CONTROL OF MAGNETIC PARTICLES IN CENTRIFUGAL MICROFLUDIC PLATFORMS

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Dedication

I dedicated this thesis to my parents, Mahmoud Givehchi and Parvaneh Javdan who have been so close to me that I found them with me whenever I needed. It is their unconditional love that motivates me to sets higher targets.

Abstract

Centrifugal microfluidic platforms, also known as CD-like microfluidics, are types of lab-on-a-chip devices that employ centrifugal force to pump liquid between micro chambers via micro channels. Magnetic particles can be used in centrifugal microfluidic platforms for bimolecular assays such as the enzyme-linked immune sorbent assay (ELISA), polymer chain reaction (PCR) and other applications. Magnetic particles can act as mobile solid supports for bio reactions due to their specific surface functionalization. For this reason, trapping, transport and detection of magnetic particles are very important operations in centrifugal microfluidic platforms for research applications and clinical diagnostics.

Magnetic forces are required for controlling the magnetic particles in CD-like microfluidic devices. Therefore, external magnetic field should be applied on micro chambers. In previous studies, external magnetic field was generated by means of sophisticated coil arrays that require skillful technicians and permanent magnets which need manual tedious procedures. In addition, other studies attempted to manipulate magnetic particle when CD is in stationary state.
This study introduces a novel electromagnetic platform that allows controlling of magnetics particles movements on CD-like microfluidics during rotational CD automatically. The required magnetic force to move magnetic particles under a centrifugal force are estimated by MATLAB software. By employing the magnetic force equation and based on the required magnetic force, the exact value of required magnetic flux density at the location of magnetic particles was calculated. Then, an electromagnetic platform which produces required magnetic flux density was designed using COMSOL simulation software.

Our results indicate that the designed electromagnetic platform with 16 solenoids inside the ring-shaped core is able to generate the required magnetic flux density (more than 1.91 T).

By utilizing the electromagnetic platform in this project, magnetic particles can be trapped in one chamber for 10 second and then can be transported from one chamber to another chamber automatically. This preliminary result will lead to the future development of electromagnetic platforms and implementation of fully automated biomedical assays in centrifugal microfluidic applications.

Abstrak

Platform microfluidic Centrifugal, juga dikenali sebagai CD-seperti microfluidics, adalah jenis peranti makmal-on-a-chip yang menggunakan daya emparan untuk mengepam cecair antara dewan mikro melalui saluran mikro. Zarah magnet boleh digunakan dalam platform microfluidic empar untuk ujian bimolecular seperti imun cerakin enzim berkaitan pengerap (ELISA), tindak balas rantai polimer (PCR) dan aplikasi lain. Zarah magnet boleh bertindak sebagai sokongan padu bimbit untuk tindak balas bio kerana functionalization permukaan khusus mereka. Atas sebab ini, memerangkap, pengangkutan dan pengesanan zarah magnet adalah operasi yang sangat penting dalam platform microfluidic empar bagi aplikasi penyelidikan dan diagnostik klinikal.

Kuasa-kuasa magnet yang diperlukan untuk mengawal zarah magnet dalam peranti microfluidic CD-suka. Oleh itu, medan magnet luaran perlu digunakan pada dewan mikro. Dalam kajian sebelum ini, medan magnet luar telah dijana melalui tatasusunan gegelung canggih yang memerlukan juruteknik mahir dan magnet kekal yang memerlukan prosedur membosankan manual. Di samping itu, kajian-kajian lain cuba untuk memanipulasi zarah magnet apabila CD adalah dalam keadaan pegun.

Kajian ini memperkenalkan platform elektromagnet novel yang membolehkan pengawalan Nizhnian zarah pergerakan pada CD-seperti microfluidics semasa CD putaran automatik. Daya magnet diperlukan untuk menggerakkan zarah magnet di bawah daya emparan adalah dianggarkan melalui perisian MATLAB. Dengan menggunakan persamaan daya magnet dan berdasarkan daya magnet yang diperlukan, nilai sebenar diperlukan ketumpatan fluks magnet di lokasi zarah magnet telah dikira. Kemudian, sebuah platform elektromagnet yang menghasilkan diperlukan ketumpatan fluks magnet telah direka dengan menggunakan perisian

simulasi COMSOL.

Keputusan kami menunjukkan bahawa platform elektromagnet yang direka dengan 16 solenoid dalam teras berbentuk cincin yang mampu menjana ketumpatan fluks magnet yang diperlukan (lebih daripada 1.91 T). Dengan menggunakan platform elektromagnet dalam projek ini, zarah magnet boleh terperangkap di dalam satu ruang selama 10 kedua dan kemudiannya boleh diangkut dari satu ruang ke ruang lain secara automatik. Ini hasil awal akan membawa kepada pembangunan masa depan platform elektromagnet dan pelaksanaan ujian automatik sepenuhnya bioperubatan dalam aplikasi microfluidic empar.

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TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF ABBREVIATIONS

POC	Point-of-Care
LOC	Lab on a Chip
LOD	Lab on a Disc
PCR	Polymerase Chain Reaction
MEMs	Microelectromechanical Systems
RPM	Revolutions per minute
IR	Infrared
MRI	Magnetic resonance imaging
AWG	American wire gauge

Chapter 1. INTRODUCTION

1.1 Overview

Medical testing in vitro plays an important role in modern health care. For this reason, the availability of high sensitive diagnostic tools is a significant issue for all people in the world. Nowadays, about 70% of medical tests are accomplished in centralized laboratories. The centralized laboratories should be equipped with sophisticated equipment to perform different processes of the medical test. In addition, working with this equipment is time-consuming and needs professional technicians. The remaining 30% of the medical tests are performed as point-of-care (POC) tests. POC testing can provide immediate and convenient tests for patients. These types of tests integrate several diagnostic steps which lead to faster and less expensive procedure compared to centralized testing approaches (Bruls *et al*., 2009). However, POC devices need large analytical equipment due to the applied high reagent volume. As a result, microfluidic technologies have been emerged as powerful enabling tools to improve the related shortcomings by reduction of reagent volume. Moreover, microfluidic technologies can increase reliability of POC tests.

Lab-on-a-chip (LOC) is one of the current POC testing systems which utilize microfluidic diagnostic technologies. There are various techniques for operating microfluidic functions. These methods are acoustics, pressure, syringe, electrokinetics, electrochemical bubble generation, and centrifuge (Madou *et al*., 2006). Among all of these techniques, centrifuge offers a number of intrinsic advantages such as, removing the need for external pump, providing wide range of rate flow and handling fluid independent to physicochemical properties of fluid. In addition, based on physical principle of centrifugal pumping, several centrifuge fluidic functions (e.g. mixing, valving, metering and switching) can be done in a CD-like plastic substrate. LOC devices which employ centrifugal force to pump liquid between micro chambers via micro channels are called centrifugal microfluidic platforms or lab-on-a-disc (LOD) platforms. LOD platforms have successfully demonstrated their capability for high performance analytical measurement for a wide range of biological assays (e.g. Cell-based assay, immunoassay, polymerase chain reaction (PCR)). Biological assays need to deliver a great analytical performance with cost-effective materials. There are various types of magnetic (e.g. magnetic particles and Ferro fluids) and non-magnetic (diamagnetic objects) materials which can be applied in biological assays.

Magnetic particles are valuable materials which can be easily manufactured in a wide range of size from nanometer to micrometer (Aytur, 2007). Different types of biomolecules such as antigens, antibodies, and DNA strands can be easily attached to these particles due to their specific surface functionalization. Spherical shape and large surface area are other important properties of these particles which are desired in mass transferring (Pamme, 2006). The related advantages of magnetic particles make them appropriate materials for using in LOD systems in a large number of applications (Strohmeier *et al*., 2013; Wadle *et al*., 2012). For example, in cell-based assays, identification, analysis, capturing, sorting, and selective manipulation of cells can be simply done by using magnetic particles inside the microfluidic channels (Chen *et al*., 2011; Siegrist *et al*., 2011; Kirby *et al*., 2012).

Magnetic forces are required for controlling the magnetic particles in LOD platform. External magnetic field should be applied on microchambers. Magnetic field strength and pattern can be designed based on the variety types of LOD platforms. In order to obtain desired magnetic field strength and pattern, many types of permanent magnets and electromagnets have been manufactured. All of the methods used to control the magnetic particles in the LOD platforms need skillful technicians for setting up the sophisticated electromagnetic arrays or manual tedious procedures to install permanent magnets. These methods make corresponding constraints on the automation and miniaturization concepts of LOD platform. By automatic controlling and manipulating magnetic particles movement from outside of the LOD platform, under a wide range of centrifugal force, more functions and flexibilities can be achieved in centrifugal microfluidic systems. For example, automatic controlling the movement of magnetic particles enables us to trap these particles inside a micro chamber (for binding particles with biomolecules) in a specified duration of time, and then transport them from one chamber to another one (for washing the weak binding). These abilities result in performing various assays on the LOD platform.

The main goal of this project is implementing a multiplex electromagnetic ring that would be designed exclusively for LOD platforms in order to gain the aforementioned abilities. This system warrants controlled movements of magnetic particles in microchambers over LOD platforms.

1.2 Objectives

The objective of this project is to design the electromagnetic platform for controlling magnetic particles in centrifugal microfluidic platform.

1.3 Scope of this Study

In order to achieve the goal of this study, the following steps have been taken into account. The corresponding literature has been reviewed to find an appropriate way to calculate the desired magnetic force for various sizes of magnetic particles under the wide range of centrifugal force. In addition, several mathematical methods to calculate the magnetic field at any interesting point, above the magnetic ring, have been reviewed. AutoCAD software has been used to design the centrifugal microfluidic platform. Then, electromagnetic platform has been designed by means of COMSOL software. Finally the equation of designed electromagnetic platform has been obtained by employing MATLAB software.

The designed electromagnetic platform consists of 16 solenoids which are located at circular shape. This electromagnetic platform is located under micro chambers of LOD platform. By this platform, magnetic particles can be trapped in one chamber in a specified duration of time and then can be transported from one chamber to another chamber automatically.

1.4 Outline of Thesis

This thesis consists of five chapters. In first Chapter, it discussed the objective, scope and summary of this project; while the Chapter 2 will be discussed more on literature review of platforms that have been simulated. It discussed about centrifugal microfluidic platform and magnetic theory. In Chapter 3 the discussion will be on the mathematical calculation, design and simulation of the electromagnetic platform. Moreover, the results and interpretations are shown in Chapter 4. The Chapter 5 is conclusion and recommendation for the overall project.

Chapter 2. LITERATURE REVIEW

This section is divided into three subsections. At the first section, the details regarding to Centrifugal microfluidic platform are provided. This section comprises; background, theoretical principle, centrifugal microfluidic functions, analytical measurement techniques and finally applications of this platform. At the second section, magnetic theory is reviewed. This section deals with the magnetic properties of different types of materials. Then, different types of magnets (ring permanent magnet and temporary magnet) are discussed in this section. At the third section, the combination of microfluidics and magnetism are reviewed.

2.1 Centrifugal Microfluidic Platform

Centrifugal microfluidic platforms which are known as lab-on-a-disk (LOD) or compact disk (CD) microfluidics are a powerful solution for medical and clinical diagnostics applications. The principal of the technique is that it exploits centrifugal force to drive liquids inside microfluidic system for properly mixing the samples and reagents and to perform diagnostic assays. So, each steps of the process will be carried out automatically by controlling the rotation speed of the CD as well as the liquid flow (Lai *et al.*, 2004). Based on physical principle of centrifugal pumping, several centrifuge fluidic functions can be implemented on LOD platform. In addition, various analytical measurement techniques can be utilized for this platform. The combination of centrifuge fluidic functions and analytical measurement techniques make a centrifugal microfluidic platform a great solution for diagnostics applications such as, immunoassay and polymerase chain reaction (PCR) (Madou *et al.*, 2006).

2.1.1 Background

The use of microfluidic technologies for carrying out miniaturization on the analytical equipment through the reduction in reagent volumes, improves the shortcomings related to the use of large and expensive instrumentations. In addition, microfluidic technologies simplify the job of analytical assays by full incorporation of analytical procedures in flowing systems. These technologies can be performed in low-cost and disposable instruments to prevent sample contamination. Furthermore, it has a potential to scale the important instrument process such as, cooling, heating, chromatographic and electrophoretic separation in micro domain (Madou *et al*., 2006). In order to increase functionality of microfluidic systems to perform analytical assays, microelectromechanical systems (MEMs) are employed. The combination of these two technologies allows the integration of different types of functions (e.g. electrical and electrochemical functions) into chips for different procedures of analytical assays such as, sensing the parameters of assay and biomolecular detection (Verpoorte *et al*., 2003). Lab-on-a-chip (LOC) is a device that utilizes the integration of these two technologies. Single or multiple laboratory functions are performed on a chip by handling small volume of fluid inside interconnected micro channels. Several technologies for handling fluid inside the micro channel exist, including acoustics, pressure, syringe, electrokinetics, electrochemical bubble generation and centrifuge. Table 2.1 displays the comparison of four important microfluidic propulsion techniques (Madou *et al*., 2006).

Table 2.1. Comparison of four important microfluidic propulsion techniques (Reproduced from Madou *et al*. (2006)).

Fluid propulsion mechanism				
Comparison	**Centrifuge**	**Pressure**	**Acoustic**	**Electrokinetic**
Valving solved?	Yes for liquids, no for vapor	yes for liquid and vapor	Yes for liquids and vapor	Yes for liquids, no for vapor
Maturity	Products available	Products available	Research	Products available
Propulsion force influenced by	Density and viscosity	Generic	Generic	pH, ionic strength
Power source	Rotary motor	Pump, mechanical roller	5 to 40 V	10 kV
Materials	Plastics	Plastics	Piezoelectric	Glass, Plastics
Scaling	L3	L3	L2	L2
Flow rate	From less than 1 nl s^{-1} to greater than 100 µl s^{-1}	Very wide range (less than nl s^{-1} to liter s^{-1})	20 µl s^{-1}	0.001–1 µl sec^{-1}
General remarks	Inexpensive CD drive, mixing is easy, most samples possible (including cells). Better for diagnostics	Standard technique. Difficult to miniaturize and multiplex	Least mature of the four techniques. Might be too expensive. Better for smallest samples	Mixing difficult. High voltage source is dangerous and many parameters influence propulsion, better for smallest samples

According to the table, centrifugal microfluidics done in a CD-like plastic substrate has got lots of advantages. This system employs centrifugal force for moving fluid while other systems need the external pump. A wide range of flow rate (i.e. less than 10 nl s^{-1} to more than 100 µl s^{-1}) can be provided by this technology compared to another technologies. Moreover, valving structures (i.e. fluid gating) play fundamental role in enabling sequential fluidic processing and multiplexing and miniaturization could be easily done in this system. Fig 2.1 shows a general figure of LOD instrument and disposable CD (Madou *et al*., 2006).

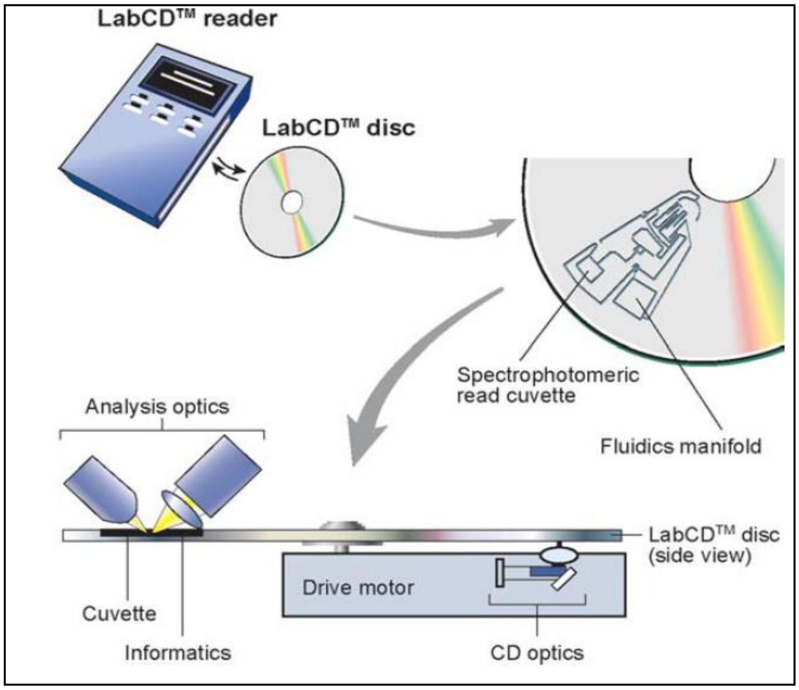


Fig 2.1.General figure of LOD instrument and disposable CD (Reproduced from Madou *et al*. (2006)).

2.1.2 Theoretical Principle

The theoretical principle of the LOD platform contains the principle of fluid rate as well as the principle of basic forces which are applied on fluid or on suspended particles. Rotation rate, geometry and location of channels and reservoirs, as well as fluid properties determine the CD fluid propulsion which is occurred via centrifugally induced pressure. The average velocity of the liquid (u) can be found by Equation 2.1(Madou *et al*., 2006).

$$U = D_h \rho \omega^2 r^- \Delta r / 32 \mu L \qquad \textbf{(Equation 2.1)}$$

Definitions:

D_h: hydraulic diameter of the channel

L: the length of the liquid in the capillary channel

r^-: the average distance of the liquid in the channels to the center of the CD

w: angular speed of the CD

μ: radial extent of the fluid

ρ: the density of the liquid

Δr: radial extent of the fluid

In addition, Equation 2.2 can be used for calculation the volumetric flow rate of liquid (Madou *et al.*, 2006). Velocity of liquid (*U*) and cross sectional area of the channel (*A*) is two parameters which they have directly effect on volumetric flow rate.

$$Q = UA \qquad \textbf{(Equation 2.2)}$$

In CD microfluidics, different combinations of rotational speeds (from 400 to 1600 rpm), channel widths (20–500 μm), and channel depths (16–340 μm) can give flow rates, ranging from 5 nls^{-1} to >0.1 mls^{-1}.

On the other hand, LOD platform utilizes the centrifugal force, Coriolis force and Euler force to manipulate and transport the liquid and suspended particles (Ducrée *et al.*, 2007; Grumann *et al.* 2005). Fluid is transferred from the inner part of CD to the outer part by means of centrifugal force. Angular speed of CD, mass density of liquid substance or particles and distance between liquid or particles and center of CD (*r*) are the parameters that have the effect on the magnitude of the centrifugal force. This force can be found according to Equation 2.3(Ducrée *et al*., 2007).

$$f_w = \rho w^2 r \qquad \textbf{(Equation 2.3)}$$

The second basic force is Coriolis force. The fluid flow can be separated in LOD platform by this force when the angular speed is high enough. The Coriolis force will be applied on the liquid when the flow velocity is in the radial direction. The effect of this force on liquid is not significant compared to the centrifugal force when the angular speed is not high. This force can be calculated by Equation 2.4(Ducrée *et al*., 2007).

$$f_c = 2\rho wu \qquad \textbf{(Equation 2.4)}$$

The Euler force is another basic force which can be applied on the liquid when the rotational speed of CD is not constant. In other words, the Euler force depends on the acceleration of angular speed. The Euler force can be determined by Equation 2.5 (Ducrée *et al*., 2007).

$$f_E = \rho r \frac{dw}{dt} \qquad \textbf{(Equation 2.5)}$$

Fig 2.2 displays a rotational CD, which the liquid inside the CD experienced three basic forces (centrifugal force, Coriolis force and Euler force) (Ducrée *et al*., 2007).

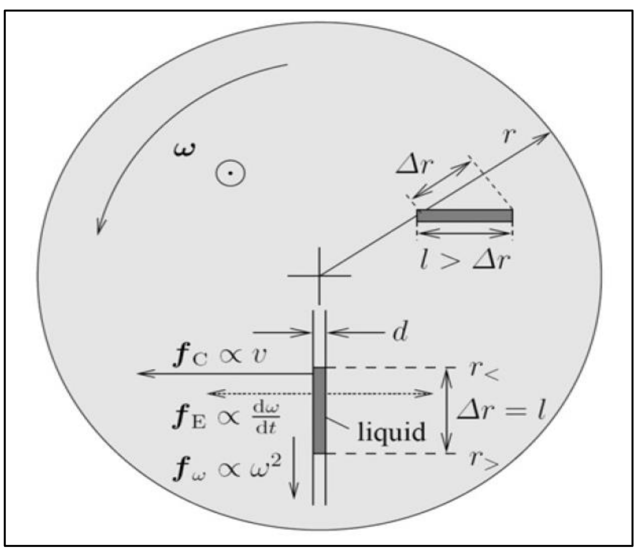


Fig 2.2. Liquid inside the rotating CD experienced three basic forces (centrifugal force, Coriolis force and Euler force (Reproduced from Ducrée *et al*. (2007)).

2.1.3 Functions

There are various types of functions in a centrifugal microfluidic structure such as, mixing, valving, metering and switching.

2.1.3.1 Valving

Controlling of fluid flow consists of ability to start and stop the fluid flow. Valving structures play fundamental role in flow control and enabling sequential fluidic processing. The valve holds until spin velocities, measured in rotations per minute (RPM), are increased above a critical threshold, known as the burst frequency. This frequency can be found according to Equation 2.6 where θ is contact angle and γ is surface tension of fluid (Lai *et al.*, 2004).

$$f_b = \left(\frac{\gamma sin\theta}{\pi^2\, \rho.\Delta R.R^{-}.D_h}\right)^{1/2} \qquad \textbf{(Equation 2.6)}$$

The microfluidic applications are multiplexed and, as such, several valving components must work simultaneously. In addition, compatibility, long-term stability, prevention of cross-contamination and actuation in accordance with the design paradigms of the instrument are important factors in related to valving. There are two kinds of valving; passive valve and active valve. The mechanism of passive valves is that centrifugal forces drive liquid outwards while surface tension created at the interface prevents from flowing. The liquid is released from the reservoir only when the applied produced pressure by rotational speed is greater than capillary force. Fig 2.3 can illustrate this mechanism. Although mechanism of passive valves is simple without barriers and external trigger they have some limitations like valving failures or decreasing burst frequency by increasing distance away from the disc center.it means passive valves are RPM-dependent. This problem makes limitation scope of use. There are different kinds of passive valves such as hydrophobic valves, pneumatic passive valves, siphon valves, etc. The active valving was introduced to overcome the limitations of passive valving and also for expanded use. The mechanism of active valve is that act as programmable control of fluidic flow elements where a physical gating material is changed or removed by an external actuation source. Depend on type of active valve gating material and actuation source will be changed. There are many types of active valves such as using wax and focused infrared (IR) lamp; using Ferro wax and laser diode; heat absorbing printer toner with Laser diodes as gating and actuation source respectively. Thus active valve is not RPM-dependent and can solve some problems in passive valving (Madou *et al*., 2001; Yusoff *et al*., 2009).

