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MICROBIOROBOTICS

Biologically Inspired Microscale Robotic Systems

Second Edition

Edited by
MinJun Kim
Anak Agung Julius
U Kei Cheang

Micro & Nano Technologies Series

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Preface

Building robotics system in the microscale is an engineering task that has resulted in many important applications, ranging from microscale assembly to cellular manipulation. However, it is also a very challenging engineering task. One of the reasons is due to the fact that many engineering ideas and principles which are used on larger scales do not scale well into the small world. For example, locomotion principles in fluidic environment do not scale because of the difference in (order of) the Reynolds numbers. The use of rotational motors is also impractical because of the challenges related to building of the components.

Similar challenges exist in the effort to realize sensing mechanisms. Macroscale positioning techniques such as global satellite positioning systems or acoustic positioning sensors simply do not offer microscale resolution. The fundamental wavelengths for such operations are much larger than the scale of the robots themselves. For vision-based sensing, components for typical on-board robotic vision are also much larger to integrate with microscale robots.

On the other hand, microorganisms have evolved various mechanisms to thrive in such an environment. Microbial cells use various structures, such as flagella and cilia to generate motion. They have also developed various chemical receptors and cellular signaling mechanisms to detect and process sensory information from their environment. This is evident in the observed motility behavior of microorganisms, which includes phenomena such as chemotaxis, phototaxis, thermotaxis, and others.

Recently, synthetic microrobots have become very common in this field. Various locomotive mechanisms are inspired by microorganisms. With the advances in microfabrication technologies, microscale actuators can be fabricated on a massive scale which is an indication of the feasibility to utilize artificially fabricated actuators. However, there exist technological limitations in creating micro or nanoscale on-board power supply and sensors, thus, synthetic microrobots are generally simplistic in geometry and rely on an external power sources such as magnetic fields. Nonetheless, future advances in fabrication technologies and biocompatible materials will enable the use of synthetic microrobots for future applications.

This book covers the use of biological and synthetic systems in microscale robotics applications. Three main topics that are covered are:

- Theoretical Microbiorobotics
- Biological Microrobots
- Synthetic Microrobots

In these topics, we have solicited contribution from leading researchers in the area so as to provide a balanced treatment between the theoretical analysis and experimental results.

Microbiorobotics is a new engineering discipline that inherently involves a multidisciplinary approach (mechanical engineering, cellular biology, mathematical modeling, control systems, synthetic biology, etc.). The documentation of relevant development in this field has been scattered in various journals and conference proceedings in areas mentioned above. With this book, we aim to provide the readers with a unique perspective and unified source for the fundamentals and the recent advances in the field of microbiorobotics.

This book is aimed at engineers with a background in robotics, physics, and biological systems. It is also aimed at teaching graduate students about the fundamentals and the recent advances in the field of microbiorobotics.

Acknowledgments

It is obvious that the work of editing this book does not represent solely the efforts of its three editors. Since microbiorobotics is an advanced and interdisciplinary topic, we aim to highlight some of the most innovative and powerful developments in microrobotics that have been based on biologically-inspired systems, and to provide a resource for research and scientists interested in learning about the techniques themselves – their capability and limitations. We owe a great debt to many who helped us in various ways, from sharing their understanding to providing original research data. We do certainly appreciate all authors for their contributions. This book would not be possible without their work. The diverse backgrounds of the authors provide multiple perspectives of microbiorobotics that we present in this book. Special thanks should be given to our reviewers for providing detailed suggestions on all aspects of this book.

Many people read and commented on specific chapters, provided figures and materials, and spent much time with us in helpful discussions. We gratefully thank these people. We have been privileged to work with many gifted graduate and undergraduate students at Drexel University and Rensselaer Polytechnic Institute, all who contributed in part to further this research: Dr. Dalhyung Kim, Dr. Wonjin Jo, Dr. Anmiv Prabhu, Dr. Kevin Freedman, Dr. Gaurav Goyal, Armin Darvish, Yan Ou, Rafael Mulero, William Hesse, David Casale, and Kiran Phuyal. We would also like to acknowledge several funding agencies, National Science Foundation, Army Research Office, Korea Institute of Science Technology (KIST), and Ministry of Trade, Industry, and Energy (MOTIE) for financial support to our current microbiorobotics research programs.

