Magnetic micro-devices for separation and manipulation of biological components

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When magnetic particles become trapped on the surface of the coil (on top of the insulating dielectric layer) the resultant coil inductance can be written as:

$$L = L_0 + \Delta L \quad (5.20)$$

where L is the overall inductance, L_0 is the coil inductance in the absence of any magnetic beads, and ΔL is the change of inductance due to the bead trapping.

The coil inductance is related the coil geometry and permeability and, according to eq. 5.19, increasing the total volume of magnetic beads on the surface of the device leads to an increase in the overall permeability and therefore, increases the coil inductance with ΔL .

Assuming the coil's surface is completely covered by a single layer of magnetic bead, the total magnetic reluctance of the magnetic circuit can be given as (Fig. 5.24b). The reluctance is defined as

$$\mathfrak{R} = \frac{l}{\mu A} \quad (5.21)$$

where l is the length of the path and A is the area. The definition of the reluctance in a magnetic circuit is analogous to the definition of the electrical resistance in a electric circuit. In the same manner, the resultant magnetomotive force (mmf) is analogous to the driving voltage in an electric circuit:

$$mmf = \mathfrak{R}\Phi \quad (5.22)$$

with Φ the magnetic flux generated by the magnetic circuit, similar to the electric current in an electric circuit. The total reluctance in the magnetic circuit shown in Fig. 5.24b is

$$\mathfrak{R} = \mathfrak{R}_b + \mathfrak{R}_d + \mathfrak{R}_s \quad (5.23)$$

where b , d , and s subscripts refer to the magnetic beads, the dielectric layer, and the silicon substrate, respectively.

5.5 Summary

This chapter showed that inserting a magnetic pillar within a planar micro-coil structure enhances the magnetic energy density gradient at the pillar surface and focuses/confines the magnetic flux as well. Furthermore, inserting a magnetic backside plate beneath the micro-coil confines the magnetic flux and closes the magnetic circuit which results in a further enhancing of the magnetic energy density gradient. The combination of a micro-coil, magnetic pillar and backside plate results in an excellent magnetic source system for magnetic particle manipulation on the micro-scale as will be shown in the next two chapters.

CHAPTER 6

FABRICATION OF THE DEVICES

6.1 Introduction

This chapter describes and discusses the fabrication methodology used to realize the devices studied in this dissertation. A novel MEMS fabrication methodology will be presented which is based on existing processes that were adapted from the IC technology. This methodology relies on creating high aspect ratio trenches in silicon substrate, filling them with a high conductivity metal (Cu). This is followed by planarization of the surface to form the micro-coil winding and finally the magnetic pillars are added using the electroless plating. In the beginning, a brief literature review of magnetic devices and of their fabrication techniques will be given. A brief presentation of the microelectronic processing fundamentals and a technical description of the processes employed in the realization of the devices described in this dissertation will be given. The fabrication issues associated with different steps will be discussed in details.

Before describing the fabrication process of the novel devices, the results obtained on simple test chips will be presented first. These test chips were fabricated in order to investigate the influence of certain geometrical shapes on the device performance and to measure the magnetic field generated by these devices.

The majority of MEMS transducers have been electrostatically driven due to their ease of fabrication and integration with other micro components. On the other hand, the fabrication of magnetically actuated transducers has generally been avoided due to the lack of processing knowledge and the difficulty of integrating magnetic components with other microsystems and circuits. In spite of the poor scaling of magnetic forces, presently there is a growing interest in magnetic micro-devices, mainly due to their

inherent unique advantages, among which is the ability of realizing magnetic-based actuators that can generate large magnetic forces.

Magnetic micro-actuators and sensors have been fabricated for many years and, until now, they were realized simply as scaled-down versions of their macroscopic counterparts, such as electromagnetic motors, magnetometers and sensors. Their electromagnetic interaction is mainly due to the use of external micro-coils or micro-permanent magnets. It is well known, however, that it is a challenging, time consuming and expensive task to construct micro-coils using classical methods, or to hand-machine large pieces of permanent magnetic materials into micro-permanent magnets, for the purposes of constructing micro-devices. The fabrication of micro-coils, in particular, poses critical problems, because the coils are three-dimensional and micro-fabrication is typically two-dimensional. The present devices not only eliminate these problems, but also integrate ferromagnetic materials into their structure. In doing so, these devices benefit from the advantages of silicon micro-machining technologies, well known in the integrated circuit (IC) industry.

In order to make use of and benefit from silicon (Si) based IC technology in the fabrication of micro-magnetic devices, the problems related to usable materials must be solved. Additionally, consideration must be given both to the Joule heating that occurs when injecting large currents into highly resistive structures and to the compatibility of bulk magnetic materials with micro-scale processing. In an initial approach to the fabrication of the devices described in the previous chapter original solutions were found for two important constitutive elements used in the structure of our devices:

- (1) Highly conductive materials, such as Cu, which are needed to withstand the large currents required to produce significant magnetic fluxes, are employed in forming a planar micro-coil that is embedded in the Si-micromachined structures; and

- (2) A magnetic core made of soft (low coercivity) magnetic materials, such as CoNiP alloys, is used to play the role of a classical magnetic core. In this case, however, the pillar is realized using electroless plating, in order to be compatible with semiconductor fabrication techniques and to obtain the desired structure at the micro-scales.

Magnetic micro-devices have found major use in Hall devices and thin film heads for magnetic discs. Recent development goes in the direction of dense thin-film magnetic heads, high-performance magnetographic printing heads, inductors, micro motors and various kinds of actuators. A common goal for magnetic micro-actuator applications is that the highest possible energy density must be achieved by the smallest possible input energy. This can be achieved by enhancing the magnetic properties of the materials used in the device.

The fundamental components of any electromagnetic device are the coil and the core. The coils which can be used for generating magnetic fields are of two types, planar and three-dimensional. Planar coils are generally shaped either as a spiral (square or circular coil of decreasing dimension) or as a meander (convoluted windings generally in the form of repeated loops). In the case of planar micro-coils, standard IC technology can be used and a current can be injected to produce an appropriate magnetic flux. In the case of three-dimensional micro-coils, however, a more advanced fabrication process is required, employing technologies such as wafer bonding and through-via connections. Because all coils, planar or three-dimensional, macroscopic or microscopic, are current-driven devices and since the maximum injected current is limited by Joule heating, the coil resistance must be minimized. To do this, it is desirable to construct coils of large cross-sectional area, short length and made of the highest conductivity material available within the fabrication process.

Most of the planar micro-coils mentioned in the literature have been fabricated by depositing the conductor material (e.g, a metal) as a thick film on top of a Si surface. These planar micro-coils can be formed with or without a core. For example, spiral inductors have been fabricated for the analysis of small volume biological samples using NMR microscopy [146]. The micro-coils used in this case were formed by depositing a Cu seed layer on a Ti adhesion layer, on an oxidized Si substrate. A thick layer of photoresist was then spun on the Ti/Cu layers and patterned to form a spiral mold. Cu was electroplated into the mold and the photoresist and Cu seed layer were subsequently removed to insulate the wires. Using a similar method, a planar micro-coil for implantable Microsystems has been fabricated [147].

The previous methods of realizing micro-coils have many disadvantages, such as: the thickness of the conductor is determined by the photoresist; and the final micro-coil has a non-planar upper surface, which can adversely affect subsequent processing steps and integration of additional components.

An electromagnetic optical switch has been fabricated for optical network communication [148]. The system consisted of a planar micro-coil and a NiFe permalloy film on a vibrating suspension diaphragm. The planar micro-coil generated the magnetic force which produced the diaphragm displacement. The system was realized using many complicated fabrication processes, including electroplating, bulk micromachining, excimer laser ablation and wafer bonding. The coil did not have a magnetic core, which resulted in significant flux leakage.

A Semi-Encapsulated Spiral Inductor has been fabricated on pyrex a glass wafer which is later bonded to a Si wafer [149]. The multi-step process included the following steps:

- (a) Seed layer deposition on the pyrex substrate;

- (b) Photolithography to form an electroplating mold using a first mask;
- (c) Copper coil electroplating;
- (d) Resist and seed layer removal;
- (e) Via patterns formation using a second photolithography process;
- (f) High temperature curing;
- (g) Seed layer evaporation;

(h) Top magnetic layer and via patterning using a third patterning process. It is obvious that this process requires several stages of photoresist and photolithography, which places stringent requirements on many related factors, such as surface planarization.

Photoresist is also used as a patterning, insulating and planarizing material in the fabrication of planar micro-coils [150]. The process involves forming a first patterned photoresist layer within which to electroplate a magnetic layer. Next, a second patterned photoresist layer is formed as an insulating/planarizing/support layer over the magnetic layer. Finally, a coil is formed by electroplating into the patterned second photoresist layer. In some specific applications, the resulting planar micro-coil was sandwiched between two layers of magnetic material, which shield the coil and restrict the magnetic field produced by the coil to the region between the layers.

The design of these types of micro-coils suffers from several limitations, the most severe being the photolithographic processes required to form high aspect-ratio electroplating molds from the photoresist layers. The photoresist insulation layer between the micro-coils must also fulfill many requirements, including photostructureability, ability to support vias for interconnections between different micro-coil layers, the capability to supply sufficiently planarizable surfaces so that successive layers can be formed and precisely photolithographed, and good dielectric

properties (e.g, low dielectric constant and high breakdown voltage). Finally, the micro-coils formed by such methods have sizes on the order of millimeters, which limits their ability to produce the desired magnetic field gradients.

Recent research has also focused on the fabrication of 3-dimensional micro-coils. For example, a toroidal-meander type integrated inductor with a multilevel meander magnetic core, was formed on a silicon wafer using multi-level metal interconnect schemes [151]. Its complex 6-step fabrication process involved

- (a) Polyimide deposition on a Si wafer;
- (b) Plasma etching of a plating mold through the polyamide using an Al mask;
- (c) Plating a lower magnetic core into the mold;
- (d) Deposition and patterning of a conductor about the core;
- (e) Plating vias;

(f) Plating an upper core onto the lower core to form the meander. The final inductor size was 4 mm x 1 mm, with 30 turns and the magnetic core material was electroplated $\text{Ni}_{81}\text{Fe}_{19}$, producing an inductance of 30 nH/mm^2 at 5 MHz.

Another 3-dimensional air-core micro-coil has been fabricated by using the deformation of a sacrificial thick polymer and electrodeposition [152]. The authors describe the formation of an inductor coil by first forming patterned electroplated planar bottom conductor pieces, then connecting the bottom conductor pieces with an upper curved conductor formed by electroplating conductor pieces on a supporting convex surface. The bell-shaped convex surface is formed by curing a positive photoresist originally deposited in a rectangular mesa formation. The deformed photoresist support core is then stripped away, leaving a completed coil with an air core. The large number of vias required to interconnect all the coil sections dramatically increases the coil

resistance, limits the magnitude of the current that can be injected and, therefore, limits the maximum achievable magnetic flux density.

Another study reports the fabrication of a solenoidal 3D micromagnetic manipulator [153]. A 25 micron copper wire is wound around a 50 micron diameter soft-magnetic wire. The resulting solenoid was used to manipulate micro-magnetic particles. The performance of such a fabrication is limited both by the number of turns that can be wound around the magnetic core and the feasibility of integrating the fabrication with other microcomponents.

More recently, a toroidal-shape inductor was fabricated on a printed circuit board (PCB) [154]. A toroidally wound coil was formed by passing conducting leads through both dielectric layers by means of vias, so that the ferromagnetic layer became the core of the coil. Primary and secondary coils were formed in this way. Another problem that needs to be considered is that the nature of the PCB may not permit the device to operate at high current densities. An additional problem arises from the fact that the ferromagnetic material forming the core is nickel deposited by electroplating or electroless plating. The use of various chemical agents in the nickel's plating process introduces phosphorus in the final layer which can adversely affect its magnetic saturation, as will be discussed later.

As can be seen from all the above cited references, several severe limitations and disadvantages are found in prior art structures and fabrication methods, which can be summarized as follows:

1. The dimensions of the fabricated devices allow that to produce only limited magnetic field gradients and, in consequence, limited magnetic forces.
2. The designs are basically scaled-down versions of macroscopic designs and, as such, require complicated fabrication processes.

3. The problems associated with the complicated designs and process steps also result in uneven surfaces, which is a disadvantage when subsequent process steps are required.
4. None of the prior methods are able to efficiently generate high magnetic field gradients along with planarized surfaces compatible with the integration of additional circuitry and components on the same chip.

6.2 The first test-fabricated device

6.2.1 Fabrication

In the initial stage simple planar micro-coils were realized for the necessary preliminary tests and magnetic field measurements. These coils were fabricated using the most conventional fabrication process and made of Al. The details of this study which we followed in this preliminary stage are published elsewhere [155].

Three micro-electromagnet meander designs were investigated, all of them realized with the same single mask fabrication technology, as will be shown later. Fig.6.2 shows a schematic view of the three types of investigated meander-shaped micro-electromagnets topologies: serpentine (EM1), mesh (EM2) and rosette (EM3), respectively. In EM1 the conductor is looped back and forth to create a series of parallel conductor segments through which the current flows in alternating directions (Fig.6.1a).

In EM2 the current flows in small current semi-loops made of three-conductor segments, the cascaded array of these loops forming the mesh-shaped micro-electromagnet (Fig.6.1b). The third type, EM3, is similar to EM1, only that instead of having a linear configuration it is applied along a circular circumference of inner radius r (Fig.6.1c). The conductors in EM3 are no longer parallel to each other as they converge towards the center of the rosette circumference. This arrangement reduces the area of the device compared to EM1 and was investigated to study the enhancement

achievable in the magnetic field and field gradient through an increase in the conductor density in a small spatial location.

Fig. 6.2a briefly illustrates the fabrication process. A 2 μm layer of silicon dioxide was deposited on a silicon substrate, then a 2 μm Al film was deposited using Physical Vapor Deposition (PVD), followed by photoresist coating, exposure and patterning. The coil conductors had the width and the spacing of 10 μm each. After Al etching the photoresist was removed to form the micro-electromagnet lines. Active micro-electromagnets areas of 0.45, 0.44, and 0.36 mm^2 and DC resistance values of 64, 22, and 39 Ω were obtained for the EM1, EM2 and EM3 micro-electromagnets, respectively. The layout designs of these microelectromagnets can be easily implemented since they require only one metal layer patterned in different configurations rather than two metal layers, as in the case of a spiral micro-electromagnet. Fig.6.2b shows microphotographs of the realized micro-electromagnets.

6.2.2 Magnetic field measurements (SQUID)

Scanning SQUID microscopes provide a powerful means to measure weak magnetic fields. It has the advantage of high sensitivity ($0.1 \text{ nT Hz}^{-1/2}$) but exhibit only a relatively modest spatial resolution ($\sim 10 \mu\text{m}$). The principle operation of the scanning SQUID microscope is described in detail elsewhere [156]. The planar microelectromagnet sample has been mounted under the SQUID sensor at the minimum allowable distance (250 μm) and a current was injected in it by a constant current source via two wire leads. DC currents in the range of 4 – 6 mA were applied to each sample and the magnetic fields were scanned at the separation distance of 250 μm between the sample and the SQUID sensor. The values of the injected DC current and the separation distance are the variable parameters that can be adjusted in order to perform the measurements in a proper way, i.e., to reduce the noise and to avoid the damage of the

(a) EM1

(b) EM2

(c) EM3

Figure 6.1: Schematic drawings of the designed microelectromagnets: (a) straight-conductors meander, (b) Mesh-shaped meander, and (c) Rosette-shaped meander of internal radius r .

Figure 6.2: (a) Fabrication process of the micro-electromagnet; (b) Photographs of the realized devices.

SQUID sensor. However, the relation between the intensity of the generated magnetic field and the injected current is linear and, on the other hand, the dependence of the magnetic field magnitude on the vertical distance is exponential, respectively. Consequently, other values of the magnetic fields at different currents and distances can be extracted based on the measured values. Indeed, as is shown in the next section, our practical tests were carried out at much higher currents between 50 – 400mA and employing and employing channels of less depth than the SQUID measurement height.

The separation distance between the sample and the sensor is relatively large in the SQUID microscope, which affects the spatial resolution and in consequence the magnetic field distribution images. Nevertheless, the SQUID magnetic field images obtained for different applied currents show the magnetic field density, with higher values being generated by the mesh-shaped electromagnet (EM2) than by the other types.

Fig.6.3 shows 3D representations of the magnetic field density distributions (in Tesla) in the xy -plane for the three types of coil designs. The current used for this scan was 6 mA and the average scanning distance was 250 μm . The dependence of the magnetic field generated by the second type of micro-electromagnets (EM2) on the applied electric current is shown in Fig.6.4. As was mentioned previously, the magnetic flux density tends to reduce in the central region of the meandering coils due to the cancellation of the fields generated by alternate conductors from either sides. This cancellation is clearly visible in the SQUID results shown in Fig. 6.3, where the magnetic flux density profile is at its lowest at the center. The non-symmetry of the B profile at the front and rear sides of each image is due to the bonding pads which have large dimensions (50 x 50 μm^2), compared to the coil conductor width (10 μm).

Figure 6.3: 3D representation of the B field distribution across the xy -plane, at a separation distance of $250 \mu\text{m}$ and for an injected DC current of $3 \times 10^8 \text{ A/m}^2$ in: (a) EM1, (b) EM2, and (c) EM3 micro-electromagnets, respectively.

Figure 6.4: Magnetic field vs electric current at a fixed separation distance of 250 μm between the micro-electromagnet and the SQUID sensor for the EM2 micro-electromagnet showing a nearly linear relation.

The large separation distance between the SQUID sensor and the micro-electromagnet surface does not allow high resolution mapping of the magnetic field. However, the measured values of the magnetic field B_0 at a distance of 250 μm from the surface of the micro-electromagnet, which agree well with the simulation results, can be used to estimate the magnetic field at any distance z from the surface using the relation $B = B_0 e^{-kz}$. Fig.6.5 shows the theoretical (analytical calculations), simulated and measured values of the magnetic flux density profiles at a distance of 250 μm from the surface, for each micro-electromagnet type, respectively.

6.2.3 Devices Testing results & discussion

Experiments to test the capability of the planar micro-electromagnets to trap magnetic beads were conducted using superparamagnetic particles (Dynal beads & Estapor magnetic microspheres) with diameters of 2.8 and 1 μm , respectively, in an aqueous solution. A drop of liquid (approximately 2 μl) with magnetic beads (at an estimated concentration of $1 \cdot 10^6$ beads/ml) was injected directly on the surface of the electromagnet. Current was supplied to the micro-electromagnet from a DC power supply within the range of 50 to 400 mA. To trap magnetic particles a magnetic force of $\sim 10^{-12}$ Newton is required and to generate this force using a planar micro-electromagnet a DC current of $\sim 200\text{--}300$ mA is required. However, for such a correct intensity, since our test coils are made of only a thin Al layer significant Joule heating was present during the measurements and testing. To partially overcome this problem a heat sink was used to cool down the silicon chip. It should be noted that the fabricated chip in this study were realized only to study the effect of different geometries on the magnetic field and field gradient. New types of coils with a much larger cross-section were implemented (as will be presented in the next section) and their design took into account the optimization

(a) EM1

(b) EM2

(c) EM3

Figure 6.5: Magnetic flux densities along a line located 250 μm above the surface of 3 types of planar micro-electromagnets, for an injected current density $J = 3 \times 10^8 \text{ A/m}^2$. (For clarification of the exact topology of each micro-coil, see again Fig. 6.2).

results of this study to realize a complete magnetic device for magnetic particle manipulation

Real time tracking of the beads motion and trapping was performed using an optical microscope and a CCD camera. Fig. 6.6 shows the magnetic beads trapped under the effect of the magnetic force on top of various types of micro-electromagnets. Beads tend to form chains oriented along the magnetic field due to the dipole-dipole interaction after applying the power but they re-suspend in the fluid after removing the magnetic field.

However, as previously mentioned the micro-coils fabricated by this simple method (with Al as the material of the coils) suffered from severe Joule heating during the experiments and a large value of current intensity was required to generate the magnetic field and force to achieve the bead trapping. The geometry of the coil's conductor (i.e., a low aspect ratio height/width) does not encourage the generation of high magnetic field gradient which is a major factor in determining the device performance.

Figs.6.3 and 6.5 show clearly that EM2 generates the strongest magnetic field and field gradient among the three meander micro-electromagnet types, due to the summation of the three magnetic field components produced by the three conductor segments contained in its geometry. Because of its structural simplicity (only a single metal layer with no vias required), relatively large magnetic field which can be generated, and its ease of integration in a microfluidic channel, this design is the most suitable for usage as an actuation tool in our targeted application, i.e., for beads trapping in a magnetic-based biomolecular separation system. Nevertheless, much stronger fields and field gradients (and hence a drastically improved performance) can be obtained with the improved design which is presented in the subsequent section. However, the EM2

Figure 6.6: Micro-graphs of magnetic beads with 4.5 μm diameter trapped on top of various types of planar microelectromagnets at an injected current of 300 mA.

micro-coil still can be attractive choice if no complex microelectronic processing is available, i.e., when the user must realize a very simple, and/or a low cost device.

In a microfabricated planar electromagnet the maximum current is limited by Joule heating and electromigration; hence the coil geometry and its layout optimization become the most significant factors in determining the magnetic field strength. Within the various types of meander micro-electromagnets the mesh-shaped design EM2 generates the highest magnetic field due to its looping profile which strengthens the z -component of B and is a good candidate for usage in simple microfluidic devices since it needs only one metal layer and thus has simpler processing sequence than the spiral coil.

Reducing the spacing between conductors (or the loop radius for the rosette design) results in increasing the magnitude of the generated magnetic field. Similarly, increasing the cross-sectional area of the conductor (by electroplating a thick metal film and increasing the conductor width) allows higher electrical current injection which results in a stronger magnetic field. At the same time, reducing one conductor dimension results in increasing the magnetic field gradient along a direction perpendicular to the reduced side.

In conclusion, the magnetic system for magnetic bead trapping and transporting should satisfy the following conditions and requirements:

1. The ability to generate large magnetic field gradients;
2. The ability to manipulate the magnetic field/force over a certain surface area;
3. The ability to focus and concentrate the magnetic energy or the magnetic flux on a small spatial location (small spot);
4. The ability to detect the magnetic particle trapping

Therefore, in order to fully meet these requirements, new and more complex magnetic systems are proposed and realized as discussed in Chapters 3, 4, 5 and shown in this Chapter.

6.3 Improved design and novel structure

The techniques described in literature and shown in the previous sub-section all enable the realization of 3D-like or actual 3D micro-coils, but at the expense of a very complex fabrication process that may not be compatible with existing CMOS standards. Furthermore, the realization of a micro-coil with very thick conductors is extremely inconvenient, due to more reasons:

- Firstly, the very thick conductor metal would hamper the realization of the similarly thick magnetic pillar. In order to deposit this pillar a much more complicated processing sequence has to be used;
- Secondly, if photoresist (PR) is used as a mould for electroplating and kept in place to offer a more planar surface suitable for subsequent processing steps, then the efficient dissipation of heat from the coil conductor through the polymer may not be optimal. If, however, the PR is removed, this may create problems due to the extremely non-planar surface with very high steps, so that very little processing can be done after the PR removal. This demands other modifications in the fabrication sequence if more processing has to be executed after the PR is removed.

Due to all these reasons, we have adopted an original fabrication approach which would eliminate all these disadvantages. Namely, instead of erecting the conductor upwards, we first etch deep ($\sim 10\text{ }\mu\text{m}$) trenches in the Si substrate, which are then filled with copper. The copper is then planarized and automatically patterned using CMP, like in a standard damascene process, followed by the deposition of a protective PECVD

oxide layer. At this moment, a fully planar Si surface allows an easy processing of any other component, e.g., depositing the soft magnetic material for the pillar using electroless plating. Moreover, because the Cu is now embedded in the Si substrate (which is a very good heat conductor), heat dissipation is now significantly eased.

There would be only three disadvantages:

- Consumption of Si: being realized by etching in the substrate itself, the coil needs obviously to be placed in regions where no electronic devices are *a priori* present in Si;
- Heat dissipation in the coil area, and
- Disturbance of correct microelectronic device operation by the strong magnetic fields generated.

All these drawbacks demand that the micro-coil(s) should be placed far away from any signal processing circuits or similar ICs. However, they are not very strong disadvantages. Clearly, they are not significant for the present microfluidic realization, and would need to be considered only when the micro-coils would be applied in high frequency RF chips. Nevertheless, even in this case these disadvantages would not be a major obstacle for their useful usage for such purposes. In this respect, the micro-coils could be considered extremely similar to the semiconductor high-power transistors: these also can dissipate large amounts of heat and therefore need to be placed not only far from the sensitive ICs but also to be judiciously placed across the layout to ensure a uniform heating of the entire Si chip. At the same time, the final packaging of the device should ensure not only the desired magnetic properties but also allow connection to an external heat sink. Similarly, just like the semiconductor high-power transistors, the upper frequency limit to which these Si-embedded micro-coils could operate efficiently may be limited, due to the magnetic coupling and losses of the Si substrate itself at

increasingly higher frequencies. In such a case, one must use a micromachined version in which the micro-coil conductors are indeed realized as deposited thick metal layers placed on a thin released membrane and insulated only by air.

