IMPRINTED MAGNETIC TRAPS FOR STUDY ON PARTICLE FLUCTUATION, ORDERING AND MICROFLUIDIC APPLICATIONS

DISSERTATION

Presented in Partial Fulfillment of the Requirements for the Degree Doctor of Philosophy in the Graduate School of The Ohio State University

By
Aaron Chen

Graduate Program in Physics

The Ohio State University

2013

Dissertation Committee:
Ratnasingham Sooryakumar, Advisor
Fengyuan Yang
Ciriyam Jayaprakash
Klaus Honscheid
ABSTRACT

Superparamagnetic particles embedded in a polymer matrix (bead) have been a cornerstone to numerous interdisciplinary studies and applications across a wide range of fields such as physics, chemistry, material science and biomedicine. Through designed magnetic field profiles, these polymeric magnetic beads have the potential to be activated to move along field gradients to realize targeted drug delivery, assembly of functional materials and marker-based cell isolation. During my pursuit of Ph.D. in Physics in Prof. R. Sooryakumar’s lab, I have worked on magnetic trapping platforms based on ferromagnetic thin-film patterns imprinted on a substrate. These design-based platforms serve as excellent candidates in functionalizing the aforementioned magnetic beads and open up a broad new scope of phenomena and applications to explore. This dissertation will summarize three major aspects of the versatile platform developed in our lab: (1) regulating Brownian fluctuations of submicron magnetic particles with monopole-like domain walls located on the vertex of a ferromagnetic zigzag wire, (2) assembly of magnetic microspheres into structures ranging from closely packed, branching chains to expanded within confinements provided by patterned time-orbiting magnetic potentials, and (3) on-chip magnetic cell separation and encapsulation into droplets for single-cell experiments.
This document is dedicated to my family.
ACKNOWLEDGMENTS

I would like to thank my research advisor Prof. R. Sooryakumar for the helpful guidance he has given me during my Ph.D. study, research group members Greg Vieira, Tom Henighan, Wei Zhou, Marci Howdyshell, Anand Harvind, Tom Byvank, Mike Prikockis, Atul Bharde for their company and helps on various projects, Adam Hauser, Josh Zhao and James Morris for introducing me to research groups, lab tools and fellowships, Professors David Stroud, John Wilkins, Nandini Trivedi, Mohit Randeria, Ciriyam Jayaparakash, Fengyuan Yang, Klaus Honscheid, Chris Hammel, Thomas Humanic, Yuri Kovchegov, Eric Braaten, Rashid Bashir for the useful discussions, lectures, being my committee and writing reference letters for me, summer program host research group Prof. Hidekazu Tanaka, Toshio Ono, Sonia Sharmin, Izumi Umegaki, Yasushi Usui, Yutaka Shirata, Kazunori Ishibashi, Taiki Amemiya, Bakusui Daidoji and Motoki Yamada for the hospitality during my stay in Japan, collaborators Adam Hauser, Jeremy Lucy, Brian Peterson, Fengyuan Yang, Justin North, Marek Simon, Michael Poirier, Brandon Miller, Jeffrey Chalmers, Dananjay Thakur, Gang Ruan, Jessica Winter, Hyunchul Chung, Wu Lu, Daniel Gallego-Perez, Jeremiah Schley, Colin Hisey, Derek Hansford, Bo Yu, Yun Wu, Xinmei Wang, Junyu Ma, Kwang Kwak, Lei Li, James Lee, Woojin Chang, Nima Jokilaakso, Bobby Reddy, Rashid Bashir for generously lending materials, human resources and experiences on projects as well as hosting my visits, department and laboratory staff including Brenda Mellett, Kris Dunlap, Pete Gosser, Josh Gueth, Jim Burns, J. D. Wear, Brian Keller, Denis Pelekov, Paul Steffen, Peter Janney, Derek Ditmer and Tom Kelch for making things happen.
VITA

2005.........................................................B.S. in Physics, National Taiwan University

2013.........................................................Ph.D. in Physics, The Ohio State University

Awards

2009.........................................................NSF EAPSI Fellow¹; JSPS Summer Program Fellow²

2012.........................................................Presidential Fellowship, The Ohio State University

2013.........................................................APS GMAG Dissertation Research Award³

¹ East Asia and Pacific Summer Institutes for U.S. Graduate Students funded by National Science Foundation
² Summer program funded by Japan Society for the Promotion of Science
³ Awarded by the American Physical Society Topical Group on Magnetism and its Applications (GMAG) to outstanding dissertation research in magnetism
Publications


A. Chen and R. Sooryakumar, “Patterned time-orbiting potentials for the confinement and assembly of magnetic dipoles” (Submitted to *Physical Review Letters* on Feb 27th, 2013).
Conference Presentations


(Presented by Prof. H. Tanaka’s Group)

(Presented by Prof. H. Tanaka’s Group)


Fields of Study

Major Field: Physics
# TABLE OF CONTENTS

Abstract .................................................................................................................................................. ii
Acknowledgments .................................................................................................................................... iv
Vita ........................................................................................................................................................ v
Table of Contents .................................................................................................................................. viii
List of Tables ......................................................................................................................................... xii
List of Figures ....................................................................................................................................... xiii

Chapters

Chapter 1 Introduction ............................................................................................................................. 1
  1.1 The Manipulation of Tiny Objects ............................................................................................... 1
  1.2 Thin-Film Based Magnetic Tweezers ......................................................................................... 2

Chapter 2 Basic Principles and Methods .............................................................................................. 3
  2.1 Physics of Thin-Film Based Magnetic Tweezers ...................................................................... 3
  2.1.1 Energy and Force on a Superparamagnetic Bead ............................................................... 3
  2.1.2 Motion of the Bead .............................................................................................................. 5
  2.2 Experimental Methods .............................................................................................................. 6
  2.2.1 Magnetic Patterning ........................................................................................................... 6
  2.2.2 Experimental Setup ............................................................................................................. 8

Chapter 3 Regulating Brownian Motion with Zigzag Wire ................................................................. 9
  3.1 Turning Randomness into Usefulness ....................................................................................... 9
  3.2 Magnetic Zigzag Wire Trap ........................................................................................................ 10
  3.2.1 Monopole Model ................................................................................................................. 12
3.2.2 Micromagnetic Model ................................................................. 13
3.3 Deterministic Confinement Force vs. Stochastic Motion .............. 13
  3.3.1 Regulating the Extent and Direction of Bead Trajectory ........... 13
  3.3.2 Weakening of the Trap and Nonlinear Magnetic Response of the
        Bead .................................................................................. 17
3.4 Spatial Relation between the Trap and Bead Trajectories .......... 18
3.5 Temporal Aspects of Confined Brownian Motion ...................... 22
  3.5.1 Diffusion ............................................................................ 22
  3.5.2 Spectral Analysis ............................................................... 23
  3.5.3 Harmonic Trap Model ....................................................... 24
3.6 DNA Hitchhiking a Ride ............................................................ 28

Chapter 4 Patterned Time-Orbiting Potentials for the Confinement and Assembly of
Magnetic Microspheres ...................................................................... 30
  4.1 Schemes for Confining Interacting Dipoles ................................. 31
  4.2 Time-Orbiting Confinement and Interactions in a Magnetic Disk .... 31
    4.2.1 Different Sources of Magnetic Fields .................................. 32
    4.2.2 Interaction Energy Decomposed ...................................... 34
    4.2.3 Time-Averaged Forms of the Interacting Energies ............. 35
    4.2.4 Elliptic Integrals in a Magnetic Disk .................................. 38
    4.2.5 Second Order Interaction Energies .................................. 39
  4.3 Two Major Interplaying Forces: Confinement and Dipolar .......... 41
    4.3.1 Forces in the x-y Plane .................................................... 42
    4.3.2 z-Dependence of the Forces .......................................... 43
  4.4 Tuning Microsphere Structures within the Confinement ............ 46
    4.4.1 Collapse and Expansion of the Cluster ................................ 46
    4.4.2 Reversible Tunability and Transient Cluster Structures ...... 49
    4.4.3 Cluster Impurities .......................................................... 50
    4.4.4 Frustrated Structure due to Competing Interactions .......... 51
# Appendices

## Appendix A Magneto-Optical Kerr Effect (MOKE) Imaging

<table>
<thead>
<tr>
<th>Section</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>A.1</td>
<td>Shaping the Incident Light</td>
</tr>
<tr>
<td>A.2</td>
<td>Operating Modes of MOKE</td>
</tr>
<tr>
<td>A.3</td>
<td>Image Processing</td>
</tr>
</tbody>
</table>

## Appendix B Determination of Experimental Parameters through Particle Tracking

<table>
<thead>
<tr>
<th>Section</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>B.1</td>
<td>Near-Wall Effect</td>
</tr>
<tr>
<td>B.2</td>
<td>Bead Susceptibility</td>
</tr>
<tr>
<td>B.3</td>
<td>Effective Thickness of Magnetic Patterns</td>
</tr>
</tbody>
</table>

## Appendix C Outlook

<table>
<thead>
<tr>
<th>Section</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>C.1</td>
<td>Potential Tweezers Platforms to Offer Individual Control</td>
</tr>
<tr>
<td>C.1.1</td>
<td>CCD Tweezers</td>
</tr>
<tr>
<td>C.1.2</td>
<td>Magnetic Memory Tweezers</td>
</tr>
<tr>
<td>C.2</td>
<td>Drafting behind a Rolling Bead: Label-Free Magnetic Manipulation</td>
</tr>
<tr>
<td>C.3</td>
<td>Portable 3D Magnetic Field Platform</td>
</tr>
</tbody>
</table>
List of Tables

Table 5.1: Summary of the parameters used in the separation and encapsulation experiments. .................................................................................................................................................. 75
LIST OF FIGURES

Figure 2.1: Three major field sources contributing to the net magnetic field....................... 4
Figure 2.2: Sample preparation and experimental setup................................................... 7
Figure 3.1: Stray magnetic field generated from a head-to-head domain wall on a zigzag wire vertex. .................................................................................................................. 11
Figure 3.2: Models for the magnetic zigzag wire trap. ....................................................... 12
Figure 3.3: Tuning the trap strength and extent of bead trajectory...................................... 15
Figure 3.4: Average (dots) and standard deviation (vertical bars) of bead trajectory in the $y$-direction as a function of $H_z$. $H_x = 0$ and $H_y = 35$ Oe are fixed. ......................... 16
Figure 3.5: Comparison of the energy profiles between the monopole and micromagnetic models.................................................................................................................. 19
Figure 3.6: Experimental trajectories (column 2) compared to energy contours plotted by the micromagnetic and monopole models (columns 3 and 4) under various external fields (rows (A), (B) and (C)). .................................................. 21
Figure 3.7: Aspect ratio of the experimental bead trajectories and that of the traps generated by the monopole and micromagnetic models.................................................. 22
Figure 3.8: Diffusion and power spectrum of a trapped bead............................................. 25
Figure 3.9: Stiffness, $k$, of the trap in (a) $y$ and (b) $x$ directions plotted as a function of the tuning field component $H_z$. ....................................................................................... 27
Figure 3.10: Trapping of a DNA-tethered bead remote from the zigzag wire. .................... 28
Figure 4.1: Magnetic microspheres in fluid randomly distributed on a permalloy disk on silicon substrate in the absence of the external field............................................... 32
Figure 4.2: Realignment of the moments in the beads due to $H_{\text{dip}}$ or $H_{\text{disk}}$. ............ 34
Figure 4.3: Energy landscapes and microsphere arrangements in the presence of a (a) fixed and (b) precessing external magnetic field. ................................................................. 37

Figure 4.4. Quantification of the two primary forces in the system: time-averaged confinement force from the disk, $F_{\text{disk}}$, and dipolar force, $F_{\text{dip}}$, between the dipoles on the x-y plane................................................................. 41

Figure 4.5: Maximum (contact) dipolar force $F_{\text{dip}}$ as a function of $\Theta$ .............................................. 43

Figure 4.6: Independent tunability on the confinement and dipolar forces. .............................................. 43

Figure 4.7: x-z cross-sections of the field of (a), confinement force, and (b), confinement force plus gravitational force, in the plane of $y = 0$. ................................................................. 44

Figure 4.8: x-z cross-section of the dipolar force field at various angle of precession $\Theta$. 45

Figure 4.9: Equilibrium and transient structures of a 45-microparticle cluster confined in the bowl-shaped potential with dipolar interaction tuned by $\Theta$ .............................................. 47

Figure 4.10: Time dependence of the mean sphere separation as the strength and sign of dipolar interaction is changed. ................................................................. 48

Figure 4.11: Nucleation and jamming effects................................................................. 49

Figure 4.12: Possible configurations obtained from simulation of a cluster of beads with different susceptibilities................................................................. 51

Figure 4.13: “Washing” a cluster of beads of different susceptibilities in simulation. .... 52

Figure 4.14: Frustrated branching chain structure observed at $H_1 = 60$ Oe and $\Theta = 57.5^\circ$ (as inset H of Figure 4.9). ................................................................. 52

Figure 4.15: Phase diagram of mixed electrostatic and magnetic interactions for two beads separated by $x$ along the x-direction (bead displacement $\mathbf{x} = x\mathbf{\hat{x}}$). ............. 55

Figure 4.16: Time-orbiting potential as a catalyst for forming frustrated structures....... 57

Figure 4.17: Loading and unloading microspheres into and out of the permalloy disk. . . 58

Figure 4.18: Time-orbiting potentials of various shapes. ................................................................. 61

Figure 5.1: Device layout and system setup. ................................................................. 68

Figure 5.2: Manipulation of a magnetic bead from one permalloy disk to the next on the disk array................................................................. 72
Figure 5.3: Snapshots showing the process of magnetic separation, encapsulation, droplet collection and analysis. ............................................................... 74

Figure 5.4: Separation efficiency for 7.9 μm diameter magnetic beads plotted as a function of the input flow rate $Q_1$, corresponding to experiment (i) in Table 5.1. 77

Figure 5.5: Trapping forces vs. hydrodynamic drag force for a 7.9 μm magnetic bead on an array of two permalloy disks that are 84 nm thick. ............................... 78

Figure 5.6: Separation efficiency for 7.9 μm diameter magnetic beads plotted as a function of (a) in-plane field strength $H_1$ and (b) rate of transport $f$. ...................... 79

Figure 5.7: Quantification of the encapsulation characteristics with 7.9 μm diameter magnetic beads. .............................................................................. 83

Figure 5.8: Separation efficiency and encapsulation characteristics of labeled BT-474 cells. ........................................................................................................ 87

Figure 5.9: Cell viability detection with PI (propidium iodide) fluorescence of the encapsulated cells at 55°C. ................................................................. 88

Figure A.1. Schematic of magneto-optical Kerr effect microscope. ....................... 111

Figure A.2: Photo of magneto-optical Kerr effect microscope............................... 112

Figure A.3: Image of the rear focal plane of various objective lenses taken while the polarizer (P) and analyzer (A) are cross-polarized. ........................................ 113

Figure A.4: The longitudinal, transverse and polar MOKE ..................................... 115

Figure A.5: Images obtained through the transverse MOKE on a CoFe zigzag wire with contrast set in the horizontal (a) and vertical (b) directions......................... 116

Figure B.1: Mean square displacements of 17 beads (8 μm in diameter, UMC4F Bangslabs) as a function of time................................................................. 118

Figure B.2: Two beads repelling as an out-of-plane external field is turned on......... 118

Figure B.3: Bead jumping away from a magnetic pattern as the external field is switched. ........................................................................................................ 121

Figure C.1: An artistic rendition of the portable 3D magnetic field platform.......... 124
Chapter 1
INTRODUCTION

1.1 The Manipulation of Tiny Objects

The ability to apply controlled forces on objects in the nanometer to micrometer range leads to fundamental studies and broad range of applications across disciplines of science, engineering and medical research[1–6]. These include, for examples, study on thermally activated processes[7–14], transitions between new phases of matter[15–18], interplay between the diverse competing and cooperating forces[19–24], design of Brownian motor which converts random force into useful work[25–28], probing the mechanical response of biological cells or DNA[29–33], targeted drug delivery[34–37] and isolation of cells[38–40]. Different methods have been developed to apply forces on objects at this length scale based on their different properties. For examples, cantilever-based techniques[41–44] physically probe the objects through van der Waals, electrostatic or receptor-ligand binding interactions; electric-field-based techniques such as optical tweezers[45–48] and dielectrophoresis[49–52] generate forces on dielectric objects through electric field gradient from lasers or electrodes; flow-based techniques such as electrokinesis[53] and electrokinetic traps[54] generates directed flow in solution to manipulate objects; magnetic tweezers[55–57] generates force or torque on objects with intrinsic or induced magnetic moments in the presence of magnetic fields.
1.2 Thin-Film Based Magnetic Tweezers

In this dissertation, magnetic tweezers technique based on imprinted magnetic patterns will be presented. Ferromagnetic thin films deposited on a flat surface have been used over the first decade of 21st century for the trapping and manipulation of magnetic objects. Localized magnetic fields are generated either through magnetic domains on a plain film[58–60] or through lithographically defined thin-film structures such as ellipses[61], disks[62–64], squares[62], [65], rings[66–70], microwires[71], [72], tracks[69], [70], zigzag wires[67], [73], [74], corners[75] as well as other periodic structures[76]. Magnetic objects seek high or low field locations based on their magnetic response relative to the fluid environment. By altering magnetization of the pattern or augmenting the localized fields with an externally applied magnetic field, the spatial profile of the magnetic field can be controlled, resulting in the manipulation of these objects in targeted directions. The commercially available superparamagnetic beads[55], [77] are utilized as magnetic objects for the studies in this dissertation. These beads are composed of spherical polymeric matrix (polystyrene or silica) embedded with superparamagnetic nanocrystals. Their surfaces are ready to be functionalized to attach to specific biological cells or DNAs for biomedical applications. The superparamagnetic property enables rapid magnetic response of the beads to fields less than 100 Oe while showing zero remnant magnetization when the field is removed, rendering them excellent force handlers in magnetic tweezers.

As an overview of the dissertation, the basic operating principles and methods underlying the thin-film-based magnetic tweezers will be presented in Chapter 2, while three projects related to studies on particle fluctuation, ordering and microfluidic applications will be presented in Chapter 3, Chapter 4 and Chapter 5 respectively. The dissertation will then end with Conclusion.
Chapter 2

Basic Principles and Methods

2.1 Physics of Thin-Film Based Magnetic Tweezers

2.1.1 Energy and Force on a Superparamagnetic Bead

The magnetic response of a superparamagnetic bead can be characterized by its magnetization \( M_{\text{bead}} \) as a function of the magnetic field \( H \) it experiences. Typical superparamagnetic beads show zero remnant magnetization in zero field but respond rapidly in the presence of a weak magnetic field, i.e. for \(|H| = H < 500 \text{ Oe}\), bead magnetization is roughly linear in \( H \):

\[
M_{\text{bead}} = \chi H
\]

where the magnetic susceptibility \( \chi \) typically lies in the range of 0.1 to 1 [78], [79] (compared to \(10^{-5}\) for paramagnetic materials [80]). Experimental determination of \( \chi \) is given in Appendix B. As shown in Figure 2.1, three major sources contribute to the spatial profile of the net magnetic field \( H(\mathbf{r}) \), which include:

1. The externally applied, spatially uniform magnetic field, \( H_{\text{ext}} \),
2. Stray magnetic fields generated from the imprinted magnetic patterns or domain walls, \( H_{\text{pattern}}(\mathbf{r}) \), and
3. Dipolar fields \( H_{\text{dip}}(\mathbf{r}) \) generated from the magnetizations induced in all surrounding superparamagnetic beads (except the one located at \( \mathbf{r} \)).

The net magnetic field \( H(\mathbf{r}) \) is given by the superposition of all these field sources:

\[
H(\mathbf{r}) = H_{\text{ext}} + H_{\text{pattern}}(\mathbf{r}) + H_{\text{dip}}(\mathbf{r})
\]
Explicit expressions for $H_{\text{pattern}}(r)$ will be given in Chapter 3, Chapter 4 and Chapter 5 based on the respective patterns used while the effect of $H_{\text{dip}}$ will be discussed in Chapter 4 where interaction between multiple dipoles are accounted for.

![Figure 2.1: Three major field sources contributing to the net magnetic field. (a) $H_{\text{ext}}$: externally applied magnetic field. (b) $H_{\text{pattern}}$: stray field generated from the magnetization divergence residing in the magnetic patterns. (c) $H_{\text{dip}}$: dipolar field generated from the induced magnetization in the beads.](image)

Given the spatial dependence of the net field, $H(r)$, energy landscape for a superparamagnetic bead located at $r$ can be calculated:

$$U(r) = -\mu_0 V \int \frac{|H_{\text{pattern}}(r')|}{|H(r')|} M_{\text{bead}}(H')dH'$$  \hspace{1cm} (2.3)

where $\mu_0$ is the magnetic permeability of free space and $V = (4/3)\pi R^3$ the volume ($R$ the radius) of the bead. The energy at $|r| \rightarrow \infty$ (far away from any magnetic patterns) is set to zero. A spatially varying magnetic field $H(r)$ results in an inhomogeneous energy landscape $U(r)$, which then gives rise to a force acting on the magnetic bead located at $r$: 4
\[ \mathbf{F}(\mathbf{r}) = -\nabla U(\mathbf{r}) \]  

(2.4)

In most experimental cases where \( H \) is weak (< 500 Oe), Equation (2.1) holds true, and the energy and force on a superparamagnetic bead can be expressed in the following simple forms:

\[ U(\mathbf{r}) = -\frac{1}{2} \mu_0 z V H(\mathbf{r})^2 \]  

(2.5)

\[ \mathbf{F}(\mathbf{r}) = \frac{1}{2} \mu_0 z V \nabla H(\mathbf{r})^2 \]  

(2.6)

2.1.2 Motion of the Bead

As manipulation is usually done in a fluid environment, motion of the bead can be described by Langevin’s Equation[81], the equation of motion for objects moving in a viscous medium while experiencing a force field \( -\nabla U \) and gravity:

\[ (\rho_{\text{bead}} V) \ddot{\mathbf{r}} + \gamma \dot{\mathbf{r}} = -\nabla U(\mathbf{r}) + (0,0,(\rho_0 - \rho_{\text{bead}}) V g) + \xi(t) \]  

(2.7)

\[ \gamma = \lambda \cdot 6 \pi \eta R \]  

(2.8)

where \( \rho_0 \) and \( \rho_{\text{bead}} \) are densities of the surrounding medium and the bead respectively. Drag coefficient \( \gamma \) accounts for the dissipative force opposing the bead motion. The mass term (first term on the left hand side of Equation (2.7)) is generally ignored since \( \rho_{\text{bead}} V / \gamma \), which relates to the time it takes for the bead to reach terminal velocity, is on the order of \( \mu s \), much less than the time scale of interest (>ms). The value for \( \gamma \) is given by Stokes’ law[82] for unbound spheres \((6 \pi \eta R, \text{where} \ \eta \text{is the viscosity of the fluid})\) corrected by a dimensionless near-wall factor \( \lambda \) accounting for the increase in drag force due to the bead moving near a surface[83]. Experimental determination of \( \lambda \) is given in Appendix B. The last term, \( \xi(t) \), on the right hand side of Equation (2.7) is a Gaussian white noise accounting for the random thermal fluctuation. It has a mean of zero and a correlation function in time as a delta-function:

\[ <\xi(t)> = 0 \]  

(2.9)

\[ <\xi(t)\xi(t')> = 2 \gamma k_B T \delta_0 \delta(t-t') \]  

(2.10)

where \( k_B \) is Boltzmann’s constant and \( T \) the temperature.
In summary, the motion of the bead can be described by Equation (2.7) given parameters such as the drag coefficient, external field, stray field generated from the magnetic patterns, bead size, susceptibility and temperature of the surrounding fluid.

