

# Precision fermentation with mass spectrometry-based spent media analysis

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## Abstract

Optimization and monitoring of bioprocesses requires the measurement of several process parameters and quality attributes. Mass spectrometry (MS)-based techniques such as those coupled to gas chromatography (GCMS) and liquid Chromatography (LCMS) enable the simultaneous measurement of hundreds of metabolites with high sensitivity. When applied to spent media, such metabolome analysis can help determine the sequence of substrate uptake and metabolite secretion, consequently facilitating better design of initial media and feeding strategy. Furthermore, the analysis of metabolite diversity and abundance from spent media will aid the determination of metabolic phases of the culture and the identification of metabolites as surrogate markers for product titer and quality. This review covers the recent advances in metabolomics analysis applied to the development and monitoring of bioprocesses. In this regard, we recommend a stepwise workflow and guidelines that a bioprocesses engineer can adopt to develop and optimize a fermentation process using spent media analysis. Finally, we show examples of how the use of MS has revolutionized the design and monitoring of bioprocesses.

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