Control of Magnetotactic Bacterium in a Micro-Fabricated Maze

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Abstract—We demonstrate the closed-loop control of a magnetotactic bacterium (MTB), i.e., Magnetospirillum magnetotacticum, within a micro-fabricated maze using a magnetic-based manipulation system. The effect of the channel wall on the motion of the MTB is experimentally analyzed. This analysis is done by comparing the characteristics of the transient- and steady-states of the controlled MTB inside and outside a micro-fabricated maze. In this analysis, the magnetic dipole moment of our MTB is characterized using a motile technique (the u-turn technique), then used in the realization of a closed-loop control system. This control system allows the MTB to reach reference positions within a micro-fabricated maze with a channel width of 10 µm, at a velocity of 8 µm/s. Further, the control system positions the MTB within a region-of-convergence of 10 µm in diameter. Due to the effect of the channel wall, we observe that the velocity and the positioning accuracy of the MTB are decreased and increased by 71% and 44%, respectively.

I. INTRODUCTION

The size of biological microrobots provides them with a wide range of applications, as opposed to miniature robots which usually fall in the range of a few millimeters to a few centimeters scale [1], [2]. These biological microrobots have the potential to perform targeted drug delivery and actuation of micro-objects [3], [4]. The natural propulsion mechanism allows for their navigation in low Reynolds number environments. Magnetotactic bacteria for instance, rotate their helical flagella to provide thrust force to overcome drag forces, while Tetrahymena pyriformis and Serratia marcescens use their cilia to provide self-propulsion [5], [6].

In order to predict how these biological microrobots will behave in vivo, key issues such as fluid flow velocity and the dynamics of the biological microrobots inside blood vessels have to be addressed. These issues can be investigated by analyzing the motion of the biological microrobots in micro-channels. Martel et al. demonstrated the open-loop control of a swarm of MC-1 bacteria inside micro-channels of 50 µm to 120 µm in diameter [7], [8]. Open- and closed-loop control of a single magnetotactic bacteria, i.e., Magnetospirillum magnetotacticum (MS-1), were accomplished inside a flat capillary tube with an inner thickness of 200 µm by Khalil et al. [9], [10].

This work addresses the closed-loop control of a magnetotactic bacterium (MTB) inside a micro-fabricated maze with channel width of 10 µm, shown in Fig. 1. Closed-loop control system is developed to accomplish point-to-point positioning of the MTB. This control capitalizes on the characterization of the magnetic dipole moment of the MTB using the u-turn technique [11], and is based on the magnetic force-current map of our magnetic system. The experimental results are done using our magnetic system, shown in Fig. 2 [12], [13]. We analyze the channel wall effect by comparing the motion control results inside and outside a micro-fabricated maze. Characteristics of the transient- and steady-states are used to evaluate the control system for each case.

The remainder of this paper is organized as follows: In Section II we discuss the theoretical background pertaining to the modeling and characterization of our MTB. First, the magnetic and drag forces and torques experienced by an MTB are modeled. Second, the u-turn technique is implemented to characterize the magnetic dipole moment of the MTB. In Section III, the characterized magnetic dipole moment is used in the realization of the magnetic force-current map of our system. This map is used as a basis of our closed-control system. Section IV describes our experimental setup and provides motion control results. Finally, Section V concludes and provides directions for future work.

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During the wireless control of an MTB, magnetic-based manipulation systems are utilized [9]. We consider a magnetic system with n-electromagnets. The magnetic field can be determined by the superposition of the contribution of each of the electromagnets [16]

$$B(P) = \sum_{i=1}^{n} B_i(P) = \sum_{i=1}^{n} \tilde{B}_i(P) I_i = \hat{B}(P) I.$$  \hspace{1cm} (5)

where $B_i(P)$ is the induced magnetic field by the $i$th electromagnet. The magnetic field ($\hat{B}(P)$) is linearly proportional to the current ($I_i$) of the $i$th electromagnet, as we use air-core electromagnets. Further, $\hat{B}(P) \in \mathbb{R}^{3 \times 1}$ is a matrix which depends on the position at which the magnetic field is evaluated, and $I \in \mathbb{R}^{n \times 1}$ is a vector of the applied current. The magnetic field due to each electromagnet is related to the current input by $\tilde{B}_i(P)$. Substituting (5) in the magnetic force equation (1) yields

