Iterative Model Based Experimental Design for Spherical Agglomeration Processes

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Abstract

Spherical agglomeration (SA) is a process intensification (PI) strategy, which can reduce the number of unit operations in pharmaceutical manufacturing. SA merges drug substance crystallization with drug product wet granulation, reducing capital and operating costs. However, SA is a highly nonlinear process, thus for its efficient operation model-based design and control strategies are beneficial. These require the development of a high-fidelity process model with appropriately estimated parameters. There are two major problems associated with the development of a high-fidelity process models – (i) selection of the appropriate model corresponding to the underlying process mechanisms, and (ii) accurate estimation of the parameters. This work focuses on the identification of the best fitting model that correlates with experimental observations using cross-validation experiments. Further, an Iterative Model Based Experimental Design (IMED) strategy is developed, which uses D-optimal experimental design criterion to minimize the number of experiments necessary to obtain accurate parameter estimates.

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