【Grant-in-Aid for Transformative Research Areas（B）】

The reason why microbes are moving: the birth of behavioral microbiology beyond the Leeuwenhoek era

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Purpose and Background of the Research

●Outline of the Research

Approximately 350 years ago, Antonie van Leeuwenhoek was the first to discover microorganisms. At that time, life sciences were not well developed, and even microbial culture techniques had not been established. How was he able to recognize that these small objects were alive? The reason lies in "motility." Single-lens microscopes of his own design and make had high resolution that allowed him to observe a myriad of moving microorganisms in a single drop of pond water. This was the discovery of microorganisms as well as their motility.

Currently, research on microbial motility has become a transdisciplinary field, combining bioengineering, physics, and natural history, and several studies have been conducted on the detailed observation of motility, atomic-level structure of locomotor devices, and mechanics of force generation. However, despite the great technological advances that have been made since the days of Leeuwenhoek, there is still a simple and essential unanswered question: "Why do these tiny organisms need to move around?"

In the past, it has been difficult to properly study microorganisms, their behavior, ecology, and evolution. However, innovative advances in sensor technology, not only in microscopy but also in high-sensitivity cameras, have enabled the capture and analysis of the behavior of individual microorganisms over a wide area and at high speeds. By incorporating new theoretical frameworks and research approaches from ethology and evolutionary ecology into advanced measurement technology and knowledge from physics, a new field of "behavioral microbiology" that will provide an adequate answer to why microorganisms move is being developed (Fig. 1).

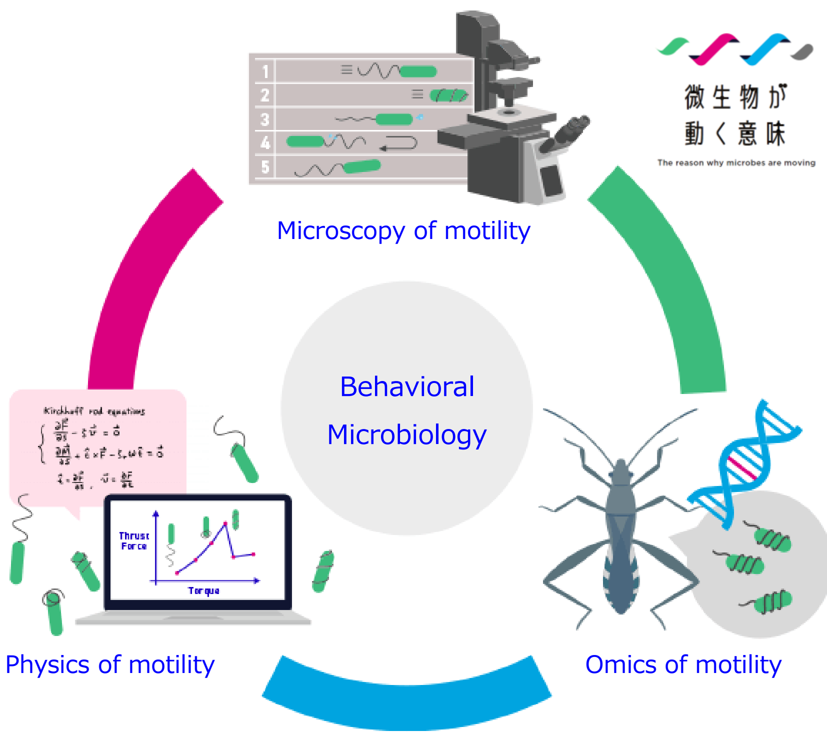

Figure 1. Overall view of behavioral microbiology. We utilized advanced microscopy technologies to measure the motility of microorganisms, analyze their physical background and genetic basis, and further understand the evolution and ecology of bacterial motility.

