Theoretical Study of Sequential Centrifugal Partition Chromatography

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Sequential centrifugal partition chromatography (sCPC) is a novel cyclic liquid–liquid chromatographic process. Each cycle comprises two steps, which differ by the liquid phase used as a mobile phase (upper or lower phase) and its flow direction. The feed is continuously separated into two product streams, which are collected alternately. The process includes six (four flow rates and two-step durations) interconnected operating parameters. In this work, by imposing a complete separation of a binary feed mixture and using the assumption of instantaneous solutes partition equilibrium, a set of constraints on the sCPC unit operating parameters is derived. Using these constraints, a region of complete separation, composed of a set of combinations of the two-step times, can be defined for a preselected feed and mobile phase flow rates. The approach is validated by simulation of a binary mixture separation in a sCPC using the cell model. © 2012 American Institute of Chemical Engineers *AIChE J,* 59: 241–249, 2013

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Introduction

In solid support free liquid–liquid chromatography (commonly referred as countercurrent chromatography, CCC), the two phases of a biphasic liquid system, obtained by mixing of at least two solvents, are used as a mobile and stationary phase. The mechanism of separation is based on the difference of the distribution (partitioning) of the solutes between the two liquid phases.[1] One of the phases is kept stationary in a specially designed column hardware assembled on a centrifuge. The whole set-up is called CCC machine or CCC instrument and replaces the classical column used in liquid–solid chromatography. There are basically two types of commercially available CCC machines (i.e., columns): (i) hydrodynamic type, with two axes of rotation and (ii) hydrostatic type, with one axis of rotation.[1–3]

In liquid–liquid chromatography, either of the phases of the biphasic liquid system (upper or lower phase) can be used as a stationary phase. Moreover, their role and flow direction can be reversed during the chromatographic separation. This creates the opportunity for several original operating options, not possible with solid stationary phases. These novel operating procedures can be used to improve the separation (increase product purity and recovery) and cut down the separation time (increasing productivity and reducing solvent consumption).

One of the alternative operating modes is the dual mode, where the separation is started in a conventional elution mode and after some time the phase's role and mobile phase flow direction is switched, that is, the phase used as a mobile phase becomes stationary phase and vice versa[4,5]; or the multiple dual mode where the phase switching is performed several times after the sample injection.[6] Another operating option is the elution-extrusion mode, where the separation run is started in a conventional elution mode and at a certain point the mobile phase is stopped and the stationary phase is pumped into the column to push out the column content.[7,8] Alternative CCC machine arrangements have also been used to perform operating procedures commonly used in extraction. As for instance, the cocurrent mode, where the stationary phase moves slowly in the same direction with the mobile phase.[9,10] In the dual flow mode (countercurrent mode), the phases move in opposite directions, while the feed is introduced in the middle of the column in a batch or continuous manner.[11–13]

The sequential centrifugal partition chromatography (sCPC) is a novel liquid–liquid chromatographic separation technology.[14] In sCPC, a feed stream is continuous introduced between two columns and two product streams are collected successively at the opposite ends of the two columns. Each cycle comprises two steps, which differ by the liquid phase used as a mobile phase and its flow direction.[14] In the patent of Couillard et al.,[14] the sCPC concept is described and demonstrated in a equipment set-up with hydrostatic columns. Recently, the sCPC concept was also applied in set-ups with two hydrodynamic, instead of two hydrostatic columns. The feed mixture was introduced either

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Additional Supporting Information may be found in the online version of this article.

