

## Solvent-gradient SMB to separate *o*-xylene and *p*-xylene

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**Abstract**—In batch chromatography, solvent-gradient operations (SG) produce significant improvement in terms of the enrichment of products and the separation time and the solvent consumption as compared with isocratic operations. This work studied solvent-gradient operation in reversed-phase simulated moving bed unit to separate *ortho*-xylene and *para*-xylene. In a solvent-gradient mode, different mobile phase compositions lead to a different retention behavior of solutes, i.e., different adsorption isotherms. Frontal analysis experiments for *ortho*-xylene and *para*-xylene were carried out with a reversed-phase column to measure adsorption parameters at several different mobile phase compositions, such as 45%, 50%, 60%, 75% and 90% acetonitrile. Therefore, the parameters in the retention model for solvent-gradient operation in the case of reversed-phase chromatography were estimated and applied to the design of an SMB system. A modified design method for solvent-gradient simulated moving bed chromatography (SG-SMB) was proposed. The robust operating conditions were obtained within the separation region on  $(\varphi_R, \varphi_E)$  plane ( $\varphi_R$  and  $\varphi_E$  are the volumetric content of organic modifier in the raffinate and the extract streams, respectively). The performance results of isocratic and solvent-gradient SMB were compared. A partial-discard strategy and increasing of the solvent gradient level were also applied to improve the performance of the SG-SMB.

Key words: Solvent-gradient, Simulated Moving Bed, SMB, *O*-xylene, *P*-xylene, Reversed Phase Liquid Chromatography

### INTRODUCTION

The SMB technology, first patented by Universal Oil Products (UOP) as the Sorbex process [1], has emerged as a powerful tool for the continuous counter-current separation of binary mixtures. The basic concept of an SMB process is to simulate the solid phase movement of the corresponding true moving bed (TMB) where the fluid and solid phases move countercurrently [2]. Countercurrent operation maximizes the driving force for mass transfer, thus providing for a better use of the adsorbent than that of the traditional batch mode. The SMB system consists of multiple identical chromatographic columns which are interconnected circularly to form a closed loop. By periodically switching the inlet and outlet ports in the same direction with the fluid flow, the countercurrent contact between the solid and liquid phases is simulated.

The conventional four-zone SMB described above has recently been used commercially in many industrial separations [3-5]. Almost all SMB operations are carried out under isocratic conditions, such as constant temperature, pressure, and mobile phase composition. However, the separation of enantiomers as well as bioseparation is often based on rather small selectivities. Many studies have demonstrated the significant effect of experimental conditions (temperature, pressure, mobile phase composition) on the adsorptivity and retention time of solutes [6-8]. It is promising to apply the gradient conditions in a SMB operation in order to improve the separation performances [8].

Gradient elution is widely applied to improve the separation of

mixtures by varying the solvent strength during the elution process. The main result of using gradient elution is to increase the resolution of early eluted components in a mixture and to decrease the retention time of a less diluted component, which will result in decreased solvent consumption and less diluted product [8-14]. The concept of applying gradients in the SMB process has been recently identified as a method for further improving separation performance. In an SG-SMB, schematically drawn in Fig. 1, the implementation of gradients using two different solvents or two different mobile phase compositions at two inlet ports was suggested [11-14]. The solvent strength is weak in the feed solution and strong in the desorbent solution. As a result, the components to be separated are more retained in the solvent regeneration zone of SMB process (zone 4) and more easily eluted in the sorbent regeneration zone (zone 1) [2].

Recently, the two-step gradient SMB process was studied theoretically and experimentally to separate two cycloketones using normal-phase silica and a different composition of n-hexane and ethyl acetate (as modifier) [11]. The model proposed follows the locally and temporally changing composition of the solvent composition and specifies from this information and the current adsorption equilibrium forming the driving force for the separation. Systematic calculations were performed in order to identify suitable operating conditions as a function of averaged desorbent concentrations. A significant improvement in the process performance as compared to the common isocratic SMB was found.

In another study on SG-SMB, Abel et al. studied design criteria for binary SMB separations operated in the solvent gradient mode in linear isotherm [8] and non-linear isotherm [9]. In particular, she tried to determine the complete separation region in the operating parameter space, and to clarify the features of the solvent gradient

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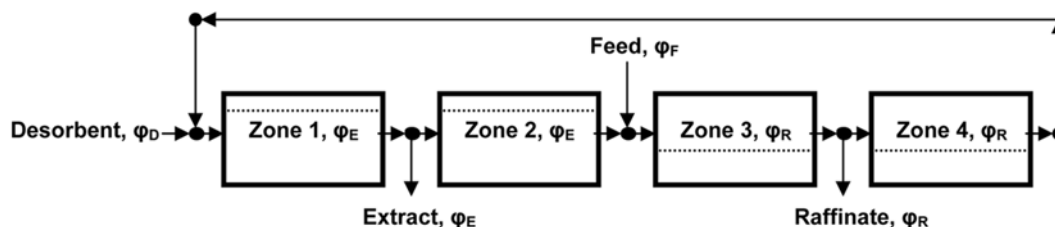


Fig. 1. Schematic illustration of the solvent gradient SMB. Dotted lines are the level of organic modifier. The levels of organic modifier in zones 1 and 2 are maintained higher as compared with those in zones 3 and 4. The concentration of strong solvent (organic solvent) in the desorbent and in the feed are indicated by the symbols  $\varphi_D$  and  $\varphi_F$ , respectively. The strong solvent concentrations are indicated as  $\varphi_E$  in zones 1 and 2, and as  $\varphi_R$  in zones 3 and 4.

operation, without actually attempting to identify optimal operating conditions, e.g., optimal solvent gradient profile and optimal operating point. To design the complete separation region, the authors tried to fix the organic concentration in zone 2 and change the organic concentration in zone 3. A set of fixed values of the organic concentration in zone 2 were chosen from the minimum value to maximum value in order to obtain the complete separation region in ( $m_2$ ,  $m_3$ ) plane when both organic concentrations in zone 1, 2 and zone 3, 4 were changing from minimum to maximum values. Two enantiomers, (R)-(+)- $\alpha$ -ionone and (S)-(+)- $\alpha$ -ionone, were separated in the methanol-water mobile phase using solvent-gradient operation in an SMB unit.

