KINEMATIC STUDY OF MOTILE MICROALGAE UNDER THE INFLUENCE OF LOW GRADIENT MAGNETIC FIELD

NG WEI MING

UNIVERSITI SAINS MALAYSIA 2018

KINEMATIC STUDY OF MOTILE MICROALGAE UNDER THE INFLUENCE OF LOW GRADIENT MAGNETIC FIELD

by

NG WEI MING

Thesis submitted in fulfilment of the requirements for the degree of Master of Science

ACKNOWLEDGEMENT

First of all, I would like to express my heartiest gratitude to my main supervisor, Professor Dr. Lim Jit Kang, who has great intelligence and attitude toward science. He continually and convincingly conveyed an enthusiasm and passion in regard to research, and an excitement in regard to teaching. I am honoured for the opportunity to work under his supervision as he keeps pushing me beyond my limit with the stress and motivation for a better me. Thanks for his great effort, consistent guidance and constructive advices throughout the project until the completion of this thesis.

Secondly, I would like to thank my co-advisor Associate Professor Dr. Derek Chan Juinn Chieh for giving me a chance to learn the microbiological culture techniques from him. His passion toward cell culture has driven me to develop my own skills and treat the cultivation of the microbes seriously as all of them are the smallest building blocks of life. Thanks for his willingness to share his first-hand experience on cultivation techniques.

Next, I would like to thank to my family members who supported me financially and mentally. A special gratitude to my beloved parents for their endless love, support and prays that motivate me to complete my research project. Special appreciation must be expressed to Associate Professor Dr. Low Siew Chun, who has been my academic advisor since my undergraduate study. Her great patience, unconditional guidance and hearty advice have led me gone through every obstacle along my way. Thanks for both spiritual and financial support from her.

Sincere thanks to all technicians and staffs for their technical assistance and kindness cooperation during my lab works. Special thanks to administrative staffs for their helps when dealing with the research related documents. Here, I would like to

gratefully acknowledge Universiti Sains Malaysia for providing me financial support

through the Fellowship scheme throughout my master study.

Last but not least, I would like to thank all my friends and colleagues who have

gone through ups and downs in my study life. I would like to convey my gratitude to

my seniors Swee Pin, Hui Xin and Sim Siong for their guidance and help whenever I

encounter problems in my research. Thanks to my colleagues Foo Kean, Wai Sing and

Sean who work close to me and have been a source of assistance in my research.

Thanks to my friends who always care about me and ask me for the date I graduate.

Without them, my study life would not be so interesting and I will cherish all the great

memories we created. Thanks everyone who have involved in this process toward its

completion in reality.

Sincerely, Wei Ming

iii

TABLE OF CONTENTS

| | | | Page |
|------|--|--|------|
| ACE | KNOWL | EDGEMENT | ii |
| TAB | BLE OF | CONTENTS | iv |
| LIST | Γ OF TA | ABLES | vii |
| LIST | r of fi | GURES | viii |
| LIST | Γ OF AF | BBREVIATIONS | xii |
| LIST | Γ OF SY | MBOLS | xiv |
| ABS | TRAK | | xvii |
| ABS | TRACT | | xix |
| CHA | APTER (| ONE: INTRODUCTION | |
| 1.1 | | ty and biohybrid microbot | 1 |
| 1.2 | | em statement | 3 |
| 1.3 | | rch objectives | 5 |
| 1.4 | | rch scope | 5 |
| 1.5 | | ization of thesis | 6 |
| CHA | APTER T | ΓWO: LITERATURE REVIEW | |
| 2.1 | Low F | Reynolds number swimming of microorganism | 7 |
| 2.2 | Microbots at low Reynolds number environment | | 9 |
| | 2.2.1 | Challenges associated with microbot | 10 |
| | 2.2.2 | Biohybrid microbots | 11 |
| | 2.2.3 | Construction of biohybrid microbots and their potential applications | 12 |
| 2.3 | Motion control of biohybrid microbots | | 21 |
| | 2.3.1 | Chemotactic and chemical control | 21 |
| | 2.3.2 | Phototactic and optical control | 24 |
| | 2.3.3 | Electrotactic and electric control | 26 |