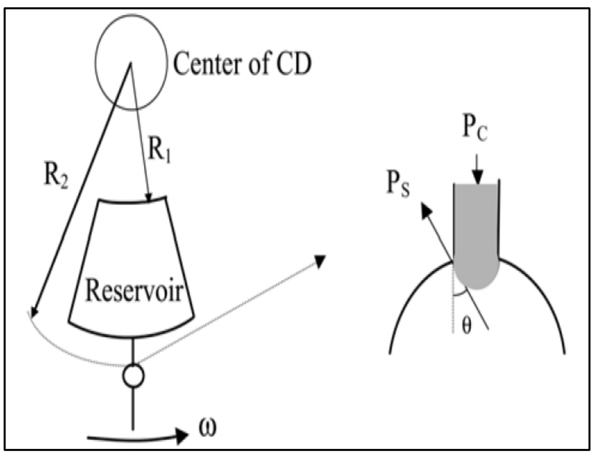


Fig 2.3. Mechanism of passive valve (Reproduced from Yusoff *et al*. (2009)).

2.1.3.2 Metering

Controlling the volume of the liquid (metering) as a function of LOD platform plays a key role in analytical sample processing procedure. This function can be achieved by connecting a common distribution channel to the metering reservoir chamber. Fig 2.4 shows the mechanism of the metering. At the specific rotational speed of CD, liquid moves from the distribution channel into reservoir channel. At the same time, the rest liquid of distribution channel move to the waste channel. When the rotational speed of CD increases the liquid will transfer from reservoir channel into the next channel. The volume of the liquid can be determined by measuring the volume of the reservoir channel (Madou *et al*., 2006).

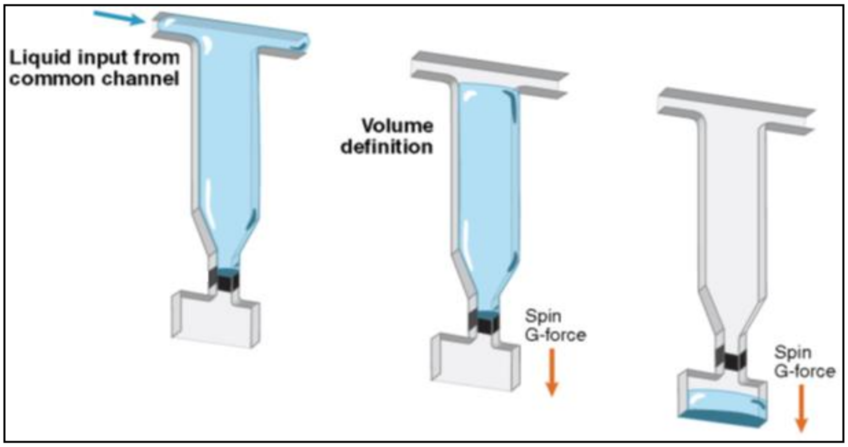


Fig 2.4. Mechanism of metering function (Reproduced from Madou *et al*. (2006)).

2.1.3.3 Switching

Controlling of a flowing fluid is necessary when routing fluid into different outlet channels. When CD is rotating, switching intend to move the liquid into the selected channels. Separation of biomolecule from the mixture of liquid is one of the significant applications of switching. There are variety techniques for performing switching. Using Coriolis force is a common technique for switching in LOD platform. Fig 2.5 display centrifugal force and Coriolis force that have the effect on the direction of fluid flow. This technique consists of two outlet channels with common inlet. At low rotational speed, centrifugal force pump the liquid toward the outer radius of Cd and liquid flow follow the original path. By contrast, when the rotational speed is increased, the Coriolis force can move the liquid in to the opposite direction of rotating CD (Kim *et al*., 2008).

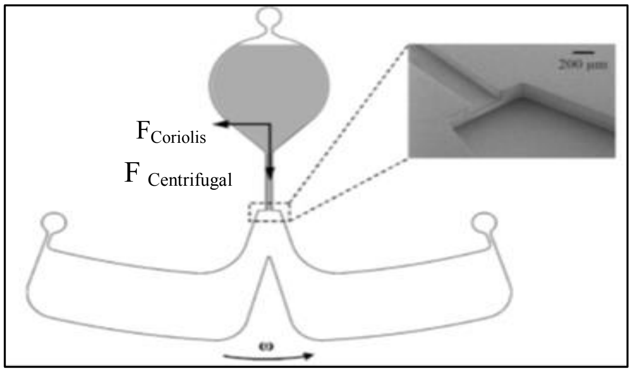


Fig 2.5. Centrifugal force and Coriolis force which have the effect on the fluid flow direction (Reproduced from Kim *et al*. (2008)).

2.1.4 Analytical Measurement Techniques

Analytical measurement techniques consist of the variety types of methods for measuring the analyte of the biological assays. The presence or the functional activity of the analyte can be measured by these methods. Type of analytical measurement techniques can be determined based on biological assay, for an instance, detection of binding between analyte and biological (sensing) element is the basic principle of the measuring techniques for affinity bioassay. Optical imaging, absorbance and fluorescence spectroscopy are some of these techniques which are used in LOD platform.

2.1.5 Application

Centrifugal microfluidic platform is a kind of multi-purpose devices which can be used for many applications such as, sample preparation, Cell-based applications, DNA purification, Immunoassay, Polymerase chain reaction (PCR) and so on.

2.1.5.1 Sample Preparation

In analytical chemistry, sample preparation is referred to the ways in which a sample is treated prior to its analysis. Because the techniques are often not responsive to the analyte in its in-situ form, or the results are distorted by interfering species, preparation is a very important step in most analytical techniques. Manual sample preparation is relatively tiresome and time consuming, and can introduce errors common to multi-step pipetting. Developing LOD platform for automation of sample preparation has shown a lot of promises in this field (Glasgow *et al*., 2003).

2.1.5.2 Cell-Based Applications

Cell separation, purification, sorting and manipulating are significant processes for clinical diagnostic applications. In addition, capturing of cell, cell counting and assaying play an important role for research usages. Cell separation and purification are primary process for cell analysis. The main objective of this process is separating the target cells from the surrounding medium. Separation of target cell from the medium can be done by different methods which depend on the characteristics of cell such as, dielectric features, size, density and morphological characteristics. In order to manipulate of cell, complex, expensive and sophisticated equipment are required. Therefore, both clinical diagnostic and research applications need to low-cost and portable systems. LOD platforms have effectively established their intrinsic advantages for Cell handling and cell identification applications (Burger *et al*., 2012; Chen *et al*., 2011).

2.1.5.3 DNA Purification

DNA purification is a process of isolation DNA from the sample. Several chemical and physical methods can be used for DNA purification. In general, isolation DNA from cellular components can be done by sequential stages including, disruption, lysis, removing proteins, removing contaminants and recovery of DNA. All of these sequential stages can be perfumed by professional techniques which are used in LOD platforms (Strohmeier *et al*., 2013; Wadle *et al*., 2012).

2.1.5.4 Immunoassay

An immunoassay is a biochemical test that measures the presence or concentration of a substance in solutions containing a complex mixture of substances. Immunoassay methods are usually used to assay analyte in biological liquids such as serum, saliva or urine. The exceptional ability of an antibody to bind with high specificity to one or a very limited group of molecules is the basic for this kind of assays. In addition to that, the other key feature of all immunoassays is a means to produce a measurable signal in response to a specific binding. Historically this was accomplished by measuring a change in some physical characteristic such as light scattering or changes in refractive index. The automation of immunoassays on microfluidic platforms is challenging because of the high number of fluidic processes and liquid reagents involved. CD platform is of interest for multiple parallel immunoassays because it can provide simultaneous and identical flow rates, incubation times, mixing dynamics and detection (Lai *et al*., 2004).

2.1.5.5 Polymerase chain reaction (PCR)

The polymerase chain reaction (PCR), an important process for nucleic acid analysis, is a scientific technique in molecular biology to amplify a single or few copies of a piece of DNA across several orders of magnitude, generating thousands to millions of copies of a particular DNA sequence. This process needs substantial sample preparation that, unless automated, is laboured extensive. Current bench-top PCR systems can take on the order of hours to complete a set of PCR cycles. As a primary example, combined sample preparation with PCR on the CD was reported by Kellogg *et al*. (Kido *et al*., 2007) They demonstrated sample preparation and PCR amplification for two types of samples, whole blood and Escherichia coli, on the CD platform and shown that the results are as good as the conventional methods.

2.2 Magnetism

2.2.1 Magnetic Theory

There are four main magnetic vectors namely, magnetic field (H), magnetization (M), magnetic flux density (B) and magnetic force (F). All of these vectors can be specified by both strength and direction.

Magnetic fields (H) are produced by magnetic materials and electric currents. Atomic structure of materials consists of positive charges (i.e. nucleus) and negative charges (i.e. electrons). Spinning of atomic components comprising, rotating electrons around nucleus and rotating nucleus and electrons relative to their axes is the reason of creation magnetic dipoles. The magnetic dipole moment of rotating electrons around nucleus is more significant than rotation electrons or nucleus around their axes. Therefore, the presence of moving charges in magnetic materials (i.e. spinning of electrons around nuclei) and electric currents (i.e. flowing of electrons along a wire) is the main reason of magnetic field generation. There are two types of magnetic field including, static magnetic field and time-varying magnetic field. Static magnetic fields are generated by permanent magnets and steady currents whereas time-varying magnetic fields are produced by time-varying currents. The unit of magnetic field vector is Ampere per meter (A/m).

The number of atoms which have the specific value of magnetic dipole moment per unit volume is the description of magnetization (M) vector. The net magnetic dipole moment of most materials is zero due to the randomly orientation of their magnetic dipoles by contrast; magnetic dipoles of permanent magnet or the materials which are placed under the external magnetic field are aligned equivalently and net magnetic dipole moment has value. The unit of magnetization vector is ampere per meter (A/m). Fig 2.6 displays the effect of external magnetic field on nonmagnetized material (Cheng, 1989).

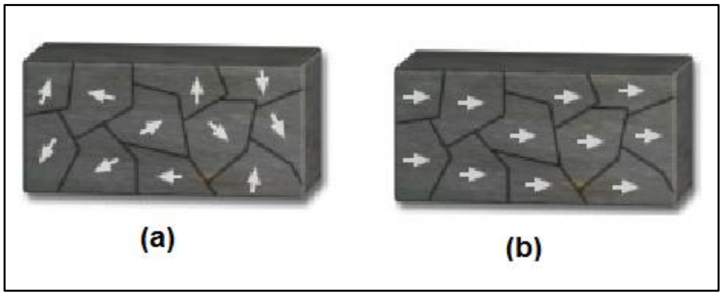


Fig 2.6. (a) Domains before magnetization. (b) Domain after magnetization (Reproduced from http://hyperphysics.phy-astr.gsu.edu/).

Different materials respond differently in terms of supporting magnetic field creation inside them, when they are placed under same magnetic field strength. In other words, the density of magnetic field lines within a material depends on its magnetic permeability (μ). The density of magnetic field lines per unit area is defined by magnetic flux density (B). Magnetic flux density value will be reduced by increasing the distance from the magnetic field source. The unit of magnetic flux density vector is Tesla (T). Fig 2.7 shows the density of magnetic field lines inside the soft iron and the effect of distance on the magnetic flux density (Pamme, 2006).

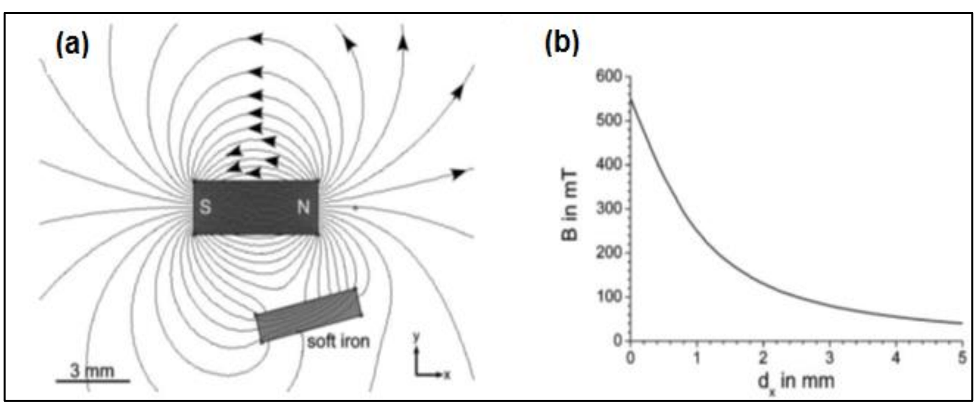


Fig 2.7. (a)The density of magnetic field lines inside the soft iron. (b) The effect of distance on the magnetic flux density (Reproduced from Pamme (2006)).

Magnets apply magnetic forces (F) on each other as a result of interactions between magnetic dipoles of first magnet and magnetic dipoles of second magnet. Attractive and repulsive magnetic force can be determined by recognizing the all magnetic dipoles of the first and second magnets. The unit of magnetic force vector is Newton (N).

2.2.2 Magnetic Properties of Materials

Produced effects within materials are different when materials are placed in magnetic field. Therefore, materials have been divided into two main groups; namely, materials which are not magnetically arranged (i.e. diamagnetic and paramagnetic materials) and materials that are magnetically well-ordered (i.e. ferromagnetic, ferrimagnetic and antiferromagnetic materials) under certain temperature. Table 2.2 displays the classification of different magnetic materials.

Table 2.2.Classification of different materials.

Class	X dependent on temperature	Hysteresis	Example	X value
Diamagnetic	No	No	Water	-9.0×10^{-6}
Paramagnetic	Yes	No	Aluminum	2.2×10^{-5}
Ferromagnetic	Yes	Yes	Iron	3000
Ferrimagneti	Yes	Yes	MnZn(Fe2O4)2	2500
Antiferromagnetic	Yes	Yes	Terbium	$9.51E^{-02}$

2.2.2.1 Diamagnetic materials:

All materials have a fundamental property which is called diamagnetism. This property is related to atomic behavior of a material when it subjected to the magnetic field. The orbital shells of diamagnetic materials are filled. For this reason, this type of material does not have the net magnetic moment. When this material is subjected to the magnetic field the molecules of this material acquire induced moment which this moment is opposite to the magnetic field. Fig 2.8 displays the Susceptibility (χ) of these kinds of materials which is negative, the effect of temperature on susceptibility values and relationship between induced magnetic flux density and applied magnetic field.

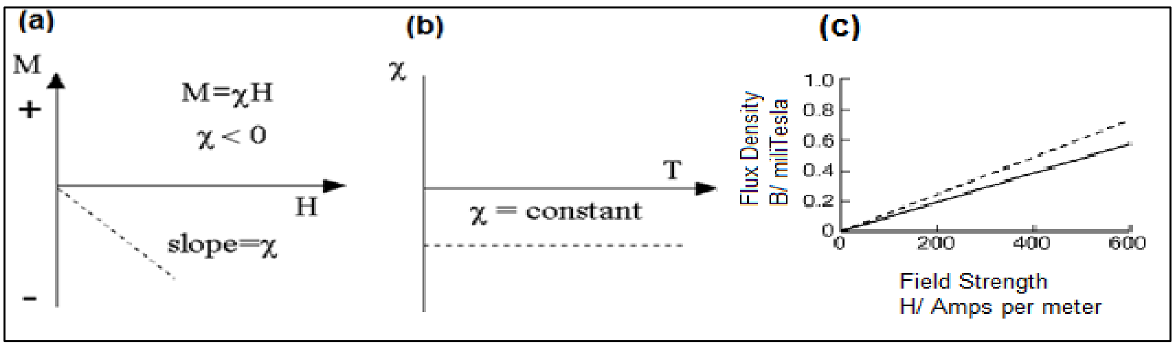


Fig 2.8. (a) Susceptibility of diamagnetic materials is negative. (b) The value of susceptability is independent of tempratures. (c) By applying magnetic field (H) on these materials the magnetic flux density (B) is less than vacume (dashed line) (Reproduced from http://www.irm.umn.edu).

2.2.2.2 Paramagnetic materials:

These materials comprising atomic structures with partially field orbital shells. Therefore these materials can be magnetized to some extent in the presence of magnetic field. Susceptibility of these materials is positive. In addition, increasing the temperature has the opposite effect on the susceptibility values. Fig 2.9 shows these features of susceptibility and relationship between applied magnetic field and induced magnetic flux density.

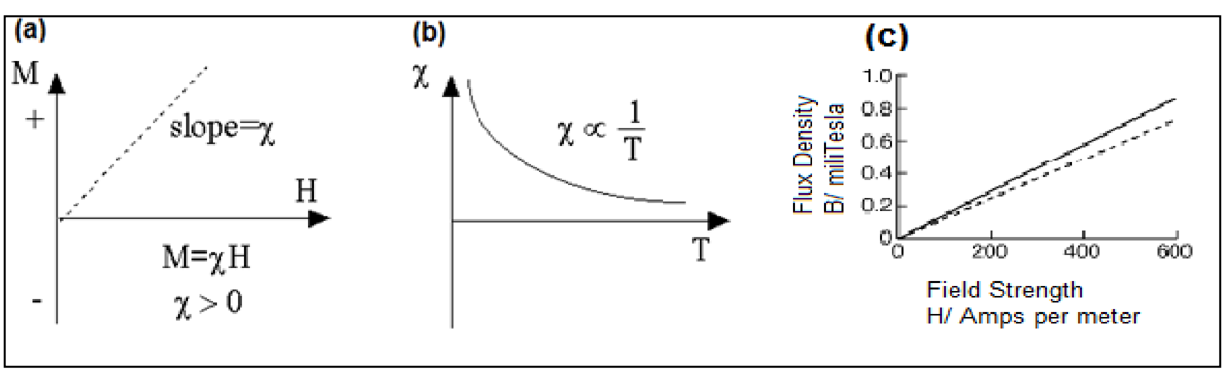


Fig 2.9. (a) The positive value of susceptability. (b) The relationship between susceptability and temprature (c) By applying magnetic field (H) on these materials the magnetic flux density (B) is more than vacume (dashed line) (Reproduced by http://www.irm.umn.edu).

2.2.2.3 Ferromagnetic materials:

These materials can be magnetized more strongly than paramagnetic materials due to the strong interactions of atomic moments when the magnetic field is applied. The magnetic moment of atoms in such materials have tendency to become parallel (Fig 2.10.(a)). By applying the magnetic field to this material, the magnetic flux density will be in the range of Tesla and the BH curve (Fig 2.10.(b)) will not be linear while both diamagnetic and paramagnetic materials have magnetic flux density in the range of milliTesla and their BH curves are linear.

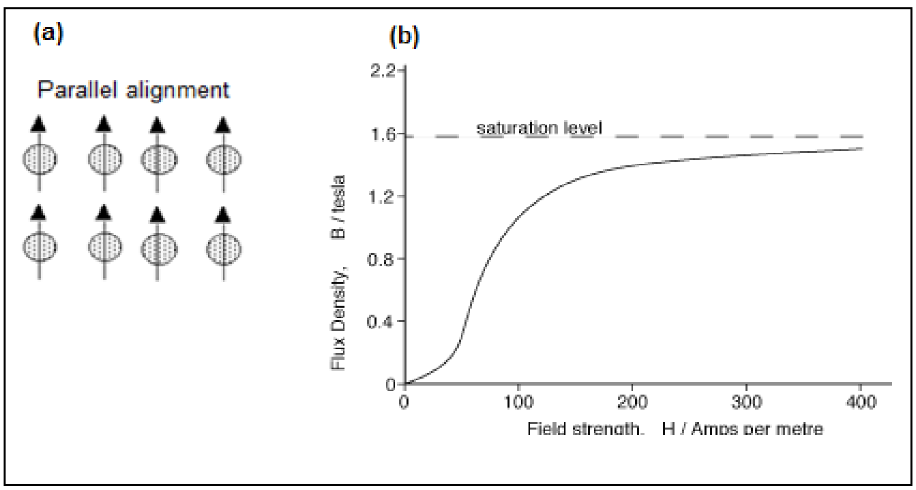


Fig 2.10. Ferromagnetic material. (b) BH curve of ferromagnetic materials. (Reproduced by http://www.irm.umn.edu).

Remanence and coercivity are two another features of ferromagnetic materials which make them distinct from paramagnetic and diamagnetic materials. Magnetic flux density of these materials is zero in the absence of external magnetic field. By applying magnetic field on the material, magnetic flux density will be appearing. Hysteresis loop is a curve which can be used for learning about the properties of some materials (Fig 2.11). In this curve, increasing magnetic field strength is the cause of growing magnetic flux density until the material reach to the saturation point (i.e. in this point all domains of material are aligned). When external magnetic field is removed, there will be a remaining magnetic flux density which is called romance. Magnetic flux density will be zero by increasing the magnetic field in opposite direction (coercivity point). Material can be magnetized in opposite direction and reach to the saturation point by increasing the magnetic field in opposite direction.

