Towards Autonomous Bacterial Microrobots

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***Abstract*—A summary of our recently developed bacterial microrobots with an overall length of a few micrometers with the main efforts, experimental data and preliminary designs towards the development of fully autonomous bacterial microrobots for future operations in an aqueous medium, is briefly presented. Due to technological constraints in microfabrication coupled with limits in electrical energy sources and conversions that can be embedded in future fully autonomous untethered microrobots only a few hundreds micrometers in overall length, the energy requirement collected through embedded photovoltaic cells is minimized by exploiting the motility of flagellated MC-1 Magnetotactic Bacteria (MTB). The encapsulation of such bacteria in special micro-reservoirs embedded in the microrobot provides the mean of propulsion. Directional control of the microrobot is achieved from an onboard microcircuit inducing a torque on a chain of single domain magnetic nanoparticles called magnetosomes embedded in each bacterium. Integrated 3D coil solenoids based on standard CMOS technology are used to generate local magnetic fields to orient the swimming directions of the bacteria inside the micro-reservoirs.**

***Index Terms*—Magnetotactic bacteria, microrobots, photovoltaic cells, untethered microsystems, magnetotaxis, controlled bacterial actuation**

I. Introduction

UNLIKE the swimming paths of most flagellated bacteria that are influenced by chemotaxis to detect nutrient gradients, the direction of displacement of Magnetotactic Bacteria (MTB) [1, 2] is influenced mainly by magnetotaxis where a magnetic field (typically 0.5 Gauss) induces a torque on a chain of membrane-based single magnetic domain nanoparticles of a magnetic iron referred to as magnetosomes. From an engineering point of view, magnetotaxis represents a more suitable interface, especially with electronics and computer-based software.

Acting like a compass, this chain of magnetosomes enables the bacteria to orient themselves and swim along the lines of a magnetic field. Hence, the basic control method consists of modifying the swimming paths of the MTB with the generation of local directional magnetic fields using small programmed electrical currents passing through special embedded conductor networks. This new method referred here to as controlled *bacterial micro-actuation* when compared to other traditionally known methods, is a serious candidate for its integration in future untethered microrobots operating in an aqueous medium for several reasons. First, because only a very small electrical current is required (typically sufficient to produce a local magnetic field > 0.5 Gauss) for controlled MTB-based micro-actuation since the motility of the bacteria is exploited, it does not have the disadvantages of many micro-actuators such as the ones based on piezo-ceramics that require relatively high voltage levels to operate which is difficult to implement at such a small scale. Second, many actuation techniques require voltage levels that are higher than the relatively low operating voltage levels of the microelectronics embedded in such microrobots, requiring voltage converters that significantly increase the overall dimensions of such microrobots while decreasing the power efficiency of the systems. This is avoided with bacterial micro-actuation. Third, bacterial actuation does not need electrical power to actuate unlike all other known micro-actuation methods used in microrobotics. Because the motility of the bacteria is exploited, electrical power requirement is minimized since electrical current is only used to change the direction of the bacteria and not to induce a force on the MTB itself. As such, besides exploiting the motility of MTB, the power requirement can be minimized by reducing the space between the conductors, and by increasing pushing surface to volume ratio in order to increase bacterial micro-actuation density, to name but a few approaches.

II. Recent Progress Towards Bacterial Microrobots

In our knowledge, the use and integration of bacteria and in particular MTB as a mean of controlled directional propulsion for any micro-objects including microrobots also sometimes referred to as bacterial carriers, Autonomous Bacterial Systems (ABS), etc., has been first proposed in [3, 4]. Unlike many efforts worldwide trying to mimic the flagellar motor of bacteria through microtechnologies, we proposed to integrate such bacteria in microsystems/microrobots to exploit the flagellar motor of the bacteria in order to provide a mean of

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propulsion/actuation suited for microrobots and microsystems operating in an aqueous medium. But more importantly, a method [5, 6] to control their swimming paths or in other words, to be able to navigate them in a controlled manner from computer software was proposed and validated experimentally. It was shown that the combination of the flagellated nanomotor and the chain of single domain nanoparticles acting as a compass and embedded in MC-1 MTB could be used as an effective bio-actuator that could be controlled through external magnetic field lines. Furthermore, it was also recorded experimentally that the particular use of MC-1 MTB could provide an average thrust force of ~4 pN per MTB, a much larger value than the average typical thrust of ~0.5 pN provided by other flagellated bacteria. The efficacy of such nanomotor and the directional control provided by the single domain nanoparticles called magnetosomes were assessed and validated in microfluidic channels. The implementation of such bio-carriers with micro-objects being propelled by a single MTB was also demonstrated. The effect of various diameters MTB-pushed beads on the velocity of this bio-carrier and the retarding effect caused by the proximity of the walls of the microchannels were also investigated.

