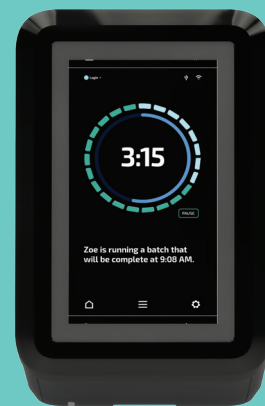


At-line spent media analysis is now a reality – don't get left behind.



BACKGROUND

There is a need for advanced process analytic technologies that can monitor cell media nutrients and cellular metabolites alongside bioreactors in process development labs. Timely analysis of media components during a process contributes to the understanding of critical environmental or nutrient influences on cell health and productivity. Biochemical analyzers based on enzymatic assays deliver useful data, but they do not give a complete picture of the bioreactor state as they are limited to a small number of analytes. Comprehensive spent media analysis of amino acids and other media components is bottlenecked by core lab turn-around times which slow media optimization and process decisions severely. To elevate process development decisions to real-time, researchers require new analytical platforms that simplify analysis and accelerate delivery of actionable intelligence.

THE EXPERIMENT

Traditional spent media analysis requires at least two separate HPLC runs for the coverage of both amino acids, vitamins, and other components. The Rebel™ eliminates this complexity by analyzing each sample for amino acids, vitamins, amines and dipeptides in a single run. In this example, tiny bioreactor samples (approx. 10 µL) were diluted 100X with Rebel diluent and run on the Rebel. For simplicity, the average from four replicate runs per sample was plotted for the amino acids present in the media only (Figure 1).

DISCUSSION

Spent media analysis should no longer be a lengthy process for any researcher. As highlighted here, a simple 7 minute daily run on the Rebel can provide quantitation for a broad set of media components like the amino acids shown here. In this fed-batch process, there were amino acids like Asn, Gln, His, Met, Pro, Ser and Trp which all were lower in concentration at the end of the process compared to their initial concentrations. Conversely, there was a buildup of the amino acids like Ala, Arg, Asp, Glu, Gly, Phe, Thr, Tyr and Val. In particular, there was a substantial increase in the amount of Gly in the culture highlighting that the media contained excessive amounts of it in the feed. With the Rebel alongside both bioreactors and conventional biochemical analyzers, process development researchers can now reveal deeper process insight via media nutrient levels in near real-time.

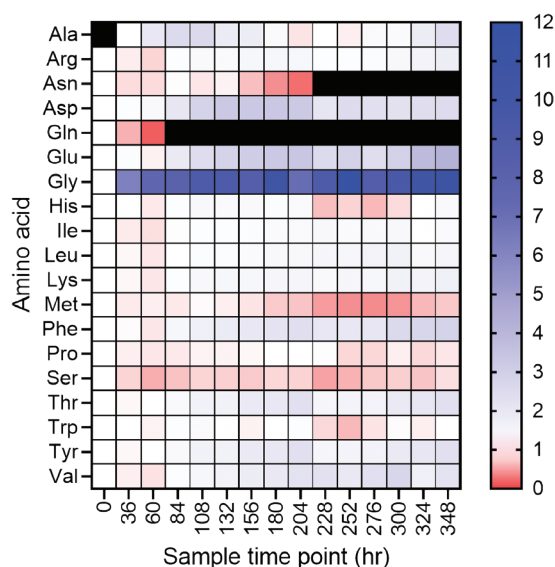


Figure 1: Selected media components from a time-lapse spent media analysis of a 14-day fed-batch process of Chinese-hamster ovary cells producing an IgG. The color scale is the normalized amount of each component relative to the first concentration it was detected at. Black squares represent time points when a component was not detected.