$$F(P) = (m \cdot \nabla) \hat{B}(P) I = \Lambda(m, P) I,$$  \hspace{1cm} (6)

where $\Lambda(m, P) \in \mathbb{R}^{3 \times n}$ is the actuation matrix which maps the input currents onto magnetic forces. This actuation matrix depends on the magnetic dipole moment of the MTB and its position. Realization of this map necessitates the characterization of the magnetic dipole moment, and the evaluation of the magnetic field gradients at the position of the MTB.

A finite element (FE) model is developed for our magnetic-based manipulation system. Gradients of the magnetic fields are calculated within the workspace of the MTB, as shown in Fig. 3. We verify the accuracy of our FE model by measuring the magnetic fields using a calibrated three-axis Hall magnetometer (Sentron AG, Digital Teslameter 3MS1-A2D3-2-2T, Switzerland) at 12 points that span the workspace of our magnetic system. The average deviation in the magnitude and direction of the magnetic field are 2.3\% and 0.7\%, respectively. We apply 16 sets of current vectors and calculate the corresponding gradients. These sets are devised based on the saturation limits of our current amplifiers, i.e., Elmo ‘Whistle’ 1/60 servo controller (Elmo Motion Control, Petach-Tikva, Israel). Fig. 3 provides the field gradients for 4 different representative sets of current vectors, indicating constant gradients within the workspace of our magnetic system. This observation simplifies the implementation of our closed-loop control system since the pseudoinverse of the actuation matrix (6) is realized to calculate the current vector (I).

### B. Characterization of the Magnetic Dipole Moment

Realization of the force-current map (6), necessitates the characterization of the magnetic dipole moment of our MTB. Under magnetic field reversals, an MTB undergoes u-turn trajectories. The diameter ($D$) of the u-turn is given by [11]

$$D = \frac{\alpha \pi |\dot{P}|}{|m||\hat{B}(P)|},$$  \hspace{1cm} (7)

where \( \alpha \) is the rotational drag coefficient.
whereas, the u-turn time ($\tau$) is given by

$$\tau = \frac{\alpha}{m \| B(P) \|} \ln \left( \frac{2 \| m \| B(P) \|}{kT} \right),$$

where $k$ and $T$ are the Boltzmann constant and the temperature of the fluid, respectively. Characterization of the magnetic dipole is carried out using our magnetic system, shown in Fig. 2. A culture of magnetotactic bacteria in 0.02 ml of growth medium are incubated within a capillary tube (VitroCom, VitroTubes 3520-050, Mountain Lakes, USA). The tube has an inner-width and inner-thickness of 1 mm and 0.2 mm, respectively. The bacterial density ranges from $10^6$/ml to $10^7$/ml. The *Magnetospirillum magnetotacticum* (MS-1) cultures utilized in our work are grown according to the protocol provided by Bertani *et al.* [17]. Electromagnets A and C (Fig. 2) are utilized to provide uniform magnetic fields, then the magnetic field is reversed. The diameter and time of the u-turn trajectory is determined from the off-line motion analysis of the MTB. Fig. 4 shows the u-turn trajectory taken by the MTB during the reversal of the magnetic field. Using (7) and (8), the average magnetic dipole moment is determined from 15 different u-turn trajectories. The magnetic dipole moment of our MTB has an average of $1.6 \times 10^{-16}$ A.m$^2$, at magnetic field of 7.9 mT, and linear velocity of 32 $\mu$m/s. In the calculation of the magnetic dipole moment using (7) and (8), the rotational drag coefficient ($\alpha$) is computed using (4) based on the morphology of the MTB and the properties of the growth medium [9], [10]. We assume that the growth medium has similar properties as water.