In this work, our objective was to separate *o*-xylene and *p*-xylene using reversed phase simulated moving bed process in a solvent-gradient mode. A modified design method for gradient SMB based on the retention model and linear isotherm was developed and the separation region was drawn on the ( $\varphi_R$ ,  $\varphi_E$ ) plane. The simulations of gradient SMB were performed with the operating conditions obtained from the separation region on ( $\varphi_R$ ,  $\varphi_E$ ) plane. These results were compared to the performance results of an isocratic SMB. A partial-discard strategy and increasing the solvent gradient level were also applied to improve the performances of the SG-SMB.

## THEORY

### 1. Isocratic Simulated Moving Bed

With reference to a binary mixture to be separated, the more retained component, called A, is collected in the extract stream, while the less retained component, called B, is collected in the raffinate stream. Both the batch and simulated moving bed (SMB) chromatographic process can be modeled by the differential mass balance equation:

$$\frac{\partial c_i}{\partial t} + \beta \frac{\partial q_i}{\partial t} + u \frac{\partial c_i}{\partial x} = D_{L,i} \frac{\partial^2 c_i}{\partial x^2} \quad (1)$$

where  $c_i$  and  $q_i$  is the concentration of component  $i$  in the mobile phase and the stationary phase, respectively,  $\beta$  is the phase ratio and equals to  $(1 - \varepsilon^*)/\varepsilon^*$  where  $\varepsilon^*$  is the bed voidage of the column,  $u$  is the interstitial velocity and  $D_{L,i}$  is the axial dispersion coefficient of component  $i$ .

For mass transfer between the mobile and stationary phase, it is common to use a linear lumped mass transfer model:

$$\frac{\partial q_i}{\partial t} = a_p k_{eff,i} (c_i - c_i^*) \quad (2)$$

with  $a_p k_{eff,i}$  is the mass transfer coefficient of solute  $i$ ,  $a_p$  is  $6/D_p$  for spherical particles, and  $c_i^*$  is concentration of solute  $i$  in the liquid film.

The triangle theory, based on the equilibrium theory of chromatography, offers simple design criteria for the operation of SMB units [15]. In its framework, the performance of the SMB unit is characterized by the ratio of the net flow of the mobile phase to that of the stationary phase, i.e., the  $m_j$  values, which are defined as:

$$m_j = \frac{Q_j t^* - V \varepsilon}{V(1 - \varepsilon^*)} \quad (j=1, \dots, 4), \quad (3)$$

where  $Q_j$  is the volumetric flow rate in section  $j$ ,  $t^*$  is the switching time, and  $V$  and  $\varepsilon$  are the column volume and void fraction.

Under the condition of dilute concentration of solutes, the adsorption equilibrium can be represented by a linear isotherm:

$$q_i = H_i c_i \quad (i=1, 2), \quad (4)$$

where  $H_i$  is the Henry constant.

Under these conditions, the necessary and sufficient operating conditions for complete separation in a SMB unit are determined by the following inequalities [16]:

$$H_A < m_1 < \infty \quad (5)$$

$$H_B < m_2 < H_A \quad (6)$$

$$H_B < m_3 < H_A \quad (7)$$

$$\frac{-\varepsilon_p}{1 - \varepsilon_p} < m_4 < H_B \quad (8)$$

### 2. Solvent-gradient Simulated Moving Bed

In a four-zone SMB, each zone has different role. In zones 1 and 2, the major role is to desorb solutes for the regeneration of adsorbent and preventing of the contamination of extract port from the less retained solute, respectively. On the contrary, the major role of zones 3 and 4 is to adsorb solutes for the preventing contamination of raffinate port from the more retained solute and the regeneration of desorbent, respectively. Therefore, in an SG-SMB, the levels of organic modifier in zones 1 and 2 are maintained higher as compared with those in zones 3 and 4. Thus, the gradient changes are located at the ports between zones 1, 2 and zones 3, 4. These gradient changes can be controlled by different compositions of the mobile phase in the feed and desorbent streams.

Let us indicate the concentration of a strong solvent (organic solvent) in the desorbent and in the feed with the symbols  $\varphi_D$  and  $\varphi_F$ ,

respectively. The composition profile for mobile phase can be illustrated in Fig. 1. When  $\varphi_D > \varphi_F$ , i.e., the concentration of a strong solvent in the desorbent is higher than that in the feed, retention time will be shorter in zones 1 and 2 than in zones 3 and 4. The mobile phase composition profiles in each section are flat at steady state in the TMB unit where axial dispersion is neglected. The strong solvent concentrations are indicated as  $\varphi_E$  in zones 1 and 2; and as  $\varphi_R$  in zones 3 and 4. Eq. (9) shows the boundaries of the organic modifier content in the extract and raffinate streams:

$$\varphi_D > \varphi_E > \varphi_R > \varphi_F \quad (9)$$

where  $\varphi_D$ ,  $\varphi_E$ ,  $\varphi_R$ , and  $\varphi_F$  are the volumetric content of organic modifier in the desorbent, the extract, the raffinate, and the feed streams, respectively. To maintain constant composition of the mobile phase in the extract and the raffinate stream, the mass balances of the organic modifier in each zone have to be satisfied by the following two equations:

$$m_3 = \frac{\varphi_E - \varphi_F}{\varphi_R - \varphi_F} m_2 \quad (10a)$$

$$m_4 = \frac{\varphi_E - \varphi_D}{\varphi_R - \varphi_D} m_1 \quad (10b)$$

If the adsorption isotherm of solutes is linear, the separation region on ( $m_2$ ,  $m_3$ ) plane is drawn as rectangular. The design criteria of a gradient SMB are similar to that of an isocratic SMB; however, the partition coefficients of solutes are different in zones 1-2 and zones 3-4. The following inequalities show the design criteria of gradient SMB:

$$H_A(\varphi_E) < m_1 \quad (11)$$

$$H_B(\varphi_E) < m_2 < H_A(\varphi_E) \quad (12)$$

$$H_B(\varphi_R) < m_3 < H_A(\varphi_R) \quad (13)$$

$$-(1 - \varepsilon_p)/\varepsilon_p < m_4 < H_B(\varphi_R) \quad (14)$$

where subscripts A and B represent the more retained solute and the less retained solute, respectively. The partition coefficient corresponding to the content of the organic modifier is obtained from the retention model. In this work, a three parameter model, Eq. (4), is adopted and the retention factor is converted to the partition coefficient by following relationship:

$$H = K = \frac{v_m}{v_s} k = \frac{1}{\beta} k \quad (15)$$

where  $H$ ,  $K$ ,  $k$  and  $\beta$  are Henry's constant, partition coefficient, retention factor and phase ratio, respectively and  $v_m$  and  $v_s$  are the volume of the mobile phase and the stationary phase in the column, respectively. A retention model for solvent gradient elution in the reversed phase liquid chromatography proposed by Lee et al. [17, 18] was used for this study. The retention behavior of solutes is described as a function of organic-modifier content:

$$\ln k = \frac{\ln k_w - S\varphi}{1 + k_s\varphi} \quad (16)$$

where  $k_w$  is the retention factor with pure water as the mobile phase,  $S$  is the empirical coefficient,  $k_s$  is the empirical coefficient for the dwindling rate of parameters  $k_w$  and  $S$ , and  $\varphi$  is the volumetric frac-

tion of the organic modifier.