| | 2.3.4 | Magnetotactic and magnetic control | 28 |
|-----|---------------------------------------|---|----|
| | 2.3.5 | Other control methods | 31 |
| 2.4 | Magnetotactic microbot system | | 35 |
| | 2.4.1 | Optical microscopy for motion tracking | 37 |
| | 2.4.2 | Motion analysis of microbot | 38 |
| | 2.4.3 | Interpretation of Reynolds number | 39 |
| | 2.4.4 | Force analysis | 39 |
| | | | |
| CHA | PTER 7 | THREE: MATERIALS AND METHODS | |
| 3.1 | Materi | als and chemical lists | 41 |
| 3.2 | Flow | of experiments | 43 |
| 3.3 | Synthesis of particles | | 44 |
| | 3.3.1 | Synthesis of iron oxide nanoparticles | 44 |
| | 3.3.2 | Synthesis of magnetic microbeads | 45 |
| 3.4 | Charac | cterization of magnetic microbeads | 46 |
| | 3.4.1 | Electrophoretic mobility measurement | 47 |
| | 3.4.2 | Transmission Electron Microscope | 47 |
| | 3.4.3 | Atomic Absorption Spectrometery | 48 |
| | 3.4.4 | Vibrating Sample Magnetometer | 48 |
| 3.5 | Cultiv | ation of Chlamydomonas reinhartii | 49 |
| | 3.5.1 | Bristol's solution composition | 49 |
| | 3.5.2 | Cell concentration measurement | 51 |
| 3.6 | Assem | ably of microbot | 51 |
| 3.7 | Microscopy study of microbot's motion | | 52 |
| | 3.7.1 | Artificial magnetotaxis study of the microbot | 52 |

| CHA | PTER | OUR: RESULTS AND DISCUSSION | |
|------|---|---|----|
| 4.1 | Synthesis of magnetic microbeads and assembly of microbot | | |
| | 4.1.1 | Synthesis of iron oxide nanoparticles | 54 |
| | 4.1.2 | Synthesis of magnetic microbeads | 55 |
| | 4.1.3 | Characterization of magnetic microbeads | 57 |
| | 4.1.4 | Assembly of microbot | 58 |
| 4.2 | Micros | scopy study of microbot | 62 |
| 4.3 | Motion | n analysis of microbot in the absence of magnetic field | 65 |
| | 4.3.1 | Motility study of freely swimming <i>Chlamydomonas</i> reinhardtii | 65 |
| | 4.3.2 | Effect of magnetic microbead attachment on the motility of microbot | 68 |
| 4.4 | Motion | n analysis of microbot under a low gradient magnetic field | 73 |
| | 4.4.1 | Magnetic field strength and gradient | 73 |
| | 4.4.2 | Artificial magnetotaxis study of microbot | 77 |
| | | | |
| CHA | PTER I | FIVE: CONCLUSION AND RECOMMENDATION | |
| 5.1 | Conclu | usion | 90 |
| 5.2 | Recon | nmendation | 93 |
| | | | |
| REF | ERENC | ES | 94 |
| | | | |
| APP | ENDIC | ES | |
| Appe | endix A: | Characterization of magnetic microbeads | |
| Appe | endix B: | Flow past a spheroid moving parallel to its major axis | |
| Appe | endix C: | Derivation of magnetic field gradient equation | |
| Appe | endix D: | Calculation of mass of microbot | |
| Appe | endix E: | Calibration curve for cell concentration | |

LIST OF TABLES

| | | Page |
|-----------|---|------|
| Table 2.1 | Construction of microbots for microscale applications. | 19 |
| Table 2.2 | Comparison between chemical, optical, electrical and magnetic control methods for bio-hybrid microbots. | 29 |
| Table 2.3 | Motion control of microbots. | 33 |
| Table 2.4 | Performances of different magnetotactic microbots under the influence of magnetic fields. | 36 |
| Table 3.1 | List of chemicals used. | 41 |
| Table 3.2 | List of chemicals used for Bristol's solution preparation. | 49 |
| Table 3.3 | List of chemicals required for A5 Trace metal solution preparation. | 50 |
| Table 4.1 | Electrophoretic mobility measurement of magnetic microbeads at each stages of synthesis. | 56 |
| Table 4.2 | Summarized FFT analysis results (frequency) and angular velocities for all microbots. | 69 |
| Table 4.3 | Regression parameters of $F_{\text{swim},\parallel}$ as a function of distance from tip and R^2 value of fitting. | 82 |
| Table 4.4 | ANOVA for regression model of $F_{\text{swim},\parallel}$ for microbot-2 μ m and microbot-4.5 μ m. | 82 |

