

USE OF SIMULATED ANNEALING FOR OPTIMIZATION OF CHROMATOGRAPHIC SEPARATIONS

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SUMMARY

The effectiveness of a hybrid of simulated annealing (SA) and the simplex algorithm for optimization of a chromatographic separation has been examined. The method has been used to solve optimization problems for separations in batch and continuous chromatographic systems under isocratic and gradient conditions. To verify the robustness of the algorithm a variety of test problems have been solved. Different objective functions have been optimized subject to different optimization constraints for several operating conditions used as decision variables. The effectiveness of the hybrid procedure has been compared with that of a random search algorithm.

The hybrid method proved particularly effective for multicondition optimization involving changes of mobile-phase composition. The method is rapid and robust in location of the global optimum. It does not, moreover, require initiation of the calculations with a “feasible point”, i.e. a point for which optimization constraints are met.

INTRODUCTION

Designing industrial chromatographic separations for batch and continuous processes (e.g. the simulated moving bed, SMB process) requires an efficient optimization tool which can be used to determine the optimum operating conditions rapidly and robustly. The objective of the optimization process is to find conditions which ensure minimum separation cost while still satisfying product purity requirements. Because of the need for high throughput, the optimum conditions correspond to severe nonlinearity of adsorption isotherm. Any optimization tool must include a

model of the process dynamics accounting for the nonlinear competitive adsorption equilibria of the components to be separated. Such a model must be solved numerically. It should be sufficiently accurate to reproduce the concentration profiles correctly and sufficiently simple to reduce the calculation time. The model must be implemented in an optimization procedure which enables calculation of the optimum operating conditions on the basis of model predictions.

Determination of the optimum conditions requires many replicate simulations of the process dynamics (evaluations). To solve optimization problems in reasonable time the optimization routine must be effective. It should guarantee location of the solution as close as possible to the global optimum with a minimum number of evaluations. The calculation time is a factor of major importance if the optimization tool is implemented online for automatic feedback control. Because, in a real industrial plant, disturbances of the process conditions are unavoidable, feedback control is frequently used to ensure the process is operated under optimum conditions. Attempts to improve the effectiveness of the optimization tool are, therefore, fully justified.

Several techniques can be used to solve nonlinear optimization problems. A recent review of optimization methods in chemical engineering is available elsewhere [1]. Deterministic methods that use information about the properties of objective functions and/or their derivatives (e.g. the Newton–Raphson method, the Powell method, the simplex method) require the fewest evaluations. With a reasonably good starting point they solve problems efficiently; they fail to find a global optimum for multimodal, hard-to-optimize objective functions [1]. A deterministic method such as the simplex algorithm has been used for optimization of non-linear chromatography by Dose [2] and by Felinger and Guiochon [3,4]. Because of the limitations of this algorithm, only a small number of operating conditions can be optimized simultaneously. To avoid trapping of the calculation in a local minimum, calculations must, moreover, be repeated several times with different sets of operating conditions as the starting point.

In the design of a chromatography process several operating conditions, e.g. mobile phase flow rate, the size of the bed particles, feed flow rate, inlet concentration, mobile-phase composition, etc., must usually be determined. A variety of objective functions can be considered as performance indicators, for example the productivity of the process, mobile-phase consumption, product purity. Some of these mutually conflict, i.e.

improvement of one objective function results in worsening of another. To solve such a problem multi-objective optimization is necessary.

Operating conditions are calculated subject to optimization constraints, e.g. purity demands for product streams. Operating conditions can, moreover, be constrained by specific process requirements. For such complex problems, calculations based on deterministic methods can be trapped in a local minimum. To solve these problems, stochastic optimization algorithms are more suitable [5]. Stochastic algorithms, for example genetic algorithms, simulated annealing (SA), random search (RS), taboo search, or the ant-colony approach, have attracted attention for optimization of the operating conditions of large-scale production processes. Such techniques are particularly suitable for solving difficult optimization problems in which the desired global optimum is hidden among many, poorer, local optima. Stochastic algorithms have recently been implemented for optimization of large-scale continuous chromatography processes. For example, a genetic algorithm has been used for multi-objective optimization of a reactive SMB process [6,7], the Varicol process [8–10], a standing wave annealing technique, has been used to optimize SMB systems with a linear adsorption isotherm [11], and the random-search algorithm of Luus and Jaakola [12] has been used to optimize mobile-phase composition in isocratic and gradient SMB processes [13, 14].

In this work the effectiveness of a hybrid of simulated annealing (SA) and the downhill simplex algorithm for optimization of batch and continuous chromatography (SMB) has been examined. The hybrid method is available in Numerical Recipes as the AMEBSA routine [5] and can be easily implemented to solve optimization problems in chromatography. The robustness of the method has been compared with that of the random search (RS) technique used in our previous study [13,14].

THEORY

The Design of Batch Chromatography

Model of Column Dynamics

For simulation of column dynamics the equilibrium dispersive model has been used [15]:

$$\frac{\partial C_i}{\partial t} + \frac{1-\varepsilon_t}{\varepsilon_t} \frac{\partial q_i}{\partial t} + w \frac{\partial C_i}{\partial z} = D_a \frac{\partial^2 C_i}{\partial z^2} \quad (1)$$

where C_i and q_i are the concentrations of solute i in the mobile and solid phases, respectively, ε_t is the total porosity, t and z are time and space coordinates, w ($= u/\varepsilon_t$) is the interstitial fluid velocity, u is superficial velocity, and D_a is the apparent dispersion coefficient, which is related to column efficiency:

$$D_a = \frac{w \times HETP}{2} \quad (2)$$

$HETP$ is related to particle diameter and fluid velocity by the van Deemter equation:

$$HETP = ad_p + bd_p^2w + c/w \quad (3)$$

where a , b , c are empirical constants and d_p is the particle diameter.