2.2 Experimental Methods

2.2.1 Magnetic Patterning

Silicon is utilized as the substrate material for magnetic patterns. The 300 ~ 500 μm thick silicon wafer (with natural or thermally grown oxide on the surface) is cleaned with acetone and isopropyl alcohol, and organic residue removed by UV-ozone treatment (UVO Cleaner 42, Jelight Company Inc) for 5 min.

The micrometer-scaled magnetic patterns are fabricated by standard lithographic techniques. For the CoFe zigzag wires and the large permalloy (Ni$_{80}$Fe$_{20}$) polygons studied in Chapter 3 and Chapter 4, electron-beam lithography is implemented: Two layers of e-beam resist (methylmethacrylate and polymethyl methacrylate) are spin-coated at 4500 rpm onto a Si substrate and each layer baked at 180 °C for 60 s. Patterns are exposed on the resist layers at 125 ~ 280 μC/cm$^2$ using a scanning electron microscope (Helios Nanolab 600, FEI Company) and developed with 25% to 33% (volume fraction) methyl isobutyl ketone in isopropyl alcohol. Photolithography is used for fabrication of the large permalloy disk and permalloy disk array in Chapter 4 and Chapter 5: Two layers of photoresist (LOR3B and S1805, MicroChem Corp) are spin-coated at 2500 ~ 4000 rpm and baked at 180°C (2 min) and 110°C (90 s) respectively. The resist layers are exposed with UV through projection photolithography (large permalloy disk) or contact photolithography (permalloy disk array) with patterned chromium-on-quartz mask and developed with 2.5% tetramethylammonium hydroxide developer for 30 ~ 45 s.

A layer of magnetic material, either CoFe or Ni$_{80}$Fe$_{20}$ (permalloy), is then deposited onto the resist-patterned surface by magnetron sputtering followed by lifting off unwanted areas with acetone or n-methyl-2-pyrrolidone assisted by 1-min sonication, 60°C bath, or a combination of the two.
Capping layer on top of the patterned magnetic film serves to protect the film from oxidation and physical wear or to enable further surface functionalization. For the CoFe zigzag wires used in Chapter 3, a several-nanometer thick Au layer is deposited to enable a hydrophilic monolayer coating of triethylene glycol prior to the experiment. For the large permalloy patterns and disk array used in Chapter 4 and Chapter 5, a 100 nm thick SiO$_2$ layer is either spin-coated or sputter-deposited.

Figure 2.2: Sample preparation and experimental setup. (a) A solution of magnetic beads is placed on the Si substrate imprinted with magnetic patterns (not shown to scale) and surrounded by a PDMS (polydimethylsiloxane) ring and cover glass. (b) A platform consisting of electromagnets and coil that generate the external field and a microscope for the observation of the sample. (c) Experimental setup diagram.
2.2.2 Experimental Setup

Figure 2.2a shows the preparation of a typical sample (for experiments conducted in Chapter 3 and Chapter 4): A solution containing objects to be manipulated such as superparamagnetic beads is injected onto the Si substrate imprinted with magnetic patterns and enclosed by a PDMS (polydimethylsiloxane) ring and cover glass to prevent fluid flow and evaporation. The sample is then placed onto a microscope platform (Figure 2.2b) consisting of a set of electromagnets and coil which generate the in-plane ($H_x, H_y$) and out-of-plane ($H_z$) magnetic field components respectively. As shown in the flow diagram of Figure 2.2c, computer program coded in LabVIEW (National Instruments) controls the current sent by the power supplies into the electromagnets and coil, allowing 3-dimensional control on $\mathbf{H}_{\text{ext}} = (H_x, H_y, H_z)$ with joystick (Xbox 360 Controller, Microsoft) as an optional user interface. A LabVIEW imaging routine captures the sequence of images from the sample at 10 to 40 frames per second through a CCD camera (QImaging Retiga-EXi) mounted on the microscope (Leica DM2500MH), while a tracking routine analyzes individual trajectories with sub-micron resolution.
Chapter 3
REGULATING BROWNIAN MOTION WITH ZIGZAG WIRE

3.1 Turning Randomness into Usefulness

Nature has proven that it is possible to engineer complex nano-scale machines in the presence of thermal fluctuations[25–28]. These biological complexes, which harness random thermal energy to provide functionality, yield a framework to develop artificial, i.e. non-biological, phenomena and devices. Indeed, thermally activated transitions in optical traps[8], diffusion in solids through activated escape from metastable states[9–14] and transport of colloidal particles[84] and DNA[85] through a combination of diffusive and electric forces are examples where the ceaseless source of thermal motion is channeled into useful outcomes. An important outcome of controlling thermally driven motion in a fluid (i.e. Brownian fluctuations) will be the ability to manipulate and generate deterministic motion of individual objects in the 100 nm to 10 micron range.

The wide tunable force range, convenience of remote access, independence of fluid properties, and selectiveness to objects with designed magnetic signatures are all advantages of a magnetic-field-based approach compared to other manipulation techniques such as those mentioned in Section 1.1. Although the trapping of paramagnetic objects in a stable, solely magnetic configuration in free space is not possible[86], control of their Brownian fluctuations in quasi three- or two-dimensions exclusively through magnetic fields would nevertheless provide much added value. While other approaches based on magnetic fields have utilized Brownian fluctuations to
characterize trapping forces[65], [87] and susceptibility of the beads[88], the method presented here serves as an experimental implementation of a magnetic trap that provides a high degree of control over the extent of the Brownian fluctuation of the bead and a quantitative understanding of the parameters that influence it.

This chapter presents a mechanism based on magnetic zigzag wire trap, recently utilized for the transport of labeled biological cells[73], to show that the strength and profile of the quasi-3D magnetic trap originating from local domain-wall field generated from the patterned zigzag wires can be tuned by weak external fields. This remote control on the local energy landscape results in the position of its energy minimum being manipulated along a predetermined pathway, and its depth varied from much greater than $k_B T$ (a measure of thermal energy) to a few $k_B T$, enabling the bead to execute stochastic motion within a tunable deterministic trapping potential. As a result, Brownian fluctuations of the bead can be varied from being tightly confined (virtually immobilizing the bead) to undergoing large excursions (expeditiously biased away from the wire vertex where a domain wall resides). Analysis of the bead trajectory allows properties of the local energy profile to be probed such as the aspect ratio and stiffness of the trap. The tunable magnetic trap also acts as a high-pass filter, suppressing the low-frequency component of the power spectrum of the bead motion, thereby tuning its power-law behavior to mimic other fluctuating phenomena observed in nature.

### 3.2 Magnetic Zigzag Wire Trap

Zigzag wires (thickness 13.5 nm, width 2 μm, arm length 16 μm) made of ferromagnetic CoFe are imprinted on a Si substrate using the e-beam lithographic technique mentioned in Chapter 2. The zigzag geometry has been exploited[89] for the ability to systematically create domain walls on its vertices. By application of a strong field (~0.3 T) along the y-direction followed by the relaxation of the magnetization ($\mathbf{M}_{\text{wire}}$) along the long axes of the wires after the field is removed (Figure 3.1), the resulting magnetization point towards (or away from) the vertices of the zigzag wire as is verified by magneto-optical Kerr effect imaging discussed in Appendix A. The resulting head-to-head (or tail-to-tail)
domain walls generate magnetic field \( (H_{DW}) \) in the outgoing (or incoming) directions. Critical to the creation of a tunable magnetic trap is the underlying principle of combining the fields generated from the domain walls \( (H_{DW}) \) with a weak external magnetic field \( (|H_{ext}| \sim 100 \text{ Oe}) \) which does not alter wire magnetization due to the strong shape-anisotropy of the wires.

![Diagram](image)

Figure 3.1: Stray magnetic field generated from a head-to-head domain wall on a zigzag wire vertex.

A solution of superparamagnetic beads (diameter 560 nm, CM-05-10 Spherotech) diluted in 0.1% Triton X-100 surfactant are placed on the zigzag wire platform as described in Figure 2.2a. This chapter studies the dynamics of single bead in a tunable trap. To prevent bead-bead interactions, the concentration has been diluted to ensure only zero or one bead per trapping site (zigzag vertex) after a settling time of several minutes. We follow the motion of the bead in trapping potentials subjected to different external fields through a 40x objective lens. A CCD camera and tracking routines resolve individual trajectories with sub-micron resolution.

As discussed in Section 2.1, \( M_{\text{bead}}(H) \), magnetization of the bead, is induced by the net field \( H = H_{DW} + H_{ext} \), where the dipolar field \( H_{dip} \) from other beads has been ignored.
The interaction between $\mathbf{M}_{\text{bead}}$ and $\mathbf{H}$ leads to a deterministic trapping force on the bead (Equations (2.3) and (2.4)) while thermal fluctuation leads to its stochastic motion. The magnetic field profile, $\mathbf{H}_{\text{DW}}(\mathbf{r})$, generated from the domain walls located on the vertex of a zigzag wire can be described by the two models discussed below.

![Figure 3.2: Models for the magnetic zigzag wire trap. Illustrations of the isotropic and irregular domain wall fields generated by (a) the monopole model and (b) micromagnetic model are respectively shown.](image)

### 3.2.1 Monopole Model

This model approximate the zigzag wires to be infinitely thin, such that $\mathbf{H}_{\text{DW}}(\mathbf{r})$ emanates only from a point, $\mathbf{r} = (0,0,0)$, on the vertex as the monopole field from a point magnetic charge (Figure 3.2a)[90]. This approximation is valid for bead-vertex distance much greater than the wire width[91]. For particles trapped in the vicinity (< 2 μm) of one vertex, monopole fields generated from other vertices of the zigzag wire can be ignored due to its decay over distance $r$ as $1/r^2$ and the long vertex-to-vertex distance (16 μm). The expression for the magnetic field emanating from the domain wall under this approximation is given by:

$$
\mathbf{H}_{\text{DW}}(\mathbf{r}) \rightarrow \mathbf{H}_{\text{monopole}}(\mathbf{r}) = \frac{q_m}{4\pi} \frac{\mathbf{r}}{|\mathbf{r}|^3} 
$$

(3.1)

$$
q_m = 2M_{\text{wire}} \cdot w \cdot d \cdot \alpha_{\text{monopole}}
$$

(3.2)
where $q_m$ is the monopole charge, $M_{\text{wire}} = 1.92 \times 10^6$ A/m the magnetization, $w = 2$ μm the width, and $d = 13.5$ nm the thickness of the CoFe wire. $\alpha_{\text{monopole}}$, set to 0.1, is a correction factor adjusted to properly simulate the trajectories observed in the experiment; it accounts for the inaccuracy of monopole field at close distance ($|r| \sim w$) as well as any reduction in wire magnetization caused by oxidation or defects.

### 3.2.2 Micromagnetic Model

A more accurate description for $H_{\text{DW}}(r)$ is based on simulation of the magnetization distribution $M_{\text{wire}}(r)$ within the zigzag wire (Figure 3.2b)[92]. The field at a given location outside the wire is now a superposition of fields generated from the divergence of magnetization:

$$H_{\text{DW}}(r) \rightarrow H_{\text{micromag}}(r) = \int dr' 3 - \nabla \cdot \frac{M_{\text{wire}}(r') r - r'}{4\pi |r - r'|^3}$$

(3.3)

The integral is over the entire space; for simplicity, we have only integrated over the volume of one vertex (where the domain wall lies) and ignored the magnetization divergence at other ends of the zigzag for the same reason as in calculating $H_{\text{monopole}}(r)$. The magnitude of $M_{\text{wire}}(r)$ is zero everywhere except for $r$ within the wire: $|M_{\text{wire}}(r)| = M_{\text{wire}} \alpha_{\text{micromag}}$, where $\alpha_{\text{micromag}} = 0.25$ is another correction factor chosen to best fit the trap depths of that yielded by the monopole model. $\alpha_{\text{micromag}}$ is closer to unity than $\alpha_{\text{monopole}}$ since the micromagnetic model is more accurate than the monopole model at close proximity of the vertex. However, the value of $\alpha_{\text{micromag}}$ is still less than unity to account for oxidation or defects that could suppress the wire magnetization.

### 3.3 Deterministic Confinement Force vs. Stochastic Motion

#### 3.3.1 Regulating the Extent and Direction of Bead Trajectory

We will adopt the simple monopole model (Equations (3.1)) for calculation of the energy profile $U(r)$ (Equation (2.3)) while using Langevin dynamics (Equation (2.7)) to provide a semi-quantitative understanding on the bead dynamics observed in experiment. Figure
3.3 provides an overview of how the externally applied field $H_{\text{ext}}$ tunes the profile of the zigzag wire trap as well as the bead trajectory. In the absence of $H_{\text{ext}}$ (row (i)), strong field gradients ($>10^4$ T/m) from the domain wall confines the 560 nm bead to the vertex. A useful quantitative measure of the trap and its influence on the bead trajectories is the relative magnitude of the energy depth $\Delta U$ (resulting in a deterministic confinement force) and the thermal energy $k_B T$ (resulting in stochastic motion). Here $\Delta U \equiv U(\infty) - U_{\text{min}}$ is the difference between energy at the minimum and that at a distant location. The computed vertical force at energy minimum, $F_z = -27 \text{ pN} = -6500 \frac{k_B T}{\mu \text{m}}$, pushes the bead towards the surface, while the calculated potential depth is $\Delta U = 527 \frac{k_B T}{\mu \text{m}^2}$ with spring constants $k_x = k_y = 96 \text{ pN/}\mu \text{m} = 23000 \frac{k_B T}{\mu \text{m}^2}$. We find the resulting fluctuation in bead position is below our measurement resolution of $\sim 100$ nm, consistent with the calculated root-mean-square (rms) displacement of 9.3 nm due to thermal fluctuations.

Application of an in-plane field on the order of tens of Oersteds, e.g. $H_{\text{ext}} = (H_x,H_y,H_z) = (0,35,0)$ Oe, breaks the symmetry, shifting the trap away from the vertex in the same direction as the in-plane field ($+y$), while an addition of a field component in the $-z$ direction, e.g. $H_{\text{ext}} = (0,35,-74)$ Oe, weakens the trap. The resulting net field leads to a local field maximum and potential energy minimum that is formed at $y \approx 0.3 \mu \text{m}$ from the vertex center (row (ii)). Concomitantly, the trap is also weakened and becomes anisotropic: $\Delta U = 22 \frac{k_B T}{\mu \text{m}}$, $F_z = -1200 \frac{k_B T}{\mu \text{m}}$, $k_x = 1400 \frac{k_B T}{\mu \text{m}^2}$ and $k_y = 250 \frac{k_B T}{\mu \text{m}^2}$ at the energy minimum. Both the simulation and experiment (third and fourth columns) showed a tightly confined bead trajectory near the vertex tip at this field value. As shown in row (ii)-(iv), when $H_z$ is progressively tuned in the $-z$ direction ($-74 \rightarrow -86 \rightarrow -91$ Oe), the energy minimum moves farther away ($y \approx 0.3 \rightarrow 0.7 \rightarrow 0.8 \mu \text{m}$) from the wire vertex, while the trap is further weakened: $\Delta U = 22 \rightarrow 10 \rightarrow 8 \frac{k_B T}{\mu \text{m}}$, $F_z = -1200 \rightarrow -140 \rightarrow -110 \frac{k_B T}{\mu \text{m}}$, $k_x = 1400 \rightarrow 72 \rightarrow 45 \frac{k_B T}{\mu \text{m}^2}$ and $k_y = 250 \rightarrow 74 \rightarrow 53 \frac{k_B T}{\mu \text{m}^2}$ at the respective energy minima. As evident in both simulation and experiment (third and fourth columns of Figure 3.3), the weakening of the asymmetric trap causes an increase in the extent of Brownian motion of the bead. The bead remains in the focal plane of the
Figure 3.3: Tuning the trap strength and extent of bead trajectory. Shown at various applied external fields \( \mathbf{H}_{\text{ext}} = (0,H_y,H_z) \) (column 1) are the calculated energy landscapes \( U(x,y,R) \) (column 2) and bead trajectories obtained in simulation (column 3) and experiment (column 4). The wire vertex and energy contours are projected on top of the energy landscape. Bead trajectories are taken for 5 min except for the experiment in row (iv), which is 3 min.
objective lens provided the sum of the vertical force provided by the trap and the buoyant weight (\( \sim 0.1 \ k_B T/\mu m \) for \( 2R = 560 \ nm \); \( \sim 1.5 \ k_B T/\mu m \) for \( 2R = 1.2 \ \mu m \)) is strong enough to confine the bead near the surface. In row (iv), the vertical trapping force drops below 1 \( k_B T/\mu m \) for \( y > 4 \ \mu m \) so that the bead can become momentarily out of focus when it is far away from the energy minimum.

Figure 3.4 shows the detailed dependence of the extent of the Brownian motion on the strength of the anisotropic trap tuned by the field component \( H_z \). As \( H_z \) is decreased from \(-70\) to \(-90\) Oe, the distribution of Brownian trajectory shifts gradually along +\( y \) direction, while extending its spread in the range of \( y = 0 \sim 2 \ \mu m \). Upon further decreasing \( H_z \) below \(-90\) Oe, experiment and simulation revealed an abrupt increase in
fluctuation up to 10–15 μm, due largely from the more frequent escapes of the bead to the flatter region of the energy landscape shown in row (iv) of Figure 3.3.

### 3.3.2 Weakening of the Trap and Nonlinear Magnetic Response of the Bead

The increase in the extent of Brownian motion as the energy depth $\Delta U$ is decreased can be understood from Boltzmann statistics, i.e. the ensemble-averaged probability for the bead to be located at $\mathbf{r}$ is proportional to $\exp[-\Delta U/(k_B T)]$. As $\Delta U$ decreases the bead can be found farther from the energy minimum, hence the increase in extent of the trajectory. When $\Delta U$ becomes comparable to $k_B T$, the bead has a higher probability to overcome the deterministic potential barrier on the time scale of interest (i.e. 5 minutes); large excursions of Brownian trajectories with motion biased away from the zigzag wires therefore happen more frequently (row (iv) of Figure 3.3). Although there seems to be a critical $H_z$ value at which this transition occurs, i.e. $H_z \sim -90$ Oe, this transition is not due to any abrupt change in the energy landscape, but it depends on the time scale of interest and is subject to statistical fluctuation in different runs of the experiment. This singularity typically implies an irreversible escape of the particle, resulting in non-repeatability of the experiment around the singular point. In the simulations, we track single trajectories (as in the experiments) for a particular realization of the noise term $\xi(t)$ in Equation (2.7) and so ensemble averages are not performed.

Since $M_{\text{bead}}(H)$ changes monotonically with $H$, $M_{\text{bead}}(H)$ only serves to modulate the energy profile $U(\mathbf{r})$ as given by Equation (2.3), i.e. while a steeper $M_{\text{bead}}(H)$ curve results in steeper $U(\mathbf{r})$, energy minima will always coincide with field maxima. The nonlinear trend of $M_{\text{bead}}(H)$ as $H$ increases, i.e. lower susceptibility $(\partial M_{\text{bead}}(H)/\partial H)$ at higher $H$, further weakens the trap as the bead is magnetized more. This is depicted in the inset shown in Figure 3.4a where the net field $H$ experienced by the bead is large enough to reduce the slope of $M_{\text{bead}}(H)$ and therefore the steepness of $U(\mathbf{r})$ after the integration in Equation (2.3). To represent this nonlinearity, we model the magnetization response $M_{\text{bead}}(H)$ of the bead as a superposition of superparamagnetic nanoparticles with a log-normal size (moment) distribution $\psi(m)$ as given in[93], while each nanoparticle carries a
classical magnetic moment \( (m) \) whose individual response is described by Langevin’s function \( L(x) = \coth(x) - 1/x \):

\[
M_{\text{bead}}(H) = M_{s,\text{bead}} \cdot \int_0^\infty \text{d}m L \left( \frac{\mu_0 m H}{k_B T} \right) \psi(m) \tag{3.4}
\]

\[
\psi(m) = \frac{1}{\sqrt{2\pi} \sigma m} \exp \left( -\frac{\log(m/m_0)^2}{2\sigma^2} \right) \tag{3.5}
\]

where \( M_{s,\text{bead}} = 1.85 \times 10^8 \mu_B/V \) is the saturation magnetization of the bead \( (\mu_B = 9.27 \times 10^{-27} \text{ J/T is the Bohr magneton}), \sigma = 1.68 \) is the width of the distribution function adopted from \([94]\), and \( m_0 = 431 \mu_B \) sets the scale of the magnetic moment per each nanoparticle. The resulting zero-field magnetic susceptibility of the entire particle determined by these parameters is \( [\partial M_{\text{bead}}(H)/\partial H]_{H=0} \equiv \chi = 0.52 \). The overall scale of the bead magnetization \( M_{\text{bead}}(H) \) is difficult to determine due to uncertainty in the exact nanoparticle size distributions within the bead and the precise wire magnetization. For the experimentally determined values of various parameters and the appropriate correction of the monopole strength \( (\alpha_{\text{monopole}} = 0.1 \text{ in Equation (3.2)}) \), the semi-quantitatively reproducible behaviors of the bead are strikingly similar to the experimental results as shown in the third and fourth columns of Figure 3.3 as well as Figure 3.4.