LIST OF FIGURES

| | | Page |
|------------|--|------|
| Figure 2.1 | Sketches of microswimmers. a) <i>Caulobacter crescentus</i> b) <i>Rhodobacter sphaeroides</i> c) <i>Escherichia coli</i> d) Mammalian sperm cell e) <i>Chlamydomonas reinhardtii</i> f) <i>Paramecium</i> . | 9 |
| Figure 2.2 | Schematic of the selective attachment and on-demand release of PS bead-carrying E. coli from patterned surfaces using either imidazole or EDTA. | 15 |
| Figure 2.3 | Microbot used for treatment and diagnosis of tumor. Carbodiimide binding of nanoliposome to the surface of magnetotactic bacteria. | 16 |
| Figure 2.4 | Assisted delivery of an immotile sperm to the oocyte for fertilization by a remotely controlled magnetic helix. | 17 |
| Figure 2.5 | Time-lapse images showing the motion of a PS bead propelled by <i>S. marcescens</i> at interval of 0.6 s for 6 s: a) The PS bead is propelled by the bacteria before copper ions are added. b) The PS bead stops moving almost instantaneously after copper ions are added. c) The PS bead resumes its motion after EDTA is added. | 23 |
| Figure 2.6 | Steering of <i>E. elegans</i> cell along arbitrarily set trajectories such as (a.1)-(a.8) zigzag and (b.1)-(b.7) triangle by using positive phototaxis. The red circle in each frame indicates and traces the position of the cell, and the red dotted line illustrates the movement trajectory of the cell. | 26 |
| Figure 2.7 | Motion of <i>S. marcescens</i> -driven microstructure a) Directional motion control using DC electric field and b) on/off motion control of microstructure using AC electric field. | 27 |
| Figure 2.8 | Microorganism that respond to magnetic field. a) A curved, rod-shaped magnetotactic bacteria with internal chains of magnetosomes. b) Microscopy images of <i>T. pyriformis</i> with the scale bars shown for 10 μ m (b.1) normal condition, (b.2) after ingestion of IONPs and (b.3) after magnetization of ingested IONPs. | 31 |

| Figure 3.1 | Schematic flow of the overall experimental work. | 43 |
|------------|---|----|
| Figure 3.2 | Schematic diagram showing the major steps involved in layer-by-layer assembly of magnetic microbead by the means of electrostatic interaction between oppositely charged species. | 44 |
| Figure 3.3 | Glass slide setup used in the microscopy study. | 53 |
| Figure 4.1 | TEM micrograph of IONPs synthesized via co-precipitation method. | 55 |
| Figure 4.2 | TEM micrographs of magnetic microbeads at initial and final stages of synthesis. a) 2 μm and b) 4.5 μm aminefunctionalized polystyrene beads, c) 2 μm and d) 4.5 μm magnetic microbeads after decoration of iron-oxide nanoparticles with layer of PDDA as the cationic outermost shell. | 57 |
| Figure 4.3 | Magnetization curve for IONPs synthesized via coprecipitation method. | 58 |
| Figure 4.4 | Chlamydomonas reinhardtii bound with a magnetic microbead. a) Pictorial representation of electrostatic interaction between the cell and microbead, b) molecular structure of 4-hydroxyproline, c) molecular structure of PDDA, and, d) optical micrograph showing a 2 µm magnetic microbead was attached to a microalgae. | 59 |
| Figure 4.5 | Time lapse images showing the motion of microbot-2µm and microbot-4.5µm before and after magnetic field was introduced. The red arrows and arcs have been added to each frame to indicate the position of the microbot and magnetic source respectively. It is noted that the position of magnetic source is marked according to the direction of field gradient and does not represent the exact position of the mu-metal tip. | 63 |

