Towards Bacterial Microfactories

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Abstract - **Our group demonstrated experimentally that the swimming paths of Magnetotactic Bacteria (MTB) could be controlled through special microelectronic circuits and software algorithms. These results may lead to the development of a new type of microfactories where manipulation at the micrometer-scale could be performed by many MTB operating under the influences of special control rules. As such, a special integrated microelectronic circuit designed specifically to embed MTB and to control their swimming directions, has been developed. The orientation of the MTB are controlled by inducing a torque on a chain of small particles named magnetosomes, acting as a compass embedded in each bacterium. Such torque is achieved by circulating a small electrical current through selected conductors in the microcircuit in order to use the motility of the bacteria to push micro-objects towards desired locations. The microcircuit containing both the bacteria and the micro-objects being manipulated are placed under an optical microscope to provide information that are processed and fed back to the microcircuit to activate specific conductors in order to achieve optimal coordination and control of the MTB. Our initial proof-of-concept where MTB are pushing microbeads under computer control suggests that the use of biological components such as bacteria could play a major role and influence the development of future microfactories dedicated to specific ranges of applications.**

Index Terms *- Magnetotactic bacteria, microfactories, microelectronic circuit, micromanipulation.*

I. Introduction

In this paper the methodology of SoC systems is used to design circuits exploiting magnetotactic bacteria as biological components [1]. The first goal of such an intermediary experimental platform is to study the characteristics of magnetotactic bacteria in view of integrating them in future hybrid microsystems, as autonomous yet controllable entities, towards the building of microfactories [2].

First, we propose an architecture capable of orienting magnetotactic bacteria in any direction. We show how the bacteria would complete diverse tasks in reaction to commands for a central control unit. Tasks like surface screening and the assembly or microobjects are possible [1,2 and 3].

II. System Architecture

We envision a bacterial microfactory for the possible application of coordinated parallel placements of microbeads. The proposed architecture for such a system consists of three main components: a platform for microfabrication, an optical microscope with a couple-charged device (CCD) for monitoring and a computer for control.

The microfabrication platform itself consists of three layers: at the highest level a swarm of magnetotactic bacteria is responsible for actuation. The bacteria swim in a special biological milieu over an electronic matrix of conductors used as magnetic fields generators. Of course the two layers are isolated. At the lowest level we find the necessary hardware for control, power and communication with the matrix. This, along with the other components, is depicted in Fig. 1.

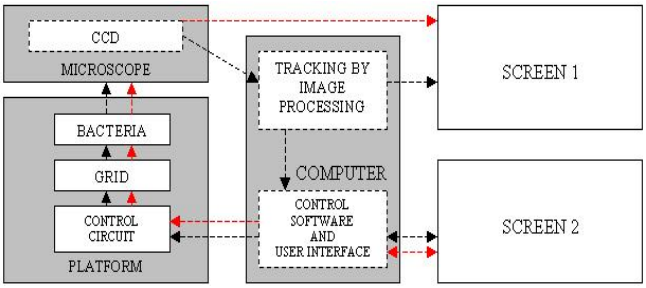

Fig.1 System architecture

Two control schemes are presented. The first is an open loop and depends heavily on user interaction. It is intended as an experimental system. It has been implemented and is detailed in the following sections. The second is closed-loop and builds upon the first one. It adds an image processing based tracking component and hence provides feedback for the automatic control of the bacteria.

This architecture is extensible. The surface of the matrix for instance can be augmented or multiple matrices can be combined with minimal changes in the tracking and control components.

III. HARDWARE

A. *Magnetic Field Generation*

The integrated electronic circuit 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 conductor and 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

$$B = \frac{\mu_c I}{2\pi d}, \qquad (1)$$

where 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 the bacterium) and the conductor. The magnetic field generated by the conductor will induce a torque on the chain of magnetetosomes of the bacteria, which will align them according to the magnetic field and thus determine the direction of swimming. The distance between a bacterium and the conductor should be kept so that the bacterium will stay inside of an influence magnetic area equal to 0.6 G. Since the bacterium naturally navigates with the earth magnetic field that is 0.5 Gauss, then if we produce a magnetic field greater than 0.5 Gauss we should be able to influence the swimming direction of the bacterium and therefore control its navigation.