## EXPERIMENTAL

### 1. Materials

Ortho-xylene (*o*-xylene) and para-xylene (*p*-xylene) were purchased from Junsei Chemical Co., Ltd, Japan. Mobile phases were prepared with acetonitrile (HPLC grade solvent) from J.T. Baker Company, USA, and deionized water was acquired from Milli-Q purification system, Millipore, USA.

### 2. Equipment

The HPLC system is composed of two pumps (model LC-6AD, Shimadzu, Kyoto, Japan), a UV detector (model SPD-M10A vp Shimadzu), an auto-injector (STL-10 AD vp Shimadzu), and a column oven (model CTS-30Younglin, Korea)

A C18 Kromasil column (1 cm×10 cm) with 100 Å-25 µm spherical silica particles was used.

### 3. Methods

#### 3-1. Test the Solubility of Solutes

In a solvent gradient operation, the solubility of solutes is very important for the separation because changing the mobile phase composition, i.e., the modifier concentration or the pH of the solution or its ionic strength, has a major effect on both the retention time and solubility. If the concentration of solutes is higher than their solubility, a portion of solutes will become immiscible and will not agree with the normal adsorption behavior. Especially in a solvent gradient SMB, the concentration of solutes often increases dramatically in zone 2 because the flow rate of the extract stream is smaller than that in an isocratic mode SMB.

The solubility of *o*-xylene and *p*-xylene as a function of the mobile phase composition was measured at 30 °C. The solvent mixtures prepared with different solvent contents were saturated with *o*-xylene and *p*-xylene at 30 °C. The samples were taken and put in a water bath at 30 °C for 1 hour. The concentration of solutes was measured by using the HPLC system.

#### 3-2. Adsorption Isotherm

Among the various chromatographic methods available to determine single-component isotherms, frontal analysis (FA) is the most accurate [19]. For chromatographic systems with low efficiency, FA is the most suitable method, because of its accuracy and its relative simplicity [20].

The five-step frontal analysis was performed using a C18 Kromasil column (1 cm×10 cm) detected by photo diode array detector, at a temperature of 30 °C and a flow rate of 3 ml/min. To study the adsorption behavior in the linear case, solutes were made at the concentrations of 0.5 g/l. The experiments were done with a column and without a column. For each step in the frontal analysis, the amount of solutes adsorbed on the solid phase calculated by a graphic method is the area difference of the elution profile between with a column and without a column. In the ( $c$ ,  $q$ ) plot, five points calculated from five-step frontal analysis can be fitted by a straight line regressed to the linear isotherm in order to obtain the Henry constant  $H_i$  in the equation  $q_i = H_i \cdot c$ . This is the linear adsorption isotherm for a single component. These experiments were done in mobile phase solutions prepared with five compositions of acetonitrile and water which included 45%, 50%, 60%, 75% and 90% acetonitrile in water.

### 3-3. Retention Behavior in the Mixed Solvents

Changing mobile phase compositions not only affect the solubility but also the retention behavior of the solutes. To operate in a solvent gradient mode, it is necessary to survey the changing retention behavior of the solutes when the solvent content in the mobile phase changes.

In reversed phase liquid chromatography, the retention behavior of solutes is described as a function of the organic-modifier concentration as shown in the Eq. (16). The retention times of solutes decrease when the organic modifier (strong solvent) concentration increases. In this work, this retention model was used to describe the retention behavior of *o*-xylene and *p*-xylene in reversed-phase liquid chromatography using an acetonitrile-water solution as the mobile phase.

To find the parameters in the retention model Eq. (16), five values of Henry constants obtained from the results of the multi-step frontal analysis experiments above at five mobile phase compositions of 45%, 50%, 60%, 75% and 90% acetonitrile were plotted on a retention model curve described by the Eq. (16).

### 3-4. Estimation of Kinetic Model

The retention behavior of solutes not only depends on the adsorption isotherm but also on the kinetic model. To estimate a suitable kinetic model for the solvent gradient operation, the elution profiles of frontal analysis for *o*-xylene and *p*-xylene at five mobile phase compositions of 45%, 50%, 60%, 75% and 90% acetonitrile were estimated using an Aspen chromatography simulator. The kinetic model was chosen when simulation results showed a good agreement with the experimental results.

### 3-5. Determination of Gradient Condition in SMB

In the isocratic-mode SMB, i.e.  $\varphi_R = \varphi_E$  (known value), the necessary and sufficient conditions to achieve complete separation in the case where the adsorption isotherm is linear follow Eqs. (5) to (8). With these four constraints, to build the complete separation region in the  $(m_2, m_3)$  plane is a simple task. The projection of the corresponding complete separation region onto the  $(m_2, m_3)$  plane is a square, of which only the portion above the diagonal, where  $m_2 > m_3$ , allows having a positive feed flow rate.

However, in the solvent gradient SMB, the operation lines obtained from the mass balance of the organic modifier, Eq. (10), have to pass through the separation region on the  $(m_2, m_3)$  plane and also the  $(m_1, m_4)$  plane. If this condition is not satisfied, it is impossible to operate the gradient SMB. A modifier design method for gradient SMB draws the separation region on the  $(\varphi_R, \varphi_E)$  plane.