The relationship between the concentrations in the mobile and solid phases is expressed by an isotherm equation. In this work the competitive Langmuir isotherm model has been used to describe adsorption equilibria:

$$q_i^*(C_1, C_2) = \frac{H_i(C_{\text{mod}})C_i}{1 + \sum_{l=1}^2 b_l(C_{\text{mod}})C_l}; i = 1, 2 \quad (4)$$

where the isotherm coefficients, i.e. the Henry constant, H_i , and the equilibrium constant, b_i , are functions of mobile-phase composition:

$$H_i(C_{\text{mod}}) = (p_{H_i} C_{\text{mod}})^{-r_{H_i}}; i = 1, 2 \quad (5)$$

$$b_i(C_{\text{mod}}) = (p_{b_i} C_{\text{mod}})^{-r_{b_i}}; i = 1, 2 \quad (6)$$

where C_{mod} is the concentration of the active component of the mobile phase (i.e. the modifier).

To quantify possible adsorption of the modifier the single-component Langmuir model was used:

$$q_{\text{mod}}^*(C_{\text{mod}}) = \frac{H_{\text{mod}}C_{\text{mod}}}{1 + b_{\text{mod}}C_{\text{mod}}} \quad (7)$$

To find the equilibrium, the terms H_{mod} and b_{mod} , and p_{H_i} , r_{H_i} , p_{b_i} , and r_{b_i} must be known. Competition between solutes and the modifiers has been neglected. Details of the model can be found elsewhere [16].

The separation factor, defined as:

$$\alpha = H_2(C_{\text{mod}}) / H_1(C_{\text{mod}}) \quad (8)$$

is also a function of modifier concentration.

Optimization Problem

To examine the effectiveness of the optimization tool the following problem has been solved:

$$\text{Max}(OF) = \text{Max}(\text{Pr or } SP) = f(u, d_p, C_{\text{Fi}}, t_{\text{inj}}, C_{\text{mod}}) \quad (9)$$

subject to the purity constraints:

$$Pu_i \geq Pu_{i,\text{min}} \quad (10)$$

Decision Variables

The operating conditions superficial fluid velocity, u , particle diameter, d_p , injection time t_{inj} , feed concentration C_{Fi} , and mobile-phase composition C_{mod} were selected as decision variables.

Objective Functions

Objective functions OF are performance indicators of batch chromatography. Two objective functions were examined – productivity and specific productivity. Productivity Pr is defined as the mass of the key product i collected (i.e. the product of the feed volume, V_{inj} , the concentration of the feed stream, C_{Fi} , and the recovery yield Y_i) during the cycle time Δt_c , normalized relative to the column cross sectional area S :

$$\text{Pr}_i = \frac{C_{\text{Fi}} V_{\text{inj}} Y_i}{S \Delta t_c} \quad (11)$$

If all the components are required as pure products total productivity is calculated as a sum of productivities for single components:

$$\text{Pr}_{\text{tot}} = \sum_i \text{Pr}_i \quad (12)$$

The specific productivity, SP , is defined as:

$$SP = \frac{Pr}{u} \quad (13)$$

SP is the productivity corresponding to unit volume of the solvent consumed.

Optimization Constraints

The purity Pu of the outlet stream can be expressed as:

$$Pu_i = \bar{C}_{i,\text{out}} / (\bar{C}_{1,\text{out}} + \bar{C}_{2,\text{out}}); i = 1,2 \quad (14)$$

where:

$$\bar{C}_{i,\text{out}} = \frac{\int_{t_{\text{start}}}^{t_{\text{end}}} C_i^{\text{out}} dt}{\Delta t_i} \quad (15)$$

and where $\bar{C}_{i,\text{out}}$ is the average concentration of component i in the outlet stream and $\Delta t_i (= t_{\text{end}} - t_{\text{start}})$ is the time interval in which component i is collected.

The decision variables u and d_p are, moreover, limited by the pressure drop constraint, which is calculated by use of the Blake–Kozeny equation:

$$u < u_{\text{max}} = \frac{\Delta P_{\text{max}}}{L} \frac{\varepsilon_e^3}{(1 - \varepsilon_e)^2} \frac{d_p^2}{150 \eta} \quad (16)$$

$$\text{or } u < u_{\text{max}} = \frac{\Delta P_{\text{max}}}{L} \frac{\varepsilon_e^3}{(1 - \varepsilon_e)^2} \frac{d_p^2}{150 \eta} \times 60 \times 10^{-10}$$

where η ($\text{kg m}^{-1} \text{s}^{-1}$) is the fluid viscosity, the pressure drop is in Pa, ε_e is the external porosity, L (cm) is the column length, and d_p (μm) is the particle diameter.

Designing an SMB Process

Operating Conditions

Designing a real SMB process performed under conditions of limited system efficiency and isotherm nonlinearity involves many operating conditions. Optimization of an SMB process is therefore more difficult than optimization of batch systems. A typical four-zone SMB unit is depicted

in Fig. 1. Each of these zones fulfils distinct tasks, i.e. separations occur in zones II and III whereas the solid and the fluid phases are regenerated in zones I and IV, respectively. Movement of the solid bed is simulated by switching of ports or columns after fixed time intervals. There are two incoming streams – the feed stream containing the mixture to be separated, \dot{V}_F , and the desorbent (or eluent), \dot{V}_{Eluant} . Two product streams are withdrawn from the unit, one enriched with the less adsorbed raffinate ($\dot{V}_{\text{Raffinate}}$) and one enriched with the more adsorbed extract (\dot{V}_{Extract}). In isocratic mode feed is dissolved in the same mobile phase as is used in the desorbent port. The principles of this process are well known [17–21]. In gradient mode the solvent strength in the feed is weaker than that in the desorbent stream, i.e. $C_{\text{modF}} < C_{\text{modD}}$. Such modulation of the solvent strength results in increased productivity and reduced mobile-phase consumption [16,22–25].

