Spring 5-11-2015

Implementation of Raman spectroscopy at manufacturing scale: Overcoming modeling challenges while implementing advanced process control

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IMPLEMENTATION OF RAMAN SPECTROSCOPY AT MANUFACTURING SCALE: OVERCOMING MODELING CHALLENGES WHILE IMPLEMENTING ADVANCED PROCESS CONTROL

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Key Words: Raman Spectroscopy, Mammalian cell culture, Glycation, Fluorescence, Manufacturing Scale

In order to improve glycation control in our new high intensity platform process, we investigated implementation of Raman spectroscopy to monitor and control glucose at low levels throughout the process. Using Raman allows a way to measure glucose near real time which in turn allows for a more responsive and flexible control algorithm. Prior literature has shown connections between elevated glucose levels and glycation when in presence of high protein concentrations, which was indicative of our process. Using Raman along with advanced process control (APC), allowed us the flexibility to reduce glycation back towards historical process levels.

We will share a case study of how Raman models were built using the RXN2-785 system and later deemed unresponsive due to high levels of fluorescence on day 5 of a 14 day process. We will discuss potential sources of the fluorescence and provide a multi-product comparison for perspective. Additional development effort was required in tight time frame to derive a manufacturing ready solution to this challenging problem. We will describe what that solution was and how we were able to successfully create new models with errors acceptable within our process control strategy design. Lastly, we will demonstrate how controlling glucose at lower levels during the process impacted glycation. Our work ended with two engineering runs at 17,000L scale where we used Raman spectroscopy to successfully monitor and control glucose at a lower set point and effectively lower glycation by 40% of its original value.