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Title: Bioreactor Process Characterization for Continuous Processes Based on Statistical Modelling Simulation

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Introduction — Continuous bioprocessing is of paramount importance in biotechnology and pharmaceuticals, as it enhances productivity, maintains product consistency, reduces waste, and offers operational flexibility. It enables real-time control, accelerates time-to-market, and deepens process understanding. Moreover, continuous bioprocessing has the potential to increase product yields, reduce costs, and promote sustainability.

Process characterization is crucial in bioprocessing because it ensures product quality, regulatory compliance, and process efficiency. It also helps in reducing risks, making informed decisions, and ultimately contributes to the success and sustainability of bioprocessing operations.

Challenges — Perfusion cultures exhibit dynamic behavior throughout their duration. To gain a comprehensive understanding of how process parameters influence both culture performance and product quality, including the entire harvest phase, it's essential to integrate time-based data into the analysis alongside the tested process variables. However, it's important to recognize that time-based data points are not independent, making it inappropriate to conduct statistical analyses for time effects while assuming no interrelationships among responses at each time point.

Proposed Approach — To address this challenge, a mixed model with repeated measures was employed for the analysis of harvest phase data. Additionally, simulations to model the entire harvest process were conducted to evaluate Proven Acceptable Ranges (PARs).

Conclusions — Utilizing predictive models with mixed models and repeated measures facilitates time-dependent analysis, enhancing process knowledge. These predictive models also enable Monte Carlo simulations for determining PARs.