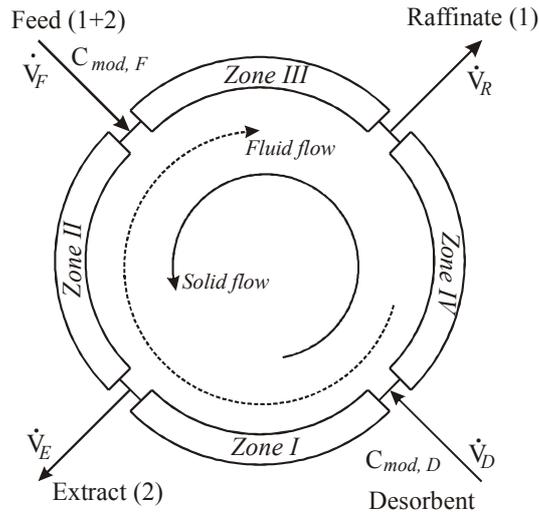


Fig. 1

Schematic diagram of a four-zone SMB

To design the process, operating regions of flow rates leading to pure product streams can be calculated. These regions are typically plotted in the (m^{II}, m^{III}) plane of the following dimensionless flow rates m^K in zone K :

$$m^K = \frac{\dot{V}^K t^* - V \varepsilon_t}{V(1 - \varepsilon_t)} \quad K = I, \dots, IV \quad (17)$$

The switching time t^* in eq. (17) is defined as:

$$t^* = \frac{V(1-\varepsilon_t)}{\dot{V}_s} \quad (18)$$

where the \dot{V}^K are the four volumetric flow rates in the zones, \dot{V}_s is the solid flow rate of the equivalent true mobile bed (TMB) process, and V is the volume of one fixed bed.

The triangle theory can be used to calculate the position of the operating regions corresponding to the equivalent TMB unit with infinite efficiency [19]. For a real SMB system with limited efficiency the size of operating regions calculated by the use of the triangle theory can be over-estimated, however. To design the process more accurately, optimization of the operating conditions should be performed on the basis of predictions of the dynamics of the process (e.g. eq. 1).

This optimization is indispensable for designing the process under gradient conditions. In this instance the concentration profiles of the components to be separated and of the mobile phase modifier in cyclic steady state must be calculated numerically.

Optimization Problem

For the SMB process two optimization problems have been considered.

Single-Objective Optimization

As a single-objective function mobile-phase consumption or productivity were optimized:

$$\text{Min}(EC) \text{ or } \text{Min}(1/\text{Pr}) = f(m^{K=I,II,III,IV}, C_F, C_{\text{modD}}) \quad (19)$$

Multiobjective Optimization

In multi-objective optimization two conflicting objective functions, productivity and purity, were optimized. Improvement of system performance with regard to productivity leads to simultaneous reduction of the purity of the product collected. The following objective function was formulated:

$$OF = \min \left(\frac{1}{PR} + (1 - Pu_E) + (1 - Pu_R) \right) \quad (20)$$

Decision Variables

The flow rate ratios m^K , the feed concentrations $C_{F1} = C_{F2}$, mobile-phase composition C_{mod} (isocratic mode), or the composition of the mobile phase in the desorbent port C_{modD} (gradient mode) were selected as the decision variables.

Objective Functions

The objective functions were defined as follows:

$$EC = \frac{\dot{V}_D + \dot{V}_F}{C_{1R}\dot{V}_R + C_{2E}\dot{V}_E} \quad (21)$$

where EC is mobile-phase consumption and corresponds to the ratio of the amount of mobile phase delivered in the inlet streams to the amount of the pure products collected; \dot{V}_D , \dot{V}_F , \dot{V}_R , and \dot{V}_E are the volumetric flow rates of the inlet (desorbent and feed) and outlet (raffinate and extract) streams, or:

$$PR = \frac{C_{R1}\dot{V}_R + C_{E2}\dot{V}_E}{V_{\text{bed}}} \quad (22)$$

where PR is the productivity defined as the mass flow rate of the product collected normalized to the total bed volume.

Optimization Constraints

The optimization problem has been solved subject to the purity constraints:

$$Pu_{\text{port}} \geq Pu_{\text{port,min}} \quad \text{port} = E, R \quad (23)$$

where Pu indicates the average purity of the raffinate and extract streams, i.e. R , E , collected during the interval of one switching time in the cyclic steady state.

If the purity constraint (eq. 23) in port j is violated the following penalty functions are active:

- for single-objective optimization (compare with eq. 19):

$$OF' = OF + \sum_{port} \frac{weight}{Pu_{port}} \quad (24a)$$

- for multi-objective optimization (compare with eq. 20):

$$OF' = OF + \sum_{port} weight(0.9 - Pu_{port}) \quad (24b)$$

Because the flow rates of the inlet and output streams must be positive, the following overall constraints of the decision variables must be met:

$$m_D = m^I - m^{IV} > 0 \quad (25)$$

$$m_{Ex} = m^I - m^{II} > 0 \quad (26)$$

$$m_{Ra} = m^{III} - m^{IV} > 0 \quad (27)$$

$$m_F = m^{III} - m^{II} > 0 \quad (28)$$

where m_E , m_R and m_F , m_D correspond to the flow rate ratios of outgoing (m_E , m_R) or incoming (m_F , m_D) streams (eq. 17 and Fig. 1).

Optimization Tool – Simulated Annealing Method

The method of simulated annealing (SA) is a numerical technique that has attracted attention for efficient solution of large-scale optimization problems, especially when a desired global extremum is hidden among many, poorer, local extrema [5,26]. At the heart of the SA method is an analogy with the way metals cool and anneal [5]. At high temperatures, the atoms of a metals move freely with respect to one another. If the metal is cooled slowly, thermal mobility is lost. The atoms are often able to align themselves and form a pure crystal. This crystal is the state of minimum energy for this system. The SA scheme based on this idea is realized in the following steps.

1. Set the starting vector of decision variables \mathbf{x}_0 (i.e. the vector of the initial values of decision variables).
2. Generate a new vector \mathbf{x}' :

$$\mathbf{x}' = \mathbf{x} + A \times (0.5 - URN)$$

where A is the algorithm variable and URN is a uniform random number.

3. If the objective function OF fulfils the condition $OF(\mathbf{x}') < OF(\mathbf{x})$, accept new point \mathbf{x}' as the best solution and return to step 2, otherwise go to step 4. The vector \mathbf{x} is the best solution.
4. Calculate probability $p1$ by use of the equation:

$$p1 = \exp\left[-(OF(\mathbf{x}') - OF(\mathbf{x}))/T\right]$$

5. Generate a random number, p , within the interval $[0,1]$ (uniform distribution).
6. If $p1 > p$ then accept new point \mathbf{x}' as the best solution and return to step 2.
7. If $p1 < p$ reject new point and return to step 2.

