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Metabolic Network Analysis of Lysine Producing *Corynebacterium glutamicum* at a Miniaturized Scale

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Abstract:

We present a straightforward approach comprising ^{13}C tracer experiments at 200- μL volume in 96-well microtiter plates with on-line measurement of dissolved oxygen for quantitative high-throughput metabolic network analysis at a miniaturized scale. This method was successfully applied for cultivation and ^{13}C metabolic flux analysis of two mutants of lysine producing *Corynebacterium glutamicum* (ATCC 13287 and ATCC 21543). Microtiter-plate cultivations showed excellent accordance in kinetics and stoichiometry of growth and product formation as well as in intracellular flux distributions as compared with parallel shake-flask experiments. These cultivations further allowed clear identification of strain-specific flux differences such as increased flux toward lysine, increased flux through the pentose phosphate pathway (PPP), decrease flux through the tricarboxylic (TCA) cycle, and increased dihydroxyacetone formation in *C. glutamicum* ATCC 21543 compared with ATCC 13287. The present approach has strong potential for broad quantitative screening of metabolic network activities, especially those involving high-cost tracer substrates.

Key-words: ^{13}C , flux, microliter plate, mass spectrometry