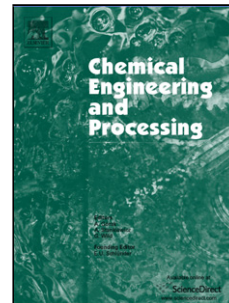


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# Optimal Campaigns in End-to-End Continuous Pharmaceuticals Manufacturing. Part 1: Nonsmooth Dynamic Modeling

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## Abstract

Increasing focus exists on process intensification of pharmaceuticals production by developing continuous manufacturing (CM) processes. However, efficient and economical CM is challenged by the short campaign times prevailing in this industry, resulting in significant transients, often exhibiting nonsmooth behavior, such as changes in flow or thermodynamic phase regimes. Thus, process intensification should be coupled with optimizing its *dynamic operation*. In this series we investigate the optimal dynamic operation of a continuous process that includes several reaction and separation steps to produce an active pharmaceutical ingredient at final dosage from advanced intermediates, inspired by a pilot plant previously tested at MIT. This paper, the first in a two-part series, illustrates the use of nonsmooth differential-algebraic equations (DAEs) as a new paradigm for modeling dynamic process systems in an equation-oriented approach. Such a formulation has been recently shown to admit a unique solution and computationally tractable sensitivity analysis, facilitating its embedding in optimization schemes to find optimal operational procedures. The nonsmooth dynamics of several units are demonstrated from start-up. The nominal overall

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