The “temperature”, T , is a decreasing function which describes the manner of “cooling”. Steps 4 to 7 enable escape from a local minimum. The probability of escaping from a local minimum is higher for high values of the “temperature”. The computations from steps 2 to 7 are repeated for slowly decreasing values of the “temperature”, T .

Optimization by use of stochastic methods, for example the SA method, can be more effective if they are coupled with a deterministic minimization procedure. Such a hybrid enables faster convergence of the solution to the optimum compared with the original stochastic algorithms. The probability of locating the global optimum is, moreover, greater than for deterministic methods. A very interesting combination of the simulated annealing method and the downhill simplex method [27] has recently been discussed [5]. The hybrid method was implemented as the procedure AMEBSA [5].

In this work the AMEBSA procedure was used for optimization of batch and continuous separations. The scheme of computation is presented in Fig. 2.

The vector \mathbf{x}_0 of initial values of the decision variables is the first simplex vertex [5,27]. The remaining vertices were generated by use of the formula:

$$x'[j,i] = x[1,i] + A(0.5 - URN); \quad A = 2[x_{\max}(i) - x_{\min}(i)]; \quad i = 1 \dots NP, \\ j = 2 \dots NP + 1$$

where NP is the number of decision variables optimized, $NP + 1$ is a number of simplex vertices, x_{\max} and x_{\min} are the lower and upper bounds of the search region and URN is a random number generated by use of the uniform random number generator RNAD described elsewhere [5].

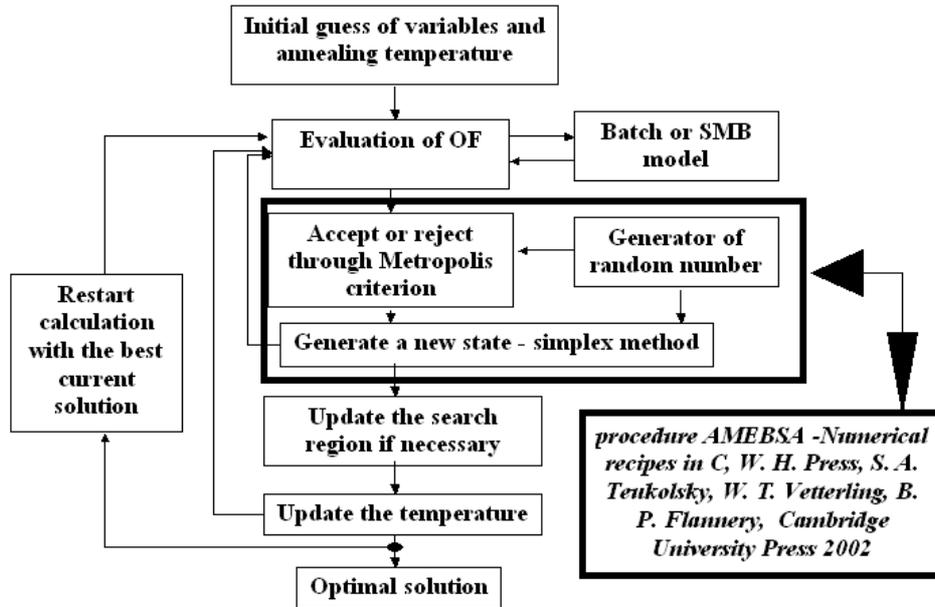


Fig. 2
Computation scheme

The initial temperature was assumed to be:

$$T_0 = \max_i (x_{\max}(i) - x_{\min}(i)) \quad i = 1, \dots, NP$$

For each value of the temperature the objective function was evaluated and a new state was accepted or rejected. These operations were repeated $\beta \times NP$ times for each value of the temperature (the most internal loop in the scheme depicted in Fig. 2).

The temperature was reduced until T was greater than $T_{\min} = 10^{-3}$ (second internal loop) in accordance with the formula:

$$T = T \times (1 - \gamma)$$

where γ is the algorithm variable, $0 < \gamma < 1$.

Finally, the computation was repeated in the external loop $\delta \times NP$ times.

The computations were restarted from the best current vector \mathbf{x} of the decision variables. The external loop was crucial for successful optimization; without it the optimum could not be located for any combina-

tions of β , γ , and T_{\min} . The efficiency of the optimization depends on the values of β , δ , and γ .

Numerical Tools

Batch Chromatography

To solve the optimization problems the algorithm was coupled with the column dynamics model. For batch chromatography the equilibrium-dispersive model (eq. 1) has been solved by use of a finite difference method. A forward-backward algorithm [15,28] was used. The size of the integration step guaranteeing numerical convergence of the solution is calculated on the basis of the isotherm equation and the system efficiency, which depends on the fluid flow rate [15,28].

The SMB Process

To solve the column dynamics model the backward-forward scheme was used; this required smaller integration steps and longer computation time than the forward-backward scheme. The integration step in this scheme is independent of the isotherm terms, however, which is advantageous if the gradient process is simulated. For numerical reasons, to correlate the concentration in the adsorbed and stationary phases a pseudo kinetic equation was introduced (i.e. the equation of the linear solid film driving force), with a sufficiently high value of the kinetic coefficient, for which the solution converged to the equilibrium-dispersive model (i.e. to eq. 1). The details of the model can be found elsewhere [13,14,16].

The computation effectiveness of the algorithm has been compared with that of an RS method using the modified Luus Jaakola algorithm [13, 14].

RESULTS AND DISCUSSION

Optimization of Batch Chromatography

To simulate batch chromatography the following model components were used.

