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# 論 文 内 容 の 要 旨
## Abstract of Dissertation

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In recent years, several severe global environmental problems are proceeding and one of the solutions is a shift to a sustainable economic system utilizing biotechnology. Biotechnology utilizing valuable microorganisms can continuously produce food and chemical compounds using bioproducts. Among the production process of bioproducts, the scale-up examination is important for production on an industrial scale. To increase the yield of useful material produced in large cultivations, monitoring the internal environment of a large cultivation tank (jar fermenter) using various sensors in real-time and controlling optimum cultivation conditions based on the results of monitoring are effective. There are various types of indicators for monitoring the jar fermenter. Since microorganisms respond to the extracellular environment and the influence is reflected in the microbial morphology, the microbial morphology may be utilized as a more useful indicator of microbial cultivation than the other conventional monitoring indicator (pH, dissolved oxygen, etc.). However, a trade-off exists between speed and image quality when acquiring morphological information, which it was difficult for the microbial morphology to be acquired at high-definition continuously as well as other sensors. In this thesis, the author aimed to develop a real-time monitoring system in a jar fermenter utilizing microbial morphology.

Chapter 1 describes the background of this research, especially the monitoring method for a large-scale cultivation of microorganism, and mentions the significance of this study.

Chapter 2 describes a module that can acquire microbial morphology in high-definition from one-batch cultivation in the jar fermenter by using a microscope, a developed microfluidic device, and a high-speed camera. By using this module, the following points were demonstrated: 1) Images could be acquired with a sufficiently high resolution to observe organelles of cell in the flowing cultivation medium through the microfluidic device. 2) A large number of images could be captured at high speed, and more than 10,000 cell images could be acquired in 2.2 seconds in one take. This image acquiring rate was comparable to cell sorter. The developed module could acquire morphological parameters of microbes in real time like the other general monitoring sensors.

Chapter 3 describes the estimation of the culture state (growth or materials productivity) through analysis of images acquired using the developed real-time monitoring system. For image analysis, a deep learning was applied. Oleaginous yeasts were used for the demonstration since these yeasts are some of the most capable for industrial use and insights in the relationship between their morphology and their growth or lipid-productivity has not been clarified. The deep learning image analysis with training data showed a high correlation between the specific cell image and the growth/lipid productivity of the microorganisms. In addition, image analysis using deep learning without training data also confirmed a high correlation between cell image and

growth/lipid productivity. Moreover, there seemed to be species-dependent differences in the relationship between the morphology and the state of cells.

Finally, in chapter 4, the results presented in this thesis are summarized and discussed the usefulness of these developed modules and future issues.