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Preliminary Investigation of Bio-carriers Using Magnetotactic Bacteria

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Abstract— **This paper proposes a novel micro-carrier based on magnetotactic bacteria (MTB). To confirm the feasibility of such carriers, the thrust force of the bacteria is evaluated. By measuring the swimming speed of MC-1 bacteria in an unbounded medium, a thrust of 4pN generated by a single MC-1 bacterium is found. The effects on the MTB's swimming speed under the control of micro-electromagnets and influenced by the wall effects when each MTB is attached to a microbead are investigated.**

Keyword— **Bio-carrier, micro-robot, magnetotactic bacteria, thrust.**

I. INTRODUCTION

Here we present a novel micro-carrier based on magnetotactic bacteria (MTB)[1-4] that can swim in a medium such as blood, a bio/chemical-reagent or water, for various tasks such as micro-manipulation, drug delivery and bio-sensing, to name but a few examples. Under the navigational control of external magnetic fields (up to a few Gauss), MTB can push functional micro- or nano-particles attached to them through an aqueous medium with prospects for their uses in human blood vessels. This paper primarily focuses on evaluating the thrust of *MC-1*MTB [2]. After briefly introducing the characteristics of magnetotactic bacteria, the thrust force of *MC-1* bacteria is evaluated. Then, the wall effects of a micro-channel on the movement of *MC-1* are considered followed by an analysis of the kinetic characteristics of the *MC-1* bacteria when attached to microbeads. Finally, the experimental results of MTB pushing microbeads in an aqueous medium are described.

First discovered in 1975 [1], magnetotactic bacteria are known particularly for their response to an external magnetic field. A chain of nanoscale magnetic particles embedded in the MTB acts as a compass to orient the MTB according to the magnetic field lines. Based on their orientation to the magnetic field, MTB are classified as axial or polar. Axial MTB can swim to either magnetic poles and randomly change their swimming direction along the magnetic field lines. Polar MTB, on the other hand, only swim towards one pole. For example, polar MTB that only swim towards the North Pole are generally discovered in the northern hemisphere, and are referred to as North-seeking MTB. As depicted in Fig. 1, North-seeking *MC-1* bacteria are swimming to the north pole of a magnetic bar.

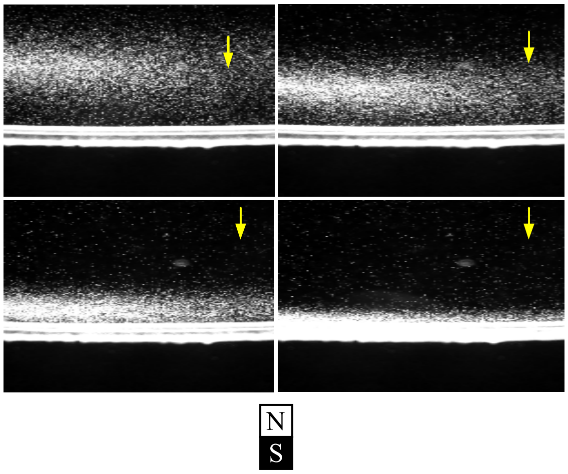


Fig. 1. MC-1 bacteria are swimming to the north pole of the magnetic bar. The white particles in the picture are bacteria

Although, different types of MTB have been identified [4], there are only a few types of MTB that can be cultivated under artificial conditions [4]. Most MTB moving by rotating their flagella with swimming speeds ranging from ~10μm/s to 250μm/s.

Initially, *MC-1* and *Magnetospirillum gryphiswaldense* [3] bacteria were considered for the preliminary investigation of our bio-carriers. Table 1 summarizes the characteristics of *MC-1* and *Magnetospirillum gryphiswaldense* bacteria. As such, one of the most important characteristics of the MTB for the implementation of micro-carriers is the thrust force provided by a single MTB.

TABLE I
Characters of *MC-1* and *Magnetospirillum Gryphiswaldense* bacteria

Type of MTB	*MC-1*	*Magnetospirillum gryphiswaldense*
Living environment	Marine water	Fresh water
Shape	Cocci	Spiral
Size	1~2μm(D)	0.7(W) μm*3μm(L)
Magnetosome size	~20nm	~40nm
flagella	One side	Both sides
Swimming speed	50~250μm/s	10~60μm/s
Magnetosome number	Up to 20	Up to 60

II. THEORY

A. Microfluidics

Due to the overall size of the proposed carriers, the MTB are operating under low Reynolds hydrodynamics inside a micro-chamber or a micro-channel such as a capillary. Assuming that the temperature and density of the fluid are similar to that of water at room temperature, the Reynolds number for the carrier is computed as:

$$\mathrm{Re} = \frac{\rho V L}{\mu} \tag{1}$$

where V and L are the characteristic velocity and the length scale of the object being pushed (here the diameter of the microbead is greater that the diameter of ~1 μm of the MTB), ρ is the density of the fluid, and μ is the dynamic viscosity of the fluid (marine water). In our experiment, Re is approximately 0.004. Under this condition, the thrust force of a single *MC-1* MTB can be calculated according to Stokes law [5].