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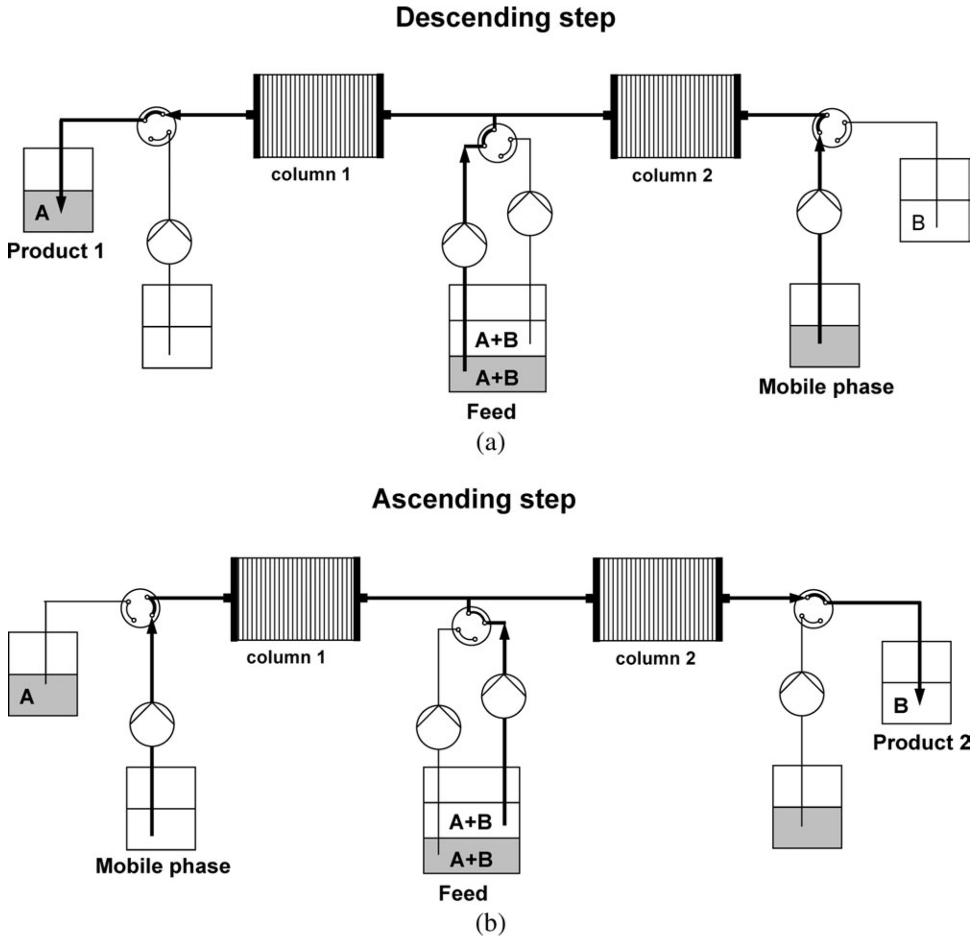


Figure 1. Technical illustration of a sCPC unit operating in (a) descending step and (b) ascending step (lower phase presented in gray color, upper phase presented in white color).

as a bolus (long pulse injection)[15–17] or continuously.[18] In these works, the same concept was named intermittent dual CCC[17] and intermittent countercurrent extraction.[15,18]

Except sCPC, all above-mentioned liquid–liquid chromatography operating modes were already described mathematically using approaches of different complexity.[19–25] Correlations for the prediction of a solute's elution times based on the solute retention volume, distribution constant, and the volumes of the two phases are also available in the literature.[8,9,17,26]

The objective of this work is to derive correlations that could be used to select preliminary operating parameters of a sCPC unit for separation of a binary mixture. By requiring that the unit achieves complete separation of the feed components, a set of implicit constraints on the operating parameters is derived using the local equilibrium theory. It is demonstrated how these constraints can be used to select the operating conditions of a sCPC for a complete separation of a model binary feed mixture. The discrete (staged) cell model is used to simulate a sCPC unit operation and to explore the applicability of the proposed approach.

sCPC

The sCPC was originally described and demonstrated in a specially designed equipment set-up with a hydrostatic type of CCC column.[14,27] The unit was commercialized recently by Armen Instrument (France) under the name True Moving Bed Centrifugal Partition Chromatograph and is schematically presented in Figure 1.

The sCPC unit has two hydrostatic CCC columns (Columns 1 and 2) placed on two rotors and four pumps. More details about the design of the columns are available in the Supporting Information. Before the separation is started, the columns are filled with a preset volume ratio of the upper and lower phase of the selected biphasic solvent system. 50v%:50v% phase ratio is normally used[15–18,28] and recommended by the producer of the equipment. In principle, different phase ratios can also be used, as soon as the preset ratio can be kept constant during the unit operation. After the columns are filled with upper and lower phase, the rotors are started. When the set rotation speed is reached, the feed is introduced continuously between the two columns, and the two products are alternately collected at the opposite ends of the two columns.