| Figure 4.6 | Complete trajectories of a) microbot-2µm, and b) microbot-4.5µm for an interval of 5 s. The sector of circle drawn in red dotted line shows the position of mu-metal tip in the dispersion of microbot. The solid dot indicates the final position of the microbot where its location can still be determined precisely. Each trajectory consists of two parts: solid line represents the motion path of microbot in the absence of magnetic field, and dotted line represents its motion path under the influence of low gradient magnetic field when the mu-metal tip is magnetized by a NdFeB magnet. Refer to section 4.3.2 and 4.4.2 for further analysis on these trajectories. | 64 |
|-------------|---|----|
| Figure 4.7 | Self-swimming microalgae. a) Trajectories of <i>Chlamydomonas reinhardtii</i> over an interval of 1 s. The solid dots indicate the final position of the cells. b) Swimming speed distribution of the cells. | 66 |
| Figure 4.8 | Individual motion paths of the microbot $1-8$ (a-h) in the absence of magnetic field. Note that x -axis and y -axis are scaled unequally. | 68 |
| Figure 4.9 | Illustration for the approximation of microbot as a spheroid moving parallel to its major axis. a and b are the semimajor and semiminor axis lengths respectively. | 71 |
| Figure 4.10 | Indication of v/f on the helical trajectory of a microbot. | 73 |
| Figure 4.11 | Magnetized mu-metal tips to produce highly localized magnetic field within the confined space. Due to the in-plane nature of this arrangement, the magnetic field generated is more focus and concentrated within the fluid layer. | 74 |
| Figure 4.12 | Magnetic field strength generated by the magnetized mumetal tip. | 76 |
| Figure 4.13 | Magnetic field gradient used in the magnetotaxis study. | 76 |

78 Figure 4.14 Microbot in the presence of low gradient magnetic field. a) Resolution of velocity into v_{\parallel} and v_{\perp} . b) Free-body diagram of the microbot visualizes the relationship of all forces acting on the microbot which dictates its motion under the influence of magnetic field. It is noted that the diagram is drawn for illustration and the vector length is not drawn according to the magnitude of the force. Figure 4.15 Scatter plot of all the magnetophoretic and resolved parallel 80 swimming forces for a) microbot-2 µm, and b) microbot-4.5 µm under the influence of low gradient magnetic field. The solid line represents the regression for the spatial changes of $F_{\text{swim.}\parallel}$. 83 Figure 4.16 Linearized logarithm regression of $F_{\text{swim},\parallel}$ for a) microbot-2 μm, and b) microbot-4.5 μm under the influence of low gradient magnetic field. The dotted lines indicate the 95% prediction interval. Figure 4.17 85 Scatter plot of v_{\perp} and v_{\parallel} for a) microbot-2 μ m, and b) microbot-4.5 µm under the influence of low gradient magnetic field. The comparisons between the experimentally measured data (v_{\parallel} represented by marker) and their model calculation (solid line) are presented in each figure. Figure 4.18 Scatter plot of acceleration a for a) microbot-2 μ m, and b) 87 microbot-4.5 µm in its motion direction. The comparisons between the experimentally measured data (a represented by marker) and their model calculation (solid line) are presented in each figure. Figure 4.19 Trajectories of all microbots and the acceleration radii under 88 the same plot. The red and blue trajectories represent the motion path traveled by the microbots carrying magnetic microbead of 2.0 µm and 4.5 µm respectively.

LIST OF ABBREVIATIONS

AAS Atomic Absorption Spectrometry

AC Alternating current

BSA Bovine serum albumin

CaCl₂ 2H₂O Calcium chloride dihydrate

Co(NO₃)₂ 6H₂O Cobalt (II) nitrate hexahydrate

CuSO₄ 5H₂O Copper (II) sulphate pentahydrate

DC Direct current

dH₂O Distilled water

EDTA-Na₂ Disodium ethylenediaminetetraacetic acid

Fe Iron

FeCl₂ 4H₂O Iron (II) chloride tetrahydrate

FeCl₃ Iron (III) chloride

FeCl₃ 6H₂O Iron (III) chloride hexahydrate

Fe₃O₄ Magnetite

FFT Fast Fourier Transform

HA Hyaluronic acid

HCl Hydrochloric acid

HNO₃ Nitric acid

H₃BO₃ Boric acid

IONPs Iron oxide nanoparticles

I₂ Iodine

KH₂PO₄ Potassium dihydrogen phosphate

K₂HPO₄ Dipotassium hydrogen phosphate

KI Potassium iodide

LEDs Light-emitting diodes

MgSO₄ 7H₂O Magnesium sulphate heptahydrate

MnCl₂ 4H2O Manganese (II) chloride tetrahydrate

NaCl Sodium chloride

Na₂MoO₄ 2H₂O Sodium molybdate dihydrate

NaNO₃ Sodium nitrate

NaOH Sodium hydroxide

NdFeB Neodymium boron ferrite

Ni Nickel

NiSO₄ Nickel (II) sulphate

PDA Polydopamine

PDDA Poly(diallyldimethylammonium chloride)

