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学 位 論 文 内 容 の 要 旨

博士の専攻分野の名称　博士(生命科学)　氏　名　熊倉　大騎

学 位 論 文 題 名

Functional Specialization and Phenotypic Plasticity: A Mathematical Modeling Approach to Microbial Growth Dynamics
（機能分業と表現型可塑性：微生物の生存戦略に基づく増殖モデル研究）

This study aims to propose a growth model that considers the functional division system to understand the phenotypic plasticity and survival strategies of microorganisms and comprehensively understand the growth dynamics of microorganisms. The growth dynamics of microorganisms vary significantly depending on cultivation time and environmental conditions. The empirical equation by Monod (1949) is a classical theory that explains the relationship between microbial growth rate and limiting substrates, but it cannot fully capture the complex growth dynamics observed. Therefore, this study seeks to construct a new mathematical model that considers the functional division of microbial subpopulations and aims to analyze the behavior of microorganisms during the cultivation process.

Conventional microbial culture models are generally divided into three phases: the growth phase, the stationary phase, and the death phase. However, these phases do not sufficiently explain microbial growth dynamics. In particular, the stationary phase is often regarded as a period where microbial growth completely ceases, but slight growth and death exist, and equilibrium is not achieved. Additionally, existing models have primarily focused on the growth phase, with little consideration given to microbial behavior in the later stages of cultivation. To address these issues, this study proposes a microbial growth model that considers the allocation of energy obtained from substrates and analyzes the formation of subpopulations and their roles.

In this study, we propose a new mathematical model for microbial growth that includes limiting substrates and metabolic products. In this model, the energy obtained by microorganisms from consuming substrates is divided between a population responsible for growth and a population responsible for decomposing metabolic products. The growth dynamics were calculated under the assumption of functional division based on the roles of each subpopulation. Furthermore, parameter estimation was conducted using actual culture data, and the impact of metabolite accumulation on microbial growth was quantitatively evaluated.

Numerical analysis revealed that microbial growth can be classified into six stages: three in the growth phase, two in the stationary phase, and one in the death phase. Notably, it was confirmed that after the death phase, the accumulation of metabolic products leads to the loss of microbial growth capacity. This suggests that microorganisms may adopt a two-stage strategy, first rapidly consuming the substrate to increase their density and then purifying the environment afterward. Exploration of parameter dependencies revealed that microorganisms might switch between a strategy of rapid growth by consuming substrates and a strategy of slow growth while purifying the environment, depending on the situation. Furthermore, based on differences in sensitivity to metabolite accumulation, microorganisms were classified into three types: resistant, moderately sensitive, and highly sensitive. Data analysis allowed for the precise definition of previously ambiguous stages and demonstrated that microorganisms grow slowly while purifying the cultivation environment. This highlighted the importance of phenotypic plasticity and subpopulation formation in the growth dynamics of microorganisms. This study has provided a new perspective on understanding the factors that inhibit microbial growth and the adaptive strategies used in response to changes in cultivation conditions. The findings are expected to significantly contribute to future applications in microbial ecology and biotechnology.