Iterative Set-Point Optimization of Batch Chromatography

Weihua Gao* and Sebastian Engell
Process Control Laboratory
Department of Biochemical and Chemical Engineering
Universität Dortmund, Emil-Figge-Str. 70, D-44221 Dortmund, Germany

Abstract

An iterative gradient-modification optimization strategy is applied to the set-point optimization of batch chromatography in presence of a plant-model mismatch. A new method is used to deal with process-dependent constraints. The methods requires the estimation of the gradient of the real process mapping which is computed by a technique which considers the influence of errors and the number of additional set-point perturbations. A simulation study illustrates the potential of the proposed strategy.

Keywords: chromatography, online set-point optimization, iterative optimization

1. Introduction

In the chemical industry, life science products are considered to be a very promising market for the near future. Since chemicals for pharmaceutical products, cosmetics, food additives etc. are subject to strict purity requirements and tight regulations, efficient methods for the separation of the valuable product from often complex mixtures are needed. These separations usually cause a significant share of the production cost. Chromatographic separations constitute an important element of downstream processing steps because they provide high purities at moderate temperatures. While quasi-continuous chromatographic methods are available and are increasingly used in industry, most chromatographic separations are still operated in the batch mode. The optimal operation of these processes with respect to throughput and solvent consumption is an important factor to reduce the overall production cost.

Dünnebier *et al.* (2001) proposed a model-based online optimization strategy for batch chromatography. To improve the model accuracy and to track changes in the plant, an online parameter estimation is performed. This technique has been tested at pilot scale plants and works well for separations with linear adsorption isotherms. However, most of the chromatographic separation processes are characterized by nonlinear adsorption isotherms which are often not reproduced exactly by the standard isotherm models (e.g. Langmuir, Bi-Langmuir). One important reason for this is the presence of additional components in the mixture. If a structural mismatch between the model and the plant occurs, a model-based optimization cannot give good results and the constraints must be established by an additional control layer (Hanisch 2002), causing a loss of performance.

* Author to whom correspondence should be adressed : w.gao@bci.uni-dortmund.de

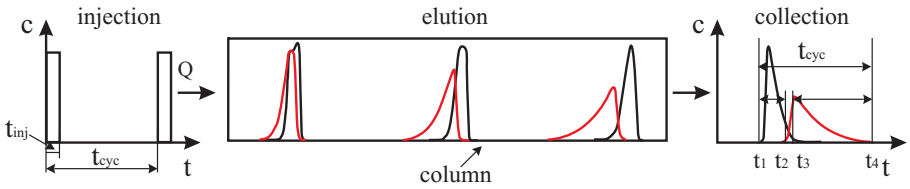

Figure 1. Principle of batch chromatography (binary separation)

In recent years, methods have been developed which perform a set-point optimization in the presence of model uncertainties. The *Integrated System Optimization and Parameter Estimation* (ISOPE) strategy combines parameter estimation and optimization. It generates a sequence of set-points which converges to the optimum of the true process. It performs an update of the model parameters to satisfy an equality constraint at every iteration. Tatjewski (2002) redesigned the ISOPE strategy such that parameter estimation is not necessary. This leads to a simple iterative gradient-modification optimization strategy. In this paper we extend this strategy to the handling of constraints on the process output and apply it to the set-point optimization of batch chromatography. The efficiency of the method is shown by a simulation study with plant-model mismatch.