The sCPC is a cyclic process. The cycle consists of two steps: descending and ascending step. In the following, the sCPC principle of operation will be explained for a separation of a binary mixture, containing Components A and B. It is assumed that Component A distributes preferentially into the lower phase, whereas Component B distributes preferentially into the upper phase.

In descending step, presented in Figure 1a, the lower phase is used as a mobile phase, and it is introduced in the unit through Column 2. Components A and B dissolved in the lower phase are used as a feed, which is introduced between Columns 1 and 2. During the descending step

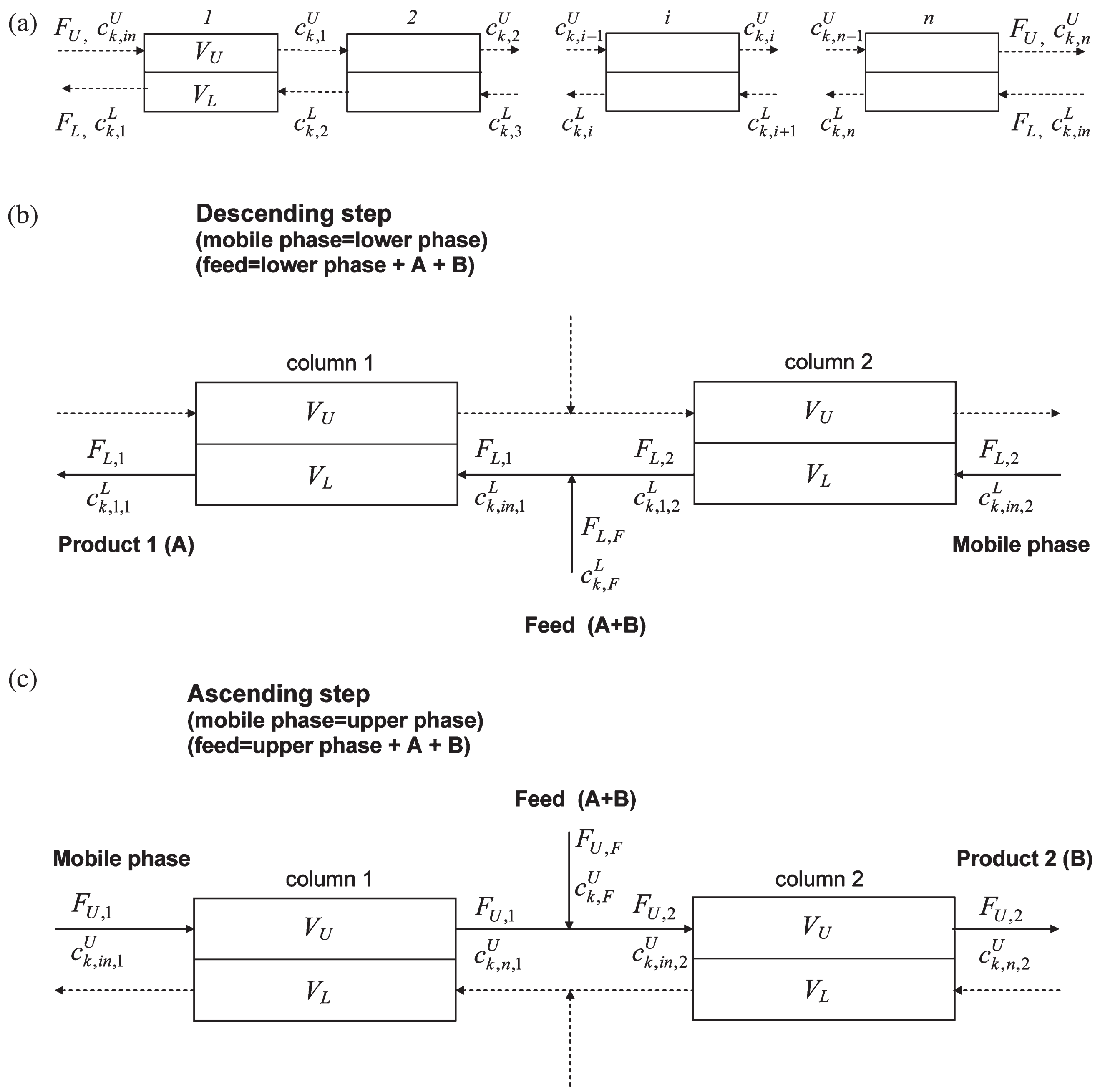


Figure 2. (a) General presentation of a single column with *n* cells, operating in ascending or descending step; (b) stream flow rates and concentrations in a sCPC unit during the descending; and (c) stream flow rates and concentrations in a sCPC unit during ascending step.