6.3.1 Basic device building blocks

The structure of the magnetic system in this research study is described in detail in § 3.12 and Figs. 3.6-3.8. The device consists of four major parts:

1. Actuation coil
2. Magnetic pillar(s).
3. Sensing coil: The sensing coil is integrated only with a few selected designs.
4. Fluidic channel, realized by etching in the top glass plate above the magnetic device, for handling the fluid in and out the device.

Fig. 6.7 shows a schematic drawing of the microsystem's structure indicating the major parts and the different devices which were drawn in the layout and subsequently implemented.

6.3.2 Coils dimensions, series resistance and Joule heating

To avoid the problem of heat dissipation, the resistance of a coil should be optimized to prevent excessive heating during the operation. Because the series resistance of a coil is directly proportional to the total length of the coil's wire, it is necessary to optimize this length with the Joule heating, which on its turn for best performance, has to match the cell/biomolecules handling.

This sub-section presents the pre-fabrication calculations of the total series resistance of the micro-coils. This was necessary to determine the length of any micro-coil, as well as other dimensions related to the electrical characteristics of the device that would allow a maximum current density to be injected with a minimal Joule heating effect.

Figure 6.7: (a) Schematic drawing of the device with its major parts. The spiral micro-coil array is shown here for example, but the device can have any of the micro-coil designs that shown in Fig. 3.8. Only the actuation coil is shown here while some devices structures have an integrated sensing coil. (b) Cross-sectional view.

The series resistance R_s of a coil can be considered as made up of two components: the first one is independent of frequency (i.e. the purely DC resistance which is easily found by using Ohm's law) whereas the second one is frequency dependent. Moreover, the micro-coil's intrinsic parasitic elements, namely the inter-wire parallel capacitance and resistance caused by the insulating layer on which the micro-coil is placed, may seriously degrade the RF performance of the micro-coil. However, in practical cases targeted only for bio-applications which do not need high-frequency operation, the influence of these parasitic components is much smaller than the series resistance and can be neglected.

The resistance of a conductor is given by the well-known relation $R = \frac{\rho l}{A}$, with l the conductor length, and $A = WT$, where W is the conductor width and T its thickness.

The dimensions of a single segment of the coils wire were selected to be $W = 3 \mu\text{m}$ and $T = 10 \mu\text{m}$, resulting in a cross-sectional area of $A = 30 \mu\text{m}^2$. The spacing between two adjacent wires is $S = 3 \mu\text{m}$. All the coils were fabricated using the same dimensions (i.e., W , T , and S). This enhances the uniformity of the surface and enables an easy copper plating during the electro-deposition processes.

Since in all our designs the cross-section of the conductor is always fixed at the value of $30 \mu\text{m}^2$, the only value needed to be determined for the resistance calculations is the total length of the micro-coil. Fig. 6.8 summarizes the total lengths of the different types of micro-coils and their corresponding resistances. For a better comparison several identical micro-coils designs of different sizes were also included in the layout was subsequently fabricated and tested, but these are not included in Fig. 6.8.

The magnetic field and magnetic force generated is a function of the current flowing through the micro-coil, and this current is limited by the heating of the metal

μ -Electromagnet /Coil	Single element	μ -Coil layout	$R_s (\Omega)$ (Calculated)
MS1: Length (μm) $= l_t = 2N(l_c + S)$	$l_c = 200 \mu\text{m}$	$N = 35, A_c = 0.084 \text{mm}^2$ $l_t = 14.2 \text{mm}, 3\text{-phases}$	8.002
MS2 Length (μm) $= l_t = 2N(l_c + S)$	$l_c = 200 \mu\text{m}$	$N = 25, A_c = 0.135 \text{mm}^2$ $l_t = 11.2 \text{mm}$	6.3/coil
MM1: Length (μm) $= l_t = 4aR_n C_n$ R_n : number of rows C_n : number of columns	$l_c = 80 \mu\text{m}$	$l_t = 3.2 \text{mm}, A_c = 0.029 \text{mm}^2$ $R_n = 8, C_n = 8$	3.6
MM2: Length (μm) $= l_t = (2\pi r + 3d)R_n C_n$	$l_c = 80 \mu\text{m}$	$l_t = 1.6 \text{mm}, A_c = 0.0125 \text{mm}^2$ $R_n = 8, C_n = 6$	2.1
CS1: Length (μm) $= l_t = 2\pi \left[r_{in} + \left(\sum_{n=1}^N r_{in} + Pn \right) \right] P$: Pitch size; $r_{in} = r_0$	$r_{in} = 50 \mu\text{m}$	$N = 10, 25, 35$ $l_t = 3.6, 15.9, 28.9 \text{mm}$ $A_c = 0.038, 0.07, 0.138 \text{mm}^2$	2 (N=10) 8.9 (N=25) 16.2 (N=35)
SS2: Length (μm) $= l_t = ND_{in} + \sum_{n=1}^N 2nP$ P: pitch size, $D_{in} = D_0$	$l_c = 50 \mu\text{m}$	$N = 10, 25, 35$ $l_t = 4.68, 20.6, 37.24 \text{mm}$ $A_c = 0.012, 0.04, 0.067 \text{mm}^2$	2.64 (N=10) 11.6 (N=25) 20.96 (N=35)

Figure 6.8: Length and area of various cells from which different micro-coil designs

were composed, each with a different total length and hence a DC resistance value. A copper conductor with a cross-sectional area of $30 \mu\text{m}^2$ was considered for all the designs.

conductor (the micro-coil wire). Assume that the conductor is made of copper with resistivity of $1.69 \times 10^{-8} \Omega\text{m}$ and that the dissipated power is conducted through the silicon substrate safely until the top silicon surface reaches a temperature of 100°C .

The resistance and the current through the coil define the power which is dissipated and conducted into the silicon substrate:

$$I^2 R = \frac{k A_c \Delta T}{h_s} \quad (6.1)$$

where k is the thermal conductivity of silicon (157 W/m.K) [157], A_c is the total area of the planar coil, and h_s is the thickness of the silicon substrate, which is assumed to be $5 \times 10^{-4} \text{ m}$. The expression in (6.1) assumed that a one dimensional thermal conduction model is appropriate. This is justified by assuming that the lateral area of the silicon substrate is equal to that of the coil. The conductor profile is rectangular with cross-sectional area of $A = W \cdot h$, where W and h are the width and the thickness of the conductor, respectively. From Eq. (6.1) we get:

$$\frac{I_{\max}^2}{A_c} = \frac{k W t \Delta T_{\max}}{\rho l h_s} \quad (6.2)$$

replacing $k=157 \text{ W/m.K}$, $W=3 \mu\text{m}$, $t=10 \mu\text{m}$, $\Delta T=100\text{K}$, $\rho=1.69 \times 10^{-8} \Omega \cdot \text{m}$ and $h_s = 5 \times 10^{-4} \text{ m}$, the condition setting the maximum Joule heating which can still be dissipated effect by heat conduction results as:

$$I_{\max} \leq 236.6 \sqrt{\frac{A_c}{l}} \quad (6.3)$$

Fig. 6.9 shows the change of the total resistance of the spiral coil as a function of its total length and the change of the maximum current allowed to be injected into the coil as a function of the number of turns.

(a)

(b)

Figure 6.9: (a) The change of the total resistance of the spiral coil with respect to its length; (b) The maximum current allowed to be injected into the coil as a function of the number of turns used in the spiral coil.

6.3.3 Fabrication processes details

In this section a detailed description of the processes employed in the fabrication of the device fabrication will be given in their sequential order, as described in Fig. 6.10, and in the following sub-sections.

As it can be clearly understood from the cross-sectional descriptions of the process flow in Fig. 6.10, the final device does have a 3D-like structure and yet achieves a very planar surface just before the magnetic pillar deposition. As it can also be seen, the process innovatively combines more bulk micromachining processes, namely DRIE trench etching, Cu electroplating, CMP, a second metal deposition and magnetic material plating.

Since the seed layer for Cu electroplating would cover the whole surface of the trenches, the Cu will grow in all directions, but slightly faster at corners. Therefore, the trench dimensions become significant factors in determining the filling profile of the metal. To ensure a good filling of the trenches, a narrow trench profile of 3 μm wide and 10 μm deep has been proposed and successfully used in this implementation.

The detailed process sequence is as follows:

- 1) Start with 6-inch (100) wafers which are oxidized to a thickness of 1 μm . This oxide will be used as an insulating layer, mask transfer and later as a CMP stop layer;
- 2) Oxide patterning for trench forming;
- 3) The trenches are formed using DRIE (3 μm wide and 10 μm deep)
- 4) Trench oxidation (1000 $\text{\AA}$);
- 5) Ti/TiN barrier layer deposition (200–500 $\text{\AA}$), to prevent Cu diffusion;
- 6) Cu seed layer deposition;
- 7) Cu electroplating;

Figure 6.10: The original process for the fabrication of a 3D-like micro-coils embedded in Si and with central magnetic pillars for magnetic field focusing.

Figure 6.10 (Continued): The original process for the fabrication of a 3D-like micro-coils embedded in Si and with central magnetic pillars for magnetic field focusing.

- 8) Cu Chemical Mechanical Polishing (CMP)
- 9) PECVD Oxide deposition (1000 Å). This oxide thickness is chosen such that it allows to trace the steps still present after Al deposition for alignment purposes;
- 10) Window opening in oxide for via;
- 11) Plasma treatment to strip CuO induced by previous processing;
- 12) Ti/TiN barrier layer deposition (200 Å);
- 13) Al (1 µm) deposition and patterning (TiN is patterned at the same time with Al);
- 14) BCB coating and patterning (open the area of magnetic pillars);
- 15) NiCoP electroless plating;
- 16) Bonding pad opening.

6.3.3.1 Layout

Based on theoretical analyses and simulations which considered the factors that enhance and focus the magnetic field, different types of planar micro-electromagnets were designed and then drawn in the layout. The final layout consists of 8 chips each 10 mm long and 5 mm wide. Each chip carries one (or more in some chips) type of device different from one chip to another. The layout was drawn using standard layout editor software (CADENCE). The final layout used for wafer processing is shown in Fig. 6.11.

Different designs have been included in the layout which consists of 8 chip dices, each with 1, 2 or 3 devices. The layout contains a matrix of micro-coil designs (see Fig. 3.8), which can be classified into:

- I. Micro-coils with magnetic pillars;
- II. Micro-coils without pillars.

Each of the above categories can also be further split into two groups:

- 1) Single micro-coil;
- 2) An array of micro-coils.

Figure 6.11: An overview of the layout for the chip with various micro-coil designs.

Each the above groups can also be further split into two sub-groups:

- 1) Device with integrated sensing coil;
- 2) Device without sensing coil.

6.3.3.2 Wafer preparation

Twenty five-6 inch P-types wafer were used in the device fabrication. The wafers were first marked from 1 to 25 and went through a preliminary cleaning process to remove any contaminants on the surface of the wafer which may have been generated during wafer fabrication and subsequent storage and process. The wafer is then dipped in aqueous diluted solution of HF for 1 minute in order to remove any native oxide grown on the silicon surface. After spin-rinse-dry cycle the wafer is ready to be transferred to the actual device fabrication process.

The first step is the growth of a sufficient thick oxide. This layer need to mask material in the next step that will etch the silicon wafer (DRIE trench etching) and also CMP etch-stop barrier later in the process (Fig.6.10 Step a). A1 μm thermal oxide is grown on the silicon substrate. For DRIE silicon etching, the thickness value typically used for the masking oxide is generally around 1- 2 microns [158].

Silicon dioxide usually grows by placing the wafer in a high temperature environment (900-1250⁰C) either in a stream of vapor in the case of wet oxidation, or O₂/N₂ mixtures in the case of dry oxidation [110]. The high temperature enhances diffusion oxidant through the surface, according to the reactions:

The ratio of silicon thickness T_{Si} converted to resulting oxide thickness T_{ox} is proportional to their respective densities as:

$$T_{\text{Si}} = 0.455 T_{\text{ox}} \quad (6.4)$$

When 1 μm of oxide is grown, it consumes 0.455 μm of Si [110]. Table 6.1 shows the thermal oxide's properties [110]. After the oxidation was completed the oxide thickness was measured using ellipsometer and was found to have an average value of 9895 Å.

6.3.3.3 Oxide patterning for trenches etching (1st mask transfer)

The first mask to be transferred to the wafer is the trenches mask. As mentioned above the width of the trench is 3 μm . The wafer was coated by a 2 μm thick positive photoresist (PR) at a spin speed of 1200 rpm. The PR thickness affects to a high extent the critical dimension (CD), so it should be optimized according to the mask features and the desired CD. In our case we chose a PR thickness of 2 μm because of the protection they must offer during the subsequent deep etching process following after the patterning.

Table 6.1: Properties of thermal oxide

Property	Value
Density (g/cm^3)	2.24 – 2.27 (dry) and 2.18 – 2.20 (wet)
Dielectric constant	3.9
Dielectric strength (V/cm)	2×10^6 (dry) 3×10^6 (wet)
Energy gap (eV)	~8
Etch rate in buffered HF ($\text{\AA}/\text{min}$)	1000
Infrared absorption peak (μm)	9.3
Melting point ($^{\circ}\text{C}$)	~1700
Molecular weight	60.08
Molecules/ cm^3	2.3×10^{22}
Refractive index	1.46
Resistivity at 25 $^{\circ}\text{C}$ ($\Omega\text{-cm}$)	3×10^{15} (dry) $3\text{--}5 \times 10^{15}$ (wet)
Specific heat ($\text{J}/\text{g } ^{\circ}\text{C}$)	1
Stress in film on Si (dyne/cm^2)	$2\text{--}4 \times 10^8$
Thermal conductivity ($\text{W}/\text{cm } ^{\circ}\text{C}$)	0.014
Thermal conductivity (W/cmK)	0.014
Thermal linear expansion coefficient ($^{\circ}\text{C}^{-1}$)	5×10^{-7} (0.5 ppm/ $^{\circ}\text{C}$)

The wafer was then soft-baked at 75 to 100°C for 10 min. to remove solvents and promote the PR adhesion. After that the wafer was transferred to the exposure system (Cannon aligner), where it was placed under the mask plate (which had been prepared previously) and UV light exposed the PR on the wafer, through the mask at an exposure energy of 100 J/cm², resulting in the transfer of mask image on to the wafer. The following step is the PR developing, i.e., selective removal of the PR in the areas that where not exposed to the UV light (Fig. 6.10b). The critical dimension CD was measured at the end of this photolithography process before the wafer would be transferred to the next step, the oxide etching process. This next step consists of dry etching the SiO₂ regions unprotected by PR. The residual oxide was measured with the ellipsometer (the residual oxide thickness was 40 Å). The wafer is now ready for the deep trench etching.

6.3.3.4 Deep Reactive Ion Etching (DRIE) for trenches

The main reason for, and the ideal result of any dry or wet etching process is to achieve the exact transfer of the mask pattern onto the substrate. However, isotropic etching (dry or wet) always enlarges the mask's features due to the lateral under etching and thus distorts the critical dimensions, whereas anisotropic wet etching is crystallographic orientation-dependent. As a consequence, in bulk micromachining critical dimensions can be maintained only if features are strategically aligned along certain crystallographic planes.

Another possible alternative is to employ Deep Reactive Ion Etching (DRIE) of silicon which enables the microfabrication of High Aspect Ratio Structures (HARS). This technique, in combination with other MEMS techniques such as wafer bonding, makes possible the realization of novel and promising applications. However, most applications impose tough requirements on HARS in terms of high silicon etching rate,

good selectivity with respect to the masking material, good trench profile control, and compatibility with other processes [159]. Specifically, the ability to micro-fabricate deep trenches in silicon substrates while maintaining high selectivity to masking material, good profile control and low non-uniformity across a wafer was an extremely difficult task until recently. In the latest period, etching deep trenches in silicon (even through-wafer holes) has been revolutionized and made possible with the current generation of DRIE tools. These are usually high-density plasma tools that use two distinct gas feeding approaches: standard and time multiplexing.

In the standard approach, all gas species are flowed in the etching chamber at the same time, and the etching results depend on the glow discharge. Consequently, in the etching chamber there will be present both the species of radicals necessary for etching, and the passivating radicals that cover and protect the trench sidewalls. In the time-multiplexing scheme, the etching and passivating gases used are introduced in the etching chamber separately and sequentially only one at a time. In other words the machine alternatively switches between an etching and a passivating cycle many times during the trench etching period [159]. This latter type of etching procedure is known as the “Bosch process”, after the German company that first developed and patented this technique. In a typical configuration SF_6 is flowed during the etching cycle and C_4F_8 during the sidewall protection cycle. This process, described as time-multiplexed deep etching (TMDE), offers the advantage of exploiting the high silicon-etching rate of fluorinated chemistries, such as SF_6 for different applications.

The high silicon-etching rate of TMDE, combined with the possibility of employing soft masking materials, for instance photoresists, and the ability to control the profile of etched devices, makes them a very attractive alternative for producing HARS. Compared with LIGA (German acronym for lithography–electroplating–

injection–molding), for instance, TMDE does not require a synchrotron radiation source for PR exposure, but it is also more compatible with integrated circuit technology and other clean room microfabrication processes. LIGA, however, offers characteristics not surpassed by any other technology, namely, the production of metallic structures with the highest aspect ratio and with reasonably smooth surfaces.

For high etch rate, and high selectivity etching of silicon, fluorine-based chemistry is the method of choice the TMDE due to the high rate at which free fluorine radicals isotropically etch silicon. In order to retain this high etch rate and keep the profile of the etched structures vertical some form of sidewall passivation must be employed. Simultaneous trench etching and sidewall passivation processes (e.g, using HBr, Cl₂ /SiCl₄, or SF₆ /O₂ chemistries) rely on establishing the chemistry within the process chamber such that the products either of the plasma or of the silicon etch generate a passivating layer on the sidewalls of the features of interest.

In the present study, the deep trench etching was performed using an STS process developed by Advanced Silicon Etch ASETM [160], which is very similar to the Bosch one. The ASE process is based on the technique invented by Larmer and Schilp [161]. By sequentially alternating etch and passivation steps anisotropic etching can be carried out on feature sizes ranging from submicron to several millimeters in size. SF₆ and C₄F₈ are used as the etching and passivation gases respectively. The SF₆ gas supplies fluorine radicals for the spontaneous isotropic etching of exposed silicon. The C₄F₈ plasma deposits a (C_xF_y)_n polymeric passivation layer on all substrate features. The directional ion energy supplied by the capacitively coupled plate electrode during the etch step preferentially removes the passivation from the base of the features hence exposing silicon for further spontaneous etching in the subsequent Si etch step. The balance

between etch and passivation determines the final process results and this balance can be controlled through a wide variety of process parameters such as:

1) Etch cycle time	7) Etch cycle time
2) SF ₆ flow rate	8) SF ₆ flow rate
3) Etch cycle platen power	9) Etch cycle platen power
4) Etch cycle coil power	10) Substrate distance from source plasma
5) Etch cycle pressure	11) Passivation cycle coil power
6) Substrate temperature	12) Passivation cycle pressure

After the DRIE trench etching process was finished, the wafer went through a resist strip process and cleaning. The trench depth was measured using SEM, and Fig.6.12 shows the SEM image of one such trench.

6.3.3.5 The sidewall insulating oxide

A1000 Å of oxide (PETEOS) layer was used to isolate the metal (which would subsequently fill in the trenches) from the substrate. This oxide was deposited by Plasma Enhanced Chemical Vapor Deposition (PECVD) technique. The oxide should be stand against breakdown at the maximum voltage at which the device expected to be operated. The quality of an oxide film is often measured in terms of the electric field at which dielectric (oxide) breakdown occurs. Good quality thick (>100 nm) oxide films typically exhibit breakdown at fields greater than about 10 MV/cm, while good quality thin (<10 nm) oxide films usually show larger breakdown fields, often in excess of 15 MV/cm [161].

6.3.3.6 Barrier and seed metal layers

Cu diffuses fast in oxide and this may lead to serious defects in the copper film and increases its resistance. To prevent Cu from diffusion and electromigration a barrier

Figure 6.12: SEM image of the DRIE etched trenches (7.15 μm deep and 2.86 μm wide). The image was taken from the first wafer in order to calculate the etch rate and the time required for different depths.

layer is usually used and deposited just before the deposition of the seed layer. Different materials have been used as a barrier in the interconnections in VLSI circuits such as Ta, TaN, Ti, TiN, TaSiN and WN. In this case a combination of Ti and TiN layers 200 and 300 Å thick were deposited using Physical Vapor Deposition (PVD) as a barrier and adhesive layers, respectively. This combination of layers is frequently used in the CMOS processes, in particular in the Dual Damascene method [162]. The step coverage of the Ti/TiN layers is very important as the aspect ratio increases, a conformal coverage of the trench is reported to be achieved even at high aspect ratios in VLSI processes using different deposition techniques like PVD [163], LPCVD [164].

As mentioned earlier, electroplating starts from an initial conductive seed layer that must be deposited on the substrate prior to electroplating by standard PVD techniques such as electron beam evaporation or sputtering. The requirements to be met by the seed layer can be summarized as follows:

1. **Good conductor:** The seed layer should be able to transfer electrons from the power supply to the metal ions in the electrolyte. The resistance of the seed layer must be sufficiently low in order to ensure a uniform potential all over the wafer. A 200-300 nm gold or copper seed layer will usually fulfill this requirement.
2. **Good adhesion:** Good adhesion of the seed layer to the substrate is important in order to prevent detaching due to residual stress in the deposited film. A thin (approximately 20 nm) layer of chromium or titanium deposited underneath the seed layer will usually fulfill this requirement. Formation of a strong bond between the seed layer and the deposited metal should also be ensured by proper cleaning of the seed layer prior to electroplating.
3. **Chemical resistance:** The seed layer should be able to withstand the aggressive chemicals of the electrolyte. This is further complicated when Pulse Reverse

(PR) plating techniques are used. In PR plating the current is reversed for short periods of time, and small amounts of deposited metal are etched again. In this case, choosing the most suitable seed layer depends very much on the type of electrolyte used.

4. **Removable:** In many cases, it is essential that the seed layer can be removed again after metal deposition, e.g., to avoid short circuits between the fabricated devices. The seed layer etching must be performed selectively with respect to the other materials present on the wafer. Alternatively, the seed layer can be patterned prior to plating. Such a strategy would require an additional masking step and also a thicker seed layer.
5. **Good step coverage:** The thickness of the Cu seed layer is a key factor attaining thick void-free electroplated copper layers which completely fill in all the trenches of features. The challenge of obtaining a complete trench fill with high aspect ratios is largely dependent on the success of achieving an initial complete trench coverage by the Cu seed layer. A poor Cu step coverage results in void formation, although the poor step coverage can be compensated to some extent by increasing the thickness of the seed layer. Due to its good conducting properties, copper is widely used as a seed layer material as it can easily satisfies the required conditions [165-167].

A non-uniform current distribution on the cathode during plating should also be avoided as it causes poor material distribution and non-uniform internal stress. Several factors can result in a poor current distribution, the most important factors being the geometrical shape of the cathode, plating tank and the voltage drop in the seed layer from the supply contacts to the location of deposition, the conductance of the seed layer

is also important especially in electrolytes without any leveling effect of the film growth.

The influence of the seed layer thickness on the current distribution has been well investigated theoretically in literature [165]. For a wafer of radius R , contacted at the entire periphery, the minimum seed layer thickness T_s can be estimated to be:

$$T_s \geq \frac{\rho_s \gamma R^2}{4\xi} \quad (6.5)$$

where ρ_s is the resistivity of the seed layer material, γ is the conductance per unit area of the electrolyte close to the cathode surface, and ξ is the maximum allowed thickness variation of the plated metal. γ can be approximated by $\frac{J}{\eta}$, where J is the current density and η is the over-voltage at the cathode. For electroplating on a 6-inch wafer with a current density of 400 mA/cm² and an estimated cathode over-voltage of 1 V, a thickness variation less than 2% requires a copper seed layer of at least 493 Å. As a consequence of this result, a 1000 Å copper seed layer, has been chosen to be used in our experiments.

6.3.3.7 Copper electroplating

The steps described previously were necessary to prepare for filling the trenches with a thick copper layer, using Cu electroplating started from an initial thin seed layer. The electroplating process thus defines the metal growth mechanism and the shape of the metal structure.

