【Grant-in-Aid for Scientific Research (S)】

Broad Section C

Title of Project : Study on active transport phenomena for predicting and controlling biological active matter

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Research Project Number : 21H04999 Researcher Number : 20313728
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Keyword : Microorganism, Taxis, Collective behavior, Biomechanics, Continuum mechanics, Simulation

【Purpose and Background of the Research】

With the recent development of molecular biology, life sciences at the molecular and cellular scales have made tremendous progress. However, engineering has not fully benefited from this progress. The main reason for this is that the development of biology at the molecular and cellular scale has not been connected to the macroscopic continuum scale, which is often important in engineering. In medicine, for example, the lack of understanding of the behavior of bacteria in the intestinal environment is a major obstacle to the diagnosis and treatment of intestinal flora. Also, in the case of red tides, which are a global environmental problem, the growth and accumulation of microalgae in the physical environment have not yet been elucidated, and this has become an obstacle in predicting outbreaks. Thus, the impact of molecular and cellular biology on continuum-scale transport phenomena remains unclear, stalling the resolution of macroscopic health and environmental problems involving microorganisms.

In this study, we regard collective nature of motile micro-organisms as biological active matter, and attempt to predict and control the behavior of biological active matter. In order to break the current bottleneck in the field, we aim to construct a study on the active transport phenomena. The study quantitatively describes macro-scale transport of cells, mass, and momentum by building up blocks from the cellular scale, which can provide a new methodology to the fields of biology, physics and engineering.

【Research Methods】

For the prediction and control of biological active matter, we construct a microbial analysis platform in this study. The theoretical basis of the platform is the study of transport phenomena incorporating cell biology, which mainly consists of three conservation laws: momentum, nutrient and cell number. The momentum conservation law describes the flow of a suspension. This flow governs the advection, diffusion, and rheotaxis of cells and nutrients. The nutrient conservation law describes the advection, diffusion, and consumption of nutrients. This concentration field affects the chemotaxis and growth rate of cells. The cell number conservation law describes the advection and diffusion of cells, their proliferation, and cell-cell inter-actions. The validity of the mathematical model is examined by comparing with the experimental results.

We focus on microorganisms such as bacteria and microalgae and confront important issues in engineering, medicine, and biology, such as intestinal flora, red tides, and the origin of multicellular organisms. Based on our world leading microbial biomechanics, we will construct a study of active transport phenomena by employing a bottom-up strategy, from cellular to meso and macro scales. The study on active transport phenomena will be a powerful methodology to pioneer the related fields.

【Expected Research Achievements and Scientific Significance】

In the study of intestinal flora, we will build a simulator to solve the coupled transport of momentum, mass, and bacteria in the intestine. We will also conduct live imaging of zebrafish intestine to elucidate the transport phenomena of intestinal flora. Intestinal flora is closely related to diseases such as colorectal cancer and ulcerative colitis. The results of this research would be useful for diagnostic and therapeutic techniques for intestinal diseases.

In the study of red tide, we will develop a simulator that can reproduce the daily vertical movement of microalgae. We will elucidate the mechanism of accumulation of microalgae depending on the physical environment. The results of this research will be useful in predicting red tide outbreaks and in reducing damage in the aquaculture industry through early shipping.

In the study of the evolution to multicellular organisms, *Volvocine* algae and sponges will be used as model organisms to elucidate the enhanced mass transport by means of multicellularity. This will help us to answer the fundamental question in biology on why organisms became multicellular.

This research can provide a new tool of prediction and control by simulation to the fields of engineering, science, and biology involving microorganism, which leads to quantitative understanding of active transport phenomena.

【Publications Relevant to the Project】

- T. Omori, H. Ito, T. Ishikawa. Swimming microorga-nisms acquire optimal efficiency with multiple cilia. *Proc. Natl. Acad. Sci. USA*, **117**, 30201-30207 (2020)
- A. Srivastava, K. Kikuchi, T. Ishikawa. The bubble induced population dynamics of fermenting yeasts. *J. R. Soc. Interface*, **17**, 20200735 (2020)
- T. Ishikawa, D. R. Brumley, T. J. Pedley. Rheology of a concentrated suspension of spherical squirmers. *J. Fluid Mech.*, **914**, A26 (2021).

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