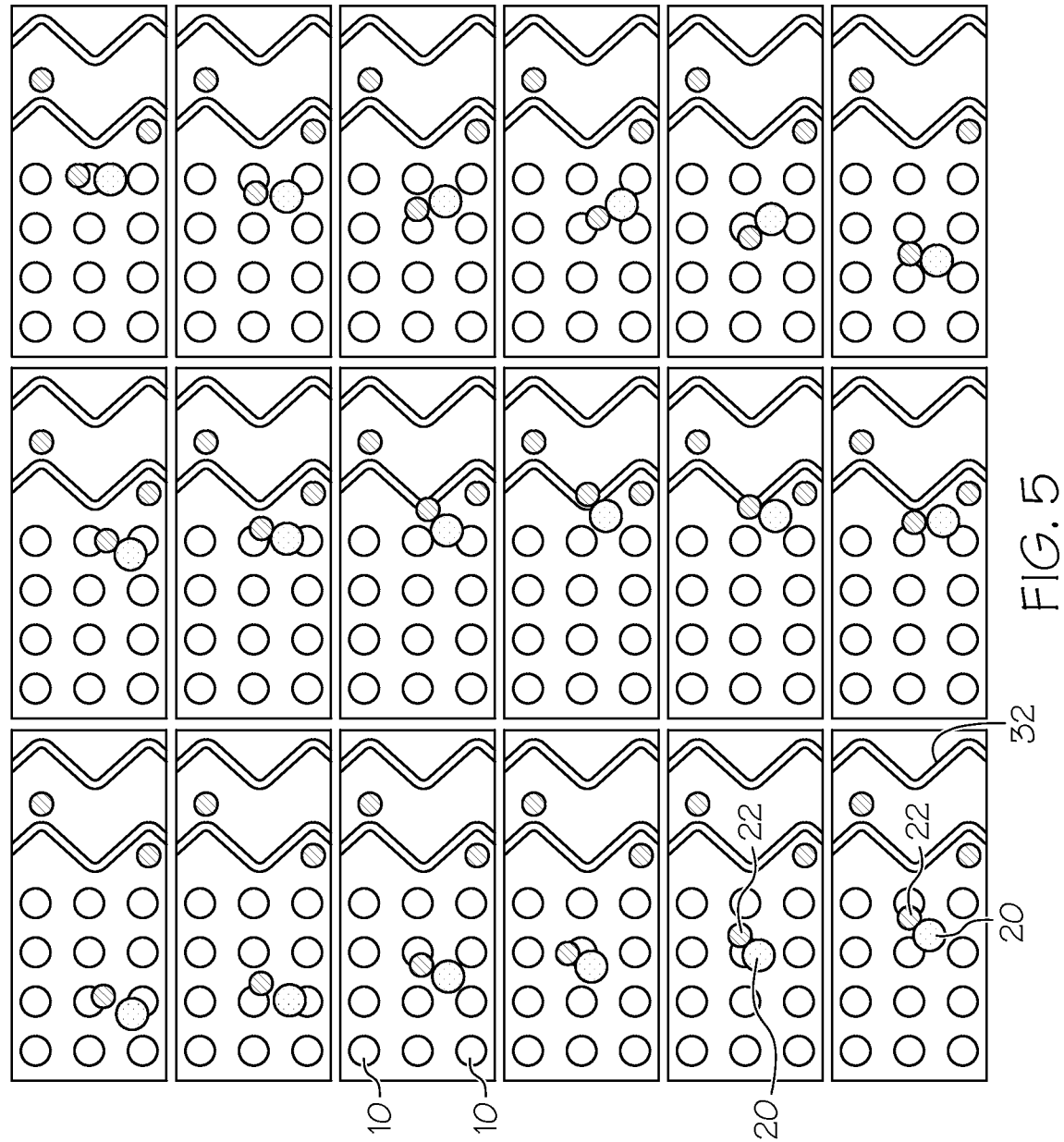


FIG. 4



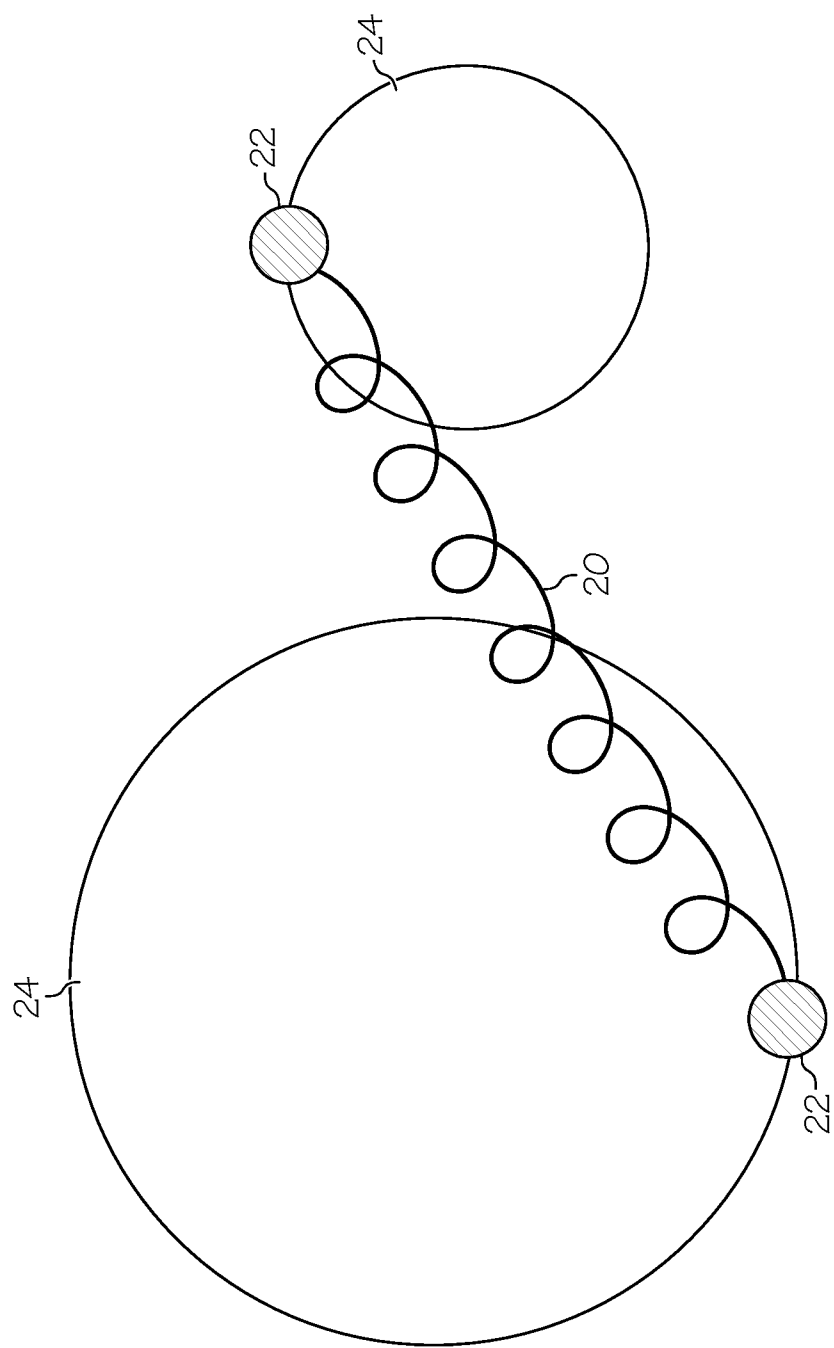


FIG. 6

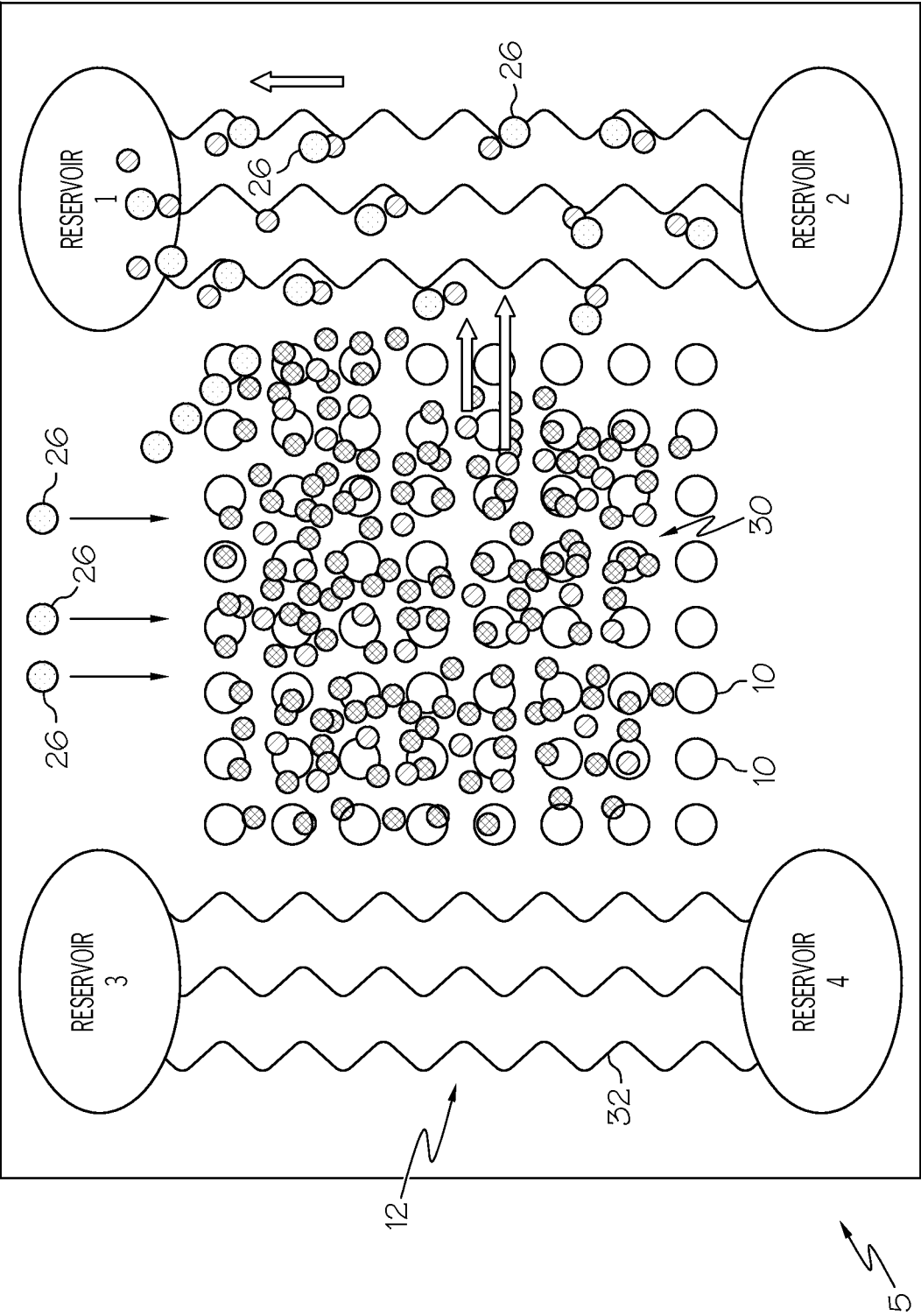


FIG. 7

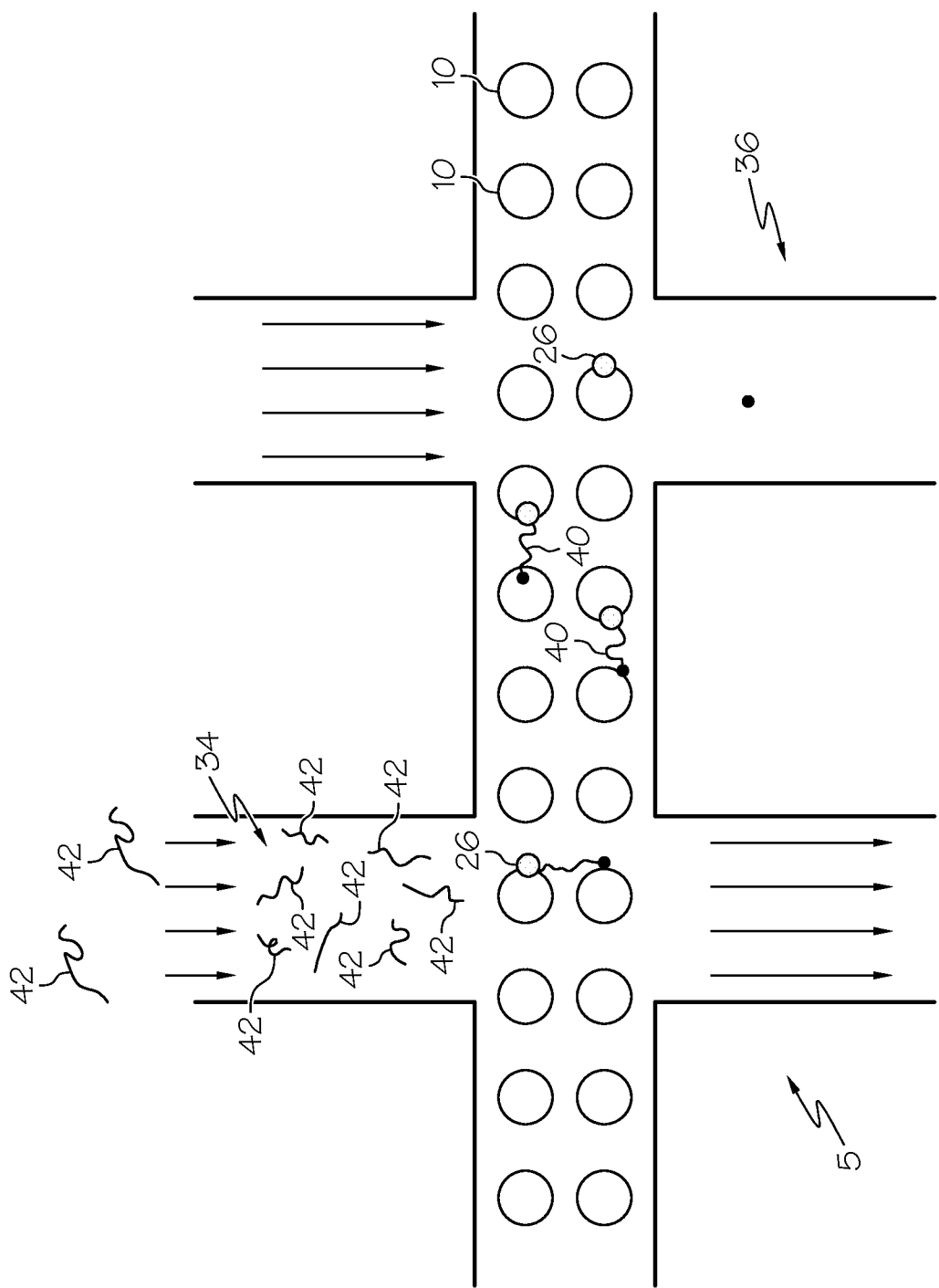


FIG. 8

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 10/23472

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - G01N 33/53 (2010.01)

USPC - 436/526; 422/50; 436/524

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

USPC: 436/526; 422/50; 436/524

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