Electroplating is performed in an electroplating cell consisting of an electrolyte, a set of electrodes and a power supply (Fig. 6.13). The electrolyte contains metal ions Me^{z+} and is usually aqueous. One of the electrodes is a bar made of the metal is intended to be deposited. When a negative voltage is applied between the item and the

counter electrode(s), metal ions are reduced and metal deposited on the item according to the cathode reaction:

If the counter electrode consists of the same metal, an oxidation reaction will take place at the anode according to:

In this way, the net amount of metal ions in the electrolyte remains the same.

Although it is quite an old and established technique with a long history, the use of electroplating in microfabrication, for the processing of ICs, microsystems and MEMS, is relatively new. The typical electroplating cell used to perform the copper electroplating contains 25 liters of electrolyte in a polypropylene container with a vertically submerged reference electrode (anode). The counter-electrode (i.e., cathode) forms a ring on top of the container, where the wafer is placed with the face to be plated facing the electrolyte. The electrolytes are continuously pumped from the outer cell to the inner cell. The electrolyte chemistry and other electroplating conditions used in the experiments are shown in Table 6.2. Fig. 6.14 shows SEM cross-sectional photos of Si trenches filled with copper from different test wafers. It has been found that the oxide undercut structure caused by the DRIE etching of silicon resulted in a poor step coverage of the Cu seed layer and maximized the current density at the trenches top. This caused fast plating at the top edges of the trench and a very poor plating rate at its bottom. Reducing the oxide thickness from 1 μm to 1000 Å eliminated this problem and provided an excellent trench filing with electroplated Cu, as shown in Fig.6.15.

Figure 6.13: Schematic representation of an electroplating cell.

Table 6.2: The electrolyte chemistry and conditions used in the electroplating process for trench-filling used in the experiments.

Description	Value
Copper Sulphate (CuSO_4)	17.5 g/l
Sulphuric Acid (H_2SO_4)	17.5 g/l
A – 2001 (Brightener)	1 ml/l
S-2001 (Suppressor)	25 ml/l
PH	4.5
Temperature	25 °C
Anode material	Cu
Current density	400 mA/cm ²
Duration per wafer	40 –80 min

Figure 6.14: SEM images of trenches etched in silicon (3 μm wide and 10 μm deep) unsuccessfully filled with copper by electroplating under various circumstances. The oxide tips at the top of the trenches wall (photo *a*) prevent complete coverage of the trench surface with the seed layer. Therefore, during the electroplating, the current is concentrated at the top of the trench where most of the Cu will be plated, which results in large voids at the bottom of the trenches (photos *b*, *c*, and *d*).

Figure 6.15: Si trenches (3 μm wide and 10 μm deep) successfully filled with electroplated copper after reducing the oxide thickness from 1 μm to 1000 $\text{\AA}$.

6.3.3.8 Chemical mechanical polishing (CMP)

Chemical-Mechanical Polishing (CMP) was first developed by IBM to enable the use of lithography in building up-multi-layer stacks [173]. Nowadays, CMP is a worldwide accepted cleanroom technique used in back-end processes for planarizing multi-layer interconnects. The main objectives of a CMP process are to smooth the surface topography of the silicon wafer and to remove the excess metal produced by electroplating. Nowadays, after decades of Al metallization domination, the advent of submicron VLSI ICs imposed Cu as the best choice and CMP is used exclusively in defining Cu-based metal interconnects using damascene and dual damascene processes [174, 175].

The principles of CMP can be found elsewhere [176, 177]. Although CMP offers an attractive solution for patterning Cu-based metallizations, many challenges exist in developing the process and adapting it for a specific purpose. In the particular case of a Cu CMP process, the key process issues which must be taken into account include across-wafer uniformity, copper dishing, oxide erosion, corrosion and post CMP cleaning. In of this particular case, there is one important advantage: the trenches used in this study have dimensions much larger than the interconnect vias used in the damascene process for VLSI ICs. Therefore, the above mentioned critical issues become less important in our devices. Moreover, these issues were found to be heavily dependent on the various CMP process parameters (such as slurry type, pad material, wafer pressure, platen speed), as well as device features (line width, spacing). The results of polishing after using different polishing parameters were first estimated on test blanket wafers globally electroplated with copper as well as on Cu patterned wafers (with the devices) as shown schematically in Fig.6.16.

The Cu CMP process was performed using an IPEC wafer polisher [178], which consists of a head (wafer carrier), a carousel, a polishing platen and a cleaning platen. All wafers were polished on a polyurethane pad (IC 1000, Rodel Inc.) [179]. The polishing system incorporates an *ex situ* pad conditioner used to recondition the surface of the pad after every CMP run. The slurries, DI water and cleaning solution were pumped unto the pad using a programmed pumping system and the wafer moved from the polishing pad to the cleaning platen with the help of a robotic arm.

The wafer polishing was conducted with alumina-based slurries (iCue™ 5001, Cabot Corporation) [180]. An oxidizer (hydrogen peroxide, H₂O₂) was added to the slurry in order to oxidize the Cu film and thus enhance its removal rate. After every polishing run, the wafers and the brush went through a post-CMP cleaning solution (CMP-M02, Kanto Chemical Inc.) [181]. The slurries were continuously agitated to prevent particle sedimentation and fresh slurry solutions were prepared before polishing each wafer. Both the Cu and the barrier layers were polished using the same slurries. Before each run the pad was soaked with slurry for around 20 sec to fully charge the pad with abrasive particles. The CMP conditions applied for the polishing procedure used for our devices are summarized in Table 6.3.

After each run, the wafer was moved with the robotic arm into the flushing brush and rinsed with deionized water and dried in a N₂ flow. The wafer was treated with the cleaning solution after the last run in order to remove most of the Cu and slurry particle residues. The thickness and uniformity of the Cu film during the CMP processes was obtained using a four point probe to measure the sheet resistance at different locations of the wafer surface, and a step profiler (Tencor Alpha-step 200 Stylus profiler) to measure the Cu step height (thickness).

Figure 6.16: (a) Schematic showing the contact surface between the wafer and the brush and the abrasive particles in between; (b) Material stacks for both test blanket wafers and patterned wafers before the CMP.

Table 6.3: The CMP process parameters

Description	Value
Oxidizer (H ₂ O ₂) wt %	(25 – 33) %
Slurry PH	4.0
Down force pressure (psi)	1 – 6
Back pressure (psi)	4 – 8
Wafer rotation speed (rpm)	50 – 75
Platen rotation speed (rpm)	50 – 75
Slurry flow rate (ml/min)	100 – 250
Single run time (min)	2 – 5
DI flush time (min)	2
Post CMP cleaning time (min)	2

The sheet resistance was measured using a four point probe: $R_S = kV/I$, where V is the measured voltage, I is the applied current and k is a constant which includes geometrical effects such as tip spacing. Once the sheet resistance is measured, the film thickness can be calculated from the relation $R_S = \rho/t$, where ρ is the bulk resistivity of the material. The thickness and uniformity of the oxide after the Cu film complete removal were measured using an ellipsometer. All the erosion and dishing measurements were made with a high-resolution profilometer. Surface defects were inspected/measured by various metrology tools including optical microscope, and SEM.

In order to establish a proper recipe for Cu CMP and to investigate its removal rate of Cu relative to that of SiO_2 , blanket test wafers were used having the same thickness of copper and other thin film (1000 Å Oxide/250 Å Ti/ $\sim 4\mu\text{m}$ Cu) as on the patterned wafers (see Fig.6.16). The thick Cu film on the test wafers was electroplated using the same conditions as for the patterned wafers (see again Table 6.2).

The Cu removal rate by CMP is directly proportional with the back pressure applied on the wafer and the wafer/platen speed, as shown in Figs. 6.17 & 6.18. The applied pressure and polishing speed determine how much mechanical action is exerted onto the wafer's surface, therefore determining the degree of abrasion and thus directly influencing the CMP removal rate. At the same time, the wafer's surface etching by the slurry chemistry also contributes to the ultimate CMP removal rate. Fig. 6.19 shows optical images of various micro-devices, or parts of them, as obtained immediately after a successful CMP process. The surface profile of the wafer in the patterned areas was studied using an optical surface profiler (Veeco). The surface profiles for one single Cu line and for dense Cu lines are shown in Fig. 6.20. From the profile of the single line it can be seen that the Cu lines surface has a rough profile. The surface roughness and dishing of copper surfaces resulted after the CMP process were observed and measured

Figure 6.17: Removal rate of copper by CMP as a function of the pressure applied on the wafer back-side at fixed platen speed.

Figure 6.18: Removal rate of copper by CMP as a function of platen speed at three different wafer pressures.

Figure 6.19: Various Cu patterns of different micro-coils and other magnetic devices immediately after CMP.

Figure 6.20: Coil surface profile measured with optical surface profiler.

using a contact profiler (Tylor Hobson). Fig. 6.21 shows the measured profiles of selected areas on the wafer around a single Cu line (Fig. 6.21a) and at high density lines (Fig. 6.21b-d).

As mentioned earlier, the dimensions of the copper lines are much bigger than the interconnect vias used in the damascene process and therefore the dishing and erosion problems are not critical in our case. Fig. 6.21d shows a global erosion in the surface of the coil which is a result not only from the Cu removal but also from the dielectric erosion between the Cu lines as well. The estimated dishing recess as shown in Fig. 6.21 is about (100 – 150 nm). These CMP effects are not critical parameters for the devices in this study and hence will not affect their performance.

6.3.3.10 Vias and aluminum

After the structure of the embedded micro-electromagnet is defined by electroplating and CMP, the device needs to be connected to the power supply connection. Therefore, a second layer of metal (in this case Al) was used for vias (to connect the center of the spiral shaped electromagnet to the periphery bonding pads) as well as a bonding pad material. As illustrated in Fig. 6.10f, first a 1000 Å thick oxide was PECVD deposited to isolate the electroplated Cu film from the second metal. Then the oxide was patterned by dry etching in order to open the contact area where Cu (M1) would be connected to Al (M2). As this etching process follows the Cu CMP, it results in copper oxidation, which can dramatically increase the impedance of the via. To ensure that Cu is completely uncovered and oxide-free at all contact areas, the wafers were first plasma-treated (i.e., went through a N₂ plasma sputtering) after oxide etching and immediately before the second metal deposition, when the resistance of the device was also measured.

Figure 6.21: Coil surface profile measured with a contact surface profiler at different locations of the coil surface (a) single Cu wire and (b-d) dense Cu wires.

(c)

(d)

Figure 6.21 (Continued): Coil surface profile measured with a contact surface profiler at different locations of the coil surface (a) single Cu wire and (b-d) dense Cu wires.

250 Å of Ti were deposited using PVD as a barrier layer between Cu and Al. Formation of Al inter-metallic compounds, such as TiAl_3 , above or below the Al metal stacked with Ti is known to be effective in preventing electromigration (EM)-related failures [180]. After that, a 1 µm thick Al layer was PVD deposited. The Al was then patterned by wet etching to form the vias and the magnetic alloy substrate areas.

The Al metal in the devices has many functions these are as illustrated in Fig. 6.22:

1. Cross-bridge to connect the center of the spiral shaped electromagnet to the periphery bonding pads.
2. Leads to connect the coil ends to the bonding pads
3. Substrate for the subsequent plating of magnetic alloy which will serve as magnetic pillar. The details of this latter process are discussed in the subsequent sub-section.
4. The upper part of the bonding pad: The bonding pad has two parts: the first one is the embedded Cu mesh which is fabricated in parallel with the coils and the second one is the Ti/Al bi-layer. In fact the bonding pads should be made from the same materials of the coils (i.e., Cu), but the horizontal dimension of the coils' trench is very small (3 micron wide) whereas that of the bonding pad should be large (e.g, 500 µm × 500 micron µm). Consequently, bonding pad can not be realized using the same approach, i.e., etching a trench 10 µm wide and 500 µm × 500 µm large since the presence of two trenches in the wafer of such different lateral dimensions (i.e., 3 µm and 500 µm) will not be filled with Cu in the same manner during the Cu electroplating, i.e., the large pad trench will not be filled completely. Therefore, the bonding pads were reshaped by dividing them into small trenches having the same size of the coils trenches (3 µm width) resulting in a mesh like structure. This means that the bonding pads actually are

Figure 6.22: (a) The second metal (M2) has three functions: top material for the bonding pad, material for the interconnectors between bonding pads and vias, and substrate for the subsequent ferromagnetic core (NiCoP); (b) Simplified cross-sectional view of the bonding pad made of a mesh of Cu-filled trenches with the same dimensions as the coil-wires, inter-metal dielectric (1000 Å) and top upper Al layer; (c) Side view showing the structure of the device with Al as bonding pad, NiCoP substrate and interconnecting Al lead.

now a mesh of Cu-filled trenches, which will make the wire bonding unto bond pads much more difficult in later stages. In order to eliminate this significant practical disadvantage, the meshes of Cu-filled trenches forming the new bond pads are covered by a Ti/Al bi-layer to allow subsequent wire bonding. In all Figures of the fabrication process the Cu mesh is shown, for simplicity, as only one trench (strip) but actually the mesh is constructed from a number of trenches (horizontal and vertical) having the same dimensions like those of the coils (Fig. 6.22 b) and therefore the bond pad are performed simultaneously with the coils fabrication processes. In Fig. 6.22 b the Cu mesh has three trenches (the actual bonding pad has more than three trenches) shown in the cross section.

Fig.6.23 shows several devices after completing the second metal deposition and patterning steps. The resistivity of Al is well known to be higher than that of Cu and to avoid creating high total resistance in the Al interconnecting leads the total cross section of the Al lead must be optimized in order to make the total resistance per unit length equal for each of the two metals (i.e., Cu and Al). The Al leads were fabricated with width of $W_{Al} \geq 40 \text{ } \mu\text{m}$.

6.3.3.7 Magnetic core fabrication

Electrochemical deposition processes have been applied to fabricate various magnetic microsystems [183-185]. For example, electroplated NiFe films are exclusively used for the core of thin film magnetic heads. Although electroplating is a well established method for preparing magnetic films, electroless plating was found to be more suitable for our specific case. (deposition of NiCoP for the magnetic pillar) due to its inherent advantages: 1) Ability to provide a uniform surface, 2) No seed layer is needed; 3) Easy covering of non-planar substrates at a low temperature. This makes it very attractive as a post-processing step, like in the present study;

Fig.6.23: Magnetic micro-devices after the deposition & patterning of the second metal (Al for vias and as a substrate for the subsequent magnetic alloy plating).

- Capability to modify the magnetic properties of the deposited film by changing the ratio of Co and Ni in the plating solution, which makes the process extremely attractive for present specific purpose;
- Simple materials and equipments that result in a low cost.

Since its discovery by Brenner and Ridell [186], electroless plating has been used frequently for the preparation of magnetic films. However, its usage for plating magnetic alloys such as CoNi and CoNiP has only been investigated in the last few years due to its promising applications in ULSI and MEMS fabrication technologies. For example electrolessly deposited thin NiP, CoP, and NiCoP films have been proposed [187] as barrier materials in the development of electroformed Cu interconnects for ULSI applications. The former electroless Cu barriers were effective up to a temperature of 400°C. It was proposed that an introduction of a third alloying element, especially W, Mo, or Re may improve the barrier efficiency. Indeed, electroless Co (W, P) thin films showed an ability to function as effective barriers layers for Cu metallization at temperatures up to 550°C [187]. However, the usage of electroless plating for realizing magnetic pillars as cores of micro-coils is not reported in the literature.

6.3.3.10.1 Basic electroless plating principles

It is widely accepted that electroless plating proceeds similarly to an electrochemical mechanism, consisting of a simultaneous cathodic metal deposition and an anodic oxidation of a reductant. The difference with respect to electroplating is that now no current needs to be injected into the system, and the reaction takes place only due to the catalytic effect of the surface. The electroless deposition of metals can then be explained as the sum of the cathodic reduction of the metal combined with the anodic oxidation of the reducing agent, both on a catalytic surface. In addition, there might be

also some interference effects between these reactions. Therefore, the complete reaction is a complex result of combination of the two different partial reactions. Those two partial reactions, however, occur at one and the same electrode, metal/solution interface.

Because in the electroless deposition processes there is no external current supply, the electrons required to perform the deposition are produced by the chemical reaction(s) in solution. In fact, there is no such thing as “electroless” deposition and the process should be described as a “chemical deposition method” or “autocatalytic deposition”. The metal electrons needed to reduce the metal ions are provided by the reducing agents R^{n+} which give z electrons (e^-), being oxidized to $R^{(n+z)}$. The equations for this [46] are:

where Me^{z+} refer to the metal ions initially present in the solution and which are finally deposited on the desired substrate as the metal film Me .

The overall reaction in the hypophosphate reduction of nickel ions is described as [186]:

The exact nature of the reactions involved when Ni is formed is not yet fully understood.

The following model was set up to explain its deposition [188]:

All the above reactions take place simultaneously in the overall plating process. The specific rate of each reaction depends on the bath composition and concentrations of the

various chemicals or intermediary compounds at a given moment, pH, and temperature. The effect of the plating parameters on the electroless deposition of Ni are summarized in Table 6.4.

Table 6.4: The effect of plating conditions on the electroless plating rate of Ni.

Parameter	Effect on plating rate	Remarks
Temperature	Increases	Many of the reactions mentioned above take place above 50° C
pH	Increases	Increasing the pH also reduces the P content in the deposition
Bath composition 1. Ni & Co ions concentration 2. Hypophosphate concentration	Slightly increases No effect	Increasing the hypophosphate results in a higher concentration of P
Contamination	Reduce/inhibit	Avoid by clean & careful processing
Immersion time	Decrease	P content increases

From all the above reactions (6.13) it is clear that besides Ni, P is also included together with Ni in the deposited film. Consequently, electroless Ni plating from hypophosphate-containing solution actually results in the deposition of NiP alloys with 3 to 15% P content. The problem is that, unlike a pure Ni film, this alloy is not a magnetic material, especially for P concentrations higher than 5% [189]. For this reason, in the recent study, NiP was replaced with the ternary alloy NiCoP which exhibits good magnetic properties.

Typically, the composition of the solution for NiCoP electroless plating is:

1. A source of Ni cations: the preferred source is nickel sulphate or nickel chloride;
2. A source of Co ions: cobalt sulphate or cobalt chloride
3. A reducing agent. Four reducing agents are used in the chemical reduction of Ni from aqueous solutions [189]:
 - a. Sodium hypophosphate ($\text{NaH}_2\text{PO}_2 \cdot \text{H}_2\text{O}$),
 - b. Sodium borohydride (NaBH_4),

- c. Dimethylamine borane=DMAB ($(\text{CH}_3)_2\text{NHBH}_3$) and
- d. Hydrazine ($\text{N}_2\text{H}_4 \cdot \text{H}_2\text{O}$).

These agents are structurally similar with one another as each contains two or more reactive hydrogen components, and Ni reduction results from their catalytic dehydrogenation.

- 4. A complexing agent: it performs three functions in the electroless plating bath [189]:
 - a. Prevents the pH of the solution from decreasing too fast;
 - b. Prevents the precipitation of the Ni salts;
 - c. Reduces the concentration of free Ni ions.
- 5. A stabilizer: it prevents the decomposition reaction of the plating solution and thus increases its lifetime;
- 6. Energy: Electroless plating requires energy in order to trigger and proceed the chemical reactions. This energy is usually supplied as heat.

6.3.3.10.2 Plating substrate

Aluminum is a catalyst for the electroless deposition of Ni and hence it was used as electroless plating 'substrate' for depositing the magnetic pillar. The size of the magnetic pillars substrate ranges from 10 to 90 μm , with circular and squared shapes, as was shown in Fig. 6.23. The thickness of this Al 'substrate' is 1 μm .

6.3.3.10.3 Passivation layer coating

Before carrying out the electroless plating process, a passivation layer is deposited on top of the silicon oxide (and Al) and patterned, i.e., opened only at places where the plating of NiCoP is desired. Even this step is not necessary in a general electroless plating process since electroless Ni, which is the common material used, is selectively deposited onto the activated area, usually Al pads. However, during the initial stages of

this process a global plating of the alloy was observed, in other words the surface of oxide was also covered with NiCoP. For this reason, and in order to prevent plating on non-desired places, the above mentioned passivation layer was added.

Normal photoresist is not stable in the plating bath (usually an alkaline solutions with $\text{pH} \geq 9$) in which it dissolves immediately. Therefore, we have employed a benzocyclobutene-based polymer (BCB). BCB series are dielectric photosensitive resins polymers developed for microelectronics applications. These materials are ideal for wafer level applications where a thin dielectric layer is required, or where a protective layer is needed for passivation or chemical resistance.

BCB is a negative acting resist, that is the exposed regions are cross-linked and remain after development, with very good dielectric and planarizing properties. This type of resist is sensitive to the I-line radiation (i.e., the 365-nm emission from a UV lamp). Table 6.5 shows some properties of BCB (Cyclotene).

The photosensitive BCB film is spun onto the pre-cleaned wafer, then the resist is soft baked at 210°C for 40 Min. After the soft bake, the wafer was exposed to UV light. The typical exposure dose corresponding to a Cyclotene BCB film $2.5\text{ }\mu\text{m}$ thick spun at 2500 rpm is 30 mJ/cm^2 . Then the resist was developed and baked again to further dry the film and stabilize the sidewalls of the etched openings. After completing the photolithographic processing, the film is cured at 250°C for 60 Min. to improve adhesion between the polymer layer and the substrate and also to give the film its maximum chemical resistance and stable mechanical and electrical properties.

Table 6.5: Properties of Cyclotene BCB [190].

Property	Value
Glass temperature (°C)	>350
Residual Stress on Si at 25°C (MPa)	28±2
Dielectric Constant (1kHz-20GHz)	2.65
Breakdown Voltage (V/cm)	3×10^6
Volume Resistivity (Ω -cm)	1×10^{19}

6.3.3.10.4 Surface pretreatment

As Al rapidly oxidizes during rinsing or exposure to air, the resulting oxide film will completely suppress metallization and/or prevent the formation of intermetallic bonds between the electroless plated material and the Al 'substrate', resulting in adhesion failure. For this reason, a detailed surface pre-treatment has to be carried out to ensure the activation of the Al surface.

In this sub-section, the activation of the Al surface and the subsequent adhesion of the electroless nickel deposit will be discussed based on experimental studies and reported literature data, and in the next section the key issues of the electroless nickel-cobalt deposition process will be presented.

The overall process used in this study is shown in Fig. 6.24. Each step was investigated to assess its impact on the plating. The process begins with cleaning/etching of the Al surface using sodium hydroxide and nitric acid, followed by a zincate activation step, before the final electroless plating step. The detailed steps of the process are presented as follows:

Figure 6.24: Process flow of the NiCoP electroless deposition.

A. Cleaning/etching solutions (Sodium Hydroxide and Nitric Acid)

For oxide removal and cleansing of the Al substrate, sodium hydroxide (NaOH) and nitric acid (HNO₃) were used. First, the wafer was etched in a 5 wt% (1.25 M) NaOH solution in water for a period of 30 s to 1 min, at a temperature of 75–80° C. The degree of etching depended on the individual device and the etch time was kept to a minimum to prevent excessive removal of Al from the substrate. Following the NaOH etch, the wafer was rinsed with water and then dipped into a 50% (10 M) nitric acid solution for 10-20 s, at room temperature. The wafer was then rinsed with deionised (DI) water before proceeding to the zincate activation step. The concentrated nitric acid etch is used to remove the metal “smut” materials left behind by the NaOH etch and helps to remove any remaining organic residues on the pad surface.

B. Zincate activation

The zincation of an Al ‘substrate’ is a widely used process that activates the Al surface for subsequent electroless deposition process, i.e., in principle, gives rise to good adhesion between the substrate and the plated Ni. Zincating relies on the electrochemical exchange reaction between zinc complexes in solution and the Al, depositing Zn crystals at the expense of Al etching. The zincation process results in a permeable Zn layer ~500 Å thick which inhibits oxide formation on the covered Al surface to be electrolessly plated. The overall reaction is:

A commercially available solution was used to activate the Al surface, which was a modified alkaline zincate bath. The zincate treatment was applied to the wafers at room temperature, immediately after the cleaning processes, by dipping them into the solution for periods of 10 to 60 seconds and then rinsing with deionised water. For samples that were to have a double zincate treatment, a second etch in 50% HNO₃ for 10

to 20 s was carried out, followed by rinsing and repeating the zincate treatment. Double zincation was also considered as is believed to give the best adhesion for electrolessly deposited nickel [189, 191]. Samples were taken at various stages of the processes and analyzed by several techniques (e.g., SEM and surface profiler) until the right recipe was established and found to be reliable.

6.3.3.10.5 Electroless plating

For the electroless plating of NiCoP unto the zincate activated Al 'substrate' different solutions were evaluated. All of them can be classified into two categories, with respect to the chemistry of their solution: sulphate- and chloride-based. Table 6.6 details the compositions of these two types of NiCoP electroless plating solutions. In general, alkaline hypophosphite baths were used, operating at a pH of 7...9, producing nickel-cobalt deposits with phosphorus incorporated into them. Plating was carried out in a plating cell with capacity of 25 liters of bath solution into which samples were suspended. The bath temperature was controlled at 75 to 85°C and the pH value was measured frequently and maintained at a constant value of 9.

