

Example 3: Comparison of Feedback Control and Bolus Fed Strategy

Materials and Methods

Cells were cultured under feedback control or bolus fed strategy as described above.

Results

Figure 11 shows the difference in PTMs in cells cultured using the feedback control or bolus fed strategy. Each pair of columns represents a batch day. For each pair of columns, the left column is the feedback control data, and the right column is the bolus fed data. The feedback control strategy (left column for each pair of columns) was confirmed to reduce the level of %PTM in the subsequent experiment as compared to the bolus feed strategy (right column for each pair of columns). The steady-state addition of a dose of nutrients continuously over time allows for the production of bioproducts having lower levels of PTM in comparison to bolus fed strategy. The %PTM was also reduced from the bolus feed strategy thus demonstrating the ability to control the antibody quality. The data are from a comparison between a bolus fed strategy that does not include Raman Spectroscopy feedback control to a feed system that does include Raman Spectroscopy feedback control.

The disclosed feedback control culture systems and methods provide real-time multi-component analysis without sample removal. Real time data enables automatic feedback control for continuous nutrient addition. Reduced, steady bioreactor concentrations of reactive nutrients results in lower level of antibody PTM by over 50% from standard bolus nutrient feed thus improving product quality and consistency.

While in the foregoing specification this invention has been described in relation to certain embodiments thereof, and many details have been put forth for the purpose of illustration, it will be apparent to those skilled in the art that the invention is susceptible to additional embodiments and that certain of the details described herein can be varied considerably without departing from the basic principles of the invention.