### 3.4 Spatial Relation between the Trap and Bead Trajectories

The Bitter technique\([95]\) utilizes an ensemble of magnetic particles to probe local energy inhomogeneity of a magnetic material. We show below that such mapping of the energy profile can be achieved with a single particle by taking advantage of the random thermal motion that prevails among micrometer or smaller sized particles suspended in a fluid.

We use the two mathematical models discussed above to plot the energy profile of the zigzag wire trap tuned by a fixed external field \( H_{\text{ext}} = (0,35,-79) \text{ Oe} \): (1) the monopole model which accounts for all the divergence of magnetization as one magnetic monopole (Figure 3.5a) and (2) the micromagnetic model which considers the detailed magnetization distribution within the vertex (Figure 3.5b). The bead trajectory simulated using the simpler monopole model as shown in Figure 3.5c does not correctly account for
the shape of the experimentally observed trajectory shown in Figure 3.5d. In actual experiment, the trapped particle tends to hover along the edge of the vertex, resulting in an elongated shape in the $x$ direction of the trajectory. This elongated trajectory distribution along $x$ matches well with the energy profile produced by the micromagnetic model shown in (Figure 3.5b).

![Figure 3.5: Comparison of the energy profiles between the monopole and micromagnetic models. Energy $U(r)$ of the bead located at the $z = R$ plane on top of the zigzag wire trap produced under an external field of $H_{\text{ext}} = (0,35,-79)$ Oe is plotted using the monopole (a) and micromagnetic (b) models. Bead trajectories (5 min) obtained through simulation using the monopole model (c) and through the experiment (d) are shown.]

While further weakening of the trap by decreasing $H_z$ results in more frequent recursions of the bead from the vicinity of the vertex, it does not change the
characteristics of the concentrated region of the trajectory distribution: elongation along the $x$ direction as shown in the second column of Figure 3.6. As can be seen from the shape of the energy contours, the trap profiles produced by the micromagnetic model (third column) display elongation matching the concentrated regions of the experimental trajectories under the external fields shown compared to those produced by the monopole model (fourth column) which is more isotropic.

A quantitative parameter suitable to compare shapes of the trajectory distribution and the trapping profile of the two models is their respective aspect ratio defined by the standard deviation in $y$ direction to that in $x$ direction:

$$\text{Aspect ratio} = \frac{\left\langle (y - \langle y \rangle)^2 \right\rangle^{1/2}}{\left\langle (x - \langle x \rangle)^2 \right\rangle^{1/2}}$$

(3.6)

where the average is performed over:

1. all the grid points enclosed by the $8 \ k_BT$ contour above the energy minimum of the trap produced by the monopole and micromagnetic models, or
2. bead positions of the experimental trajectory.

The aspect ratio is plotted as a function of the tuning field component $H_z$ as shown in Figure 3.7. The aspect ratio of the experimental trajectories largely follows the trend of the micromagnetic model, except in weaker traps ($H_z < -83$ Oe) where large and loose excursions of the trajectories result in deviations from the calculated aspect ratio. The $H_z$ value at which the singularity occurs, i.e. $H_z = -91$ Oe in the plot of Figure 3.7, depends on the time scale of interest and is subject to statistical fluctuation in different runs of the experiment as discussed in Section 3.3.2. We conclude that, given sufficient spatial coverage of its Brownian trajectory, a single particle in combination with digital tracking allows one to probe the local energy landscape.
Table 3.6: Experimental trajectories (column 2) compared to energy contours plotted by the micromagnetic and monopole models (columns 3 and 4) under various external fields (rows (A), (B) and (C)). The energy contours are plotted at 2, 4, 6 and 8 $k_B T$ above the respective energy minima.

<table>
<thead>
<tr>
<th>External field $H_{\text{ext}}$ (Oe)</th>
<th>Experiment</th>
<th>Micromagnetic model</th>
<th>Monopole model</th>
</tr>
</thead>
<tbody>
<tr>
<td>(A) $(0.35, -79)$</td>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
<td><img src="image3.png" alt="Image" /></td>
</tr>
<tr>
<td>(B) $(0.35, -84)$</td>
<td><img src="image4.png" alt="Image" /></td>
<td><img src="image5.png" alt="Image" /></td>
<td><img src="image6.png" alt="Image" /></td>
</tr>
<tr>
<td>(C) $(0.35, -91)$</td>
<td><img src="image7.png" alt="Image" /></td>
<td><img src="image8.png" alt="Image" /></td>
<td><img src="image9.png" alt="Image" /></td>
</tr>
</tbody>
</table>

Figure 3.6: Experimental trajectories (column 2) compared to energy contours plotted by the micromagnetic and monopole models (columns 3 and 4) under various external fields (rows (A), (B) and (C)). The energy contours are plotted at 2, 4, 6 and 8 $k_B T$ above the respective energy minima.
Figure 3.7: Aspect ratio of the experimental bead trajectories and that of the traps generated by the monopole and micromagnetic models. The aspect ratio is plotted as a function of tuning field component $H_z$ while $H_x = 0$ and $H_y = 35$ Oe. External field values used in Figure 3.6 are indicated by (A), (B) and (C) in the plot. Starting from strong trap strength ($H_z = -74$ Oe), trajectories are recorded for 300 s at each data point except at $H_z = -91$ Oe (C), where the irreversible escape of the particle at 187 s results in a singularity for this particular data set.

3.5 Temporal Aspects of Confined Brownian Motion

3.5.1 Diffusion

The time dependence of the confined Brownian motion of the bead offers additional insight into the characteristics of the local energy landscape. From the temporal perspective, the diffusion of the bead is limited by the magnetic trap as shown in Figure 3.8a, such that the mean square displacement $<\Delta r^2>$ of the bead does not increase as rapidly as that of a two-dimensional freely diffusive particle, which is linear in time $t$:

$$<\Delta r^2> = 4Dt$$

(3.7)

where $D$ is the diffusion constant given by Stokes-Einstein equation[82], [96]:

22
\[ D = k_B T / \gamma \]

where the drag coefficient \( \gamma = \lambda \cdot 6 \pi \eta R \) is as discussed in Chapter 2 for a spherical bead of radius \( R \) in a fluid with viscosity \( \eta \). The near-wall factor \( \lambda \) is set to 1 here as a qualitative comparison. For tightly confined trajectories, i.e. bead in a strong trap as (A) and (B) in Figure 3.6, \( \langle \Delta r^2 \rangle \) saturates at a certain value (\(< 1 \mu m^2\)) within one second. In contrast, for trajectories with large excursions that occur within weak traps such as (C) in Figure 3.6, \( \langle \Delta r^2 \rangle \) continues to increase at a slower rate than the free diffusion case and with larger statistical fluctuation. The relation between trap strength and the rate at which the trajectory undergoes large excursions has long been studied[9–14] in the context of thermally activated processes. Due to the finite energy depth of the trap, it is expected that even a tightly confined bead should be able to escape the trap in time scales much greater than 5 min.

### 3.5.2 Spectral Analysis

With the diffusion limited by the magnetic trap, an immediate consequence is on the power spectrum of the Brownian trajectory defined by (for example, in the \( y \) position of the bead):

\[
P_y(f) = \frac{1}{\tau} \left| \int_0^\tau e^{i2\pi f t} y(t) \right|^2
\]

where \( \tau \) is the time period of bead trajectory. The stronger the trap, the more suppression there is to the low frequency part of the spectrum, as shown in Figure 3.8b; in other words, the magnetic trap acts as a high-pass filter for the Brownian noise. Further analysis shows that the trap changes the power-law behavior of the spectrum (fitted by the \( f^{-p} \) curves in the figure). Two well understood fluctuations with power-law behavior are the completely random white noise (\( p = 0 \)) and the time-correlated Brownian noise (\( p = 2 \)) for a free particle. One of the long-existing puzzles in contemporary science is the ubiquity of fluctuations with \( 0 < p < 2 \) found in nature, yet lacking a generic physical explanation[97–99]: For example, voltage across vacuum tubes[100], human heart beats[101], flow of traffic[102], stock markets[103], sea current[104], and even the sound
intensity in music[105] have all been shown to exhibit spectra following certain power laws. The presented magnetic trap easily tunes the order, $p$, of the power law of the fluctuating spectrum and lends itself as a simple candidate model explaining the $f^{-p}$ noise, thereby illustrating that these phenomena could originate from confined Brownian-type fluctuations.

### 3.5.3 Harmonic Trap Model

Also depicted in Figure 3.8b are the Lorentzian curves resulting from the harmonic trap model[106]. In this model, particle fluctuates in a harmonic potential of the form $(1/2)kx^2$ within a viscous medium, where $k$ is the stiffness (spring constant) of the trap. The resulting equation of motion is (in 1D):

$$\gamma \ddot{x} + kx = \xi(t)$$

(3.10)

By taking the Fourier transform of Equation (3.10) while noting that the power spectrum of the fluctuating force $\xi(t)$ is a constant as a consequence of its delta-function time-correlation (Equation (2.10)), one obtains the power spectrum of the particle as:

$$P_{\text{harmonic}}(f) = \frac{D/2\pi^2}{f_c^2 + f^2}$$

(3.11)

$$f_c = k/(2\pi\gamma)$$

(3.12)

where $D$ is the diffusion constant given by Equation (3.8), $f_c$ the corner frequency, and $\gamma$ the drag coefficient given by Equation (2.8). By fitting $P_{\text{harmonic}}(f)$ to the experimental spectrum $P_{x,y}(f)$ (Equation (3.9)) with parameter $f_c$, stiffness constants $k_x$ and $k_y$ can be extracted. Despite deviation of the Lorentzian curve from the experimental spectrum at strong trap strength, i.e. plot (A) in Figure 3.8b, this model qualitatively accounts for the flattening of power spectrum at low frequency. However, at intermediate trap strengths, e.g. plot (B) in Figure 3.8b, neither the flattening of the curve at low $f$ or the $f^2$ trend at high $f$ matches with the experimental spectrum, which exhibits a power law $f^{-p}$ with $p \approx 1.24$ across two decades of $f$ (from 0.1 Hz to 10 Hz). This misfit stems from the non-harmonic nature of the zigzag wire trap – the flattening of the energy landscape farther from the energy minimum results in the bead exhibiting an excursion-type dynamics that
involves occasional escapes and returns. At weak trap strengths, e.g. plot (C) in Figure 3.8b, both the Lorentzian curve derived from the harmonic trap model and the power law function converge well with the experimental spectrum since the $p$ value now approaches 2, that of a free particle.

Figure 3.8: Diffusion and power spectrum of a trapped bead. (a) Mean square displacements, $\langle \Delta r^2 \rangle \equiv \langle (r(t)-r(0))^2 \rangle_{\text{traj}}$ (averaged over 1-second segments of trajectories), as a function of time $t$ are plotted for trajectories (A), (B) and (C) shown in Figure 3.6. The dashed line represents the theoretical curve for a two-dimensional freely diffusive particle that follows $\langle \Delta r^2 \rangle = 4Dt$, where $D$ is the diffusion constant described in the text. (b) Power spectrum, $P_y(f)$, of the y-position of the bead is averaged over 10-second segments of trajectories and plotted as a function of frequency ($f$) for the same three trajectories. The data points are fitted to a power-law functions $f^{-\beta}$ (red solid lines) and Lorentzian curves (blue dashed curves) based on the harmonic trap model with y-direction spring constants $k_y$ shown in each plot.
Stiffness of the trap can be calculated from either the monopole or micromagnetic model, given the two-dimensional energy profile $U(x,y)$ by Equation (2.3):

$$k_{x,\text{model}} = \frac{\partial^2 U}{\partial x^2} \bigg|_{(x,y)=(x_0,y_0)} = \frac{U(x_0 + \Delta x, y_0) + U(x_0 - \Delta x, y_0) - 2U(x_0, y_0)}{\Delta x^2}$$  \hspace{1cm} (3.13)

$$k_{+,\text{model}} = \frac{\partial^2 U(y > y_0)}{\partial y^2} \bigg|_{(x,y)=(x_0,y_0)} = \frac{2(U(x_0, y_0 + \Delta y) - U(x_0, y_0))}{\Delta y^2}$$ \hspace{1cm} (3.14)

$$k_{-,\text{model}} = \frac{\partial^2 U(y < y_0)}{\partial y^2} \bigg|_{(x,y)=(x_0,y_0)} = \frac{2(U(x_0, y_0 - \Delta y) - U(x_0, y_0))}{\Delta y^2}$$ \hspace{1cm} (3.15)

where $(x_0, y_0)$ is the position of energy minimum, and $\Delta x = \Delta y = 0.5 \, \mu\text{m}$ is the step size used in taking the derivatives. Stiffness in $+y$ and $-y$ directions are separately determined due to the anisotropy of the trap in the presence of an in-plane field component ($H_y$). In these cases, to determine the stiffness constant (e.g. $k_{+,\text{model}}$ along $+y$ direction), trap profile in the $y > y_0$ half is mirrored to the $y < y_0$ half before a second derivative at $y = y_0$ is evaluated. Figure 3.9 shows comparison between the stiffness $k$ extracted from the experiment (by fitting experimental spectrum, Equation (3.9), with the Lorentzian curve, Equations (3.11) and (3.12)) and those from the models (Equations (3.13), (3.14) and (3.15)). Despite deviation of the Lorentzian curve from the experimental spectrum at intermediate to strong trap strengths, the stiffness deduced from the experiment using this model agrees well with that from the monopole (in $+y$ direction) and micromagnetic (in both $+y$ and $x$ directions) models within an order of magnitude for $|H_z| < 83 \, \text{Oe}$ as shown in Figure 3.9. At weaker trap strengths, however, the more free-particle-like motion results in deviation of the experimentally deduced stiffness from those determined by the two models and tends towards zero. The higher (10 times) stiffness of the trap in $-y$ than that in $+y$ direction biases particle motion in the $+y$ direction, as evident by the energy contour and bead trajectory in Figure 3.6. This bias thus makes $k_{+,\text{monopole}}$ or $k_{+,\text{micromag}}$ a more realistic representation than $k_{-,\text{monopole}}$ or $k_{-,\text{micromag}}$.
Figure 3.9: Stiffness, $k$, of the trap in (a) y and (b) x directions plotted as a function of the tuning field component $H_z$. The contours on each panel illustrate $y$-asymmetry of the trap with minimum position at “$\times$”, whereas the arrows indicate the direction the stiffness constant is calculated. Long-dashed lines and dotted lines are based on the monopole and micromagnetic models respectively, where stiffness along the $+y$ and $-y$ directions from the energy minimum are plotted separately as indicated in (a); filled circles are experimentally derived values. External field values used in Figure 3.6 are indicated by (A), (B), and (C) in the plot. The experimental value of $k_x$ at $H_z = -91$ Oe is $3.5 \times 10^{-15}$ pN/μm, which is not shown within the plotted range.
Figure 3.10: Trapping of a DNA-tethered bead remote from the zigzag wire. (a) The applied external field $\mathbf{H}_{\text{ext}}$ with respect to the zigzag wires and trapped DNA-tethered bead (diameter 1.2 μm) is shown. (b) Calculated energy landscape. Interval of the energy contours projected above the landscape is 1.9 $k_B T$. (c) Experimental snapshot and trajectories (in red) of the trapped DNA-tethered bead are shown in bright field and fluorescent modes.

3.6 DNA Hitchhiking a Ride

Figure 3.10 demonstrates the ability of this platform to confine Brownian motion of a bead of diameter $2R = 1.2$ μm with strands of DNA tethered to it, as illustrated in Figure 3.10a. Each strand of DNA (Integrated DNA Technologies) is a 20 base pair of adenine, labeled with biotin on the 3’ end and an amine group on the 5’ end. After attaching Cy5 dye to the amine group on the DNA, ethanol precipitation and high performance liquid chromatography (HPLC) are used to remove any excess unlabeled DNA or dye from the
solution. The resulting concentration of the solution is measured to be 292 µM. The DNA solution is then mixed with a solution of streptavidin-labeled beads (MyOne, Dynabead) at a DNA-to-bead ratio of $\sim 6 \times 10^5$ and incubated for about 15 minutes minimum. After a final diluting process to $\sim 10^5$ beads/mL, the DNA-tethered bead is ready for experiment.

Using the Y5 filter (Leica) on the microscope with exposure time of 0.6 s and gain 25, the fluorescence from the DNA-tethered bead could be clearly observed, but it faded away in a few minutes. Since no excess dye was in the solution, and non-tethered beads were confirmed to show no fluorescence, a fluorescing bead is evidence of DNA tethering. As shown in Figure 3.10a and b, application of an external field in the $+y$ and $-z$ direction shifts the energy minimum for the DNA-tethered bead towards $+y$ direction while weakening it ($\Delta U = 8 k_B T$). DNA attachment is confirmed by fluorescence of DNA-conjugated dye molecules as shown in Figure 3.10c. As expected, since the DNA is short, we observed no qualitative difference between the DNA tethered and non-tethered beads of the same radii in their Brownian motion and response to the tunable trap. The more confined motion of the larger bead ($2R = 1.2 \mu m$) compared to that of the smaller bead ($2R = 560$ nm) in traps of similar depth ($\Delta U = 8k_B T$) can be attributed to the fact that the diffusion coefficient scales as $1/R$, i.e. smaller bead has the tendency to diffuse farther than the larger bead given the same energy profile and time scale.
Chapter 4

Patterned Time-Orbiting Potentials for the Confinement and Assembly of Magnetic Microspheres

Advances in semiconductor devices during the mid-twentieth century\cite{107} have revolutionized the way people communicate and store information. These progresses stem from the ability to design miniature, complex barriers for the confinement and manipulation of electrons. Despite such ability, a purely magnetic analogy to provide designable confinements for magnetic dipoles while achieving simultaneous tunability on the confinement and dipolar forces has remained elusive. In this chapter, we present a straightforward realization by simply activating a micro-patterned permalloy thin film with a precessing magnetic field. With the angle of precession and amplitude of the rotating field as the only two parameters, strengths of various patterned time-orbiting confining potentials are independently controlled from the dipolar forces, manifesting in the pattern-coded assembly of fluid-borne magnetic microspheres (dipoles) into tunable structures. The presented magnetic confinement scheme could serve as a prototype realizable at all scales, enabling fundamental studies such as artificial atoms\cite{108–112}, nucleation\cite{113–117}, jamming\cite{118–120} and frustration\cite{21–23} as well as applications in biomedicine\cite{121–128}, material assembly\cite{129–134}, photonics\cite{135–139}, magnetic logic\cite{140–142} and atom traps\cite{143–148}. 
4.1 Schemes for Confining Interacting Dipoles

As early as 1878[149], various schemes for the confinement of interacting magnetic dipoles have been proposed[16], [137], [150–152] in the context of the ordering phenomena of macroscopic (micrometer to centimeter) magnets. However, limitations are typically inherent in existing systems, such as:

1. Hard-wall confinements that prohibit regulation of the size of the dipole cluster,
2. Restriction of the dipolar interaction to only repulsive or attractive, and
3. Lack of control on placing and removing a desired number of dipoles that are smaller than the millimeter scale within the interacting landscape.

Magnetic traps have also been developed over the last three decades for the confinement of dipolar atoms[143–148]; however, these schemes are based on current-carrying coils that do not offer flexibility on the spatial design and scaling of the trap. In contrast, the patterned time-orbiting potentials presented in this study overcome these disadvantages, enabling in-situ loading and unloading of confined dipoles at the micrometer scale and independent tunability of the soft-confinement force and dipolar interactions (from attraction to repulsion). Moreover, the lithographically defined confinement scheme allows, as discussed below, complex designer landscapes of desired length scales to be readily fabricated.

4.2 Time-Orbiting Confinement and Interactions in a Magnetic Disk

Defining the architecture of the confining potential for magnetic dipoles are permalloy (Ni0.8Fe0.2) thin-film patterns imprinted on a silicon substrate. For the disk pattern, a 150–200 nm layer of SiO2 is spin-coated (Silicafilm, Emulsitone) on the permalloy disk pattern at 4000 rpm followed by baking at 180 °C for 15 min for protection from the environment and further surface treatment. Prior to experiment, the spin-coated SiO2 surface is treated with 0.1 M NaOH for 10 min and rinsed with de-ionized water. Figure 4.1 illustrates a solution of superparamagnetic microspheres (8.18 μm in diameter) (UMC4F/9560, Bangs Laboratories, Inc.) being placed on a substrate patterned with a
permalloy disk (210 μm in diameter, 40 nm thick) to yield a random distribution of microspheres drawn to the surface by gravity in the absence of magnetic fields. The solution contains 0.01~0.05% Tween-20 (Sigma-Aldrich) for the prevention of surface adhesion.

Figure 4.1: Magnetic microspheres in fluid randomly distributed on a permalloy disk on silicon substrate in the absence of the external field. The microspheres are 8.18 μm in diameter, and the disk 210 μm in diameter and 40 nm in thickness.