The mass balance equations at the feed node and desorbent node are written as follows:

$$\varphi_E = \frac{m_3}{m_2}(\varphi_R - \varphi_F) + \varphi_F \quad (17)$$

$$\varphi_E = \varphi_D - \frac{m_4}{m_1}(\varphi_D - \varphi_R) \quad (18)$$

From Eqs. (11) to (14) for the conditions in the flow rate ratios

to achieve complete separation, we can have some inequalities:

$$\frac{m_3}{m_2} > \frac{H_B(\varphi_R)}{H_A(\varphi_E)} \quad (19)$$

$$\frac{m_3}{m_2} < \frac{H_A(\varphi_R)}{H_B(\varphi_E)} \quad (20)$$

$$\frac{m_4}{m_1} < \frac{H_B(\varphi_R)}{H_A(\varphi_E)} \quad (21)$$

To replace the  $m_3/m_2$  and  $m_4/m_1$  in two mass balances at the feed node (17) and at the desorbent node (18) by the inequalities (19), (20), and (21), we can obtain three boundary equations for the  $(\varphi_R, \varphi_E)$  plane:

$$\varphi_E < \frac{H_A(\varphi_R)}{H_B(\varphi_E)}(\varphi_R - \varphi_F) + \varphi_F \quad (22)$$

$$\varphi_R < \frac{H_A(\varphi_E)}{H_B(\varphi_R)}(\varphi_E - \varphi_F) + \varphi_F \quad (23)$$

$$\varphi_R < \varphi_D - \frac{H_B(\varphi_R)}{H_A(\varphi_E)}(\varphi_D - \varphi_E) \quad (24)$$

These three inequalities are nonlinear, so a numerical method is required to solve these equations. The right triangle shows the region obtained by Eq. (9). Owing to these three lines and one right triangle region, the separation region on the  $(\varphi_R, \varphi_E)$  plane can be decided when the mobile phase compositions of the feed and the desorbent streams are fixed. According to the selected operation point on the  $(\varphi_R, \varphi_E)$  plane, the mobile phase compositions in the extract and raffinate streams are obtained, and it is possible to draw the separation regions which are passed through by the operation lines on the  $(m_2, m_3)$  plane and the  $(m_1, m_4)$  plane. Finally, the flow rate ratio,  $m$ , in each zone can be obtained.

## RESULTS AND DISCUSSIONS

### 1. Solubility

The solubility of solutes is affected by the organic volumetric fraction of the solution used for dissolving solutes. Therefore, in solvent-gradient chromatography, it is important to consider the solubility of solutes in the mixed solvents with different compositions. Fig. 2 and Table 1 shows the solubility of *o*-xylene and *p*-xylene in the mobile phase solution with different acetonitrile concentrations. The solubility of these solutes rises rapidly when the acetonitrile concentration in the mobile phase increases.

### 2. Adsorption Isotherms and Retention Behavior of Solutes in the Mixed Solvent

In the linear case, the adsorption behavior of *o*-xylene and *p*-xylene follows Eq. (4) when the Henry constant  $H$ , i.e., the partition coefficient  $K$ , is calculated from the frontal analysis for each solute with five different mobile phase compositions, 45%, 50%, 60%, 75% and 90% acetonitrile in water. The equilibrium isotherms ob-

**Table 1. The solubility of *o*-xylene and *p*-xylene in the mobile phase solution with different acetonitrile concentrations**

AcN concentration (%)	30	40	50	60	70	80	90
Solubility of <i>o</i> -xylene in AcN solution (%)	0.42	0.48	1.08	2.35	3.93	6.81	15.56
Solubility of <i>p</i> -xylene in AcN solution (%)	0.41	0.46	1.01	1.94	3.41	6.31	14.14

tained for the adsorption of *p*-xylene and *o*-xylene on C18 are presented in Fig. 3. In this case, both components are linear isotherms.

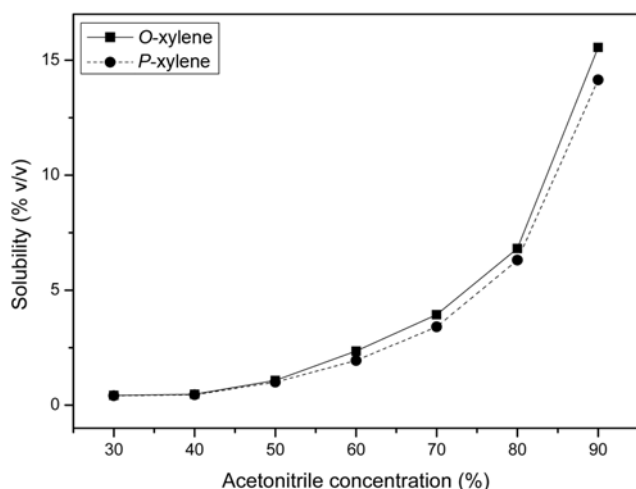


Fig. 2. The solubility of *o*-xylene and *p*-xylene in the mobile phase solution with different acetonitrile concentrations. The samples were taken and put in a water bath at 30 °C for 1 hour before being measured at 30 °C using HPLC.

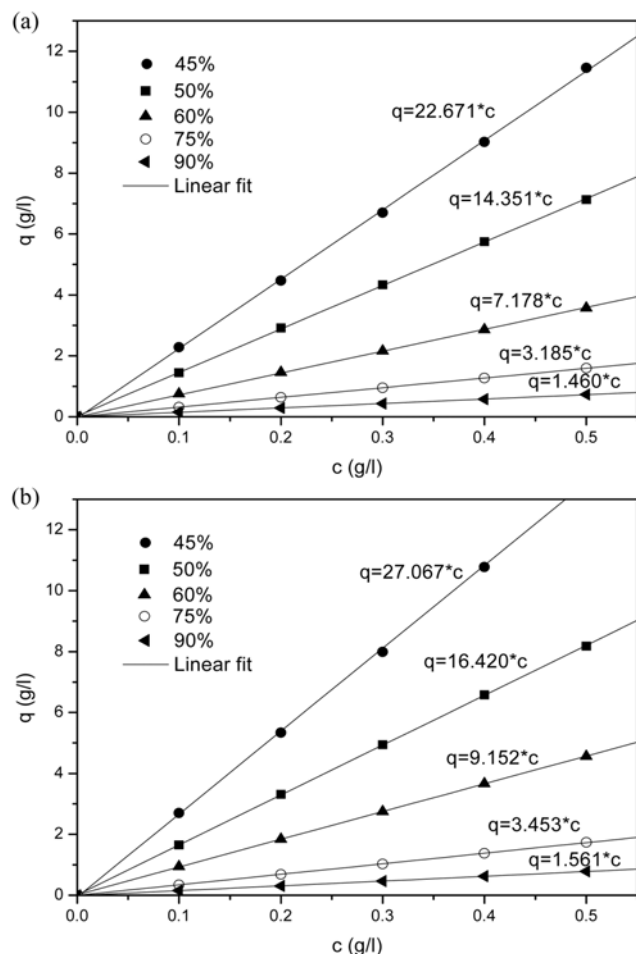


Fig. 3. The comparison of the experimental data and calculated isotherm curve of (a) *o*-xylene and (b) *p*-xylene on C18 at 30 °C.