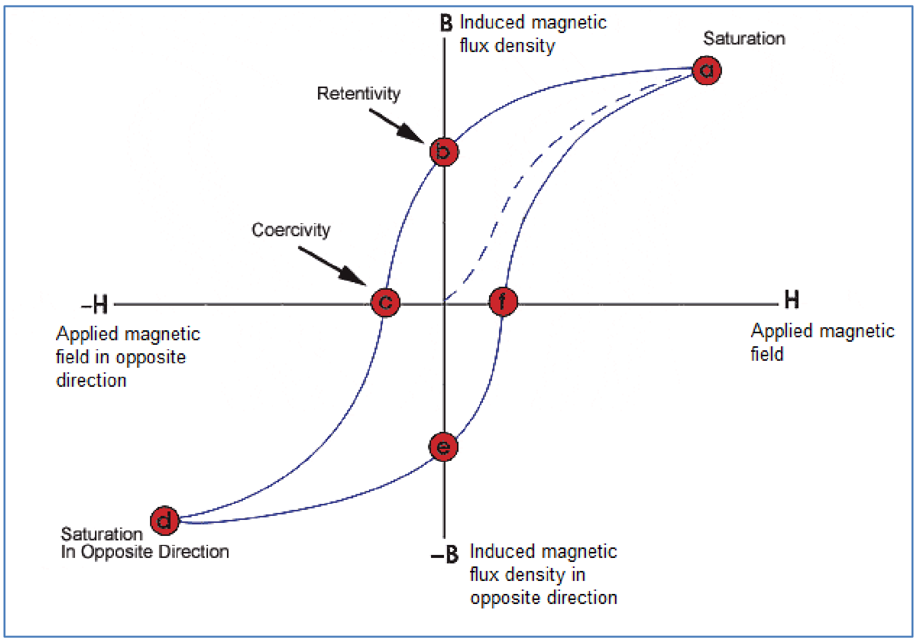


Figure 2.11. (a) Saturation point. (b)Retentivity point. (c) Coercivity point. (d) Saturation point in opposite direction. (e) Retentivity point in opposite direction. (f) Coercivity point in opposite direction (Reproduced from http://www.ndt-ed.org).

2.2.2.4 Ferrimagnetic materials:

The atomic structure of these kinds of materials consist of opposite and parallel magnetic moments. In addition, magnetic moments of one direction are stronger than the magnetic moment in opposite direction (Fig 2.12.(a)). There is wide range of application for these types of materials such as, sensors, inductors, motors and so on.

2.2.2.5 Antiferromagnetic materials:

The magnetic moments of these materials are opposite and parallel. Unlike ferromagnetic materials, the magnetic moments of antiferromagnetic materials are equal (Fig 2.12.(b)).

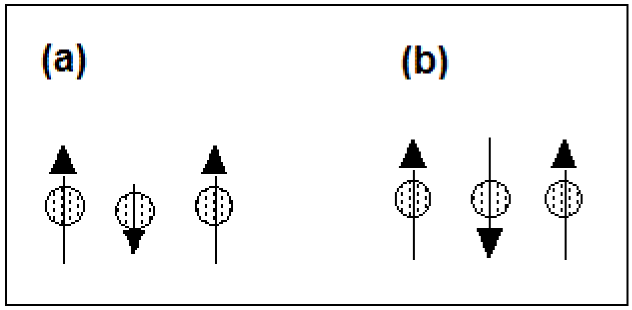


Fig 2.12. (a) Ferrimagnetic material. (b) Antiferromagnetic material(Reproduced from http://www.irm.umn.edu).

2.2.3 Types of Magnets

Magnetic field can be generated by magnets. There are two types of magnets based on the source of magnetism; namely, Permanent magnet and Temporary magnet.

2.2.3.1 Permanent Magnet

These types of magnets are made of materials which are magnetized and they can retain their magnetism properties. So, there is no control on this type of magnet to increase or reduce the magnetic field strength. In general, for selecting permanent magnet for specific application different parameters should be considered such as, material (e.g. neodymium iron boron, samarium cobalt and ceramic or ferrite), shape (e.g. disk, cylinder, block, ring and spheres), and direction of magnetization (e.g. axially and diametrically magnetization). Colombian method is used to calculate the parameters of permanent magnet.

2.2.3.1.1 Ring Magnet

There is wide range of applications for axially and radially magnetized ring permanent magnet for instance, sensors and actuators, magnetic bearing and magnetic separating devices. Therefore, calculation the magnetic parameters (e.g. magnetic field, magnetic flux density and magnetic force) of such structures are very significant. In order to calculate the magnetic force of ring at any point of interest, the exact value of magnetic field at that point is required. So far variety analytical and numerical methods have been used for calculation the magnetic field strength around a ring magnet which is axially or radially magnetized (Ravaud *et al*., 1989; Babic *et al*., 2008; Ravaud *et al*., 2009). Fig 2.13 shows axially and radially magnetized ring. This study deals with axially magnetized ring permanent magnet.

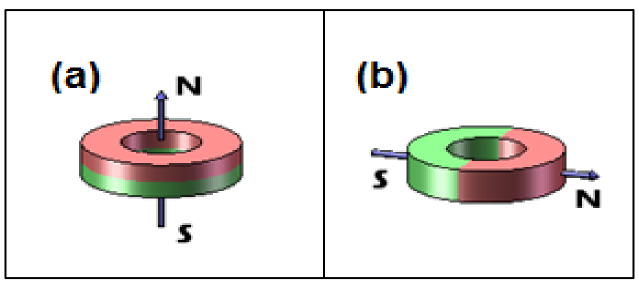


Fig 2.13. (a) Axially magnetized ring. (b) Radially magnetized ring (Reproduced from http://www.kjmagnetics.com)

Cylindrical coordinate is used in order to calculate three components of magnetic field (i.e. H_r, H_θ, H_z) around permanent ring magnet. Coulombian method (Equation 2.7) is one of the analytical methods for calculation the magnetic parameters of permanent magnet. Fig 2.14 displays the parameters which were used in this method.

$$\vec{H}(r,\theta,z) = \vec{H}^{+}(r,\theta,z) + \vec{H}^{-}(r,\theta,z) \quad \textbf{(Equation 2.7)}$$

$$\vec{H}^{+}(r,\theta,z) = \frac{\sigma}{4\pi\mu_0}\int_{\theta=0}^{\theta=2\pi}\int_{r_1=r_{in}}^{r_1=r_{out}} \frac{P_1+M}{|P_1+M|^3} r_1 dr_1 d\theta \quad \textbf{(Equation 2.8)}$$

$$P_1 + \vec{M} = (r - r_1 \cos\theta)\,\vec{\iota_r} - r_1 \sin\theta\,\vec{\iota_\theta} + (z-h)\vec{\iota_k} \quad \textbf{(Equation 2.9)}$$

$$\vec{H}^{-}(r,\theta,z) = \frac{-\sigma}{4\pi\mu_0}\int_{\theta=0}^{\theta=2\pi}\int_{r_1=r_{in}}^{r_1=r_{out}} \frac{P_1-M}{|P_1-M|^3} r_1 dr_1 d\theta \quad \textbf{(Equation 2.10)}$$

$$P_1 - \vec{M} = (r - r_1 \cos\theta)\,\vec{\iota_r} - r_1 \sin\theta\,\vec{\iota_\theta} + (z+h)\vec{\iota_k} \quad \textbf{(Equation 2.11)}$$

<u>*Definitions:*</u>

σ: Surface magnetic pole density (Tesla)

μ_0: Magnetic permeability of vacuum (Henry per meter)

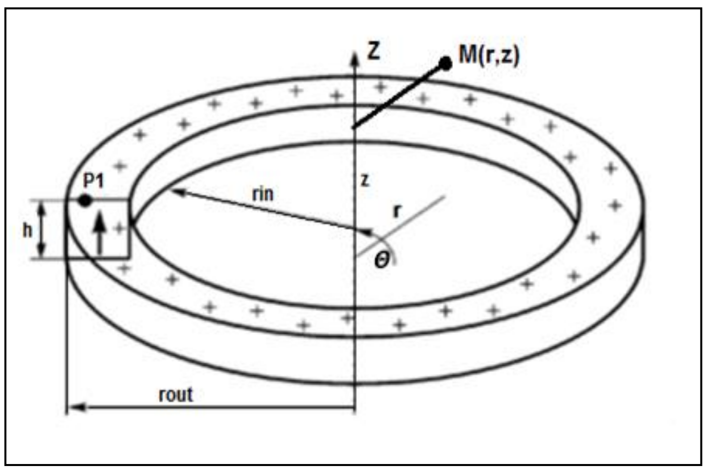


Fig 2.14. Axially magnetized ring permanent magnet at cylindrical coordinate (Reproduced from Babic *et al*. (2008)).

Coulombian method was employed by (Ravaud *et al*., 1989) for calculating three components of magnetic field around ring but this method was not successful for all points (i.e. just for regular points) around the ring. The equations of this method were modified by (Babic *et al*., 2008) in order to calculate magnetic field components for any point of interest (i.e. regular and singular points) around ring permanent magnet. Radial component (r) of magnetic field can be calculated by Equation 2.12. Table 2.3 shows the parameters were used in this equation.

$$\overrightarrow{H_r}(r,\theta,z) = \vec{H}^{+}{}_{r}(r,\theta,z) + \vec{H}^{-}{}_{r}(r,\theta,z) \quad \textbf{(Equation 2.12)}$$

$$H^{+}{}_{r}(r,\theta,z) = \frac{\sigma}{\pi\mu_0}\sum_{n=1}^{2}(-1)^{n-1}\frac{1}{k^{+}{}_{n}}\sqrt{\frac{r_n}{r}}\left[E(k^{+}{}_{n}) - \left(1-\frac{k^{+2}{}_{n}}{2}\right)K(k^{+}{}_{n}\right) \quad \textbf{(Equation 2.13)}$$

$$H^{-}{}_{r}(r,\theta,z) = \frac{-\sigma}{\pi\mu_0}\sum_{n=1}^{2}(-1)^{n-1}\frac{1}{k^{-}{}_{n}}\sqrt{\frac{r_n}{r}}\left[E(k^{-}{}_{n}) - \left(1-\frac{k^{-2}{}_{n}}{2}\right)K(k^{-}{}_{n})\right] \quad \textbf{(Equation 2.14)}$$

Definitions:

r_1: inner radius and r_2: outer radius

K (k): complete elliptical integral of first kind

E (k): complete elliptical integral of second kind

Table 2.3. Required parameters for Equation 8.

Parameters	
$\boldsymbol{k^{+2}{}_{n}} = \frac{4rr_n}{(r+r_n)^2+(z-h)^2}$	$\boldsymbol{k^{-2}{}_{n}} = \frac{4rr_n}{(r+r_n)^2+z^2}$

Azimuthal Component (θ) of this field is zero due to the cylindrical symmetry (Equation 2.15).

$$\overrightarrow{H_\theta}(r,\theta,z) = \vec{H}^{+}{}_{\theta}(r,\theta,z) + \vec{H}^{-}{}_{\theta}(r,\theta,z) = 0 \quad \textbf{(Equation 2.15)}$$

Equation 2.16 is used for calculation the axial component (z) of magnetic field. Table 2.4 defines the parameters of equation 2.16.

$$\overrightarrow{H_z}(r,\theta,z) = \vec{H}^{+}{}_{z}(r,\theta,z) + \vec{H}^{-}{}_{z}(r,\theta,z) \quad \textbf{(Equation 2.16)}$$

$$H^{+}{}_{z}(r,\theta,z) = \frac{\sigma}{2\pi\mu_0}\sum_{n=1}^{2}(-1)^{n-1}\left\{\frac{k^{+}{}_{n}(z-h)\sqrt{r^2+(z-h)^2}}{\sqrt{rr_n}\left(\sqrt{r^2+(z-h)^2}+r\right)}K(k^{+}{}_{n}) + \frac{\pi}{2}sign\,(z-h)sign\left(\sqrt{r^2+(z-h)^2}-r_n\right)[1-\Lambda_0(\theta^{+}{}_{1n},k^{+}{}_{n})] + \frac{\pi}{2}sign(z-h)[1-\Lambda_0(\theta^{+}{}_{2n},k^{+}{}_{n})]\right\} \quad \textbf{(Equation 2.17)}$$

$$H^{-}{}_{z}(r,\theta,z) = \frac{-\sigma}{2\pi\mu_0}\sum_{n=1}^{2}(-1)^{n-1}\left\{\frac{k^{-}{}_{n}z\sqrt{r^2+z^2}}{\sqrt{rr_n}\left(\sqrt{r^2+z^2}+r\right)}K(k^{-}{}_{n}) + \frac{\pi}{2}sign\,(z)sign\left(\sqrt{r^2+z^2}-r_n\right)[1-\Lambda_0(\theta^{-}{}_{1n},k^{-}{}_{n})] + \frac{\pi}{2}sign(z)[1-\Lambda_0(\theta^{-}{}_{2n},k^{-}{}_{n})]\right\} \quad \textbf{(Equation 2.18)}$$

Definitions:

Π (h, k): complete elliptical integral of third kind

Λ (ε, k): Heuman's Lambda function

Table 2.4.The required parameters for Equation 2.10.

Parameters	
$\boldsymbol{\theta^{+}{}_{1}} = sin^{-1}\sqrt{\frac{1-h^{+}{}_{1}}{1-k^{+2}{}_{n}}}$	$\boldsymbol{\theta^{+}{}_{2}} = sin^{-1}\frac{\lvert z-h\rvert}{\sqrt{r^2+(z-h)^2}+r}$
$\boldsymbol{\theta^{-}{}_{1}} = sin^{-1}\sqrt{\frac{1-h^{+}{}_{1}}{1-k^{+2}{}_{n}}}$	$\boldsymbol{\theta^{-}{}_{2}} = sin^{-1}\frac{\lvert z\rvert}{\sqrt{r^2+z^2}+r}$
$\boldsymbol{h^{+}{}_{1}} = \frac{2r}{r+\sqrt{z^2+(z-h)^2}}$	$\boldsymbol{h^{+}{}_{2}} = \frac{2r}{r-\sqrt{z^2+(z-h)^2}}$
$\boldsymbol{h^{-}{}_{1}} = \frac{2r}{r+\sqrt{z^2+r^2}}$	$\boldsymbol{h^{-}{}_{2}} = \frac{2r}{r-\sqrt{z^2+r^2}}$

Magnets apply magnetic forces on each other when they are placed close together. Based on the polarization of each magnet, the applied forces can be attractive or repulsive. Magnetic field strength of source magnet (external magnetic field) should be measured firs in order to calculate the applied magnetics force on target magnet. There are several methods for computation the magnetic force comprising, Surface integration (Maxwell's Stress Tensor approach), volume integration (Virtual Work Method) and finally surface and volume integration (Equivalent Source Method) (Delfino *et al*., 2001). Among all of these methods, equivalent source method has got a lot of interests. This method is based on replacing of permanent magnet with surface and volume distribution of currents, dipoles or magnetic charges. Then, magnetic force of each element is calculated. The total force is the result of summation the calculated magnetic force of each element. The Equations 2.19, 2.20 and 2.21 represent the magnetic force which is applied on target magnet by replacing magnets with surface and volume distribution of currents, dipole and magnetic charges respectively.

$$F = \int_{\Omega} J_{mv} \times B_{ext} d\Omega + \oint_{\Sigma} J_{ms} \times B_{ext} d\Omega$$ **(Equation 2.19)**

$$F = \int_{\Omega} M.\nabla H d\Omega + \frac{1}{2\mu_0} \oint_{\Sigma} (M.n)^2 d\Omega$$ **(Equation 2.20)**

$$F = \int_{\Omega} \rho_m H_{ext} d\Omega + \oint_{\Sigma} \sigma_m H_{ext} dS$$ **(Equation 2.21)**

Definitions:

Jmv: Volume density of current $J_{mv} = 1/\mu_0 \nabla \times M$

Jms: Surface density of current $J_{ms} = 1/\mu_0 M \times n$

ρ_m: *Volume density of magnetic charges* $\rho_m = -\nabla . M$

σ_m: *Surface density of magnetic charges* $\sigma_m = M.n$

B_{ext}: *External magnetic flux density*

H_{ext}: *External magnetic field*

M: Magnetization

Ω: Volume occupied by permanent magnet

Σ: External surface

Equivalent surface method with magnetic dipole is one of the common methods which are used for calculation magnetic force between permanent magnets. In most of studies this method has been used for calculation the levitation force between permanent magnets. This method was employed by (Delinchant *et al*., 2011) to calculate the magnetic force between ring permanent magnet and other shapes of permanent magnets. The only volume contribution of Equation 2.12 can be used in the case of rigid, isotropic and linear magnets. (Alqadi *et al*., 2008) calculated the levitation force between cylinder superconductor and ring permanent magnet. Furthermore, this method was utilized for calculation the magnetic force for MEMS applications such as micro valves (Williams *et al*., 2008; Rakotoarison, H. L., 2006). Moreover, many studies have been done which they considered permanent magnet as magnetic charges in order to calculate the magnetic force between two ring permanent magnets. By contrast the magnetic dipole methods, only surface contribution of Equation 13 can be used for rigid, isotropic and linear magnets. (Ravaud *et al*., 2009) used this method for calculation the magnetic force between two axially magnetized ring permanent magnets for bearing applications. In addition, axially magnetized permanent ring magnets which act as rotor and stator (inner ring as a rotor and outer ring as a stator) can be used for many other applications such as turbo molecular pumps. The (Bekinal *et al*., 2012) deals with the calculation of the force which is applied from outer ring on the inner ring when inner ring moves. While (Ravaud *et al*., 2010) utilized this method to calculate magnetic force between axially ring permanent magnet and radially ring permanent magnet.

2.2.3.2 Temporary Magnet

The principle of this type of magnets is based on transmission of electrical current through the wire which leads to produce electromagnetic field around wire. The magnetic field of this type of electromagnets can be controlled by changing the current. The electromagnets are classified based on different parameters such as, winding shape (e.g. solenoid coil, toroid coil and etc.), geometry of core (e.g. “E” core, “I” core, planer core, “U” core, ring core and etc.), materials of core (e.g. ferromagnetic or ferromagnetic materials) and the polarization of electromagnets (e.g. axially magnetization, diametrically magnetization) . Ampere’s law is used in order to calculate the magnetic parameters of an electromagnet.

2.2.3.2.1 Solenoid

A solenoid is a type of electromagnet that it acts as a permanent magnet when an electrical current is passed through it. A solenoid consists of a long straight coil of wire which can generate a nearly uniform magnetic field in a volume of space. The strength of generated magnetic field can be increased by the addition of iron core at the center of solenoid. Fig 2.15 shows the magnetic field lines around a solenoid without core and solenoid with core. Solenoids have an enormous number of medical applications such as medical analysis of fluids, blood analysis, medical transfusion, medical sterilization, medical ventilation, medical laser, medical imaging and etc.

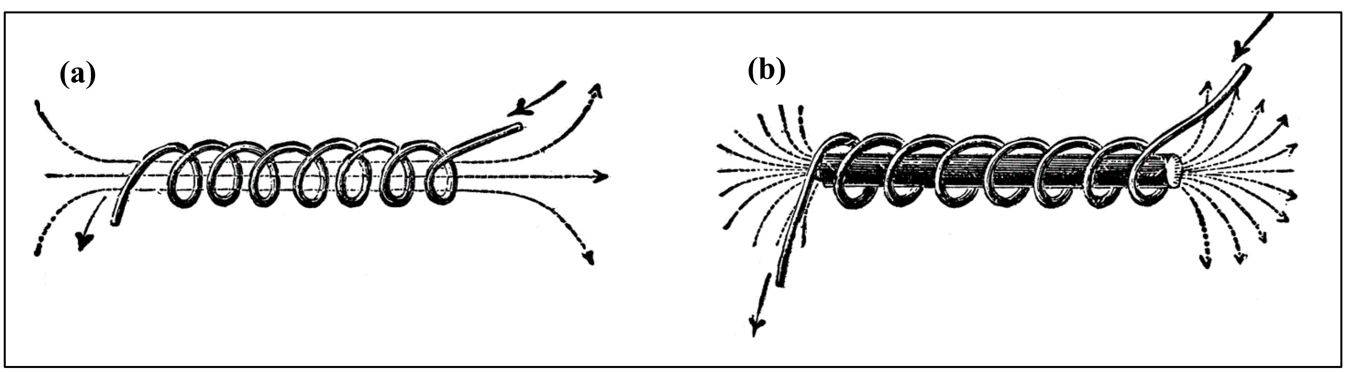


Fig 2.15. (a) Magnetic field lines of solenoid without core. (b) Magnetic field lines of solenoid with metallic core. (Reproduced from http://etc.usf.edu).

Magnetic field of a solenoid which has length “L” and “N” current loops of radius “a” is calculated at the point of “P” in the solenoid axis by Equation 2.22 (Cheng, 1989). Fig 2.16 shows different parameters of following equation.

$$B = \frac{\mu_0 IN}{2L}\int_{\beta_1}^{\beta_2}(-\sin\beta)d\beta = \frac{\mu_0 IN}{2L}(\cos\beta_2 - \cos\beta_1) \quad \textbf{(Equation 2.22)}$$

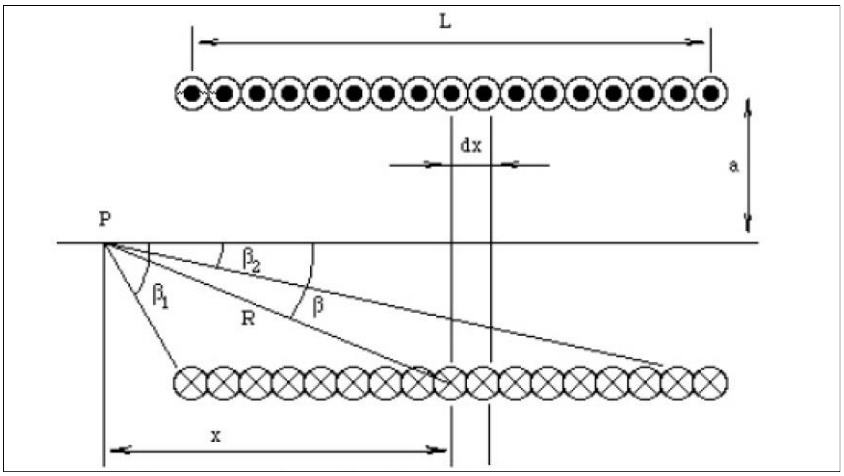


Fig 2.16. Different parameters of Equation 2.14 (Reproduced form http://physics.aalto.fi/pub/kurssit).

