

FEEDBACK CONTROL OF INTENSIFIED FED-BATCH MAMMALIAN CELL CULTURE USING INLINE RAMAN SPECTROSCOPY

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The monitoring and control of mammalian cell culture processes are critical for the development of biotherapeutics in drug development. Current control of fed-batch processes using offline sampling is infrequent and can miss important metabolic shifts that can impact product quality and consistency. Raman spectroscopy can provide in-line monitoring of multiple metabolites and critical process parameters for improved process control. In this research a generic model was developed for monitoring and control of a Lonza intensified fed-batch platform process across multiple cell lines. Parameter estimates for glucose, phenylalanine and methionine were measured hourly by Raman and then used for the feedback control of three supplemental nutrient feeds. Automated control in this manner provided more consistent nutrient feed-rate additions compared to traditional fed-batch cultures that use daily offline sampling.