B. Thrust Force of MTB in Unbounded Marine Water

Compared with the different MTB reported, until now, *MC-1* is the fastest MTB ever found. Their swimming speed ranges from 50μm/s to 250μm/s. An example of distribution of the swimming speed from a sample of MTB measured in our laboratory is given in Fig. 2. The swimming speeds of most MTB range from 150 to 200μm/s in the unbounded marine water.

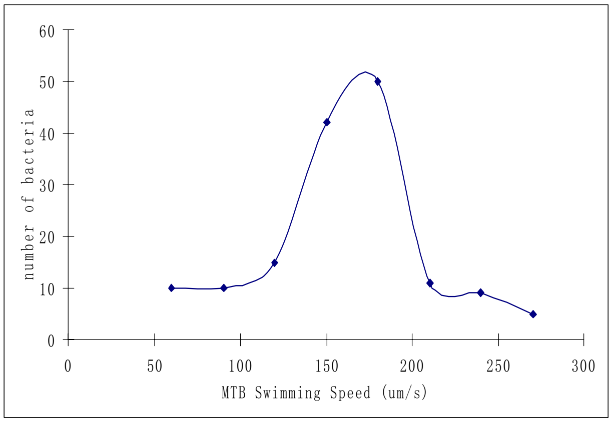


Fig. 2. Velocity distribution of the *MC-1* bacteria.

Due to their very small radius, the inertial force on MTB is negligible compared to the fluid drag on the MTB and thus, due to the fluid drag, the MTB will always move with an equilibrium velocity, meaning that the fluid drag force equals the thrust force. Since Re is very low (<< 1), Stokes equations can be used to estimate the drag force exerted on the *MC-1* cell. Hence, the thrust force of the MTB is:

$$F = 6\pi\mu\upsilon R\,. \tag{2}$$

With Eq. 2 and a speed of 200μm/s, a thrust of 4 pN in the unbounded marine water is computed.

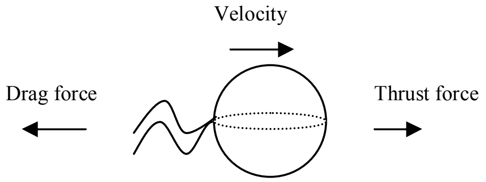


Fig. 3. MTB with a radius R moving to the right at a velocity ν in a fluid with viscosity μ

C. Wall Effect on the Swimming Speed of MTB

For such micro-carrier moving in a micro-chamber or micro-channel such as a capillary or a lymphatic vessel, MTB have to deal with the larger drag force caused by the wall effect. This effect becomes more significant as the diameter of the micro-channel approaches the diameter of the carrier.

$$\frac{v}{v_\infty} = \left\{\frac{1-(\frac{d}{D})}{1-0.475(\frac{d}{D})}\right\}^4 \tag{3}$$

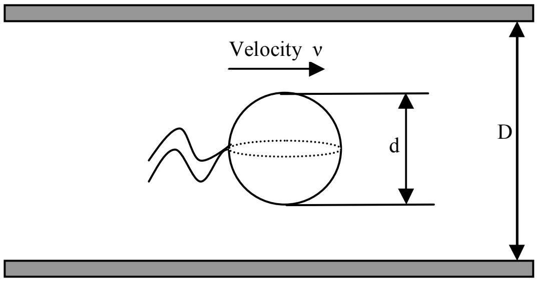


Fig. 4. According to Eq..3, with a fluidic channel (diameter of 10μm) and a velocity of the MC-1 bacteria of 200μm/s in unbounded conditions, the velocity of the bacteria will be decreased to approximately 120μm/s due to the wall effect.

For example, assuming a capillary with a diameter of 10μm, from Eq. 3 [6], the swimming speed of *MC-1* will decrease to 122μm/s compared to 200μm/s in an unbounded environment (see Fig. 4). Such theoretical result is also confirmed by another model proposed in [5] where a velocity of 119μm/s is obtained.

D. Swimming Speed of the MTB when Attached to a Microbead

Micro-particles or microbeads are the most suitable payloads that MTB can transport. Currently, there are many reports in the literature dealing with the fabrication of nano or microscale functional beads [7, 8].

After a microbead or microsphere is attached to a MTB, the drag force increases due to the change of surface area and combined geometry. Consequently, assuming that the MTB maintain the same thrust force as calculated above, the swimming speed of the MTB with a microbead will decrease significantly. Fig.5 illustrates the relationship between the diameter of the microbead and the displacement speed when attached to a MTB.