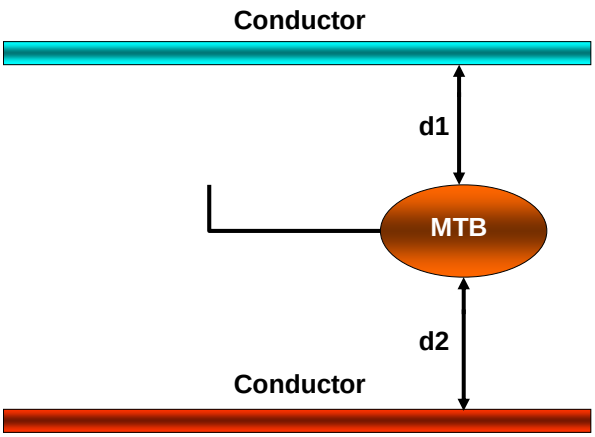

Fig.2 Magnetic field influence

B. *Internal Architecture of the Bacteria Control Microchip*

The system contains two decoders that translate the commands coming from a local computer. These decoders will select the corresponding columns and lines to direct the bacteria in order to achieve a specific task. In addition, the system contains voltage to current converters that provide current to the different lines of the matrix. Fig. 3 presents the schematic block of the hardware system.

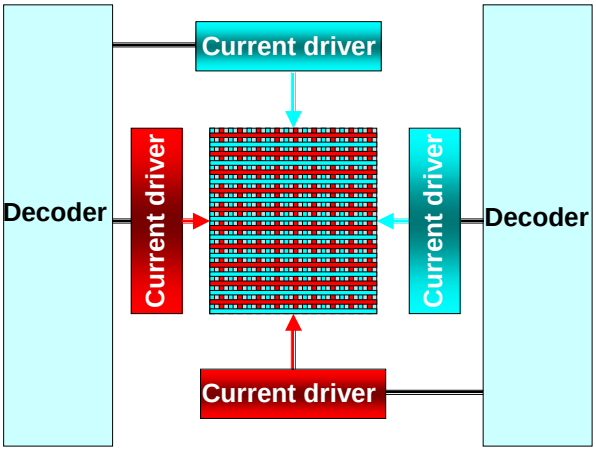

Fig.3 Bloc diagram of the hardware architecture

Current lines and columns alternate in directions so as to allow the generation of adjacent magnetic fields in opposite directions and hence a larger flexibility in terms of bacterial control.

Cadence layout editor is used to simulate the circuit. The matrix is composed of 32 horizontals lines and 32 vertical lines; the dimensions of the matrix are estimated to be 16µm x 20 µm. Fig. 4 presents the matrix layout designed in cadence.

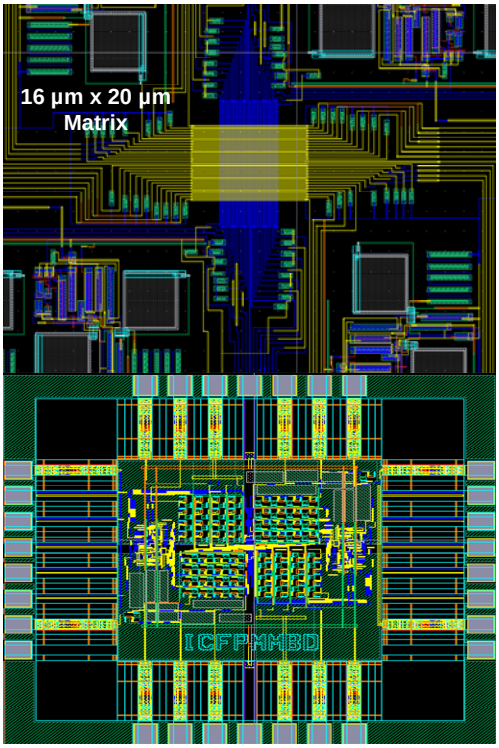

Fig.4 Matrix layout in Cadence

A very thin layer of parylene of about 200 nm is added on top of the silicon die in order to isolate the microchip from the medium. The bacteria are hence located at a distance of 2 µm from metal 1 and at a distance of 3 µm from metal 2. To observe the trajectory and reaction of the controlled bacteria, an optic microscope is used. Therefore, the control is done in two steps: first we track the bacteria with the use of a microscope equipped with specialized image-processing software and secondly, we send commands to the matrix for control.