Isotherm Equation

Two isotherm equations were considered, isotherm I exemplifying an easy separation with a relatively high separation factor and isotherm II for a difficult separation. For isotherm I the separation factor increases with

modifier concentration whereas for isotherm II the opposite occurs. Optimization of a difficult separation described by isotherm II requires more computations than that described by isotherm I. The terms of the isotherm model expressed by eqs (5) and (6) are summarized in Table I. These terms correspond to the separation system designed in Ref. [16] and have been already used in previous studies [13,14]. The dependence of the isotherm terms on mobile phase modifier concentration are illustrated in Figs 3 and 4.

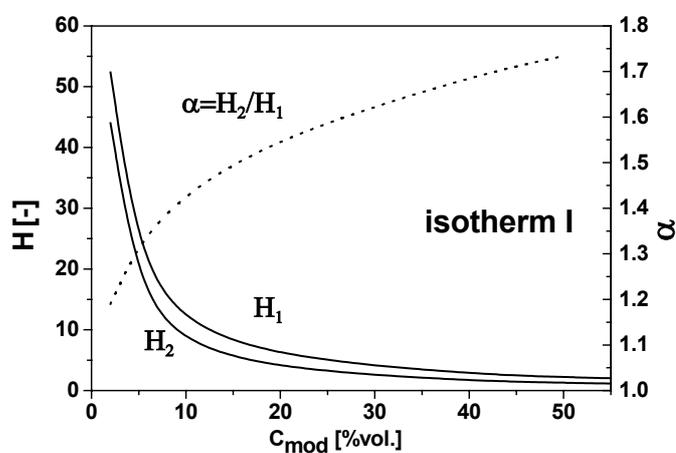


Fig. 3

Dependence on modifier concentration of separation factor and Henry constants

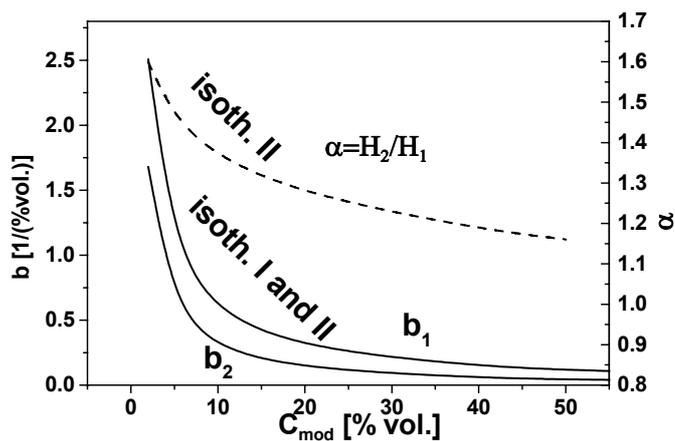


Fig. 4

Dependence on modifier concentration of the separation factor for isotherm II and equilibrium constants for isotherms I and II

Table I

The terms of eqs (8) and (9) for components 1 and 2. For the modifier (eq. 7) $H_{\text{mod}} = 0.92$, $b_{\text{mod}} = 0.05$, and C_{mod} is expressed in % (v/v)

	Component 1	Component 2
p_b	0.316	0.1903
r_b	1.126	0.951
Isotherm I		
p_H	0.0161	0.009
r_H	1.102	0.985
Isotherm II		
p_H	0.0085	0.008
r_H	0.846	0.9457

Terms of the van Deemter Equation

The empirical values of a , b , and c , 4.17×10^{-4} , 2.78×10^{-6} , and 0, respectively, correspond to the data obtained for the experimental system studied elsewhere [16].

A few test examples have been selected for study of the terms with increasing complexity of the optimization problem, i.e. the number of conditions optimized, the objective functions, and the optimization constraints.

Example 1

Optimization problem:

$\max(SP_i)$ for $i = 1, 2$, or $1 + 2$ – see eqs (11)–(13) – subject to the purity constraints $Pu_1 > 0.99$ and $Pu_2 > 0.99$ (eq. 14)

Decision variables:

1. Inlet concentration of the components to be separated, C_{F1} , C_{F2} ; initial values $C_{F1} = C_{F2} = 1$ (% v/v); search region 0.3–20
2. Injection time, t_{inj} ; initial value $t_{\text{inj}} = 1$ s; search region 0.1–30
3. Concentration of the modifier, C_{mod} ; initial value of $C_{\text{mod}} = 5\%$, search region 5–100%
4. Superficial velocity, u ; initial value $u = 0.2 \text{ cm min}^{-1}$, search region 0.2–0.3.

Constant model conditions: Column length $L = 25$ cm, column diameter $D_c = 1$ cm, total column porosity $\varepsilon_t = 0.7$, particle diameter $d_p = 12 \mu\text{m}$.

Terms of the SA method: $\gamma = 0.5$, $\beta = 4$, and $\delta = 5$ (see above).

The optimization problem presented above is relatively easy; it involves few decision variables and a single constraint (purity demand). For both isotherms and all the objective functions considered similar computational efficiency has been achieved. The optimum was located very quickly after ca. 200 evaluations. Further increasing the number of evaluations did not improve the value of the objective function.

The same calculations were repeated with the RS method (random search) with the same initial values and sizes of the search regions. The RS method usually required more evaluations and the value of the optimum was lower than that located with the SA method. Because of the random manner of selection of the decision variables the RS method cannot locate the optimum with the same precision as the hybrid SA method proposed, which uses the advantages:

1. deterministic algorithm of fast (compared with stochastic algorithms) convergence of calculations to the optimum; and
2. random-search methods enable escape from local minima.

A typical comparison of both methods is shown in Fig. 5; for all the remaining examples the efficiency of both the methods was almost the same.

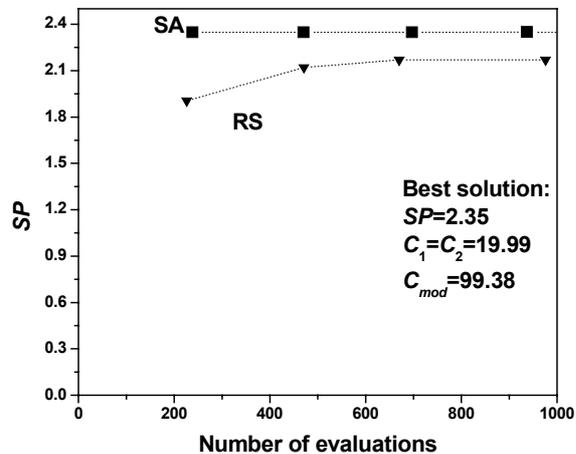


Fig. 5

Convergence of the solution to the optimum for SP ; component 1; isotherm I; Example 1

Example 2

This optimization problem is more complicated. The number of the decision variables has increased, i.e. the particle diameter d_p was set as

another decision variable and the search regions of the mobile phase velocity were enlarged. The number of constraints was increased. The following problem was considered.