According to Fig 2.16, when a permanent magnet or an electromagnet is placed at the point of “P”, the solenoid applies magnetic force on the magnet. Variety methods are used for calculation the applied magnetic force on magnet by solenoid such as the filament method, the shell method, an integral method, the integral method of Babic *et al* which are employed for calculation the applied force on cylindrical permanent magnet (Robertson *et al*., 2012). Equation 2.23 is employed for calculation the applied magnetic force on cylindrical magnet by solenoid. Fig 2.17 illustrates the parameters of following equation.

$$F_{z3} = \frac{B_r NI}{l_c[R_c - r_c]} \int_{-l_c/2}^{l_c/2} \int_{r_c}^{R_c} \sum_{e_1}^{\{1,-1\}} [e_1 m_6 f_{z3}] dr_2 dz_2 \quad \textbf{(Equation 2.23)}$$

Definitions:

Br: Magnet remanence

N: Coil turn

I: Coil current

lc: Coil length

R_c: Coil outer radius

r_c: Coil inner radius

$$f_{z3} = \left[1 - \frac{1}{2} m_5\right] K(m_5) - E(m_5) \quad \textbf{(Equation 2.24)}$$

$$m_5 = \frac{4R_m r_2}{m_6^2} \quad \textbf{(Equation 2.25)}$$

$$m_6^2 = [R_m + r_2]^2 + [z + \frac{1}{2} e_1 l_m - z_2]^2 \quad \textbf{(Equation 2.26)}$$

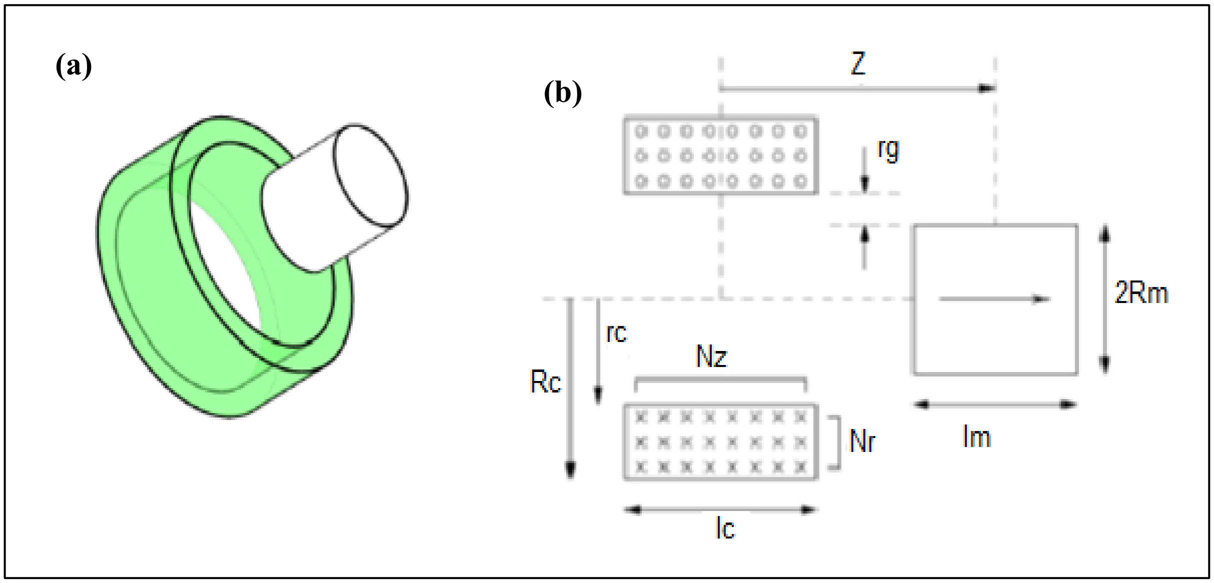


Fig 2.17. (a) Three dimensional sketch of solenoid and cylindrical magnet. (b) This geometry describe the terms of Equation 2.16 (Reproduced from Robertson *et al*. (2012)).

2.2.4 Magnetic Particles

Magnetic particles are valuable materials which can be easily manufactured in a wide range of size from nanometer to micrometer (Aytur, 2007). Magnetic particles are used for a wide range of medical applications such as immunoassay, separation, magnetic resonance magnetic resonance imaging (MRI), drug delivery systems and etc. Different types of biomolecules such as antigens, antibodies, and DNA strands can be easily attached to these particles due to their specific surface functionalization (Fig 2.18). Spherical shape and large surface area are other important properties of these particles which are desired in mass transferring (Pamme, 2006).

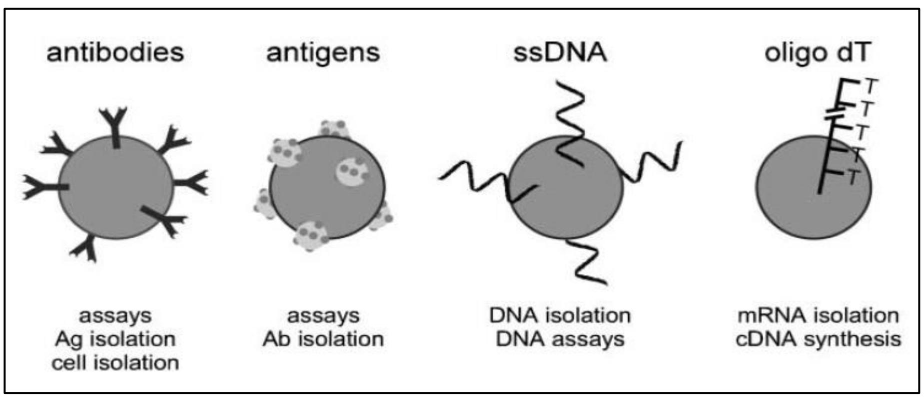


Fig 2.18. Biomolecules such as antibodies, antigens, DNA strand can be attached to the surface of magnetic particles for biomedical applications (Reproduced from Pamme, (2006)).

2.2.4.1 Force on Magnetic Particles

Magnetic force is applied on magnetic particles when they are placed inside a magnetic field. This force depends on strength and gradient of the applied magnetic field, the volume of the particles and the difference in magnetic susceptibilities of particles and their medium. Equation 2.27 is utilized for calculation the applied force on magnetic particles (Gijs, 2004).

$$F = \frac{V.\Delta x}{\mu_0}(B.\nabla)B \quad \text{(Equation 2.27)}$$

Definition:

V: Volume of particles

Δx: The difference in magnetic susceptibilities

(B.∇)B: Strength and gradient of magnetic particles

2.3 Combination of Microfluidics and Magnetism

In recent years the microfluidics and the magnetism have been combined. Combination of microfluidics and magnetism is very useful especially for medical applications. Two approaches are used for controlling the magnetic particles inside the microfluidic systems. Firstly, permanent magnets or electromagnets which they are used outside of the microfluidic systems. Secondly, micro fabricated permanent magnets or electromagnets which they are used inside the microfluidic systems (Pamme, 2006). Magnetic particles are controlled for many purposes such as trapping of particles within a microfluidic chamber, transporting of magnetic particles between reagents, washing and detection of magnetic particles and so on.

2.3.1 Trapping of Magnetic Particles

Trapping of magnetic particles is useful for cell sorting and cell identification applications. For cell sorting or cell identification applications, cells are labeled by magnetic particles. In order to trap magnetic particles in a specific chamber of microfluidic platform, saw-tooth shaped permanent magnets or electromagnetic arrays which they are turned on alternatively are used. By employing these types of magnets, magnetic particles are trapped at locations with maximum magnetic field. As a final step, target cells are sorted and identified from background population (Wirix *et al*., 2005; Lee *et al*., 2001; Burger *et al*., 2012).

2.3.2 Transporting of Magnetic Particles

Magnetic particles are transported between different chambers of a microfluidic platform for different applications such as DNA separation, mRNA purification and so on. In this method biomolecules are labeled with magnetic particles and they moved between different reagents by employing variety shapes of permanent magnets or electromagnetic arrays. Shapes of permanent magnets and numbers of electromagnetic arrays are chosen based on the shape of microfluidic platforms. Strohmeier *et al* (2013) presented a magnetic platform for manipulation of magnetic particles within a centrifugal microfluidic platform. This platform was designed and fabricated by permanent magnet for transporting magnetic particles between three chambers for binding, washing and elution of DNA. In this method, spinning speed of centrifugal microfluidic platform should be zero during the manipulation of magnetic particles.

2.3.3 Detection of Magnetic Particles

Bimolecular detection assays are very challenging issues for diagnosis purposes. Magnetic platform can be used for reduce the time-consuming problem of biological bead-based assays in detection of biomolecules. Bruls *et al* (2009) described using magnetic nanoparticles in stationary microfluidic system for immunoassays and detection of these particles by employing optomagnetic technology. This method is based on actuating magnetic particles by using two electromagnetic at the top and bottom of the microfluidic system.

Chapter 3. METHODOLOGY

The procedure to design and development of an electromagnetic platform for manipulation magnetic particles is discussed in the following sections. This platform can be used for several usages such as, washing and detecting steps in sandwich immunoassays and purification of biomolecules from background populations (e.g. DNA purification). This part of study is divided into six divisions; designing the microfluidic disc platform by AutoCAD software, finding the best design of electromagnetic platform to produce desired magnetic field pattern by COMSOL software, calculating the forces which act on magnetic particles by MATLAB software, changing the variables of the platform and measuring the values of produced magnetic flux density over limited space of microfluidic chamber (COMSOL), obtaining the general magnetic flux density equation for this platform by MATLAB, and finally acquiring appropriate parameters of electromagnetic platform to generate desired force. The following block diagram (Fig 3.1) shows the procedures of this study. Although the mentioned procedures have been done for DNA applications, this platform can be designed easily for other applications by obtaining the general magnetic force equation.

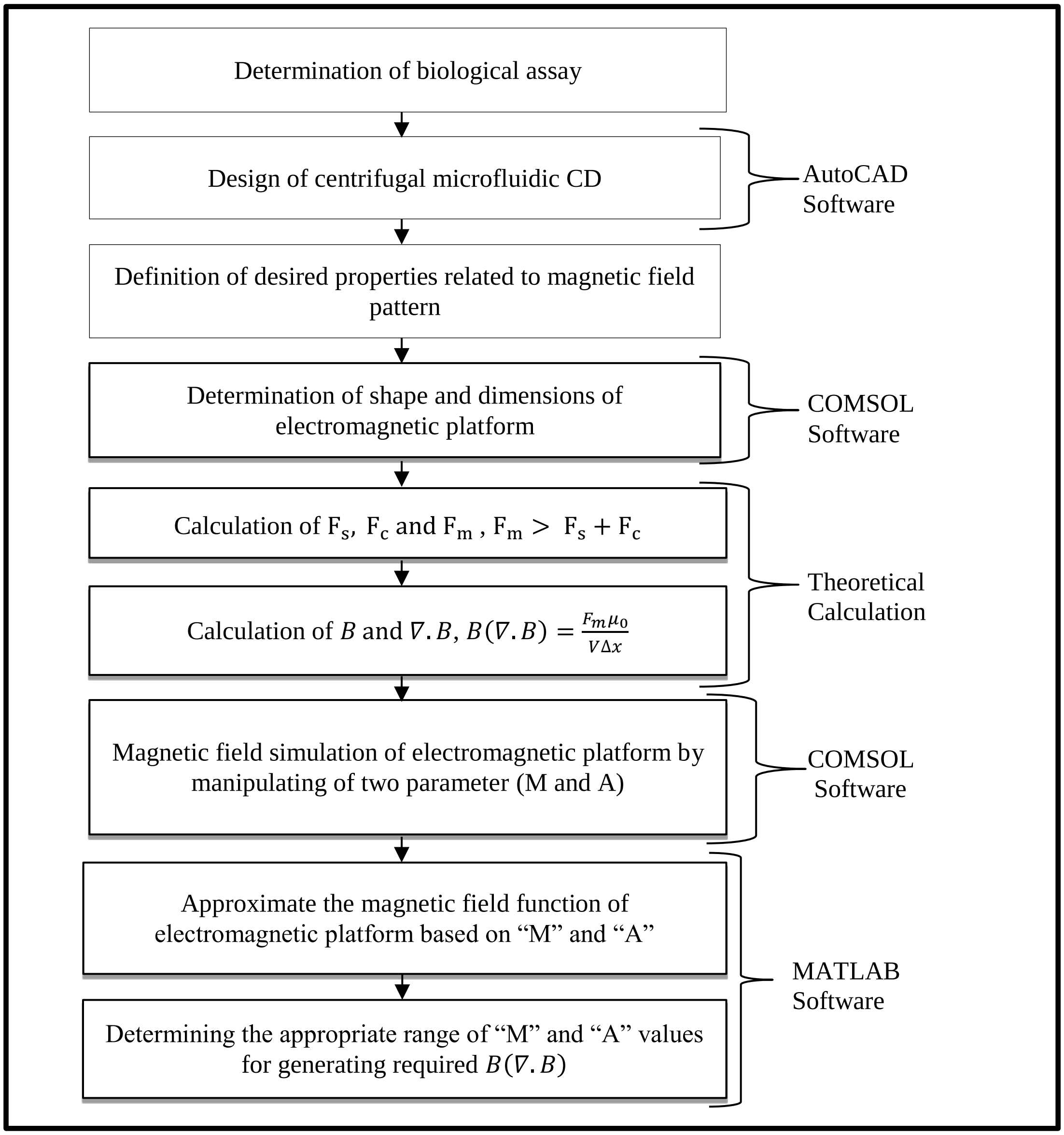


Fig 3.1. Block diagram shows the procedures of design electromagnetic platform.

3.1 Design the Microfluidic Disc Platform

Microfluidic disc platform can be designed in different forms based on its application. The application and design of LOD platform should be specified in order to design electromagnetic platform for manipulation of magnetic particles inside the chambers. Manipulation of magnetic particle can be done for many purposes such as washing, detection, purification, separation and so on. In this study AutoCAD software was used for drawing the CD design for DNA purification.

Magnetic particles act as mobile solid support in some biological assays (e.g. DNA extraction and mRNA purification). These magnetic particles play fundamental role in such assays by displacing between different reagents. DNA purification is an example of these kinds of assays. Hence, complex set-up and design for CD is required in order to transportation of fluid and manipulation magnetic particles between different chambers. The complexity of the CD design can be reduced by applying suitable external magnetic field on CD. This magnetic field helps to move particles from one chamber to another one easily. Therefore, DNA purification was implemented on CD with three chambers. Design of CD for this application consists of binding chamber, washing chamber, and elution chamber (Strohmeier *et al*., 2013). Fig 3.2 displays the design of CD for DNA purification. In this study following design was used for displaying the movement of magnetic particles inside the chambers.

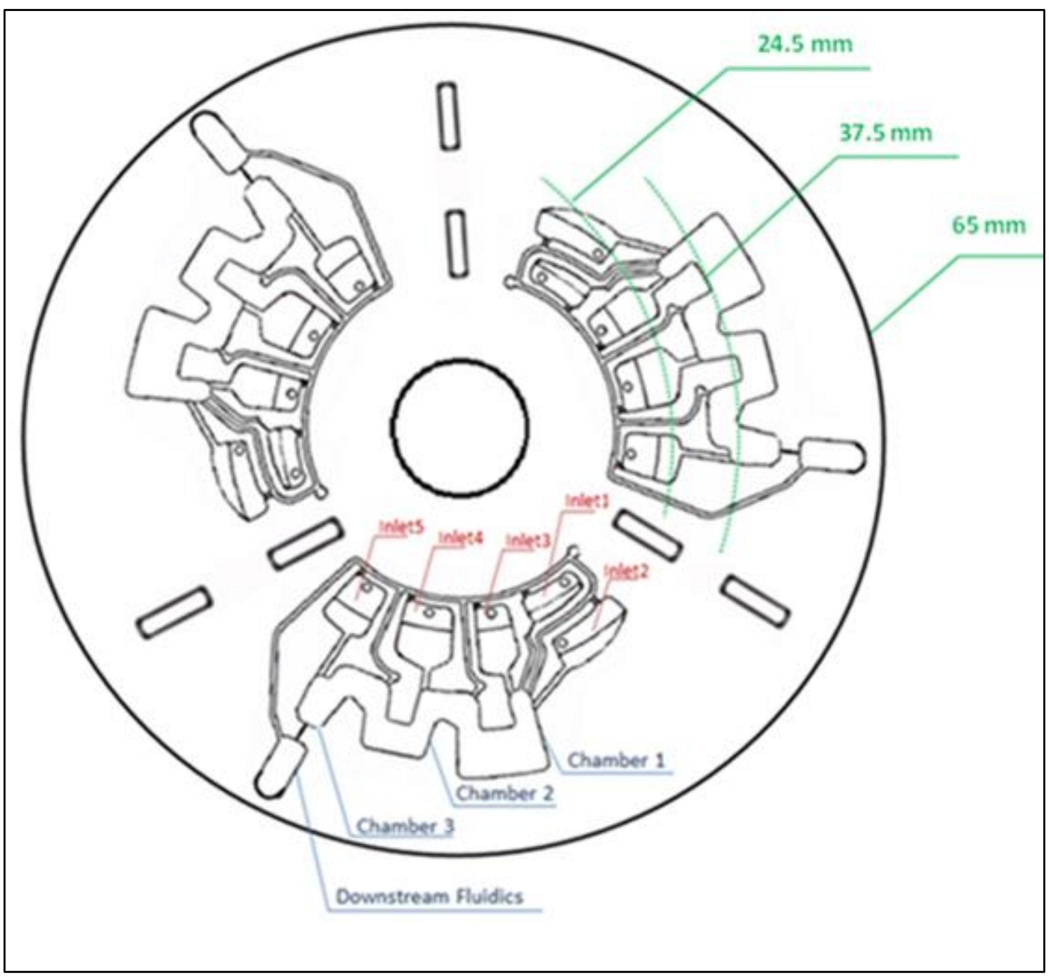


Fig 3.2. Design of CD for DNA purification (Reproduced from Strohmeier *et al*. (2013)).

3.2 Developing the Magnetic Field Pattern

This study aims to design an electromagnetic platform which produce desired magnetic field pattern over centrifugal microfluidic CD. As mentioned in Chapter 2, rotational motion of microfluidic CD provides many advantages to perform biological assays. Therefore, manipulating of magnetic particles during the rotation of CD plays a key role in time-reducing of process and integration of assay. On the other hand, CD platforms are designed in standard size (limited size) with different shapes of chambers and channels to perform sequential steps of bioassay. So, the chambers are very close together and magnetic particles should be controlled very accurately. Magnetic particles can be controlled within the chambers accurately during the rotation of CD by applying desired magnetic field pattern. There are three main objectives in order to get desired pattern. Firstly, the magnetic field pattern should be symmetry relative to z-axis in cylindrical coordinate. Secondly, the maximum values of magnetic field pattern should be located at the target places (chambers that contain magnetic particles) over the CD. Finally, the magnetic field pattern should be constant for the points which have constant distance from centre of coordinate.

Ring permanent magnet is proper option as a magnetic platform to provide these three objectives. The ring shape of magnet produces symmetric magnetic field pattern relative to z-axis. Additionally, axially magnetized rings produce maximum magnetic field over the surface of magnet and this magnetic field pattern is constant for any points with specific distance from centre of coordinate as well (Fig 3.3). Although permanent ring magnet provides many benefits, the magnetic field is not controllable.

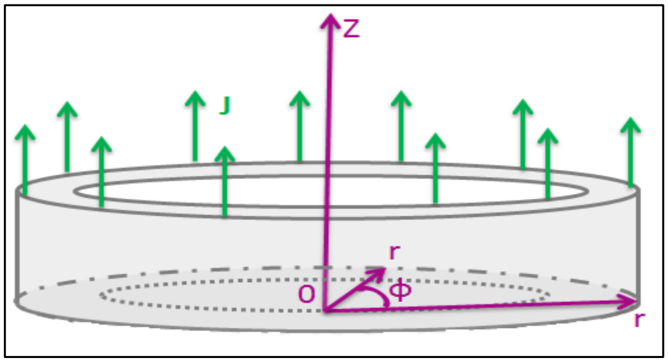


Fig 3.3. Magnetic field lines around ring permanent magnet.

In this study electromagnetic platform has been employed to overcome this problem. Consequently, this study has attempts to design electromagnetic platform which is switched between "on" and "off" positions. In "on" positions it produces magnetic field pattern same as ring permanent magnet while in "off" positions it does not produce magnetic field. COMSOL software was used for simulation the magnetic field pattern around the electromagnetic platform.

3.2.1 Electromagnetic Platform (Symmetric Magnetic Field Pattern)

There are several reasons why symmetric magnetic field pattern is necessary. First of all, CD obviously has the round shape (i.e. it is axially symmetric). In the second place, microfluidic CD is divided into several partitions for performing several assays simultaneously. So, symmetric magnetic field should be applied on the CD to affects all partitions identically. In addition, the magnetic field should be applied on the small area of each partition. For these reasons, ring-shaped electromagnetic platform has been used for generating symmetric magnetic field pattern. Dimensions of an electromagnetic ring platform are based on CD design and its application. On the other hand, the efficacy of magnetic platform on magnetic particles depends on the distance between them. Table 3.1 demonstrates the dimensions of ring electromagnetic platform which are designed for microfluidic CD for DNA purification.

Table 3.1.Dimensions of electromagnetic platform.