6.3.3.10.6 Obtained results

The above described electroless plating procedure was applied practically and the obtained results are shown in Figs. 6.25 & 6.26. Fig.6.25a to c show optical photos of magnetic pillars on test wafers, whereas Fig.6.25d to h show optical photos of magnetic processed devices at the end of the entire fabrication in which the pillars are clearly visible in the center of the micro-coils. Fig. 6.26 shows SEM photos of various devices where only the magnetic pillars are visible (the micro-coils are not visible due to the passivation layer on top of them). The thickness values of the magnetic pillars were measured during the plating experiments using a contact profilometer. Fig. 6.27 shows some measurement results at different plating times.

Figure 6.25: (a) to (c) Optical photos of various magnetic pillars on a test wafer; (d) to (h) Optical photos of various magnetic fabricated micro-coils with their corresponding magnetic pillars.

Figure 6.26: SEM photos of magnetic pillars for various magnetic devices (the micro-coils are not visible due to the passivation layer on top of them).

(a) Single pillar, (Plating time ~30 min)

(b) Single pillar, (Plating time ~30 min)

Figure 6.27: Ferromagnetic pillars heights measured by a contact surface profiler.

(c) An array of pillars, Plating time ~20 min

(d) An array of pillars. Plating time ~25 min

Figure 6.27 (Continued): Ferromagnetic pillars heights measured by a contact surface profiler.

Table 6.6: Compositions of the electroless path used to deposit NiCoP.

Chemicals	Concentration g/l		Function
	Sulphate	Chloride	
Nickel sulphate	25		Nickel source
Nickel chloride		25	Nickel source
Cobalt sulphate	17.6		Cobalt source
Cobalt chloride		35	Cobalt source
Sodium hypophosphate	18.8	18.8	Reducing agent
Sodium citrate	80	80	Buffer for PH control
Ammonium sulphate	40		Complexant
Ammonium chloride		40	Complexant
Boric acid	30	30	Accelerator
Thiourea (mg/l)			Stabilizer
PH value	7-9		
Temperature	75-85		
Deposition rate	0.4...1 $\mu\text{m}/\text{min}$		

The materials properties of the electroless deposited magnetic pillars were characterized for both the composition and the magnetic properties. Fig. 6.28 shows the energy-dispersive X-ray (EDX) spectrum of CoNiP. The average composition of the materials was measured as $\text{Co}_{31}\text{Ni}_{60}\text{P}_9$. Fig. 6.29 shows the hysteresis loop of CoNiP as measured after plating using Vibrating Sample Magnetometer (VSM). The shape of the hysteresis loop seems to be very similar to that exhibited by partially or totally amorphous materials [192,193]. It is well known that magnetic characteristics of amorphous materials are significantly smaller than those of crystalline materials [194]. The NiCoP deposits in the current study exhibit soft magnetic characteristic with a coercivity (H_c) of 43.5 G and a magnetization M_s of 95.5 emu/g.

According to Tarozatie et al. [195] the formation of certain crystallite shapes, which determine high coercivity, takes place only a definite boundaries, differs for film

deposit under different conditions, because the grains with different size and shape formation.

According to them, electroless NiCoP deposits exhibit a high coercivity when the phosphorus content of the deposit lies 4 and 6 wt. %. When the phosphorus content is lower than 4 wt. %, films of coarse crystallite are deposited, resulting in lower coercivity. If phosphorus content exceeds 6 wt. %, films consisting of very fine grains are deposited which also leads to a decrease in coercivity. Rivero et. al. [196] report a linear increase in magnetic moment when increasing the cobalt content for electrodeposited NiCoP amorphous ribbons.

The measured resistance and inductance (with and without magnetic pillars) for the different types of coils studied in this dissertation and compared with the theoretical (calculated) ones are shown in Table 6.7.

6.4 Summary

The fabrication of the novel magnetic devices has been presented. These devices were implemented using a combination of MEMS and Cu interconnect processes, namely, deep trenches etching, Cu electroplating, CMP and magnetic ternary alloy electroless plating. The realized devices have void-free Cu conductors electroplated in a high aspect ratio trenches. Different micro-coil designs have been realized together with magnetic pillars made of a high permeability material and positioned at specific locations to focus the magnetic field. These devices can be used for manipulation of magnetic micro-particles as will be shown in the next chapter.

Figure 6.28: EDX spectrum of CoNiP.

Figure 6.29: Hysteresis loop obtained for electroless NiCoP ternary alloy deposit after plating process. Notice the extremely thin loop, typical for soft magnetic materials which can be easily magnetized in the presence of an magnetic field, and then demagnetized with the same rapidity once the magnetic field is removed.

Table 6.7: Measured and calculated resistance and inductance for various planar micro-coils with and without magnetic pillars.

Micro-coil (single)	Resistance		Inductance		
			Without pillar(s)		With pillar(s)
	Calculated	Measured	Calculated	Measured	Measured
MS1	8.002	14.6	0.8	1.22	NA
MS2	6.3	10.82	0.77	1.19	NA
MM1	3.6	5.8		1.02	1.24
MM2	2.1	2.55		1.16	1.26
CS1(N=35)	16.2	20.25	0.95	1.52	1.75
SS1(N=35)	20.96	21.03	1.08	1.49	1.53
CS2 (inner)	2	2.45	0.21	0.28	
CS2(outer)	8.9	13.21	0.76	0.88	1.05
CS3	14.63	16.3	1.22	1.52	1.81

CHAPTER 7

MEASUREMENTS, RESULTS & DISCUSSION

7.1 Introduction

The goal of this chapter is two-fold, as it presents:

- a) First, the measurements carried out on the fabricated devices, and
- b) Secondly, the various performance parameters of the realized devices, which will prove the successful implementation of the designs proposed in this dissertation, and their suitability for the intended μ -fluidic applications.

More specifically, in this thesis it was proposed that micro-coils with Cu conductors having the smaller side of their rectangular cross-section in the plane of the chip, and with magnetic pillars (made of ferromagnetic materials, acting as magnetic cores) located in the point of maximal field can create deep magnetic potential wells at the micro-scale. These wells are capable to generate large forces on magnetic beads and can also be controlled so as to be variable in time, and/or space and/or magnitude. This is in contrast to both conventional methods of magnetic field/force generation and classical miniaturized devices, due to the aggressive scaling down of the dimensional features of the proposed and realized devices and to the ability to construct various planar geometries of current-carrying conductors. All the magnetic devices proposed, designed and presented in this dissertation were realized using an original combination of standard fabrication processes typically used in the semiconductor industry. Therefore, all the proposed devices have the great advantage of being integratable with other micro-components on the same chip.

To briefly summarize again, in this dissertation the following essential concepts were proposed:

- To generate large magnetic forces on magnetic micro/nano particles by maximizing the magnetic field gradient. As discussed in Chapter 3, the field gradient can be increased by reducing the size of the device. In the present study the magnetic field gradient was enhanced successfully by:
 1. Miniaturizing the individual coil's conductors, which in turn results in a reduced size of the whole device;
 2. Orienting the cross-section of the coil's conductor with the long side normal to the chip surface;
 3. Placing a magnetic micro-pillar(s) in the point(s) of maximal magnetic field in order to play the role of the magnetic core in the conventional coils.
- Various magnetic particle trapping profiles can be achieved by creating different arrangements (geometries) of current carrying conductors (micro-coils). These devices can be used in applications that require biomolecular separation/manipulation. The study presented the following 8 designs of micro-coils:
 1. Simple meander micro-coil (MS1)
 2. Interdigitated meander micro-coil (MS2)
 3. Semi-squared loop meander micro-coil (MM1)
 4. Circular loop meander micro-coil (MM2)
 5. Circular spiral micro-coil (CS1)
 6. Coaxial spiral micro-coils (CS2)
 7. Interdigitated spiral micro-coils (CS3)
 8. Square spiral micro-coil (SS1)

- The magnetic field generated by a planar micro-coil can be confined on one side of the device by placing a backside plate made of high permeability material and hence with the magnetic pillar this would close the magnetic circuit and maximize the force on magnetic particles in the separation chamber which is positioned on the active side (top) of the device. This minimizes magnetic losses and further enhances magnetic focusing thus allowing creation of deeper potential wells.
- Magnetic potential wells created by the previous mentioned devices, and hence the attracted/trapped cell-magnetic, particles composite can be manipulated by tuning/programming the current through an array of these devices.
- The trapping rate of the magnetic particles can be quantified by employing a sensing micro-coil integrated with the actuation micro-coil. The operation of sensing coil is based on the change of inductance that results from the accumulation of the magnetic particles to the micro-coil's surface.

This chapter studies the performance for the following structural devices:

- Different designs of planar micro-coils;
- Planar micro-coils without magnetic pillars vs. micro-coils with magnetic pillars;
- Planar micro-coils without magnetic backside plate vs. planar micro-coils with backside plate.
- The trapping and manipulation performance of the above listed devices arranged in arrays.

All these proposed devices and arrangements/arrays were first introduced in Chapter 3, analyzed theoretically and using FEA methods in Chapters 4 and 5, respectively, and their realization was described in Chapter 6.

This Chapter is organized into three main sub-sections:

1. Experimental: This sub-section describes the device packaging (the initial preparation for testing), as well as the parameters and variables that were tested and measured in the experiments in order to prove the scheme functionality and materials and experimental methodology and setup used through the experiments;
2. Results: The measured performance of the different designs with/ without magnetic pillars for various parameters, will be described in this part of the Chapter.
3. Finally, a general discussion of all the results presented in this Chapter and their connection with the simulation results of Chapters 4 & 5 will be presented.

The simulation and measurement results will be compared and discussed through this Chapter in view of the above listed parameters to examine the agreement between the proposed (simulated) models and the actually implemented devices.

7.2 Experimental

7.2.1 Device packaging

7.2.1.1 Electrical connections

After wafer dicing (dice size= $10 \times 5 \text{ mm}^2$), the chip to be tested/used has been mounted on a previously fabricated printing circuit board (PCB) using an epoxy resin bond as shown in Fig. 7.1. The PCB allows the connection of the chip to the power supply and the measurement equipment. The PCB size is $30 \times 15 \times 1 \text{ mm}^3$. The bonding pads on the chip were connected to the PCB with gold wires $80 \text{ }\mu\text{m}$ diameter by thermocompression wire bonding.

7.2.1.2 Fluidic connection

To allow precise and sealed fluidic injection to the device, a fluidic connection block has been fabricated to accommodate the device and allow fluid dispensing with minimum sample volumes. The fluidic block is schematically illustrated in Fig 7.2. The bottom part of the block is made from copper with a small protrusion contacting the backside of the silicon chip through a hole made in the PCB. This small protrusion provides a path for sinking the heat that may be generated in the chip during the device operation. The top part of the fluidic block is made of Perspex and consists of a fluidic chamber, with the fluidic inlet and outlet channels drilled through it. Due to its transparency, the top part of the block allows visualization and particle tracking during the experiments. A silicon rubber sheet, with a cutout in its center at the chip site, surrounded the chip and was sandwiched between the copper block and the Perspex cover to ensure complete sealing and to prevent fluid leakage. The size of the fluidic chamber is $10 \times 5 \times 0.1 \text{ mm}^3$ which results in a total sample volume of $5 \text{ }\mu\text{l}$. The fluidic inlet and outlet, with inner diameter of 1 mm, were connected to the external apparatus setup using Teflon tubing with an inner diameter of 0.5 mm.

7.2.2 Magnetic particles

Different types and sizes of magnetic beads were used in the experiments, all of which are listed in Table 7.1. The magnetic beads were diluted from their original stock solution using DI water and phosphate buffered saline (PBS) solution into different concentrations to result in samples containing $(10^5\text{-}10^9)$ bead/ml. Lower bead concentrations were used for bead tracking.

Figure 7.1: Device mounted on PCB.

Figure 7.2: Fluidic connection block, (a) Schematic drawing; (b) Final fluidic block with chip inserted in.

Table 7.1: Magnetic beads used in the experiments and their properties.

Magnetic bead		Average diameter (μm)	Density (g/cm^3)	Ferrite %	Surface area	Surface coating property
Dynabeads $\rightarrow$	M-500	5	1.5	20	$7 \times 10^{-4} \text{ m}^2/10^7$	Streptavidin
	M-450	4.5	1.5	20	1-4 m^2/g	Streptavidin
	M-280	2.8	1.3	12	4-8 m^2/g	Streptavidin
	Myone	1	$7-12 \times 10^9$ bead/ml	20		Streptavidin
Estopor	EM1-100	1.03	1.65	43		COOH
	EM2-70	1.20	1.65	54		NH ₂
	M1- 200	1.88	2.2	34		COOH
	M1-70	1.05	2.2	59		COOH
	EM4-100	1.62	1.65	46		OH group
	R99-44	0.87	1.65			Fluorescence

7.2.3 Experimental setup

The general experimental arrangement used in testing the magnetic beads separation and tracking consists of the fluidic connection block described in the previous sub-section, Teflon tubing, a programmable syringe pump fitted with a 1-ml syringe, a DC power supply, an optical microscope with a CCD camera, and a PC with image/video recorder (Fig. 7.3). The additional experimental setup for other measurements will be discussed in the next sections.

The prepared magnetic bead samples with known concentration (number of beads per volume) were pumped into the fluidic chamber through the Teflon tubing using the programmable syringe pump as shown in Fig. 7.3. Table 7.2 summarizes the geometries and conditions for sample injection. The magnetic devices were excited by injecting a DC current from a DC power supply, and the current was increased until bead trapping was observed. Real time tracking of the magnetic beads' behavior was obtained using the CCD camera and the image/video recording system.

Figure 7.3: Experimental setup for magnetic beads separation and tracking.

Figure 7.4: Experimental schemes used in the magnetic beads separation experiments.

Q is the flow rate.

Extensive measurements based on direct visualization and their interpretation employing different quantification methods were carried out. The different experimental procedures and schemes are shown in Fig. 7.4.

Table 7.2: Sample flow parameters of the magnetic beads separation experiments.

Parameter	Notation (unit)	Numerical value
Inlet flow channel diameter (mm)	D (mm)	1
Flow channel cross-sectional area	$A = \pi \left(\frac{D}{2} \right)^2$ (mm ²)	0.785
Volumetric flow rate of the suspension	Q (μl/min)	10 – 100
Estimated particle velocity at the channel end (at the inlet of the chamber)	$v = \frac{Q}{A}$ (mm/s)	0.212 – 2.12

7.2.4 Parameters and variables

To prove the proposed scheme functionality, the above mentioned characteristics were studied by measuring the following parameters and variables:

1. Magnetic particle trapping rate employing two different methods:
 - i. Direct counting of the particles;
 - ii. Change of inductance using an additional sensing coil;

The dependence of the trapping rate was studied with respect to the following variables: a. Device design; b. Flow rate; c. Injected current; d. Time.

2. Trapping profile: this parameter was described using image processing using frame by frame image recording for the different designs and structures.
3. Magnetic particle transportation/manipulation: the manipulation of particles was also measured using the image processing method.

4. The long range influence of the device: this parameter was studied by using all the above three mentioned methods (direct counting, inductance change measurements and image processing).

7.2.5 Methods

Three measurement methods were used throughout these experiments:

7.2.5.1 Direct counting of particles

The trapping rates for the different designs of micro-electromagnets have been measured by directly counting the magnetic beads at the fluid inlet and at the fluid outlet. The counting of beads was made using a haematocytometer (NEUBAUER-Germany) and the initial concentration of magnetic beads was fixed at 6×10^5 beads/ml. The experimental conditions for these measurements are listed in Table 7.3 and the process is illustrated in Fig.7.5. Before injecting the sample into the device a fixed volume of sample was frequently taken at the beginning of every measurement and spread over the haematocytometer which is divided into several squares and then the beads were counted in each square and summed. The same counting was made using a sample with the same volume but taken from the outlet. The trapping rate then was calculated using the following relation:

$$\text{Trapping Rate} = \frac{\text{Total number of trapped beads}}{\text{Total number of injected beads}} \times 100\%, \text{ where,}$$

$$\text{Total number of trapped beads} = \text{Total number of injected beads} - \text{Total number of beads counted at the outlet}$$

7.2.5.2 Change of inductance

As described in Chapters 3 and 5, the devices MS2 and CS3 consist of two interdigitated micro-coils. In the quantification experiments one of the micro-coils was used for bead actuation and the second one (connected to an LCR-meter) was used as a sensing coil that measured the variation of inductance which resulted from the

accumulation of magnetic beads on the device surface. Magnetic beads with diameters of 1-5 μm were used in these experiments.

Large bead concentrations (3.2×10^9 bead/ml) were used in these particular experiments to ensure that the surface of the micro-coil is covered by a quasi-uniform layer of permeable material (i.e. the magnetic beads) in order to enhance the signal obtained by the sensing coil (i.e. the change of inductance). Moreover, for the same reason, for these experiments we used beads with high ferrite contents (e.g., Estapor M1-70 and Estapor EM2-70 with ferrite contents of 59% and 54%, respectively). This would allow easier bead trapping and the creation of a permeable layer with low reluctance which would increase the inductance variation of the sensing coil. Fig. 7.6 illustrates the experimental setup and the micro-coil connections for these experiments.

Table 7.3: Experimental conditions of the magnetic beads counting experiments for the various designs of micro-electromagnets

Parameter	Unit	Numerical value
Flow rate	$\mu\text{l}/\text{min}$	20
Beads concentration at the inlet	Beads/ml	6×10^5
Bead size (diameter)	μm	2.8
Current intensity	mA	150 – 250
Separation time	Second	30

Figure 7.5: Diagram illustrating magnetic beads counting before and after the device operation using a hematocytometer.

Figure 7.6: Two types of devices (MS2, and CS3) consisting of coupled actuation and sensing micro-coils. The first coil is connected to the power supply and the second one is linked to an inductance measurement system. The CS3 micro-coil can also be realized in two versions: with and without magnetic pillars in the center, respectively.

7.2.5.3 Magnetic beads trapping and movement profile assessment using image processing

A large number of images and videos were taken during the experiments. The still images were taken at pre-determined time intervals. These images were then arranged in sequence to study the magnetic bead movement due to the magnetic force during the experiments. The software associated with the image capturing system shown in Fig. 7.3 allows image processing, objects counting, and extraction of line and surface profiles based on the image under study. In the following analysis image sequences will be shown at different periods of time for an individual device, and a comparison between the two main design types of coils, i.e. meander and spiral coil (with and without magnetic pillars), will be drawn. For this type of image assessment the following important considerations should be taken into account:

1. Pre-calibration and setup of the colors were performed before starting the experiments;
2. The software counts only the objects with a predefined color in the image;
3. The line or surface profile reflects the dark/light area in the image;
4. A reference line /surface was drawn before any line or surface profile was taken. This reference was then subtracted from the subsequent line/surface in the collected image;
5. The object counting and surface profiling gives an estimation and not the exact quantification of magnetic beads trapped on the surface of the micro-coil(s).

7.3 Results and discussion

The experimental results in the following sub-sections will be presented in a sequence similar to the measurements methods mentioned above:

7.3.1 Magnetic bead trapping rate (using direct counting)

Initially, the magnetic beads trapping experiments were carried out on all the fabricated devices previously described in Chapters 3-6. The trapping of magnetic beads was successfully demonstrated and visualized for all the devices. However, each different device has a different trapping profile, rate, behavior, and operation conditions as will be presented further. These differences are due to the particular configuration and structure of each device (e.g. the geometrical shape, and the existence or the absence of the magnetic pillars). The magnetic bead trapping was observed for both static condition (no flow) and continuous flow, at different flow rates and with or without the magnetic pillars.

The trapping rates for the devices with two different structures, without and with magnetic pillars (except in the case of MS-type coils, which have no pillars in their structures) are listed in Table 7.4 and illustrated in Fig.7.7a. Fig. 7.7b compares the calculated magnetic field using FEA and the measured trapping rate. The diagram shows an agreement between the simulation and measurement since larger magnetic field results in a stronger magnetic force and in consequence larger trapping rates. It should be noted that these measured trapping rates compare the trapping efficiencies of different micro-electromagnet designs and do not measure the exact efficiency of an individual micro-electromagnet. This is explained by the fact that the device occupies only a small area of the fluidic chamber, and the magnetic force generated by it affects only a fraction of the magnetic beads injected into the chamber, as illustrated in Fig. 7.8a.

Table 7.4: The trapping rate for all the devices having two different structures, without and with magnetic pillars.

Device	Index (on Fig. 7.7)	Geometrical parameters	Operation mode	Fill factor (%)	Trapping Rate (%)	
					Without pillars	With pillars
MS1	A	S=3 μ m	100,010,001	5	18.7	NA
	B		110,101,011	10	27.3	
	C		111	15	35.4	
MS2	D	S1=3, S2=15 μ m	01 or 10	10	24.3	
	E		11 parallel	10	33.5	
	F		11 antiparallel	10	21.7	
MM1	G	G=40 μ m	1	17	20.7	25.4
	H	G=20 μ m	1	8.5	23.4	28.1
MM2	I	R _{Loop} = 25 μ m	1	11	24.6	29.4
	J	R _{Loop} = 10 μ m	1	4.5	23.6	28.2
CS1	K	NA	100,010,001	7	29.7	39.6
	L	NA	110,101,110	14	38	66.5
	M	NA	111	21	67.3	84.3
CS2	N	NA	Inner (1), Outer (0)	1.5	13	24.4
	O	NA	Inner (1), Outer (1)	9.5	36.1	76.5
CS3	P	NA	10, 01	21	32.8	60.6
	Q	NA	11 parallel	21	48.6	79.4
	R	NA	11 antiparallel	21	20.6	29.3
SS1	S	NA	100,010,001	7	27	48.8
	T	NA	110,101,110	14	34	58.3
	U	NA	111	21	49.6	80.8

$$\text{Fill factor} = \frac{\text{Total surface area occupied by the device}}{\text{Total surface area of the fluidic chamber}} \times 100\%$$

Total number of trapped beads = Total number of injected beads – Total number of covered beads

S: spacing between two adjacent conductors,

G: Square loop dimension

R_{Loop}: loop radius,

R_{Loop}: The radius of the elementary loop,

0: Device OFF, 1: Device ON, (e.g. **100**: coil 1 is ON, coil2 is OFF, and coil 3 is OFF)

(a)

(b)

Figure 7.7: Trapping rate of magnetic beads achieved by different micro-electromagnet designs for both cases with and without magnetic pillars. The flow rate during the experiments was 20 µl/min, and the current injected in an individual device was ~150 mA. The micro-coils types A to U are index in the previous Table 7.4.

The ratio between the total surface area of the magnetic device and that of the chamber is expressed as the “Fill factor”, which can be given as:

$$\text{Fill factor} = \frac{\text{Total area occupied by the device}}{\text{Total area of the fluidic chamber}} \times 100\%$$

The trapping rate as a function of the Fill factor for two devices (MS1 & CS1) is shown in Figs 7.8b & c.

The beads in the fluidic chamber are distributed in three zones (Fig. 7.8a):

Zone A: This corresponds to the top surface area of the micro-electromagnets array. The beads passing through this area are subjected to the strongest magnetic force (maximal at the center) and the observations confirm that they are always trapped.

Zone B: The beads passing through this zone are affected by moderate magnetic forces. The smaller magnitude of the attracting force is due to the increased distance from the micro-electromagnet. The bead trapping in this zone is determined by the magnetic force, the flow rate, and the separation distance of the bead from the micro-electromagnet. Only a fraction of the beads will be trapped while the remainder will continue to flow out. However, the magnetic force can be increased by injecting higher currents in order to fully trap a larger number (theoretically all) of beads. Consequently, one can define a so-called bead capture radius determined by a device, which will be discussed in the next section.

Zone C: This zone is far from the electromagnet and the beads are barely affected by a weak magnetic force and therefore have a small chance to be trapped.

The relation between the magnetic force, the beads distribution and flow will be discussed in detail in the next section.

(a)

(b)

(c)

Figure 7.8: a) The magnetic beads in the fluidic chamber are distributed in three zones: (A): The surface of the micro-electromagnets array. The beads passing through this zone are subjected to the strongest magnetic force and they are always trapped, (B) The beads passing through this zone are affected only by moderate magnetic forces due to the increased distance from the micro-electromagnet; (C) Far from the electromagnet the beads are hardly affected by the weak magnetic force existing in this area and therefore, they have a small chance to be trapped; b) Trapping rate as a function of the fill factor for MS1; c) Trapping rate as a function of the fill factor for CS1.