We also developed several experimental platforms to conduct further tests and we estimated and concluded from preliminary data that it would be possible although challenging to develop an autonomous microrobot pushed by MTB considering all aspects that may have an impact on the behavior of such a microsystem (e.g. buoyancy, etc.). By exploiting the motility of MTB, the electrical energy required to propel such a robot is null and we estimate that by pushing the limit of miniaturization or feature sizes to what is possible with actual microfabrication methods, a small current as low as 100 µA could be sufficient to control groups of pre-selected and most responsive MTB from a microcircuit embedded in the microrobot. As such, photovoltaic cells were simulated and developed to be implemented in such microrobots to power the embedded electronics. Our recent progress is described in several papers with experimental results showing the feasibility of such method and describing the use of such bacterial microrobots in many applications including but not limited to the fast detection of pathogenic bacteria [7, 8], as biosensors [9], bio-carriers [10] particularly in microfluidic systems [11], for the implementation of bacterial microfactories [12], fully autonomous aqueous microrobots [13, 14], and even for operations in the complex arteriolocapillar networks of the human cardiovascular system [15, 16].

But just prior to use MTB as micro-actuators in microrobots, the integration of bacteria as functional components was demonstrated [17, 18] where *Serratia marcescens* flagellated bacteria were attached to polydimethylsiloxane or polystyrene to form a *bacterial carpet* for moving fluid. But these bacteria were operating without a control or coordination method appropriate for actuation of micro-objects including microrobots. For instance as shown in [17], without coordination, when N bacteria are attached to an object of size L, the propulsion force F will scale like F α $N^{1/2}$ assuming N α L^2 and such bacteria will swim in a pattern described by the so-called run-and-tumble that can be explained by chemotaxis [19] models while remaining unpredictable when used for the propulsion of an aqueous untethered microrobot. On the other hand, controlling the direction of motion of N bacteria attached to an object or microrobot with pushing surfaces of size L could lead to a propulsion force F that could be proportional to N. As such, MTB can be more appropriate to carry out computer-based controlled micromanipulation or micro-actuation of micro-objects and microrobots. In other studies involving MTB, some mass-scale applications to exploit the motility of MTB have been done using permanent or electromagnets. As an example, low field Orientation Magnetic Separation (OMS) [20] is a process, where motile, magnetic field susceptible MTB can be separated. In other studies, micromanipulation of biological systems or controlled assembly of MTB using micro-electromagnets arrays, have also been described [21, 22]. But in all these previous examples, MTB were the entities being manipulated instead of being used to manipulate or actuate other micro-objects such as untethered microrobots.

III. Main Types of Bacterial Microrobots

A. Bacterial Carriers: Non-autonomous Bacterial Microrobots for Transport

A schematic of one of our non-autonomous bacterial microrobots is depicted in Fig. 1a with the real implementation depicted in Fig. 1b as observed under an optical microscope.

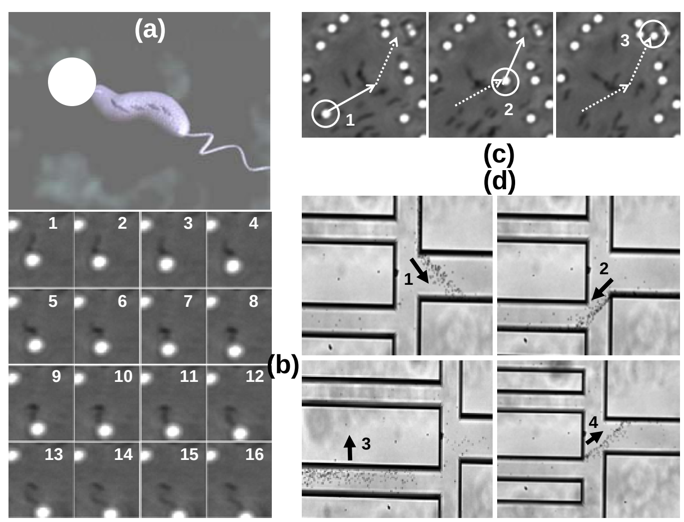

Fig. 1. (a) Basic concept of the bacterial carrier or microrobot; (b) Closed-up view of the real implementation using a 3 µm diameter bead showing the displacement of the microrobot in an aqueous solution; (c) Example of navigational control of a single bacterial microrobot; (d) Navigational control of a swarm of magnetotactic bacteria in microfluidic channels observed under an optical microscope.