MinJun Kim
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Part 1

Introduction

Motivation for microbiorobotics

For much of the history of robotics, research has focused on systems that have some relation in operational capability or length scale to humans. From the perspective of the layman, the very definition of robot is most often closely tied to the subclass of robotics relating to humanoids. Perhaps this isn't particularly surprising, since the methods of machining and the tools that we first developed are correlated with our ability to easily observe and manipulate objects at macroscopic length scales. That is, with the naked eye we can easily see objects down to the millimeter, and our hands are not adept at working with smaller objects. It is also not surprising that we have developed strong capabilities at developing much larger structures such as bridges and skyscrapers. In a sense, the bottom of the scale limits engineers more than the top, and we can consider the largest structures to be considered 'bottom-up,' a concept that is prevalent in nanotechnology. In the last decade, significant advances have been made in the field of microrobotics due to relatively recent advancements in both micromachining and microscopy. With the proliferation of several advanced tools for imaging and analysis, such as atomic force, electron, and confocal microscopies, coupled with the increasing availability of microfabrication technology, we can expect to see tighter integration between fundamental discovery and engineering applications.

Experimentalists in microscale robotics are inevitably led to consider two fundamental questions. Firstly, what can we learn from cells in terms of mimicking or integrating natural phenomena with robots? Secondly, how can we apply new microrobotic technologies to the fields of cell biology and medicine?

Cells are, in a sense, highly optimized and specialized microrobots. If we look at the function of a cell from the perspective of a beginning robotics course, we find striking analogs between cells and robots. Motor proteins perform as actuators, neurons and ion channels act as wiring, DNA and RNA act as memory and software, etc. The cellular systems are composed of elements that are self-assembled in the truest, atomistic sense from the bottom up. Proteins are the functional subunit of the cellular machinery, assembled into myriad actuators and sensors. In the current state of micro- and nanorobotics, we either mimic behaviors that are otherwise performed by these proteins, or we use whole, intact cells. For example, the behavior of the flagellum is currently replicated not by proteins, but by external magnetic fields [1–4], and the sensing of chemical compounds may be interfaced with mechanical measurements and solid-state microelectronics [5]. In the long view, however, it is only reasonable to expect that cellular subsystems will be successfully integrated with microfabricated, inorganic elements. Indeed, there is a significant progress being made in the effort to harness the power of motor proteins as microactuators.

The branches of bioengineering related to genetic engineering and synthetic biology will also inevitably be interfaced with microbiorobotics, from both the standpoint of sensors and actuators, or even combinations. In the field of optogenetics, we see a step toward this combination, the coupling of light exposure with muscle actuation [6]. If we're willing to expand our definition of robotics, another viable option is to reprogram whole cells to suit our needs. Bacterial and yeast cells have been reprogrammed to perform basic operations such as counting and timing [7,8].

One of the great challenges in microrobotics is expanding the current control capabilities from single or few-robot systems to many-robot systems. Since many of the current techniques are field based, it is no small task to accomplish. That is, individual control is limited by the divergence or resolution of the applied fields. In many current systems, sensing and control are performed at a much larger scale using the microscope as an interface. Despite the current limitations on the ability to create systems of independent microrobots, it is easy to imagine how such capabilities would greatly enable otherwise difficult tasks, such as the collective propulsion of large objects relative to the robot size, or collecting data in from disparate locations.

From the biomimetic point of view, multirobot systems seem like an obvious step along the continuum of technological advancement. Although there are certainly countless examples of microorganisms that go about their life cycle in a largely independent manner, there are also many examples of single-cell organisms that demonstrate collective behaviors, such as swarming bacteria [9].

Passive, circulating multirobotic systems can also easily be envisioned. Although much of the focus to date has been on actuation methods, sensing networks of passively flowing, perhaps even communicating robots. For instance, leukocytes detect and defend against infection in the human body. Although many of these cells circulate freely in the blood, they are able to sense and respond to foreign bodies. One can imagine another layer of robotic protection tasked with monitoring or even responding to disease.

As described, there are clearly myriad options for fundamental study on several levels with direct applicability to microbiorobotics. While the fundamental research by itself serves to motivate the subject as a whole, the application of microbiorobots to cellular research, drug delivery, or as working tools for other microscale tasks should prove to be fascinating.