4.2.1 Different Sources of Magnetic Fields

An externally applied magnetic field of:

\[ H_{ext} = (H_x, H_y, H_z) = (H_1 \cos \Phi, H_1 \sin \Phi, H_1 \cot \Theta) \]  

magnetizes the permalloy disk along the in-plane field direction: (\( \cos \Phi, \sin \Phi, 0 \)). For the in-plane field strengths \( H_1 \) used in this chapter (> 60 Oe), disk magnetization along the in-plane field direction is higher than 99% of the net magnetization according to micromagnetic simulation[92]. Therefore a uniform magnetization serves as a good approximation to the magnetization distribution of the disk. In this approximation, stray magnetic fields are generated only from magnetic charges lying along the circumference of the disk:

\[ H_{disk}(r) = \frac{1}{4\pi} M_{disk} R_{disk} \int_0^{2\pi} d\phi \frac{r-r'}{|r-r'|^3} \cos(\phi' - \Phi) \]
where $M_{\text{disk}} = 8.6 \times 10^5$ A/m, $R_{\text{disk}} = 105$ μm and $d = 23.7$ nm are the magnetization, radius and effective magnetic thickness (see Section B.3) of the disk respectively. The integral is performed over the positions $\mathbf{r}'=\left(R_{\text{disk}} \cos \phi', R_{\text{disk}} \sin \phi', 0\right)$ along the periphery of the disk, where we have made the assumption that the disk situates within an infinitely thin circular area centered at the origin (0,0,0).

The external field also transforms the microspheres into dipoles, emanating dipolar fields:

$$H_{\text{dip}}(\mathbf{r}) = \frac{1}{4\pi} \chi V \sum_{\mathbf{r}_{\mathbf{x}}} \frac{3\mathbf{\hat{r}}_{\mathbf{i}} \cdot \mathbf{H}_{\text{ext}}}{|\mathbf{\hat{r}}_{\mathbf{i}}|^3} - \mathbf{H}_{\text{ext}}$$

(4.3)

where $\chi = 0.051$ and $V = (4/3)\pi R^3$ ($R = 4.09$ μm the bead radius) are the susceptibility and volume of the bead respectively (experimental determination of $\chi$ is given in Section B.2). The relative displacement between beads is defined as $\mathbf{\nu}_i \equiv \mathbf{r} - \mathbf{r}_i$, and the symbol “$$\mathbf{\hat{r}}$$” above the vector denotes unit vector form, i.e. $\mathbf{\hat{r}}_i \equiv \mathbf{\nu}_i / |\mathbf{\nu}_i|$. The summation is performed over the positions $\mathbf{r}_i$ of all the microspheres except the one located at $\mathbf{r}$. As $H_{\text{ext}}$ is generally greater than 60 Oe while $H_{\text{dip}}(\mathbf{r}) < 0.5$ Oe for $|\mathbf{\nu}_i| > 2R$, and $H_{\text{disk}}(\mathbf{r}) < 1$ Oe for all $\mathbf{r}$ located within 80% of the disk radius, we have omitted contributions to the magnetic moment of bead from the $H_{\text{dip}}$ and $H_{\text{disk}}$ terms. As shown in Figure 4.2a, moments of the beads are aligned with $H_{\text{ext}}$ and unaffected by $H_{\text{dip}}$ and $H_{\text{disk}}$ terms for the parameters used in this study. These terms will only come into play on the alignment of the moments under $\chi$ values that are ~100 times higher or large film thickness $d$ that are ~10 times higher as shown in Figure 4.2b-e.

The $H_{\text{dip}}$ term, if included, would require a self-consistent realignment of the magnetic moments from all the beads since each bead moment $\mathbf{m}_i$ is now a function of $H_{\text{dip}}(\mathbf{r}; \mathbf{r}_1, \mathbf{m}_1, \mathbf{r}_2, \mathbf{m}_2, \ldots)$, which depends on all other $\mathbf{m}_i$’s. This realignment of the moments could result in many-body interaction, an interaction that exists only in the presence of many beads, resulting in chain formation when all other forms of interactions are negligible[133].
Figure 4.2: Realignment of the moments in the beads due to $\mathbf{H}_{\text{dip}}$ or $\mathbf{H}_{\text{disk}}$. In each panel, a cluster of beads (small circles) is randomly distributed atop the magnetic disk (a portion of the large circle) in the presence of an external field of $\mathbf{H}_{\text{ext}} = (60,0,-60)$ Oe. The direction of the magnetic moment of each bead is represented by the arrow for the in-plane component and color-coded background for the z-component (inset below) in each circle. Note the magnitude of the moment of each bead may vary but is not shown here. Realignment of the magnetic moments of the beads is shown in (a) for the susceptibility $\chi$ and film thickness $d$ used in this study, in (b,c) for increased susceptibility, and in (d,e) for increased thickness.

4.2.2 Interaction Energy Decomposed

Given Equations (4.2) and (4.3) as well as (2.2) and (2.5) discussed in Section 2.1.1, the energy profile $U(r)$ for a bead located at $r$ can be determined. For a better understanding on the interactions involved, we further decompose the energy into two major terms: $U_{\text{disk}}$...
and $U_{\text{dip}}$, omitting the constant term involving $H_{\text{ext}}^2$ as well as terms that are second order in $H_{\text{disk}}$ and $H_{\text{dip}}$:

$$U(r) = -\frac{1}{2} \mu_0 \chi V \left[ H_{\text{ext}} + H_{\text{disk}}(r) + H_{\text{dip}}(r) \right]^2$$

$$\approx U_{\text{disk}}(r) + U_{\text{dip}}(r) + \text{constant}$$

(4.4)

where

$$U_{\text{disk}}(r) \equiv -\mu_0 \chi V H_{\text{ext}} \cdot H_{\text{disk}}(r)$$

(4.5)

$$U_{\text{dip}}(r) \equiv -\mu_0 \chi V H_{\text{ext}} \cdot H_{\text{dip}}(r)$$

(4.6)

The beads (dipoles) interact with each other as well as the disk, arranging themselves into configurations that minimize the total energy $U$, with primary contributions from the dipole-disk ($U_{\text{disk}}$) and dipole-dipole ($U_{\text{dip}}$) interaction energies. As shown in Figure 4.3a, in the presence of a fixed, oblique external field of $H_{\text{ext}} = (60,0,60)$ Oe oriented between the $+x$ and $+z$ directions, each dipole on a plane above the pattern experiences an asymmetric energy landscape, $U_{\text{disk}}(r)$, where a strong energy barrier and trench exist on disk edges facing the $-x$ and $+x$ directions respectively. The dipoles are attracted towards local energy minima that form on the $-x$ side of the strong barrier, inside the disk, and the trench on the $+x$ side. The constant field also causes the magnetic dipoles induced in the beads to align along the direction of $H_{\text{ext}}$, forming chains of aggregates. Simulation of equilibrium bead arrangement is performed by iterating bead positions over 5 min (Equation (2.7)), ignoring the inertial term and thermal fluctuating force while incorporating boundary conditions of a hard sphere and substrate surface. Experimental determination of the near-wall correction factor that contributes to the drag coefficient $\gamma$ in Equation (2.8) is given in Section B.1.

### 4.2.3 Time-Averaged Forms of the Interacting Energies

Typical force experienced by a microsphere situated within 80% of the disk radius is less than 1 pN, which corresponds to a time scale of greater than 1.5 s for the microsphere to move by a distance of its own diameter. Therefore, precessing $H_{\text{ext}}$ about the $z$-axis at 20 Hz (time period 0.05 s) results in the microsphere motion insensitive to the fast varying
component of the energy profile, but instead, it responds to a time-averaged energy
landscape, $\overline{U_{\text{disk}}}$, in the form of a bowl-shaped confinement surrounded by a circular
trench as shown in Figure 4.3b. The precessing field also renders rotational symmetry to
the time-averaged dipole-dipole interaction ($U_{\text{dip}} \rightarrow \overline{U_{\text{dip}}}$), facilitating formation of a
planar ordered cluster rather than aggregated chains within the confining potential. Note
that to prevent net rotation and drifting of the microsphere cluster in the experiment,
the rotation of the in-plane field is programmed to cycle through the following sequence of
angles at a speed of 20 revolutions per second: $180^\circ$, $-360^\circ$, $180^\circ$, $-360^\circ$, $360^\circ$,
$-180^\circ$, $360^\circ$ and $-180^\circ$.

Theses time-averaged forms of the interaction energies can be computed by letting $\Phi = \omega t$
in Equation (4.1), where $\omega$ is the angular frequency of precession, and then taking
the averages of Equations (4.5) and (4.6) over time $t$, i.e.

$$\overline{U_{\text{disk}}}(r) = -\mu_0 \chi V \mathbf{H}_{\text{ext}}(t) \cdot \mathbf{H}_{\text{disk}}(r, t)$$

$$= -\frac{H_0}{4\pi} \chi VM_{\text{disk}} R_{\text{disk}}^2 \int_0^{2\pi} d\phi' \frac{\mathbf{r} - \mathbf{r}'}{|\mathbf{r} - \mathbf{r}'|^3} \left[ \begin{array}{c} H_1 \cos \omega t \cos (\phi' - \omega t) \\ H_1 \sin \omega t \cos (\phi' - \omega t) \\ H_2 \cos (\phi' - \omega t) \end{array} \right]$$

(4.7)

$$\overline{U_{\text{dip}}}(r) = -\mu_0 \chi V \mathbf{H}_{\text{ext}}(t) \cdot \mathbf{H}_{\text{dip}}(r, t)$$

$$= -\frac{\mu_0}{4\pi} \chi^2 \nu^2 H_{\text{ext}}^2 \sum_{r_i, r_f} 3 \cos \theta_i \cos \phi_i \sin \theta_i \cos (\omega t - \phi_i) \sin \phi_i |\mathbf{r}_i|^2 - 1$$

(4.8)

where $\mathbf{r}_i = |\mathbf{r}_i|(\sin \theta_i \cos \phi_i, \sin \theta_i \sin \phi_i, \cos \theta_i)$ is the relative dipole displacement $\mathbf{r}_i = \mathbf{r} - \mathbf{r}_i$
in spherical coordinates. These expressions can be further simplified by noting that

$$\cos(\omega t + \delta) = \sin(\omega t + \delta) = \cos(\omega t + \delta) \sin(\omega t + \delta) = 0$$

(4.9)

and

$$\cos^2(\omega t + \delta) = \sin^2(\omega t + \delta) = 1/2$$

(4.10)

for any angle $\delta$ and non-zero angular frequency $\omega$. 

36
Figure 4.3: Energy landscapes and microsphere arrangements in the presence of a (a) fixed and (b) precessing external magnetic field. Shown from top to bottom are the calculated energy landscapes, simulated and experimental snapshots of the system 5 min after application of a fixed or precessing external field $H_{\text{ext}}$. The contour intervals drawn on the energy landscape are $2000 \ k_B T$ ($T = 300$ K). Projections of the simulated microsphere positions on the surface are drawn in circles to distinguish levitated microspheres.
The expressions for $U_{\text{disk}}(r)$ and $U_{\text{dip}}(r)$ then become:

$$U_{\text{disk}}(r) = -\frac{\mu_0 H_1}{8\pi} \chi V M_{\text{disk}} dR_{\text{disk}} \int_0^{2\pi} d\phi \frac{r - r'}{|r - r'|^3} \begin{pmatrix} \cos \phi' \\ \sin \phi' \\ 0 \end{pmatrix}$$

(4.11)

$$U_{\text{dip}}(r) = -\frac{\mu_0}{8\pi} \chi^2 V^2 H_{\text{ext}}^2 \left( 3 \cos^2 \Theta - 1 \right) \sum_{r_1 \neq r} \frac{(3 \cos^2 \Theta - 1)}{|s_1|^3}$$

(4.12)

These time-averaged forms of the first-order interaction energies will be utilized in simulation in this chapter for the confinement and assembly of the microsphere (dipole) cluster.

### 4.2.4 Elliptic Integrals in a Magnetic Disk

Quantities containing $H_{\text{disk}}$ involve integration of the fields generated from magnetic charges along the periphery of the disk as in Equation (4.2). It may greatly enhance the computation speed using built-in analytical functions in the programs (as is the case for Mathematica, Wolfram) instead of performing actual integrals. For this reason, it is beneficial to express terms such as $U_{\text{disk}}(r)$ in terms of complete elliptic integrals of the first, second and third kind defined respectively by:

$$K(n) = \int_0^{\pi/2} d\phi (1 - n \sin^2 \phi)^{-1/2}$$

(4.13)

$$E(n) = \int_0^{\pi/2} d\phi (1 - n \sin^2 \phi)^{1/2}$$

(4.14)

$$\Pi(n,n') = \int_0^{\pi/2} d\phi (1 - n \sin^2 \phi)^{-1/2} (1 - n' \sin^2 \phi)^{-1/2}$$

(4.15)

It can be shown through suitable change of variables that $U_{\text{disk}}$ in Equation (4.11) can be expressed as:

$$U_{\text{disk}}(r) = -\frac{\mu_0 H_1}{8\pi} \chi V M_{\text{disk}} d \frac{1}{\rho} \left[ \left( 2 - n - 4 \frac{R_{\text{disk}}^2}{\rho^2} \right) \Pi(n,n) - 2K(n) \right]$$

(4.16)
where $\rho(r)$ and $n(r)$ are defined, in spherical coordinate $r = r(\sin \theta \cos \phi, \sin \theta \sin \phi, \cos \theta)$, as:

$$\rho(r) \equiv \left( r^2 + R_{\text{disk}}^2 - 2rR_{\text{disk}} \sin \theta \right)^{1/2} \quad (4.17)$$

$$n(r) \equiv -\frac{4rR_{\text{disk}} \sin \theta}{\rho(r)^2} \quad (4.18)$$

Other terms such as $H_{\text{disk}}(r)$ and $U_{\text{disk}}(r)$ as well as second order terms $\overline{U^{(2)}_{\text{disk}}(r)}$ and $\overline{U_{\text{dip-disk}}(r)}$ discussed below can also be expressed by $K(n)$, $E(n)$, and $\Pi(n,n)$ through the same change of variables and algebra. Due to the lengthiness of those expressions, they will be left as exercises for interested readers.

### 4.2.5 Second Order Interaction Energies

As discussed in Section 4.2.1, for dipoles confined within 80% of the disk radius, $|H_{\text{disk}}|$ and $|H_{\text{dip}}|$ are, even at their maximum values, one order of magnitude smaller than $|H_{\text{ext}}|$. Therefore terms involving $H_{\text{disk}}^2$, $H_{\text{dip}}^2$ and $H_{\text{disk}} \cdot H_{\text{dip}}$ has been ignored in calculation of the interaction energy $U$ in Equation (4.4). For completeness, we will qualitatively discuss the consequences of these higher order terms in this section.

Terms that are second order in $H_{\text{disk}}$ or $H_{\text{dip}}$ in Equation (4.4) for $U(r)$ are given, in their time-averaged forms along, with order-of-magnitude estimates for $\rho \sim R_{\text{disk}}$ as:

$$\overline{U^{(2)}_{\text{disk}}(r)} = -\frac{1}{2} \mu_0 \chi V \overline{H_{\text{disk}}^2} \sim -\mu_0 \chi V \left( \frac{M_{\text{disk}} d}{R_{\text{disk}}} \right)^2 \quad (4.19)$$

$$\overline{U^{(2)}_{\text{dip}}(r)} = -\frac{1}{2} \mu_0 \chi V \overline{H_{\text{dip}}^2} \sim -\mu_0 \left( \chi V \right)^2 H_{\text{ext}}^2 \left[ 1 - \frac{1}{4} \left( 3 \cos^2 \Theta - 1 \right) \right] \frac{1}{|\mathbf{r}|^6} \quad (4.20)$$

$$\overline{U_{\text{dip-disk}}(r)} = -\mu_0 \chi V \overline{H_{\text{dip}} \cdot H_{\text{disk}}} \sim -\mu_0 \left( \chi V \right)^2 H_{\text{ext}} \left[ \frac{M_{\text{disk}} d}{R_{\text{disk}}} \right] \frac{1}{|\mathbf{r}|^5} \quad (4.21)$$

where we have assumed that there exists a dipole located at $(r - \mathbf{u})$, in the same $x$-$y$ plane as the dipole located at $r$, i.e. angle between $\mathbf{u}$ and the $z$-axis is $\Theta = 90^\circ$. 

39
It is worth noting that \( U_{\text{disk}}^{(2)}(r) \), arising from interaction between stray field from the disk \( (H_{\text{disk}}) \) and the dipole moment induced by it, does not depend on the external field, and its magnitude is a factor of \( (M_{\text{disk}}/H_1)(d/R_{\text{disk}}) \sim 0.05 \) times that of the first order dipole-disk interaction energy \( U_{\text{disk}}(r) \) (Equation (4.16)). Since the second order dipole-disk interaction energy \( U_{\text{disk}}^{(2)} \) scales as \( \rho^{-6} \) compared to \( U_{\text{disk}} \) which scales as \( \rho^{-3} \) for small dipole-edge distance \( \rho \) (i.e. \( \rho \ll R_{\text{disk}} \)), it becomes non-negligible only for dipoles situated near the edge of the disk; however, as \( U_{\text{disk}}^{(2)}(r) \) is negative for all \( r \), i.e. no energy barrier, this second order term does not qualitatively transform the first order energy landscape \( U_{\text{disk}}(r) \).

The term \( U_{\text{dip}}^{(2)}(r) \) arises from the interaction between field from other dipoles \( (H_{\text{dip}}) \) and the dipole moment induced by it. This second order dipole-dipole interaction energy is negative for all dipole-dipole displacements \( \mathbf{r} \), resulting in an attractive interaction from all directions; however, it depends slightly on the orientation of the external field \( H_{\text{ext}} \), increasing by 25% as \( H_{\text{ext}} \) is changed from out-of-plane (\( \Theta = 0^\circ \)) to in-plane (\( \Theta = 90^\circ \)). It scales as \( 1/|\mathbf{r}|^6 \), decaying faster than the first order dipole-dipole interaction energy \( U_{\text{dip}}(r) \), which scales as \( 1/|\mathbf{r}|^3 \) (Equation (4.12)). For beads that are in contact (\( |\mathbf{r}| = 2R \)), the relative magnitude of \( U_{\text{dip}}^{(2)} \) compared to \( U_{\text{dip}} \) scales as the susceptibility, i.e. \( U_{\text{dip}}^{(2)}/U_{\text{dip}} \sim \chi \); therefore, the second order dipole-dipole interaction is only negligible for small bead susceptibilities, large dipole spacing, or low first order interaction when \( \Theta \) is close to the transitioning angle \( \Theta_c \) (discussed below).

The term \( U_{\text{dip-disk}} \) involves interaction between \( H_{\text{disk}} \) and the dipole moment induced by \( H_{\text{dip}} \), plus the interaction between \( H_{\text{dip}} \) and the dipole moment induced by \( H_{\text{disk}} \). This cross-coupling between \( H_{\text{disk}} \) and \( H_{\text{dip}} \) is only relevant when a dipole is near other dipoles while situated in the vicinity of the disk edge.
In the following sections, only first order terms will be accounted for in the discussion for the interacting forces unless otherwise noted.

Figure 4.4. Quantification of the two primary forces in the system: time-averaged confinement force from the disk, $F_{\text{disk}}$, and dipolar force, $F_{\text{dip}}$, between the dipoles on the $x$-$y$ plane. In the presence of a precessing $H_{\text{ext}}$ as in Figure 4.3b ($H_1 = 60$ Oe, $\Theta = 45^\circ$), the $x$-component of (a) $F_{\text{disk}}$ and (b) $F_{\text{dip}}$ (exerted by a microsphere located at $x = 0$) are plotted as a function of $x$. $F_{\text{disk}}^*$ and $F_{\text{dip}}^*$ are defined as the maximum in-plane confinement and dipolar forces respectively.

### 4.3 Two Major Interplaying Forces: Confinement and Dipolar

We will first obtain a quantitative understanding on the interplay between two primary forces – the confinement force (time-averaged) that arises from dipole-disk interaction ($U_{\text{disk}}$) and the dipolar force from dipole-dipole interaction ($U_{\text{dip}}$).
4.3.1 Forces in the $x$-$y$ Plane

As shown in Figure 4.4a, in the presence of a precessing $\mathbf{H}_{\text{ext}}$ oriented at $\Theta = 45^\circ$ from the $z$-axis and with a horizontal component $H_1 = 60$ Oe as in Figure 4.3b, the time-averaged confinement force ($\mathbf{F}_{\text{disk}}$), obtained by taking the negative gradient of $U_{\text{disk}}$, on a dipole situated inside the disk has an in-plane component directed towards the center with a maximum amplitude of $F_{\text{disk}} \approx 1$ pN. As can be seen from Equation (4.16), $U_{\text{disk}}$ is proportional only to the in-plane component ($H_1$) of $\mathbf{H}_{\text{ext}}$, and therefore the confinement force, $\mathbf{F}_{\text{disk}} = -\nabla U_{\text{disk}}$, is also proportional to $H_1$—an interesting property that enables the strength of the confinement force to be controlled simply by $H_1$.

Figure 4.4b shows that under the same precessing field, the corresponding time-averaged dipolar force, $\mathbf{F}_{\text{dip}} = -\nabla U_{\text{dip}}$, between two dipoles on the $x$-$y$ plane is repulsive with a maximum value of $F_{\text{dip}} \approx 0.2$ pN when they are in contact and weakens with their separation ($x$) as $1/x^4$. Moreover, it can be shown by taking the negative gradient of Equation (4.12) that $\mathbf{F}_{\text{dip}}$ is proportional to $H_{\text{ext}}(3\cos^2\Theta - 1)$, or $H_1^2(2\cot^2\Theta - 1)$ in terms of $H_1$, for any given positions of the interacting microspheres. Given a fixed $H_1$, the dipolar force $\mathbf{F}_{\text{dip}}$ within the $x$-$y$ plane can be tuned by $\Theta$ from being repulsive ($\Theta < \Theta_c$) to attractive ($\Theta > \Theta_c$), crossing over at $\Theta = \Theta_c = \cos^{-1}(1/\sqrt{3}) \approx 54.7^\circ$ as shown in Figure 4.5.

Separate and independent control of the confinement ($\mathbf{F}_{\text{disk}}$) and dipolar ($\mathbf{F}_{\text{dip}}$) forces can thus be achieved, as illustrated in Figure 4.6, by tuning $H_1$ and $\Theta$ along contours of constant $F_{\text{disk}}^*$ or $F_{\text{dip}}^*$. 
Figure 4.5: Maximum (contact) dipolar force $F_{\text{dip}}$ as a function of $\theta$. The curve crosses over zero at $\theta_c \approx 54.7^\circ$.