Application	**DNA Purification**
Inner Radius (Rin)	30(mm)
Outer Radius (Rout)	45(mm)
Height (h)	19(mm)
Distance to magnetic particles (d)	10(mm)

3.2.2 Electromagnetic Platform (Maximum Values of Magnetic Field Pattern)

Imagine electromagnetic platform which is located at the centre of Cartesian coordinates. The maximum values of magnetic field have been distributed in magnetic field pattern along “x” direction. The location of maximum values on this pattern plays fundamental role in controlling magnetic particles. Therefore, magnetic platform should be designed with specific features to produce desired magnetic field pattern (i.e. the pattern which have maximum values at target places). The locations of maximum values can be determined based on the CD design and its application. Moreover, the maximum values of magnetic field should be applied on the small areas of CD (specific chambers) due to the chambers proximity to each other.

The CD for declared application (i.e. transporting of magnetic particles for DNA purification) require the maximum values of magnetic field above the electromagnetic ring. In other word, the magnetic field pattern along “x” direction should have two maximum values at the overhead of ring. Fig 3.4 displays the desired location of maximum magnetic field along “x” direction.

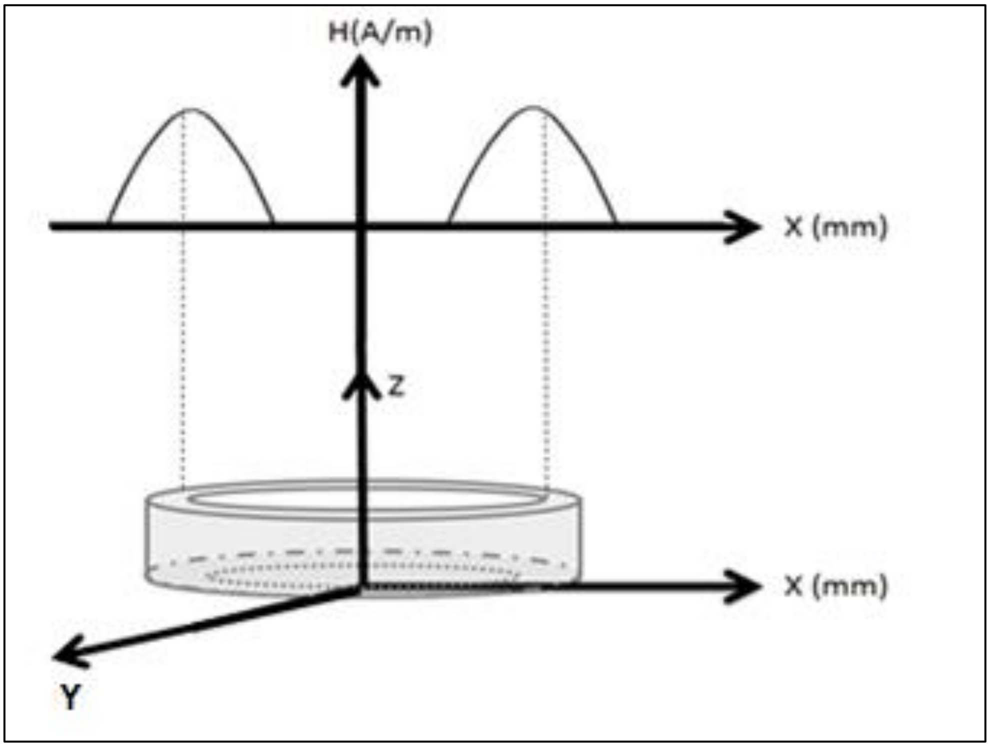


Fig 3.4. Desired locations of maximum magnetic field along "x" direction.

Once the desired locations for peak of pattern were determined, different designs of solenoid electromagnet (simple solenoid and combination of solenoids) were simulated to meet the desired pattern. Solenoid was chosen for simulation due to its ability to produce axial magnetic field. According to the magnetic field equation of solenoid, simple solenoid with air core produces maximum value of magnetic field at the centre. Fig 3.5.a displays the simple solenoid with air core. Thus, the following factors have been applied on the simple solenoid to disperse the maximum value from centre toward the edges.

- Using the combination of solenoid in circular configuration.
- Using material with permeability higher than air as a core of solenoid.

The proposed electromagnetic platform is shown in Fig 3.5.b.

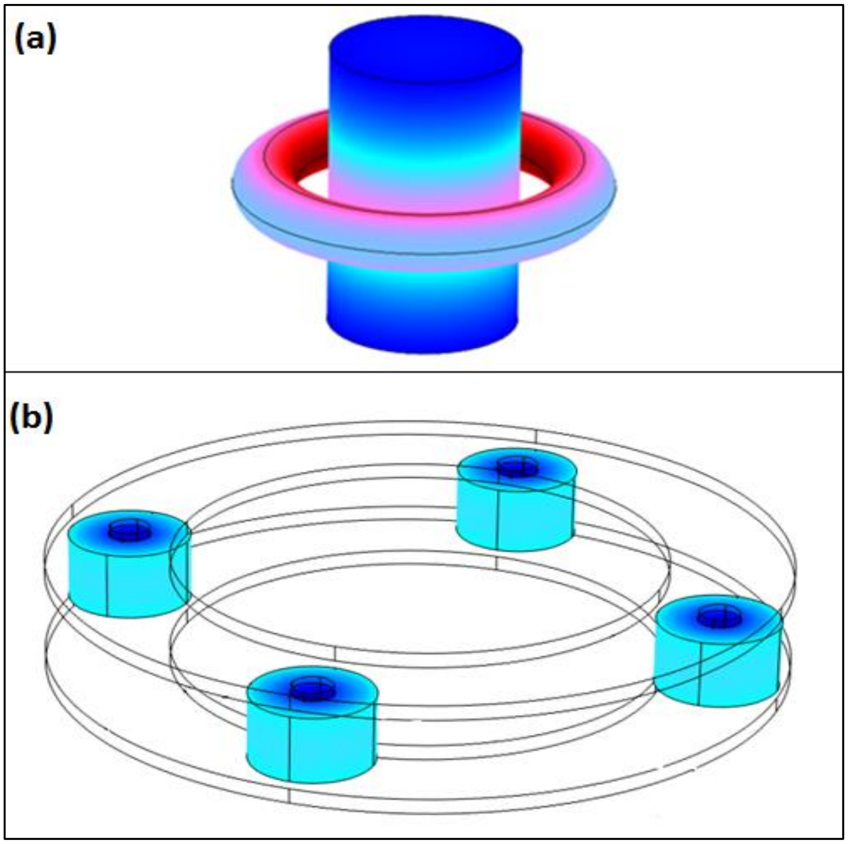


Fig 3.5. (a) Simple solenoid with air core (red color indicates maximum magnetic field strength around solenoid). (b) Electromagnetic platform which constructed from combination of solenoids (4 solenoids).

3.2.3 Electromagnetic Platform (Nearly Homogenous Magnetic Field Pattern)

In this section another type of magnetic field pattern is considered. This pattern is related to the magnetic field value of points which are located with specific distance directly above the electromagnetic platform in a circular shape. The homogeneity characteristic of this magnetic field pattern is another objective of the platform design. As discussed earlier about this parameter, the rotational motion of CD provides many advantages for performing bioassays. Additionally, CD is used for performing several assays simultaneously. Hence, magnetic field should be same for all points which have specific radial distance from the centre of platform (Fig 3.6). In this condition, during the rotation of CD, all target chambers experience same magnetic field.

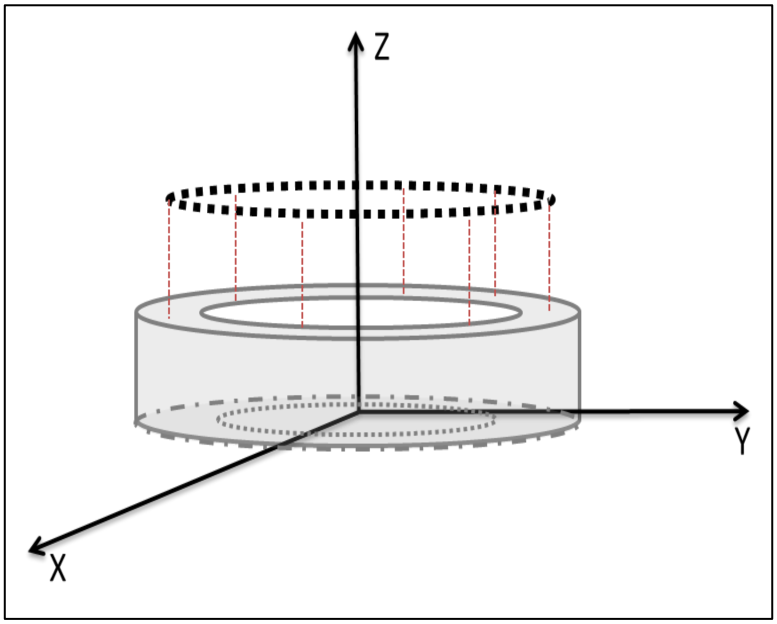


Fig 3.6. The magnetic field pattern should be homogenous for black points which have specific distance from center of platform.

In proposed electromagnetic platform (combination of solenoids in circular configuration), the homogeneity is affected by number of solenoids which are used. Number of solenoids specifies the distance between two solenoids. By using large number of solenoid in electromagnetic platform the homogeneity of magnetic field pattern will be increased. In order to calculate the number of solenoids which can be used in specific area of platform (circular configuration) the following procedures has been used (Fig 3.7). Firstly, the diameter of each solenoid was specified based on the width of ring platform. Secondly, the area of solenoid and the area of ring were calculated. Thirdly, the area of ring was divided by the area of solenoid and the result can approximately show the maximum number of solenoids which can be used in the ring platform.

For this application, according to Table 3.1, width of ring platform for a CD is 13 mm, so the radius of solenoid should be 6.5mm. As a result, the exact number of solenoids which can be used in circular configuration is 16. Finally the location of each solenoid should be specified in "XY" plane by employing trigonometric functions.

$y = r\, sin\, \theta\, , x = r\, cos\theta$ .... **(Equation 3.1)**

Definition:

The distance of solenoid from centre of ring (r): $r = R_{in} + \frac{R_{out} - R_{in}}{2}$ .... **(Equation 3.2)**

Θ: the angle of each solenoid

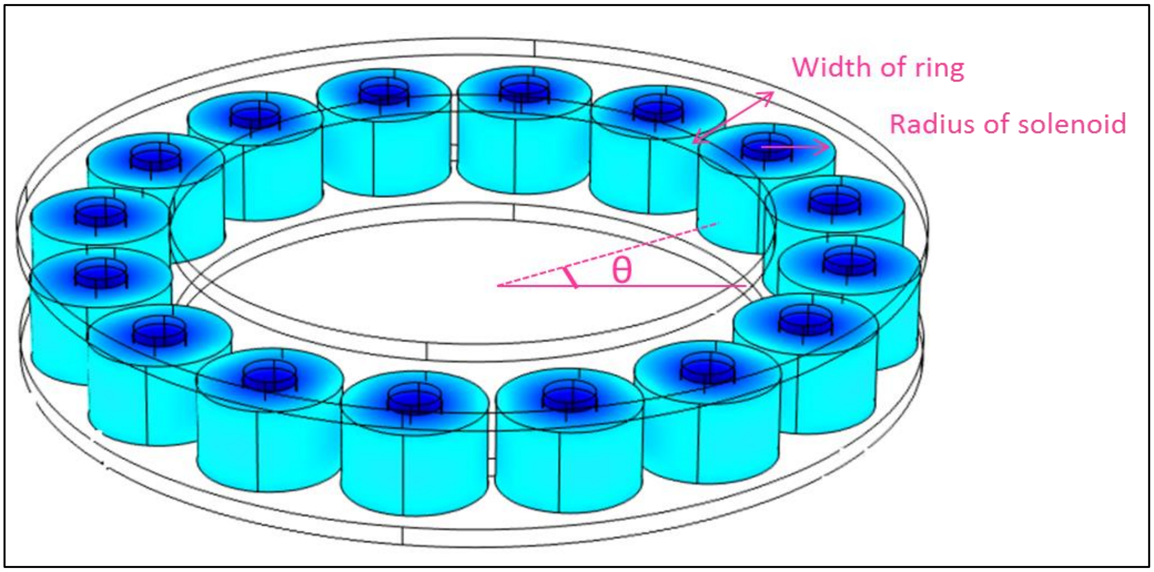


Fig 3.7. The number of solenoid which is used to create homogeneity inside the electromagnetic platform.

3.3 Calculating the Applied Forces on Magnetic Particles

Force should be applied on magnetic particles to transfer them from one chamber into another one. So, calculation of required magnetic force is essential. The required magnetic force for moving magnetic particles should be bigger than the summation of other forces which act on magnetic particles in opposite direction of movement. This section deals with the calculation of applied forces on magnetic particles. All calculations have been done by MATLAB software.

3.3.1Centrifugal Force

This force is due to the rotational speed of microfluidic CD. In fact, when CD is rotating with specific rotational speed, all points of CD will experience the centrifugal force. As explained in microfluidic section, this force is proportional with the density of magnetic particles, the radial distance of magnetic particles from the centre of CD and rotational speed of CD. Table 3.2 shows the required information about the magnetic particles and conditions of rotating CD for different steps of DNA purification (Strohmeier *et al*., 2013).

Table 3.2.The information about the magnetic particles and condition of rotating CD (Reproduced from Strohmeier et al.(2013)).

Parameters	**Value**
Rotational Speed (w)	20.94(rad/sec)
Diameter of magnetic sphere (D)	$1.05e^{-6}$(m)
Density of magnetic sphere (d_{sphere})	1.8 (g/cm^3)
Volume of magnetic particles ($V_{magnetic\ partticles}$)	4e-5 (L)
Mass of Volume particles(m)	$7.2e^{-6}$ (Kg)
Density of volume particles (ρ)	1.8 (Kg/L)
Radial distance form centre of CD(r)	0.04(m)

The centrifugal force density is calculated by Equation 3.3. In order to calculate the centrifugal force, the density of magnetic particles should be multiplied to centrifugal force density equation.

$$F_{Centrifuge} = V_{magnetic\ particles} \times \rho \times w^2 \times r = 1.262e^{-3}(N) = 1.262\ (mN) \quad \textbf{(Equation 3.3)}$$

3.3.2 Surface Tension Force

Another type of force which should be considered is surface tension force. Actually magnetic particles are in liquid phase when they are in binding chamber and they should cross from the gas phase to get to another chamber (washing chamber). Surface tension force is a result of transporting magnetic particles from liquid phase to gas phase. Table 3.3 shows required parameters for calculation this force (Strohmeier *et al*., 2013).

Table 3.3. The required information for calculating surface tension force. (Reproduced form Strohmeier *et al*. (2013)).

Parameters	**Value**
Susceptibility of magnetic particles(X_{mag})	0.29
Susceptibility of liquid (water) (X_{liquid})	$9e^{-63132}$
Permeability of vacuum (μ_0)	$1.25e^{-6}(NA^2)$
Surface tension of liquid(water) (σ_{liquid})	$72.5(mNm^{-1})$
Volume of magnetic particles ($V_{magnetic\ particles}$)	$4(mm^3)$

The following calculation was done based on the information of Table 3.3 and the Equation 3.4 is used to calculate surface tension force.

$$F_{surface\ tension} = 6^{1/3} \times \pi^{2/3} \times \sigma_{liquid} \times V_{magnetic\ particles}{}^{1/3} = 0.448e^{-3}(N) = 0.448\ (mN)$$

(Equation 3.4)

The total forces which apply in the opposite direction of movement magnetic particles were calculated by summation centrifugal force and surface tension force. The total value of applied force is 1.71 mN. Fig 3.8 illustrates directions of centrifugal force, surface tension force and magnetic force which are applied on magnetic particles.

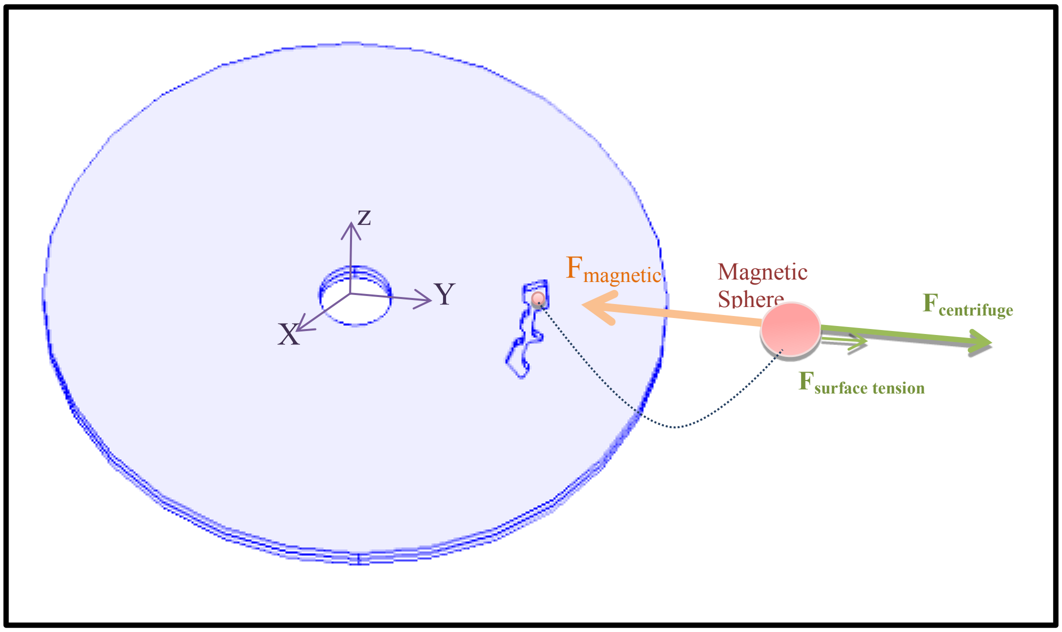


Fig 3.8. The directions of forces which act on the magnetic sphere.

3.3.3 Magnetic Force

In order to transfer magnetic particles from binding chambers toward the electromagnetic platform, magnetic force should overcome the summation of centrifugal force and surface tension force. So, magnetic force should be bigger than 1.71mN. Equation 3.5 shows that the value of magnetic force is related to the volume of magnetic particles, susceptibility of magnetic particles, susceptibility of background liquid, and permeability of vacuum. The values of all these parameters have been specified in Table 3.3. In addition magnetic force is related to the magnitude and gradient of magnetic flux density at the point of magnetic particles.

$$F_{mag} = \frac{V_{cluster}(X_{mag} - X_{liquid})}{\mu_0}.\left(grad\ (B)\right).B \quad \textbf{(Equation 3.5)}$$

Definition:

B_{xyz}: magnetic flux density

$$\left(grad\ (B)\right).B = \begin{matrix} B_x\frac{\partial Bx}{\partial x} & B_y\frac{\partial Bx}{\partial y} & B_z\frac{\partial Bx}{\partial z} \\ B_x\frac{\partial By}{\partial x} & B_y\frac{\partial By}{\partial y} & B_z\frac{\partial By}{\partial z} \\ B_x\frac{\partial Bz}{\partial x} & B_y\frac{\partial Bz}{\partial y} & B_z\frac{\partial Bz}{\partial z} \end{matrix} \quad \textbf{(Equation 3.6)}$$

Definition:

(Grad (B)) $_{xyz}$: gradient of magnetic flux density

The range of (grad (B)).B can be determined by employing the specified parameters in magnetic force equation. Therefore, the value of (grad (B)).B should be at least 1.84 T. According to Fig 3.8, the magnetic particles should move toward the centre of CD (radial direction in cylindrical coordinate). On the other hand, COMSOL software calculates the magnetic flux density in Cartesian coordinate. Hence, the gradient of magnetic flux density was calculated for a point on CD which in this point the radial direction of cylindrical coordinate is parallel with y direction of Cartesian coordinate. Although CD is rotating and the point is displaced, the gradient of magnetic flux density keeps constant due to the homogeneity of the electromagnetic platform. Thus, (grad (B)).B can be calculated as following in order to reduce the complexity of calculation (Gijs, 2004).

$$\left(grad\ (B)\right).B = B_x\frac{\partial By}{\partial x} + B_y\frac{\partial By}{\partial y} + B_z\frac{\partial By}{\partial z} = 1.84(T) \quad \textbf{(Equation 3.7)}$$

3.4 Measuring the Magnetic Flux Density

Different designs of electromagnetic platform produce the different magnetic flux density at the location of magnetic particles. The design of an electromagnetic platform depends on several parameters such as dimension of platform, the material of platform, the number of solenoids which are used in the platform structure, the current of solenoids, the number of turns in solenoid, distance of particle from platform and so on. Some of these parameters must be kept constant and some of them can be varied in specific range. Hence, the main objective of this part is investigation the effect of each parameter on produced magnetic flux density and obtaining the design which can produce 1.84T or more magnetic flux density at the target point.

3.4.1 Dimensions of Electromagnetic Platform

The size of electromagnetic platform has effect on the produced magnetic flux density. In fact, bigger electromagnetic platform provides more spaces to increase the number of turns in each solenoid. As a result magnetic flux density will be amplified around platform. The size of inner radius and outer radius of platform should be kept constant based on the design of microfluidic CD. Height of platform is only variable parameter in platform. Nevertheless, miniaturization is one of the main purposes of “point of care" devices and it limits the size of electromagnetic platform. Therefore, in this study the dimension of platform was considered as a constant parameter (inner radius=24.5mm, outer radius=37.5mm and height=15mm). Fig 3.9 displays the dimension of electromagnetic platform.

