Supervisory Control of Modular Continuous Pharmaceutical Manufacturing for Enhanced Economic Resilience

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ABSTRACT

Continuous pharmaceutical plants have demonstrated significant advantages over traditional batch processes. However, conventionally, they rely on custom-built equipment with fixed capacities; therefore, they lack the flexibility to respond to market demand volatility. To address this, a modular design and supervisory control framework is presented in this study for managing volume flexibility in modular plants that are constructed from multiple standardized and interchangeable reactor modules. In this framework, the active process volume is adjusted by activating or bypassing modules to match production needs. The configuration of the reactor modules is determined in the design phase based on reaction kinetics: a parallel topology to maintain selectivity, or a series topology to ensure conversion. During operation, a Python-scripted supervisory layer, integrated via the AVEVA™ Python interface, adjusts the number of active reactor modules by communicating discrete control signals to automated on/off switching valves acting as actuators. These decisions are informed by offline sensitivity analyses that identify economic crossover points across the uncertainty space for different configurations. Control actions are complemented by a regulatory layer within AVEVA™ Process Simulation, which automatically calculates and enforces operational parameters, such as reflux and boil-up ratios for distillation columns, to maintain product quality. This integrated approach ensures that both economic performance and product quality are preserved across all stochastic demand trajectories.

The framework is demonstrated using a two-step catalytic reaction route involving hydrogenation and carbonylation for the continuous production of ibuprofen. Simulations of both conventional and modular plants are carried out using AVEVA™ Process Simulation, incorporating reaction kinetics and appropriate thermodynamic models for upstream and downstream processes. For the modular plant, parallel and series topologies are used for hydrogenation and carbonylation processes, respectively. To model market demand uncertainty, two scenarios are evaluated: fixed-rate compound annual growth rate (CAGR), in which CAGR is assumed to remain constant over the entire project lifetime, and time-dependent CAGR, in which CAGR is allowed to vary annually. Results indicate that the proposed design and control strategy enhances economic resilience, reducing the mean levelized cost of production (LCOP) and lowering the ruin probability in the modular configuration compared to the conventional plant. This study highlights the potential of logic-based supervisory control to enable flexible and economically resilient pharmaceutical production.

Keywords: Process simulation, modularity, supervisory control, demand uncertainty, risk analysis

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