PDMS Polydimethylsiloxane

PLL Poly-L-lysine

PNIPAM Poly(N-isopropylacrylamide)

PPY Polypyrrole

PS Polystyrene

TEM Transmission Electron Microscope

Ti Titanium

UV Ultraviolet

VSM Vibrating Sample Magnetometer

ZnSO₄ 7H₂O Zinc sulphate heptahydrate

LIST OF SYMBOLS

a Semimajor axis length

a(r) Acceleration as a function of r

b Semiminor axis length

B Magnetic field strength

 B_r Remanence field strength

 $\frac{dB}{dr}$ Magnetic field gradient with respect to r

 $\frac{dr}{dt}$ Rate of change of distance from tip surface

 $\frac{dv}{dt}$ Rate of change of velocity

 $\frac{d^2B}{dr^2}$ Derivative of magnetic field gradient with respect to r

f Frequency

f_{inertial} Inertial force

 $f_{\rm viscous}$ Viscous force

F Applied force

 $F_{\rm b}$ Buoyant force

 $F_{\rm drag}$ Viscous drag force

 $F_{\text{drag},\parallel}$ Component of viscous drag force parallel to the reference axis

 $F_{\rm drag,\perp}$ Component of viscous drag force perpendicular to the reference

axis

 $F_{\rm mag}$ Magnetophoretic force

 F_{swim} Swimming force

 $F_{\text{swim.}\parallel}$ Component of swimming force parallel to the reference axis

 $F_{\text{swim},\perp}$ Component of swimming force perpendicular to the reference

axis

 $F_{\rm thrust}$ Thrust force

g Gravitational acceleration

H Height of magnet

K Geometric correction factor

1 Longitudinal length of synthetic cargo

ℓ Characteristic length

L Length of magnet

 $m_{\rm m}$ Mass of microbot

r Distance from tip surface

Re Reynolds number

R Radius

 $R_{\rm c}$ Radius of microalgal cell

t Time

v Velocity

 v_{\parallel} Component of velocity parallel to the reference axis

 v_{\perp} Component of velocity perpendicular to the reference axis

 $v_{\rm c}$ Velocity of microalgal cell

 $v_{\rm m}$ Velocity of microbot

V Volume

W Width of magnet

 η Dynamic viscosity of fluid

μ Magnetic moment

 ρ Density of object

 ρ_f Density of fluid

 $au_{
m mag}$ Magnetic torque

 ω Angular velocity

 ∇B Magnetic field gradient

Ø Diameter

-COOH Carboxyl functional group

-OH Hydroxyl functional group

KAJIAN KINEMATIK TERHADAP MIKROALGA MOTIL DI BAWAH PENGARUH MEDAN MAGNET BERKECERUNAN RENDAH

ABSTRAK

Mikrosfera magnet, yang terdiri daripada teras polistirena (PS), nanopartikel oksida besi (IONPs) dan polielektrolit kationik, disintesis melalui teknik penyusunan secara berlapis-lapis. IONPs disintesis melalui kaedah pemendakan bersama. Pengendapan IONPs diikuti dengan polielektrolik pada permukaan teras PS dikenal pasti melalui pemeriksaan kegerakan elektroforesis. Morfologi teras-petala mikrosfera magnet dibuktikan melalui mikrograf mikroskopi transmisi elektron manakala jisim magnet dan sifat magnetnya dikaji dengan menggunakan spektroskopi serapan atom dan magnetometer sampel bergetar. Mikro-robot magnetik buatan dibentuk dengan mengikatkan mikrosfera magnet dengan mikroalga melalui saling tindak elektrostatik. Tingkah laku kinematik mikro-robot yang membawa mikrosfera magnet dengan diameter 2 µm dan 4.5 µm telah dikaji di bawah pengaruh dan tanpa pengaruh medan magnet berkecerunan rendah ($\nabla B < 100 \text{ T/m}$). Dalam keadaan tanpa pengaruh medan magnet, mikro-robot bergerak secara heliks akibat daripada salah jajaran antara daya tujah dan paksi simetri mikrosfera. Mikro-robot yang diikat dengan mikrosfera magnet yang bersaiz besar bergerak dengan halaju translasi yang tinggi tetapi berputar perlahan pada paksi putarannya. Keseimbangan antara daya kelikatan bendalir dengan daya tujah mikro-robot menyebabkan mikro-robot bergerak secara rawak dengan halaju terminal. Sebaliknya, di bawah pengaruh medan magnet berkecerunan rendah, kawalan terarah mikro-robot tercapai berdasarkan prinsip-prinsip berikut: (1) daya magnetoforesis tidak berperanan untuk mempengaruhi pergerakan seranjang mikrorobot, dan, (2) pergerakan selari mikro-robot bergantung pada kemotilan mikro-robot