This simple bacterial microrobot or carrier consists of one MTB (~1 to 1.5 µm) attached (typically by using rabbit polyclonal antibody already developed in our laboratory) here to a 3 µm polymer bead but other microstructures or micro-objects can be used. A chain consisting typically of 5 to 12 or

14 of a few tenths of nanometers in diameter cubo-octahedral (Fe_3O_4) magnetosomes (single magnetic domain) is embedded in each MC-1 bacterium. Figure 1c shows one of the same type of bacterial microrobots being controlled to swim in a straight line between location 1 and 2 and then to turn to the left in order to reach location 3. The control of the swimming direction of a swarm of MC-1 MTB in micro-channels is also shown in Fig. 1d through sequences 1 to 4 as seen under an optical microscope.

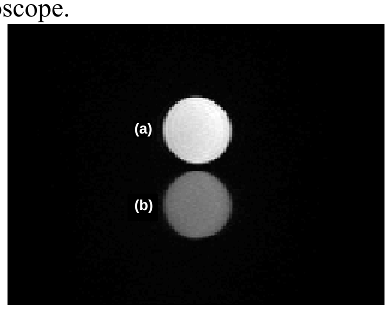

Fig. 2. MR images of two samples containing a concentration of 10^6 MC-1 bacteria/ml (Fig. 2a) and 10^{10} MC-1 bacteria/ml (Fig. 2b). The sequence used was a spin echo with TE/TR = 84/1000 ms, FOV = 300×300 mm, matrix size = 256×256, slice thickness = 2 mm, magnetic field strength = 1.494 Tesla.

The possibility of detecting and then controlling swarms of MTB inside the human body, in our particular case using Magnetic Resonance (MR) Imaging (MRI), is shown in Fig. 2 where different concentrations of MC-1 bacteria alone have been detected by our group in a 1.5T clinical MRI system. This demonstration is quite significant in sight of using such bacterial microrobots for applications such as targeted chemotherapies, chemo-embolization, or hyperthermia, to name but a few applications. In these interventional procedures, targeting tumoral regions through small capillary vessels (as small as 4-6 µm in diameter) is essential for enhancing the efficacy of treatments. As such, the thrust provided by the flagellated MC-1 bacteria may be an effective complementary means of transport of therapeutic agents to cancer cells when navigating in small capillaries while being guided by computer from MR detection and tracking. Although tracking could be enhanced by ferromagnetic or superparamagnetic beads being pushed by the MTB, being able to detect MTB without MR image artifacts created by the beads as depicted in Fig. 2 allows more flexibility for the implementation of the bead itself. This in turn may lead to potentially higher density of therapeutic agents being delivered per bacterial carrier.

B. Non-autonomous Bacterial Microrobots for Cooperative Tasks

As stated previously, the orientation of the MTB are controlled by inducing a torque on a chain of magnetosomes, acting as a compass embedded in each bacterium. Such torque is achieved by circulating a small electrical current through selected conductors in a microcircuit in order to use the motility of the bacteria to push micro-objects towards desired locations. Here, the microcircuit in the form of a CMOS Integrated Circuit (IC) containing both the bacteria and the micro-objects being manipulated is placed under an optical microscope. The images captured by a CCD connected to the microscope provide information that are processed and fed back to the microcircuit that switches an electrical current to specific conductors in order to achieve optimal coordination and control of the MTB. The integrated electronic circuit as depicted in Fig. 3 contains an embedded matrix that is made of two layers of vertical and horizontal conductor lines. One of the objectives of such a matrix is to determine the minimum current intensity and corresponding distance between the conductors and the bacteria in order to provide the minimum magnetic field capable of influencing the swimming direction of the magnetotactic bacteria.

A current flowing into a metal conductor will generate a magnetic field according to Biot-Savart law. The expression of that field is given by Eq. 1.

$$B = \frac{\mu_c I}{2\pi d}. \quad (1)$$

In Eq. 1, B is the magnetic field, μ_c is the conductor permeability, I the intensity of the current flowing into the wire and d the distance between the object (which is chain of magnetosomes in the bacterium) and the conductor. This equation suggests that lower electrical energy requirement can be achieved through miniaturization or smaller distances between the conductors and conductor-bacteria. The magnetic field generated by the conductor will induce a torque on the chain of magnetosomes of the bacteria, which will align them according to the magnetic field and thus determine the direction of swimming. Using several bacteria on the matrix, coordinated tasks such as micro-manipulations can be performed by independent control of the bacteria.

