ADVANCED RAMAN MICROSPECTROSCOPY FOR SINGLE-CELL METABOLOMICS OF MARINE MICROORGANISMS

Masahiro Ando*†[1], Kaori Sugiyama[1], Koya Kubo[2], Shumpei Horii[2], and Haruko Takeyama[1,2,3]

[1]Research organization for Nano and Life Innovation, Waseda University – Japan
[2]Graduate School of Advanced Science and Engineering, Waseda University – Japan
[3]Institute for Advanced Research of Biosystem Dynamics, Waseda Research Institute for Science and Engineering, Waseda University – Japan

Abstract

We present an innovative analytical platform for single-cell metabolomics of marine microorganisms using confocal Raman microspectroscopy with multivariate curve resolution (MCR) analysis. While single-cell genomics has revolutionized our understanding of microbial diversity, it provides limited insight into cellular metabolism. Our Raman-based approach bridges this gap by enabling label-free, non-destructive metabolite profiling with subcellular resolution (_˜0.5 μm), complementing genomic data with direct metabolic insights. Unlike conventional techniques requiring cell extraction, our method visualizes metabolites in their native cellular environment without sample preparation artifacts. By applying physicochemically reasonable constraints during MCR analysis, we extract distinct metabolite signatures from complex cellular Raman data. We demonstrated this using the marine diatom *Chaetoceros tenuissimus* (1), identifying polyunsaturated fatty acids that distinguish between proliferative and non-proliferative states. The non-destructive nature of our approach enables sequential analysis, where cells can first undergo Raman profiling and subsequently be subjected to genomic analysis, creating a powerful multi-omics workflow. This non-destructive approach opens new frontiers in marine biotechnology by enabling real-time visualization of metabolic processes, detection of transient metabolic states, and direct observation of cellular responses to environmental stimuli-capabilities impossible with conventional destructive methods. The ability to observe metabolites in their native cellular context represents a significant advancement for understanding the chemical ecology of marine microorganisms.
(1) Ando, M., et al., *J. Phys. Chem. B*, **127** (2023) 5027.

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*Speaker
†Corresponding author: mando@aoni.waseda.jp