and magnetoforesis, di mana kesan koperatif ini dipengaruhi oleh jarak pemisahan antara mikro-robot dengan magnet. Apabila mikro-robot mendekati magnet, penahanan daya magnetoforesis terhadap kemotilan mikro-robot diri membawa kepada pergerakan magnetotaksis positif mikro-robot ke arah sumber medan magnet. Penggunaan mikrosfera yang mempunyai jisim magnet yang tinggi boleh meningkatkan pecutan mikro-robot dan memperluas jejari pecutan. Keputusan ini menandakan kawalan magnetotaktik terhadap mikro-robot dalam medan magnet dapat dicapai dengan memanipulasikan jisim magnetnya.

KINEMATIC STUDY OF MOTILE MICROALGAE UNDER THE INFLUENCE OF LOW GRADIENT MAGNETIC FIELD

ABSTRACT

Magnetic microbead composed of a polystyrene (PS) core, iron oxide nanoparticles (IONPs) and cationic polyelectrolyte, was prepared via layer-by-layer assembly. The IONPs were synthesized by co-precipitation method. The successful deposition of IONPs followed by polyelectrolyte onto the PS bead was monitored with electrophoretic mobility measurement. The core-shell morphology of the magnetic microbead was confirmed by transmission electron microscopy technique, and its magnetic mass and magnetic property was determined by using atomic absorption spectroscopy and vibrating sample magnetometer respectively. An artificial magnetotactic microbot was created by attaching a magnetic microbead onto a microalgal cell by the means of electrostatic interaction. The kinematic behaviors of the microbots carrying magnetic microbeads of two different sizes, with diameter of 2 μm and 4.5 μm, in the absence and the presence of low gradient magnetic field $(\nabla B < 100 \text{ T/m})$ were characterized. In the absence of magnetic field, the microbot exhibited a helical motion as a result of the misalignment between its thrust force and the symmetry axis after the attachment. The microbot bound with a larger magnetic microbead moved with higher translational velocity but rotated slower about its axis of rotation. The viscous force was balanced by the thrust force of the microbot, resulting in a randomized swimming behavior of the microbot at its terminal velocity. Meanwhile, under the influence of a low gradient magnetic field, the directional control of the microbot was achieved based on following the principles: (1) magnetophoretic force was insignificant on influencing its perpendicular motion, and, (2) its parallel motion was dependent on both self-swimming and magnetophoresis, in which this cooperative effect was a function of separation distance from the magnet. As the microbot approached the magnet, the magnetophoretic force suppressed its self-swimming behavior, leading to a positive magnetotaxis of the microbot toward the source of magnetic field. The use of a high magnetic mass of microbead enhanced the acceleration of the microbot and expanded the acceleration radius, suggesting that the spatial magnetotactic control of microbot in the magnetic field can be achieved by varying its magnetic mass.

CHAPTER ONE

INTRODUCTION

1.1 Motility and biohybrid microbot

Motility is the ability of an organism to exhibit motion and to perform mechanical work using its metabolic energy (Allen, 1981). Swimming organisms range in sizes from a few micrometres as motile microorganism up to several metres as a large marine animal. However, the physics governing swimming at the micrometer length scale is completely different from the physics of swimming at the macroscopic scale (Eric and Thomas, 2009). The underlying physics are dictated by the ratio of the inertial forces to the viscous forces, which is represented by a dimensionless quantity known as Reynolds number (Chisholm et al., 2016). The fundamental differences between motion in microscale and macroscale were discussed by Edward Mills Purcell, a Nobel Laureate in Physics in his famous lecture "Life at low Reynolds number" in 1977 (Purcell, 1977). Microorganisms use cilia or flagella to swim at small characteristic length scale in the low Reynolds number regime, where viscous forces dominate inertial forces. The specific beating pattern of these appendages creates a time-irreversible deformation of the appendages for cell propulsion which later contribute to its translational (and, to some extent its rotational) motion.