Optimization problem:

Max(Pr) (eq. 9), subject to the purity constraints $Pu_1 > 0.99$ and $Pu_2 > 0.99$ (eq. 10), $\Delta t_i > 0.1$ min, the minimum practically feasible fractionating time

Decision variables:

1–3. The same as for Example 1

4. Particle diameter, d_p ; initial value $d_p = 10$ μm , search region 4.9–50

5. Superficial velocity, u ; initial value $u = 0.2$ cm min^{-1} , search region $u_{\min} > 0.01$ cm min^{-1} , $u < u_{\max}$, where u_{\max} is limited by the pressure drop constraint (eq. 16). The maximum pressure drop was $\Delta P_{\max} = 4 \times 10^7$ Pa.

The bed porosity, ε_e , was assumed to be 0.35. The remaining model terms were the same as in Example 1.

The results of the calculations are presented in Table II. The number of evaluations, NE , needed to locate the optimum depends strongly on the difficulty of the problem solved. The largest number of evaluations was necessary for isotherm II for the second component as key product. The optimum mass overloading is obviously higher for isotherm I at a high modifier concentration than for isotherm II. In all instances concentration overloading was preferable to volume overloading; the injection volume was low and reached the boundary of the search region.

Table II

Optimum values of the decision variables for Example 2

C_i (%, v/v)	C_{mod} (%, v/v)	t_{inj} (min)	d_p (μm)	u (cm min^{-1})	Pr ($\text{mL}_{\text{product}} \text{min}^{-1} \text{cm}^{-2}$)	NE
Isotherm I, production rate for the first component						
14.1	99.7	0.100	5.00	15.5	38.5	1500
6.61	97.6	0.106	8.61	24.3	38.5	
Isotherm I, production rate for the second component						
17.0	97.7	0.103	8.98	44.7	52.3	1400
Isotherm II, production rate for the first component						
1.25	5.95	0.101	17.0	153	19.4	3400
Isotherm II, production rate for the second component						
0.533	5.11	0.100	25.8	416	19.2	7000
0.588	5.29	0.100	29.0	414	19.0	

NE is the number of evaluations required to locate the optimum

A very important feature of the method presented is that it enables location of several equivalent optima corresponding to the same or similar values of the objective function; this is typical of multimodal objective functions. From analysis of the first two rows and the last two rows in Table II it follows that several equivalent sets of decision variables can be found corresponding to the same value of the goal function.

To verify the robustness of the procedure, calculations were repeated for a reduced number of conditions, i.e. the particle diameter d_p was set equal to the optimum reported in Table II and the remaining decision variables were considered. Optimization converged to similar results; the best value of the objective function did not differ from that presented in Table II by more than 4%.

To achieve comparable robustness the random search algorithm required a many more evaluations. Similar effectiveness could be achieved only when the decision variables C_{mod} and d_p were optimized discretely, i.e. for each discrete change of C_{mod} and d_p the remaining operating conditions were optimized. The RS procedure was, moreover, efficient if the calculations were initiated with a feasible point for which the optimization constraints were met, otherwise a large number of evaluations was needed to solve the problem.

Optimization of SMB Processes

Optimization of SMB processes is usually more difficult than for batch separations. This is particularly true if mobile-phase composition is optimized. Variation of the modifier concentration involves changes in the isotherm equation, which strongly affects the position and shape of the separation region in the plane of $m^{\text{II}}-m^{\text{III}}$.

For gradient separation the region is no longer a triangle and the shape changes rapidly with any change of modifier concentration. Simultaneous optimization of all four flow rates m^K and the modifier concentrations is, therefore, very difficult. It is important to note that the algorithm does not require a good starting point; calculation can be initialized with an unfeasible point. In gradient elution the operating conditions can be determined only by use of numerical solution. Analytical solution of the gradient problem which takes into account changes of the isotherm and of the concentration profile of the modifier is not possible. Note that all methods reported in the literature for optimization of the SMB process [6,7, 8–11] exploit the triangle theory developed on the basis of the analytical solution for the steady-state TMB process.

Three numerical experiments were performed with increasing complexity of the optimization problem.

Example 3

Optimization problem:

$OF = \min (EC)$ (eq. 21) subject to the constraints $Pu_E > 0.9$ and $Pu_R > 0.9$; the weight in the penalty function, eq. (24a), was $weight = 1000$

Decision variables:

- 1–4. Flow rate ratios m^{I-IV} : the calculations were started with an unfeasible point, for which purity constraints were not met; initial values: $m^I = 15$, $m^{II} = 10$, $m^{III} = 15$, $m^{IV} = 10$; search region 0.1–20
5. $C_{mod} = C_{modF} = C_{modD}$, modifier concentration in the SMB unit (isocratic mode); initial value $C_{mod} = 10$; search region 5–100%

Constant model conditions: model conditions as for the batch system except the inlet concentration of species: $C_{F1} = C_{F2} = 5\%$ (v/v)

Calculations were performed for both isotherms. Convergence of the solution to the optimum is illustrated in Fig. 6 for the most difficult case of isotherm II. Each point in the plot corresponds to an optimization success (i.e. a better value of the solution was found).