Our experiments showed that the trapping rate decreases with increasing flow rate. This relation is investigated for flow rates in the range 10-120 $\mu\text{l}/\text{min}$. Fig. 7.9 shows this variation for the MS1 and CS1 micro-electromagnets types. The critical flow rates at which the device is not able to trap the beads are 65 $\mu\text{l}/\text{min}$ for MS1 and 85 and 120 $\mu\text{l}/\text{min}$ for CS1 without and with pillar, respectively. Because the magnetic fields generated by the devices are directly proportional to the injected current, this means that increasing the injected current into the device, by maintaining temperature quasi-constant through heat dissipation into the substrate, would result in increasing the trapping rate as well. Figure 7.10 shows the trapping rate of the CS1 micro-electromagnet as a function of the injected DC current. The magnetic pillar within the device not only maximizes the magnetic energy but also reduces the power consumption or the current required to generate the magnetic force necessary for efficient bead trapping. The decrease in the consumed power in turn reduces the heating effect which is a desired feature in such devices.

To insure that the magnetic force is the major factor in magnetic beads trapping and to test the effect of the gravitational force as an opposing force, the trapping rate was measured again by setting the device up-side-down i.e. the micro-electromagnet becomes the top of the fluidic chamber instead of the normal position when it lies at its bottom. Fig. 7.11 shows the trapping rate for both cases: when the micro-coil (CS1-type) is on the top and at the bottom, respectively.

The existing but rather small difference between the two cases clearly highlights two facts: a) The micro-electromagnets are efficient in trapping beads, even at large separation distances (e.g., $z=100\text{ }\mu\text{m}$, which is the fluidic chamber depth), and b) The gravitational force is negligible for such a system, as was initially assumed in § 3.7.

(a)

(b)

Figure 7.9: Trapping rate as a function of the flow rate for: (a) MS1 and (b) CS1 micro-electromagnets at current intensities of 200 mA.

Figure 7.10: The trapping rate for a CS1 micro-electromagnet with/without pillar as a function of the injected DC current.

Figure 7.11: Trapping rate versus the flow rate for CS1 micro-coil for two positions: micro-coil at the bottom and at the top of the fluidic chamber, respectively.

7.3.2 Quantification of magnetic bead trapping (using sensing coil)

The change of inductance due to the magnetic bead trapping on the surface of the device was measured using the integrated sensing micro-coil in two devices: MS2 and CS3. Figs. 7.12 and 7.13 show the measured variation of inductance as a function of the injected current intensity, and time during the bead trapping for the MS1 micro-coil and the CS3 device with and without magnetic pillar, respectively.

The observed increase of the inductance indicates a corresponding increase of the permeability of the layer on top of the device, i.e., it is a result of an accumulation of magnetic beads.

7.3.2.1 The interpretation of the change of inductance due to magnetic bead trapping

The inductance change obtained by the sensing coil can be correlated to the number of beads captured from the solution and therefore the number of trapped biological targets can be calculated if the properties of the magnetic particles are known.

To establish a relation between the change of inductance and the number of trapped magnetic beads, different concentrations of magnetic beads were prepared and the changes of inductance due to the trapping of these beads were measured. Table 7.5 shows the concentrations and number of beads used in the experiments. The number of beads inside the fluidic chamber at a certain time is: $N_{bead} = C_{bead} \times V$, where C_{bead} is the beads concentration and V the fluidic chamber volume. However, as explained earlier and illustrated in Fig. 7.8, not all the beads are trapped by the magnetic device and those beads which are trapped on the surface of the coils will contribute to the change of the sensing coil's inductance. The effective number of these beads can be given as $N_{eff} = N_{bead} \times TR$, where TR is the trapping rate.

Fig. 7.14 shows the predicted effective number of beads (trapped beads) as a function of the change of inductance for the CS3 micro-coil. Thus for a ~36% trapping rate of the micro-coil CS3 at no-flow condition ($Q=0$ $\mu\text{l}/\text{min}$) the effective number of beads will be $N_{\text{eff}} = 0.36N_{\text{bead}}$.

7.3.3 The effect of magnetic backside plate

As shown in § 5.2.2.4, when a magnetic backside plate is introduced under the coil the simulation results show a 5 times increase in the magnetic field in the case of the spiral micro coil with magnetic pillar and 1.5 times in the case of the meander micro-coil without a magnetic pillar. To measure the effect of this magnetic plate a hole with dimensions of $400\text{ }\mu\text{m} \times 400\text{ }\mu\text{m} \times 400\text{ }\mu\text{m}$ was created in the Si substrate on the backside of the device and subsequently filled with a fine powder of the same magnetic material as that used to fabricate the pillars i.e. a CoNiP. Fig. 7.15 shows a schematic of the device with an incorporated backside magnetic plate. Trapping rate tests were performed for selected devices with a backside plate, namely MS1 and CS1 with and without magnetic pillars, respectively. The trapping rates of these devices were quantified using both direct bead counting and measurement of the inductance change due to the bead trapping. Fig. 7.16 shows the trapping rate with and without the existence of the backside plate for MS1 and CS1 micro-coils. Fig. 7.17 shows the trapping rate exhibited by the MS1 micro-coil as a function of the flow rate for both cases: with and without the existence of backside plate, respectively. Fig. 7.18 shows the measured change of inductance as a function of current for the spiral micro-coil (CS3) for both cases with and without the existence of a backside plate.

(a)

(b)

Figure 7.12: Variation of inductance due to the accumulation of magnetic beads on top of the device as a function of: (a) The injected current intensity; and (b) Time, for the MS2 micro-electromagnet.

(a)

(b)

Figure 7.13: Variation of inductance due to the accumulation of magnetic beads on top of the device as a function of the injected current intensity for the CS3 micro-electromagnet: (a) Without and; (b) With magnetic pillar, respectively. In both cases the separation time = 30 seconds.

(c)

(d)

Figure 7.13 (Continued): Variation of inductance due to the accumulation of magnetic beads on top of the device as a function of time for the CS3 micro-electromagnet: (c) Without, and; (d) With magnetic pillar, respectively.

Table 7.5: The concentration and the corresponding number of beads in the fluidic chamber for the calibration experiments.

Beads Concentration ($10^{10} \times \text{beads/ml}$)	Number of beads in the fluidic chamber ($N_{\text{bead}} \times 10^7$)
1.6	8
0.8	4
0.4	2
0.2	1

Figure 7.14: Calibration of the number of trapped beads and the resultant change of inductance for a spiral micro-coil with magnetic pillar (CS3).

Figure 7.15: Schematic representation of the magnetic device with magnetic side plate. The magnetic plate enhances the magnetic field confinement and reduce the flux leakage which result in more efficient magnetization of the beads and, consequently, in higher trapping rates.

Figure 7.16: A comparison between the trapping rates for the meander micro-coil with and without a magnetic backside plate and for a spiral micro-coil with pillar only and with both pillar and magnetic plate.

Figure 7.17: The beads trapping rate for the MS1 micro-coil as a function of the flow rate for both the cases with and without the backside plate.

Figure 7.18: The inductance variation due to the accumulation of magnetic beads on top of the device as a function of current for the CS3 micro-electromagnet with both magnetic pillar and backside plate.

7.3.4 Magnetic bead trapping and movement profile assessment using image processing

The magnetic bead trapping, transportation, and relocation were successfully visualized under the optical microscope. Because of the many types of micro-electromagnet designs and structures investigated in this research, qualitative and quantitative assessment methods for the performance of a single device and for comparing the performance of many devices were needed.

7.3.4.1 Time sequences of beads trapping by micro-coils

The frame by frame image capture and sequencing were done for all the different devices. However, due to the large size of these pictures only a few sequences for selected devices will be presented. Figs 7.19-7.24 show bead trapping sequences for different examples of micro-coils. Each line of these figures shows the optical image, the line profile and a 3D surface profile of the coil surface at a certain time.

The line and surface profiles shown in the second and third columns are typically the profile of the magnetic bead distribution shown in the optical image of the first column. When the beads accumulate on the conductors or around the pillars, the line and surface profiles exhibit a significantly reduced reflectivity. Hence, a dip normally appears in the line and surface profiles and the change of the intensity in these profiles is directly proportional to the number of magnetic beads accumulated at the area where the profile is measured or drawn. The following considerations should be taking into account for the accurate interpretation of the line and surface profiles:

1. When beads are randomly distributed over the surface of the device, when the device is OFF, the light intensity as shown by the line profile (2nd column) and surface profile (3rd column) has a non-uniform shape with a number of small peaks/dips distributed along the line/surface;

2. When magnetic beads start to move toward the active device, the light intensity decreases at the place corresponding to the place where the beads are trapped and an intensity dip will be created;
3. With continuous trapping of the beads with time the depth of the intensity dip increases due to the continuous accumulation of beads and the width of this dip shrinks with time as well due to the bead confinement at the active device (coil). At the same time this leads to a decrease of bead concentration at the non-active area of the device or the area surrounding the coil which in turn results in an increase in the light intensity reflected from this region until a maximum light intensity from this peripheral region is reached ultimately corresponding to a bead-free region.

Using image processing the trapping profiles of a meander (MS1) and of a spiral micro-coil (CS1) have been compared. Many tracking images (frames) have been taken at different time intervals and the number of trapped magnetic beads was counted by dividing the area of the micro-coil into several sectors as shown in Fig 7.25 a and c. The trapping profiles for the MS1 and CS1 micro-coils are shown in Fig 7.25 b and d. These profiles show that the meander coil traps the beads in a periodic pattern over the whole micro-coil surface such that the beads align themselves along the coil's conductors. In contrast, for the spiral coil, in particular the one with magnetic pillar, the beads are strongly confined in the center, where the concentration of beads is significantly higher than in the area surrounding the center as shown in Fig. 7.25 d.

The presented results showed strong agreement between the simulated magnetic flux distribution profiles and the observed magnetic particles profile and this shown again in detail in Figs 7.26 - 7.28, where the locations of maximal magnetic flux density shown observed to be the same location, on the realized devices, with high beads concentration.

Figure 7.19: Magnetic beads trapping sequence for a meander μ -coil (MS2/11-mode) with four conductors, $I = 100$ mA, $R_{bead} = 0.55$ μ m, $Q = 20$ μ l/min.

Figure 7.20: Magnetic beads trapping sequence for a meander μ -coil (interdigitated MM2 with pillars/11-mode), $I = 100$ mA, $R_{bead} = 0.55$ μ m, $Q = 20$ μ l/min.

Figure 7.21: Magnetic beads trapping sequence for a meander μ -coil (MM1), $I = 100$ mA, $R_{bead} = 0.55 \mu\text{m}$, $Q = 20 \mu\text{l/min}$.

Figure 7.22: Magnetic bead trapping sequence for a circular spiral μ -coil (CS1-with magnetic pillar), $I = 100$ mA, $R_{bead} = 0.55$ μ m, $Q = 20$ μ l/min.

Figure 7.23: Magnetic bead trapping sequence for a circular spiral μ -coil (CS1with magnetic pillar), $I = 100$ mA, $R_{bead} = 0.5$ μ m, $Q = 20$ μ l/min

Figure 7.24: Magnetic bead trapping sequence for a circular spiral μ -coil (CS1 without pillar), $I = 100$ mA, $R_{bead} = 0.55$ μ m, $Q = 20$ μ l/min.

(b)

Figure 7.25-i: a) Magnetic bead trapping sequence captured in frames taken at different time intervals for a meander (MS1) micro-coil trapping sequence; b) Trapping profile of MS1 micro-coil as obtained from counting the beads within the frames shown in (a).

(c)

(d)

Figure 7.25-ii: c) Magnetic bead trapping sequence captured in frames taken at different time intervals for meander (CS1) micro-coil; d) Trapping profile obtained from counting the beads within the frames shown in (c).

Figure 7.26: A comparison between the distribution profiles of the magnetic flux on the simulated devices and the magnetic bead trapping profile on the tested devices shows a strong agreement between the simulation and measurement results.

Figure 7.27: A comparison between the magnetic force profile generated by two conductors carrying currents in the opposite directions and the corresponding magnetic bead trapping profile of the tested device. The results show a strong agreement between simulation and measurements.

Figure 7.28: A comparison between the magnetic force profile generated by CS1 micro-coil and the corresponding magnetic bead trapping profile of the tested device. The results show a strong agreement between simulation and measurements.

7.3.5 The long-range influence of micro-coils

As predicted, one advantage of using micro-coils over micro-electrodes (i.e. employing magnetic instead of electric fields) is that the magnetic field has a long-range force influence on magnetic particles. This allows a more effective interaction with particles in a thick layer of liquid suspension. To detect the range of influence of the micro-coils spacer sheets made of a non-magnetic dielectric polymer of 50 μm thickness were laminated successively on top of the micro-coil (Fig. 7.29) and the same previously described experimental procedures were used to quantify the trapping rate. The spacer was made of a stack of individual sheets each 50 μm , allowing spacings of 50, 100, 150, ..., 500 μm . The polymer sheet was replaced by a glass cover when the desired thickness of the space was 200 or 400 μm (Fig. 7.29b). Trapping magnetic beads was successfully observed even with the spacer inserted in the system. Table 7.6 summarizes the experimental results, showing the measured maximum thickness of the spacer (using the stack made of polymer sheets each 50 μm thick) at which the micro-coil was still capable to move the beads i.e. the maximum thickness after which no movement of beads was further observed when another sheet was added. For example, when bead movement is observed at maximum sheet thickness of 250 μm this implies that movement was not observed anymore for the next stack thickness of 300 μm .

The measurements have an inherent error of 50 μm along the vertical axis, due to the intrinsic limitations of the method itself. The experiments were performed using magnetic particles with a diameter of 1 μm , at no-flow condition and at an injected current of 200 mA.

Figure 7.29: Schematic representation of the devices with dielectric spacer positioned on the top in order to examine the range of influence of the magnetic force generated by the micro-coils. (a) Plastic; (b) Glass sheet; (c) A fluidic chamber etched in silicon with $100\ \mu\text{m}$ thick membrane at its bottom and with glass cover positioned on top of the magnetic device.

The trapping rates for the micro-coil CS1 (110-mode) with a spacer thickness of 100 μm as a function of the injected current and flow rate were also determined by the bead counting method and the results are shown in Figs. 7.30 and 7.31, respectively. By comparing these results with those obtained without any spacer, it can be deduced that the addition of the 100 μm spacer results in a 34% reduction of the trapping rate. By comparing the results of Fig. 7.30 with those of Fig. 7.10 this relation can be expressed as ($TR_{Z=100\ \mu\text{m}} = 0.41\ TR_0$) with TR and TR_0 as the trapping rates at a given vertical distance from the micro-coil's surface with/without spacer, respectively. These results show that it is possible to position a separate fluidic chamber, with a thin bottom, on top of the magnetic device to perform the target separation and the magnetic device can be re-used again as shown schematically in Fig. 7.29c. This trapping rate reduction is explained by the expected exponential decay of the magnetic force generated by a micro-coil as predicted previously, e.g. as shown in Fig. 4.68b.

Table 7.6: Maximum spacer thickness at which the micro-coil was still able to trap magnetic beads. Flow rate = 20 $\mu\text{l/min}$, magnetic particle size = 1 μm .

Micro-coil	Maximum spacer thickness at which the μ -coil was capable to trap magnetic beads.	
	Without magnetic pillar	With magnetic pillar
MS1	50	NA
MM2	50	50
CS1	200	250
CS2 (11-mode)	200	300
CS3 (11-mode)	250	350

Figure 7.30: Trapping rate for the circular spiral micro-coil CS1 with a 100 μm thick polymer spacer added on top of its surface for different injected current intensities and at a flow rate of 20 $\mu\text{l/min}$. The magnetic particles used in these measurements had a diameter of 2.8 μm .

Figure 7.31: Trapping rate for the circular spiral micro-coil CS1 with a 100 μm thick polymer spacer added on top of its surface for different flow rates.

7.3.6 Manipulation of magnetic beads using micro-electromagnets arrays

As discussed in Chapters 3, 4 and 6, different micro-electromagnets were designed to allow magnetic beads manipulation i.e. transportation, concentration and guiding. These designs generate local maxima in the magnetic density gradient that can be used to move beads from one location to another. The different modes of bead manipulation, illustrated in Figs.7.32 to 7.37 are discussed in the following subsections.

7.3.6.1 Beads manipulation by MS2 micro-coil

When a current is injected in one coil only (the inner one) of MS2 (i.e. 1,0 mode) a local maximum of the magnetic field is created along the edges of the inner loops and the magnetic beads will be trapped along these wires (Fig.7.32 a & b). By switching on the current in the other coil and switching it off in the first coil (i.e. 0,1 mode), the local maximum will shift towards the edges of the outer loop and the magnetic beads follow these maxima. Another operation mode can be obtained by injecting different current intensities in each coil (e.g. $I_1=100$ mA & $I_2=10$ mA) which can make the beads move only along short distances (5-10 μ m). The magnetic field profile and vectors for the different two modes are shown in Fig. 7.32c, d & e, f, respectively, and the corresponding image sequences and line profile are shown in Fig. 7.33. The magnetic forces profiles of the two coils for current intensities of 100 mA injected in each micro-coil at a time are shown in Fig. 7.34a, for only one loop in Fig. 7.34b, and for a single wire in Fig. 7.34 c. The particles trapping pattern is typical to these force profile.

Each individual loop (either the inner loop or the outer one) generates a magnetic force capable to move or trap the beads that were initially trapped around the other loop. This implies that all the magnetic particles can be moved from one loop to the other one without losses and consequently, can be easily manipulated alternatively between various locations. Trapping all the beads at one single spatial location can be explained

Figure 7.32: Magnetic beads guiding by MS2 micro-coil. The magnetic beads are moved between two interdigitated meander micro-coils by alternatively injecting currents into each micro-coil or tuning different values of current through them: (a & b) Schematic representation of the beads distribution when the current in the two coils are alternatively switched on and off; (c & d) Magnetic field profile; and (e & f) Magnetic vectors distribution for the two cases shown in (a & b).

Figure 7.33: Magnetic beads trapping and transporting sequence for the MS2 meander micro-coil, $I = 100 \text{ mA}$, $R_{\text{bead}} = 0.55 \text{ }\mu\text{m}$, $Q = 20 \text{ }\mu\text{l/min}$.

(a)

(b)

(c)

Figure 7.34: (a) Magnetic force distribution profile for an MS2 micro-coil with two interdigitated loops; (b) Magnetic force profile for a single MS2 loop (inner); (c) Magnetic force profile for a single wire.

by the fact that the capture-cross section and radius of each individual loop are large enough for capturing the beads that were previously attracted by the other micro-coil, as shown in Fig. 7.35.

7.3.6.2 Bead manipulation by an array of MM2-type micro-coil

Consider employing two independent sets of micro-coils, each of which has the design similar to that of the MM2 micro-coil (Fig.7.36a). By injecting a current I in the first set (i.e. 10 mode), local maxima will be created at the center of each loop of the set and the magnetic beads will be trapped there. By switching on the current flowing through the other set (i.e. 01 mode), the local maxima shift towards the centers of this second set of loops and the magnetic beads will move correspondingly, for distances as large as $\sim 20\text{ }\mu\text{m}$, as illustrated in Fig. 7.36a. The magnetic forces exerted on a magnetic particles with a $1\text{ }\mu\text{m}$ radius by two independent conductor loops carrying current intensities of 100 and 20 mA, respectively, are shown in Fig. 7.36b.

7.3.6.3 Beads manipulation by an array of spiral micro-coils

In a spiral array (Fig.7.37) beads can be transported over longer distances, equal to one diameter of the coil ($\sim 150\text{ }\mu\text{m}$), by alternatively injecting a current in each spiral (i.e. 100, 010, and 001) or injecting different values of current intensities in the array (e.g. $I_1=100\text{ mA}$, $I_2=20\text{ mA}$, $I_3=20\text{ mA}$ followed by $I_1=20\text{ mA}$, $I_2=100\text{ mA}$, $I_3=20\text{ mA}$ etc.). The magnetic energy maximum is created around the central area i.e., at the magnetic pillar surface of the spiral which is either switched ON, or carries the highest value of current intensity. It was realized that the magnetic field and field gradient generated by a single micro-coil was not strong enough to magnetize and move magnetic particles located far from the outermost turn of this coil, i.e. particles typically located on the surface of the neighboring coils.

Figure 7.35: (a) Schematic representation of the capture cross-sections of two interdigitated MS2 loops; (b) Their capture radius.

Figure 7.36: (a) Beads manipulation using two sets of MM2 micro-coils. When a current I is injected in the left row, local maxima will be created at the center of each loop of the row and the magnetic beads will be trapped there. By switching on the current flow through the other set, the local maxima shift towards the center of these loops and the magnetic beads will move correspondingly for distances as large as $\sim 20 \mu m$. (b) Magnetic force exerted on a magnetic particle with a $1 \mu m$ radius by two independent conductor loops carrying current intensities of 100 and 20 mA, respectively.

Figure 7.37: Magnetic beads transportation along an array of three spiral micro-electromagnets by sequentially operating the array with triphasic signals. When a current is injected in the first spiral a magnetic energy density maximum is created at the magnetic pillar located at its center and therefore magnetic beads are collected there (100-mode). Then the first spiral is switched OFF and the second spiral micro-coil is ON, so that the maximum will be shifted towards the corresponding pillar of the second micro-coil and the beads will follow it (010-mode). The process is repeated for the third spiral micro-coil (001-mode). In the 0-mode the coil may carry a small value of current for magnetizing the beads at its vicinity.

For successful magnetic beads transportation from one coil's surface to another the micro-coil must be able to magnetize the particles and to create a strong magnetic field gradient. Consequently, the magnetic force required in order to achieve a successful bead transportation results from the interaction between the magnetic moment of the particle and the field gradient generated by the system as

$$F_{mag} = (\vec{m} \cdot \nabla) \vec{B} = m \nabla B \quad (7.6)$$

with

$$m = V \chi \frac{B_0}{\mu_0} \quad (7.7)$$

The effective magnetic moment of the particle can be written in term of its magnetization saturation M_s by replacing $\frac{B_0}{\mu_0}$ by H_0 and χH_0 by M_s and eq. (7.7)

becomes

$$m = V M_s \quad (7.8)$$

and eq. (7.6) becomes

$$F_{mag} = V M_s \nabla B \quad (7.9)$$

The magnetic particles used in our experiments have a saturation mass magnetization of 35-40 A·m²/kg and they saturate at an external magnetic field of 40000 A/m. If an external magnetic flux density of 50 mT is applied using an external rare earth magnet or electromagnet, as illustrated in Fig. 7.38, a magnetic particle with the diameter of 1 μm would have $m = 7.2 \times 10^{-14}$ Am² and it can be transported by creating a magnetic field gradient generated by the micro-system (the micro-coil and the pillar). A magnetic field gradient of 28 T/m is enough to move the particle towards the pillar surface. It should be noted that applying an external magnetic field B_0 would result in forming beads chains due to the magnetic dipole interaction between the beads which in

Figure 7.38: Magnetic particle transport between two micro-coils with pillars. The source of the external magnetic field used to magnetize particles is located far from any micro-coil. The coil which generates the magnetic field gradient will determine the beads movement towards its corresponding pillar.

Figure 7.39: Magnetic flux density profile (a), Intensity vector plots (b) and flux lines (c) for two spiral micro-electromagnets carrying current intensities of 100 mA and 20 mA, respectively.

turn results in a much higher magnetic moment (due to the larger size of the chain compared to that of a single bead) and thus a lower magnetic field gradient will be required to move the chain. Fig. 7.39 shows the magnetic flux density profile, vectors and lines for two spiral micro-electromagnets carrying current intensities of 100 and 20 mA, respectively, while Fig. 7.40 shows the magnetic force on a magnetic particle with 1 μm radius due to two these micro-coils.

The corresponding image sequences and line profiles for CS1 micro-coil are shown in Fig. 7.41.

As discussed earlier the most important force competing with the magnetic force is the viscous hydrodynamic one and the equilibrium between these forces can be expressed as

$$VM_s \nabla B = 6\pi\eta R(v_b - v_f) \quad (7.10)$$

where v_b and v_f are the bead and fluid (medium) velocities, respectively. Multiplying eq. (7.10) by the concentration of beads in the fluid C_b

$$C_b VM_s \nabla B = 6\pi\eta R(v_b - v_f) C_b \quad (7.11)$$

The term between the brackets in eq. (7.11) can be termed as the mass flux of the magnetic beads i.e. $J = C_b(v_b - v_f)$ and can be expressed as

$$J = \frac{2C_b M_s R^2}{9\eta} \nabla B \quad (7.12)$$

Eq. (7.12) states that the mass flux of the magnetic beads in the present magnetic transporting system is related to the magnetization of the beads M_s and the field gradient generated by the system at the vicinity of the pillar. The mass flux becomes independent of the magnetization after the beads become saturated. The bead magnetization depends on the applied magnetic field H_0 , (which can be an external field

Figure 7.40: Magnetic force on a magnetic particle with radius 1 μm due to two micro-coils carrying current intensities of 100 and 20 mA, respectively.

