THE POWER OF AT-LINE AMINO ACID MEASUREMENTS FOR ACCELERATED PROCESS AND MEDIA DEVELOPMENT OF A MAB-EXPRESSING CHO CELL LINE

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Biologics production development for intensified processes aims to achieve desired product quality attributes and high productivity. Running multiple micro-bioreactors in parallel enables expedited optimization, but low microbioreactor volumes limit the media available for daily sampling for analysis. Cell culture media (CCM) optimization can be a lengthy and complex process involving multiple DoEs. Fast, at the point-of-need, analytical tools with only minimal sample consumption, are required to assess key-nutrient consumption and provide feedback to enable feed strategy optimization.

Presented here are data-driven and accelerated CCM selection, screening, and optimization leveraging an automated at-line capillary electrophoresis - mass spectrometry analyzer (the REBEL) requiring only 10 µL per sample. High throughput CCM panel screening and feed optimization experiments were performed using a mAb producing GS-CHO cell line in the Ambr 15. Daily monitoring of the spent media for typical metabolites (cell counts, viability, ammonia, lactate etc); amino acids (AA) using the REBEL, and CQAs at harvest were measured. CHO cell growth and production were correlated to CCM components consumption to optimize the feeding strategy for this cell line.

The first experiment, Ambr15#1, was a media screening of 8 commercially available CCM utilizing 48 vessels. From this, four media were taken forward to the next experiment Ambr15#2, in which feeding strategy was tested: AA identified to have depleted in Ambr15#1 were fed as a separate bolus, in addition to three levels of the commercial feed.

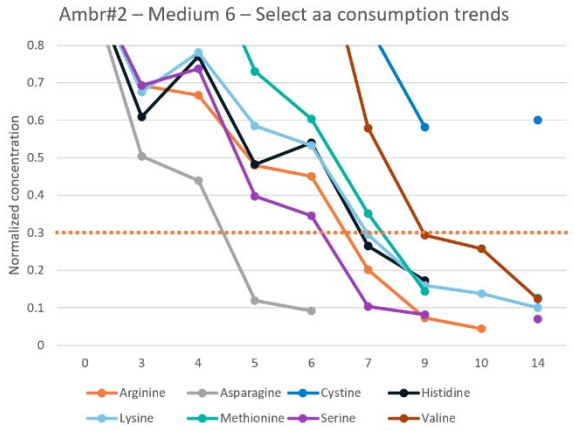

Figure 1. The REBEL analysis of the media screening experiment Ambr15#1showed several AAs depleting during the time course in the best performing (by growth and titer) CCM.

Ambr15#2 run showed how a lower level of feed, combined with the highly consumed AA feeding provided an advantageous profile of productivity and low toxic metabolites. A higher level of the commercial feed increased the toxic metabolites in the CCM.

The project proceeds to further experimentation: defining the feeding strategy (commercial feed and AA) as well as scale-up up to 10Lscale.

The effect of amino acid concentration adjustments on titer, growth, toxic metabolites, and critical quality attributes is presented. Data-driven media and process optimization of a mAb expressing cell line using an at-line REBEL analyzer for targeted metabolite quantitation.