

# 嫌気条件下での出芽酵母を用いた生育結合増産の可能性

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## Growth-coupled overproduction is theoretically possible for most metabolites in *Saccharomyces cerevisiae* under anaerobic conditions

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**Abstract:** Metabolic network analysis through flux balance is an established method for the computational design of production strains in metabolic engineering. A key principle often used in this method is the production of target metabolites as by-products of cell growth. Recently, the strong coupling-based method was used to demonstrate that the coupling of growth and production is possible for nearly all metabolites through reaction deletions in genome-scale metabolic models of *Escherichia coli* and *Saccharomyces cerevisiae* under aerobic conditions. However, it is unknown whether this coupling, using reaction deletions, is always possible under anaerobic conditions. In fact, when growing *S. cerevisiae* under anaerobic conditions, deletion strategies using the strong coupling-based method were possible for only 3.9% of all metabolites. Here, we found that the coupling of growth and production is theoretically possible for 91.3% metabolites in genome-scale models of *S. cerevisiae* under anaerobic conditions if any reaction deletion strategy is allowed. This analysis was conducted for the worst-case-scenario using flux variability analysis. To demonstrate the feasibility of the coupling, we derived appropriate reaction deletions using a new algorithm for target production in which the search space was divided into small cubes (CubeProd). Our results are fundamentally important for computational metabolic engineering under anaerobic conditions. The developed software, CubeProd, implemented in MATLAB, and the obtained reaction deletion strategies are available at (<http://sunflower.kuicr.kyoto-u.ac.jp/~tamura/CubeProd.zip>). Details of this research are available on (<https://www.biorxiv.org/content/10.1101/563437v2>).

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