USPC: 436/526; 422/50; 436/524 (text search)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

PubWEST (PGPB,USPT,EPAB,JPAB), Google Scholar, DialogWEB

Search terms used: magnetic platform, magnetic elements, electromagnet, coil, biomolecule, DNA, virus, protein, cell, joystick, substrate, silicon, silica, glass, polymer

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 2007/0141728 A1 (MORELAND et al.) 21 June 2007 (21.06.2007), para [0001], [0019]-[0022], [0027]-[0032], [0043], [0052]-[0055], [0061], [0064]-[0067], [0078]; Fig 8A-8C.	11, 12, 14 ----- 1-10, 13, 15-20
Y	US 2008/0176762 A1 (HEROLD et al.) 24 July 2008 (24.07.2008), para [0067], [0069], [0090]-[0091], [0098], [0148]	1-10, 16-20
Y	US 2004/0262210 A1 (WESTERVELT et al.) 30 December 2004 (30.12.2004), para [0145], [0155]	4, 13
Y	US 2007/0182517 A1 (HUMPHRIES et al.) 09 August 2007 (09.08.2007), para [0244]-[0246]	15
Y	US 2006/0073540 A1 (MARTEL) 06 April 2006 (06.04.2006), para [0051]-[0055]	10, 19
Y	US 2008/0124779 A1 (OH et al.) 29 May 2008 (29.05.2008), para [0005], [0012], [0014], [0015], [0034], [0038], [0120]	16-20



Further documents are listed in the continuation of Box C.



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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

16 March 2010 (16.03.2010)

Date of mailing of the international search report

29 MAR 2010

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450

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