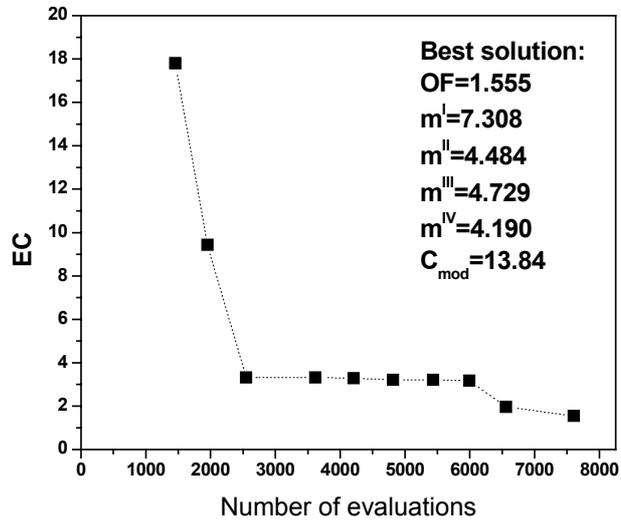


Fig. 6

Convergence of the solution to the optimum for EC ; isotherm II, Example 3

Terms of the algorithms: $\gamma = 0.2$, $\beta = 2$, and $\delta = 5$ (see above).

Column length was assumed to be $L = 15$ cm, column diameter was assumed to be $D_c = 0.46$ cm, total column porosity was assumed to be $\varepsilon_t = 0.75$, and the number of theoretical plates was assumed to be 50.

In this instance the computer time needed to locate the optimum was the longest because, as mentioned above, the optimization problem was very difficult – it corresponded to very severely nonlinear conditions, for which the separation region is narrow. Variation of modifier concentration also resulted in large changes of the shape and position of the triangle. Also, the calculations were initiated with unfeasible point. The procedure was able to locate a feasible point after approximately 1500 solutions of the SMB model and the optimum was found after 8000 solutions. The number of evaluations could be substantially lower if the sizes of search regions of the decision variables were reduced.

Example 4

In the next example optimization of the SMB gradient in the closed loop arrangement was examined.

Optimization problem:

$$OF = \min(EC) \text{ or } \max (PR)$$

Decision variables:

- 1–4. Ratios m^I – m^{IV} ; initial point: $m^I = 12$, $m^{II} = 10$, $m^{III} = 12$, $m^{IV} = 10$ (unfeasible); search region 0.1–15
5. Modifier concentration in the desorbent stream, C_{modD} ; initial value $C_{\text{modD}} = 50\%$; search region 4.5–100%

Constant model conditions: feed concentration $C_{F1} = C_{F2} = 0.3\%$ (v/v); concentration of the modifier in the feed stream $C_{\text{mF}} = 0$; other model conditions and constraints as in Example 3

The progress of optimization for isotherms I and II is presented in Figs 7 and 8 and the optimum conditions are reported in Table III. Irrespective of isotherm model, maximum productivity was obtained after approximately 2000 solutions of the SMB model. A more difficult problem was minimization of mobile-phase consumption, particularly for isotherm II, for which the optimum was found after about 4000 evaluations. Optimization of modifier concentration in isocratic or gradient mode using a single stochastic method was effective only when the optimization was performed discretely; with step changes of the modifier concentration [14], and calculations were initiated with a feasible point.

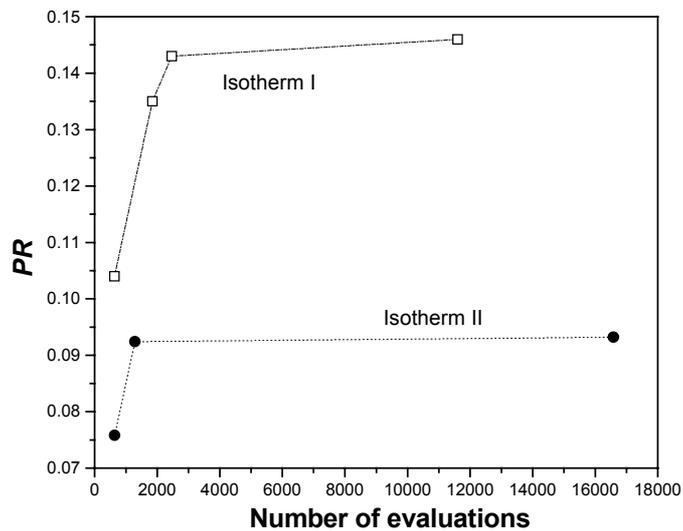


Fig. 7
 Convergence of the solution to the optimum for *PR*. The square symbols denote isotherm I and the circles denote isotherm II; Example 4

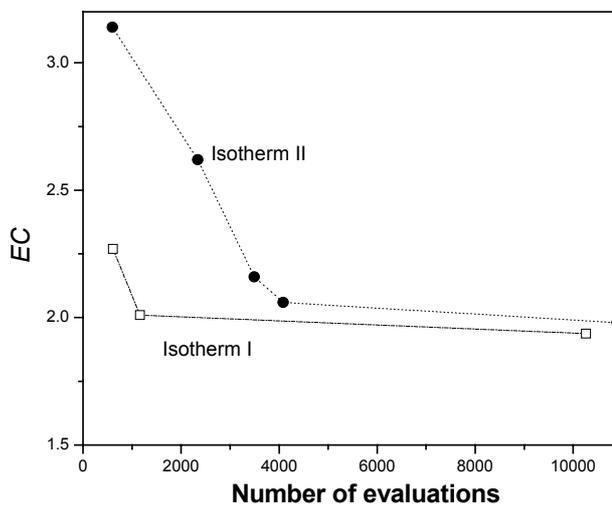


Fig. 8
 Convergence of the solution to the optimum for *EC*. The square symbols denote isotherm I and the circles denote isotherm II; Example 4

Table III

Optimization of SMB separation in gradient mode

m^I	m_I^I	m^{III}	m^{IV}	C_{mod}	Pu_R	Pu_E	PR	EC
Isotherm I								
1.47	0.574	7.37	0.102	99.99	0.911	0.944	0.146*	2.16
8.04	4.44	8.62	7.5	98.8	0.976	0.957	0.084	1.94*
Isotherm II								
9.62	4.37	9.87	4.86	19.5	0.914	0.900	0.093*	3.42
8.87	4.73	9.73	8.34	99.9	0.969	0.901	0.088	1.98*

*Optimized value

Example 5

The efficiency of the method was examined for multi-objective optimization of isocratic and gradient SMB operation.