Figure 7.41: Magnetic beads trapping and transporting sequence over an array of circular spiral μ -coils (CS1 with magnetic pillars), $I = 100 \text{ mA}$, $R_{\text{bead}} = 0.55 \mu\text{m}$. $Q = 20 \mu\text{l/min}$. For simplicity, the figures show only two micro-coils.

as discussed earlier) up to a certain value where the beads become magnetically saturated. Since $M_s = \chi H_0$, eq. (7.12) can be rewritten as

$$J = \frac{2C_b \chi R^2}{9\eta\mu_0} B_0 \nabla B \quad (7.13)$$

7.3.7 Magnetic bead capture radius

In this section the magnetic bead capture by the magnetic pillars is treated in a similar manner to the macro-scale High Gradient Magnetic Separation (HGMS) which is used in different industrial applications such as steel industry, power plants and mineral processing. The technique is based on the use of small magnetic elements (such as a stainless-steel wire) that generate gradients in a uniform magnetic field background. These gradients give rise to large attractive magnetic forces that allow for the removal of magnetic particles from aqueous solutions.

The theory of HGMS is described elsewhere else and therefore will not be detailed here [196, 197]. Consider a ferromagnetic pillar with radius a and saturation magnetization M_s situated in the origin of the z -axis and placed in the magnetic field (H_0) generated by the corresponding planar coil. The magnetic field is assumed to be large enough to saturate the magnetic pillar. The superparamagnetic particles of magnetic susceptibility χ , volume $V_p (= \frac{4}{3}\pi R^3)$ and density ρ_p flow past the pillar. The fluid has a viscosity η and flow with a uniform velocity v_0 and at low Reynolds number along the x -direction. The equations of motion for the magnetic particles in this configuration can be given in cylindrical polar coordinates as [197, 198]:

$$\frac{dr_a}{dt} = \frac{v_0}{a} \left(1 - \frac{1}{r_a^2} \right) \cos \theta - \frac{v_m}{a} \frac{\cos 2\theta}{r_a^3} \quad (7.14)$$

$$r_a \frac{d\theta}{dt} = -\frac{v_0}{a} \left(1 + \frac{1}{r_a^2} \right) \sin \theta \quad (7.15)$$

where v_m is the particle velocity due to the magnetic force generated by the system which now can be termed as the “magnetic velocity” and is given as:

$$v_m = \frac{2(\chi_p - \chi_f)M_s H_0 R^2}{9\eta a} \quad (7.16)$$

where p and f refer to the particle and fluid, respectively. Eq. (7.16) can be rewritten in terms of the particle and fluid magnetization as

$$v_m = \frac{2(M_p - M_f)M_s \mu_0 R^2}{9\eta a} \quad (7.17)$$

Assuming that the fluid has negligible magnetic susceptibility, the magnetic velocity can be written as

$$v_m = \frac{2\chi M_s H_0 R^2}{9\eta a} = \frac{2M_p M_s \mu_0 R^2}{9\eta a} \quad (7.18)$$

For known properties of the magnetic particle, magnetic pillar and fluid, the magnetic velocity is directly proportional to the magnetic field H_0 generated by the planar micro-coil at the vicinity of the magnetic pillar. Assuming that $\chi = 0.5$, $M_s = 95.5 \text{ emu/cm}^3$, $R = 0.9 \times 10^{-6} \text{ m}$, $\eta(\text{water}) = 1 \times 10^{-3} \text{ Kg/m.s}$, and $a = 10 \times 10^{-6} \text{ m}$, the magnetic velocity results as $v_m = 5.3 \times 10^{-7} H_0$. Fig. 7.42 shows the calculated magnetic velocity along a line starting from the vicinity of the magnetic pillar and ending at the most outer turn of a circular spiral micro-coil. The capability of the device to capture beads was investigated in terms of the distance between the center of the device (e.g. the pillar) and the farthest point at which its magnetic field is still able to captured beads. This distance will hence forth be referred to as the “Capture Radius R_C ” and the corresponding capture cross-section will therefore be given by $A_C = \pi R_C^2$.

Figure 7.42: The calculated magnetic velocity V_m along a line starting from the vicinity of the magnetic pillar and ending at the most outer turn of a circular spiral micro-coil.

The capture radius of the device was measured by recording the trapping process at different injected current intensities at no-flow condition. Several video clips were recorded for each value of the current intensities at low-microscope magnification to allow visualization of a wide area around the coil (i.e. the view area is larger than the capture-cross section). Concentric circles were drawn on each image such that their centers coincided with the center of the device. These circles were used as a reference for measurements of frames captured by the microscope camera. A schematic drawing of this setup is shown in Fig. 7.43 a. The capture radius was measured as $R_c = \frac{h}{m}$, where h is the distance measured on the captured image and m is the magnification used during the video recording.

A similar technique was used to measure the velocity of a magnetic particle due to either the fluid flow, i.e. when magnetic field is OFF (V_0) or the magnetic force, i.e. when the magnetic field is ON (V_m), as illustrated in Fig. 7.43 b & c. Several single frame pictures were taken from the video play back and particle tracking was measured from these frames using a mesh superposed on the captured image. The velocity was calculated as $v = \frac{h}{mn\Delta t}$, where v can be v_0 or v_m , h is the measured distance on the monitor after n frames, and Δt is the time interval between the two analyzed frames. The capture radii for two wires carrying equal currents in opposite directions, a single loop with pillar and a spiral micro-coil (CS1) as a function of the injected currents are shown in Fig. 7.44 a, b, c, while the capture radius for the spiral as a function of the ratio between the magnetic velocity and the fluid velocity is shown in Fig. 7.53 d. It can be clearly seen that the capture radius increases both with the current intensity and the $\frac{v_m}{v_0}$ ratio until the magnetic pillar reaches its saturation state.

Figure 7.43: Schematic drawing of the setup for the measurement of: (a) Capture radius, (b) and (c) Particle velocity v_0 and v_m .

Figure 7.44: Capture radius of: (a) Two wires carrying currents in opposite direction (MS1 with only two wires); (b) Single current loop with magnetic pillar (MM2); (c) Circular spiral micro-coil with magnetic pillar (single CS1) as a function of the injected current; and (d) as a function of $\frac{V_m}{V_0}$ for CS1.

The discrepancy between the simulation and measurement results, in particular for the CS1 micro-coil, can be explained by the supplementary contribution brought by the via resistance which was not considered in the simulations.

7.4 General discussion

In this thesis the interaction between the geometry, the structure and the shape of the magnetic field and field gradient and their effect on micro-magnetic particles was studied for applications dealing with the manipulation of biomolecules.

The shape of the micro-coil winding influences the nature of the resultant magnetic field due to the current flowing through it, according to the well-known Biot-Savart law. This magnetic field is necessary to magnetize the magnetic particle whereas the magnetic field gradient generates the magnetic force required to trap/move these particles. In addition, inserting a micro-pillar made of a permeable ferromagnetic material at locations with maximal magnetic field intensities results in magnetic flux focusing in a very small region. This is due to the fact that the magnetic pillars play the same role as the core in a macroscopic coil, i.e. present a low reluctance path for the magnetic flux generated by its corresponding micro-coil. Therefore, each magnetic pillar is magnetized by its corresponding micro-coil. Once the pillars are magnetized the magnetic flux is concentrated through them and large magnetic field gradients are created at the pillars' locations. Thus, deep potential wells are established in the immediate vicinity of each pillar which will determine a more efficient trapping of magnetic beads. Finally, the magnetic particle trapping on the surface of the device can be detected using an integrated sensing micro-coil which measures the change of inductance due to the magnetic particle accumulation.

The combination of planar micro-coils, ferromagnetic pillars, a magnetic backside plate, and an integrated sensing micro-coil results in a complete system for magnetic

particle manipulation and detection on a chip. Chapters 4 and 5 presented the simulation analysis of various types of micro-coils and of complete magnetic systems. The analysis also optimized the parameters that maximize the magnetic force exerted on magnetic particles. Chapter 6 presented the fabrication technology used to realize such a system and Chapter 7 describes the measurement results and the discussions of the results. In the following subsection a general discussion of the simulation and measurements results and the connection between the theoretical and experimental work will be presented.

7.4.1 The influence of the winding profile of the micro-coil (geometry) on the device performance

The influence of the geometrical parameters on the device performance was studied by FEA simulations as presented in Chapter 4. The simulation results showed that different magnetic flux profiles and field gradients result when the current is injected in different micro-coils wound in different profiles or shapes. This winding profile affects the coupling between the conductors or the loops that form the micro-coil, i.e. it affects the interactions between adjacent conductors or the interaction between conductors located at different locations (e.g. a conductor at the center and another one at the periphery of the micro-coil). This interaction is obvious when the two major types of micro-coils studied (i.e. the meander and spiral) are compared. The meander micro-coils generate an array of magnetic potential wells (i.e. alternating maximal and minimal values of magnetic energy density gradient) distributed in a periodic manner over the surface of the device. In contrast, the spiral micro-coil generates a single potential well at its center. These potential wells are shown to be steeper when a magnetic pillar is present at the location of a maximum magnetic field value. The distribution of these potential wells will dictate the attraction of magnetic particles, which become trapped.

As shown in Table 7.4 and Fig. 7.7, the highest trapping rate among all the studied devices was achieved by the circular spiral micro-coil with a magnetic pillar (trapping rate= 84.3% at a flow rate of 20 $\mu\text{l}/\text{min}$, and when a three coil-array was used) while the highest trapping rate among the meander devices was achieved by the device with circular loops and magnetic pillars positioned at each loop's center (trapping rate= 40.6% at flow rate of 20 $\mu\text{l}/\text{min}$). The highest trapping rate among the micro-coils that include no pillars in their structure was achieved by the triphasic array of meander micro-coils of the MS1-type (trapping rate= 35.4% at a flow rate of 20 $\mu\text{l}/\text{min}$). Table 7.7 compares different micro-coil designs in terms of the magnetic force (simulation results) and their trapping rate (measured results). The design of the planar micro-coils allowed the generation of high magnetic field gradients due to two important features: a) Firstly, the orientation of the micro-coil's conductor was changed, i.e., the small side of the conductor is now placed in the plane of the device surface. The resulting high aspect ratio and small micro-coil diameter generate a high magnetic field gradient as discussed in §4.8.3. It was observed that even a single conductor of this geometrical type was able to capture magnetic beads located in its vicinity, as shown in Fig. 7.45. Secondly, adding magnetic micro-pillars to the coils enables the devices to achieve a higher magnetic field gradient. After this is magnetized (i.e. magnetically saturated) by the field of the surrounding micro-coil, a stronger field gradient than that of a single conductor and thus a maximal magnetic energy gradient, will also be created in the immediate vicinity of the pillar. Consequently, the magnetic particles follow this gradient and will be trapped at or around the pillar. The trapping of magnetic particles around a single conductor and the very concentrated bead trapping around the pillars successfully prove what had been proposed earlier for generation of high magnetic field gradients and hence magnetic forces. These results showed the significance of the

Table 7.7: The magnetic force generated by three types of micro-coils and the corresponding trapping rate achieved using these devices when operated at the same current and flow rate.

Micro-coil	Fill factor	F_{magz} (pN)		TR (%)	
		Without pillars	With pillars	Without pillars	With pillars
MS1	5	6	NA	18.7	NA
MM2	11	8.25	25	24.6	29.4
CS1	7	60	700	29.7	39.6

Figure 7.45: Magnetic particles trapped due to the magnetic force generated by a single wire. The images show two wires that are carrying independent currents (I_1 and I_2).

geometrical features of the single conductor (i.e. the high aspect ratio) for allowing large currents to be injected and hence generation of large magnetic fields and generation of large magnetic field gradient along the small side and the importance of the magnetic pillars in concentration of beads. This conclusion is supported also by the results of the previous simple version of devices presented in §6.2.3 where it was shown that planar devices with Al conductors with low aspect ratio (10/2) were not able to trap magnetic beads at the same injected current. The simple Al micro-coils were able to perform very simple magnetic bead trapping (over the whole surface) at very large currents (250-300 mA, see Fig. 6.6) for which Joule heating becomes very significant, while the new magnetic devices tested here performed multiple profile trapping at moderate currents (less than 100 mA). The winding profile of the micro-coil and the presence or absence of the magnetic pillar explain the differences in the trapping rates shown in Table 7.7 for various devices. Simulations and measurements both show that the winding profile and the presence of a magnetic pillar influence the trapping profile. This was discussed in §4.8, §5.3, and §7.3.1, where it was shown that the meander micro-coil traps the beads periodically on the whole surface while the spiral micro-coil focuses the beads at the central point of the device. These geometry-dependent trapping profiles also prove the proposed model of creating different distribution profiles of magnetic field by designing different arrangements of current carrying conductors (micro-coils) and consequently the trapping profile typically follows the magnetic field and field gradient profile.

Another important contribution of this thesis is the insertion of a magnetic backside plate. This can further enhance the magnetic field concentration and therefore significantly improve the trapping of magnetic beads and the overall performance of the device.

It was also found that the meander micro-coil MM2 resembles an array of single/two spiral loop(s) and therefore it concentrates the beads in an array of bead niches. The magnetic bead trapping profile using such designs offers a platform for the manipulation of beads, and hence for biomolecular applications.

It should be noted that the trapping rate can also be scaled proportionally with the area occupied by the device (the fill factor) and the density of the conductors in the device. Each micro-coil with/without pillar has a different capture radius, which will determine the ratio of the surface area of the device to that of the fluidic channel so that the trapping rate can be maximized to values close to 100 %. Our experimental data (see Fig. 7.44) show that capture radii of 50, 100, and 500 μm were measured for the MS1, MM2, and CS1 devices, respectively. It was also determined that the capture radius of a particular device increases with both the injected current and the ratio between the magnetic velocity and the flow velocity $\frac{v_m}{v_0}$. Therefore, trapping all the magnetic beads injected into the fluidic chamber can be achieved by:

1. Increasing the injected current. This choice is limited due to the heat dissipation, although a significant improvement can be achieved for discrete devices by mounting them on metal heat sinks;
2. Increasing the magnetic velocity v_m by employing magnetic pillars and using magnetic beads of large sizes (e.g. 2 μm in diameter). As predicted by eq. (7.5), v_m can also be increased by increasing the injected current as well;
3. Reducing the flow velocity as the trapping rate decreases with increasing the flow rate (see Fig. 7.44d);
4. Applying an external uniform magnetic field from a permanent magnet or electromagnet to magnetize beads located very far from the center of the device,

i.e. where the device is not able to magnetize them. In this case the magnetic field gradient generated by the device can generate the force required to move the beads (see Fig. 7.38).

5. The last option is to increase the conductor density of the micro-coil i.e. increasing the fill factor to extend the capture radius to the edges of the fluidic chamber. In other words, this requires either an increase in the active area of the device for a given microfluidic chamber, or a decrease in the size of the microfluidic chamber for a given micro-coil of fixed size.

It was shown in §7.3.7 that the capture radius of one turn of the MS1 micro-coil (two conductors carrying equal currents in opposite directions) is $\sim 45 \mu\text{m}$ (at $I = 150 \text{ mA}$). Moreover, in sections §4.7.1 and §4.8.1 it was shown that the number of turns of the meander type does not contribute to increasing the magnetic flux density of the micro-coil, in particular near its surface (see Fig. 4.57). Therefore, adding one turn to the structure of a meander micro-coil (e.g. MS1) increases the active area of the device with the capture cross-section area of one turn. The capture radius of the device is extended transversally with $\sim 45 \mu\text{m}$ (i.e. along the x -direction which is perpendicular to the conductor which oriented along the y -axis). On the other hand, the capture radius of a spiral micro-coil (e.g. CS1) is $\sim 500 \mu\text{m}$ (at $I = 150 \text{ mA}$) which is much larger than the radius of the spiral itself ($220 \mu\text{m}$). This means not only that the spiral micro-coil can easily concentrate and focus the magnetic beads at its center, but it also effectively confines and traps beads located at large distances (e.g. $500 \mu\text{m}$) from the center. Furthermore, in § 4.7.2 it was shown that the magnetic field is proportional to the number of turns N of the spiral micro-coil and the magnetic energy density gradient is proportional to N^2 . This implies that, in addition to the options mentioned above, one can capture the beads by optimizing the ratio between the total surface area of the

micro-coil and that of the fluidic chamber, as highlighted previously (see point 5 in the list above). This can be particularly true in the case of the spiral micro-coil, where the ratio between the surface area of the coil and that of the chamber will be small (e.g. 0.4).

It was also demonstrated and discussed earlier, that the magnetic force is a long range force and it was shown that the studied micro-devices were able to trap/move magnetic beads suspended in different fluid layers, i.e. at different distances from the device surface (the plane $z=0$), as discussed in §7.3.5. If the device has a meander micro-coil in its structure the fluidic channel can be 50 μm deep. On the other hand, the channel can be up to 350 μm deep when a spiral micro-coil with a magnetic pillar is employed.

7.4.2 The influence of the magnetic pillars on the device performance

All the presented micro-coil designs were studied theoretically, simulated by FEA, fabricated and tested in three versions namely: micro-coils without magnetic pillars, with magnetic pillars and with magnetic pillars and a backside plate. Adding magnetic pillar(s) in the magnetic system is an important factor in enhancing the overall performance of the magnetic devices presented in this thesis. This is because the magnetic pillar plays the role of the magnetic core in the conventional solenoid, and therefore, it concentrates and focuses the magnetic flux in a small spatial location (micrometer size pillar) by creating a low reluctance path that reduces the flux leakage (as compared with the case when no pillar is used). Consequently, the addition of a magnetic pillar in the center of a micro-coil enhances the magnetic field, field gradient and the magnetic force exerted by the micro-coil unto a magnetic particle and this ultimately results in a significant increase of the magnetic particle trapping rate and particle confinement. This was shown through the comprehensive FEA simulation

presented in Chapter 5 and was experimentally verified in this Chapter (Chapter 7), when magnetic bead trapping was demonstrated using our magnetic devices.

The influence of the magnetic pillar on the device performance was analyzed in two ways: First, the trapping rate of magnetic particles for micro-coils with pillars was compared to that of the micro-coils without pillars and the increase for the former case was evident, as shown in Table 7.7. Secondly, we also studied and measured the confinement/focusing of particles that resulted from the deep potential wells created by the pillars. This 3-dimensional motion was first predicted by the FEA results shown in Figs. 5.6 and 5.23 and then visualized in our experiments. The FEA simulation results also showed the favorable influence of the pillars on the magnetic force by increasing the magnitude of the x and z - components of the magnetic force, as shown in Figs. 5.20 and 5.22. For example, the magnetic force exerted on a magnetic particle is increased from 42 to 1500 pN along the x -direction and from 200 to 3000 pN along the z -direction, for an injected current of 100 mA, when inserting a magnetic pillar at the center of a spiral micro-coil. This example shows the significant increase in the magnetic force, especially along the x -direction, which can be achieved by adding a magnetic pillar ($F_{magx}(\text{with pillar}) = 35.7 F_{magx}(\text{without pillar})$ and $F_{magz}(\text{with pillar}) = 15 F_{magz}(\text{without pillar})$). In the spiral micro-coil the z -component of the magnetic force dominates over the

x -component: $\left(\frac{F_{magz}}{F_{magx}} \right)_{\text{without pillar}} \approx \frac{200}{42}$. This implies that, in the case without a

magnetic pillar the trapping of magnetic particles in the z -direction is dominated by the

motion of the beads, whereas, in its presence $\left(\frac{F_{magz}}{F_{magx}} \right)_{\text{with pillar}} \approx \frac{3000}{1500}$, and the x -

directional motion of the particles becomes more significant. This force enhancement

results in a significant deepening of the magnetic potential well, which in turn leads to a 3-dimensional projectile movement of the magnetic particle.

Furthermore, this thesis work has successfully demonstrated both theoretically and practically that creating a magnetic backside plate beneath the micro-coil also significantly increases the resultant magnetic field by confining the backside-magnetic flux lines which, otherwise, are considered as a leakage. Therefore, the presence of a magnetic backside plate provides an additional low reluctance path, besides that provided by the pillar, and this enables confinement of all the flux lines in the pillar, as shown in Figs. 5.13-5.18. This combination close the magnetic circuit as discussed earlier. As a result, the device performance has been dramatically improved by increasing the trapping rate of the particles as shown in Table 7.7 and Fig. 7.46 and this proves again the earlier proposed model of confining the magnetic field.

7.4.3 Magnetic beads manipulation

Different design arrangement (arrays) of micro-coils were studied and tested in this dissertation and their corresponding bead manipulation was demonstrated as summarized below.

MS2: Two interdigitated meander micro-coils

The magnetic beads were aligned in alternating manner between two locations. It was observed that all the magnetic beads were initially aligned at the first potential well site (e.g. the inner loop through which current was injected). Then, when the current was switched on only in the second loop, all the magnetic beads re-aligned with the second potential well created by the second loop (see Fig. 7.33). A moderate current intensity (i.e. 60-100 mA) injected successfully in the loops was enough to actuate the beads. It was observed from the magnetic beads motion between the two micro-coils that the MS2 design can be effectively used as a passive mixer in a microfluidic channel,

Figure 7.46: Trapping rates for three main types of micro-coils for different structures: without magnetic pillars, with magnetic pillars and with magnetic backside plate.

as it is well known that mixing fluids at the micro-scale is not nearly as simple as at the macro-scale. At very small dimensions, the Reynolds number of a fluid is usually quite small and no turbulence occurs. As a result, streams of fluid do not interfere with each other and the mixing of fluid streams does not occur to an appreciable extent. The only driving force for mixing is diffusion. The micro-coil configurations, in particular MS2, offer a good alternative to fluid mixing by making use of magnetic particles to stir liquids, increasing their diffusion contact surface area. Small magnetic particles can be rapidly moved from side-to-side by either switching the current on and off or by reversing current directions in micro-coil configurations. Furthermore, the chaotic perturbation of the suspension would enhance and maximize the probability of the attachment of the functionalized magnetic beads to the bio-molecular target rather than performing this step outside the chip.

MM2: 2-phase array of meander micro-coil with circular loops

A magnetic potential well was created in the center of each loop of one row as shown in Fig. 7.36. This allowed the beads to be accumulated there and when the current was switched on into the other row the beads moved to the new potential well that was created. The step size for this movement is equal to one diameter of the loop (e.g. 20 μm).

CS1 & SS1: 3-phase spiral array

Using a 3-phase array (but other numbers larger than three can be used, too) of the micro-coil CS1/SS1 and by applying an external uniform magnetic field to create a magnetic moment in the magnetic bead, long range magnetic bead transport was achieved (e.g. for a distance of 150 μm). The magnetic pillars within the structure of the device helped in extending the range of influence by moving/trapping beads located outside the local coil's area. The capture radius of the device was extended in

comparison with that of the spiral micro-coil which was able to trap only the beads located within the local area of the micro-coil. The results of magnetic bead manipulation successfully prove the proposal and satisfy the objectives of the thesis.

7.4.4 Other functions of superimposed micro-coils (CS2)

Two concentric micro-coils can also be used for various other purposes too. The outer large micro-coil magnetizes the beads, i.e. creates a magnetic moment within the particle, which allows an easy trapping by the magnetic field gradient created by the inner micro-coil (with pillar). The current in the outer micro-coil can be optimized to the minimum intensity value at which the particle reaches the maximum saturation. Using this arrangement of superimposed micro-coils one can expect an increase in the capture radius of the system and consequently an increase in the trapping rate. The outer micro-coil can occupy a large area in the fluidic channel or several concentric micro-coils can be superimposed in the same manner to maximize the efficiency of the device. The magnetic particles can reach their maximum magnetization by applying an external magnetic field. Creating a weak magnetic field at the vicinity of the surface of the fluidic chamber (e.g. $\sim 8 \times 10^{-4}$ A/m) was sufficient to create a magnetic moment in the particles. The outer micro-coil for this purpose can be a winding of any shape such as a circular, square or meander structure, as shown in Fig. 7.47a. A meander/spiral micro-coil surrounding an array of spiral micro-coils (CS1-type) can also be employed to generate a global magnetic field for bead magnetization (Fig. 7.47b). In this arrangement the outer micro-coil replaces the permanent magnet used to apply an external magnetic field as discussed in § 7.3.6.3 (see Fig. 7.38). The magnetic flux of the outer micro-coil in this case has less effect on magnetization of the pillar because its most inner loop is far away from the pillar. Fig. 7.48 shows the magnetic flux profiles and flux line contours of the outer meander micro-coils.

Figure 7.47: Schematic illustration of: (a) A circular meander micro-coil surrounding a spiral micro-coil. The former generates the magnetic field required for the beads magnetization whereas the latter traps them; (b) A meander micro-coil surrounding an array of spiral micro-coils. Again, the former generates the magnetic field required for the beads magnetization whereas the latter transports them due to the magnetic field gradient generated.

