*E. coli* in Motion

The bacterium *Escherichia coli*—*E. coli* for short—has long been the organism of choice for unraveling biochemical pathways, deciphering the genetic code, learning how DNA is replicated and read, and even for manufacturing proteins of commercial interest. For some thirty years, it also has been a model for studying the molecular biology of behavior. *E. coli* swims in a purposeful manner, propelled by long thin helical filaments, each driven at its base by a reversible rotary engine. As a microscopic organism immersed in an aqueous environment, it has mastered physical constraints utterly different from any that we know, devising sensors, comparators, and motors on the nanometer scale.

This cross-disciplinary monograph describes these feats in a manner accessible to scientists, engineers, and others not trained in microbiology who would like to learn more about living machines. It treats the history of the subject, the physiology, physics, biochemistry, and genetics, largely from first principles. It is all about a small but remarkably sophisticated friend who lives in your gut.

Topics discussed include:

- How does *E. coli* move about?
- How do cells decide whether life is getting better or worse?
- What is the machinery that makes this behavior possible?
- How is the construction of this machinery programmed?
- How does this machinery work?
- What remains to be discovered?

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Howard C. Berg

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# Preface

Most bacteria are small, about one micrometer in diameter: ten thousand cells laid out side by side span the width of one's finger. Nevertheless, many species are motile. They swim using propellers (called flagella) that extend out into the external medium or, in the case of spirochetes, that rotate within the cell envelope. One marine bacterium appears to use submicroscopic external oars. Other common bacteria, equipped with large numbers of flagella, swarm rapidly over surfaces. Some bacteria glide over surfaces by extending and retracting thin filaments (called pili) that stick to the substratum at their distal ends, a kind of fly casting. Others move particles linked to the substratum along their outer membranes, by a mechanism as yet unknown. Bacteria of all kinds respond to changes in their environment, for example, to changes in temperature, light intensity, or chemical composition. In short, they move in a purposeful manner.

I have been interested in this world for more than 30 years. When I began, more was known about the genetics and biochemistry of the bacterium *Escherichia coli* than of any other free-living thing. So that has been the organism of choice. The emphasis has been on the responses of this organism to chemical stimuli: chemotaxis. Early work on the motile behavior of bacteria had been done with larger species, more easily seen in the light microscope, so these also are of interest.

How, exactly, does *E. coli* behave? What is the machinery that makes this behavior possible? How is the construction of this machinery programmed? How does this machinery work? And finally, what remains to be discovered?

Since *E. coli* is microscopic and lives in an aqueous environment, the physical constraints that it has had to master are very different from those that we encounter. For example, *E. coli* knows nothing about inertia, only about viscous drag: it cannot coast. It knows nothing about transport by bulk flow, only about diffusion;

as we will see, it can go where the grass is greener, but it has to wait for its dinner. So the methods that its cells use to move and sample their environment are strange to us. This is part of *E. coli's* charm.

This book is designed for the scientist or engineer, not trained in microbiology, who would like to learn more about living machines. However, it also should be accessible to the educated layman and of interest to the expert. I try to build on first principles. However, if you are overwhelmed by the facts that appear in a given chapter, please read on: the figures might suffice. References are given as entrée to the literature and a tribute to those who have done the work.

My own research has been supported by the Research Corporation, the U.S. National Science Foundation, the U.S. National Institutes of Health, and the Rowland Institute for Science. Much of the writing was done while a Fellow of the John Simon Guggenheim Foundation. Space for thought was provided by the Lorentz Institute, Leiden.

A large number of capable people have contributed to the body of knowledge to be described here: molecular geneticists, biochemists, microbial physiologists, physicists. Some, no doubt, will disagree with my emphasis. I can claim only a small part of this work as my own, built on the labor of students, postdocs, and other colleagues. The real hero is *E. coli.* If nothing else, I hope that this book will convince you that *E. coli* demands our admiration and respect.

HOWARD C. BERG

*Cambridge, Massachusetts*
August 2003

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