2. Batch Chromatographic Separation

Batch chromatography is most often operated in the elution mode (Fig. 1). A mixture is periodically injected into a column filled with solid adsorption particles. Due to different adsorption affinities, the components in the mixture migrate at different velocities and therefore they are gradually separated. At the outlet of the column, the purified components are collected between cutting points whose locations are decided by the purity requirements on the products. The flow rate Q and the injection period t_{inj} are considered as the manipulated variables here. The cycle period t_{cyc} is fixed to the duration of the chromatogram. The performance criterion is the production rate $Pr=m_{product}/t_{cyc}$. The set-point optimization of batch chromatography is formulated as the following nonlinear optimization problem:

$$\begin{aligned} \underset{Q,t_{inj}}{\text{Maxmize}} \quad & \Pr(Q,t_{inj}) \\ \text{s.t.} \quad & \text{Rec}(Q,t_{inj}) \geq \text{Rec}_{\min} \\ & 0 \leq Q \leq Q_{\max} \\ & t_{inj} \geq 0 \end{aligned} \tag{1}$$

where Rec denotes the recovery yield of the valuable component. The set-point optimization is based on the general rate model (Guiochon *et al.*, 1994). For a given set-point, the model is simulated. Then the production rate and the recovery yield can be calculated from the chromatogram. When a model mismatch exists, the chromatogram predicted by the model is different from the actual chromatogram. As a result, the optimization generates a suboptimal or even infeasible set-point at which the recovery yield constraint is violated.

3. Iterative Optimization Strategy

The *Integrated System Optimization and Parameter Estimation* strategy was proposed first by Roberts (1979). Tatjewski (2002) proposed a new variant of this strategy. By introducing a model shift term in the performance function, an iterative parameter estimation is no longer necessary. The strategy requires the knowledge of the gradient of the real performance function (which depends on variables which are continuously measured) with respect to the optimization parameters. The optimization problem is assumed to be stated as

$$\begin{aligned} \underset{\mathbf{u}}{\text{Minimize}} \quad & J(\mathbf{u},\mathbf{y}) \\ \text{s.t.} \quad & \mathbf{g}(\mathbf{u}) \le 0 \\ & \mathbf{u}_{\min} \le \mathbf{u} \le \mathbf{u}_{\max} \end{aligned} \tag{2}$$

where J(**u**,**y**) is the performance function, **u** is the set-point, **y** is the model output, **g**(**u**) is the constraint function. As the output of the real system $\mathbf{y}^*$ differs from the model prediction due to plant-model mismatch, the performance function of the i^{th} iteration is modified using the measured information $\mathbf{y}^*_{i-1}$ at the previous set-point $\mathbf{u}_{i-1}$:

$$\underset{\mathbf{u}}{\text{Minimize}}\ J_i^m = \left\{ J(\mathbf{u},\mathbf{y}+\mathbf{a}) + [\nabla_{\mathbf{y}} J(\mathbf{u}_{i-1},\mathbf{y}_{i-1}+\mathbf{a})]^T \cdot \left[\frac{\partial \mathbf{y}^*_{i-1}}{\partial \mathbf{u}} - \frac{\partial \mathbf{y}_{i-1}}{\partial \mathbf{u}} \right] \cdot \mathbf{u} \right\} \tag{3}$$

where $\mathbf{a} = \mathbf{y}^*_{i-1} - \mathbf{y}_{i-1}$.represents the difference between the model output and the process output at the previous set-point. If the constraint function **g**(**u**) is known exactly, the modified optimization problem can be solved by any nonlinear optimization algorithm. Let $\mathbf{u}^m_i$ denote the solution to (3) computed in step i, then the next set-point is chosen as:

$$\mathbf{u}_i = \mathbf{u}_{i-1} + \mathbf{K}[\mathbf{u}_i^m - \mathbf{u}_{i-1}] \tag{4}$$

where **K** is a diagonal gain matrix whose diagonal elements are in the interval (0,1], i.e. **K** is a damping term. Starting from an initial set-point, the strategy will generate a sequence of set-points which, for an appropriate gain matrix, will converge to a set-point which satisfies the necessary optimality conditions of the actual process.