Optimization problem:

Min (OF) (eq. 20) subject to the constraint: $Pu_E > 0.9$ and $Pu_R > 0.9$; the weight in the penalty function eq. (24b) was $weight = 1000$; constant model conditions: feed concentration: $C_{F1} = C_{F2} = 0.3\%$ (v/v).

Decision variables:

Case 1: isocratic mode

- 1-4. Flow rate ratios m^K ; initial point: $m^I = 12$, $m^II = 10$, $m^{III} = 12$, $m^{IV} = 10$ (unfeasible); search region 0.1–15
5. Modifier concentration $C_{\text{modF}} = C_{\text{modD}}$; initial value $C_{\text{modF}} = C_{\text{modD}} = 50\%$; search region 4.5–100%

Case 2: gradient mode

- 1-4. Flow rate ratios m^K ; initial point, search region the same as in Case 1
5. Modifier concentration C_{modD} ; initial value: $C_{\text{modD}} = 50\%$; search region 4.5–100%

The other conditions were the same as in Example 4.

In both the cases calculations were performed for the isotherm I.

The sets of best solutions obtained for these two examples are compared in Fig. 9.

The best values of productivity were found to be very similar to that obtained in Example 4, which confirmed the robustness of the multi-objective optimization technique.

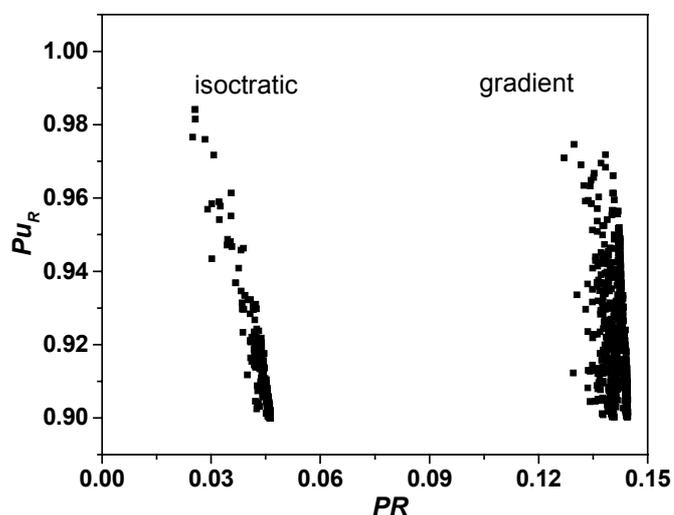


Fig. 9

Results from multi-objective optimization of P_{u_R} and PR for gradient and isocratic modes

The same number of evaluations as reported for example 4 was needed to locate the optimum for both cases.

CONCLUSIONS

In this work the effectiveness of a hybrid method of simulated annealing (SA) and the downhill simplex algorithm for optimization of chromatography has been examined. The method used the advantages of deterministic methods of fast convergence of calculations to the optimum and the advantage of random search methods to escape from local minima when finding the solution.

The method was used to solve optimization problems for separations in batch and continuous chromatographic systems under isocratic and gradient conditions. To verify the robustness of the algorithm several test examples of different complexity were solved. For a batch separation few decision variables, for example flow rate, mass overloading, mobile-phase composition and particle diameter, were simultaneously optimized subject to purity constraints and other specific process constraints. SMB optimization involved such decision variables as flow rates in SMB zones and mobile-phase composition under isocratic and gradient conditions. The procedure was found to be more robust and efficient than a random search

algorithm based solely on a stochastic procedure. The method robustly and rapidly locates the global optimum and does not require initiation of the calculations with a feasible point, i.e. to initiate calculations very approximate information about process performance is required, which is important for systems of low efficiency, for which predictions of operating conditions on the basis of the triangle theory may be inaccurate, and for gradient conditions, for which operating conditions must be determined numerically and locating a good point for initialization is problematic.

NOTATION AND ABBREVIATIONS

Term	Unit
a, b, c = coefficients of the van Deemter equation	
b = equilibrium constant	1/(% v/v)
C = concentration in mobile phase	% (v/v)
d_p = diameter of bed particle	μm
D_a = apparent dispersion coefficient	$\text{cm}^2 \text{min}^{-1}$
D_c = column diameter	cm
EC = eluent consumption	$\text{mL}_{\text{eluent}} (\text{mL}_{\text{product}})^{-1}$
$F = \frac{1 - \varepsilon_t}{\varepsilon_t}$ = phase ratio	–
H = Henry constant	–
L = column length	cm
m = flow rate ratio	–
NE = total number of evaluations	–
p_b = term in eqs (5) and (6)	–
p_H = term in eqs (5) and (6)	–
Pr = productivity for batch chromatography	$\text{mL}_{\text{product}} \text{cm}^{-2} \text{min}^{-1}$
PR = productivity for SMB process	$\text{mL}_{\text{product}} (\text{mL}_{\text{stat.phase}})^{-1} \text{min}^{-1}$
Pu = purity	%
q = concentration in the solid phase	% (v/v)
r_b = term in eqs (5) and (6)	–
r_H = term in eqs (5) and (6)	–
S = column cross-sectional area	cm^2
SP = specific productivity	$\text{mL}_{\text{product}} (\text{mL}_{\text{eluent}})^{-1}$
t = time coordinate	min
t^* = switching time	in
t_{inj} = injection time	in
T = “temperature” – condition of simulated annealing	–
u = superficial velocity	cm min^{-1}
V = column volume	mL
\dot{V} = volumetric flow rate	mL min^{-1}
w = interstitial velocity	cm min^{-1}

\mathbf{x} = vector of decision variables	
Y = yield	–
z = axial coordinate	cm
Greek letters	
α = separation factor	–
β, γ, δ = parameter of simulated annealing method	–
$\varepsilon_t, \varepsilon_e$ = total and external porosity	–
η = viscosity	kg m ⁻¹ s ⁻¹
Subscripts	
D = desorbent	
E = extract	
F = feed	
i = component index	
mod = modifier	
R = raffinate	
Superscripts	
K = zone index	

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