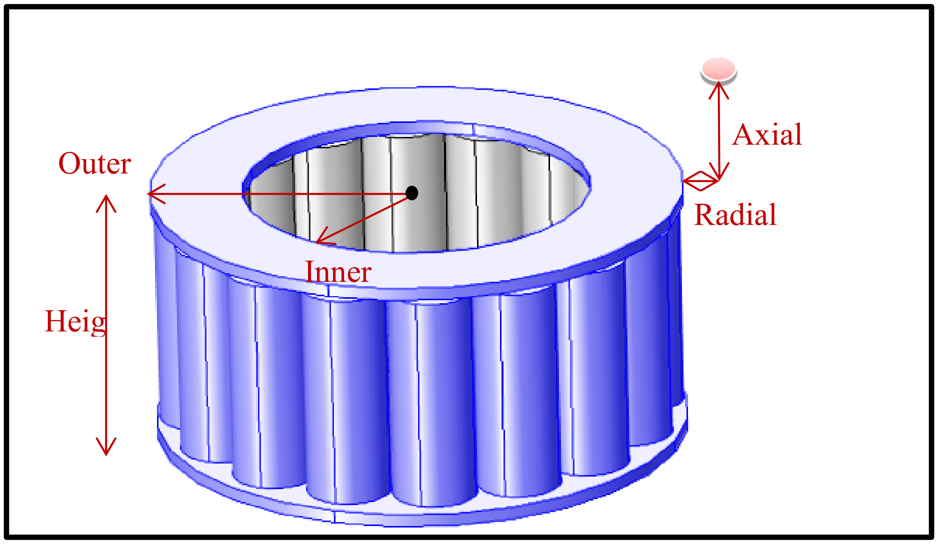


Fig 3.9. Dimension of an electromagnetic platform and the distance of magnetic particles from platform.

3.4.2 The Distance between Magnetic Particles and Electromagnetic Platform

Magnetic flux density decreases extremely by increasing the distance between magnetic particles and the surface of electromagnetic platform. The magnetic particles should be located at particular axial distance from platform due to the fluctuation of microfluidic CD during the rotation. On the other hand, based on the design of CD magnetic particles are placed at specific radial distance from platform. For these reasons changing these parameters is impossible. In this design the axial distance is 6 mm and the radial distance is 2.5 mm (Fig 3.9).

3.4.3 Material of electromagnetic platform

There are variety types of materials which can be used as core of electromagnetic platform. Relative permeability is one of the parameters which should be considered for selecting the material. Materials with high relative permeability have the ability to support magnetic flux formation inside the platform. Therefore, material of core is appropriate parameters to obtain the desired magnetic flux density at a point. For selecting best material as core of platform, the effect of each material on produced magnetic flux density should be investigated. COMSOL software was employed to measure the magnitude and gradient of magnetic flux density when the material of core is changed. Table 3.4 shows several materials with different relative permeability and electrical conductivity which were used in this study. The relative permeability of these material is higher than 1.0 (relative permeability of air).

Table 3.4. Relative permeability and electrical conductivity of materials.

Material	Relative permeability μ/μ_0	Electrical conductivity σ(S/m) at 20° C
Nickel	650	1.43e7
Mild steel	2000	6.99e6
Iron(99.8% pure)	4000	1.00e7
Silicon iron	8000	6.96e6
Mu-metal	100000	1.74e6
Purified iron (99.95%)	200000	1.029e7

3.4.4 Ampere Turns of Coils

As mentioned earlier, the proposed electromagnetic platform consists of 16 solenoids in its structure. In order to preserve the homogeneity of electromagnetic platform, all solenoids should generate equal magnetic flux density at the point of interest. So, the features of all solenoids should be similar. These features consist of the resistance of wire and current which pass through the wire. The resistance of wire depends on three parameters; resistivity, length and cross sectional area of wire. So, the material, length and diameter of wires in all solenoids must be selected equally. Another parameter is current. For passing same current through all solenoids, both parallel and series connection can be used to connect solenoids to the source of voltage. In this study, all solenoids were connected to each other in parallel.

By increasing the current, magnetic flux density of platform will be increased dramatically. However, this platform has been designed for “point of care” testing and portable devices and there is limitation for the usable range of current. So, understanding the value of the current which produce the desired magnetic flux density is very significant. The selected current for this platform are (50 mA, 150 mA, 250mA, 350 mA, 450 mA, 550 mA, 650 mA, 750 mA, 850 mA and 950 mA).

On the other hand, number of turns in coils play important role in the magnitude of magnetic flux density. Specific number of turns can be used in limited area. Therefore number of turns depends on the size of wire. And size of wire is selected based on current. American wire gauge (AWG) table has been used to select appropriate size of wire for coils. Table 3.5 indicates a part of this table. Twice of maximum current should be supported by selected size of wire. In this study the maximum current is 0.95A, hence, the size of wire should support 2 A.

Table 3.5. American wire gauge (AWG) to select the size of wire (Reproduced from http://www.powerstream.com).

AWG	Diameter (mm)	Area (mm^2)	Copper resistance (Ω/km) ($m\Omega$/m)	Fusing current, copper		
				~10 s	1 s	32 ms
22	0.644	0.326	52.96	41 A	94 A	525 A
23	0.573	0.258	66.79	35 A	74 A	416 A
24	0.511	0.205	84.22	29 A	59 A	330 A
25	0.455	0.162	106.2	24 A	47 A	262 A
26	0.405	0.129	133.9	20 A	37 A	208 A
27	0.361	0.102	168.9	17 A	30 A	165 A
28	0.321	0.081	212.9	14 A	23 A	131 A
29	0.286	0.0642	268.5	12A	19 A	104 A
30	0.255	0.0509	338.6	10 A	15 A	83 A
31	0.227	0.0404	426.9	9 A	12A	65 A
32	0.202	0.032	538.3	7 A	9A	52 A
33	0.18	0.0254	678.8	6 A	7A	41 A
34	0.16	0.0201	856	5 A	6A	33 A
35	0.143	0.016	1079	4 A	5A	26 A
36	0.127	0.0127	1361	4 A	4A	20 A
37	0.113	0.01	1716	3 A	3A	16 A
38	0.101	0.00797	2164	3 A	2A	13 A
39	0.0897	0.00632	2729	2 A	2A	10A
40	0.0799	0.00501	3441	1 A	2A	8A

On the other hand, duty cycle of solenoid play key role in selecting size of wire. If the time of applying current on wire was long the bigger size of wire should be selected to prevent the melting of wire. In this study solenoids are on for 10 second. Based on mentioned parameters, all sizes of wire is appropriate for this study except AWG40. Number of turns depends on the size of solenoid and size of wire. For an instance, the number of turns is 156 for each solenoid when AWG 24 (diameter=0.205mm) is selected for solenoid with inner radius= 2.6 mm, outer radius=5.8mm and h=13mm. In an attempt to find the appropriate value of ampere turns, COMSOL software was used. The proposed electromagnetic platform was simulated for mentioned currents and number of turns. Then, the magnitude and gradient of magnetic flux density was obtained. In fact the effect of ampere turn was investigated on the produced magnetic flux density.

3.4.5 Simulation by COMSOL Software

The effects of using different types of materials and also using different ampere turns in producing magnetic flux density at point of interest above electromagnetic platform were investigated by COMSOL software. Magnetic flux density was calculated by AC/DC physic in three dimension space. In addition, stationary domain was selected as a type of study due to the using DC current on solenoids. The simulation of electromagnetic platform was repeated 60 times for six different materials and ten different ampere turn values. In each simulation, the effect of specific type of material with specific ampere turn value was surveyed. COMSOL software uses the meshing method (i.e. finite element method) for division a portions of the geometry into small units of a simple shape. To obtain the result with high accuracy, this software has ability to use meshing with better performance for high sensitivity spaces. In this study, finer meshing method was employed for getting the high accuracy results along the shape.

Fig 3.10 shows the meshing of electromagnetic platform for calculation the magnetic flux density values.

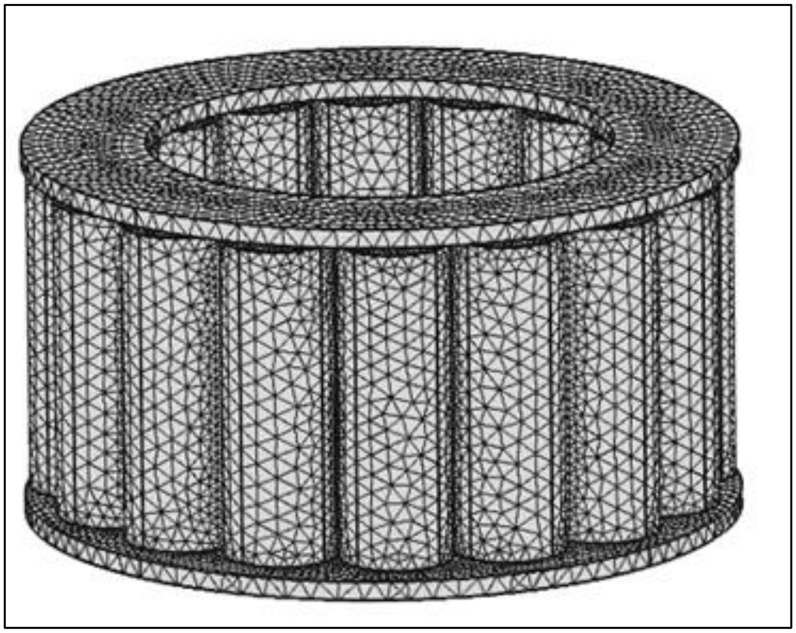


Fig 3.10. Meshing (fine mesh) on electromagnetic platform.

3.5 Magnetic Flux Density Equation of Electromagnetic Platform

Finding the relationship between material, ampere turn value and produced magnetic flux density play fundamental role in design the parameters of electromagnetic platform. MATLAB software has a function (curve fitting) which can be used to find the relationship between parameters. Hence, the value of permeability of each material and the value of ampere turns and obtained magnitude and gradient of magnetic flux density are required for acquiring the relationship between them. In the first step, all parameters should be defined in MATLAB. MATLAB assigns a point in space for each parameter. Therefore these three parameters are defined in three dimension space. In the second place, curve fitting function is applied on the parameters. MATLAB proposes a curve which covers some parts of defined points in space. The accuracy of covering points by curve can be changed, when the method of fitting is changed. The SSE value shows the error of method. So, the value of SSE helps to find the best method of fitting. In this study linear model poly 34 was selected. In this equation the order of ampere turn is 3 and the order of material is 4. This model can cover all values of three parameters in 3D space. In addition the SSE value of this model is minimum compared to other model. Finally, MATLAB shows the relationship between the parameters as an equation. By employing above procedures, the obtained equation shows the relationship between magnetic flux density ((grad (B)).B), permeability of material and ampere turn. Based on the selected method for fitting, the order of equation and the value of coefficients are changed.

3.6 Acquiring Appropriate Parameters for Design

The final step is acquiring the exact value of parameters for design the electromagnetic platform. The magnetic force should be at least 1.71mN and for producing this force 1.84 T magnetic flux density is required at the point of magnetic particles. Therefore, desired value of magnetic flux density will be gained by employing the obtained equation and changing the variable parameters in allowed ranges. In this study MATLAB software has been used to define the allowed ranges of materials and ampere turns and also for calculation the magnetic flux density by magnetic flux density equation.

Chapter 4. RESULTS AND DISCUSSION

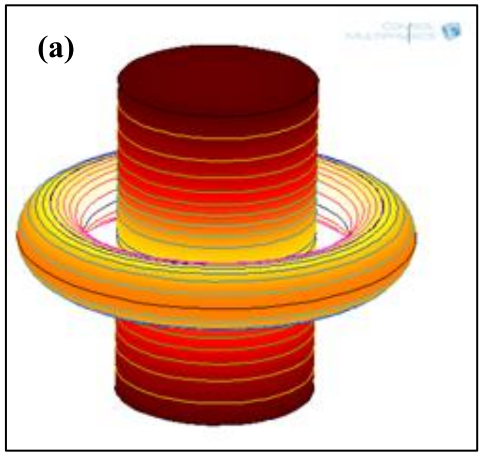
The results generated by proposed electromagnetic platform are described in the following sections. The first section, presents all simulation results which are related to procedures for obtaining desired magnetic field pattern. In this section, the effects of the desired pattern on the manipulation of magnetic particles will be discussed. After that the simulation outputs and the results of mathematical calculations regard to obtain required strength of magnetic field will be shown in the second section. Third section, deals with the significance of proposed electromagnetic platform and finally the performance of this platform in controlling magnetic particles within CD will be compared with existing methods.

4.1 Simulation Results for Developing the Desired Magnetic Field Pattern

This part is divided into two subsections; first subsection shows simulation results of modifying the locations of maximum values on magnetic field pattern and second subsection deals with the simulation results of improving the homogeneity of magnetic field over the electromagnetic platform.

4.1.1 Simulation Results for Improving the Locations of Peaks on Magnetic Field Pattern

The washing and detecting functions which are applied on CD for sandwich immunoassay and also the transporting of magnetic particles within the CD for DNA purification require the magnetic field pattern along “X” direction with two peaks. The desired pattern is defined with two maximum values at the top of the edges of ring and the zero values for rest of the points. Manipulation of magnetic particles within chambers will be facilitated by possessing two maximum values at the top of the edges. The effect of magnetic field on the neighbour chambers leads to incompatible manipulating of magnetic particles. For this reason, the magnetic field should be zero at the rest of the points along this pattern. Fig 4.1, Fig 4.2 and Fig 4.3 show the improvement of magnetic field pattern by altering the design of electromagnetic platform.



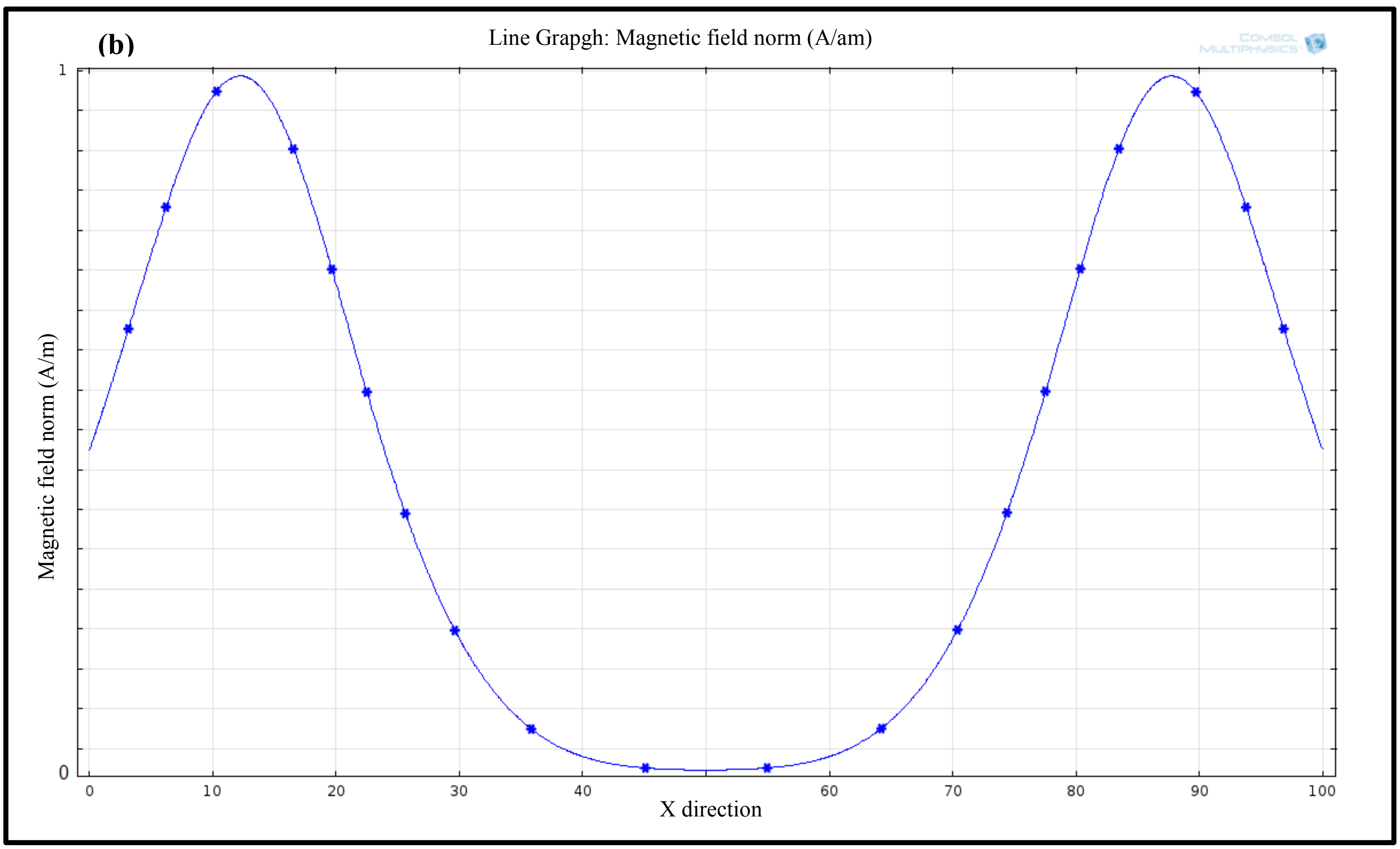


Fig 4.1. (a) Single solenoid with air core (yellow color shows the maximum magnetic field, red color shows the minimum magnetic field). (b) The magnetic field pattern along "x" direction of simple solenoid.

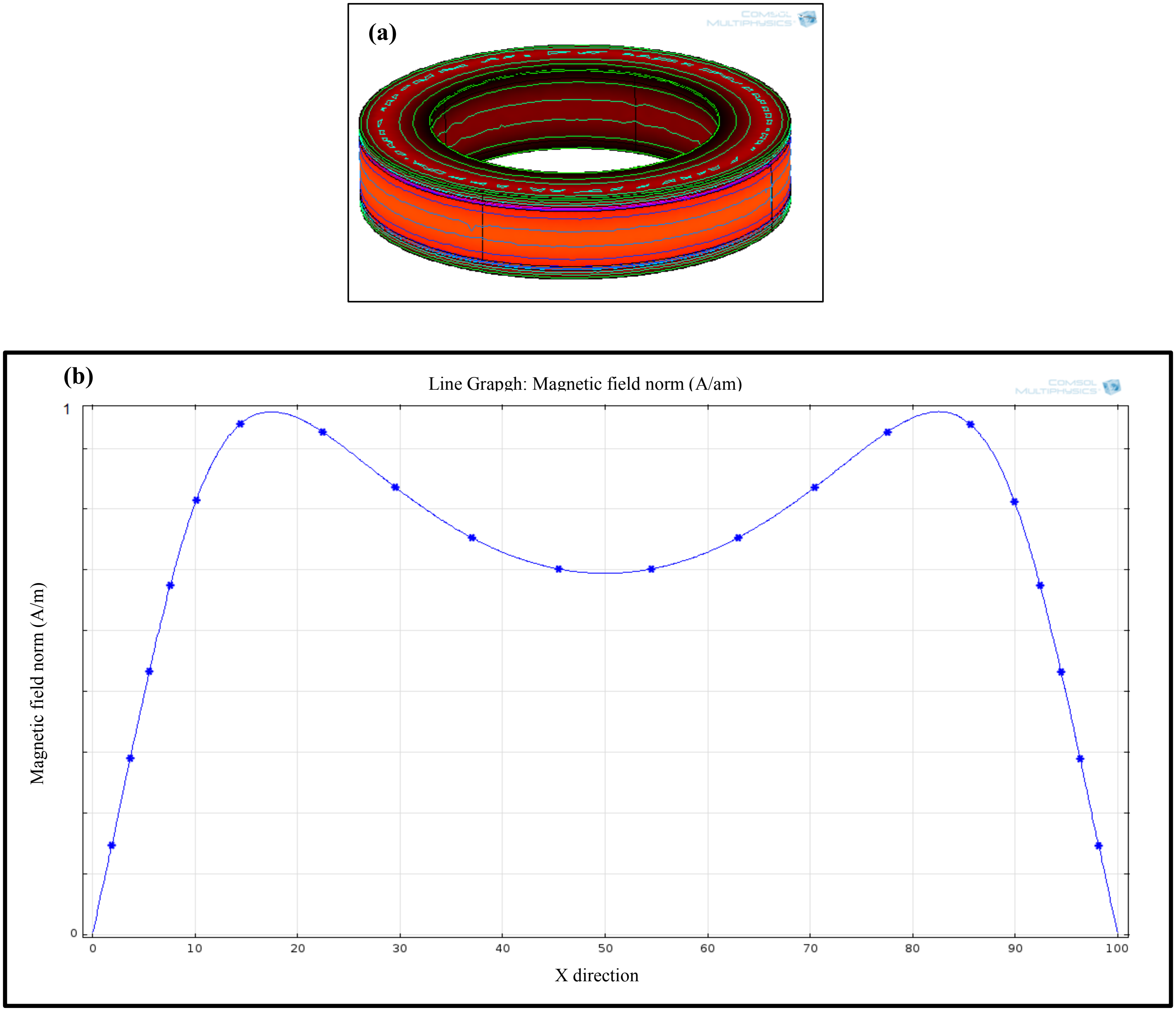


Fig 4.2. (a)Solenoid with ring-shaped of aluminum core (red color shows maximum values of magnetic field). (b) The magnetic field pattern along "x" direction of solenoid with ring-shaped of aluminum core.