As the results illustrated in the Table 2 show, the partition coefficient *K* of both *o*-xylene and *p*-xylene is high in the mobile phase with low acetonitrile content (45%), but decreases dramatically when the acetonitrile content increases up to 90%. It is worth noting that the difference of the partition coefficient *K* between two solutes means their resolution, which is high in the mobile phase, has low acetonitrile content.

To express the retention behavior of *o*-xylene and *p*-xylene when changing the acetonitrile concentration in the mobile phase, we used the retention model in Eq. (16) proposed by Lee et al. The retention factors of *o*-xylene and *p*-xylene decrease exponentially when the acetonitrile concentration in the mobile phase increases, as shown in Fig. 4. To estimate three parameters in the retention model  $k_w$ ,  $k_s$  and  $S$ , five points in the  $(\varphi, \ln k)$  plot obtained from the frontal analysis experiments were fitted by a curve defined by the retention model Eq. (16). Table 3 shows the empirical coefficients of the retention model. Consequently, retention models for *o*-xylene and *p*-xylene

Table 2. The partition coefficient (*K*) of *o*-xylene and *p*-xylene in the mobile phase with different acetonitrile concentrations

Acetonitrile concentration (%v/v)	Partition coefficient ( <i>K</i> )	
	<i>O</i> -xylene	<i>P</i> -xylene
45	22.671	27.067
50	14.351	16.420
60	7.178	9.152
75	3.185	3.453
90	1.460	1.561

Table 3. The empirical coefficients of the retention models

Component	$\ln k_w$	<i>S</i>	$k_s$	* <i>R</i> <sup>2</sup>
<i>O</i> -xylene	8.968	0.094	0.014	0.999
<i>P</i> -xylene	7.854	0.082	0.008	0.998

\*: Regression coefficient

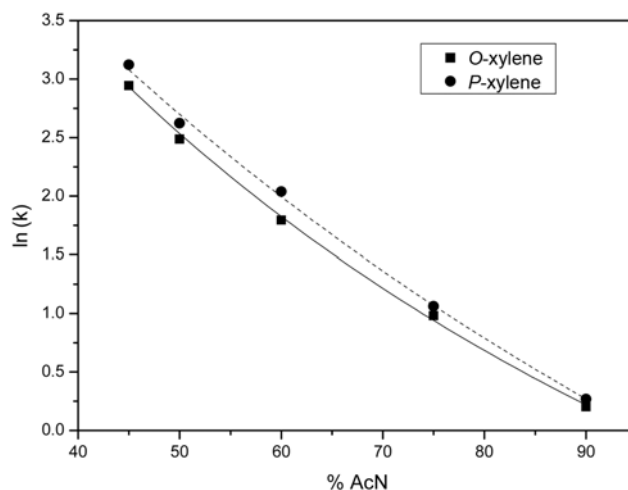


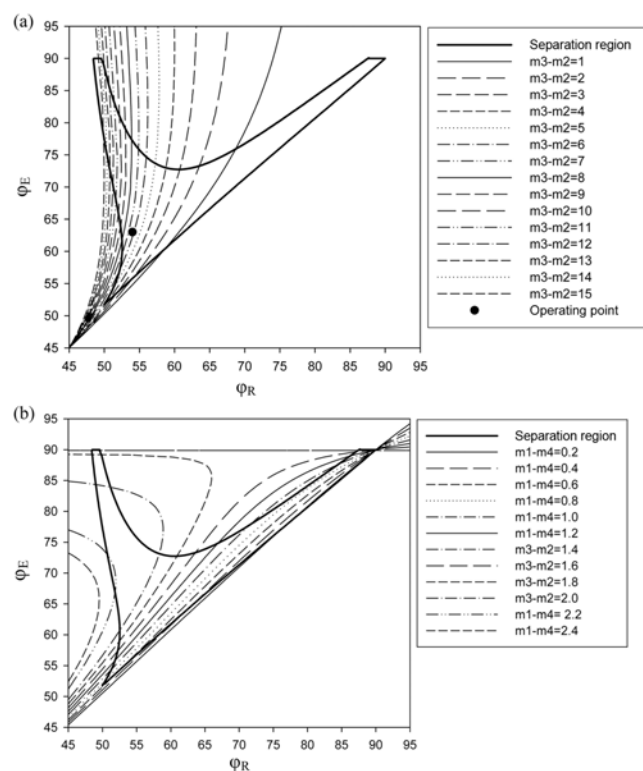
Fig. 4. The comparison of experimental data and calculated retention model curve of *o*-xylene and *p*-xylene on C18 at 30 °C.

**Table 4. Column specifications**

Description	Value	Units
Length of packed section	10.0	cm
Internal diameter of packed section	1.0	cm
Inter-particle/external voidage	0.336	m <sup>3</sup> void/m <sup>3</sup> bed
Intra-particle voidage/porosity	0.314	m <sup>3</sup> void/m <sup>3</sup> bed
Particle radius of adsorbent	25.0	micron
Adsorbent shape factor	1.0	n/a
Mass density of eluent	996.0	kg/m <sup>3</sup>
Liquid (Solvent) viscosity	0.89	cP
Constant mass transfer coefficient	1000.0	1/min

**Table 5. Simulation parameters for SG-SMB**

Partial differentiate equation discretization method	Biased upwind differencing scheme (BUDS)
Number of elements	40
Material balance	Convection with Estimated dispersion coefficient
Kinetic model	Linear lumped resistance
Lumped resistance film model	Fluid
Mass transfer coefficient	Constant
Isotherm model	Linear
Simulating step size	0.05



**Fig. 5.** The separation zone of SG-SMB in  $(\phi_R, \phi_E)$  plane and the contour lines of (a)  $m_3$ - $m_2$  and (b)  $m_1$ - $m_4$  on  $(\phi_R, \phi_E)$  plane. Black thick lines in (a) and (b) are the separation regions. The circle symbol is the operating point for the simulation of SG-SMB.