III. Closed-Loop Control

Closed-loop control of an MTB is accomplished by directing the field lines towards a reference position, then the MTB performs a flagellated swim towards this reference position. Due to the self-propulsion force provided by the rotation of the helical flagella, the closed-loop control system can only locate the MTB within the vicinity of the reference position.

A. Control System Design

In a low Reynolds number environment (inertial terms are ignored), motion of an MTB is governed by

$$| F(P) | + F_d + f = 0 \quad \text{and} \quad \| T(P) \| + T_d + \Omega = 0,$$

where $f$ and $\Omega$ are the force and torque generated by each helical flagella, respectively. We use the force equation in (9), to generate the desired currents at each of the electromagnets. In order to realize the closed-loop control system, we calculate the position and velocity tracking errors as follows:

$$e = P - P_{\text{ref}} \quad \text{and} \quad \dot{e} = \dot{P} - \dot{P}_{\text{ref}} = \ddot{P}.$$  

(10)

In (10), $e$ and $\dot{e}$ are the position and velocity tracking errors, respectively. Further, $P_{\text{ref}}$ is a fixed reference position. We devise a controlled magnetic force ($F_{\text{des}}(P)$) of the form

$$F_{\text{des}}(P) = K_p e + K_d \ddot{e},$$

(11)
where \( K_p \) and \( K_d \) are the controller positive-definite gain matrices and are given by

\[
K_p = \begin{bmatrix} k_{p1} & 0 \\ 0 & k_{p2} \end{bmatrix} \quad \text{and} \quad K_d = \begin{bmatrix} k_{d1} & 0 \\ 0 & k_{d2} \end{bmatrix}. \tag{12}
\]

In (12), \( k_{pi} \) and \( k_{di} \), for \( i = 1, 2 \), are the proportional and derivative gains, respectively. Substitution of (11) in (9), i.e.,

\[
F_{\text{des}}(P) = F(P),
\]

and assuming zero propulsion force \( (f = 0) \) yields the following position tracking error dynamics:

\[
\dot{e} + (K_d + \gamma \Pi)^{-1} K_p e = 0,
\tag{13}
\]

where \( \Pi \in \mathbb{R}^{2 \times 2} \) is the identity matrix. We only consider motion control of the MTB in a two-dimensional workspace, and based on (13), the controller gains must be selected such that the matrix \( (K_d + \gamma \Pi)^{-1} K_p \) is positive definite.

B. Region-of-Convergence

Since motile MTB provides propulsion by its helical flagella, \( f \neq 0 \). Therefore, the closed-loop control system does not allow the position tracking error to go to zero, it rather locates the MTB within the vicinity of the reference position, i.e., region-of-convergence. Positioning accuracy of the control system can be evaluated by the diameter of the region-of-convergence. From (13), the size of the region-of-convergence depends on the gains of the control system, the propulsion force of the flagella and the dynamic viscosity of the growth medium.

IV. Experimental Results

Our motion control experiments are done using a magnetic-based manipulation system with four orthogonally-oriented electromagnets (Fig. 2). Position of the MTB is determined by a microscopic system and a feature tracking software. This software is based on subtracting the consecutive images obtained by our microscopic system to suppress the static edges of the channels, then motion of the MTB is tracked by computing the image gradients within a window (shown by the blue circle in inset B of Fig. 1) around the MTB. Detailed explanations of this magnetic system are provided in [12], [13]. The array of electromagnets surrounds a capillary tube or a micro-fabricated maze. Experiments are conducted using the capillary tubes to analyze the performance of the control system in the absence of the channel wall effect, whereas the micro-fabricated channel provides this effect for the control system.