Component A travels faster with the mobile phase and is collected in Product 1 at the left end of Column 1. Before Component B elutes from Column 1, the unit operation is switched to the ascending step (Figure 1b). Components A and B dissolved in the upper phase are now used as a feed stream. During the ascending step, the upper phase is the mobile phase, and it is introduced in the unit through Column 1. In this step, Component B travels faster with the mobile phase and is collected in Product 2 at the right end of Column 2. Before Component A elutes out of Column 2, the unit is switched back to the descending step. The time durations of the descending and ascending step are called here descending step time (t_{Des}) and ascending step time (t_{As}), respectively. The duration of one sCPC cycle is equal to the sum of the descending and ascending steps times ($t_{\mathrm{Des}} + t_{\mathrm{As}}$).

In summary, the main feature of sCPC is the possibility to switch from descending to ascending step (and vice versa) and thereby separate a binary mixture continuously. With a correct choice of the operating parameters, highly pure products can be obtained.

Results and Discussion

Mathematical modeling of sCPC operation

The liquid–liquid chromatography can be modeled using conventional chromatographic models. Some of the most commonly used models are the Craig's countercurrent distribution model,[19,20,24] the cell model,[24,25] and the axial dispersion model.[21,23–25]

In this work, the cell model was used to model the sCPC unit operation. The sCPC model was derived based on the model for a single column. According to the assumption of the cell model, the CPC column can be divided into n ideal mixed cells, that is, hydrodynamically and thermodynamically equilibrated stages. The following assumptions were used in the derivation of the sCPC model:

- The sCPC consists of two identical columns (Columns 1 and 2).
- The off column volume is negligible.
- The volume of the two liquid phases is equal in all cells in both columns.
- The volume of each phase (upper or lower phase) is the same during the ascending and descending step. The phases are instantaneously reversed (mobile phase in descending becomes stationary phase in ascending step), and no phase is lost during the step switch.
- The solutes distribution constants are constant (independent of the solute concentration).
- The distribution constant of a solute k in each step is defined as the ratio of the solute concentration in the stationary over the mobile phase, consequently: $K_{k,\mathrm{As}} = \frac{1}{K_{k,\mathrm{Des}}}$.
- The number of cells per column is equal in ascending and descending step.

In Figure 2a, a generic drawing of a single column with n cells during the ascending and descending step is presented. In the figure, k refers to the solute (k = A, B); i is the cell number (i = 1,2,…n); V_U and V_L are the volumes of the upper and lower phase, respectively; F_U and F_L are the volumetric flow rates of the upper phase (during the ascending step) and lower phase (during the descending step), respectively; $c^\mathrm{U}_{k,i}$ is the concentration of Component k in the upper phase in cell i; $c^\mathrm{L}_{k,i}$ is the concentration of Component k in the lower phase in cell i; $c^\mathrm{U}_{k,\mathrm{in}}$ is the inlet concentration of Component k in the upper phase during the ascending step; and $c^\mathrm{L}_{k,\mathrm{in}}$ is the inlet concentration of Component k in the lower phase during the descending step.

The schematic presentation of the two CPC columns during the descending and ascending step, with corresponding stream concentrations, flow rates and directions, used in the derivation of the sCPC model equations, is given in Figures 2b, c.

