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Simultaneous modeling and optimization of nonlinear simulated moving bed chromatography by the prediction–correction method

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ABSTRACT

This work demonstrates a systematic prediction–correction (PC) method for simultaneously modeling and optimizing nonlinear simulated moving bed (SMB) chromatography. The PC method uses model-based optimization, SMB startup data, isotherm model selection, and parameter estimation to iteratively refine model parameters and find optimal operating conditions in a matter of hours to ensure high purity constraints and achieve optimal productivity. The PC algorithm proceeds until the SMB process is optimized without manual tuning. In case studies, it is shown that a nonlinear isotherm model and parameter values are determined reliably using SMB startup data. In one case study, a nonlinear SMB system is optimized after only two changes of operating conditions following the PC algorithm. The refined isotherm models are validated by frontal analysis and perturbation analysis.

1. Introduction

Simulated moving bed (SMB) chromatography is a continuous separation technology that can be used to resolve complex mixtures. Selective separation of a binary mixture can be achieved using SMB even if the separation factor is close to one. The SMB process has advantages over batch chromatography such as increased productivity and decreased solvent consumption. It is currently being used in a number of applications in the life sciences including sugars, enantiomers, and proteins. More details on SMB processes can be found in numerous references [1–3]. The attractive feature of SMB is that it simulates the counter-current flow of the stationary phase by rotating the positions of the inlet and outlet ports in the direction of fluid flow. This process allows for both continuous feeding and withdrawal of purified extract and raffinate products.

Although SMB technology has been in use for about 50 years, finding optimal operating conditions for most systems is not yet a straightforward task due to the discontinuous motion of the inlet/outlet ports and complex kinetics and equilibria. For a new separation problem, if there is only a small amount of feed mixture available for lab and mini-plant tests, it may be impossible to systematically optimize the SMB process consuming a large amount of the feed mixture. Therefore the SMB is usually operated under conservative conditions to ensure high purity constraints are satisfied with some safety margins; this is achieved, however, at the cost of reduced productivity and increased desorbent consumption.

The typical process development scheme for a new separation problem relies on modeling with results from batch experiments, steady state SMB experiments, and manual tuning. In Fig. 1 there is an illustration of the typical steps of SMB process development. A new separation problem poses many challenges for the process designer including the estimation of reliable SMB model parameters for each component of the mixture. Once model parameters are determined, usually by batch experiments, operating conditions are selected based on design criteria that approximate SMB dynamics [4]. By observing the steady state SMB performance, the operating conditions are tuned manually until process specifications are met. Sometimes mini-plant experiments and computer simulation of a process model are used to aid in the design [5]. Once the desired operation is satisfied, the process may be controlled to maintain the target performance.

Perhaps the most important aspect of SMB process design is the selection of a process model, including adsorption isotherm, and the determination of model parameters. Some detailed process models for liquid chromatography have been developed and there are a number of techniques that chromatographers have used for obtaining adsorption isotherm and kinetic parameters in the literature [2,6]. Details on moment analysis of pulse injections, frontal analysis, elution by characteristic points, perturbation analysis and inverse methods can be found [2,3,7,8]. Grosfils et al. [9] compared different single-column models for SMB modeling, such as the equilibrium-dispersion model and the kinetic model,

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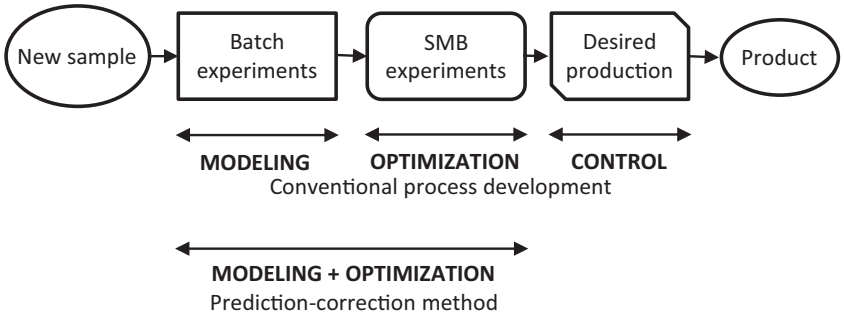

Fig. 1. Illustration of steps of SMB process development starting with a new mixture. The prediction–correction method is proposed to streamline SMB process development by simultaneous modeling and optimization.

and studied the identifiability of model parameters using pulse injections. These researchers used design of experiments to reduce the effort required to obtain reliable model parameters for SMB, although they do not consider isotherm model selection.