7.4.5 Biomolecular applications

Magnetic bead trapping, transportation and detection have been discussed in detail in this dissertation. The design, structure and properties of the various devices realized and successfully tested in this research study create a wide platform for several applications in the separation, manipulation and detection of biomolecular particles and compounds. These devices can be an effective core component in a more complex total micro-analysis system. One of the possible uses for these devices is the separation of different types of bio/chemical materials from their surrounding environments such as: DNA, RNA, enzymes, proteins, chemical agents, rare cells (e.g. cancer cells) and other bio/chemical compounds. The separation of the target can be performed with a small volume of sample and in continuous flow conditions to achieve high sample throughput and selectivity with an automated process, without the need for elaborate protocols and expensive equipments and consumables. The small features of the devices and their ability to generate high magnetic energy gradients allow fast and efficient immunoassay procedures that are routinely used in the biomolecular laboratories.

7.5 Summary

This chapter demonstrates successfully the achievement of satisfying the proposed objective and ultimately reaching the goals of realizing the magnetic system. Trapping of magnetic particles was demonstrated and achieved by using all the proposed and realized devices with/without magnetic pillars and with/without magnetic backside plates. Transportation of magnetic beads for short and long distances was also demonstrated using different designs. To avoid repetition, the overall conclusions including those related to this chapter are all listed in the next chapter.

Figure 7.48: Magnetic flux profile (a) and flux line contours (b) for a meander micro-coil with circular shape. Magnetic flux profile (c) and vectors (d) in a plane parallel to the surface at a vertical distance of $1\ \mu\text{m}$ of an inner spiral and outer meander micro-coils carrying currents of 150 and 50 mA, respectively. Magnetic flux lines (e) and vectors (f) in a plane perpendicular to the surface of the same micro-coils.

CHAPTER 8

CONCLUSIONS AND RECOMMENDATIONS

8.1 Summary

In this thesis, a micro-system for magnetic particle separation, transportation and guiding based on an original micro-coil design has been proposed, designed, fabricated and successfully demonstrated. The unique MEMS-fabrication process used to implement and realize embedded micro-coils in silicon proposed and demonstrated in our original micro-coil design offers many advantages over other processes. To our knowledge, we have reported the first embedded high aspect ratio magnetic devices with unique structures, designs and materials that generate the highest reported magnetic field gradients. This multidisciplinary thesis work offers improvements in BioMEMS magnetic trapping, separation, and transportation and takes the immunomagnetic assay a step further.

8.2 Conclusions

The following specific conclusions could be drawn from the results of this research work:

1. Because of their small size micro-coils are excellent tools for producing high magnetic field gradients and therefore they are capable to generate strong localized and tunable magnetic forces for magnetic particle manipulation;
2. Integrating ferromagnetic pillar(s) within the structure of the planar micro-coils increases the stored energy of the system and a large magnetic field gradient will be created at the surface of the pillars, in comparison with the device without pillars;

3. The magnetic pillars confine the magnetic flux in a very small spatial location which leads to the creation of a deep magnetic potential well at that location;
4. Trapping magnetic particles was achieved under both static and continuous flow conditions and the maximum flow rate at which the device was still able to trap the particles was 120 $\mu\text{l}/\text{min}$ for the spiral micro-coil with pillar and trapping rates up to 84% were achieved;
5. Integrated sensing micro-coils were successfully used to detect the trapping rate of the magnetic particles;
6. Micro-coils were capable to trap magnetic particles suspended in the fluidic layer that were situated far away ($\sim 200\text{ }\mu\text{m}$) from the surface. This excellent performance even in very high microfluidic channels is due to the magnetic force's long range of action;
7. The micro-coils reported in this study have large capture radii: magnetic particles situated within the micro-coil xy -plane as far away as $500\text{ }\mu\text{m}$ from the center of the spiral micro-coil were captured;
8. Three magnetic particle transport modes were demonstrated using our magnetic devices with transport step sizes of: $6\text{ }\mu\text{m}$, $20\text{ }\mu\text{m}$ and $150\text{ }\mu\text{m}$;

8.3 List of original contributions

To our knowledge, the novel achievements realized for the first time during this thesis work are:

1. A comprehensive comparison of different designs of planar micro-coils based on thorough theoretical and FEA analyses, including the calculation and simulation of their corresponding magnetic flux

- profiles, magnetic field gradients, magnetic energy density gradients and developed magnetic forces;
2. New superimposed micro-electromagnets designs which can be used to manipulate magnetic particles with various degree of freedom of movement;
 3. Generating large magnetic field gradients (up to 20 T/mm) and large magnetic forces (in the range of 10^{-8} Newton) on magnetic particles;
 4. A new magnetic circuit structure based on the combination of high aspect ratio planar micro-coils and ferromagnetic pillars and back-plates for focusing the magnetic flux;
 5. A new fabrication process for producing magnetic devices, with micro-coils embedded in silicon, which based on DRIE, electroplating, CMP and electroless plating;
 6. MEMS magnetic pillars made of the ternary alloy CoNiP (reported as magnetic thin films);
 7. Fabrication process for producing bonding pads using a mesh of Cu-filled trenches embedded in silicon and covered at the top with a layer of Al for easier wire bonding;
 8. Trapping magnetic particles with the previous mentioned micro-coils under continuous flow conditions with a long range magnetic force influence in both the horizontal and vertical directions;
 9. Demonstrating short and long range transportation of magnetic particles

8.4 Outlook

The immediate applications of this work are in the field of biomolecular separation and manipulation. However, in addition to such usages, the devices structures and their characteristics are very attractive and suitable for a whole new range of applications other than those previously discussed in this thesis, such as:

1. In-vivo nuclear-magnetic resonance imaging (NMR) analysis of small volume samples;
2. Actuation of various MEMS devices such as micro-mirrors, switches, fluidic valves and micro-motors;
3. Manipulation of ferrofluids in microfluidic channels;
4. Inductors for RF and high frequency applications;
5. Magnetic self-assembly: the benefit of this approach is that micro-components fabricated from various materials, e.g. made of III-V semiconductors, can be assembled onto a large substrate. The binding energy in this case is the magnetic energy. The receptor binding sites on the substrate act as potential-energy wells for the micro-components to be assembled. The process of assembly, which is very similar to the process of the magnetic particle trapping, can be performed in a fluidic environment as it would reduce the surface interaction effect. The components to be assembled in this case should have a magnetic structure/film (which can be added at in their final step of their processing) to enable the attractive force to guide them to the potential wells. When the binding sites come into contact there will be a large probability that the micro-component falls into the energy well created by the current-carrying conductors (micro-

coils) and align themselves in the template, or would be transported by the fluid to be captured in another downstream well.

The fabrication processes adapted in realizing these devices are CMOS compatible and can be reproduced in normal cleanroom facilities. In addition, these characteristics allow the integration of any desired devices with systems and circuits towards a “system in package” scheme, and this opens a wide platform for using these devices in the applications listed above.

8.5 Recommendations for further research

The work and the techniques adapted and discussed through this thesis and the results obtained are very versatile, very efficient and open many directions of research and other investigations possibilities. Based on this study, the following applications can be further investigated:

1. Fractionation of various types of magnetic beads based on their magnetic susceptibilities. This would allow the fractionation of a mixture of bio/chemical compounds, not just separation of a single type of particles from the mixture;
2. Integration of the magnetic devices with other analytical and microfluidic devices towards the realization of “Lab-on-a-chip” micro-system.
3. Investigation of the parameters which influence the mass flow during the magnetic bead transport from one spot to another. This concept seems to be acting as a “magnetofluidic transistor”. We have noticed this effect and started the work on this topic after the concept was established in this thesis and therefore further work is required to fully elucidate this phenomenon and apply it in a practically useful device.

List of author's publications

1. **Qasem Ramadan**, Victor Samper and Daniel Poenar, An integrated microfluidic platform for manipulation of magnetic carriers, Pacific Polymer Federation IX meeting, Maui (Hawaii, USA), 11-14 Dec, 2005, (Invited paper).
2. **Qasem Ramadan**, Victor Samper, Daniel Poenar and Chen Yu, Fabrication of three-dimensional magnetic micro-devices with embedded micro-coils for magnetic potential concentration, *J. Microelectromechanical Systems*, in press.
3. **Qasem Ramadan**, Victor Samper, Daniel Poenar and Chen Yu, An Integrated Microfluidic Platform for Magnetic Microbeads Separation & Confinement, *Biosensors and Bioelectronics*, 2005, in press (available online).
4. **Qasem Ramadan**, Victor Samper, Daniel Poenar and Chen Yu, Microcoils for transport of magnetic beads, *Applied Physics Letters*, 88, 032501, 2006.
5. **Qasem Ramadan**, Daniel Poenar, Victor Samper, and Chen Yu, Evaluation of current-carrying conductors for manipulation of magnetic micro/nano particles for biomedical application, *International Journal of Nanotechnology*, 4(4) 489-499, 2005.
6. **Qasem Ramadan**, Victor Samper, Daniel Poenar and Chen Yu, Integrated Microfluidic Platform for Magnetic-based Biomolecular Separation, *Biomedical Micro devices*, 2005 (In press).
7. **Qasem Ramadan**, Soft & hard magnetic layers for micro manipulation in bio & electronic applications, Workshop on self assembly, Institute of Microelectronics, Singapore 1 April, 2005.
8. **Qasem Ramadan**, Victor Samper, Daniel Poenar, Zhu Liang Chen Yu and Lim Tit Meng. Simultaneous cell lysis and bead trapping in a continuous flow microfluidic mevice, *Sensor Actuat B-Chem*, 113, 944-955, 2005.

9. **Qasem Ramadan**, Daniel Poenar, Victor Samper, and Chen Yu, Evaluation of current-carrying conductors for manipulation of magnetic micro/nano particles for biomedical application, 1st International Conference on the Nanotechnology, Singapore 13-17 July, 2004.
10. Victor Samper, **Qasem Ramadan**, Microfluidic sample preparation for nucleic acid analysis, CAS 2004, Romania, (Invited paper).
11. **Qasem Ramadan**, Victor Samper, Poenar Daniel, and Chen Yu, On-chip micro-electromagnets for magnetic-based bio-molecules separation, *J. Magnet. Magn. Mat.*, 281(2-3), 2004, 150-172.
12. **Qasem Ramadan**, Victor Samper, Daniel Poenar and Chen Yu, Integrated Microfluidic Platform for Magnetic-based Biomolecular Separation, 3rd International Conference on Materials for advanced Technologies (ICMAT), 3-8 July, Singapore 2005.
13. **Qasem Ramadan**, Poenar Daniel, Chen Yu, and Victor Samper, Magnetic micro-devices for bio-molecular separation and transportation utilizing magnetic microspheres, Estapor Microsheres n^o 10, Merck newsletter, 2004.
14. **Qasem Ramadan**, Victor Samper, and Daniel Poenar Puiu, Magnetic based μ -fabricated system for manipulation of micro/nano particles for biomolecular applications, EEE Bulletin, Nanyang Technological University, Singapore, 2004.
15. **Qasem Ramadan**, Chen Yu, Victor Samper, and Poenar Daniel, Magnetic micro-system for biomolecular separation and transportation, Symposium on Microelectronics, Institute of Microelectronics, September 2003, Selected as best paper.
16. **Qasem Ramadan**, Victor Samper, Pavel Neuzil, Lesaicherre Marie, Lim Tit Meng, Heng Chew Kiat, Yao Shao Qin, Poenar Daniel Puiu. Optomization of

On-Chip Micro-Electromagnets for Biomolecular Separation. Proceedings of IEEE sensors 11-14, June, 2002, Orlando, Florida, USA.

17. **Qasem Ramadan**, Victor Samper, Zhu Liang, Daniel Poenar Puiu Lim Tit Meng, Heng Chew Kiat, Christina Teh, Chen Yu. Microfluidic DNA sample preparation by Dielectrophoresis and Electroporation. Proceedings of EuroSensors XVI, 14-18 September 2002, Prague, Czech Republic.
18. H. M. Ji, V. D. Samper, W. M. Shu, **Qasm Ramadan** and Y. Chen, Microfluidic bead based valve, Proceedings of EuroSensors XVI, 14-18 September 2002, Prague, Czech Republic.
19. M. Lesaicherre, L. P. Tan, A. J. Rufaihah, Y. J. G. Chen, L. Zhu, C. K. Heng, T. Yan, T. M. Lim, **Qasem Ramadan**, D. Poenar, V. D. Samper, H. K. Lee and S. Q. Yao, Fast Nucleic Acid Extraction on a Microchip Device, BioMed Asia 19-21, Singapore (2001).

PATENTS

1. **Qasem Ramadan**, Victor Samper, Chen Yu, and Daniel Poenar, Microfabricated system for magnetic field generation and focusing, US Patent Application No: 10/988,266, International Application No: PCT/SG2005/000184.

Bibliography

1. I. L., Weissman, Translating stem and progenitor cell biology to the clinic: Barriers and opportunities. *Science*, 287, 2000, 1442-1446.
2. M. B. Koh; H. G. Prentice; M. Corbo; M. Morgan; F. E. Cotter; M. W. Lowdell. Alloantigen-specific T cell depletion in a major histocompatibility complex fully mismatched murine model provides effective graft-versus-host disease prophylaxis in the presence of lymphoid engraftment. *Br. J. Haematol.*, 118, 2002, 108-116.
3. T. Murohara, H. Ikeda; J. Duan; S. Shintani; K. Sasaki; H. Eguchi; I. Onitsuka; K. Matsui; T. Imaizumi. Transplanted cord blood-derived endothelial precursor cells augment postnatal neovascularization. *J. Clin. Invest.*, 105, 2000, 1527-1536.
4. H. Shapiro, *Practical Flow Cytometry*; Wiley: New York, 1995; pp 1-2.
5. Q. Ramadan, V. Samper, D. Poenar, Z. Liang, C. Yu , T.M. Lim. Simultaneous cell lysis and bead trapping in a continuous flow microfluidic device. *Sensors and actuators B*, 2005 (Accepted).
6. L. R. Moore, M. Zborowski, L. Sun, and J. J. Chalmers, Lymphocytes fractionation using immunomagnetic colloid and a dipole magnet flow cell sorter, *J. Biochem. Biophys. Methods*, 37(1-2), 1998, 11-33.
7. W. H. wing, On neutral particle trapping in a quasistatic electromagnetic fields, *Prog. Quant. Electro*, 8, 1984, 181-199.
8. R. Becker, *Electromagnetic fields and interactions*, New York: Dover Publications, 1982, pp.112
9. N. E. Kay, M. O. Ackerman, and D. Douglass, Anatomy of the immunesystem.

- Semin. Hematol.* 16, 1979, 252-282.
10. S. Gupta and R. A. Good, Marks of human lymphocyte subpopulations in primary immunodeficiency and lymphoproliferative disorders. *Sem. Hematol.* 17 (1), 1980, 1-29.
 11. T. E. Fisher, A. F. Oberhauser, M. Carrion-Vazquez, P. E. Marszalek, and J. M. Fernandez, The study of protein mechanics with the atomic force microscope. *Trends Biochem. Sci.* 24, 1999, 379–384.
 12. P. Cluzel, DNA: an extensible molecule. *Science* 271, 1996, 792–794.
 13. R. J. Davenport, G. J. Wuite, R. Landick & C. Bustamante, Single-molecule study of transcriptional pausing and arrest by *E. coli* RNA polymerase. *Science* 287, 2000, 2497–2500.
 14. S. B. Smith, L. Finzi. & C. Bustamante, Direct mechanical measurements of the elasticity of single DNA molecules by using magnetic beads. *Science* 258, 1992, 1122–1126.
 15. K. Svoboda, C. F. Schmidt, B. J. Schnapp and S. M. Block, Direct observation of kinesin stepping by optical trapping interferometry. *Nature* 365, 1993, 721–727.
 16. J. M. Crowley, *Fundamentals of Applied Electrostatics*, Wiley, New York, 1986
 17. C. Bustamante; J. C. Macosko; and G. Wuite. Grabbing the cat by the tail: Manipulation molecules one by one. *Nature*, November, 2000, 130-136.
 18. F. M. Ali. *Separation of human blood and bone marrow cells*, Bristol, 1986, pp. 1-25.
 19. H. Andersson, W. Wijngaart, P. Enoksson and G. Stemme. Micromachined flow-through filter-chamber for chemical reactions on beads. *Sensors and Actuators B*: 67, 1-2, 2000, 203-208

20. R. D. Oleschuk, A. B. Jemere, L. L. Shultz-Lockyear, F. Fajuyigbe and J. Harrison, Utilization of beads based reagents in microfluidic system. *Proceedings of the μ TAS Symposium*, 11, 2000, 11-14.
21. J. K. Tu, T. Huen, R. Szema, and M. Ferrari, Filtration of sub-100 nm particle using a bulk-micromachined direct-bonded silicon filter. *J. Biomedical microdevices*, 1(2), 1999, 113-119.
22. X. Yang, J. M. Yang, Y. C. Tai, and C. M. Ho, Micromachined membrane particle filters. *Sensors and actuators A*: 73, 1999, 184-190.
23. J. P. Brody, T. O. Osborn, K. K. Froster, and P. Yager, A planar microfabricated fluid filter. *Sensors and actuators A*, 54, 1996, 704-708.
24. T. Desai, D. J. Hansford, L. Kulinsky, A. H. Nashat, J. Tu, W. Yuchun, M. Zhang, and M. Ferrari, Nanopore technology for biomedical application. *Biomedical microdevices* 2(1), 1999, 11-40.
25. C. D. Platsoucas, R. A. Good, and A. S. Gupta. Separation of human T lymphocyte subpopulations by density gradient electrophoresis. *Proc. Natl. Acad. Sci. USA*, 1979, 1972-1976.
26. A. R. Timerbaev. Recent advances and trends in capillary electrophoresis of inorganic ions. *Electrophoresis*, 23, 2002, 3884-3906.
27. P. R. Haddad, P. Doble and M. Macka. Developments in sample preparation and separation techniques for the determination of inorganic ions by ion chromatography and capillary electrophoresis, *J. Chromatography A*, 856, 1999, 145-177.
28. P. E. Jackson, P. R. Haddad. Capillary electrophoresis of inorganic ions and low-molecular-mass ionic solutes, *Trends Anal. Chem.* 12, 1993, 231-238.
29. V. Kasicka. Capillary electrophoresis of peptides. *Electrophoresis*, 20, 1999,

3084-3105.

30. P. G. Righetti, C. Gelfi, *Capillary Electrophoresis Anal. Biotechnol.* 1996, pp. 431–476, CRC Press, Boca Raton.
31. A. D. Wilson, E. R. Edlard, M. Cooke, and C. F. Poole. *Encyclopedia of separation science*. Academic press, New York, pp. 103-118, 2000.
32. M. A. Rodriguez and D. W. Armstrong. Separation and analysis of colloidal/nano particles including microorganisms by capillary electrophoresis: a fundamental review. *J. Chromatography B*, 800, 2004, 7–25.
33. D. A. Kevin (ed.). *Capillary electrophoresis Guide-book: Principles and practice*. Berlin/New York: Springer-Verlag, 1996.
34. D. R. Baker, *Capillary electrophoresis*. New York, Wiley, 1995.
35. V. M. Okun, B. Ronacher, D. Blaas, and E. Kenndler. Analysis of Common Cold Virus (Human Rhinovirus Serotype 2) by Capillary Zone Electrophoresis: The Problem of Peak Identification. *Anal. Chem.* 71, 1999, 2028-2032.
36. D. W. Armstrong, G. Schulte, J. M. Schneiderheinze, and D. J. Westenberg. Separating Microbes in the Manner of Molecules. 1. Capillary Electrokinetic Approaches, *Anal. Chem.* 71, 1999, 5465 - 5469.
37. J. C. Giddings. The field-flow fractionation family: understanding principles. In: *Field-flow fractionation handbook*, M. E. Schimpf, K. Caldwell, and J. C. Giddings (ed.), Wiley, New York, pp. 3-30, 2000.
38. M. E. Hovingh, G. H. Thompson, and J. C. Giddings. Column parameters in thermal field-flow fractionation. *Anal. Chem.* 42, 1970, 195-203.
39. J. C. Giddings. Nonequilibrium Theory of Field-Flow Fractionation. *J. Chem. Phys.* 49, 1968, 81-85.
40. R. J. Hunter. *Foundation of colloidal science*, Clarendon Press, Oxford, England,

1987.

41. K. D. Caldwell and Y. S. Gao. Electrical field-flow fractionation in particle separation. 1. Monodisperse standards. *Anal. Chem.* 65, 1764-1772, 1993.
42. T. M. Vickrey and J. A. Garcia-Ramirez, Magnetic Field-Flow Fractionation: Theoretical Basis, *Sep. Sci. Technol.*, 15, 1980, 1297-1304.
43. J. C. Giddings, F. J. Yang, and M. N. Myers. Sedimentation field-flow fractionation, *Anal. Chem.* 46, 1974, 1917-1924.
44. J. Ashkin. Acceleration and trapping of particles by radiation pressure, *Phys. Rev. Lett.* 24, 1970, 156-159.
45. W. H. Wright, G. S. Sonek, and M. W. Berns. Parametric study of the forces on microspheres held by optical tweezers, *Appl. Opt.* 33(9), 1994, 1735-1748.
46. J. Ashkin, J. M. Dziedzic, J. E. Bjorkholm, and S. Chu. Observation of single-beam gradient force optical trap for dielectric particles, *Opt. Lett.* 1, 1986, 188-190.
47. J. Ashkin, J. M. Dziedzic, and T. Yamane, Optical trapping and manipulation of single cells using infrared laser beams, *Nature* 330, 1987, 769-771.
48. S.C. Grover, A. G. Skirtach, R. C. Gauthier, and C. P. Grover, Automated single-cell sorting system based on optical trapping, *J. Biomed. Optics* 6(1), 2001, 14-22.
49. R. Steubing, S. Cheng, W. H. Wright, Y. Numajiri, and M. W. Berns, Laser-induced cell fusion in combination with optical tweezers: The laser-cell fusion trap, *Cytometry* 12, 1991, 505-510.
50. H. Liang, W. H. Wright, S. Cheng, W. He, and M. W. Berns, Micromanipulation of chromosomes in PTK2 cells using laser microsurgery (optical scalpel) in combination with laser-induced optical forces (optical tweezers), *Exp. Cell Res.*

204, 1993, 110-120.

51. H. A. Pohl, *Dielectroporesis*, Cambridge University Press, 1978.
52. R. Pethig. Dielectrophoresis: using inhomogeneous AC electrical fields to separate and manipulate cells, In: *Critical reviews in biotechnology*”, 16, 1996, 331-348.
53. M. P. Hughes. *Nanoelectromechanics in engineering and biology*, CRC Press, London, pp. 15-50, 2002.
54. M. P. Hughes, R. Pethig, X. P. Wang. Dielectrophoretic forces on particles in traveling electric field, *J. Phys. D: Appl. Phys.* 29, 1996, 474-482.
55. Y. Huang, R. Holzel, R. Pethig and X. Wang. Differences in the AC electrodynamics of viable and non-viable yeast cells determined through combined dielectrophoresis and electrorotation studies, *Phys. Med. Biol.* 37, 1992, 1499-1517.
56. R. Hölzel, Non-invasive determination of bacterial single cell properties by electrorotation, *Biochimica et Biophysica Acta (BBA) - Molecular Cell Research*, 1450, 1999, 53-60.
57. F. F Becker, X Wang, Y Huang, R Pethig, J Vykoukal, and PRC Gascoyne, Separation of Human Breast Cancer Cells From Blood by Differential Dielectric Affinity, *Proc. Nat. Acad. Sc.* 92, 1995, 860-864.
58. Y. Huang, K. Ewalt, M. Tirado, R. Haigis, A. Forster, D. Ackley, M.Heller, J. O’Connel, and M. Krihak, Electric manipulation of bioparticles and macromolecules on microfabricated electrodes, *Anal. Chem.*, 73, 2001, 1549-1559.
59. T. Muller, A. Gerardino, T. Schnelle, S. G. Shirley, F. Bordoni, G. De Gasperis, R. Leoni and G. Fuhr, Trapping of micrometer and sub-micrometer particles by

- high frequency electric fields and hydrodynamic forces, *The Journal of Physics, D: Applied Physics*, 29, 1996, 340-349.
60. M. Washizu, S. Suzuki, O. Kurosawa, T. Nishizaka, and T. Shinohara, Molecular dielectrophoresis of polymers, *IEEE Trans. On Industry applications*, 30, 1994, 835-843.
 61. Pethig and D B Kell, The passive electrical properties of biological systems: their significance in physiology, biophysics and biotechnology, *Phys. Med. Biol.* 32, 1987, 933-970.
 62. Y. Tsong, Electroporation of cell membranes: Mechanism and applications" in: *Electroporation and electrofusion in cell biology*, E. Neumann, A. Sowers, and C. Jordan, Ed, Plenum Press, New York 1989, pp. 149-163.
 63. E. Neumaa, A. E. Sowers, and C. A. Jordan, *Electroporation and electrofusion in cell biology*, Plenum Press, 1989.
 64. F. F. Becker, X -B Wang, Y Huang, R Pethig, J Vykoukal, P R C Gascoyne. The removal of human leukaemia cells from blood using interdigitated microelectrodes, *J. Phys. D: appl. Phys.* 27, 1994, 2659-2662.
 65. I. Safarik and M. Safarikova, Overview of magnetic separations used in biochemical and biotechnological applications, In: *Scientific and clinical applications of magnetic carriers*, U. Hafeli, W. Schutt, J. teller, and M. Zborowski (Eds.), Plenum Press, New York, pp. 323-340,1997.
 66. M. D. Graham, Efficiency comparison of two preparation mechanisms for magnetic separation of erythrocytes from whole-blood, *J. Appl. Phys.* 52, 1981, 2578-2580.
 67. M. Takayaso, D. R. Killand, J. V. Minervini, Continuous magnetic separation of blood components from whole blood. 16th International conference on magnet

technology, Florida, USA, 1999.

