A Machine Learning Framework for Optimized and Reduced Experimentation in Cell Culture Process Characterization

by

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Abstract

Process characterization (PC) studies are important for demonstrating the robustness of biologics manufacturing processes, but they are resource-intensive, requiring extensive factorial experiments that consume laboratory capacity and extend timelines. As AMGEN's biologics pipeline grows, laboratory and workforce capacity cannot scale proportionally, creating urgency for more data-efficient approaches. This thesis investigates whether hybrid mechanistic machine learning models can reduce the experimental burden of PC studies while maintaining predictive accuracy. Using hybrid models developed via the DataHowLab software, we benchmark against a standard JMP regression approach across multiple product quality attributes (PQAs). The central finding was that hybrid models trained on approximately 35 PC experiments, augmented with 24 upstream commercial process development experiments as a prior, matched or exceeded JMP accuracy for the best-performing PQAs, a 54% reduction relative to the 75-experiment design analyzed, and a 61% reduction relative to a standard 90-run campaign. Learning curves flattened around 35–45 experiments on average, though convergence behavior varied by PQA. Additional findings include that measured time-series inputs outperformed idealized setpoint perturbations, space-filling sampling strategies outperformed boundary-focused designs, and the shared mechanistic backbone was the dominant performance lever over PQA-specific tuning. Even conservatively, a 30% reduction in experimental workload could translate to meaningful cost savings and freed up capacity across AMGEN's network.

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