Figure 4.6: Independent tunability on the confinement and dipolar forces. Contours of constant $F_{\text{disk}}$ and $F_{\text{dip}}$ are plotted in the parameter space spanned by $H_1$ and $\Theta$.

4.3.2 $z$-Dependence of the Forces

The confinement force plotted above considers dipoles that are located in the plane defined by $(x,y,R)$. Such confinement within the $x$-$y$ plane just above the disk surface is made possible with the help of gravity. As shown in Figure 4.7a, without gravity, the profile of the confinement force resulting from dipole-disk interaction, though providing
an in-plane confinement, contains a z-component that pushes the dipole away from the disk, preventing confinement on the surface. With the addition of a gravitational force (buoyant weight) of \((\rho_{\text{bead}}-\rho_0)Vg\) in the -\(y\) direction (\(\rho_{\text{bead}} = 1090\, \text{kg/cm}^3\) and \(\rho_0 = 1000\, \text{kg/cm}^3\) are densities of the bead and water; \(g = 9.8\, \text{m/s}^2\) is gravitational acceleration), Figure 4.7b shows that confinement within the \(x-y\) plane above the disk is made possible provided the dipoles are not too close to the disk edge (up- and outward force is still present within a small region near the inner edge of the disk).

Figure 4.7: \(x-z\) cross-sections of the field of (a), confinement force, and (b), confinement force plus gravitational force, in the plane of \(y = 0\). The confinement force includes both the first and second order terms, \(F_{\text{disk}}(r)\) and \(F_{\text{disk}}^{(2)}(r)\). Black arrows denote the direction of force while red curves represent force lines starting from various positions at \(z = R\) on the disk. Zones on the disk where confinement inside the disk is possible are highlighted in blue while those not possible in red.
Figure 4.8: x-z cross-section of the dipolar force field at various angle of precession $\Theta$. The black narrow triangles indicate direction of the dipolar force experienced by a bead due to another bead located at the origin. The force fields on the top (bottom) row are plotted for dipolar forces up to first (second) order in $H_{\text{dip}}$. Regions with repulsive/zero/attractive dipolar interaction in the plane (same $z$ for the two microspheres) are highlighted in red/white/blue below each plot.

As discussed in the section above, dipolar force between two beads in the same $x$-$y$ plane can be tuned with $\Theta$ from being repulsive to attractive (Figure 4.5). As far as first order dipolar force is concerned, the dipolar interaction for two beads not in the same $x$-$y$ plane can be described by Equation (4.12). As depicted in the $x$-$z$ cross-sectional force field in the first row of Figure 4.8, due to the factor of $\left(3\cos^2 \vartheta_i - 1\right)$ in the dipolar interaction energy between two spheres displaced by $\vartheta_i$ (Equation (4.12)), the sign of the dipolar force is opposite for $\vartheta_i = 90^\circ$ (two spheres in the same $x$-$y$ plane) and $\vartheta_i = 0^\circ$ (two spheres stacked along $z$ direction). In other words, for $\Theta < \Theta_c$ for example, the dipolar interaction is repulsive for two spheres in the plane but attractive for two spheres on top of each other; whereas for $\Theta > \Theta_c$, it is the other way around. To facilitate formation of a planar bead cluster when $\Theta < \Theta_c$ such as that shown in Figure 4.3b in the experiment, beads are made to settle in the same $x$-$y$ plane on the disk surface either by
gravity or precessing the field at $\Theta = 90^\circ$ prior to the in-plane dipolar interaction made repulsive (attractive out-of-plane).

Even though the second order dipolar interaction energy $U^{(2)}_{\text{dip}}(r)$ decays faster and is a factor of $\chi$ (~0.051) times the first order term as mentioned above, it can become non-negligible when $\Theta$ is tuned near $\Theta_c$ (where the first order term vanishes). This is best reflected in the $x$-$z$ cross-sectional plot of the dipolar force field up to second order as shown in the second row of Figure 4.8. As the second order term is stronger in the short range and always attractive (compare between Equations (4.12) and (4.20)), it can compete with the first order term that is tuned weakly repulsive in- or out-of-plane. The force plots depict that at $\Theta = 54^\circ$ (slightly below $\Theta_c$), in-plane dipolar force is attractive in the short range but repulsive in the long range; at $\Theta = 55^\circ$ (slightly above $\Theta_c$), out-of-plane dipolar force is attractive in the short range but repulsive in the long range. This competition between short and long ranged forces can potentially lead to frustrated dipolar structures discussed below.

4.4 Tuning Microsphere Structures within the Confinement

4.4.1 Collapse and Expansion of the Cluster

As a demonstration of the tunability on the interplaying forces, the angle of precession $\Theta$ is adjusted under a given in-plane field component $H_1$, i.e. tuning the dipolar interaction while the confinement force is fixed. The dipoles reassemble over a time scale of seconds into:

1. expanded structures of tunable sizes, resembling the two-dimensional version of J. J. Thomson’s atomic “plum pudding model”[153] (insets A, B, C, F and G in Figure 4.9), or

2. a hexagonal lattice centered on the disk (insets D, E, I and J in Figure 4.9).
Figure 4.9: Equilibrium and transient structures of a 45-microsphere cluster confined in the bowl-shaped potential with dipolar interaction tuned by $\Theta$. The mean separation between microspheres, $<|r_{ij}|>$ (angled brackets denote average over $i$ and $j$), determined by the bonding lengths $|r_{ij}|$ given by Delaunay triangulation (lower left inset in the plot) is plotted as a function of $\Theta$ while $H_1 = 60$ Oe. Snapshots of the equilibrium microsphere configurations at corresponding values of $\Theta$ are shown below for both simulation (insets A-E) and experiment (insets F-J). Scale bars are 50 μm.

This tunability on the equilibrium cluster size is characterized by the average microsphere center-to-center separation, $<|r_{ij}|>$, determined by Delaunay triangulation[154] as plotted in Figure 4.9 for both the experiment and simulation. The transition from an expanded structure to an ordered lattice occurs at $\Theta = \Theta_c \approx 54.7^\circ$ in the simulation where the lowest order dipolar interaction vanishes as predicted by the calculation shown in Figure 4.5. A small deviation of the observed transitioning angle to
Θ \sim 60° in the experiment could arise from the weakly repulsive hydrodynamic forces due to rotational motion of the microspheres in a precessing field.

The expanded cluster structure forming in the time-orbiting potential presented here could serve as a model experimental platform for various studies on a cluster of confined repelling objects (artificial atom)[108–112], such as the Mendeleev-type table that accounts for the shell structure of the cluster, “magic number” clusters that are found to be more stable, and the Wigner crystal that forms under strong confinement.

Figure 4.10: Time dependence of the mean sphere separation as the strength and sign of dipolar interaction is changed. At time \( t < 0 \), dipolar interaction is attractive with \( \Theta = 90° \) and \( H_1 = 60 \text{ Oe} \); at \( t = 0 \), \( \Theta \) is switched to various values shown in the legend on the right; at \( t = 300 \text{ s} \), \( \Theta \) is switched back to 90°. The top and bottom rows show data obtained from the experiment and simulation respectively.
Figure 4.11: Nucleation and jamming effects. Snapshots are taken at (a) 0 s, (b) 12.6 s and (c) 50.0 s after the instant switching of $\Theta$ from $35^\circ$ to $90^\circ$ while $H_1 = 60$ Oe. Lines are drawn between beads with center-to-center distance $|r_{ij}|$ less than $\sim 2.48R$ (10.14 µm) to emphasize these effects.

4.4.2 Reversible Tunability and Transient Cluster Structures

The rapid tunability of the dipolar interactions achieved by the precessing magnetic field offers one the opportunity to study cluster transformation. As shown in Figure 4.10, bead cluster can be reversibly transformed between closely packed and expanded structures of different sizes by abruptly changing $\Theta$ to various values (within 1 µs). The transformation from a closely packed lattice to an expanded structure takes place over a time scale of 30 s for both the experiment and simulation; however, the transformation from an expanded structure to a closely packed lattice takes longer in the simulation than in the experiment as is depicted by the plots on the right column of Figure 4.10. This is attributed to the fact that magnetic anisotropy exists in the beads used in the experiment. Such anisotropy could cause beads that are within several $R$ apart to rotate as a whole with respect to the 20 Hz precessing field, aligning their moments over a larger portion of the precessing period and hence larger attractive dipolar force.

Several other noteworthy phenomena, e.g. nucleation and jamming, are observed by abruptly tuning the dipolar interaction. For example, reorienting the precessing $\mathbf{H}_{\text{ext}}$ from the repulsive ($\Theta = 35^\circ$) to the attractive ($\Theta = 90^\circ$) regime nucleates dipoles originally in a
2D plum pudding configuration into fragments of small clusters as depicted in Figure 4.11a and b. The rapid tunability between repulsive and attractive interactions has only been realized in simulations[155], and it could become a new handle for the study of first-order phase transitions due to nucleation. The formation of large fragments of dipole lattices prior to their mergence is responsible for the jamming effect – failure of fragments to coalesce into one closely packed lattice – shown in Figure 4.11c.

### 4.4.3 Cluster Impurities

Due to challenges such as imperfections on the surface and non-uniform distribution of bead size or susceptibility, the expanded clusters experimentally observed usually do not exhibit perfect symmetries. Such experimental imperfections offer one the opportunity to study impurities. As an example, Figure 4.12 demonstrates the simulated equilibrium structure of a cluster of 6 beads, of which one has a susceptibility that is 10, 1, or 1/10 times that of the rest. In the case where all beads have the same susceptibility, the resulting cluster is symmetric as expected with possible shell configurations of (inner, outer) = (1, 5) or (3, 3). For beads with different susceptibilities, one observes the interesting fact, besides the asymmetric arrangement of the cluster, that low-susceptibility beads tend to surround large-susceptibility beads if they out-number the large-susceptibility ones, but when left alone, they are excluded from the large-susceptibility bead cluster. Figure 4.13 further illustrates this effect by “washing” (expanding and collapsing multiple times) a cluster of beads with populations of 40 and 5 that have different susceptibilities. After the washing steps, bead population with a higher susceptibility tends to settle towards the center, excluding those with a lower susceptibility to the outer shell of the cluster. This can be understood from the fact that beads with larger susceptibility experience a larger confinement force as is evident from Equation (2.6), and therefore they tend to dominate the center of the confinement.
**Figure 4.12**: Possible configurations obtained from simulation of a cluster of beads with different susceptibilities. Susceptibility of the bead shown as red filled circle ($\chi_{\text{red}}$) is adjusted by different factors shown on the top to those of the black empty circles ($\chi_{\text{black}} = 0.05$). The parameters for the precessing field are $\Theta = 45^\circ$ and $H_1 = 100$ Oe.

### 4.4.4 Frustrated Structure due to Competing Interactions

The delayed transition of the bead cluster into a closely packed lattice as $\Theta$ is increased beyond the critical angle $\Theta_c$ due to hydrodynamic repulsion also leads to the frustration effect observed at $\Theta = 57.5^\circ$. In this weakly attractive regime of dipolar coupling, competition sets in between the shorter-ranged dipolar attraction and longer-ranged hydrodynamic repulsion whose forces scale with inter-particle distance ($x$) as $1/x^4$ and $1/x^3$ [152] respectively. With the distance between dipoles restricted by the soft-confining time-orbiting potential from the disk, their attempt to satisfy these competing forces results in the formation of a branching chain cluster as shown in Figure 4.14; this feature is not revealed prior to the collapse in the simulation shown in inset C of Figure 4.9, which accounts only for the magnetic forces.
Figure 4.13: “Washing” a cluster of beads of different susceptibilities in simulation. Susceptibility of the beads shown as red filled circles ($\chi_{\text{red}}$) are adjusted by different factors shown on the left to those of the black empty circles ($\chi_{\text{black}} = 0.05$). The angle of precession $\Theta$ is switched between $45^\circ$ and $90^\circ$ once every 2-minute period for 4 times, resulting in expansion and collapse of the cluster. The in-plane field $H_1 = 100$ Oe.

Figure 4.14: Frustrated branching chain structure observed at $H_1 = 60$ Oe and $\Theta = 57.5^\circ$ (as inset H of Figure 4.9). Lines are drawn between beads with center-to-center distance $|r_{ij}|$ less than $\sim 2.48R$ (10.14 µm) to emphasize the chaining effect.
Although the realignment of magnetic moments in beads due to dipolar fields $H_{\text{dip}}$ could also cause the formation of chains[133] as discussed in Section 4.2.1, this effect, screened by hydrodynamic repulsion and weakened by the low $\chi$ value, is not observed in the work presented here. Using beads with larger $\chi$ but lower magnetic anisotropy (smaller bead rotation and weaker hydrodynamic repulsion) could enable study on such many-body effects.

4.4.5 Simulation of Frustration due to Competing Electric and Magnetic Interactions

The frustrated branching chain structure could arise through other possible combinations of competing interactions, such as:

(1) second order dipolar attraction (shorter ranged) vs. first order dipolar repulsion (longer ranged) discussed above, and

(2) dipolar attraction (shorter ranged) vs. electrostatic repulsion (longer ranged).

Since the angle $\Theta$ at which frustration occurs ($57.5^\circ$) in the experiment lies in the attractive regime for both the first and second order dipolar interactions, and electrostatic repulsion is not observed between beads in a closely packed configuration once the external field has been removed, we come to the conclusion that the shorter-ranged dipolar attraction and longer-ranged hydrodynamic repulsion are the competing forces responsible for the branching chain structure observed in Figure 4.14. It would nevertheless be useful to incorporate electrostatic repulsion as the competing force of dipolar attraction for the study of frustration as it can be tuned by the charge carried per bead ($q$) as well as the ionic strength ($I$) of the solution, both independent of the magnetic dipolar interaction.

In the following, we will simulate the behavior of bead cluster within the time-orbiting potential in the presence of a screened electrostatic interaction (Coulomb repulsion) that competes with the magnetic dipolar interaction tuned by a precessing magnetic field oriented at $\Theta = 90^\circ$ and $H_1 = 100$ Oe (attraction). The resulting
electrostatic and magnetic dipolar energy (Equation (4.12)) of a bead displaced by \( x = x\hat{x} \) from another bead is given by:

\[
\overline{U}_c(x) = U_c(x) = \frac{q^2}{4\pi\varepsilon_0} \frac{e^{-x/\lambda_D}}{x} \quad (4.22)
\]

\[
\overline{U}_{\text{dip}}(x) = -\frac{\mu_0}{8\pi} \chi^2 V^2 H_1^2 \frac{1}{x^3} \quad (4.23)
\]

where \( \varepsilon_0 \) is the permittivity of free space. The Debye length \( \lambda_D \) is the length scale over which the electric field decays due to the screening effect from ions present in the solution, and it can be expressed in terms of the ionic strength \( I \) as:

\[
\lambda_D = \sqrt{\frac{\varepsilon_r \varepsilon_0 k_B T}{2e^2 N_A I}} \quad (4.24)
\]

where \( \varepsilon_r \) is the relative permittivity of the solution (~80 for water at room temperature), \( e = 1.6 \times 10^{-19} \) coulombs the charge per electron, and \( N_A = 6 \times 10^{23} \) mole\(^{-1}\) the Avogadro’s number.

Two independent, unit-less parameters defining the form of the mixed interaction energy, \( U_{\text{mix}}(x) = U_c(x) + \overline{U}_{\text{dip}}(x) \), are:

1. \( A \equiv \left| \frac{U_c}{U_{\text{dip}}} \right| = \left| \frac{U_c(2R)_{\lambda_D \to \infty}}{\overline{U}_{\text{dip}}(2R)} \right| \), the relative strength of unscreened electrostatic to magnetic dipolar interaction when to beads are in contact, which depends on \( q \) (given \( H_1 \) and \( \Theta \)), and

2. \( B \equiv \lambda_D / (2R) \), the relative screening length to bead diameter, which depends on \( I \).

As a result, the mixed interaction energy can then be expressed as:

\[
\frac{U_{\text{mix}}(X)}{U_{\text{dip}}} = A \frac{1}{X} e^{-X/B} - \frac{1}{X^3} \quad (4.25)
\]

where the normalized distance \( X \) is defined as \( X \equiv x/(2R) \).
Figure 4.15: Phase diagram of mixed electrostatic and magnetic interactions for two beads separated by $x$ along the $x$-direction (bead displacement $x = x\hat{x}$). The phases are separated, within the parameter space spanned by ionic strength ($I$) and charge per bead ($q$), according to the form of $U_{\text{dip}}(x) + U_c(x)$ into regimes of attraction for all $x$ (inset A), attraction for $x > 2R$ (inset B), repulsion for $x > 2R$ (inset C), and competing short-ranged attraction and long-ranged repulsion (inset D). Energy difference $\Delta U$ between the first local energy maximum and minimum that exist in phases of B, C and D is color-coded in the phase diagram.

There are several distinct phases within the parameter space spanned by $A$ and $B$ according to the form of $U_{\text{mix}}(X)$ as shown in Figure 4.15:

1. Region containing point A: Interaction is attractive for all $x$, and the beads arrange into a closely packed lattice.
2. Region containing point B: Interaction is attractive for $x > 2R$. Since hard-sphere condition prevents $x$ to be smaller than $2R$, the spheres do not experience
the repulsive part of the interaction that exists at $x < 2R$. The resulting bead arrangement is a closely packed lattice.

(3) Region containing point C: Interaction is repulsive for $x > 2R$. The resulting structure is an expanded cluster.

(4) Region containing point D: Interaction is attractive in the short range but repulsive in the long range. The spheres form branching chain structure as a result.

It is evident in inset D of Figure 4.15 that beads confined in the time-orbiting potential with short-ranged attractive force competing with long-ranged repulsive force will result in the formation of a branching chain structure as that observed in the experiment (Figure 4.14), even though the origin of the repulsive force is electrostatic rather than hydrodynamic. In phases containing point C and D in the diagram, very weak attractive interaction exists at even longer range due to the repulsive electrostatic interaction decays exponentially over the Debye length due to ionic screening.

For competing interactions in the form of a short-ranged attraction and long-ranged repulsion as shown in inset D of Figure 4.15, time-orbiting potential plays an important role in facilitating the formation of a branching chain structure. As evident from the simulation shown in Figure 4.16, a dilute, randomly distributed cluster of microspheres are unable to form connected chains in the absence of a confinement; they, if started off far away, will repel each other and expand forever. In the presence of a time-orbiting potential, the confining force compresses the microsphere cluster, enforcing some beads to overcome the energy barrier $\Delta U$ between them and fall within the short range attraction regime. The soft confining potential therefore serves as a catalyst for forming the frustrated structure.
Figure 4.16: Time-orbiting potential as a catalyst for forming frustrated structures. (a) Initial arrangement of the beads in simulation. The mixed interaction energy as a function of bead separation is plotted in the inset below. Snapshots taken after 11 min of simulation time show resulting bead arrangements with (b) and without (c) a confinement provided by the time-orbiting potential.

4.5 Controlling the Number of Confined Dipoles

As discussed in Section 4.4.1, the number of confined interacting objects is an important aspect in various fundamental studies of cluster structure. However, experimental control on the number of confined magnetic dipoles has only been achieved through direct physical placement into and out of the confinement zone for millimeter- and larger-scale objects[137], [149], [152] or through the random compartmentalization at certain concentrations for much smaller objects[16], [150]. Here we demonstrate a simple mechanism to load and unload the micrometer-sized dipoles in-situ into the confinement potential. By application of a sequence of fixed $H_{\text{ext}}$ with a weak in-plane and stronger
out-of-plane field components, e.g. $H_{\text{ext}} = (0, -5, 100) \text{ Oe}$ followed by $(5, 0, 100) \text{ Oe}$, the disk is only partially magnetized along the in-plane field direction (Figure 4.17a), producing local domain-wall fields that allow the beads into the disk to join the existing cluster at the disk center (Figure 4.17b-c). Microspheres can also be easily “rolled” towards the edge and out of the disk by rotating the external magnetic field, for example, about the $y$-axis as shown in Figure 4.17d-f. These loading (unloading) steps thus control the number of isolated dipoles within the time-orbiting potentials.

Figure 4.17: Loading and unloading microspheres into and out of the permalloy disk. (a) Micromagnetic simulation of the magnetization distribution on the disk in the presence of an external field of $H_{\text{ext}} = (0, -5, 100) \text{ Oe}$. (b) Snapshot of the system, originally confining 19 closely packed microspheres, 3.3 s after application of the same field as in (a). (c) 5.4 s after application of the field. Arrow indicates the microsphere circled in (b) entering the disk periphery. (d) Snapshot of the system originally confining 54 microspheres in the presence of a precessing external field. (e) 10.4 s after application of a rotating field about the $y$-axis (with 100 Oe in magnitude and two revolutions per second in the clockwise direction when viewed from $-y$). Arrows indicate motion of the microspheres out of the disk. (f) Confinement of the remaining 34 microspheres with a precessing field.
4.6 Various Shapes of Time-Orbiting Potentials

The time-orbiting bowl-shaped profile can be readily extended to other shaped confining potentials with surrounding barriers and trenches defined by permalloy patterns. As examples, triangle (Figure 4.18a), square (Figure 4.18b), long rectangle (Figure 4.18c), and more complex octagonal ring (Figure 4.18d) are illustrated that maintain the same independent control on the confining and dipolar forces through $\Theta$ and $H_1$. The dimensions of the patterns are: circular disk 210 µm in diameter, triangle 260 µm in side length, 150 µm x 150 µm square, 75 µm x 300 µm rectangle and 200 µm x 250 µm octagonal ring with a 50 µm x 100 µm hole. A 100 nm protective layer of SiO$_2$ is deposited on these permalloy patterns through magnetron sputtering. We find that a magnetron-sputtered SiO$_2$ surface does not require the NaOH treatment used in Section 4.2, and an addition of 0.02–0.05% Triton X-100 (Sigma-Aldrich) surfactant in the bead solution serves well in the prevention of surface adhesion.