The sCPC model equations are:

Generic mass balance of Component k in cell i of Column j

$$\frac{V_\mathrm{U}}{n}\frac{dc^\mathrm{U}_{k,i,j}}{dt} + \frac{V_\mathrm{L}}{n}\frac{dc^\mathrm{L}_{k,i,j}}{dt} = F_{\mathrm{U},j}\left(c^\mathrm{U}_{k,i-1,j} - c^\mathrm{U}_{k,i,j}\right) + F_{\mathrm{L},j}\left(c^\mathrm{L}_{k,i+1,j} - c^\mathrm{L}_{k,i,j}\right) \tag{1}$$

In descending mode (Figure 2b):

The upper phase is the stationary phase, and the mobile phase is introduced in Column 2

$$F_{\mathrm{U},j} = 0 \quad j = 1,2 \tag{2}$$

$$c^\mathrm{L}_{k,\mathrm{in},2} = 0 \tag{3}$$

The flow rate and mass balance at the feed node are

$$F_{\mathrm{L},1} = F_{\mathrm{L},2} + F_{\mathrm{L,F}} \tag{4}$$

$$F_{\mathrm{L},1}c^\mathrm{L}_{k,\mathrm{in},1} = F_{\mathrm{L},2}c^\mathrm{L}_{k,1,2} + F_{\mathrm{L,F}}c^\mathrm{L}_{k,\mathrm{F}} \tag{5}$$

The distribution constant of Component k is

$$K_{k,\mathrm{Des}} = K_k = \frac{c^\mathrm{U}_{k,i,j}}{c^\mathrm{L}_{k,i,j}} \quad k = \mathrm{A,B} \quad i = 1,2 \ldots n \quad j = 1,2 \tag{6}$$

In ascending mode (Figure 2c):

The lower phase is the stationary phase and the mobile phase is introduced in Column 1

$$F_{\mathrm{L},j} = 0 \quad j = 1,2 \tag{7}$$

$$c^\mathrm{U}_{k,\mathrm{in},1} = 0 \tag{8}$$

The flow rate and mass balance at the feed node are

$$F_{\mathrm{U},2} = F_{\mathrm{U},1} + F_{\mathrm{U,F}} \tag{9}$$

$$F_{\mathrm{U},2}c^\mathrm{U}_{k,\mathrm{in},2} = F_{\mathrm{U},1}c^\mathrm{U}_{k,n,1} + F_{\mathrm{U,F}}c^\mathrm{U}_{k,\mathrm{F}} \tag{10}$$

The distribution constant of Component k is

$$K_{k,\mathrm{As}} = \frac{1}{K_k} = \frac{c^\mathrm{L}_{k,i,j}}{c^\mathrm{U}_{k,i,j}} \quad k = \mathrm{A,B} \quad i = 1,2 \ldots n \quad j = 1,2 \tag{11}$$

$F_\mathrm{U,F}$ and $F_\mathrm{L,F}$ are the feed flow rates in ascending and descending step, respectively. The feed composition is different during the descending and ascending mode. $c^\mathrm{U}_{k,F}$ and $c^\mathrm{L}_{k,\mathrm{F}}$ are the feed concentrations of Component k in the upper and lower phase, respectively.

The set of the model equations (Eqs. 1–11) was numerically solved with the commercial software gPROMS V3.1.4.[29]

Approach for selection of a sCPC unit operating parameters

Due to the continuous and cyclic nature of the sCPC unit operation the selection of the operating parameters leading to a successful separation is not a straightforward task. Six operating parameters have to be selected: the feed flow rate during the descending ($F_\mathrm{L,F}$) and ascending ($F_\mathrm{U,F}$) step, the mobile phase flow rate in ascending ($F_\mathrm{U} = F_{\mathrm{U},1}$) and descending step ($F_\mathrm{L} = F_{\mathrm{L},2}$), as well as the duration of the ascending (t_As) and descending (t_Des) step.

The proposed approach for selecting the sCPC unit operating parameters refers to a complete separation of a binary feed mixture of Components A and B. Component A is distributed preferentially in the lower phase and Component B preferentially in the upper phase of a selected biphasic liquid system. This means that Component A will be collected during the descending step (from Column 1) in Product 1, and Component B will be collected during the ascending step (from Column 2) in Product 2 (see Figures 2b, c).

To achieve a complete separation of the feed mixture, the following requirements should be fulfilled:

1. At the end of the descending step, Component B should stay in Column 1;
2. At the end of the ascending step, Component B should be completely eluted from Columns 1 into 2;
3. At the end of the ascending step, Component A should stay in Column 2;
4. At the end of the descending step, Component A should be completely eluted from Columns 2 into 1.

