Hedging your bet(-hedging): A population-level strategy for optimizing microbial growth

MCCLELLAND HLO[12*], FIKE DA[1], JONES C[1], CHUBIZ L[3] & BRADLEY AS[1]

(*correspondence to: hl.mcclelland@gmail.com)

1. Department of Earth and Planetary Sciences, Washington University in St. Louis, USA
2. Department of Earth and Planetary Sciences, Weizmann Institute of Science, Israel.
3. Department of Biology, University of Missouri – St. Louis, USA

Natural environments at the scale of microbial life are heterogeneous and mutable. The ability of microbial cells to optimize growth in the presence of new substrates or multiple substrates is a key component of fitness, and thus an important feature on which natural selection operates. Selection acts on individual cells, and newly emergent single-cell technologies have shown that there is significant heterogenetiy in gene regulation across microbial populations, challenging the canonical model in which shifts in substrate specialization always occur on a population-wide basis. However, direct measurements of metabolic rates or biomass synthesis in individual cells have largely remained elusive.

Here, we have employed the use of isotope labels and secondary ion mass spectrometry (SIMS) to provide the first direct evidence of anabolic specialization in single cells throughout a period of diauxic growth. In the model methylotroph *Methylobacterium extorquens* AM1, we find that although metabolic specialization may be heterogeneous within the population, ultimately all cells utilize the same substrate for biomass synthesis throughout the period of growth. This is likely achieved through the sharing of metabolic intermediates. We propose that this apparent cooperation between clonal cells represents a powerful population-level strategy for substrate specialization, which arises through the stochastic expression of part of the metabolic pathway, and that the sharing of metabolic intermediates acts to minimize the risk associated with bet-hedging for individual cells.