The stray magnetic field $H_{\text{poly}}(r)$ generated from these polygon-type patterns, assuming uniform in-plane magnetization, is given by:

$$H_{\text{poly}}(r) = \frac{1}{4\pi} M_{\text{poly}} d \sum_i \cos(\phi_i - \Phi) \int_{p_{i,1}}^{p_{i,2}} \frac{r - r'}{|r - r'|^3} ds'$$

(4.26)

where $M_{\text{poly}}$ and $d$ are the magnetization and thickness of the pattern respectively. The summation is performed over all polygon sides, where $p_{i,1}$ and $p_{i,2}$ are the starting and ending vertices of polygon side labeled by $i$. We use the convention that when facing along the direction of the side vector $s_i = (p_{i,2} - p_{i,1})$, the magnetic pattern lies on the left. The integral is performed over the length of side $i$ in increments of $ds'$ from $r' = p_{i,1}$ to $r' = p_{i,2}$. The azimuthal angle $\Phi$ of $H_{\text{ext}}$ is given in Equation (4.1), and $\phi_i$ with respect to side $i$ is defined as:

$$\phi_i = \arcsin(\hat{x} \times (\hat{s}_i \times \hat{z}) \cdot \hat{z})$$

(4.27)

which is the azimuthal angle of vector $\hat{s}_i \times \hat{z}$ that is normal to side $i$ and pointing away from the pattern. Equation (4.26) can be further simplified as:
\[
\mathbf{H}_{\text{poly}}(r) = \frac{1}{4\pi} M_{\text{poly}} \sum_i \cos(\phi_i - \phi) \left( \hat{s}_{i\perp} s' - \hat{s}_i s_{i\perp} \right) \left( s_{i\perp}^2 + s'^2 \right)^{1/2} \]

(4.28)

where

\[
s_{i\perp} = \hat{s}_i \times (r - p_{i\perp}) \times \hat{s}_i
\]

(4.29)

is the shortest perpendicular displacement from side \(i\) to \(r\), and

\[
s_{i,j} = \hat{s}_i \cdot (r - p_{i,j}), \quad j = 1,2
\]

(4.30)

The first-order, time-averaged form of the dipole-polygon interaction energy can then be derived, as that of the dipole-disk interaction in Equation (4.7):

\[
\frac{U_{\text{poly}}(r)}{J} = -\mu_0 \chi V \mathbf{H}_{\text{ext}}(t) \cdot \mathbf{H}_{\text{poly}}(r,t)
\]

\[
= -\frac{1}{4\pi} \mu_0 \chi VM_{\text{poly}} \sum_i \left( \frac{H_1 \cos \omega t}{H_z} \right) \cos(\phi_i - \omega t) \cdot \int p_{i\perp} \frac{r - r'}{|r - r'|^3} ds'
\]

(4.31)

The resulting time-orbiting potential landscapes unveil previously unexplored opportunities to study the behavior of field-responsive magnetic dipoles beyond conﬁnements with cylindrical symmetry or simple topology. For instances, in the repulsive dipolar interaction regime, the dipole cluster expands to reﬂect the different trap motif and symmetries (Figure 4.18a-d); the long rectangle (Figure 4.18c) serves as a quasi 1D magnetic channel; the discrete clusters decorating the octagonal ring (Figure 4.18d) show the rare competition among inter-particle attractive force and the conﬁnement force, two forces that are typically cooperative, to minimize the total system energy. The intricate balance between inter-particle attractive-or-repulsive forces and soft confining potentials of various strengths, dimensions and geometries leads to the emergence of a complex and design-specific behavior of the dipoles.
Figure 4.18: Time-orbiting potentials of various shapes. Time-averaged energy landscapes generated from various permalloy patterns are calculated for (a) triangle, (b) square, (c) long rectangle, and (d) octagonal ring. Simulations (below the landscapes) and experimental snapshots (on the right) of the system in equilibrium are shown in each panel for a precessing $\mathbf{H}_{\text{ext}}$ with $H_t = 100$ Oe and $\Theta = 90^\circ$ or $35^\circ$. Contour intervals on the energy landscapes are $2000 \ k_B T$. Scale bars shown below the images are 100 µm.
4.7 Applications

We expect the presented scheme based on patterned time-orbiting potentials to have useful applications, for instance, in the following:

1. Biomedical devices[121], [122]: On-chip control of local concentration and optimal mixing can be achieved by the expansion and collapse of the dipole cluster; attracting the dipoles from different directions to the center of the disk serves as a simultaneous, multi-directional force probe on a biological entity attached to the center; dipole clusters of tunable spacing can also be fixed as filters to sort out objects of different sizes within a narrow flow channel.

2. From materials stand point[129–131], [135], [136], through multiplexing an array of patterned traps, a tunable two-dimensional photonic crystal whose response can be varied with modest magnetic fields becomes feasible. The resulting planar photonic crystal systems offer a length scale relevant for near-visible wavelength, wide tunability of the inter-sphere separation, and simplicity of fabrication and operation.

3. As its electric counterpart, semiconductor devices, in revolutionizing the electronic age, the all-magnetic scheme presented may also become a powerful platform in the fast-growing fields that seek to achieve faster and more energy efficient information processing through magnetic dipoles than with electric charges: The patterned time-orbiting potential could serve as a lithographically defined virtual circuit or wave guide for electron spins or magnons in spintronics[140] and magnonics[141], while the ability to create clusters of various sizes serves as a strategy to build islands of nanomagnets that are dipole-coupled to produce logic operations[142].

4. We further envision the confinement scheme as a possible candidate in the trapping of cold quantum gases of magnetic dipolar atoms[143–148]. Given other means to confine these atoms to within two dimensions, a 10 μm wide circular cavity (inverted disk) on the permalloy film for example, is capable of confining diamagnetic atoms carrying 1 Bohr magneton with an effective spring
constant\(^1\) of \(~10^{15}\) N/m under \(H_1 = 100\) Oe and \(\Theta = 45^\circ\). Such a pattern-based confinement scheme would allow the effect of trap geometry on the wave function of the condensate atoms to be investigated.

\(^1\) Calculated by taking the second derivative of \(U_{\text{disk}}(\mathbf{r})\) along x-direction at \(\mathbf{r} = (0,0,0)\).
Chapter 5

MAGNETIC SEPARATION AND ENCAPSULATION OF CELLS INTO DROPLETS ON A CHIP

Single cell study is gaining importance because of the cell-to-cell variation that exists even within isogenic cell population[156–159]. Analysis of such variation at the gene expression level could impact single cell genomics, cancer research, and biotechnology[160]. The on-chip monitoring of individual cells in an isolated environment would prevent cross-contamination, provide high recovery yield, and enable study of biological traits at a single cell level. These advantages of on-chip biological experiments[38], [40], [161–163] are a significant improvement for a myriad of cell analyses methods compared to conventional methods[164], which require bulk samples and provide only averaged information on cell structure and function. This chapter of the dissertation report on a device that integrates a mobile magnetic trap array with microfluidic technology to provide the possibility of separation of immunomagnetically labeled cells and their encapsulation with reagents into pico-liter droplets for single cell analysis. The simultaneous reagent delivery and compartmentalization of the cells immediately following sorting are all performed seamlessly within the same chip. These steps offer unique advantages such as the ability to capture cell traits as originated from its native environment, reduced chance of contamination, minimal use of the reagents, and tunable encapsulation characteristics independent of the input flow. Preliminary
assay on cell viability demonstrates the potential for the device to be integrated with other up- or downstream on-chip modules to become a powerful single-cell analysis tool.

5.1 Key Components for Single-Cell Studies

Two key processes required prior to performing single-cell analyses are:

1. The sorting of cells into subpopulations, and
2. The compartmentalization of these cells of interest with dedicated reagents into individually isolated environments.

A brief introduction of the existing sorting and compartmentalization techniques as well as the rationale underlying the integration of these two on-chip processes will be given in the following sections.

5.1.1 Sorting techniques

Different sorting techniques have been developed over the past decade[38–40], [165]. For example, conventional flow cytometry[158], [166] sorts cells based on their sizes and biological signatures. While it is a well-developed and commercially available technique, this approach requires expensive instrumentation. Hydrodynamic techniques[167–172] sort objects based on their sizes without the need for external forces or pre-labeling of biological entities. Electric-field-based techniques such as optical trap[173], [174], dielectrophoresis[174–178] and electrokinesis[53] utilize the dielectric property or charge of the objects to be sorted. However, these schemes generally have strict requirements on the optical and ionic properties of the surrounding fluid, and challenges such as heating and electrolysis (bubbling) need to be addressed. In contrast, magnetic-field-based sorting, achieved by the intrinsic or extrinsic (through marker-specific magnetic bead labeling) magnetic moment of the cells[55], serves as an inexpensive technique without the same difficulties that plague its electric counterparts. Schemes such as external magnets[179–185], ferromagnetic channels[186], strips[187–189], films[58–60] and periodic patterns[61–76] have been shown to generate the magnetic field gradient required to trap or manipulate magnetic objects to desired locations.
5.1.2 Compartmentalizing techniques

Compartmentalization of the sorted cells of interest into individually isolated environments is a crucial step towards single-cell analysis. Various schemes have been utilized for the purpose of compartmentalization[39]. For examples, array of wells on a proprietary chip[158] and microfluidic chambers[190–192] act as containers for single cells while delivering reagents through pumps and valves. However, the nature of these rigid confining structures limits the ability to scale up (provide as many compartments as possible) and could potentially be contaminated or worn off over multiple uses. In contrast, compartmentalization based on microfluidic droplet devices serves as an alternative technique[193–198] where the containers (droplets) are created anew during the encapsulation of single cells. The number of droplets generated by the device is practically unlimited, allowing easy scale-up.

5.1.3 Integration of sorting and compartmentalization on a chip

In order to compartmentalize the cell while it still maintains the property as derived from the native heterogeneous environment, it is advantageous to perform the compartmentalization immediately following sorting in the same setup. However, existing work on single-cell analysis generally require transfer between instruments[158] or containers[159] from one step to another, or purification of the samples elsewhere prior to introducing them onto the compartmentalization platforms[190–192], [195–198]. These steps could potentially lead to contamination during transfer, loss through non-specific binding, and denaturation. While each of the chip-based sorting techniques mentioned above has its own merits, so far none has yet provided an on-chip mechanism for the compartmentalization of the sorted entities. Although sorting after compartmentalization exists in droplet microfluidics, e.g. post-encapsulation processing of droplets through hydrodynamic sorting[199], detection-based electric sorting[195], [196] and droplet splitting[195], [196], [200], unwanted effects and chemicals secreted from other cells could not be remove from the droplets through such sorting or splitting.
In this work, we have integrated for the first time, the magnetic sorting capability of previously developed mobile magnetic trap array[64] immediately before the compartmentalization of cells provided by droplet microfluidics on the same device. This integration not only eliminates the steps needed between sorting and compartmentalization, but it also offers the combined advantage of low cost, biocompatibility and ease of scaling up. The rationales behind choosing mobile trap array over other chip-based sorting technologies for the integration are its:

1. Well-defined pick-up and drop-off locations compared to external magnet based schemes,
2. Active separation against the flow compared to the passive ferromagnetic strips, channels or hydrodynamic sorting, and
3. Tolerance on the ionic content of the liquid environment compared to electric field based techniques.

These unique features couple well with the dropletization by continuously guiding magnetically labeled cells across a zero- or reverse-flow zone, leaving behind unwanted chemicals from other cells, and into an independently controlled reagent flow for encapsulation. The streamed output of droplets containing cells separated afresh from their heterogeneous environment serves as a production line ready for further integration with other on-chip analysis techniques such as single-cell polymerase chain reaction and electrical measurements. As proof of concept, preliminary assay on the viability of encapsulated cells through fluorescence detection is demonstrated.
Figure 5.1: Device layout and system setup. (a) Microscope image (top) showing the channel layout on an array of permalloy (Ni$_{0.8}$Fe$_{0.2}$) disks and a schematic side view of the device (bottom). Fluid flow rates $Q_1$, $Q_2$, $Q_3$ and $Q_4$ are indicated at corresponding channels while the three T-junctions are labeled with $T_1$, $T_2$ and $T_3$. (b) Schematic of full layout of the microfluidic channel. (c) Photograph of the device. (d) Photograph of the system consisting of four electromagnets and a solenoid that apply external magnetic field on the device. Tubings connected to computer-controlled syringes transfer fluid to or from the microfluidic channels of the device situated within the setup. Note the fifth tubing has not been connected yet to the droplet collection port in the picture.
5.2 Integration of Magnetic Tweezers with Droplet Microfluidics

5.2.1 Device fabrication

A mask design with transparent patterns of disk arrays and microchannels is produced on a chromium-on-quartz plate (Advance Reproductions Corporation). As shown in Figure 5.1a, an array of permalloy (Ni$_{0.8}$Fe$_{0.2}$) disks with 10 µm diameter, 15 µm centre-to-centre spacing and 84 nm height are imprinted onto a Si substrate by contact photolithography using the mask aligner followed by sputter deposition and lift-off (Section 2.2.1). A final deposition of 100 nm SiO$_2$ on the entire surface served as a protective layer. The same photolithography is used to create microchannel molds (SU-8 2025, MicroChem) on the Si substrate. Polydimethylsiloxane (PDMS) (Dow Corning Sylgard 184) is mixed with curing agent at 10:1 ratio, poured onto the microchannel molds, cured at room temperature for 2 days, peeled from the mold, cut to desired size and then punched with holes at the end of the channels for tubing connection. The resulting PDMS channel, with layout as illustrated in Figure 5.1b, is permanently bonded to the disk array substrate to form the integrated device shown in Figure 5.1c by the following procedure: The channel side of the PDMS as well as the SiO$_2$ surface of the disk array are treated with UV-ozone (UVO Cleaner 42, Jelight Company Inc.) at ~1 cm sample-lamp distance for 3 minutes, aligned and attached to each other using ethanol as a temporary lubricant in between, and then baked at 80 °C for 30 min. To facilitate droplet formation, the channel surface is made hydrophobic prior to the experiment by treating the channel inner surface with Sigmacote (SL-2, Sigma-Aldrich) for 5–10 s followed by baking at 110°C for 30 min. Channel dimensions are: height 30 µm, width of $Q_1$ flow 400 µm, left width of $T_1$-$T_2$ channel 200 µm, right width of $T_1$-$T_2$ channel 100 µm, length of $T_1$-$T_2$ channel 500 µm, width of $Q_3$ flow 50 µm, and narrowest width of $Q_4$ flow 30 µm.

5.2.2 Microfluidics

Fluid flow in the microfluidic channel are remotely controlled by computer program coded in LabVIEW (LabVIEW, National Instruments Corporation), which interfaces
with syringe pumps (PHD Ultra Syringe Pump, Harvard Apparatus) mounted with 25 or 50 μL syringes (7636-01 and 7637-01, Hamilton Company). Polyethylene tubings (inner diameter 0.40 mm, 720191, Harvard Apparatus) connected between the syringes and channel ports transfer fluid to and from the microfluidic device as shown in Figure 5.1d. Unless otherwise noted, temperature fluctuation around the tubings is minimized (thereby stabilizing the flow) by wrapping Kimwipes (Fisher Scientific) around them and utilizing cooling fans. As there are a total of 5 ports on the channel, flow rates are controlled only at 4 ports (flow $Q_1$, $Q_2$, $Q_3$ and $Q_4$ in Figure 5.1a and b) through 4 individual syringe pumps; flow rate at the fifth port (droplet collection port) is given by $Q_1 + Q_2 + Q_3 + Q_4$. The solutions sent into or out of the channel ports are detailed below.

*Magnetic and nonmagnetic input (flow $Q_1$)*

Experiments on bead separation and encapsulation are performed with a mixed magnetic and non-magnetic bead solution that contains:

1. 7.9 μm diameter superparamagnetic microspheres (UMC4N/10150, Bang Laboratories, Inc.), and
2. 3.34 μm diameter nonmagnetic beads (CP-30-10, Spherotech, Inc.).

Above beads are suspended in 0.1% Triton X-100 (X100, Sigma-Aldrich) at final concentrations of roughly $1.8 \times 10^6$ and $6.4 \times 10^6$ beads/mL for the magnetic and nonmagnetic beads respectively.

Suspension for cell experiments contains a mixture of:

2. Human breast cancer cells BT-474 labeled with 2.8 μm magnetic particles (Dynabeads M-270 Streptavidin, Life Technologies Corporation) functionalized with anti-HER2 antibodies, and
3. Red blood cells (RBCs).

These cells are suspended in phosphate buffered saline (PBS) with 5 mg/mL Pluronic F-68 (P1300, Sigma-Aldrich), 5mM ethylenediaminetetraacetic acid (EDTA) and 1% bovine serum albumin (BSA). Final cell concentrations used in separation and encapsulation experiment are roughly $5 \times 10^5$ cells/mL (BT-474) and $1 \times 10^5$ cells/mL.
(RBCs), while final concentrations used for the cell viability experiment are $2.5 \times 10^5$ cells/mL (BT-474) and $2 \times 10^5$ cells/mL (RBCs). The observed average number of beads labeling a BT-474 cell is 1.5 with standard deviation 0.8 (out of 485 cells) after an incubation time of ~30 min. This labeling yield could increase over time as the bead-to-cell (BT-474) ratio in solution is intentionally made higher than ~10 beads/cell to achieve maximum magnetic force on the labeled cells.

*Non-magnetic output (flow $Q_2$)*

Although flow $Q_2$ withdraws fluid from the microfluidic channels, a buffer solution same as that used in flow $Q_1$ to suspend beads or cells is infused into the non-magnetic output channel (along with flows $Q_1$, $Q_3$ and $Q_4$ from other channels) during the initial phase to fill the entire channels with fluid. After air has been removed from all the channels, $Q_2$ is then set to the desired withdrawal rate.

*Reagent solution (flow $Q_3$)*

Three types of solutions are used for the reagent channel, i.e. flow $Q_3$ in Figure 5.1a and b, depending on the experiment conducted:

1. 0.1% Triton X-100 in de-ionized water for magnetic bead separation and encapsulation experiments,
2. PBS with 5 mg/mL Pluronic F-68, 5mM EDTA and 1% BSA for cell separation and encapsulation experiments, or
3. PBS with 1% BSA and 1.5 μM PI (propidium iodide) for cell separation and encapsulation followed by droplet collection and fluorescence analysis of cell viability.

*The continuous phase solution (flow $Q_4$)*

Mineral oil (O121, Fisher Scientific) with 0–15% Span 80 (sorbitan monooleate, S6760, Sigma-Aldrich) as emulsifier is used as the continuous phase that surrounds the aqueous droplets.
**Droplet collection output**

The output port of droplet collection channel is not connected to any tubings during the initial air-removal phase. After removal of the air and stabilization of droplet generation, a small segment (several centimeters long) of tubing is then connected to this port for the collection of droplets.

Figure 5.2: Manipulation of a magnetic bead from one permalloy disk to the next on the disk array. Shown from top to bottom are the applied external magnetic field \( \mathbf{H}_{\text{ext}} \), calculated energy landscape (with legend of the energy scale shown on the right) for a magnetic bead (7.9 μm in diameter) on top of the disk array, and the experimental snapshot (bead appears as black dot and disks white dots). Manipulation of the bead is shown in chronological order from the left to right.

### 5.2.3 Magnetic manipulation

Shown in Figure 5.1d, are the four electromagnets (OP-2025, Magnetech Corp.) and coil that provide the in-plane \( (H_x \text{ and } H_y) \) and out-of-plane \( (H_z) \) components of the external magnetic field, \( \mathbf{H}_{\text{ext}} = (H_x,H_y,H_z) \). A LabVIEW program controls the current driving the electromagnets and solenoid, allowing fields up to ~150 Oe to be produced and remotely tuned. Using the expression for the stray magnetic field generated from a disk, \( \mathbf{H}_{\text{disk}}(\mathbf{r}) \),
obtained in Chapter 4 (Equation (4.2)), one can take a superposition of such fields to obtain the stray field from an array of disks:

\[
H_{\text{disk array}}(r) = \sum_i H_{\text{disk}}(r - r_i)
\]

(5.1)

where the summation is done over all disk positions \( r_i \). With Equations (2.2) and (2.5), the energy landscape for a magnetic bead on the disk array can be calculated. As shown in Figure 5.2, magnetic trap array (local energy minima on the edges of the imprinted permalloy disks that attract magnetic objects) is mobilized with respect to the fixed disk array by application of a sequence of magnetic fields: rotation of the in-plane field, i.e. \( H_{\text{ext}} = (H_1 \cos \Phi, H_1 \sin \Phi, H_z) \), \( \Phi = 0^\circ \) to \( 180^\circ \), followed by reversing the orientation of \( H_z \)[64]. These steps result in the transport of magnetic beads or labeled cells around the disk periphery (e.g. from \(-x\) end to \(+x\) end) during the field rotation phase followed by its hopping to the adjacent disk (e.g. from \(+x\) end of one disk to \(-x\) end of next) when \( H_z \) is reversed. One period of the transport cycle consists of a rotation time \((\tau/2)\) and wait times before \((\tau/4)\) and after \((\tau/4)\) the inter-disk hopping is completed. The rate of transport is hence defined as \( f = 1/\tau \), i.e. the number of disks traversed by the magnetic object per unit time. With the ratio of \(|H_z|\) to \(H_1\) set fixed at 1.5 to 1, the two central parameters for magnetic manipulation are the magnitude of the in-plane field \(|H_1|\) and the transport rate \(f\).