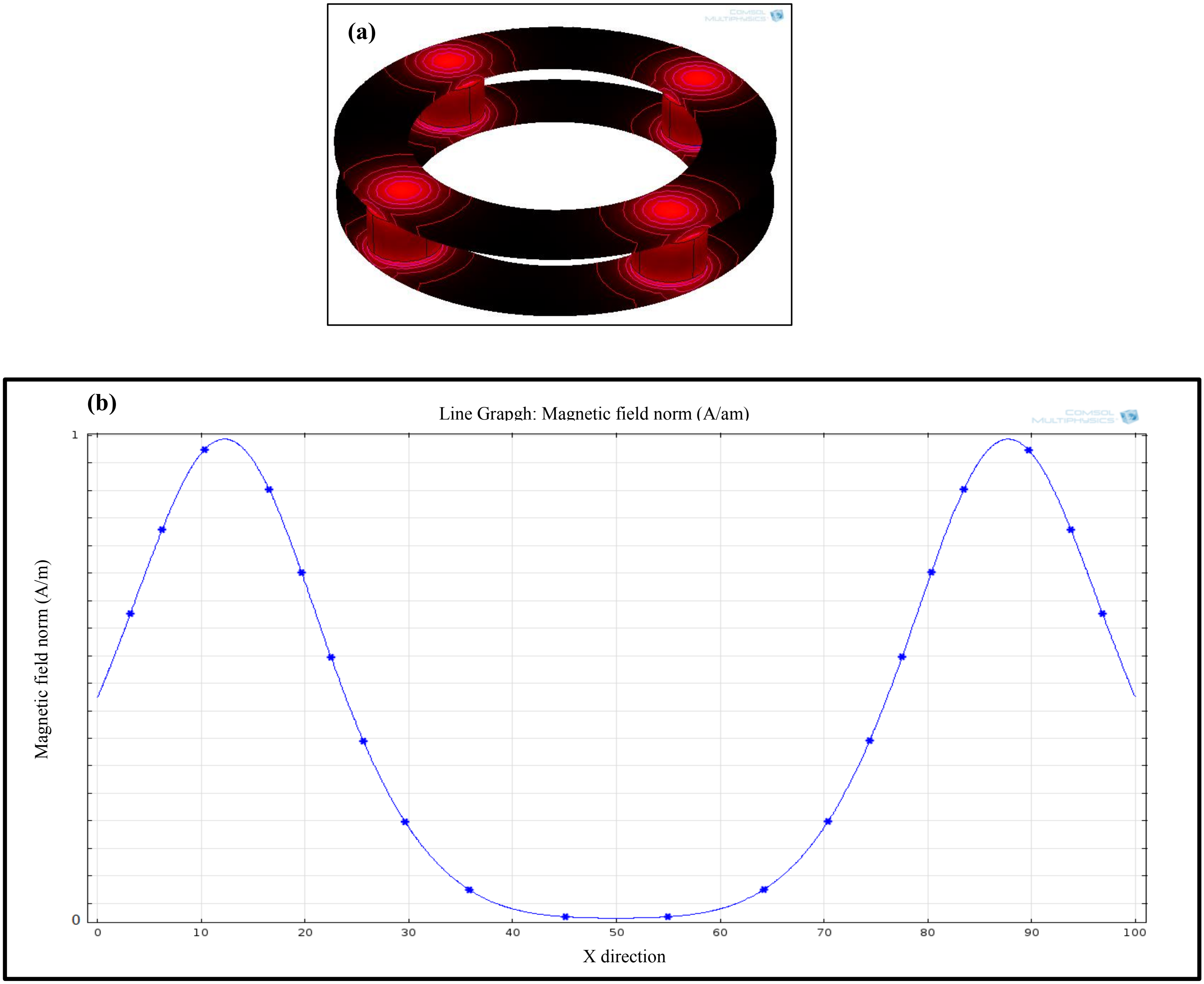


Fig 4.3. (a) Combination of solenoids inside the aluminum ring-shaped core (red color shows maximum magnetic field, black color shows minimum magnetic field). (b) The magnetic field pattern along "x" direction of multiplex solenoids.

In these figures, firstly simple solenoid with air core was simulated and magnetic field pattern along "x" direction was obtained. The magnetic field pattern displays that magnetic field lines have concentrated at one point in center of solenoid. Therefore, the material of core was changed. The magnetic field pattern of simple solenoid with aluminum core (material which has the permeability higher than air) was simulated. The obtained result shows that the magnetic field lines concentrate at two points which are at the top of the cores. This variation happened due to the permeability index of core. As a result the magnetic field lines tend to concentrate at the edges of the core. Fig 4.4 indicates the magnetic field line in this solenoid.

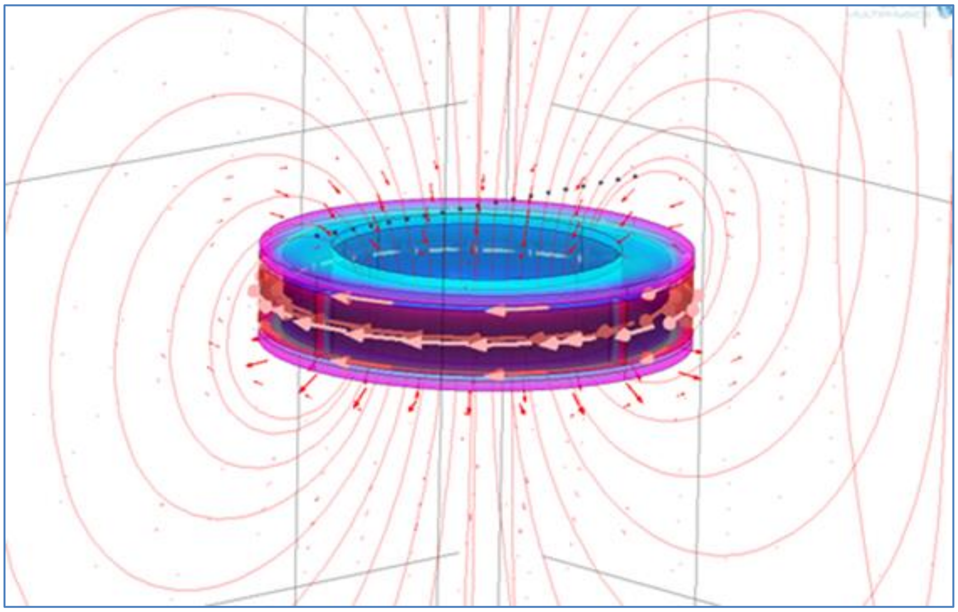


Fig 4.4. concentration of magnetic field around the edge of core.

The problem of using this kind of platform is that, magnetic field value at the rest of the points is not zero. Hence, the electromagnetic platform was proposed which has been constructed from a number of solenoids. These solenoids were located inside the ring core (the material of core has permeability higher than air) in a circular configuration. The simulation results of this platform indicated that the density of magnetic field lines is maximum at two points at the top of the edges. Moreover, the magnetic field values for rest of the points are approximately zero. Consequently, this design of electromagnetic platform could provide the requirements of desired magnetic field pattern.

4.1.2 Simulation Results for Improving the Homogeneity of Magnetic Field Pattern

One of the objectives of this study is the control on magnetic particles during the rotation of microfluidic CD and performing the several biological assays simultaneously as well. Therefore, to achieve this end, homogeneity of magnetic field pattern along the circle-shaped area is essential. In order to improve the homogeneity of magnetic field pattern, the proposed design of an electromagnetic platform was modified. As previously described, increasing the number of solenoids leads to improving the homogeneity of magnetic field patter. Fig 4.5, 4.6, 4.7 shows the progress of improvement the homogeneity of the magnetic field pattern.

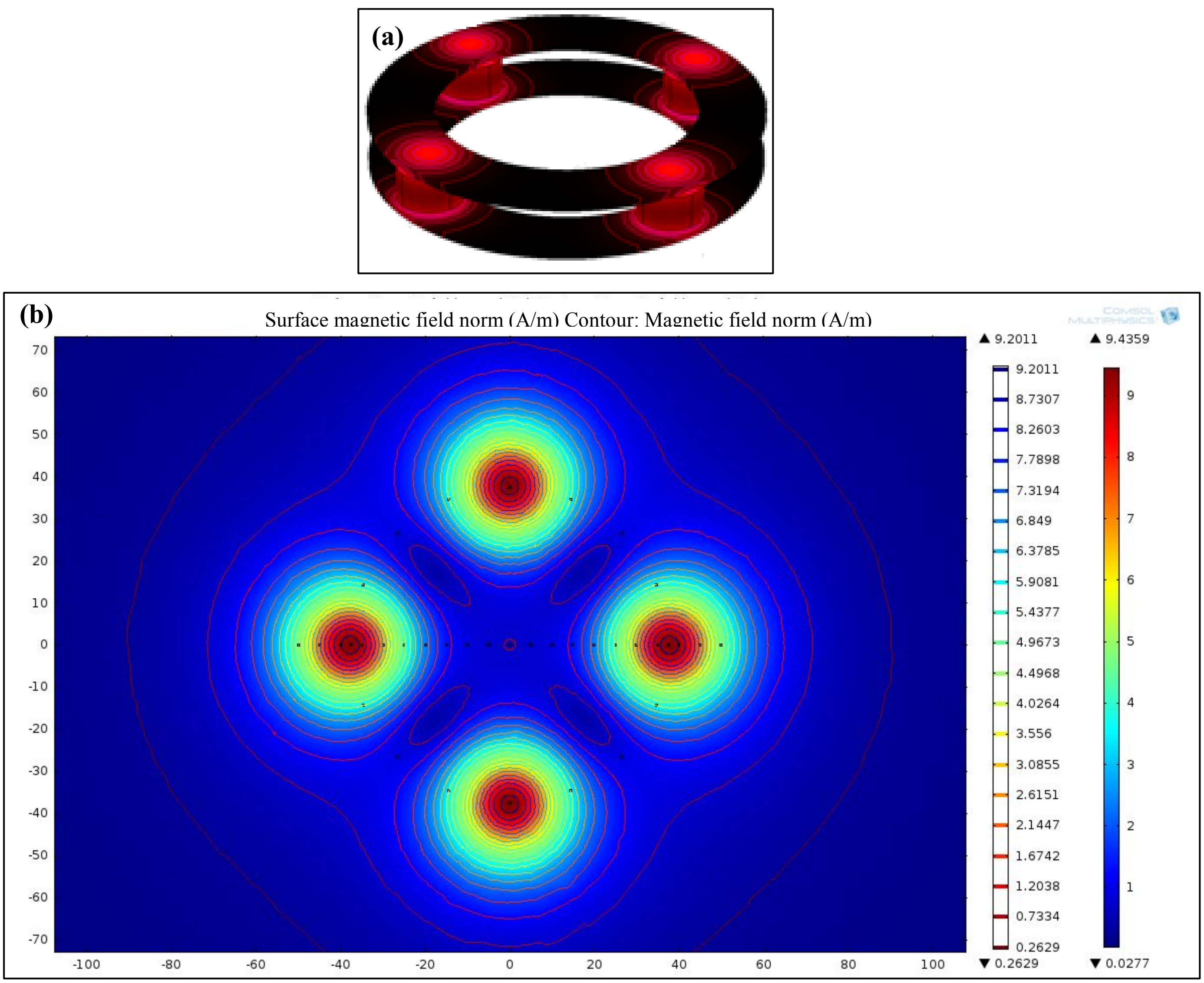


Fig 4.5. (a) Electromagnetic platform with 4 solenoids. (b) Magnetic field pattern of ring electromagnetic platform with 4 solenoids.

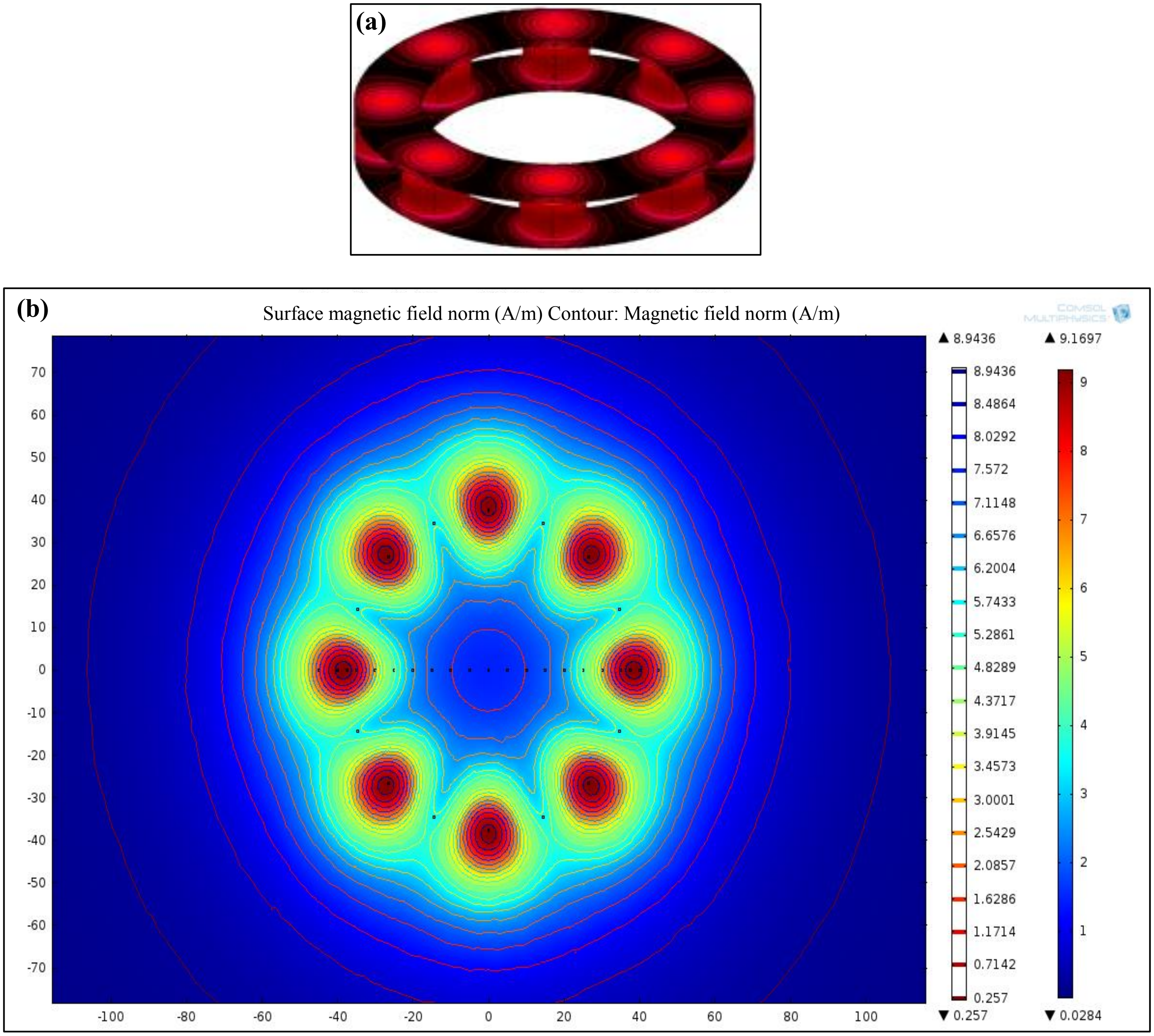


Fig 4.6. (a) Electromagnetic platform with 8 solenoids. (b) Magnetic field pattern of ring electromagnetic platform with 8 solenoids.

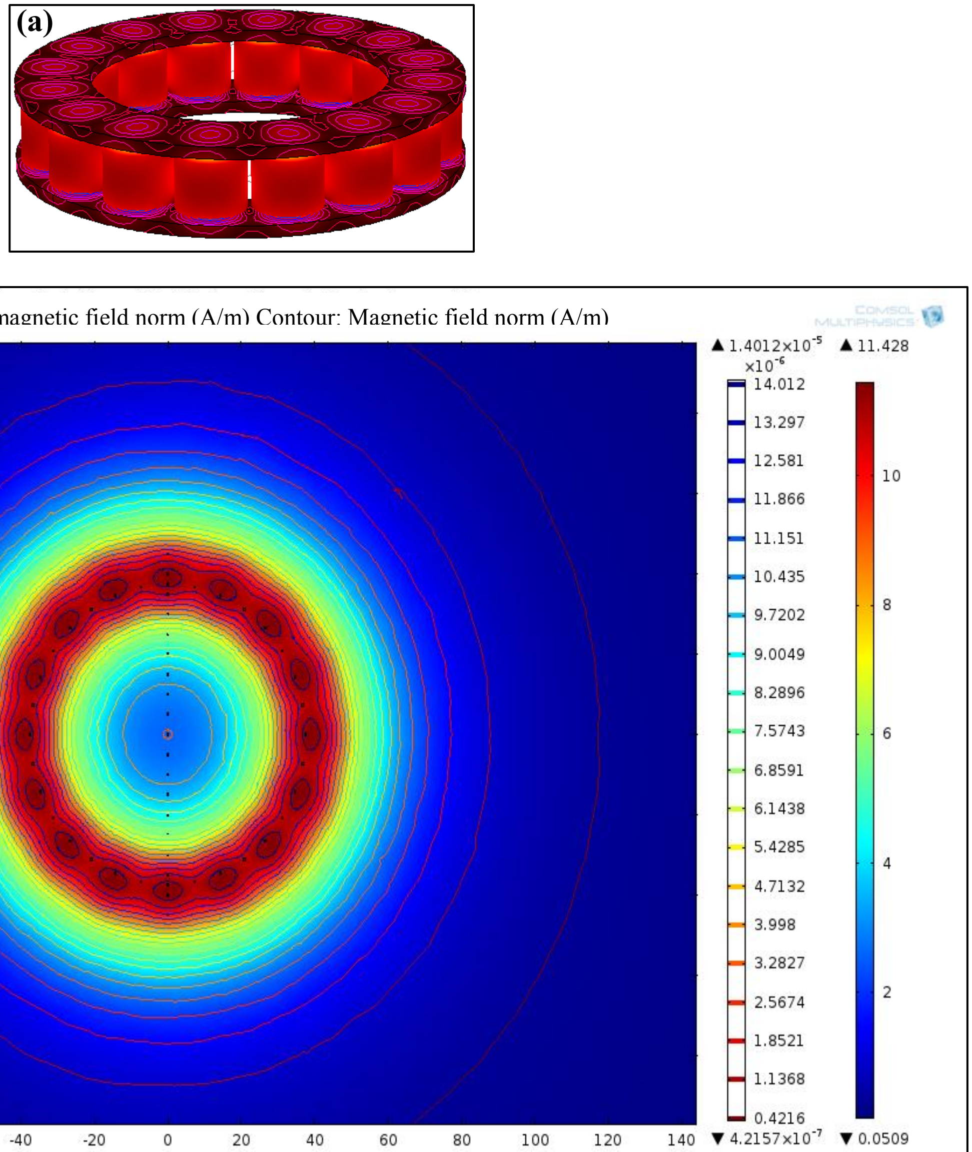


Fig 4.7. (a) Electromagnetic platform with 16 solenoids. (b) Magnetic field pattern of ring electromagnetic platform with 16 solenoids.

In electromagnetic platform with four solenoids, the magnetic field pattern shows the magnetic field lines are concentrated on only four points. Increasing the number of solenoid to eight creates more homogeneity in the magnetic field pattern. Lastly, the simulation result indicates that magnetic field pattern in nearly homogenous for all point by increasing the number of solenoids to 16. Fig 4.8 demonstrates the difference between these three patterns.

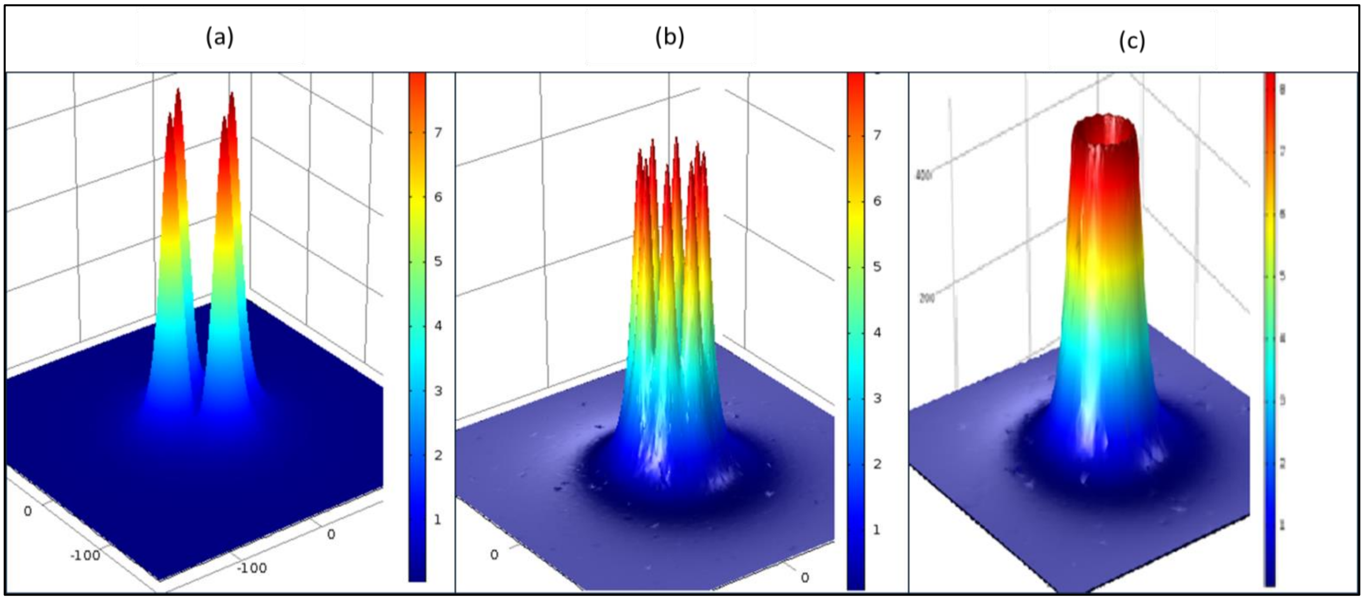


Fig 4.8. (a) The magnetic field pattern of electromagnetic platform with 4 solenoids (N=4) (b) The magnetic field pattern of electromagnetic platform with N=8 (c) The magnetic field pattern of electromagnetic platform with N=16.

Fig 4.8(a) shows that the magnetic field pattern has 4 peaks and other points have zero magnetic fields. The magnetic field of Fig 4.8(b) has 8 peaks but the magnetic field of other points are not zero. While the in Fig 4.8(c) the magnetic field values for all points are nearly same. This design of electromagnetic provides many advantages for manipulation of magnetic particles within the CD. By employing this platform the magnetic field is applied only on the target chamber, magnetic particles are manipulated within the microfluidic CD in several biological assays simultaneously during the rotation of CD. Consequently, this design enhances the accuracy of controlling on magnetic particles, improve the integrity and automation of LOD devices and reduce the time for performing the procedure of bioassays.

