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RESEARCH ARTICLE

Model-Based Control-Loop Performance of a Continuous Direct Compaction Process

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Abstract This study is concerned with enhanced model-based control of a continuous direct compression pharmaceutical process. The control-loop performance is assessed in silico and results obtained will be incorporated into the pilot plant facility of the continuous direct compaction process at the NSF Engineering Research Center of Rutgers University. The models used in the study are obtained via system identification from a combination of first principles-based dynamic models, experimental data, and/or literature data. The main objective of the paper is to formulate an effective control strategy at the basic/regulatory level, for the integrated continuous operation of the direct compaction process, and to maintain the process at the desired set-points, taking into account the multivariable process interactions and disturbances. Simulations show that that at very mild interactions, the proposed regulatory control strategy is able to maintain set-points at desired values. However, at moderate to high process interactions, oscillatory behavior of controlled variables is seen. The presence of disturbances also resulted in poor control-loop performance. Results also lend credence to the development of advanced control strategies in such scenarios and will be addressed in future work. Optimal control tuning parameters are obtained from a derivative-free optimization algorithm.

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Introduction and Objectives

The pharmaceutical industry is a tightly regulated industry where all production must comply with good manufacturing practices and quality requirements should be strictly satisfied. Historically, manufacturing in the pharmaceutical industry has been carried out in batch configuration which potentially results in expensive, inefficient, and poorly controlled processes [1, 2]. Recently, both pharmaceutical industries and regulatory authorities have recognized that continuous manufacturing has significant potential to improve product quality [3–7]. Moreover, environmental, health, and safety issues are driving the industry towards a better understanding of the processes via a model-based approach leading to more efficient operations of the overall processing line [8]. Therefore, a great opportunity arises for developing a generic continuous manufacturing platform that will benefit from state of the art strategies, modeling tools, and process analytical technologies (PAT) to implement this transition.

The application of process systems engineering to pharmaceutical processes remains at an early stage of development [9]. As mentioned above, an important area of research is the conversion of traditional batch processes to fully integrated continuous operations, which include safe and efficient start-up and shut down procedures [9]. A model-based systems approach plays an increasingly important role in process design and control to reduce time and cost for process–product development [10]. Such a model-based approach can be used to efficiently evaluate the process design space with the notion that if process