Development of glucose and biomass predictive models for real time monitoring of fermentation using Raman spectroscopy

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In 2004, the FDA issued a guidance document to encourage pharmaceutical industrial partners to develop and implement Process Analytical Technologies (PAT), i.e., technological means to monitor in quasi real time key parameters of an industrial process.[1] The benefits of this approach were clear: unlike historical offline analysis – collecting in-process samples , transporting them to the on-site laboratory, analyzing them and reporting the results – PATs are online by design. The analytical results are obtained in quasi real time 24 hours a day 7 days a week. Yet, the industry is slowly evolving. Twenty years later, PATs are still not universally adopted, particularly in the bioprocess field. Performing online analysis in a fermenter means dealing with a very complex matrix while avoiding direct contact that could cause contamination. Vibrational spectroscopies, such as Raman spectroscopy, enable data to be collected remotely and non-destructively, and are therefore a common technique in this field. They need to be coupled to powerful chemometrics tools to overcome the complexity of the matrix and generate results that meet industry standards for accuracy and robustness.[2]

In the context of industrial fermentation, two key parameters to monitor are the glucose concentration and the Optical Density at 600 nm (OD600), a common proxy for biomass concentration. Due to the technical challenges mentioned above, relatively few studies have reported the implementation of PATs dedicated to these key parameters in fermentation.[3-5] While producing seemingly functional tools, prior reports have lacked proper analysis with regard to the robustness of the tools in the context of long-term monitoring, which is crucial for their implementation in the full-scale industrial process.

In this work is reported the implementation of a tool that monitors glucose and OD600 during a type of fermentation. The tool was thoroughly tested on 14 fermenters, over 6 months and consistently produced analytical results significantly superior to the current state-of-the-art. Moreover, an easy-to-use interface was developed to help the fermentation operators to get the most of the analytical results.

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