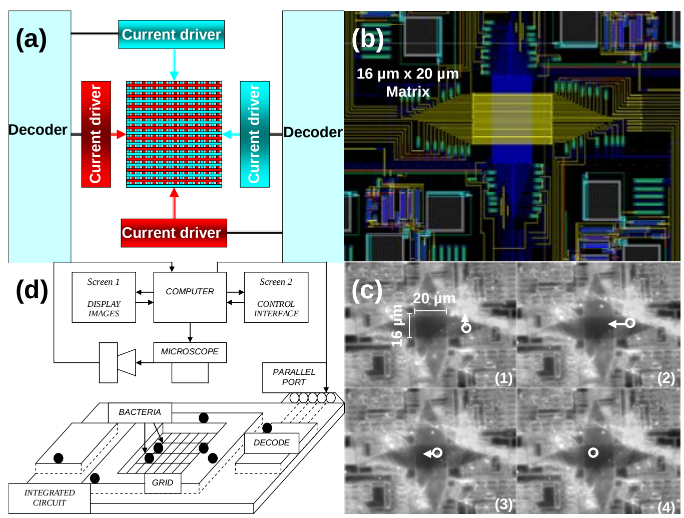

Fig. 3. (a) Bloc diagram of the hardware architecture; (b) Matrix layout as shown by the Computer-Aided Design (CAD) software; (c) Influence of the magnetic field on the bacterium's trajectory; (d) General overview of the platform.

C. Autonomous Bacterial Microrobots

The proposed autonomous microrobot is a microsystem built with silicon MEMS using standard CMOS processes, integrating electronics with bacteria. As depicted through a simple conceptual schematic in Fig. 4a, this microrobot consists of a single die containing micro-reservoirs (Fig. 4b and Fig. 4c) that shelter magnetotactic bacteria to form a "bacterial propulsion system". As depicted in Fig. 4d, a coil is embedded in each micro-reservoir. With an electrical current flowing along the conductive coil, a magnetic field likely to influence through magnetotaxis the swimming direction of the bacteria is generated as shown in Fig. 4e. Their swimming directions can be changed towards a wall of the micro-reservoir towards the intended direction of movement of the untethered microrobot. The magnetic field emanating from the inside of the solenoid coil is then used to control an agglomeration of MTB for controlled pushing or propelling force of the microrobot. In Fig. 4, initial designs of the bacterial reservoirs acting as "bacterial engines" are 90 µm × 54 µm, and 90 µm × 186 µm (length × width).

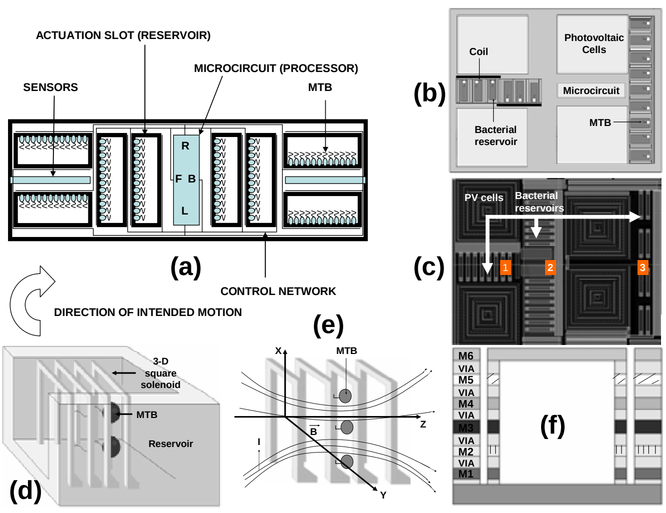

Fig. 4. (a) Bloc diagram explaining the concept of the autonomous bacterial microrobot (R, L, F, B stand for Right, Left, Forward, and Backward motions respectively); (b) Initial simplified architecture of the microrobot with left and right propulsion control; (c) CAD layout showing the micro-reservoirs, and the photovoltaic cells; (d) bacterial reservoir inside which is embedded a 3D solenoid coils; (e) bacteria swimming a long the magnetic field inside the coil. The (x, y, z) axis allows us to determine the exact magnetic field acting on the bacteria according to its position; (f) Cross-sectional view of the different layers used in the design of the bacterial reservoir.

Photovoltaic cells to be embedded in such untethered aqueous microrobots, a few hundred micrometers in overall length, have been developed. A total of 4 cells with an estimated efficiency of 12.5% should provide up to 100 microamperes (µA) of photonic current to the electronics embedded in each untethered microrobot and used to control the swimming or pushing direction of the MTB in the micro-reservoirs.

IV. Conclusion

New types of untethered microrobots based on controlled bacterial actuation have been briefly described with preliminary experimental results. Although several types of bacteria could be used, here, MC-1 magnetotactic bacteria have been chosen providing directional control through magnetotaxis and thrust forces superior to other flagellated bacteria. Our experimental results and implementations of bacterial untethered but non-autonomous microrobots also suggest that autonomous untethered aqueous microrobots a few hundreds micrometers long and propelled by bacteria is possible with present technologies. As such, a short description of initial versions of the design of such an autonomous bacterial microrobot has been briefly described.

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