4.2 Results for Developing the Desired Magnetic Flux Density Strength

According to Chapter 3, several steps have been done to design the electromagnetic platform which can produce desired magnetic flux density at the point of interest. The first step was calculation the required magnetic force. This force should be more than summation of centrifugal force and surface tension force. The calculated value of this force was 1.71 mN. Then according to the magnetic force equation, the value of magnetic force depends on the susceptibility of liquid, susceptibility of magnetic particles and the value of magnetic flux density. Therefore, the required magnetic flux density was calculated. The require value of magnetic flux density was 1.84 T. Third step attempted to investigate the effects of different parameters on produced magnetic flux density. So, magnetic flux density was measured by changing the parameters of platform. The measured values of magnetic flux density were used to find an equation. This equation presented the relationship between different parameters and produced magnetic flux density. Finally, the appropriate values of theses parameters were obtained to design desired electromagnetic platform.

4.2.1 Results of the Values of Magnetic Flux Density

As mentioned in Chapter 3, among all parameters, the material of core and the ampere turn values of solenoids are most effective parameters in producing desired magnetic flux density. Therefore, electromagnetic platform was simulated for 60 times by COMSOL to investigate the effect of different types of materials and ampere turn values on the produced magnetic flux density. The results of each part consist of three components of magnetic flux density (Bx, By, Bz) and the gradient of magnetic flux density just for "y" component (∂By/∂x, ∂By/∂y, ∂By/∂z). Finally, obtained results were used to calculate the (grad (B)).B. Finding the relationship between type of material, ampere turn and produced magnetic flux density is necessary to find out appropriate values of these parameters (best type of material for core of platform and ampere turn values of solenoids).

4.2.2 Result of the Relationship between Produced Magnetic Flux Density and Variable Parameters

Finding the equation between magnetic flux density and other parameters of electromagnetic platform is useful for design the platform. MATLAB software was used to identify the relative permeability of material, ampere turn value and magnetic flux density as a point in 3 dimension spaces. Then the equation between them was found by applying curve fitting function on identified points. Fig 4.9 displays MATLAB analysis results. In this figure X, Y and Z represent the relative permeability of material, ampere turn value and the value of (grad (B)).B respectively.

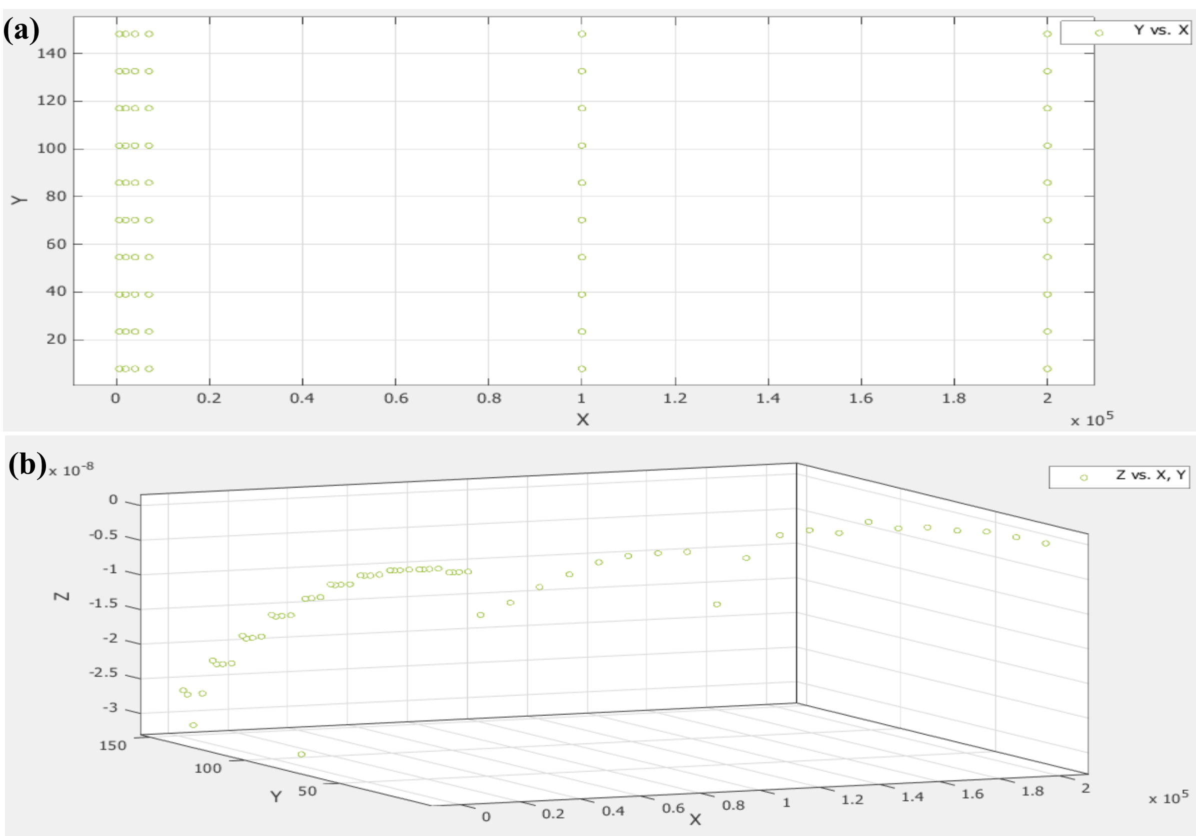


Fig 4.9. (a) Relative permeability value of material and ampere turn values of solenoids in 2D space. (b) The relative permeability of materials, ampere turn values and the results of (grad (B)).B in 3D.

For covering all identified points in 3D spaces, the correct model of fitting should be selected. At the first time polynomial 11 was selected to obtain the equation (Fig 4.10). This model was not suitable for fitting. Equation 4.1 shows the obtained equation by this model. In following equation F(x,y) is Z which is the function of X and Y. The SSE of this model is $1.063e^{-15}$.

F(x,y) = 1.655e-09 + 3.775e-14 *x + -1.591e-10 1*y..........**(Equation 4.1)**

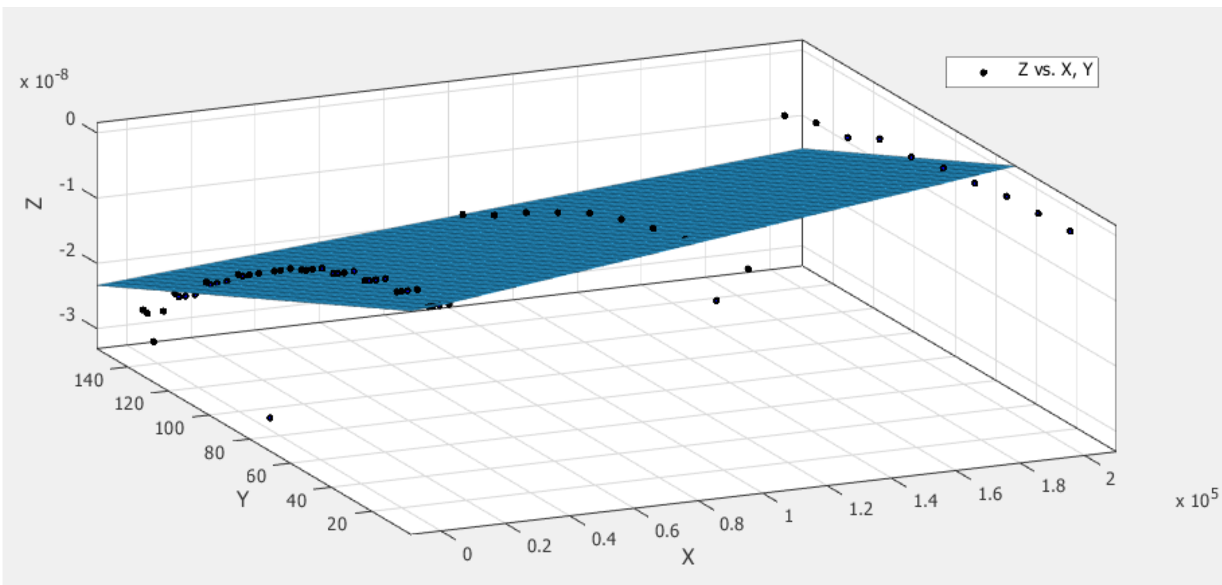


Fig 4.10. The covering of points by polynomial 11.

Desired covering obtained by changing the degree of X and Y in polynomial model. The best degree for X is 2 (in this condition SSE value is lowest). Fig 4.11 shows the covering of points by polynomial 23(X=2, Y=3).

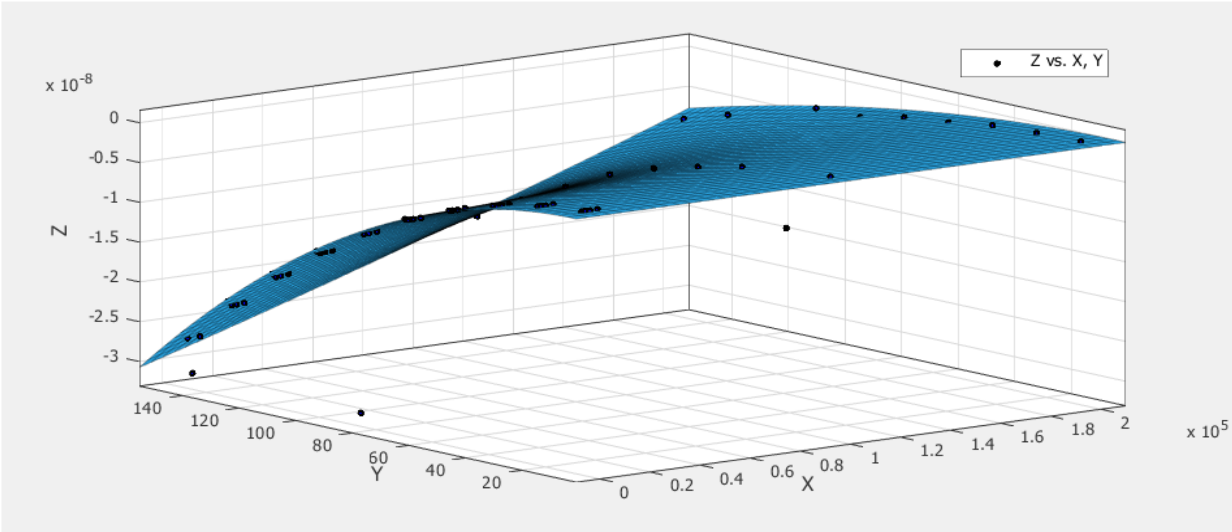


Fig 4.11. The covering of points by polynomial 23.

Equation 4.2 shows the obtained equation by this method.

F(x, y) = p00 + p10*x + p01*y + p20*x^2 + p11*x*y + p02*y^2 + p21*x^2*y + p12*x*y^2 + p03*y^3 .... **(Equation 4.2)**

The coefficients with 95% confidence bounds are described as following.

p00 = -2.098e-11, p10 = 5.577e-16, p01 = 3.007e-12, p20 = -2.518e-21, p11 = -7.031e-17

p02 = -1.295e-12, p21 = 3.325e-22, p12 = 4.362e-18, p03 = 2.455e-16

The obtained equation represents the relationship between the relative permeability of materials, ampere turn values and the value of (grad (B)).B. Therefore, the appropriate values of permeability of materials and ampere turn values can be obtained by employing this equation.

4.2.3 Results of Appropriate Values for Permeability of Materials and Ampere-Turn of Solenoids

The appropriate values of variable parameters (permeability of materials and ampere turn values) can be gained by using MATLAB software. The first step is identifying the wide range of values for these tow parameters in MATLAB. After identifying the ranges of inputs, the obtained equation was employed to calculate the produced magnetic flux density at the point of interest. Table 4.1 displays the results of this part. According to Table 4.1, material with relative permeability 200000 can produce desired values of (grad (B)).B (i.e. (grad (B)).B > 1.9). As mentioned in Chapter 3, this material is 99.95% purified iron. The availability to other materials such as silicon iron is easier than this material. Hence, there are different methods to increase the magnetic flux density of an electromagnetic platform when the other materials are chosen as a core of platform. One of these methods is using a thin layer of ring permanent magnet on the surface of electromagnetic platform. In this case, the value of produced magnetic flux density by electromagnetic platform and permanent magnet should be 1.84 T.

Table 4.1. The appropriate values of relative permeability of materials and ampere-turn value.

Number	Relative permeability of materials	Ampere turn values of solenoids	(grad (B)).B	Number	Relative permeability of materials	Ampere turn values of solenoids	(grad (B)).B
1	650	78	-4.78E-07	31	8000	78	0.11741
2	650	234	-4.77E-07	32	8000	234	0.117415
3	650	390	-4.77E-07	33	8000	390	0.117419
4	650	546	-4.77E-07	34	8000	546	0.117423
5	650	702	-4.77E-07	35	8000	702	0.117428
6	650	858	-4.76E-07	36	8000	858	0.117432
7	650	1014	-4.76E-07	37	8000	1014	0.117437
8	650	1170	-4.76E-07	38	8000	1170	0.117441
9	650	1326	-4.75E-07	39	8000	1326	0.117445
10	650	1482	-4.75E-07	40	8000	1482	0.11745
11	2000	78	-3.21E-06	41	100000	78	0.232554
12	2000	234	-3.21E-06	42	100000	234	0.232561
13	2000	390	-3.20E-06	43	100000	390	0.232567
14	2000	546	-3.20E-06	44	100000	546	0.232574
15	2000	702	-3.20E-06	45	100000	702	0.232581
16	2000	858	-3.20E-06	46	100000	858	0.232588
17	2000	1014	-3.19E-06	47	100000	1014	0.232595
18	2000	1170	-3.19E-06	48	100000	1170	0.232601
19	2000	1326	-3.19E-06	49	100000	1326	0.232608
20	2000	1482	-3.18E-06	50	100000	1482	0.232615
21	4000	78	-4.99E-06	51	200000	78	1.912214
22	4000	234	-4.98E-06	52	200000	234	1.912241
23	4000	390	-4.97E-06	53	200000	390	1.912269
24	4000	546	-4.96E-06	54	200000	546	1.912296
25	4000	702	-4.95E-06	55	200000	702	1.912323
26	4000	858	-4.94E-06	56	200000	858	1.91235
27	4000	1014	-4.93E-06	57	200000	1014	1.912378
28	4000	1170	-4.91E-06	58	200000	1170	1.912405
29	4000	1326	-4.90E-06	59	200000	1326	1.912432
30	4000	1482	-4.89E-06	60	200000	1482	1.912459

4.3 Manipulation of Magnetic Particles

The designed electromagnetic platform can be used for different application. As explained in chapter 3 force=1.71 mN was required to transfer magnetic particles from binding chamber toward the electromagnetic platform. In order to generate this value of magnetic force, 1.84 T magnetic flux density is required. According to the results of previous section, the designed electromagnetic platform can generate magnetic flux density approximately 1.9(T) at the point of interest when this platform is "on". Therefore, this platform can transfer magnetic particles from binding chamber toward electromagnetic platform while microfluidic CD is rotating. The electromagnetic platform is "on" for 10 second. After 10 second, the electromagnetic platform will become "off". In this condition, Coriolis force is applied on magnetic particles. This force can transfer the magnetic particles from the electromagnetic particles toward the opposite direction of rotating CD. Finally, centrifugal force transfer magnetic particles toward the washing chamber. Fig 4.12 displays the different steps of manipulation of magnetic particles.

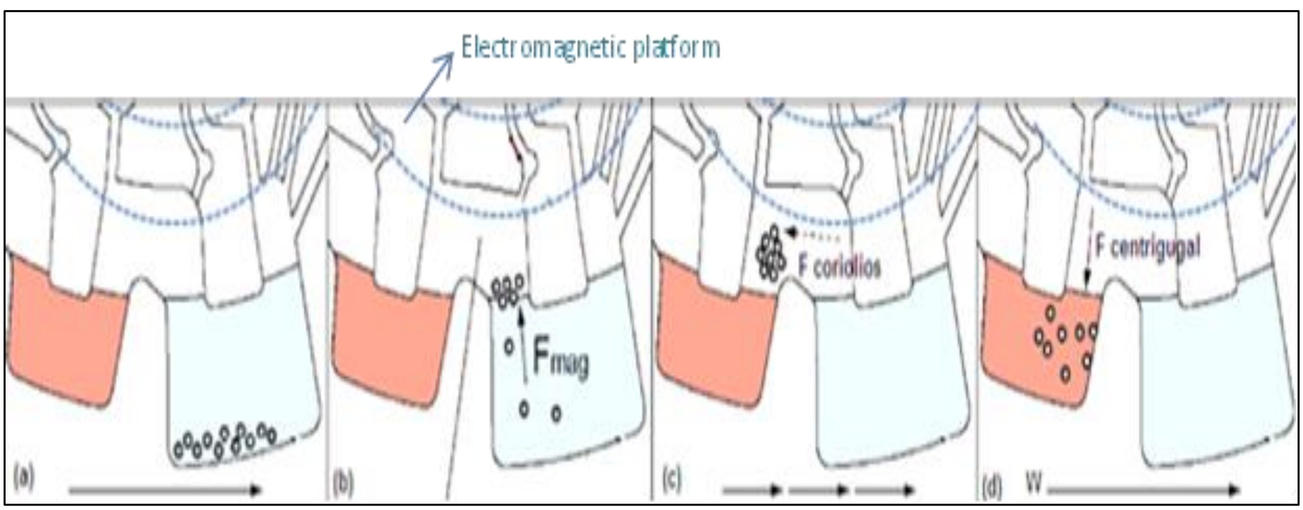


Fig 4.12. (a) Magnetic particles inside the binding chamber. (b) Magnetic chamber move toward electromagnetic platform. (c) Coriolis force is applied on magnetic particles to move them toward the opposite direction of rotation CD. (d) The centrifugal force transfer magnetic particles to the washing chamber (Reproduced from Strohmeier *et al*. (2013)).

Chapter 5. CONCLUSION AND RECOMMENDATION FOR FUTURE WORK

5.1 Conclusion

In this study, an electromagnetic platform for controlling magnetic particles in a centrifugal microfluidic platform is designed and simulated. The dimensions of electromagnetic platform have been selected based on the design of microfluidic CD which provided by (Strohmeier *et al*., 2013) for DNA purification. Then geometrical shape of electromagnetic platform has been designed based on producing the magnetic field pattern with three features including; symmetrical shape of magnetic field pattern relative to the z axis, the maximum magnetic field strength at the specific locations and finally homogeneity of produced magnetic field pattern above electromagnetic platform. Magnetic field pattern which have these three features is called desired magnetic field pattern. In order to obtain desired magnetic field pattern, an electromagnetic platform has been designed. This platform consists of the circular-shaped core with 16 solenoids.

The value of produced magnetic flux density is another objective of this study. So as to obtain the required magnetic flux density, the following procedures have been done. At the first place, the required magnetic force for transporting magnetic particles has been calculated. The value of the required magnetic force should be more than the summation of centrifugal force and surface tension force which are applied at the opposite direction of magnetic force. At the second place, required magnetic flux density has been calculated by employing the magnetic force equation. Then, the effects of structural parameters of electromagnetic platform on producing magnetic flux density have been investigated. The value of some of these parameters should be considered constant such as the axial and radial distance between magnetic particles and electromagnetic platform. While other parameters can be considered as variables including the type of material which is used as a core of platform and ampere turn of solenoid. The effects of these two parameters on produced magnetic flux density have been investigated by COMSOL software. Electromagnetic platform has been simulated for 60 times to obtain magnitude and gradient of magnetic flux density when the variable parameters were changed. The obtained results have been used to find the relationship between variable parameters and produced magnetic flux density. The equation of these parameters has been obtained by employing the curve fitting function in MATLAB software. This equation is general for designed electromagnetic platform. The wide ranges of variable parameters have been identified as inputs. Finally, appropriate values of variable parameters have been gained by employing obtained equation to design the desired electromagnetic platform. This procedure can be used in different conditions such as, changing the rotational speed of microfluidic CD or changing the size or susceptibility of magnetic particles. The electromagnetic platform with purified iron as a material of core and different ranges of ampere turn values can produced desired value of magnetic flux density at the location of magnetic particles. The magnetic force caused by the designed electromagnetic platform can overcome the centrifugal force and surface tension force. As a result, magnetic particles are transferred toward the electromagnetic platform when this platform is “on”. The electromagnetic platform is “on” for 10 seconds and then it will be “off”. When electromagnetic platform is “off”, magnetic particles are transferred toward washing chamber by the effect of Coriolis force and centrifugal force.

5.2 Limitations and Recommendation for Future Work

Accessibility of purified iron is less than other material such as, silicon iron. There are variety methods to produce desired magnetic flux density value by using other types of materials. One of the methods is using thin layer of ring permanent magnet on the surface of electromagnetic platform.

Designed electromagnetic platform has been used for different applications such as DNA purification. This platform can be used for other applications such as, different types of sandwich immunoassay. In these assays washing step is used for presenting the target in a measurable form. This step requires the additional chambers on the LOD platform for storage the washing liquid. In addition, mechanical actuation of washing liquid is time consuming process. In the magnetic particles-based assays, employing magnetic field facilitates the washing step. As mentioned earlier these types of assays are based on labelling analyte with magnetic particles. Thus magnetic field acts as washing solution to remove the analyte which have a weak bind with immobilized specific antibodies. Therefore, washing chambers were eliminated in the design of LOD platform. On the other hand, detection chambers are required in immunoassay to measure target (analyte). The antibodies should be immobilised on the surface of detection chamber. So, magnetic field can be used in this chamber for binding the analyte and immobilized antibodies. As a result, the design of CD for sandwich immunoassay can be included only four chambers namely; sample chamber, mixing chamber, waste chamber and detection chamber.

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