IV. Software

A. *Specifications*

The currently envisioned software system does not integrate automatic bacteria tracking. The present experimental setup requires active user interaction and at this stage of experimentation this is more of an advantage. Many parameters need to be measured, like the minimum current necessary to influence effectively the bacteria, the spatial resolution of the grid lines and columns, or the effective height of the isolating layer between the grid and the bacteria.

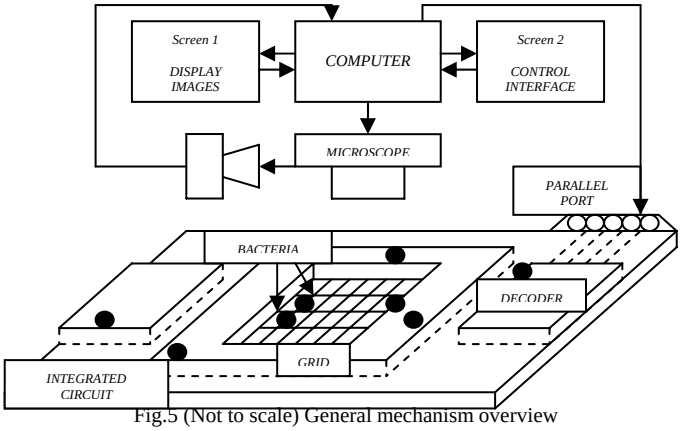

Fig.5 (Not to scale) General mechanism overview

After having the experimental setup in place: a bacteria layer on top of the grid's die, which itself sits in an integrated circuit connecting it to a parallel port, the whole under the 50x objective of an optical microscope in dark field reflection, an experimenter controls the grid magnetic field through a control software and its user interface, and then observes the behavioural reaction of the bacteria with the microscope's CCD images and integrated software. This mechanism is depicted in Fig. 5 and first results are shown in section V.

B. *Description*

According to the decoders' hardware interface, 5 data bits are necessary to specify the grid line or column and an extra bit is necessary to select the decoder. Communication is done through the computer's parallel port. Under Windows XP and with Visual Basic, this is straightforward using the inpout32.dll and output32.dll libraries [4].

The lines and columns of the grid have been numbered from 0 to 63, the lines having the even numbers and the columns the odd ones. This simplifies the mapping. A fundamental function have been written that takes as a parameter a line or a column number and generates the corresponding series of bits to the parallel port according to a simple mapping function. For more complicated setups, (i.e. for a larger grid and a greater number of decoders) a mapping table becomes probably necessary and is easily integrated.

Various functionalities that use the above-described fundamental method are then implemented. They are also combined to program higher level predefined behaviours. For example, all necessary lines could be triggered in series, with a certain frequency, in order to generate a global magnetic field across the chip whose resultant is to the left. This will act as a global vortex, attracting all vicinity bacteria in the same general direction (here to the left). Hence, four basic macros corresponding to the four basic directions are included in addition to two special functions: a "trap" method (whose purpose is to imprison the bacteria inside the outer limits of the grid by alternating the activation of the contouring lines), and an "attract center" method (that triggers a magnetic field towards the center of the grid). The frequency of alternation for all the methods is controllable through the user-interface.

For ease of use, the control of the grid is mapped graphically into the user interface by highlighting triggered lines and columns on a graphical grid. The resulting software user interface can be seen in Fig. 6. It includes control buttons for magnetic fields in the four directions (west, east, north and south), the special "trap" and "attract center" functionalities, as long as a "stop" button. Once experimentation is started camera images are recorded automatically and when the stop button is pressed a video is generated and saved automatically along with other relevant data. For experimentation purposes, lines can also be triggered individually by inputting the corresponding line number.