●Flagella drill motility of bacteria

It is assumed that Leeuwenhoek observed that flagellar motility of bacteria. The flagellum is a typical locomotor device of bacteria, in which a motor inside the cell rotates a helical fiber structure, enabling bacteria to swim smoothly in water (Fig. 2, top). However, we recently discovered that the flagellum has a new, unprecedented mode of motility: some bacteria can reverse their motors, wrap their flagella around their own bodies, and swim like drills (Fig. 2, bottom). This research area specifically targets "flagella drill motility" and promotes three different approaches, "A01 Measurement of Motility"; "A02 Physics of Motility" (Fig. 3); and "A03 Omics of Motility" (Fig. 4), in a parallel and coordinated manner to understand its mechanics and ecological significance.

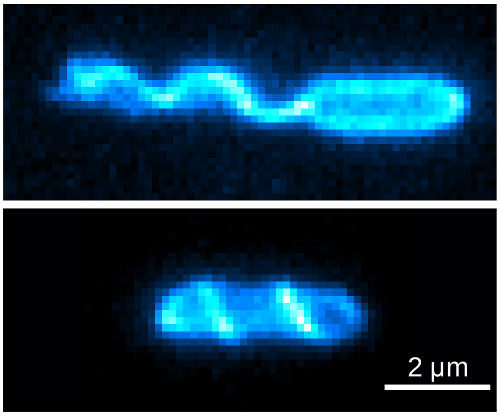

Figure 2. Commonly reported swimming-type motility (upper row). Drill motility, which we identified (bottom row).

Expected Research Achievements

●Elucidation of the mechanics and ecological significance of flagella drill motility in symbiotic and pathogenic bacterial model species.

What is the purpose of flagella drill motility? Until now, microbial motility has been studied under limited laboratory conditions, such as in culture media with model species including *Escherichia coli*. However, to understand the ecological significance of microbial motility, it is necessary to know when, where, and how motility functions and to observe and analyze microbial motility in native environments. Observation in a native environment, which is quite common in ethology, is still neglected when dealing with microbial behavior because of the technical hurdles involved.

Flagella drill motility has been observed in particularly viscous environments and exclusively in several symbiotic and pathogenic bacteria in animals. This suggests that it is likely used to break through viscous environments, such as the gut of host animals, to establish symbiosis and infection. In this study, we focused on the *in vivo* flagella drill motility of *Burkholderia*, an insect gut symbiont, and *Campylobacter*, a cause of food poisoning, in hosts as model systems to elucidate the ecological significance of their behavior and conduct interspecies comparisons and gene transplantations.

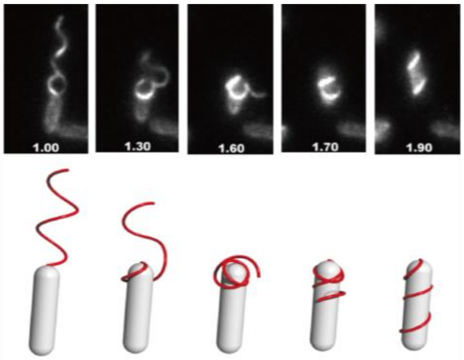

Figure 3. Simulation of flagella drill motility.

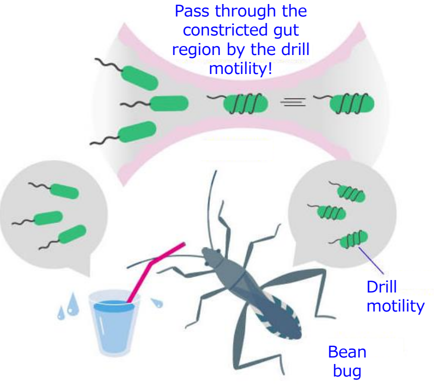

Figure 4. Critical role of flagella drill motility in insect-microbe symbiosis.

We believe that the success of this research area will help us understand the significance of flagella drill motility as well as open a new window in behavioral microbiology to elucidate the significance of "motility of microorganisms," which exhibit amazingly diverse movements.

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