5.2.4 Imaging

The sequence of events are observed through an optical microscope (Leica DM2500MH) with a 10x objective lens and recorded with a digital camera (QImaging Retiga EXi) interfaced with LabVIEW at a frame rate of 10~20 fps as mentioned in Section 2.2.2. The fluorescence signal from the PI dye is picked up with Leica’s Texas Red Filtercube (TX2).
Figure 5.3: Snapshots showing the process of magnetic separation, encapsulation, droplet collection and analysis. (a) At time $t = 0$ s, one magnetically labeled BT-474 cell and two unlabeled red blood cells are indicated by boxes and enlarged as insets, where an additional inset shows a typical labeled cell in higher resolution (scale bar is 10 μm). The cells enter from the top left branch of the channel with flow rates $Q_1 = Q_2 = 75$ nL/min, $Q_3 = 15$ nL/min and $Q_4 = 30$ nL/min. (b) At $t = 53.3$ s, movements of the three cells from $t = 0$ s are traced with lines. The labeled cell magnetically separated to the right is indicated by the box. (c) Sequential snapshots taken at $t = 57.2$, 57.4 and 57.6 s show the encapsulation process of the same labeled cell (indicated by the box) mixed with the reagent solution from flow $Q_3$. (d) Snapshot taken from a separate experiment than that of (a-c) showing droplets being transferred down the output channel. Droplets contain solution of PI (propidium iodide) at 1.5 μM concentration, and those encapsulating labeled cells are indicated by the boxes. (e) Droplets collected from (d) are placed between a glass substrate and cover glass for detection of fluorescence signal from the PI dye (inset next to the enlarged picture of a droplet containing cell). Size variation on the droplets is a result of droplet merging and breaking during the transfer step.
5.3 Experiment overview

Magnetic and non-magnetic beads or cells are sent down the input channel at flow rate $Q_1$ while withdrawn at a rate $Q_2$ same as $Q_1$ as shown in Figure 5.1a and b. As an example, Figure 5.3a shows magnetically labeled and unlabeled cells entering the input channel on the left. While the unlabeled ones follow the flow down the channel as shown in Figure 5.3b, the labeled one is magnetically manipulated to the far right of the disk array, mixed with the reagent flow ($Q_3$), and subsequently encapsulated into a droplet with the reagent as depicted in Figure 5.3c. High purity can be achieved, prohibiting unlabeled cells into the separation channel between junctions T1 and T2, by increasing $Q_2$ slightly (~10 nL/min) higher than $Q_1$. As a preliminary viability assay on the encapsulated cells, the droplets are transferred down the output channel (Figure 5.3d), collected in a tubing and then re-dispersed onto a glass substrate for the fluorescence detection of PI (propidium iodide) inside the encapsulated cells (Figure 5.3e). Table 5.1 lists all the experiments conducted within the scope of this work and the respective parameters used.

Table 5.1: Summary of the parameters used in the separation and encapsulation experiments.

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Manipulation rate $f$(Hz)</th>
<th>In-plane field $H_1$(Oe)</th>
<th>Flow rates (nL/min)</th>
<th>$Q_1$</th>
<th>$Q_2$</th>
<th>$Q_3$</th>
<th>$Q_4$</th>
</tr>
</thead>
<tbody>
<tr>
<td>(i) Bead</td>
<td>5</td>
<td>100</td>
<td>$Q_1$ + 10</td>
<td>150 ~ 700</td>
<td>100</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>(ii) Bead</td>
<td>2</td>
<td>20 ~ 100</td>
<td>250</td>
<td>260</td>
<td>100</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>(iii) Bead</td>
<td>0.5 ~ 50</td>
<td>100</td>
<td>250</td>
<td>260</td>
<td>100</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>(iv) Bead</td>
<td>5</td>
<td>100</td>
<td>$Q_1$</td>
<td>50 ~ 350</td>
<td>15</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>(v) Cell</td>
<td>1</td>
<td>100</td>
<td>$Q_1$ + 10</td>
<td>50 ~ 125</td>
<td>15</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>(vi) Cell</td>
<td>1</td>
<td>100</td>
<td>$Q_1$</td>
<td>50</td>
<td>100</td>
<td>50</td>
<td></td>
</tr>
</tbody>
</table>

* Flow not controlled.
5.4 Quantification of device performance with magnetic beads

5.4.1 Separation efficiency

Separation of targeted magnetic entities is achieved by the sequence of external magnetic fields (described in Section 5.2.3), manipulating magnetic objects towards junction T2 (Figure 5.1a) perpendicular to the flow direction. An important parameter characterizing the separation aspect of the device is the separation efficiency, defined by the number of magnetic objects separated to junction T2 to that entering the disk array, where the magnetic object can be magnetic beads or labeled cells. For the quantification purpose in this section, magnetic and nonmagnetic bead solutions (described in Section 5.2.2) are used to evaluate the separation efficiency. The smaller nonmagnetic beads (3.34 μm) compared to the magnetic beads (7.9 μm) allow visualization of the flow and distinguishability between the two types of beads. Based on prepared bead concentration, we find the recovery rate of magnetic beads entering the disk array to be 58% as some beads may settle on tubing surface. As discussed below, the influence of the input flow rate $Q_1$, in-plane magnetic field strength $H_1$ ($|H_z| = 1.5 H_1$), transport rate $f$ as well as various other factors on the separation efficiency of magnetic beads will be investigated.

Effect of Flow Rate

For fixed $H_1 = 100$ Oe and $f = 5$ Hz, Figure 5.4 depicts that high separation efficiency (>90%) is maintained until the input flow rate $Q_1$ exceeds ~300 nL/min. Beyond this threshold, separation efficiency steadily decreases to less than 10% at $Q_1 \geq 600$ nL/min. As an increasing hydrodynamic drag force could account for the decrease in the efficiency, we estimate the minimum force required to detach a bead, with typical magnetic susceptibility of 0.1 (Section B.2), off the magnetic trap to be ~110 pN along the tangential direction of the disk edge as shown in Figure 5.5a. On the other hand, diverting the hopping of the bead requires a force of greater than ~100 pN as shown in Figure 5.5b. This 100 pN hydrodynamic drag force corresponds to a flow rate of $Q_1 = 970$ nL/min based on Stokes’ law (Equation (2.8)), neglecting near-wall effects. However,
the observed flow rate at which the separation efficiency starts decreasing from its high value of > 90% is ~300 nL/min, which is much lower than the estimated flow rate (970 nL/min). Our observation suggests other explanations for the decrease in separation efficiency as $Q_1$ increases. Higher $Q_1$ results in:

1. Higher bead throughput and therefore fewer vacant disks on the array to accommodate incoming beads into the $T_1$-$T_2$ channel,
2. Less time for beads floating above the array surface to be pulled towards the disks by the magnetic trapping force or gravity, and
3. Longer time (>20 ms under a drag force of 100 pN in the -y direction) for the bead to hop to the next disk and therefore higher chance to miss the adjacent mobile trap within the allocated wait time of $1/(4f)$ (Section 5.2.3).

Figure 5.4: Separation efficiency for 7.9 μm diameter magnetic beads plotted as a function of the input flow rate $Q_1$, corresponding to experiment (i) in Table 5.1. Data points (filled diamonds) are based on measured number of separated magnetic beads over a single run of experiment. Vertical bars at the data points represent the effect of flow fluctuation discussed in the text (not measurement errors). The number of magnetic beads counted for each data point is above 400, yielding an estimated statistical error of $\sim 400^{1/2}/400 = 5\%$ due to finite sample size.
Figure 5.5: Trapping forces vs. hydrodynamic drag force for a 7.9 μm magnetic bead on an array of two permalloy disks that are 84 nm thick. (a) Maximum trapping forces are calculated along the -x, +x, -y, +y and +z directions from the energy minimum for the bead in the presence of an external field of $H_{\text{ext}} = (100,0,150)$ Oe. (b) Bead trajectories (shown as red curves) as $H_{\text{ext}}$ is switched to (100,0,-150) Oe are plotted in the presence of a fluid drag force of various shown magnitudes in the -y direction. Starting points of the trajectories at different values of the drag force are equilibrium positions of the bead before switching of the field. The trajectories are plotted for durations of 20 ms long while incorporating a near-wall factor (discussed in Section B.1) of 2.77.

Effect of the Strength and Rate of Magnetic Manipulation

As expected, Figure 5.6b illustrates that a greater magnetic field strength ($H_1$) results in an enhanced magnetic force and therefore higher separation efficiency for a given flow rate $Q_1$ and transport rate $f$. 
Figure 5.6: Separation efficiency for 7.9 μm diameter magnetic beads plotted as a function of (a) in-plane field strength $H_1$ and (b) rate of transport $f$. Data points (filled diamonds) are based on measured number of separated magnetic beads over a single run of experiment ((ii) and (iii) in Table 5.1) for each plot. Vertical bars at the data points represent the effect of flow fluctuation discussed in the text (not measurement errors). The number of magnetic beads counted for each data point range from 200 to 450, yielding an estimated statistical error of $\sim 200^{1/2}/200 = 7.1\%$ due to finite sample size.

Figure 5.6c illustrates that increasing the transport rate $f$ while keeping other parameters fixed yields more effective separation for $f$ up to $\sim 5$ Hz. In this case, rapid transport of the beads into the separation channel yields more vacant disks to accommodate incoming beads, hence the increase in separation efficiency for $f$ in the range of 0.5 to 5 Hz. Transport rates higher than 5 Hz become less effective at separation since:

1. Motion of the trap against the flow ($Q_1$) during the field rotation cycle decreases the minimum flow rate required to detach the bead from 970 nL/min ($f = 5$ Hz) to 480 nL/min ($f = 25$ Hz) and to zero ($f = 50$ Hz) according to calculation, and
(2) Too short a wait time, e.g. $1/(4f) < 10$ ms, during the inter-disk hopping phase may result in stalling (inability to hop away from the disk) of the bead. The optimal manipulation rate of $f = 5$ Hz implies a maximum separated bead throughput of about 30 beads/s, assuming that all the disks (~6 rows) are outputting beads into junction T2 at a maximum occupancy with 1 bead per disk. This yields an estimate on the maximum bead concentration for effective separation to be $\sim 7.2 \times 10^6$ beads/mL for $Q_1 = 250$ nL/min. Though this limitation on the separation throughput is an inherent property of the manipulation scheme, increasing the number of rows of the disk array could potentially enhance the throughput.

Effect of Flow Fluctuation

We find that flow fluctuation due to temperature variation (from heat generated from the electromagnets) around the tubing plays an important factor in separation efficiency. In the bead experiments performed above, i.e. (i), (ii) and (iii) in Table 5.1, thermal insulation (described in Section 5.2.2) is not applied on the tubings, and the amount of fluid flowing unwantedly in the T1-T2 channel ranges from none (when the electromagnets has not been turned on) to about 7 nL over a time scale of 10 s (maximum fluctuating flow rate of ~40 nL/min) after extended use of the electromagnets (~1 hour). The effect of such flow fluctuation on the separation efficiency is best reflected by the vertical bars drawn on the data points in Figure 5.4 and Figure 5.6: The upper bound of the vertical bar on the data point takes into account magnetic beads that are successfully separated into the T1-T2 channel but pushed off into the nonmagnetic output channel due to flow fluctuation; similarly, the lower bound is set by excluding magnetic beads that are pushed into the T2-T3 channel by flow fluctuation without being magnetically manipulated. The observed flow fluctuation is able to occasionally overcome the reverse flow of $Q_2 - Q_1 = 10$ nL/min at the T1-T2 channel to have a significant impact on the separation efficiency under very high and very low manipulation rates as depicted by the large vertical bars at $f = 0.5$ Hz and $f = 50$ Hz in Figure 5.6c. This can be reasoned as the following: At very low $f$, manipulation rate cannot keep up with the bead input, and the
disk array is jammed with magnetic beads such that those untrapped are easily pushed by flow fluctuation; at very high $f$, stalled magnetic beads (discussed above) are easily knocked off or pushed forward by flow fluctuation. Flow stabilization by thermal insulation on the tubings is applied for the experiments in the later sections, i.e. (iv), (v) and (vi) in Table 5.1, where the fluctuation can be reduced to much less than 10 nL/min to facilitate the low-rate encapsulation process.

**Other Factors Affecting the Separation Efficiency**

We will qualitatively discuss several other factors that could affect the separation efficiency. For example, the higher placement of the disk array with respect to the channel in Figure 5.1a compared to the lowered one in Figure 5.3a allows greater chance of the magnetic objects to be separated into channel T₁-T₂, but it may also cause piling up of these objects as they hit the tilted upper channel wall if the objects tend to stick. Same device was used within each set of experiment, and the quantitative effect of different disk array-channel alignments on the separation efficiency is not investigated here.

The size of the magnetic beads is chosen to be comparable to that of the disk size and gap. Much smaller beads are oversensitive to localized fields and may not be able to hop from one disk to the next, whereas oversized beads average out the energy landscape to experience little manipulation force compared to the drag force.

**Summary of Optimal Separation for Magnetic Beads**

To summarize, achieving high separation efficiency for the magnetic beads used in this device requires:

1. Low input flow rate ($Q_1 < 250$ nL/min),
2. High field strength ($H_1 > 100$ Oe),
3. Optimal manipulation rate ($f \sim 5$ Hz),
4. Low bead concentration ($< 7.2 \times 10^6$/mL),
5. Optimal bead size (comparable to disk size and spacing),
6. Thermally insulated tubing, and
Optimal disk array shape and position for increased accommodation in channel T₁-T₂ while avoiding piling up.

5.4.2 Separation purity

Purity of separation is defined as the ratio of number of nonmagnetic objects entering the nonmagnetic output channel (flow $Q₂$) to that of the total number of nonmagnetic objects entering the disk array. We find two major factors contributing to the purity:

1. The amount of reverse flow ($Q₂ - Q₁$) at channel T₁-T₂, and
2. The amount of flow fluctuation.

Under a fixed reverse flow of $Q₂ - Q₁ = 10$ nL/min, purity is found to be 100% with stabilized flow but 98% when without, as flow fluctuation (discussed in the previous subsection) can occasionally overcome the reverse flow. For zero reverse flow ($Q₁ = Q₂$), purity is found to be 96% even with stabilized flow. Each of the percentages above are obtained through counting >500 nonmagnetic beads.

5.4.3 Encapsulation characteristics

To quantify the encapsulation aspect of the device, the same magnetic bead solution described above (see Section 5.2.2) is used. As shown in Figure 5.7a, droplet throughput, i.e. droplet generation rate, is maintained at 5~8 droplets per second, while the separated bead throughput (entering the dropletization junction T₃) is varied from 1 to 6 beads per second by tuning the input flow rate $Q₁$ (note $Q₂$ is set equal to $Q₁$). This feature enables the number distribution of magnetic beads encapsulated within the droplets to be manipulated as shown in Figure 5.7b.

The encapsulation can be approximated as discrete independent events that occur randomly in time. The probability for a droplet to encapsulate $k$ beads is given by the Poisson distribution function $P(k)$[201]:

$$P(k) = \frac{\lambda^k e^{-\lambda}}{k!} \quad (5.2)$$

where $\lambda$ is the mean of $P(k)$, i.e. average number of beads per droplet.
Figure 5.7: Quantification of the encapsulation characteristics with 7.9 μm diameter magnetic beads. (a) Separated bead (filled circles) and droplet (filled diamonds) throughputs as a function of input flow rate $Q_1$. Experimental parameters are given by (iv) in Table 5.1. (b) Extracted from the same experiment as in (a), fraction of droplets (corresponding to the left vertical axis) containing various number of beads are plotted as dots with underlying color-coded bars at flow rates $Q_1 = 50$, 150 and 250 nL/min. Dashed curves at each $Q_1$ represent Poisson distribution function (Equation (5.2)) with mean value $\lambda$ set by the measured average number of beads per droplet (plotted as filled diamonds with values corresponding to the right vertical axis). Total number of droplets taken into account ranges from 840 to 1251, and an estimate on the statistical deviation due to finite sample size is $\sim 840^{1/2}/840 = 3.5\%$.

It has long been a challenge in microfluidic-based approaches to overcome the inherent Poisson statistics in typical encapsulation processes and to achieve single-cell encapsulation[202], [203]. As an example of the limitation imposed by Poisson statistics, taking the derivative of Equation (5.2) with respect to $\lambda$, one finds that the percentage of
single-object droplets can be maximized to $P(1) = 36.8\%$ at $\lambda = 1$; however, this is accompanied by a comparable number of empty droplets (also 36.8%) and multi-object droplets (26.4%). On the other hand, reducing $\lambda$ (average number of objects per droplet) could increase the ratio of single- to multi-object droplets but at the expense of having a large fraction of empty droplets, e.g. at $\lambda = 0.1$, $P(1)/(P(2) + P(3) + P(4) + \ldots) = 9.0\% / 0.47\% \approx 19$ but $P(0) = 90.5\%$.

Figure 5.7b illustrates that the number distribution of beads in a droplet at each flow rate $Q_1$ largely follow Poisson distribution based on the measured average number of beads per droplet. Interestingly, the fraction of single-bead droplets in our study exceeds that imposed by Poisson statistics by a small yet observable amount of $\sim 11\%$ (greater than the estimated statistical error of 3.5%) at $Q_1 = 150$ and 250 nL/min in Figure 5.7b. We attribute this to the fact that at higher throughput, i.e. shorter bead-to-bead distance, a rotating magnetic field with $|H_2|/H_1 = 1.5$ results in repulsive dipolar interactions between the beads travelling from junction $T_2$ to $T_3$, causing them to self-arrange into a more evenly spaced configuration before being encapsulated. This feature increases the fraction of single-bead droplets. Increasing the length of channel $T_2$-$T_3$ could potentially further enhance the fraction of single-bead droplets.

5.5 Separation and encapsulation of labeled cells

A heterogeneous mixture of labeled BT-474 and unlabeled red blood cells (RBCs) described in Section 5.2.2 serves as a sample solution to demonstrate the separation-encapsulation function of the device. RBCs are chosen as unlabeled cells due to their lack of HER2 expression and the distinctive smaller sizes compared to the labeled BT-474 cells, offering visualization on the flow. Other cell types or concentrations are not investigated here but could potentially be used in the device, provided they do not adhere to surfaces of the channel or disk array to hinder device function. Based on prepared concentration, recovery rate of the labeled cells used in this study entering the disk array is found to be 39% since cells have a higher tendency to adhere to tubing surface. A high separation purity of 100% (out of >1200 red blood cells) is achieved with flow
stabilization and reverse flow at channel T$_1$-T$_2$ (see discussion in above section). As shown in Figure 5.8a, due to the lower magnetic moment of the labeling particle, larger cell size and propensity to aggregate, the optimal flow rate to achieve efficient separation of the cells ($> 75\%$), is at $Q_1 < 50$ nL/min while the optimal transport rate is $f \sim 1$ Hz. Both the size and shape of the cells or aggregates affect the separation efficiency. Non-aggregating or smaller single cells have a higher $\gamma_{\text{cell}}$ than aggregates or larger cells due to smaller fluid drag force; linear chain-shaped aggregates tend to orient parallel to the flow direction and thereby experience less drag force when compared to round-shaped aggregates. Although the number of beads attached per cell (labeling yield) is maximized for optimal separation, it differs from cell to cell (Section 5.2.2) due to the amount of receptors present on cell surface; higher labeling yield can increase the magnetic force for a given cell size and therefore higher separation efficiency. To summarize, the marker-specific separation scheme presented here is also selective based on variation of cell size, shape and extent of cell aggregation as well as the amount of receptors expressed per cell.

Encapsulation of labeled cells proves to be fundamentally different from encapsulating magnetic beads. The reduced flow rate for effective separation, tendency of cell aggregation and adhesion to surfaces lowers the separated cell throughput to below 0.15 cells per second and an average of lower than 0.1 cells per droplet at flow rates of $Q_1 = 50 \sim 125$ nL/min. Although at such a low $\lambda$ value of 0.1, Poisson statistics predicts a high single-cell to multi-cell droplet ratio of 19 (see above section), the observed difference between single-cell and multi-cell droplet fractions still falls within an order of magnitude as depicted in Figure 5.8b. This can be understood from the assumption of the encapsulation process as independent random events in Poisson statistics – a feature that becomes less valid due to the tendency for a cell to carry other cells into the same droplet through aggregation. As shown in Figure 5.8b, measured multi-cell droplet fractions are indeed higher than those predicted by the Poisson distribution functions $P(k)$ ($k = 2, 3$), whereas measured single-cell droplet fractions are lower than $P(1)$ at corresponding flow rates. Such deviation from Poisson statistics may offer opportunities for investigating the probability of time-correlated events and insights on cell-cell interaction.
While high throughputs have been achieved in existing chip-based sorting techniques (e.g. $\sim 10^4$ cells/s with dielectrophoresis[178] and $>10^5$ cells/s with ferromagnetic strips[187]) and microfluidic encapsulation devices (>100 droplets/s[195–198]), the novelty of the work presented here lies not in achieving high throughput of cells or droplets but rather the coupling of the two; challenges such as flow stability exist at low rather than high droplet generation rates. The ability of the presented device to down-tune droplet generation rate below 10 Hz to match with the low separated cell throughput has the advantages of increased single-cell droplet fraction, minimized reagent consumption and reduced chance of cell rupture due to strong shear flow. This feature of coupling a large input flow of cells to a slow dropletization is particularly suitable for the processing of rare cells.
Figure 5.8: Separation efficiency and encapsulation characteristics of labeled BT-474 cells. (a) Separation efficiency is plotted as a function of input flow rate $Q_1$. Experimental parameters are given by (v) in Table 5.1. Each cell aggregate is counted as one entity, where single-cell (filled circles) and multi-cell (filled diamonds) entities are plotted separately. Total cell entity counts range from 33 to 58 for each $Q_1$, and the estimated statistical error due to finite sample size is $\sim 33^{1/2}/33 = 17\%$. (b) Extracted from the same experiment as in (a), fraction of droplets containing various number of cells are plotted as dots with underlying color-coded bars at flow rates $Q_1 = 50, 75, 100$ and 125 nL/min. Bottom plot is a log-scaled plot with droplet fraction ranging from $10^{-4}$ to $10^{-1}$. Dashed curves at each $Q_1$ represent Poisson distribution function with mean value $\lambda$ set by the measured average number of cells per droplet. Total number of droplets taken into account ranges from 230 to 2400, and an estimate on the statistical deviation due to finite sample size is $\sim 230^{1/2}/230 = 6.6\%$. 

87
5.6 Preliminary cell staining and viability assay

The unique channel layout of the device shown in Figure 5.1 opens up a broad range of downstream applications after the encapsulation of selected cells. The reagent flow ($Q_3$) from the branch channel (Figure 5.1b) not only draws the separated magnetic object from junction $T_2$ to $T_3$, thereby facilitating the encapsulation process, it also offers several advantages:
(1) Separated objects enter a fresh chemical environment of the reagent several seconds before encapsulation, reducing contamination from the non-separated objects and degradation of the reagent over time.

(2) Minimal use of the reagent, i.e. all fluid from flow $Q_3$ (except a slight reverse flow into channel $T_1$-$T_2$) is encapsulated in the droplet.

