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論文審査の要旨及び審査員

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論文審査の要旨（2000 字程度）

This thesis is entitled “Genomes and Single-Cell Phenotypes at Life’s Temperature Extremes: A Case Study of Methanogenic Archaea”. It is composed of five chapters, each of which describes the adaptive features of methanogenic archaea observed at the genome level or through single-cell observable growth phenotypes.

Chapter 1 gives a brief introduction to methanogenesis and its impact on the global carbon cycle on Earth today, as well as its biogeochemical role through Earth’s history.

In Chapter 2, differences in genome function and composition between psychrotolerant and thermotolerant methanogens are investigated across 86 cultured species using comparative genomics approaches. The author finds that (1) The conserved genomic core of methanogens makes up around one third of a genome on average, and the shared genome content of two species decreases with increasing phylogenetic distance, (2) Throughout the core and pangenomes, charged amino acids, leucine, and isoleucine contents increase with temperature, while polar uncharged amino acids are more abundant at lower temperatures, and (3) Thermotolerant methanogens are enriched in metal and other transporters, and psychrotolerant methanogens are enriched in proteins related to structure and motility. The author concludes physiology shapes genome content more than phylogenetic relatedness in the methanogens.

Chapter 3 focuses on physiological responses to temperature at the single cell level. Using stable isotope probing in combination with high resolution spatial mass spectrometry, physiological responses are assessed for two psychrotolerant, two mesophilic, and two thermotolerant methylotrophic species grown in pure cultures. The author examines single cell phenotypic heterogeneity at different growth temperatures, and finds that carbon uptake heterogeneity is high in cold growth, and nitrogen uptake heterogeneity increases with growth temperature. The results show that while low temperatures slow down growth, they do not necessarily induce cellular stress responses. The author also examines spatial heterogeneity for cells of *M. burtonii* which occur in microcolonies, and finds that in the cold condition cells on the outside of the aggregates incorporate more substrate than the inner cells. The author attributes this heterogeneity to asymmetric cell division or cellular interactions.

Chapter 4 introduces the use of metabolic modeling to study the different metabolic modes responsible for the observed phenotypes of *M. burtonii*, giving an insight into metabolic flux variations and differences, in an attempt to explain the causes of phenotypic heterogeneity. A core metabolic model for methylotrophic methanogens is created in a top-down approach from an existing genome scale model, by maximizing random gene deletions while maintaining sufficient biomass and methane output fluxes. Flux boundaries in the core model are then modified based on media composition and observed cell growth. The flux simulation for the phenotype with the mean carbon and nitrogen assimilation rates at 23°C is found to be similar to carbon limited phenotypes of both temperatures, while methanogenesis fluxes remain high.

Chapter 5 describes conclusions and outlook.

In summary, this thesis documents adaptive mechanisms of methanogens to varying growth temperatures from standpoints of (1) compositional, functional, and structural differences in genomes, (2) single cell phenotypes and population heterogeneity, and (3) the underlying metabolic modes of single cells. The author deserves to receive a Doctor of Science from the Tokyo Institute of Technology.