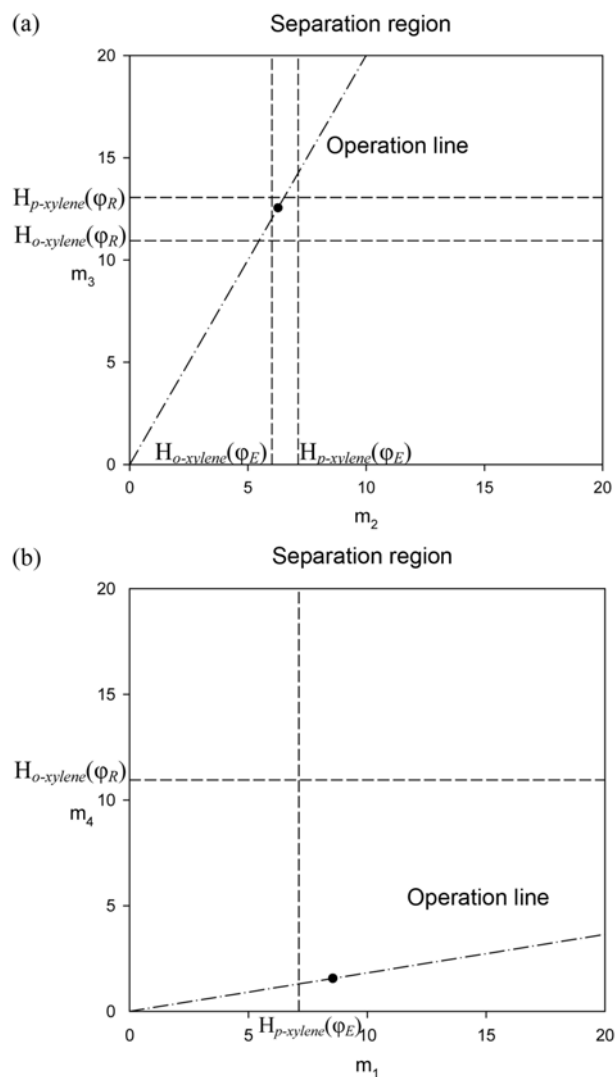
in reversed phase chromatography using acetonitrile as an organic modifier were determined as the equations:

$$\ln k_{o\text{-xylene}} = \frac{8.968 - 0.094\phi}{1 + 0.014\phi} \quad (25)$$

$$\ln k_{p\text{-xylene}} = \frac{7.854 - 0.082\phi}{1 + 0.008\phi} \quad (26)$$

### 3. Estimation of Kinetic Model

The kinetic model, which plays an important role in predicting the eluting profile of solutes in liquid chromatography, was estimated by simulating the frontal analysis of these solutes using an Aspen chromatography simulator. The column specifications used for simulation are shown in Table 4. The simulation results must have a good agreement with the experimental results. The estimated parameters of the kinetics model are shown in Table 5.



**Fig. 6.** The operation lines and operation points in (a) the  $(m_2, m_3)$  plane and (b) the  $(m_1, m_4)$  plane.  $m_2$  and  $m_3$  values were obtained at the middle of the operation lines in the separation regions on the  $(m_2, m_3)$  plane and  $m_1$  and  $m_4$  were obtained with safety margin value was 20%, i.e.  $m_1 = 1.2 \cdot H_{p\text{-xylene}}(\phi_E)$ .

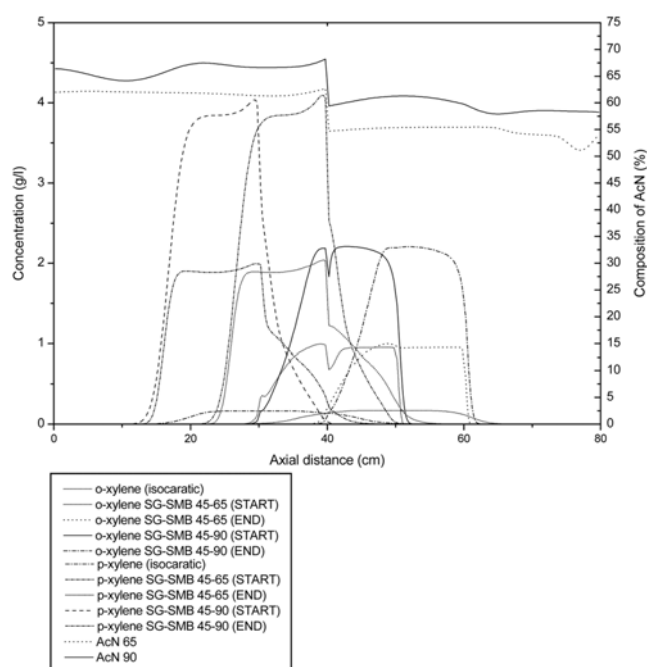
**Table 6. The operating condition of an isocratic and gradient SMB**

	Isocratic operation	Solvent gradient operation
Feed		
Concentration (g/l)		
<i>O</i> -xylene	0.25	0.25
<i>P</i> -xylene	0.25	0.25
Flow-rate (ml/min)	1.00	1.00
Modifier content (vol%)	54	45
Desorbent		
Flow-rate (ml/min)	4.28	1.12
Modifier content (vol%)	54	65
Extract flow-rate (ml/min)	2.84	0.36
Raffinate flow-rate (ml/min)	2.44	1.76
Recycle flow-rate (ml/min)	10.48	0.44
Switching time (min)	3.77	22.46

#### 4. Comparison between Solvent-gradient SMB and Isocratic SMB

With the simulation parameters and column specifications obtained above, the solvent-gradient operation in the SMB unit to separate *o*-xylene and *p*-xylene was simulated by using Aspen Chromatography 2006®. The design of solvent gradient region in the ( $\phi_R$ ,  $\phi_E$ ) plane is shown in Fig. 5. The operating point in the completed separation region was chosen to determine the solvent gradient value used for the SG-SMB process. In particular, the organic concentration of the mobile phase in the zones 1, 2 ( $\phi_E$ ) and in the zones 3, 4 ( $\phi_R$ ) was 63% and 54%, respectively. When  $\phi_D$ ,  $\phi_F$ ,  $\phi_E$  and  $\phi_R$  are known, the complete separation region in the ( $m_2$ ,  $m_3$ ) plane and in the ( $m_1$ ,  $m_4$ ) plane can be designed easily as shown in Fig. 6. The  $m_2$  and  $m_3$  values were obtained at the middle of the operation lines in the separation regions on the ( $m_2$ ,  $m_3$ ) plane, and  $m_1$  and  $m_4$  were obtained with a safety margin value of 20%, i.e.  $m_1 = 1.2 \cdot H_{p\text{-xylene}}(\phi_E)$ . The operating conditions for the SG-SMB to separate *o*-xylene and *p*-xylene were determined as shown in Table 6.