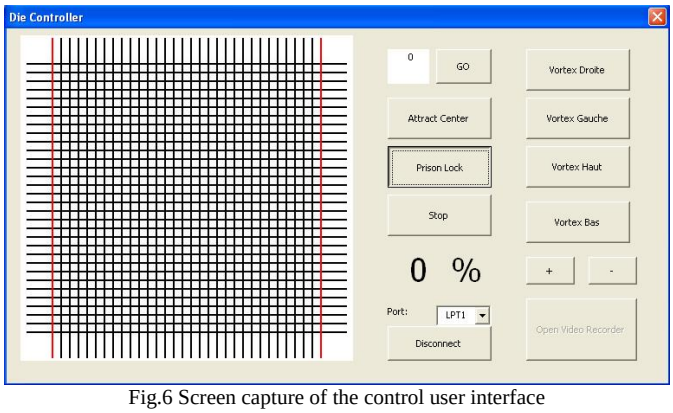

Fig.6 Screen capture of the control user interface

In Fig. 7 preliminary experimental results are depicted. We can distinguish in the background the conductors' rectangular matrix in the center of each of the four images. The white dots in the foreground are the magnetotactic bacteria.

The experimenter sent the commands for repetitive generation of a horizontal magnetic field vector pointing at 180^{o} (sending current in the corresponding columns of the conductors' matrix). When one bacterium, heading north, reached the grid as highlighted in (1), it changed its trajectory in accordance with the magnetic field exerted at that time.

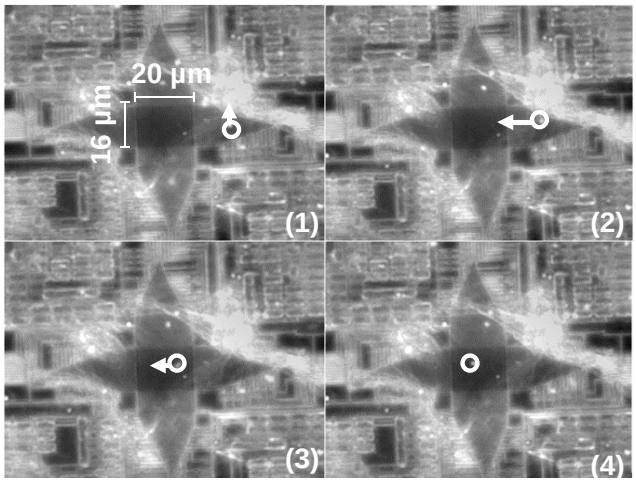

Fig.7 Influence of the magnetic field on the bacterium's trajectory

VI. Conclusion

In this paper we showed how we laid the foundations for our microelectronic control of magnetotactic bacteria that can be used for the manipulation of micro-objects. We have designed and fabricated a special control matrix and implemented control and communication software as first step towards our new proposed concept of bacterial microfactories.

Acknowledgment

This project is supported in part by a Canada Research Chair (CRC) in Micro/Nanosystem Development, Fabrication and Validation, the Canada Foundation for Innovation (CFI), the National Sciences and Engineering Research Council of Canada (NSERC), and the Government of Québec.

References

[1] S. Martel, "Controlled bacterial micro-actuation", In. Proc.of the Int. Conf. On Microtechnologies in Medicine and Biology, Okinawa, Japan, May 9-12, 2006

[2] D. Schuler and R.B. Frankel, "Bacterial magnetosomes: microbiology, biomineralization and biotechnological applications", Appl. Microbiol. Bitoechnol. (1999) 52 p.470.

[3] G. Harasko and H. Pfutzner, "Domain Analysis by Means of Magnetotactic Bacteria", IEEE Transaction on magnetics, Vol 31. No.2 March 1995.

[4] J. Axelsons, http://www.lvr.com/parport.htm