The recent decades have witnessed great progress in the realization of various miniature mobile robots for potential applications in biomedicine, bioengineering and lab-on-a-chip devices. However, the key challenges in the further miniaturization of mobile robots down to micrometer scale are (1) the miniaturization of the on-board actuators and (2) power sources for the microrobotic systems (Behkam and Sitti, 2007). The capability of the highly motile microorganism to swim in low Reynolds number

environment proposes that they could be a promising solution to the aforementioned challenges faced especially in overcoming miniaturization issue. In this regard, various motile microorganisms (microswimmers) such as bacteria (Akin et al., 2007; Sahari et al., 2012; Behkam and Sitti, 2008; Fernandes et al., 2011; Arabagi et al., 2011), algae (Weibel et al., 2005) or motile sperm cell (Magdanz et al., 2013) combined with synthetic functional materials for the assembly of biohybrid microbot have been studied. This approach exploits the biological cells as an efficient on-board power source for propulsion of the biohybrid microbot because they can harvest chemical energy from the surroundings and efficiently convert the chemical energy into mechanical work, provided that there are sufficient nutrient present in the working environment (Carlsen and Sitti, 2014).

Besides, biological cells not only exhibit high motility but show huge potential to serve as on-board sensors due to their intrinsic and versatile sensing abilities (Zhuang et al., 2015). Different motion control strategies have been developed, from the cell's sensory and behavioral response to external stimuli, in order to utilize the swimming locomotion for microscale cargo transport and delivery by microbots. These control strategies include chemotaxis (Kim et al., 2012a; Zhuang and Sitti, 2016; Park et al., 2014; Uthaman et al., 2016), pH-taxis (Zhuang et al., 2015), magnetotaxis (Ma et al., 2012; Martel et al., 2006), phototaxis (Steager et al., 2007; Weibel et al., 2005), and electrotaxis (Steager et al., 2011). Among these strategies, magnetotaxis offers an attractive advantage over others in which it can be used in both homogeneous and heterogeneous environments as the magnetic fields can be generated remotely (Carlsen and Sitti, 2014). Furthermore, this method is less invasive and does not interfere with chemical and biological activities of the microorganism.

1.2 Problem statement

In general, magnetotaxis of microbots can be achieved by the integration of magnetically responsive biological components into nonbiological components, or vice versa. The primary approach is to use biological cells that are responsive to magnetic fields. Such biological cells can be either a magnetotactic bacteria (Ma et al., 2012; Martel et al., 2006) that possesses naturally occurring intracellular magnetosomes, or an artificial magnetotactic cell (Kim et al., 2010) with ingested magnetic nanoparticles. However, these approaches are either dependent on cells with magnetoception capability or cells that can remain viable after the ingestion of magnetic nanoparticles, limiting the type of cells that can be utilized (Carlsen et al., 2014).

For the latter approach which is also the most popular way to achieve magnetotaxis, it incorporates magnetic materials onto nonmagnetic biological cells, creating artificial magnetotaxis for the motion control. Magdanz et al. (2013) presented the development of a microbiorobot comprising a magnetic tube driven by a spermatozoid. In other work, Carlsen et al. (2014) described the directional magnetic steering control of a superparamagnetic bead propelled by a swarm of rod-shaped gram-negative bacteria, *Serratia marcescens*. From all these studies, the reported cell velocities driven by micron sized magnetic particle were surprisingly low and were approaching the magnetophoretic velocity (10 μ m/s) of an individual iron oxide nanoparticle with diameter at ~ 35 nm (more than 100 times smaller than those microbead used) reported by Lim et al. (2011). There is a huge mismatch between the theoretical predictions of magnetophoretic velocity with recorded velocity. In most likelihood, the thrust force associated with the self-swimming has randomized or even suppressed the migration of entire microbead-microswimmer system under artificial