(3) Different surface chemistries can be introduced via flow $Q_1$ than to $Q_3$. For example, while a hydrophilic surfactant is desirable in $Q_1$ as it reduces cell adhesion to the surface, it hinders the stability of water-in-oil droplets if encapsulated. The reagent channel therefore allows the chemistry surrounding the separated cells to be switched from adhesion-prevention (with 5 mg/mL Pluronic F-68 surfactant) to droplet-friendly solvent (no surfactant).

As a proof of concept, Figure 5.9 demonstrates a preliminary assay on the viability of encapsulated cells at a raised temperature of 55°C by utilizing the reagent channel to transfer PI dye. PI is generally excluded outside the membrane by live cells, and since the fluorescence intensity of PI increases by many fold when it enters a dead cell to bind with nucleic acids, it serves as an indicator of cell viability. 31 labeled BT-474 cells are observed to be magnetically separated from red blood cells and encapsulated in droplets containing PI within the presented device using parameters given by (vi) in Table 5.1. Due to the difficulty in processing small amount of droplets with this preliminary method, $Q_3$ and $Q_4$ are increased for more droplets. Subsequent collection of the droplets in the tubing and re-dispersion onto a glass substrate mounted with a cover glass allow for preservation and ease of observation as shown in Figure 5.9a-c. Though these transferring steps resulted in large shear flow that merges or breaks about 33% of droplets into larger or smaller sizes, four droplets containing 1, 2, 2 and 3 cells are observed (Figure 5.9d-g), yielding a recovery rate of $8/31 \approx 26\%$ from the device. Prior to and within the first 25 min of heating at 55 °C, only 1 out of the 8 encapsulated cells appears to be alive based on their PI fluorescence retention as shown in Figure 5.9h-k. After 35 min of heating, the fluorescence image shown in Figure 5.9l-o compared to those in Figure 5.9h-k indicates eventual death of the one live cell (top cell in Figure 5.9f). Both the recovery rate ($\sim 26\%$)
and portion of recovered live cells (~12.5%) are not ideal in this preliminary assay. However, we believe that through integration with suitable on-chip observation platforms after the encapsulation step, the device has the potential to offer high recovery yield of live cells and allow detection on cell-to-cell variation with high spatiotemporal resolution.

5.7 Potential modules for integration

We envision other useful experimental modules that could be integrated with the separation and encapsulation functionalities of the device:

1. Analysis techniques such as single-cell PCR (polymerase chain reaction) for the amplification and detection of rare biological signatures of individual cells could be realized by introducing temperature zones on the microfluidic channels.

2. Electrical measurement could be performed by replacing mineral oil with, for example, the conductive ionic liquid for determining properties as the conductance or stiffness of the cell or detecting the change in surrounding solvent.

3. On-chip labeling, upstream of separation, through properly designed channels to mix the functionalized magnetic particles with cells would reduce the preparation time and amount of reagent needed for the immunomagnetic labeling of targeted cells.

4. Overcoming the Poisson statistics of encapsulation by incorporating real-time feedback on the rate of transport ($f$): By monitoring the traffic of magnetic objects in channels $T_1$-$T_2$ and $T_2$-$T_3$, one could achieve a more uniform throughput of separated objects and thus encapsulating a more consistent number of objects per droplet.
CONCLUSION

A key component in the advancement of nanotechnology is the development of precision tools for the manipulation and transport of nano-objects and biomolecules in solution. The advantages of an all-magnetic approach include easy, non-contact manipulation of the magnetic objects and absence of intricate wiring patterns, screening or heating effects that are generally present in charge-based approaches. By tuning a weak magnetic field (~100 Oe) applied through a set of electromagnets and coil (Chapter 2) and attaching magnetic beads to chemical or biological objects of interest, magnetic trapping schemes based on patterned magnetic thin films on a silicon substrate have been presented in this dissertation for studies on particle fluctuation, ordering and microfluidic applications:

1. The CoFe zigzag wire geometry (Chapter 3) produces high magnetic field gradient from local domain wall on the zigzag vertex that traps sub-micrometer magnetic beads, allowing Brownian trajectory of the bead to be tuned by external field from tightly confined to undergoing large recursions biased in targeted directions. This enables studies such as Brownian motor, 1/f noise, thermally activated processes, and drug delivery or chemical reaction with controlled spatial coverage.

2. The large, 100 μm scaled permalloy (Ni0.8Fe0.2) patterns (Chapter 4) provide time-orbiting potential for the confinement and assembly of a planar cluster of 8 μm magnetic beads. The independent tunability between the soft-confining force and dipolar interactions allows dipole cluster to be reversibly transformed between closely packed, expanded as well as frustrated configurations. This platform enables studies on artificial atoms, cluster impurity, first order transitions associated with nucleation, glass transition due to jamming,
frustration arising from competing interactions, many-body interactions, biomedical devices such as on-chip filter, force probe, or washer, material assembly such as field-tunable photonic crystals, magnetic logic devices, and the trapping of dipolar atom condensates.

(3) An array of 10 μm permalloy disks integrated with microfluidics (Chapter 5) allows on-chip separation of magnetically labeled cells and their encapsulation into droplets. The separation-encapsulation functionality serves as a key module that can be integrated with other on-chip techniques such as single-cell PCR for the analysis of biological signatures of cells at an individual level rather than averaging over bulk properties.

Besides the broad range of useful applications and fundamental studies that stem from the three main aspects of the dissertation mentioned above, I envision several projects as future work that could potentially impact the interdisciplinary fields of micro- and nano-manipulation. They will be discussed in Appendix C.
REFERENCES


Appendix A

MAGNETO-OPTICAL KERR EFFECT (MOKE) IMAGING

Light reflected off of a magnetized material will change its polarization or amplitude depending on the relative orientation between sample magnetization (M) and the direction and polarization of the incident light. This change, to first order in M, is known as the magneto-optical Kerr effect (MOKE)[204–206]. It originates from the coupling between the electric field component of light and the magnetization of the material through spin-orbit coupling. To control the direction and polarization of the incident light on the sample while being able to pick up the MOKE signal, a microscope with schematic shown in Figure A.1 is desired. As can be seen in the figure, by properly blocking light with the aperture stop (AS), the direction of incident light can be tuned, while polarizer P, placed before the sample, defines the polarization. Polarizer A, placed after the sample, determines the polarization of reflected light to be collected by the CCD camera for further image analysis and extraction of the MOKE signal. An actual photo of the microscope setup is shown in Figure A.2.
Figure A.1. Schematic of magneto-optical Kerr effect microscope.
A.1 Shaping the Incident Light

Using a convex lens (L4, the “Bertrand lens”, in Figure A.1) to bring the rear focal plane (RFP) of the objective lens into focus at the CCD camera, one can observe the direction of reflected light and tune AS accordingly: For example, a hole on the left side of AS will result in a bright spot on the right side of the RFP image, corresponding to a cone of light reflected off the sample obliquely towards the right. Due to the sensitivity of MOKE to the polarization of light, non-polarizing beam splitter (BS in Figure A.1) and objective lens are used to avoid unwanted modification to the polarization of light. In ideal situation, a dark cross should appear on the RFP image as shown in Figure A.3a and b.
when the two polarizers (P and A) are crossed (oriented at 90° with respect to each other). The dark cross indicates the region of good extinction, i.e. light incoming from the top, bottom, left, right or normal directions onto the sample will retain the same polarization after passing through the objective lens, whereas light incoming from the top-left, top-right, bottom-left or bottom-right directions will not. A strained objective lens such as that shown in Figure A.3c yields a distorted region of extinction that changes shape as one rotates the objective lens along the optical axis. The direction of incident light (positioning of the hole on AS) should fall in the region of good extinction (the dark cross) to obtain MOKE signal, which is typically 1000 to 100 times weaker than light intensity.

Figure A.3: Image of the rear focal plane of various objective lenses taken while the polarizer (P) and analyzer (A) are cross-polarized.

### A.2 Operating Modes of MOKE

As shown in Figure A.4, various modes of MOKE can be utilized for extracting information on sample magnetization (M) in different directions:

1. **Longitudinal MOKE:** M falls in the sample plane and the plane of incidence (plane defined by the directions of incident and reflected light). Both s-/p-polarized (polarization normal/parallel to the plane of incidence) light with
oblique incidence (offset hole on AS) will acquire a slight rotation to the polarization due to MOKE after reflecting off the magnetized sample, and the direction of rotation depends on the direction of $\mathbf{M}$. In order to pick up this rotation, the polarizer $A$ is oriented slightly off the crossed orientation with respect to $P$, such that the rotation in polarization of reflected light in one direction yields higher intensity on the CCD than that in the other direction.

(2) Transverse MOKE: $\mathbf{M}$ falls in the sample plane but perpendicular to the plane of incidence. Only oblique, $p$-polarized light will acquire an increase or decrease in magnitude due to MOKE, and this change depends on the direction of $\mathbf{M}$. Although polarizer $A$ may not be required in this case to pick up the change in magnitude of the reflected light, placing $A$ parallel to $P$ allows one to pick out signal solely due to the transverse component of $\mathbf{M}$ while ignoring the longitudinal component.

(3) Polar MOKE is utilized to detect out-of-plane sample magnetization. In this mode, incident light is normal to the sample plane (centered hole on AS). As in the longitudinal case, the reflected light will acquire a slight rotation in its polarization due to MOKE, and the direction of rotation depends on the direction of $\mathbf{M}$. Polarizer $A$ is oriented slightly off the crossed orientation with respect to the $P$ to pick up this difference at the CCD.

For detection of arbitrary in-plane magnetizations $\mathbf{M}$, it is best to use longitudinal MOKE with $s$-polarized light or transverse MOKE with $p$-polarized light to obtain contrast of well-defined magnetization components, i.e. no mixing from different modes of MOKE due to the other component of $\mathbf{M}$. 
A.3 Image Processing

Digital processing of the acquired images is required to amplify the weak MOKE signal to an observable extent. This includes subtraction of the pixel intensities between the images taken (averaged over 100 to 1000 frames for enhancement of signal-to-noise ratio) at opposite sample magnetizations and multiplication of the subtracted images. For example, Figure A.5 shows digitally processed MOKE images of a strand of CoFe zigzag wire with pads on the two ends. The contrast shows the magnetization of the zigzag wire after application of a momentary strong field in the vertical direction – the magnetization lies along the long axes of the zigzag wire arms after relaxation. Opposite magnetization is achieved for image subtraction by application and removal of a strong field (several hundreds of Oe) in one vertical direction versus the other.
Figure A.5: Images obtained through the transverse MOKE on a CoFe zigzag wire with contrast set in the horizontal (a) and vertical (b) directions. Black-gray-white corresponds to negative-zero-positive magnetization. The objective lens used is AO 20X 0.5 N.A. as that in Figure A.3a.
Appendix B
Determination of Experimental Parameters through Particle Tracking

Digital tracking of bead positions in fluid not only provides basic information such as bead velocity, but it also offers insights on additional parameters. In the following sections, we will exploit the dynamics of magnetic beads (UMC4F Bangs Laboratories, Inc.) under the influences of bead-surface, bead-bead and bead-pattern interactions to extract useful quantities of the near-wall correction factor, magnetic susceptibility and effective magnetic thickness of the patterns respectively.

B.1 Near-Wall Effect

As discussed in Chapter 2, a bead moving in a viscous medium is subject to a drag force $-\gamma \ddot{r}$ opposing its velocity $\dot{r}$ (Equation (2.7)), where the drag coefficient $\gamma$ given by Equation (2.8) contains a factor $\lambda$ accounting for the increase in drag force due to the bead near a surface. The near-wall factor $\lambda$ can be experimentally determined by tracking the Brownian motion of beads on a surface without the influence of any forces (e.g. no magnetic traps). For example, Brownian motion of the 8 μm beads used in Chapter 4 are tracked to yield the time dependence of their mean square displacements as given in Figure B.1. By fitting the experimental data with $<\Delta r^2> = 4Dt$ (Equation (3.7)) to extract the diffusion constant $D$, the near-wall factor $\lambda$ contained within can be determined from Equation (3.8). We find $\lambda \approx 2.77$ for this type of beads used.
Figure B.1: Mean square displacements of 17 beads (8 μm in diameter, UMC4F Bangslabs) as a function of time. Each bead trajectory is broken into 30 segments of 60-second trajectories for averaging, i.e. total tracking time of 30 min. The experimental data is fitted with a linear function $\langle \Delta r^2 \rangle = 4Dt$.

Figure B.2: Two beads repelling as an out-of-plane external field is turned on. (a) Illustration of the external field $H_{ext}$, the two beads and their induced magnetic moments $m$, and the repulsive dipolar force $F_{dip}$ they experience. (b) Bead separation $r$ as a function of time is plotted for 5 different pairs of beads (black curves). Simulation using bead susceptibility $\chi$ as the fitting parameter is shown as the red curve.
B.2 Bead Susceptibility

Bead susceptibility can be experimentally obtained by tracking the motion of two beads repelling each other on the surface in the presence of an out-of-plane field (Figure B.2a). Since the net field experienced by one bead is \( \mathbf{H} = \mathbf{H}_{\text{ext}} + \mathbf{H}_{\text{dip}} \), the force experienced by the bead only consists of dipolar interaction:

\[
\mathbf{F}(\mathbf{r}) = \frac{1}{2} \mu_0 \chi V \nabla H(\mathbf{r})^2 \approx \mu_0 \chi V \nabla \mathbf{H}_{\text{ext}} \cdot \mathbf{H}_{\text{dip}}(\mathbf{r}) = \mathbf{F}_{\text{dip}}(\mathbf{r}) \quad \text{(B.1)}
\]

where the dipolar field experienced by one of the beads is:

\[
\mathbf{H}_{\text{dip}}(\mathbf{r}) = \frac{1}{4\pi} \frac{3(\mathbf{r} - \mathbf{r}')[(\mathbf{r} - \mathbf{r}') \cdot \mathbf{m}] - \mathbf{m}[(\mathbf{r} - \mathbf{r}') \cdot (\mathbf{r} - \mathbf{r}')]}{|\mathbf{r} - \mathbf{r}'|^5} \quad \text{(B.2)}
\]

and the moment \( \mathbf{m} \) induced in that bead can be estimated as \( \mathbf{m} \approx \chi V \mathbf{H}_{\text{ext}} \). Therefore, given the external field, position and size of the beads, the dipolar force involves only the square of bead susceptibility, \( \chi^2 \).

As the motion of bead experiencing a force \( \mathbf{F}_{\text{dip}} \) in a viscous media can be described by Equation (2.7) (ignoring the fluctuation term for large bead radius and large \( \mathbf{F}_{\text{dip}} \)) given the near-wall-corrected diffusion constant obtained in the section above, one can simulate the motion of two beads repelling when an external field is turned on. By fitting the simulated curve of bead separation \( (r) \) as a function of time to that obtained in the experiment through tracking bead positions (Figure B.2), one can extract bead susceptibility \( \chi \). We find \( \chi \approx 0.051 \) for the 8.18 \( \mu \)m bead used in Chapter 4. For the 7.9 \( \mu \)m magnetic beads (UMC4N Bangs Laboratories, Inc.) used in Chapter 5, one can approximate their susceptibility to be \( \chi \sim 0.1 \) since the magnetic content is roughly 2 times higher than that of the 8.18 \( \mu \)m bead (4% to 2.4%).
B.3 Effective Thickness of Magnetic Patterns

Another parameter obtained through bead tracking is the effective thickness of the deposited magnetic patterns. In this case, the motion of beads jumping away from a magnetic pattern triggered by the external field offers one some insight on the properties of the magnetic pattern. As bead-bead interaction involves $\chi^2$ as mentioned in the section above, bead-pattern interaction involves the factor $\chi M_{\text{pattern}} d$ ($M_{\text{pattern}}$ the magnetization and $d$ the thickness of the pattern), i.e. the force experienced by one bead and a pattern is:

$$F(r) = \frac{1}{2} \mu_0 \chi V \nabla H(r)^2 \approx \mu_0 \chi V \nabla H_{\text{ext}} \cdot H_{\text{pattern}}(r) = F_{\text{pattern}}(r) \quad \text{(B.3)}$$

where $H_{\text{pattern}}(r)$ is proportional to $M_{\text{pattern}} d$. Knowing the near-wall-corrected drag coefficient and bead susceptibility discussed in the above sections as well as the external field, pattern geometry and magnetization (e.g. $M_{\text{pattern}} = 8.6 \times 10^5$ A/m for permalloy), one can simulate the motion of the bead jumping away from a magnetic pattern with Equation (2.7) (ignoring the fluctuation term due to the large bead radius and large $F_{\text{pattern}}$) as the external field changes (Figure B.3a and b). Using pattern thickness $d$ as the fitting parameter to simulate the distance traversed by the bead as a function of time (Figure B.3c), we find $d = 23.7$ nm for the magnetic disk pattern used in Chapter 4, which is 52% of the thickness measured by the atomic force microscope (46 nm). This is due possibly to the oxidation in deposited magnetic patterns causing a reduction in the effective magnetic thickness.
Figure B.3: Bead jumping away from a magnetic pattern as the external field is switched. (a) The bead is originally trapped on the edge of a magnetic pattern under an external field of $H_{\text{ext}} = (50,0,100)$ Oe. (b) At time = 0, the external field is switched to $H_{\text{ext}} = (50,0,-100)$ Oe, resulting in the bead jumping away from the edge of the pattern. (c) Bead distance $r$ from its original position is plotted as a function of time for the experiment (black curves) and simulation (red curve) using pattern thickness $d$ as the fitting parameter.
Appendix C

OUTLOOK

C.1 Potential Tweezers Platforms to Offer Individual Control

An inherent limitation in the work presented in this dissertation is the degree of individual control on object motions. For example, the mobile magnetic trap array presented in Chapter 5 is only capable of moving all the magnetic objects in the same direction since the external magnetic field generated by the setup shown in Figure 2.2b is uniform everywhere in solution. It would thus be desirable to investigate platforms with the ability to create arbitrary energy landscape for the manipulation of micro- to nanoscale objects at an individual level. Two possible candidates are proposed in the following.

C.1.1 CCD Tweezers

Charge-coupled devices (CCD) transfer light-induced charges across the semiconductor chip for reading out the spatial profile of light intensity as voltages. With some modifications on the CCD, it could serve as a platform for the manipulation of individual dielectric objects in solution. Such modification involves reversing the usual functionality of a CCD: Generate a desired spatial distribution of charges on the semiconductor chip by transferring voltage-induced charges across the platform with reversed clocking. The distribution of charges generates desired electric potential landscape for the trapping of dielectric objects at specific locations. Since the frame rate of CCDs are commonly above 10 fps, the shifting of the charge distribution between frames can be faster than what
micrometer-scaled dielectric objects can respond to, allowing the objects to react to the electric potential landscapes “frame by frame”. With a suitable feedback loop of object positions on the resulting trapping landscapes, control of individual object motion can be as simple as a drag-and-drop of a mouse click.

C.1.2 Magnetic Memory Tweezers

This proposal is based on similar concept as above. By modifying the domain pattern on the magnetic film with the existing write mechanism of a hard disk drive, arbitrary magnetic potential landscape can be generated to trap paramagnetic objects such as magnetic beads at desired locations. Manipulation is achieved by refreshing the energy landscape (magnetic memory) frame by frame as in the CCD discussed above. This scheme, however, suffers from the drawback of the need for moving mechanical components for writing the memory. Magnetic shift register could be a possible solution to eliminate the electromechanical needs, but would, at the current stage, require large current densities or magnetic fields for shifting the domains.

C.2 Drafting behind a Rolling Bead: Label-Free Magnetic Manipulation

Another drawback in typical magnetic-field-based manipulation schemes is the requirement of magnetic labeling if the object of interest is non-magnetic. However, label-free magnetic manipulation is still possible with the help of ferrofluids[62] or by pushing nonmagnetic objects such as cells[64] through magnetic beads without chemical attachments. Though less intuitive, a rolling magnetic bead can also pull without touching a cell that trails behind[207]. It may be worth investigation through fluid dynamics the non-contact hydrodynamic pulling force provided by the rolling bead and its relation to the “drafting effect” in aerodynamics – A technique used by bicycle and car racers to reduce drag force by trailing behind others.
Figure C.1: An artistic rendition of the portable 3D magnetic field platform. (a) The 4 wire-wrapped C-magnets and a sample (shown as a blue square chip) placed at the center on a glass slide. (b) Cross-sectional view of the cased platform. (c) The platform packaged into a box with sample insertion slots, microscope observation ports (top and bottom) and power/data ports.

C.3 Portable 3D Magnetic Field Platform

As shown in Figure 2.2b and c, the external field is generated by a platform of electromagnets occupying roughly 23 cm × 23 cm of space, which is supported by three bulky and heavy power supplies interfaced with the computer through expensive data acquisition card and developing software. Such a setup could be unfriendly for personal use – an ultimate goal of chip-based magnetic tweezers is its integration into point-of-care medical devices that is portable and can be operated without complex equipment.

It is possible to accommodate the magnetic field platform, power supplies and interfaces all onto a portable device that is compatible with typical personal computers. Miniaturization of the electromagnets or coil can be achieved by shaping magnetic shielding materials such as μ-metal (a soft-magnetic material with low coercivity and relative permeability as high as $10^5$) into “C” shapes and wrapping thin enameled wire around it such that relatively strong magnetic field can be generated between the tips of these C-magnets with weak currents. As shown in Figure C.1a, instead of 3 sets of magnets along the $x$, $y$, and $z$ directions, a set of 4 C-magnets that apply fields along, e.g., (1,1,1), (-1,1,1), (-1,-1,1) and (1,-1,1) directions would allow open space for observation
on the sample from the \(+z\) or \(-z\) directions as well as sample insertion from the side. The currents sent into the electromagnets are programed through integrated logic circuits and amplified through operational amplifiers within the device, eliminating the need for power supplies and data acquisition cards. With properly designed driver and software, the resulting portable device should be as simple as a box, as shown in Figure C.1b and c, of dimensions less than $10 \times 10 \times 5$ cm$^3$ (width $\times$ length $\times$ height) that requires only power and data connections such as a USB port.