A. Micro-Fabricated Maze

Our micro-fabricated maze is made of glass owing to its mechanical robustness and optical transparency. Procedures of fabrication are provided in Fig. 5. First, a glass (Borofloat) wafer is cleaned using nitric acid solutions. The thickness and diameter of this wafer are 500 \( \mu \text{m} \) and 100 mm, respectively (Fig. 5(a)). The layout of our micro-fabricated maze is transferred on the top-side of the wafer by spin-
coating a 3.5 µm photoresist layer (Olin OiR 908-35) and ultraviolet (UV) exposure (Fig. 5(b)). This photoresist layer is then used as a mask in the realization of microchannels of 5 µm in depth, through a deep reactive-ion etching process (Fig. 5(c)). The bottom-side of the wafer is coated by a 100 µm photoresist layer (Ordyl BF410). One inlet and six outlets with diameter of 1.7 mm are defined by UV-exposure (Fig. 5(d)), then developed by etching the glass wafer using powder blasting with 29 µm alumina particles (Fig. 5(e)). The wafer is then washed with deionized water, immersed in acetone and isopropanol, and cleaned by nitric acid solutions. Finally, the wafer is thermally bonded to an unprocessed glass wafer (Fig. 5(f)), then each micro-fabricated maze is diced to fit into a chip holder (FC-FC4515 chip holder, Micronit Microfluidics, Enschede, The Netherlands).

B. Control Outside the Micro-fabricated Maze

In the absence of the channel wall effect, the control law (11) allows for the positioning of the MTB within the vicinity of two reference positions, shown by the representative motion control result in Fig. 6. In this experiment, the MTB is incubated in a capillary tube (Section II-B). We observe that the MTB follows the reference positions at an average velocity of 28 µm/s. In addition, the closed-loop control system positions the MTB within an average region-of-convergence of 18 µm in diameter. The average is calculated from 10 motion control trials inside a capillary tube.

C. Control Inside the Micro-fabricated Maze

We control the MTB inside the micro-fabricated maze (Fig. 2), to analyze the channel wall effect on the velocity and the positioning accuracy of the controlled MTB. Fig. 7 provides the experimental result of the MTB inside the maze. Control system (11) allows the MTB to follow two reference positions indicated by the small blue circles. We observe that the MTB is positioned within the vicinity of the reference positions, and the region-of-convergence is 10 µm. The control system positions the MTB at a velocity of 8 µm/s. Table I provides a comparison between the characteristics of the controlled MTB outside and inside the micro-fabricated maze. The transient- and steady-states are analyzed by the velocity of the MTB and the size of the region-of-convergence, respectively.

V. CONCLUSIONS AND FUTURE WORK

We investigate the closed-loop motion control of an MTB inside a micro-fabricated maze to analyze the effect of the channel wall. Motion control experiments are conducted outside and inside a maze with a channel width of 10 µm. We do not only observe a 71% decrease in the linear velocity of the MTB, inside the maze, but we are also able to obtain 44% higher positioning accuracy.

Future work in this field should focus on the investigation of the effect of variable flow rate of the fluid. This investigation should be done to predict whether the flagella and magnetic forces are capable of holding the MTB at a reference position against a fluid flow. In addition, a three-dimensional (3D) magnetic system with auto-focusing is...
Fig. 7. Closed-loop control of a magnetotactic bacterium (MTB) inside a micro-fabricated maze with inner-width and -thickness of 10 µm and 5 µm, respectively, at various (t) instants. The MTB is controlled using the control law (11). The controller gains are: $k_{p1} = k_{p2} = 15.0 \text{ s}^{-2}$ and $k_{d1} = k_{d2} = 15.5 \text{ s}^{-1}$. This control system positions the MTB at a velocity of 8 µm/s and within a region-of-convergence of 10 µm. The black and blue arrows indicate the first and second reference positions, respectively. The small blue circles indicate these reference positions, whereas the large blue (light) circle is assigned by our feature tracking software [12]. The red (light) line represents the velocity vector of the MTB. The red arrows indicate the controlled MTB. The upper right inset shows a Transmission Electron Microscope image of an MTB, the white arrow indicates a chain of magnetite nano-crystals. Please refer to the attached video that demonstrates the results of the closed-loop control of the MTB inside the micro-fabricated maze.

essential to study the behavior and control the motion of the MTB in 3D space. Therefore, our magnetic system will be redesigned to allow for the visual tracking and control of the MTB in 3D space, and will be incorporated with a clinical imaging modality.

REFERENCES


