

## **BIOPROCESS INTELLIGENT FOR THE IMPROVEMENTS AND PREDICTION ON FED-BATCH CELL CULTURE IN BIOREACTOR**

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With advances in biotechnology, the antibody productivity is not the only issue in biopharmaceutical manufacturing; moreover, how to control the quality and quantity of antibody production in bioprocess has become prominent. In typical fed-batch cell culture, it is not easy to control the dynamic cultivation and feeding conditions. The study is to present an intelligent bioprocess make use of design of experiments (DOE) and multivariate data analysis (MVDA). In the culture medium optimization, we performed the medium screening with the DOE method in shake spin tubes and shake flasks. DOE provides a cost-effective methodology for medium development and optimization, and furthermore we utilized multivariate data analysis methodology to build up the fed-batch intelligence bioprocess in 5 L bioreactor. We analyzed mass data transferred from 5 L bioreactor process and established the fed-batch culture model with SIMCA software. Combination of the batch process and big data sets, we can be easy to do batch-to-batch comparison, cell culture profile prediction, and key parameter finding to improve the process performance with more steady product quality and less error. In this fed-batch culture model, we achieved more than 5 g/L cell productivity consistently and predictably in 5 L bioreactor cultivation with CRISPR-mediated targeted gene site-specific integration CHO cell line.