3.1 Handling of process-dependent constraints

If the constraint function depends on the behaviour of the actual process, e. g. the recovery yield constraint in batch chromatography, it cannot be assumed to be precisely known, and using a model for the computation of the constraint function will not assure that the constraints are actually satisfied. In the original derivation of the ISOPE strategy, the constraints were assumed to be process-independent. An extension of the ISOPE strategy which considers process-dependent constraints can be found in (Brdyś *et al*., 1986). In this formulation, a recursive Lagrange multiplier is used. Tatjewski et al. (2001) proposed to use a follow-up constraint controller which is responsible for satisfying the output constraints in the ISOPE strategy.

A different method to handle the process-dependent constraint is proposed here. It is based on the idea to use the acquired process information to correct the model-based constraint function. The corrected constraint function approximates the true constraint function of the actual process in the vicinity of the correction point. Let **g**(**u**) denote the model-based constraint function and $\mathbf{g}^*(\mathbf{u})$ denote the actual constraint function of the real plant. Then the modified constraint function for iterative online optimization is:

$$\mathbf{g}_i^m(\mathbf{u}) = \mathbf{g}(\mathbf{u}) + \mathbf{g}^*(\mathbf{u}_{i-1}) - \mathbf{g}(\mathbf{u}_{i-1}) + \left[\frac{\partial \mathbf{g}^*(\mathbf{u}_{i-1})}{\partial \mathbf{u}} - \frac{\partial \mathbf{g}(\mathbf{u}_{i-1})}{\partial \mathbf{u}} \right] \cdot \left[\mathbf{u} - \mathbf{u}_{i-1} \right] \cdot \tag{5}$$

As the corrected constraint is only valid in the vicinity of the correction point, a bound is added at every iteration to limit the search range for the next set-point. This guarantees that the constraints are not violated greatly. The optimization problem with process-dependent constraints at the ith iteration is thus formulated as:

$$\begin{aligned} &\underset{\mathbf{u}}{\text{Minimize}} \quad J_i^m \\ &\text{s.t.} \qquad \mathbf{g}_i^m(\mathbf{u}) \le 0 \\ &\qquad\quad \mathbf{u}_{i-1} - \Delta\mathbf{u} \le \mathbf{u} \le \mathbf{u}_{i-1} + \Delta\mathbf{u} \\ &\qquad\quad \mathbf{u}_{\min} \le \mathbf{u} \le \mathbf{u}_{\max} \end{aligned} \tag{6}$$

3.2 Computation of the gradient from measured data

A key element of the iterative optimization strategy is the computation of the gradient of the process mapping with respect to the optimization variables. A novel method which considers both the influence of errors and the number of additional set-point perturbations is proposed here. It uses the information gained from the measurements at the previous set-points as a basis for the finite difference approximation of the gradient at the current set-point. Let n denote the dimension of the set-point vector **u**. To estimate the gradient at the jth set-point, n+1 set-points, $\mathbf{u}_j$, $\mathbf{u}_{j-1}$, …., $\mathbf{u}_{j-n,}$ are used. Assume first that the vectors $\Delta\mathbf{u}_{jk}=\mathbf{u}_j-\mathbf{u}_{j-k}$ (k=1, …, n) are linearly independent. Let $\mathbf{y}^*_j$, $\mathbf{y}^*_{j-1}$, …, $\mathbf{y}^*_{j-n}$ denote the measured process outputs at these set-points. We define the matrix $\mathbf{S}_j=(\Delta\mathbf{u}_{j1}\ \Delta\mathbf{u}_{j2}\ \cdots\ \Delta\mathbf{u}_{jn})^T$, and approximate the gradient by :

$$\frac{\partial \mathbf{y}_j^*}{\partial \mathbf{u}} \approx \mathbf{S}_j^{-1} \cdot \begin{bmatrix} \mathbf{y}_j^* - \mathbf{y}_{j-1}^* \\ \vdots \\ \mathbf{y}_j^* - \mathbf{y}_{j-n}^* \end{bmatrix} \tag{7}$$