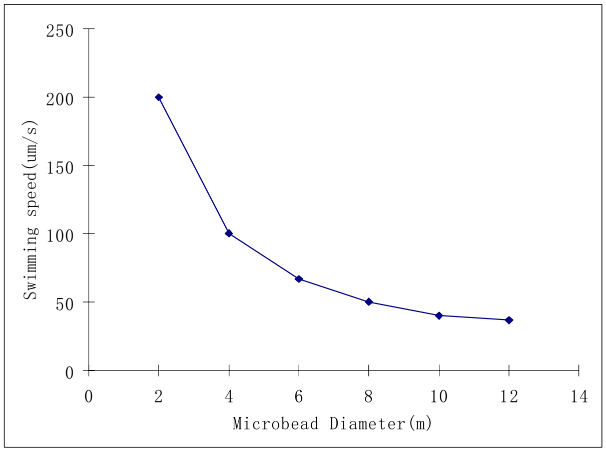


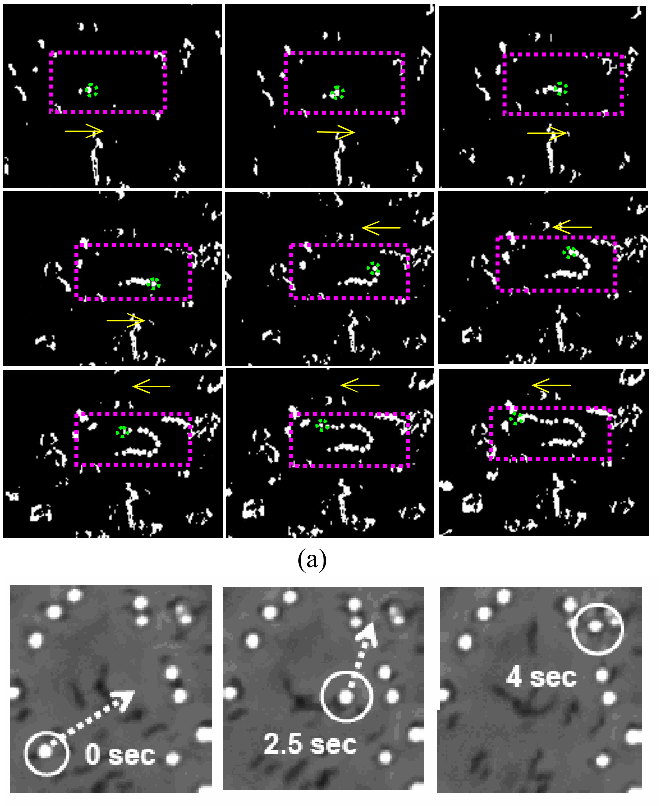
Fig. 5. Velocity of a microbead being pushed by a single MTB for various bead diameters, assuming that the swimming speed of MTB is 200μm/s before being attached to the microbead.

III. EXPERIMENTS

The experiments are designed to evaluate two important aspects for the MTB-based micro-carrier, first, the controllability of the micro-carrier; and second, the kinetic characteristics of the MTB loaded with a microbead. The fabrication of micro-electromagnets and the experimental set-up are described in [9]. Our experiments show that MTB can be attached to microbeads just by mixing two mediums together for several minutes. Before the mixing procedure, fresh MTB are withdrawn from the medium and stressed in the old medium (with less nutrition and oxygen) for 15 minutes. The fluorescent microbeads (2μm in diameter with yellow-green fluorescent from *Molecular Probes, Oregon USA*) are diluted. Then, the two mediums are mixed together and let settle for 15 minutes. Finally, drops of the solution are checked under a fluorescent microscope. With this procedure, the number of bacteria attached is presently very low with less than 1% yield.

. In Fig.6a, a *MC-1* MTB is pushing a microbead and executes a U-turn when the pole of the magnetic field is suddenly reversed. In Fig.6b, a *Magnetospirillum Gryphiswaldense* MTB is depicted pushing a microbead under the control of an external electromagnet

The 4 pN calculated according the Stokes' law relies on the assumption that the there is an equilibrium between the thrust force generated by the rotating flagella and the drag force exerted on the bacteria. For a single *MC-1* MTB pushing a microbead, we observed that some of the MC-1 bacteria can sustain the same swimming speed when not attached to a bead. This observation may suggest that *MC-1* bacteria increase their thrust force up to a certain limit in order to maintain a constant swimming speed.



(a)

(b)

Fig. 6. a) A *MC-1* bacterium is pushing a fluorescent microshpere (2μm in diameter) to execute a U-turn when reverse the magnetic field (12Gauss). b) A *Magnetospirillum gryphiswaldense* bacterium is pushing a microsphere (3μm in diameter) to the north pole of an electromagnet (100 Gauss)

IV. CONCLUSION

This paper proposes a novel micro-carrier based on magnetotactic bacteria. The working principle of this micro-carrier and an analysis of the thrust force of MTB were described. This micro-carrier may have potential applications in microscopic environments such as in human blood capillaries and in microfluidic systems. The controllability of this micro-carrier can be accomplished by modifying the direction of the lines of a magnetic field. Although there are still several challenges to overcome such as the development of an effective attachment method with microbeads, compared to other known techniques, MTB-based micro-carriers have significant advantages for many applications from an engineering perspective.

V. ACKNOWLEDGMENT

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