68. A. Kuznetsov, V. I. Filippov, O. A. Kuznetsov, V. G. Gerlivanov, E. K. Dobrinsky and S. I. Malashin, New ferro-carbon adsorbents for magnetically guided transport of anti-cancer drugs, *J. Magn. Magn. Mater.*, 194, 1999, 22-30.
69. A. W. Arnold, P. Hulin, R. J. Klein, H. Renz, F. G. Parak, C. Bergemann and A. S. Lübke, Magnetic mitoxantrone nanoparticle detection by histology, X-ray and MRI after magnetic tumor targeting, *J. Magn. Magn. Mater.*, 225, 2001, 187-193.
70. S. B. Field, J. W. Hand, *An introduction to the practical aspects of clinical hyperthermia*, London: Taylor and Francis, 1990.
71. D. W. Inglis, R. Riehn, R. H. Austin, and J. C. Sturm, Continuous microfluidic immunomagnetic cell separation, *Appl. Phys. Lett.*, 85, 2004, 5093-5095.
72. T. Deng, M. Prentiss, and G. M. Whitesides, Fabrication of magnetic microfiltration systems using soft lithography, *Appl. Phys. Lett.*, **80**, 2002, 461-463.
73. J. W. Choi, K. W. Oh, A. Han, N. Okulan, C. A. Wijayawardhana, C. Lannes, S. Bhansali, K. T. Schlueter, W. R. Heineman, H. B. Haslall, J. H. Nevin, A. J. Helmicki, H. T. Henderson, and C. H. Ahn, *Biomedical Microdevices*, **3**, 191 (2001).
74. H. Lee, A. M. Purdon, and R. M. Westervelt, Manipulation of biological cells using a microelectromagnet matrix, *Appl. Phys. Lett.*, **85**, 1063 (2004).
75. Jiles, *Introduction to magnetism and magnetic materials*, Chapman and Hall, London, 1991.
76. G. Bertotti, *Hysteresis in magnetism*, Academic Press, San Diego, pp.3-29, 1998.
77. J. Guedsdon, and A. Avrameas, magnetic solid phase enzyme-immunoassay, *Immunochemistry*, 14, 1977, 443-447.

78. <http://www.dynal.no/>
79. <http://www.bangslabs.com>
80. <http://www.merck.fr/estapor>
81. M. Zborowski, c. B. Fuh, R. Green, L. Sun, and J. J. Chalmers, Analytical magnetophoresis of ferretin-labeled lymphocytes, *Anal. Chem.* 67, 1995, 3702-2712.
82. B. Sinclair, To Bead or Not To Bead: Applications of Magnetic Bead Technology, *The Scientist* 12 (13), 1998, 17.
83. U. Hafeli, W. Schutt, J. teller, and M. Zborowski (Eds.), *Scientific and clinical applications of magnetic carriers*, Plenum Press, New York, 1997.
84. M. Iman. S. S. Celebi, and A. R. Ozdural, Preparation of photooxidized magnetic polystyrene beads for enzyme immobilization, *Reactive Polymers*, 17, 1992, 325-340.
85. H. Kbayashi, and Tmatsunaga, Amino-silane modified superparamagnetic particles with surface immobilized enzyme, *J. coll. Inter. Sci.*, 141, 1991, 505-511.
86. R. Tyaga, and M. N. Gupta, Purification and immbilization of *Aspergillus niger* pectinase on magnetic latex beads, *Biocatalysis and bio transformation*, 12, 1995, 293-298.
87. P. Nyren, Apyrase immobilized on paramagnetic beads to improve detection limits bioluminnometric ATP, monitoring, *J. Biolumin. Chemilumin.*, 9, 1994, 29-34.
88. M. A. Dasilva, H. D. Buuows, S. I. Kazlauskas, Immobilization of acrylimide onto magnetite particles-preparation of magnetic supports for enzyme immobilization, *Materials Letters*, 11, 1991, 96-100.

89. K. Barnes, L. J. Murphy, and A. J. Turner, Immunoseparation of membrane peptidase from pig lung membrane using magnetic beads, *Biochemical society transactions*, 22, 1994, 451S-451S.
90. H. Lochmuller. And L.S. Wigman, Affinity separation in magnetically stabilized fluidized beads: synthesis and performance of packing materials, *separation science and technology*, 22, 1987, 2111-2125.
91. I. Safarik, M. Safarikova, and M. Forsythe, The application of magnetic separation in applied microbiology, *J. applied Bacteriology*, 78, 1995, 575-585.
92. *RaPID Assay, technical Handbook*, Ohmicron, Newtown, USA.
93. B. Grinde, T. O. Jonassen, and H. Ushijima, Sensitive detection of group A rotaviruses by immunomagnetic separation and reverse transcription polymerase chain reaction, *J. Virology Methods*, 55, 1995, 327-338.
94. N. Seesod, J. Lundeberg, and A. Hedrum, Immunomagnetic purification to facilitate DNA diagnosis of plasmodium flaciparum, *J. of clinical Microbiology*, 31, 1993, 2715-2719.
95. G. L. Rorrer, T. Y. Hsein, and J. D. Way, Synthesis of porous-magnetic chitosan beads for removal of cadimium ions from waste water, *Industrial & Engineering Chemistry Research*, 32, 1993, 2170-2178.
96. N. Buske, application of magnetite sols in environmental technology, *Progress in Colloid and Polymer Science*, 95, 1994, 175-180.
97. J. G. Atherton, S. S. Bell, Adsorption of viruses on magnetic particles-I, *Water Research*, 17, 1983, 943-948.
98. V. Hencl, and P. Mucha, The application of High-gradient magnetic separation to water treatment by means of chemically precipated magnetite, *Magnetic and Electrical separation*, 5, 1994, 155-167.

99. L. Pauling, and C. Coryell, The magnetic properties and structure of Hemoglobin Oxyhemoglobin and carbonmonoxy hemoglobin, *Proc. Nat. Acad. Sci.*, 22, 1936, 210-216.
100. T. Higashi, A. Yamagishi, T. Takeuchi, N. Kawaguchi, S. Sagawa, and M. Date, Orientation of erythrocytes in a strong static magnetic fields, *J. Blood*, 82, 4, 1993, 1328-1334.
101. Y. Haik, V. Pai, and C. J. Chen, Apparent viscosity of human blood in a high static magnetic field, *J. Mag. Mag. Mater.* 225, 2001, 180-186.
102. N. Shalygin, S. B. Norina and E. I. Kondorsky, Behaviour of erythrocytes in high gradient magnetic field, *J. Mag. Mag. Mater.* 31, 1983, 555-556.
103. Y. Haik, V. Pai, C.J. Chen, in: W. Shyy, R. Narayanan (Eds.), *Fluid Dynamics at Interfaces*, Cambridge University Press, Cambridge, pp. 439, 1999
104. N. Nakano, J. Ostuka, A. Tasaki, Paramagnetic anisotropy measurements on a single crystal of deoxyhemoglobin, *Biochem. Biophys. Acta*, 278, 1972, 355-371.
105. M. N. Graber, H. M. Widmer, Miniaturized total chemical-analysis systems—a novel concept for chemical sensing. *Sensors and Actuators B-Chem*, 1, 1990, 244–248.
106. K. Huikko, R. Kostianen, T. Kotiaho, Introduction to micro-analytical systems: bioanalytical and pharmaceutical applications, *European Journal of Pharmaceutical Sciences*, 20, 2003, 149–171.
107. P. A. Auroux, D. Iossifidis, D. R. Reyes, A. Manz., Micro total analysis system. 2. Analytical standard operations and applications. *Anal. Chem.* 74, 2002, 2637–2652.
108. J. Khandurina, A. Guttman, Bioanalysis in microfluidic devices. *J. Chromatogr. A* 943, 2002, 159–183.

109. R. Reyes, D. Lossifidis, P. A. Auroux, and A. Manz, Micro total analysis system. Introduction, theory and technology, *Anal. Chem.* 74, 2002, 2623-263.
110. M. J. Madou, *Fundamentals of microfabrication*, 2nd edition, CRC press, 2002.
111. M. Gad-El-Hak, The fluid mechanics of microdevices, *J. Fluids Engineering*, 121, 1999, 5-33.
112. G. E. Karniadakis, and A. Beskok, *Micro flows: Fundamentals and simulation*, Springer, New York, pp. 1-37, 2001.
113. S. D. Senturia, *Microsystem Design*, Kluwer Academic Publishers, 2001.
114. S. M. Speraing, Materials issues in microelectromechanical systems (MEMS), *Acta. Mater.*, 48, 2000, 179-196.
115. Z. J. Yao, S. chen, S. Eshleman, D. Denniston, and C. Goldsmith, Micromachined low-loss microwave switches, *J. MEMS*, 8, 1999, 129-134.
116. H. Toshiyoshi, H. Fujita, Electrostatic microtorsion mirrors for an optical switch matrix, *J. MEMS*, 5, 1996, 231-237.
117. P. Dubois, B. Guldima, M. a. Gretillat, N. F. de Rooji, Electrostatically actuated gas microvalve based on a Ta-Si-N membrane, In: Proceedings of the 14th international conference on microelectromechanical systems (IEEE MEMS'01), Interlaken, Switzerland, 21-25, January, 2001, 535-538.
118. T. N. Pornsin-Sirirak, Y. C. Tai, H. Nassef, C. M. Ho, Flexible paralyne actuator for micro adaptive flow control, In: Proceedings of the 14th international conference on microelectromechanical systems (IEEE MEMS'01), Interlaken, Switzerland, 21-25, January, 2001, 511-514.
119. V. T. Srikar, and S. M. Spearing, Materials selection for microfabricated electrostatic actuators, *Sensors and actuators A*, 102, 2003, 279-285.
120. S. A. Zhou, On forces in microelectromechanical systems, *International Journal*

- of Engineering Science*, 41, 2003, 313–335.
121. H. Fujita, electrostatic and superconducting microactuators, In Proceedings: Micro system technologies'90, Berlin, Germany, pp818, 1990.
 122. H. Fujita and A. Omodaka, Electrostatic actuators for microelectronics, in proceedings: IEEE Micro robots and teleoperators workshop, Hyannis. Mass. Pp 14, 1987, 1-10.
 123. N. Takeshima, K.J.Gabriel, M.Ozaki, J.Takahashi, H.Horguchi, and H. Fujita, Electrostatic parallelogram actuators, in 6th international conference on solid state sensors and actuators (Transducers'91), san Francisco, 63-66, 1991.
 124. M. Babric, Magnetic wires in MEMS and bio-medical application, *J. Magnet. Matter.* 249, 1, 2002, 357-367.
 125. H. Guckel, Progress in magnetic microactuators, *Microsystem Technologies*, 5, 1998, 59-61.
 126. *CRC Handbook of chemistry and physics* (1986), CRC Press, Boca Raton, E119-W135.
 127. R. E. Rosensweig, *Ferrohydrodynamics*, Cambridge University press, London, 1985, pp. 74-99.
 128. R. Becker, *Electromagnetic fields and interactions*. Dover publication Inc. New York, 1982, pp. 112.
 129. M. Zborowski, C. Fuh, R. Green, L. Sun, and J. Chalmers. Analytical magnetophoresis of Ferritin-labeled lymphocytes. *Anal. Chem.* 67, 1995, 3702 – 3712.
 130. J. F. Doyle, Characterization of a magnetic separation process and its application to magnetostatic bacteria, PhD dissertation, 2000.
 131. H. C. Heitmann, In: Y. A. *Industrial applications of magnetic separation*, pp.

- 115, 1979, New York, IEEE Inc.
132. Y. Tereshima, T. Ozaki and M. sekine, removal of dissolved heavy metals by chemical coagulation, magnetic seeding and high gradient magnetic filtration, *Water Research*, 20, 1986, 537-545.
133. R. R. Dauer and E.H. Dunlop, High gradient magnetic separation of yeast, *Biotechnology and bioengineering*, 37, 1991, 1021-1028.
134. G. Bitton and R. Mitche, The removal of Escherichia coli-bacteriophage T7 by magnetic filtration, *Water Research*, 8, 1974, 549-551.
135. G. P. Hatch, and R.E. Stelter, Magnetic design considerations for devices and particles used for biological high-gradient magnetic separation (HGMS) systems, *J. Magn. Magn. Matter.* 225, 2001, 262-276.
136. J. V. Bladel. *Electromagnetic fields*. Hemisphere publishing corporation, Washington. Pp. 173-175.
137. M. R. Spiegel, *Mathematical Handbook of Formulas and Tables*. McGraw-Hill, New York, 1968, pp. 37-39.
138. E. Weber, *Electromagnetic theory*, Dover, New York, 1965, pp.131.
139. M. Misakian, Equations for the magnetic field produced by one or more rectangular loops of wire in the same plane, *J. Res. Nat. Inst. Stand. Tech.*, 105, 2000, 557-564.
140. R. K. Wagsness, *Electromagnetic fields*, Wiely, New York, 1986.
141. I. J. Busch-Vishniac, The case for magnetically driven micro-actuators, *Micromechanical sensors, actuators and systems ASME*, DSC-Vol. 32, 1991, 287-302.
142. M. Drindic, K. S. Johnson, J. H. Thywissen, M. Prentiss, and R. M. westervelt, Micro-electromagnets for atom manipulation, *Appl. Phys. Lett.* Vol. 72, No. 22,

- 1998, 2906-2908.
143. C. Tsouris, T.C. Scott. Floccution of paramagnetic particles in a magnetic field , *J. Colloid. Interface Sci.* 171, 1995, 319-330.
144. X. De latour. Magnetic separation in water pollution control. *IEEE Trans. Magn.* 9, 1973, 314-316.
145. G. H. Hatch, and R. E. Stelter, Magnetic design considerations for devices and particles used for biological high-gradient magnetic separation (HGMS) systems, *J. Magn. Magn. Mater.*, 225, 2001, 262-276.
146. L. Renaud, M. Armenean, L. Berry, P. Kleimann, P. Morin, M. Pitaval, J. O'Brien, M. Brunet, H. Saint-Jalmes, Implantable planar rf microcoils for NMR microspectroscopy, *Sensors and Actuators A-Phys.*, 99, 2002, 244-248.
147. C. R. Neagu; H. V. Jansen; A. Smith; J. G. Gardeniers.; M. C. Elwenspoek, Characterization of a planar microcoil for implantable microsystems, *Sensors and Actuators A-Phys.*, 62, 1997, 599-611.
148. C. C. Sheng, C. T. Pan, H. P. and Chou, Electromagnetic optical switch for optical network communication, *J. Magnet. Magnet. Mater.*, 239, 2002, 610-613.
149. D. J. Sadler, W. Zhang, and C. H. Ahn, Microfabricated semi-encapsulated spiral inductors for microelectromechanical systems applications, *IEEE trans. on Magnetics*, Vol. 33, No. 2, 1997, 3319-3321.
150. US patent 6,495,019,B1. Devices comprising micromagnetic components for power applications and process for forming device.
151. C. H. Ahn, and M. G. Allen, A new toroidal-meander type integrated inductor with multilevel meander magnetic core, *IEEE Trans. Magn.* 30, 1, 1994, 73-79.
152. N. Chomnawang, and J. B. Lee, On-chip 3D micro-inductor for high-frequency applications using deformation of sacrificial polymer, *Proc. SPIE*, Vol. 4334,

- 2001, 54-62.
153. M. Babric, J.J. Mock, A. P. Gray, and S. Schultz, Scanning probe electromagnetic tweezers, *Applied physics letters*, 79(12), 2001, 1897-1899.
154. US patent 6,696,910,B2. Planar inductors and methods of manufacturing thereof.
155. Q. Ramadan, V. Samper, D. Poenar, and C. Yu, On-chip micro-electromagnets for magnetic-based bio-molecules separation, *J. Magn. Magn. Mat.* 281 (2-3), 2004, 150-172.
156. W. Jenks, S. Sadeghi, and J. Wikso, SQUIDS for nondestructive evaluation. *J. Phys. D: Phys.* 30, 1997, 293 – 323.
157. K. E. Peterson, Silicon as a mechanical material. *Proc. IEEE*, 70, 420-457, 1982.
158. K. A. Shaw, Methods of integrating SCREAM micromachined devices with integrated circuits. PhD thesis, Cornell University, 1998.
159. A. A. Ayon, K. S. Chen, S. M. Lohner, S. M. Spearing, H. H. wain, and M. A. Schmidt. Deep reactive ion etching. In: *Materials research society symposium proceedings*, Ed.: A. H. Heuer. and S. J. Jacobs: Materials science of Microelectromechanical systems (MEMS) devices, 1999, Vol. 546.
160. *Surface Technology Systems*, Ltd., Redwood City, CA.
161. Y. Taur and T. Ning, 1998. *Fundamentals of modern VLSI devices*, Cambridge University Press, Cambridge, UK.
162. J. Laier, H. Stori and P. Rodhammer, Plasma assisted chemical vapor deposition of Titanium Nitride in a capacitively coupled radio frequency discharge, *J. Vac. Sci. Techol.*, A-7, 1989, 2952
163. A. Sherman. (1990). Growth and properties of LPCVD Titanium Nitride as a diffusion barrier for silicon device technology, *J. Electrochem. Soc.*, 137, 1892.
164. J. T. Ravnkilde, V. Ziebart, O. Hansen, and H. Baltes. Mechanical

- characterization of electroplated nickel-iron. *Sensors and Materials*, 12(2): 2000, 99–108.
165. J. M. Quemper, S. Nicolas, J. P. Gilles, J. P. Grandchamp, A. Bosseboeuf, T. Bourouina, and E. Dufour-Gergam. Permalloy electroplating through photoresist molds. *Sensors and Actuators A-Phys.*, 74, 1999, 1–4.
166. C. Liu. Development of surface micromachined magnetic actuators using electroplated permalloy. *Mechatronics*, 8, 1998, 613–633.
167. R. Puers, G. Vandevoorde and D. De Bruyker. Electrodeposited copper inductors for intraocular pressure telemetry. *J. Micromech. Microeng.* 10, 2000, 124-129.
168. K. Y. Lee, N. LaBianca, S. A. Rishton, S. Zolgharnain, J. D. Gelorme, J. Shaw, and T. H.-P. Chang. Micromachining applications of a high resolution ultra thick photoresist. *J. Vacuum Science and Technology B*, 13, 1995, 3012–3016.
169. A. B. Frazier and M. G. Allen. Metallic microstructures fabricated using photosensitive polyimide electroplating molds. *J. MEMS*, 2, 1993, 87–94.
170. M. McCormick, E. Chowanietz, and A. Lees. Microengineering design and manufacture using the LIGA process. *Engineering Science and Education Journal*, 1994, 255–262.
171. J. T. Ravnkilde, Metallic microdevices for monolithic integrated Microsystems. PhD Thesis, 2001.
172. N. V. Parthasaradhy. *Practical electroplating handbook*. Pp. 18, Prentice Hall, New Jersey, 1989.
173. K.D. Betyer, W. L. Guthrie, S. R. Markarewcz, E. Mendel, W. J. Patrick, K. A. Perry, W. A. Pliskin, J. Riseman, P. M. Schiabile, C. L. Standley. Chemical-mechanical polishing method for producing coplanar metal/insulator films on a substrate, US Patent 4, 1990, 944,836.

174. W. J. Patrick, W. L. Guthrie, C. L. Standley, P. M. Schiabile. Application of Chemical mechanical polishing to the fabrication of VLSI circuit interconnections. *J. Electrochem. Soc.*, 138 (6), 1991, 1778-1874.
175. H. M. Dalal, R. V. Joshi, H.S. Rathore, and R. Fillipi. A dual damascene hard metal capped Cu and Al-alloy for interconnect wiring of ULSI circuits, *Tech. Dig. IEDM*, 976, 1992.
176. W. Fyen, R. Vos, I. Teerlinck, E. Vrancken, J. Grillaert, M. Meuris, P. Mertens, and M. Heyns, Cleaning, rinsing and drying effects in post Cu CMP clean, CMP-MIC Conference, 507-510, March, 2000, California.
177. P. Wrschka, J. Hernandez, G. S. Oehrlien, and J. King, Chemical mechanical planarization of copper Damascene structures, *J. Electrochemical Society*, 147(2), 2000, 706-712.
178. <http://www.sfamipec.com>
179. <http://www.rodel.com>
180. <http://www.cabotcmp.com>
181. <http://www.kantocorp.com>
182. T. Kouno, M. Hosaka, H. Niwa, and M. Yamada. Effect of Al₃Ti intermetallic compound on electromigration lifetime of Al alloy interconnections. *J. appl. Phys.* 84, 1998, 742-750.
183. H. J. Choi and C. H. Ahn. A bi-directional magnetic microactuator using electroplated permanent magnetic arrays. *J.MEMS*, 11, 1, 2002, 78 –84.
184. C. A. ross, M. Hwang, M. Shima, H. I. Smith, M. Farhoud, T. A. Savas, W. Schwarzacher, J. Parrochon, W. Escoffier, H. N. Bertram, F. B. Humphrey, M. Redjidal. Magnetic properties of arrays of electrodeposited nanowires. *J. Magn. Mag. Materials.* 249, 2002, 200-207.

185. W. Watanabe, M. Edo, H. Hakazawa, E. Yonezawa. A new fabrication process of a planar coil using photosensitive polyimide and electroplating. *Sensors and Actuators A-Phys.*, 54, 1996, 733-738.
186. A. Brenner and G. Riddell. Deposition of nickel and cobalt by chemical reduction, *J. Res. NBS*, 1947, 385-395.
187. E. J. O'Sullivan, A. G. Schrott, M. Paunovic, C. J. Sambucetti, J. R. Marino, P. J. Bailey, S. Kaja, and K. W. Semkow. Electrolessly deposited diffusion barriers for microelectronics. *IBM J. Res. Dev.* 42(5), 1998, 607.
188. W. Riedel, Electroless Nickel plating, ASM International, Finishing publications Ltd., England, 1989, pp. 104-106.
189. G. O. Mallory, J. B. Hajdu. Electroless plating: fundamentals and application. American electroplaters and surface finishers society, Florida, USA,
190. <http://www.dow.com/cyclotene/index.htm>
191. D. A. Hutt, C. Liu, P. P. Conway, D. C. Whalley, and S. H. Mannan, Electroless Nickel Bumping of Aluminum Bond pads, Part I: Surface Pretreatment and Activation, *IEEE trans. Compo. Pack. Techn.* 25(1), 2002, 87-97.
192. M. R. Khan and E. L. Nicholson, Magnetic properties and microstructure of electroless plated Co-Ni-P and Co-P thin films for longitudinal recording, *J. Magn. Magn. Mater.*, 54-57, 1986, 1654-1656.
193. T. S. Narayanan, S. Selvakumar, A. Stephen, Electroless Ni-Co-P ternary alloy deposit: Preparation and characteristics, *Surf. Coat. Technol.*, 172, 2003, 298-307
194. K. Hüller, M. Sydow and G. Dietz, Magnetic anisotropy, magnetostriction and intermediate range order in Co-P alloys, *J. Mag. Mag. mater.*, 53, 1985, 264-274.
195. R. Tarozaitė, G. Stalnionis, A. Sudavicius, M. Kurtinaitiene, Change of magnetic properties of autocatalytically deposited CoNiP films by electrolysis

- simultaneously applied, *Surf. Coat. Technol.* 138, 2001, 61.
196. G. Rivero, M. Multigner, J. M. García, P. Crespo and A. Hernando, Magnetic and structural properties of electrodeposited Co-Ni-P amorphous ribbons, *J. Magn. Magn. Mater.* 177-181, 1998, 121-122.
197. J. H. P. Watson, Magnetic filtration, *J. appl. Phys.* 44 (9), 1973, 4209-4213.
198. A. D. Ebner and J. A. Ritter, New correlation for the capture cross section on High-gradient magnetic separation, *AIChE journal*, 47 (2), 2001, 303-313.