These requirements can be used to derive constraints to the unit operating parameters based on the distance traveled by each component during the ascending and descending step.

According to the Requirement 1, the distance traveled by Component B in Column 1 during the descending step, $x_{\mathrm{B,1,Des}}$, should be shorter than the length of the column, L_{c}

$$x_{\mathrm{B,1,Des}} < L_{\mathrm{c}} \tag{12}$$

To fulfill Requirement 2, the distance passed by Component B in ascending step in Column 1, $x_{\mathrm{B,1,As}}$, should be longer than the distance passed during the descending step in the same column, $x_{\mathrm{B,1,Des}}$. In terms of net distance this can be written as

$$x_{\mathrm{B,1,As}} - x_{\mathrm{B,1,Des}} > 0 \tag{13}$$

Requirement 3 demands that the distance passed by Component A in Column 2 during the ascending step, $x_{\mathrm{A,2,As}}$, is shorter than the length of this column

$$x_{\mathrm{A,2,As}} < L_{\mathrm{c}} \tag{14}$$

Requirement 4 is fulfilled when the distance traveled by Component A in descending step in Column 2, $x_{\mathrm{A,2,Des}}$, is longer than the distance traveled by Component A in ascending step in the same column, $x_{\mathrm{A,2,As}}$

$$x_{\mathrm{A,2,Des}} - x_{\mathrm{A,2,As}} > 0 \tag{15}$$

The distance traveled by each component in Columns 1 and 2 during each step depends on the component propagation velocity and the step duration. Namely

$$x_{k,j,\mathrm{As}} = v_{k,j,\mathrm{As}} t_{\mathrm{As}} \tag{16}$$

$$x_{k,j,\mathrm{Des}} = v_{k,j,\mathrm{Des}} t_{\mathrm{Des}} \tag{17}$$

The velocity of Component k in Column j during the descending step is

$$v_{k,j,\mathrm{Des}} = \frac{F_{\mathrm{L},j} L_{\mathrm{C}}}{V_{\mathrm{L}} + K_k V_{\mathrm{U}}} \tag{18}$$

and during the ascending step is

$$v_{k,j,\mathrm{As}} = \frac{F_{\mathrm{U},j} L_{\mathrm{C}}}{V_{\mathrm{U}} + \frac{1}{K_k} V_{\mathrm{L}}} \tag{19}$$

According to the Eqs. 18 and 19, the velocities of Component k in Column j during the descending and ascending steps are correlated as follows: $v_{k,j,\mathrm{As}} = v_{k,j,\mathrm{Des}} \frac{K_k F_{\mathrm{U},j}}{F_{\mathrm{L},j}}$.

Most importantly, Eqs. 16–19 can be used to express the above derived constraints, Eqs. 12–15, in terms of the unit operating parameters. The obtained constraints of sCPC unit operating parameters are presented in the second column in Table 1.

The sCPC operating parameters, four flow rates and two-step times, are interconnected and cannot be selected at the same time. Namely, to calculate the $t_{\mathrm{Des}}/t_{\mathrm{As}}$ interval in which a complete separation of Components A and B is possible, using Eqs. 21–23 from Table 1, besides the distribution constants and the volume of the upper and lower phase, the flow rates of the feed and mobile phase in each of the two steps must be selected.

Table 1. sCPC Unit Operation Restrictions and Operating Parameter Constraints for a Complete Separation of a Binary Feed Mixture

Restrictions	Operating parameters constraints
At the end of descending step Component B should stay in Column 1	$t_{\mathrm{Des}} < \frac{V_{\mathrm{L}} + K_{\mathrm{B}} V_{\mathrm{U}}}{F_{\mathrm{L,1}}}$ (20)
At the end of the ascending step Component B should be completely eluted from Column 1	$\frac{t_{\mathrm{Des}}}{t_{\mathrm{As}}} < \frac{F_{\mathrm{U,1}}}{F_{\mathrm{L,1}}} K_{\mathrm{B}}$ (21)
At the end of the ascending step Component A should stay in Column 2	$t_{\mathrm{As}} < \frac{V_{\mathrm{U}} + \frac{1}{K_{\mathrm{A}}} V_{\mathrm{L}}}{F_{\mathrm{U,2}}}$ (22)
At the end of the descending step Component A should be completely eluted from Column 2	$\frac{t_{\mathrm{Des}}}{t_{\mathrm{As}}} > \frac{F_{\mathrm{U,2}}}{F_{\mathrm{L,2}}} K_{\mathrm{A}}$ (23)