Theoretically, the smaller the difference between the set-points the more accurate will the approximation of the gradient be. On the other hand, because the measured process outputs are usually corrupted by errors, $\mathbf{S}_j$ should be sufficiently well conditioned in order to obtain a good approximation of the gradient. Let $d_j=\sigma_{min}(\mathbf{S}_j)/\sigma_{max}(\mathbf{S}_j)$ denote the conditioning of $\mathbf{S}_j$ in terms of its singular values. If d_j is too small, the errors in the measurements will be amplified considerably and the gradient estimation will be corrupted by noise. Therefore if d_j is less than a given constant δ ($0<\delta<1$), an additional set-point $\mathbf{u}^a_{j-1}$ is added between $\mathbf{u}_j$ and $\mathbf{u}_{j-1}$ to keep the new matrix $\mathbf{S}^a_j=(\Delta\mathbf{u}^a_{j1}\ \Delta\mathbf{u}_{j1}\ \cdots\ \Delta\mathbf{u}_{j\,n-1})$ well conditioned. The location of the additional set-point $\mathbf{u}^a_{j-1}$ is optimized such that $d^a_j=\sigma_{min}(\mathbf{S}^a_j)/\sigma_{max}(\mathbf{S}^a_j)$ becomes maximal under the constraints (6). By the choice of δ, the propagation of the measurement errors and the reduction of the convergence speed by the additional set-point perturbations can be balanced.

4. Simulation Study

The iterative optimization strategy was tested in a simulation study of a nonlinear enantiomer separation process which has been used as a test case in laboratory experiments before (Hanisch, 2002). A model with a Bi-Langmuir isotherm that was fitted to measurement data is considered as the “real model” in the simulation study. A

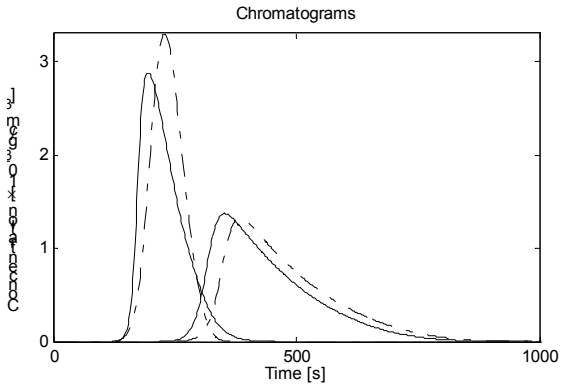

Figure 2. Illustration of the model mismatch, solid line: "real" model, dash-dot line: optimization model

model with isotherms of a different form is used in the set-point optimization. Fig. 2 shows the chromatograms of the "real" and the perturbed plant for the same set-point. The second component is considered to be the valuable product, the purity requirement is 98%. The recovery yield should be greater than 80%. There is an upper-limit for the flow rate: 2.062 cm^3/s. The flow rate and the injection period are normalized to the interval [0, 1]. The gain coefficients in **K** are set to 0.5. The bounds of the change of the inputs at each iteration are Q_{i-1}-0.1≤ $Q_i \le Q_{i-1}$+0.1 and $t_{inj,i-1}$-0.1≤$t_{inj,i}$≤$t_{inj,i-1}$+0.1, where Q_{i-1} and $t_{inj,i-1}$ denote the previous operating parameters. In order to approximate the gradients at the initial set-point, two additional initial set-points (Q_0-0.02, $t_{inj,0}$-0.02) and (Q_0-0.02, $t_{inj,0}$) were used. The iterative optimization procedure is performed as follows:

Step 1. At the i^{th} iteration, apply the $i\text{-}1^{th}$ set-point (and the additional set-point if it is needed) to the real model and calculate the production rate and the recovery yield. Random measurement errors are added to the results.

Step 2. Approximate the gradients using the proposed method. Modify the performance function and correct the constraint function. Then solve the modified model-based optimization problem and update the set-point using Eq. (4);

Step 3. If the distance between the previous set-point and the new set-point is less than 0.01, stop the optimization procedure. Otherwise go to the next step;

Step 4. Check $d_j=\sigma_{min}(\mathbf{S}_j)/\sigma_{max}(\mathbf{S}_j)$. If it is less than δ, an additional set-point is generated by maximizing $d^a_j=\sigma_{min}(\mathbf{S}^a_j)/\sigma_{max}(\mathbf{S}^a_j)$. i=i+1. Go to step 1.

