APPLICATION OF METABOLOMICS AND FLUXOMICS TO INCREASE PRODUCTIVITY AND PREDICT PRODUCT QUALITY

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Process development is routinely performed at different scales, amongst different clones, and with different optimization goals. In this work, we examine how these variables impact and relate to cell metabolism in fed-batch process, with the goal of increasing productivity and tuning product quality. Three unique CHO clones producing different IgGs were evaluated at the 250mL, 2L, and 500L scales. The impact on cell metabolism from clonal variation, reactor designs, and batch time was quantified in this work. Likewise, metabolism in turn influences final product titers and product quality profiles. To comprehensively understand this influence, over 500 extracellular metabolite time-course profiles were considered by empirical modeling, including principal component analysis (PCA) and orthogonal partial least squares (OPLS) models.

Through empirical modeling, we examined the impact of metabolism on final titer. With the objective of increasing final titer, the model identified a cluster of six metabolites (out of 500+) with a shared pathway at the interface of amino acid and glycerophospholipid metabolism. The expression of these clustered metabolites correlated strongly with final product titer at multiple stages of the fed-batch run. In addition to these findings, we will share how metabolism correlated with product quality.

As development batches often have different initial cell densities and growth kinetics, we also converted all supernatant metabolite expression profiles into specific consumption rates. This enabled a less biased and more straightforward comparison between batches. Likewise, a unique model comparison was enabled, one based upon metabolite concentrations (metabolomics) and one based upon metabolite fluxes (fluxomics). Both will be presented at this conference.