In most case studies of nonlinear SMB process development in the literature, the adsorption isotherms of each component are characterized by batch experiments and then an isotherm model is assumed and used to fit the data. For example, Heuer et al. [10] used a careful perturbation analysis to estimate modified competitive Langmuir isotherm parameters for the design of enantiomer separation by SMB. Even though the estimated parameters were reliable for single-column tests, there was still significant model mismatch in the prediction of product concentrations and purity values. Indeed, there is no guarantee that the SMB modeling based on results of batch experiments will accurately predict SMB performance. Grosfils et al. [11] used a inverse method to determine competitive Langmuir isotherm parameters from two pulse injections. Using an SMB model with careful measurements of dead volumes in a real SMB plant, the process simulation was compared with plant data *via* UV detector signals. The inverse method has been shown to be a reliable parameter estimation technique in predicting batch experimental results for enantiomer separations [8], and is useful for isotherm model.

Some other work has been done to attempt parameter estimation using SMB data. Küpper et al. [12] proposed and demonstrated a concept for SMB model parameter estimation using online measurements and computational simulation. They conclude that the model parameters can be estimated online by measurements of the extract, raffinate and recycle lines and can be adapted to physical changes in the column properties such as porosity. Yet their work requires online detection of entire internal concentration profiles over a step, and no optimization is performed using the estimated parameters. Araújo et al. [13] used a hybrid inverse method to determine competitive Langmuir isotherm parameters for an SMB model using numerous batch experiments and a periodic state represented on single-column set-up. The model parameters are refined by parameter estimation using the single-column cyclic steady state data, but these are only an approximation of real SMB dynamics and no optimization of the SMB process is performed.

There are other researchers who have worked on optimizing control to maintain the desired production of the SMB process (see Fig. 1), by correcting operating conditions in the presence of disturbances. Klatt et al. [14] described a control strategy where the operating conditions and the assembled elution profile are measured during the periodic SMB operation and adjustments are made automatically to correct deviations from the target product purities. Further work on optimizing control for SMB has been done at ETH Zurich by Grossmann et al. [15] where average product concentrations are measured during a cycle as feedback information for a controller. This measurement strategy uses HPLC to analyze the product concentrations, which is a more accurate measurement than online UV spectra. Their methodology assumes that a reliable set of process model parameters and optimal operating conditions for the SMB are known *a priori*. They do not consider updating the SMB model parameters using product concentration data.

The goal of this work is to propose and demonstrate a systematic method for SMB process development, the prediction–correction (PC) algorithm, for nonlinear SMB optimization starting from a new separation problem and ending with optimal operating conditions. This algorithm uses a surrogate model (see Biegler et al. [16]), infrequent sampling of SMB outlet streams, parameter estimation, and dynamic optimization to reduce the time and effort to obtain reliable model parameters and simultaneously optimize nonlinear SMB processes in a systematic manner. It should be emphasized that the PC method is not designed as a technique for online control, but is an integrated modeling and optimization technique which can be used with a controller in a complementary manner.

This paper is organized as follows: The detailed steps of the prediction–correction algorithm are discussed in Section 2, our laboratory equipment is detailed in Section 3, and case studies with a nonlinear isotherm system are presented in Section 4. The case studies show that the model selection and parameter estimation steps are successfully performed and the PC algorithm converges efficiently and robustly to optimize the SMB operation for a nonlinear system.

2. Methodology

The PC method is an iterative scheme that uses SMB startup experiments, parameter estimation, and model-based optimization to rapidly achieve optimal operating conditions for a new separation problem. This method is described and demonstrated in our previous work for a linear isotherm system [17], which is modified in this work to allow isotherm model selection. Here, we assume that SMB column configuration, operating scheme, mobile phase, feed composition and operating temperature are decided *a priori*.

The PC algorithm with model selection is shown in Fig. 2. During process development for a new separation problem the adsorption isotherm is unknown. Instead of spending valuable time and resources performing batch experiments to explore the adsorption isotherm for each component, we use a set of SMB startup data to perform model selection and parameter estimation. Here is a step-by-step walkthrough of the updated PC algorithm:

1. Initialize $k = 0$. A set of batch experiments are performed on a single column to estimate isotherm and kinetic parameters for the SMB model.