δ was set to 0.2. The procedure stopped after 18 iterations and generated a set-point close to the real optimum. Fig. 3 shows the trajectory of the set-point and the performance and constraint contours of the real model and the mismatched model. The stars denote the set-points generated by the iterative optimization procedure. The circles denote the additional set-point perturbations used for the gradient computation. Although there is a considerable model mismatch, the iterative optimization terminates near the real optimum while keeping the recovery yield constraint. The slight difference between the final set-point and the real optimum (about 0.04 in the normalized search space) is due to the indirect influence of the added measurement errors on the termination constraint. When there is no error, the difference is about 0.02.

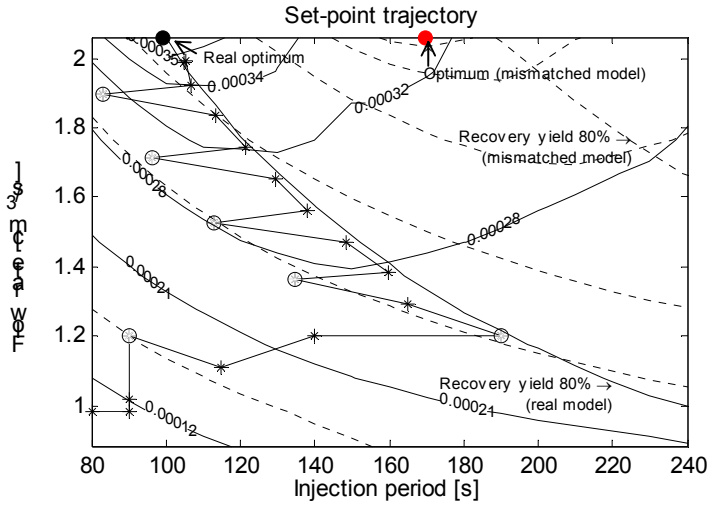

Figure 3. Set-point trajectory, solid lines: performance contours of the "real" model, dotted lines: contours of the mismatched model

5. Conclusions

The identification of an accurate model requires considerable efforts for batch chromatography of multi-component mixtures. In practice, inaccurate models must be used for set-point optimization. A purely model-based optimization will generate a suboptimal or even infeasible set-point. The iterative gradient-modification optimization strategy discussed here converges to a neighbourhood of the real optimum in a few steps while respecting the constraints. Additional set-points are introduced to reduce the effect of measurement errors on the gradient approximation.

Acknowledgements

The work of the first author was supported by a scholarship of the NRW Graduate School of Production Engineering and Logistics at Universität Dortmund. This support is very gratefully acknowledged.

References

Brdyś, M., S. Chen and P:D: Roberts, 1986, Int. J. Systems Sci. 17, 1229.

Dünnebier, G., S. Engell, A. Epping, F. Hanisch, A. Jupke, K.-U. Klatt and H. Schmidt-Traub, 2001, AIChE J. 47, 2493.

Guiochon, G., S. Golshan-Shirazi and A. Katti, 1994, Fundamentals of Preparative and Nonlinear Chromatography. Academic Press, Boston.

Hanisch, F., 2002, Prozessführung Präparativer Chromatographieverfahren (Operation of preparative chromatographic processes). University of Dortmund. (Dr.-Ing dissertation, in German)

Roberts, P.D., 1979, Int. J. Systems Sci. 10, 719.

Tatjewski, P., 2002, Iterative optimizing set-point control - the basic principle redesigned. In preprints of the 15th triennial world congress of the IFAC, Barcelona.(CD)

Tatjewski, P., M. Brdyś and J. Duda, 2001, Int. J. Control 74, 1510.