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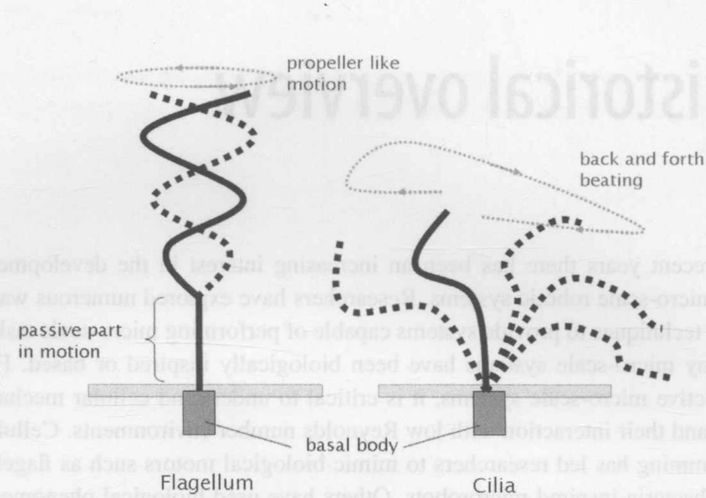
Historical overview

In recent years there has been an increasing interest in the development of micro-scale robotic systems. Researchers have explored numerous ways and techniques to provide systems capable of performing micro-scale tasks. Many micro-scale systems have been biologically inspired or based. For effective micro-scale systems, it is critical to understand cellular mechanics and their interaction with low Reynolds number environments. Cellular swimming has led researchers to mimic biological motors such as flagella for bacteria-inspired microrobots. Others have used biological phenomena and external stimuli for micro-scale robotic systems such as magnetotactic bacteria. Using bacteria as well as other microorganisms as a power source for a microrobot has also been investigated. Furthermore, mathematical modeling has been used to characterize cell behavior for control of microbiorobotic systems. Microbiorobotics has vast potential for creating robust micro-scale robotic systems.

LOW REYNOLDS NUMBER SWIMMING

The first step to building micro-scale robotic systems is to understand fluid mechanics at low Reynolds numbers. In low Reynolds number environments, viscosity is the dominating force, as inertia plays no role whatsoever. Motion at very low Reynolds number is entirely determined by the forces exerted on the organism at that moment and by nothing in the past [1]. Purcell's scallop theorem says that to achieve propulsion at low Reynolds numbers, reciprocal motion cannot be used. Purcell describes reciprocal motion as, "I change my body into a certain shape and then I go back to the original shape by going through the sequence in reverse. So, if the animal tries to swim by a reciprocal motion, it can't go anywhere." [1] The scallop theorem forms the basis of aquatic locomotion for micro-swimming devices [2].

To create efficient propulsion at low Reynolds numbers, the mechanics of biological motors such as flagella and cilia have been examined. Many bacteria, such as *Escherichia coli* and *Salmonella*, have several flagella attached at points distributed over the surface of the cell. The flagella, which are typically helical in shape, rotate in a corkscrew-like motion. While bacteria are swimming, the flagella come together in a synchronous flagellar bundle, which propels the cell [3]. For microorganisms with cilia, such as



■ **FIGURE 1** The swimming motion of bacterial flagellum and cilium. *From https://commons.wikimedia.org/wiki/File:Flagellum-beating.svg.*

Tetrahymena pyriformis and *Paramecium*, the locomotive cilium motion can be described in terms of two swimming strokes, effective (forward) and recovery (back). The cilia are aligned in arrays along the cell body and beat in a phase relationship with neighboring cilia [4]. The mechanics of flagella and cilia are shown in Fig. 1. These biological motors are efficient in low Reynolds number environments and are a source of inspiration for microbiorobotics.

TAXIS OF MICROORGANISMS

For the control of microbiorobots for micro-scale applications, external stimuli can be utilized. Many biological microorganisms respond to stimuli, such as magnetotaxis (magnetic fields), galvanotaxis (electric fields), phototaxis (light), and chemotaxis (chemicals). Based on the characterized behavior of microorganisms, these taxes can be applied to produce a desired response from the micro-scale robot. Responses from microbiorobots can be used as a method for chemical detection [5] or the manipulation of objects [6].

Magnetotaxis is used to change the direction of locomotion in motile organisms by inducing a magnetic stimulus [7,8]. Two different magnetotactic mechanisms, polar and axial, are found in different magnetotactic bacteria strains. Strains that swim in only one direction along the magnetic field are polar magnetotactic. These magnetotactic bacteria always swim towards either the north or south direction of the magnetic field, and will only reverse direction if exposed to a more powerful magnetic field. They always move