The simulation of the SG-SMB process was compared to simulation of the isocratic-condition SMB process. To compare the gradient to an isocratic SMB, an isocratic operating condition which had similar purity, yield, and productivity of products was simulated. The results in Table 7 were calculated from the simulation results at the 15<sup>th</sup> cycle of the SMB simulation. With the same feed flow rate, by the gradient operation, it is possible to concentrate *p*-xylene 2.77 times higher as compared with the feed concentration. Also, the desorbent consumption decreased to almost 4 times lower. Another advantage of the SG-SMB shown in Table 6 is that the zone flow



**Fig. 7. The simulated column profiles of *o*-xylene, *p*-xylene and volumetric percentage of acetonitrile in the mobile phase in the cases of an isocratic SMB and a SG-SMB.**

rates in the case of the SG-SMB are much lower than those in the isocratic case.

#### 5. Improvement of the SG-SMB

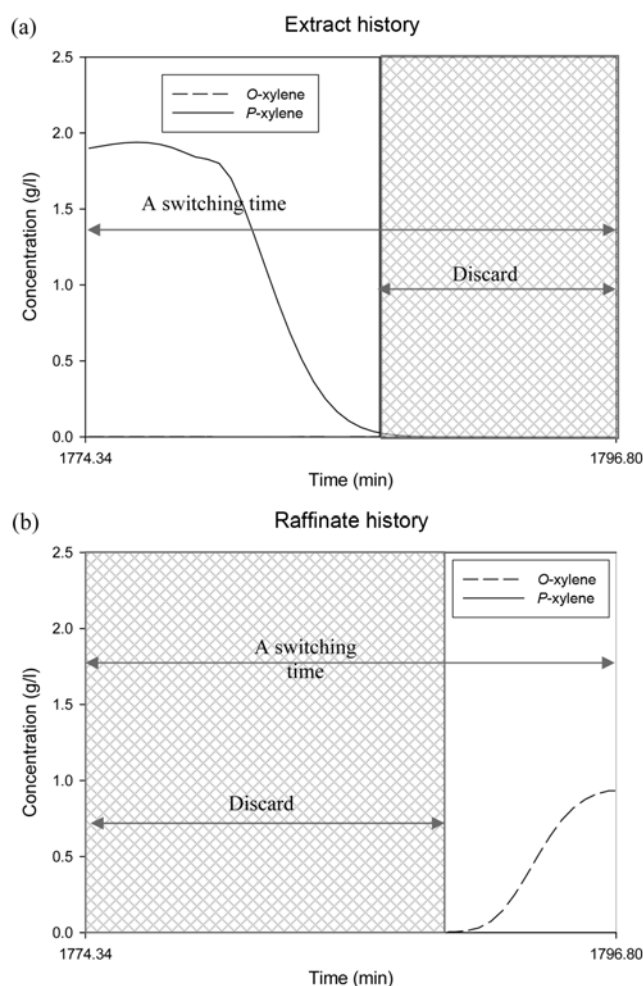
##### 5-1. Partial-discard Strategy for Obtaining Higher Enrichment Products

Fig. 8 illustrates the history product concentrations from both product ports. In the case of the extract product, at the last state of switching time, there was almost no product. The raffinate product exhibited the same phenomenon but it appeared at the initial stage of switching time. So a partial-discard operation was applied to improve the enrichment of product [21].

In the partial discard operation, a portion of the extract and raffinate products were discarded at the last and the initial stage of switching time, respectively. Adjustment of the discard time played a key role in optimizing the SMB process in relation to improving enrichment. Fig. 9 demonstrates the effect of the discard time on enrichment and yield when the partial discard operation was applied. During the partial discard operation, the enrichment of product at the extract port and also the raffinate port improved dramatically when the discard time was increased. The improvement is explained by Fig. 8, which shows that most of the non-product portion was ob-

**Table 7. The comparison of performance of the SMB between isocratic and gradient operations**

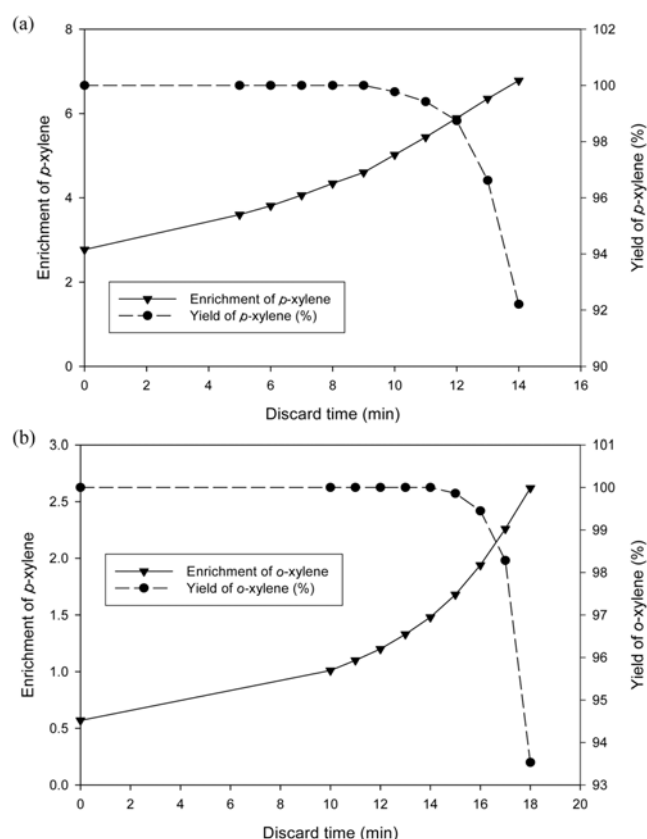
System	SMB Results								
	Purity (%)		Productivity (g/(min×cm <sup>3</sup> ))		Yield (%)		Enrichment		Desorbent consumption (ml/min)
	<i>O</i> -xylene	<i>P</i> -xylene	<i>O</i> -xylene	<i>P</i> -xylene	<i>O</i> -xylene	<i>P</i> -xylene	<i>O</i> -xylene	<i>P</i> -xylene	
Isocratic	99.83	99.89	$0.87 \times 10^{-5}$	$0.86 \times 10^{-5}$	99.71	99.33	0.41	0.35	4.28
Solvent gradient ( $\phi_F=45$ , $\phi_D=65$ )	100.00	100.00	$0.87 \times 10^{-5}$	$0.87 \times 10^{-5}$	100.00	100.00	<b>0.57</b>	<b>2.77</b>	<b>1.12</b>
Solvent gradient ( $\phi_F=45$ , $\phi_D=90$ )	100.00	100.00	$0.87 \times 10^{-5}$	$0.87 \times 10^{-5}$	100.00	100.00	<b>0.79</b>	<b>4.76</b>	<b>0.47</b>



**Fig. 8.** The history of extract and raffinate in one switching time with partial discard strategy. A portion of the extract and raffinate products was discarded at the last and initial stage of the switching time, respectively, (a) the extract port and (b) the raffinate port.

served at the last stage and initial state of switching time at the extract port and raffinate port, respectively. However, this operation can make the yield decrease as the discard time is increased, which can be seen in Fig. 9. At the extract port and the raffinate port,  $t_{\text{discard}}$  was optimized at values of 9 min and 14 min, respectively.