By combining Eqs. 21 and 23 (given in Table 1), and replacing $F_{\mathrm{L,1}}$ and $F_{\mathrm{U,2}}$ using Eqs. 4 and 9, respectively, the lower and upper borders of the $t_{\mathrm{Des}}/t_{\mathrm{As}}$ interval of complete separation can be written as follows

$$\frac{F_{\mathrm{U,1}} + F_{\mathrm{U,F}}}{F_{\mathrm{L,2}}} K_{\mathrm{A}} < \frac{t_{\mathrm{Des}}}{t_{\mathrm{As}}} < \frac{F_{\mathrm{U,1}}}{F_{\mathrm{L,2}} + F_{\mathrm{L,F}}} K_{\mathrm{B}} \tag{24}$$

As it can be seen from Eq. 24, for a selected mobile phase flow rate in ascending ($F_{\mathrm{U,1}}$) and descending step ($F_{\mathrm{L,2}}$) the $t_{\mathrm{Des}}/t_{\mathrm{As}}$ interval expands with the decrease of the feed flow rates, $F_{\mathrm{U,F}}$ and $F_{\mathrm{L,F}}$. The $t_{\mathrm{Des}}/t_{\mathrm{As}}$ interval vanishes when

$$\frac{\left(F_{\mathrm{U,1}} + F_{\mathrm{U,F}}\right)\left(F_{\mathrm{L,2}} + F_{\mathrm{L,F}}\right)}{F_{\mathrm{L,2}} F_{\mathrm{U,1}}} = \frac{K_{\mathrm{B}}}{K_{\mathrm{A}}} \tag{25}$$

and under these operating conditions a complete separation is not possible.

According to Eqs. 20 and 22, the maximum absolute value of the descending and ascending step time is inversely proportional to the mobile phase flow rates in Columns 1 and 2, respectively, that is, higher mobile phase flow rates lead to shorter step times.

In summary, to calculate the $t_{\mathrm{Des}}/t_{\mathrm{As}}$ interval for complete separation (Eq. 24) the unit flow rates should be selected first.

Selection of the sCPC unit operating parameters

In centrifugal partition chromatography, the physical properties of the biphasic liquid system, applied centrifugal force and flow rate as well as which phase (upper or lower) is used as mobile phase have great influence of the hydrodynamics and mass transfer. In general, better separation efficiency is obtained, when high flow rates and centrifugal force are used.[21,23,30] Both parameters determine the pressure drop along the columns (which is limited by the unit specifications) and the retention of the stationary phase in the column. To ensure similar conditions in both sCPC columns low feed flow rates in comparison to the mobile phase flow rate in each step should be used. This is of course not beneficial for the unit productivity. A detail description of the

Table 2. sCPC Unit Operating Conditions and Model Parameters Used for the Calculation of the Separation Region Presented in Figure 6b and for Simulation of sCPC Separation of Binary Feed Mixture

Parameter	Value
$c^{L}_{A,F}$ (g/L)	5
$c^{U}_{B,F}$ (g/L)	5
$F_{U,F}$ (mL/min)	1
$F_{L,F}$ (mL/min)	1
$F_{L,2}$ (mL/min)	10
$F_{U,1}$ (mL/min)	8
V_C (mL)	100
$V_U = V_L$ (mL)	50
K_A $(= K_{A,Des})$	0.8
K_B $(= K_{B,Des})$	1.2

steps (experiments) needed for the selection of the sCPC unit flow rates for a particular separation task can be found in Hopmann et al.[31]

The approach proposed here, developed using the equilibrium theory assumptions, can be used for a preliminary selection of the sCPC unit operating parameters. A more rigorous mathematical model, supported by experimental determined hydrodynamics and mass transfer parameters, is needed for a further optimization of the unit operation.

