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Improved Time Resolved KPI and Strain Characterization of Multiple Hosts in Shake Flasks Using Advanced Online Analytics and Data Science

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Abstract:

Shake flasks remain one of the most widely used cultivation systems in biotechnology, especially for process development (cell line and parameter screening). This can be justified by their ease of use as well as their low investment and running costs. A disadvantage, however, is that cultivations in shake flasks are black box processes with reduced possibilities for recording online data, resulting in a lack of control and time-consuming, manual data analysis. Although different measurement methods have been developed for shake flasks, they lack comparability, especially when changing production organisms. In this study, the use of online backscattered light, dissolved oxygen, and pH data for characterization of animal, plant, and microbial cell culture processes in shake flasks are evaluated and compared. The application of these different online measurement techniques allows key performance indicators (KPIs) to be determined based on online data. This paper evaluates a novel data science workflow to automatically determine KPIs using online data from early development stages without human bias. This enables standardized and cost-effective process-oriented cell line characterization of shake flask cultivations to be performed in accordance with the process analytical technology (PAT) initiative. The comparison showed very good agreement between KPIs determined using offline data, manual techniques, and automatic calculations based on multiple signals of varying strengths with respect to the selected measurement signal.

Keywords: shake flask; key performance indicator; strain characterization; online-analytics; growth rate estimation; specific oxygen consumption; microbial cultivation; plant suspension cultures; mammalian cell cultures; optrodes