Table 8 presents the comparison of performance of SMB between conventional SG-SMB and partial-discard SG-SMB operations. The yield did not change, 100% for both extract port and raffinate port. Moreover, the enrichment of *o*-xylene at extract port in the case of partial-discard SG-SMB operations was increased nearly three times as compared with that in the case of a conventional SG-SMB. Especially, enrichment of *p*-xylene at the extract port increased from 2.77



**Fig. 9.** The effects of discard time on the SMB performance at (a) the extract port and (b) the raffinate port.

to 4.60 times as compared with the feed concentration when we carried out the partial discard operation. The portion not collected as a product was reused. We could make the discarded portions have the same concentration of acetonitrile with that in the desorbent, which allowed reuse as a desorbent.

#### 5-2. Increasing the Solvent-gradient Level from (45-65) to (45-90)

The main result of using gradient elution is increased retention time of the early eluted components in a mixture and decreased retention time of the latest eluted components, which will result in decreased solvent consumption and less diluted product. Therefore, the improvement of SMB performance can be predicted when we increase the solvent-gradient level.

When the gradient level was increased, the concentration of component in the column increased as shown in Fig. 7. From the results shown in Table 7, by the gradient operation, it is possible to concentrate *p*-xylene to 2.77 times higher as compared with the feed concentration. It can be improved by changing the compositions of acetonitrile in the desorbent from 65% to 90%. The results showed higher enrichment of *o*-xylene with increases from 0.57 to 0.79, as well as

**Table 8.** The comparison of performance of the SMB between conventional SG-SMB and partial-discard SG-SMB operations

System	Productivity (g/(min×cm <sup>3</sup> ))		Yield (%)		Enrichment		Desorbent consumption (ml/cycle)
	<i>O</i> -xylene	<i>P</i> -xylene	<i>O</i> -xylene	<i>P</i> -xylene	<i>O</i> -xylene	<i>P</i> -xylene	
Conventional SG-SMB	$0.87 \times 10^{-5}$	$0.87 \times 10^{-5}$	100.00	100.00	0.57	2.77	1.12
Partial-discard SG-SMB	$0.87 \times 10^{-5}$	$0.87 \times 10^{-5}$	100.00	100.00	<b>1.48</b>	<b>4.60</b>	1.12



the enrichment of *p*-xylene, which increased dramatically from 2.77 to 4.76.

The desorbent consumption also decreased to almost four times lower when the concentration of acetonitrile in the desorbent was 65% and nearly nine times lower when it increased from 65% to 90%. This can be explained: when we increase the composition of the desorbent, the retention times of *o*-xylene and *p*-xylene decrease, which makes the process result in lower desorbent consumption.

## CONCLUSIONS

In a gradient SMB, it is difficult to design the completed separation region on the ( $m_2$ ,  $m_3$ ) plane. Therefore, in this work, a modified design method for a gradient SMB was proposed. Robust operating conditions were obtained with the separation region on the ( $\varphi_R$ ,  $\varphi_E$ ) plane. This design method for a solvent gradient SMB is able to determine the gradient level and to easily obtain robust operation conditions. To do this, the retention model, which has three parameters used to explain the nonlinear relationship between the logarithm of the retention factor and the volumetric fraction of the organic modifier in the mobile phase, was estimated and applied to the design of the completed operating zone of the SMB.

By the simulation of gradient SMB, it is possible to obtain a more concentrated product as compared with the concentration of feed solution and the desorbent consumption, which was decreased to one-fourth of the isocratic SMB. A partial discard operation was applied to improve the enrichment of products. When the partial discard strategy was applied to the extract port at the last stage of the switching time and to the raffinate port at the initial stage, the enrichment of *o*-xylene and *p*-xylene increased dramatically as the discard time was increased. The performance of SMB also increased after the solvent-gradient level was increased.

## NOMENCLATURE

$c$	: fluid phase concentration of solute [g/l]
$D_L$	: the axial dispersion coefficient [cm <sup>2</sup> /min]
$H$	: Henry constant
$a_p k_{eff}$	: the mass transfer coefficient [1/min]
$K$	: the partition coefficient of solute between the stationary phase and the mobile phase
$k$	: the retention factor
$k_s$	: the empirical coefficient
$k_w$	: the retention factor with pure water as the mobile phase
$m$	: flow rate ratio between the desorbent and adsorbent flow rate
$q$	: solid phase concentration of solute [g/l]
$Q$	: volumetric flow rate [ml/s]
$S$	: the empirical coefficient
$t_w$	: switching time [min]
$u$	: interstitial velocity of the mobile phase
$V$	: column volume [ml]
$v_m$	: the volume of the mobile phase in the column
$v_s$	: the volume of the stationary phase in the column

### Greek Letters

$\varepsilon$  : the total void fraction of the column

$\beta$	: the phase ratio of the column
$\varphi$	: the volumetric content of organic modifier [%]
$\varphi_D$	: the volumetric content of organic modifier in the desorbent stream [%]
$\varphi_E$	: the volumetric content of organic modifier in the extract stream [%]
$\varphi_F$	: the volumetric content of organic modifier in the feed stream [%]
$\varphi_E$	: the volumetric content of organic modifier in the raffinate stream [%]

## Subscripts and Superscripts

D	: desorbent
E	: extract
F	: feed
$H_A(\varphi_E)$	: Henry constant of the more retained component in zone 1, 2
$H_A(\varphi_R)$	: Henry constant of the more retained component in zone 3, 4
$H_B(\varphi_E)$	: Henry constant of the less retained component in zone 1, 2
$H_B(\varphi_R)$	: Henry constant of the less retained component in zone 3, 4
i	: component
j	: section of SMB
R	: raffinate

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