To illustrate how the derived constrains can be applied to select a preliminary sCPC unit operating parameters, a model (hypothetical) binary mixture of Components A and B is considered. All parameters needed for the determination of the t_{Des}/t_{As} interval for complete mixture separation are summarized in Table 2. It should be mentioned that these parameters were selected merely for calculation purposes. The chosen feed and mobile phase flow rates are in the commonly used flow rate range for the chosen size of the sCPC column.[32,33] In this example, the same feed flow rate was selected for both steps. There are experimental indications that under the same operating conditions (mobile phase flow rate and centrifugal force) the CPC column efficiency is lower in descending mode than in ascending mode.[30] This is related to the phase mixing and mass transfer in these two modes. To ensure similar column efficiency in both steps, we have selected a higher mobile phase flow rate in descending step than in ascending step (see Table 2). The selected feed concentration (5 g/L of each component) is relatively low, but it actually does not affect the final result of the calculation, because it does not appear in the equations used for the calculation of the t_{Des}/t_{As} interval of complete separation (Eqs. 20, 22, and 24). It is important to state that the derived constrains are applicable for any feed concentration for which the assumption of a constant distribution constant is valid (i.e., $K_{k,As} = \frac{1}{K_{k,Des}}$). In reality, the maximum feed concentration will be restricted by the solubility limit of the solutes in the used biphasic solvent system.

Once the sCPC unit flow rates are fixed (see Table 2), the interval of the t_{Des}/t_{As} ratio, in which a complete separation of the feed mixture is expected, can be calculated using Eq. 24

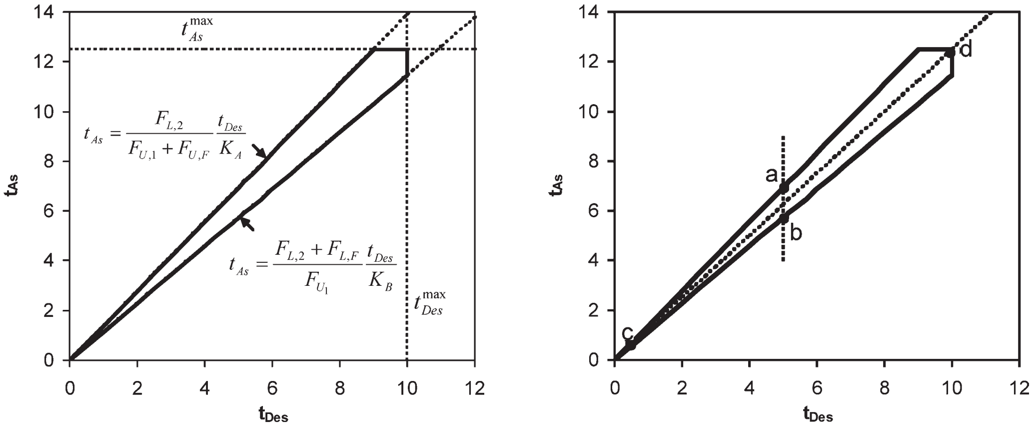
$$0.72 < \frac{t_{Des}}{t_{As}} < 0.87$$

The maximum values of the descending and ascending step times can be now calculated from Eqs. 20 and 22 given in Table 1: $t^{max}_{Des} = 10$ min and $t^{max}_{As} = 12.5$ min.

In fact, there are several combinations of the absolute values of the ascending and descending step time that lead to a value of the t_{Des}/t_{As} ratio in the interval of a complete separation. Also, a particular value of the t_{Des}/t_{As} ratio can be obtained by several combinations of the absolute values of the descending and ascending step times.

To better visualize the possible combinations of the duration of the two steps, the four t_{Des}/t_{As} constrains (Eqs. 20–23 from Table 1) are presented in a plot $t_{As} = f(t_{Des})$, in Figure 3a. The region of complete separation is marked with a thick line. For all (t_{Des}, t_{As}) pairs lying inside this region, a complete separation of Component A and B is expected. As shown in Figure 3a, for a shorter step times, the range of possible combinations of the descending and ascending step times, (t_{Des}, t_{As}), leading to a complete mixture separation is smaller than for longer step times.

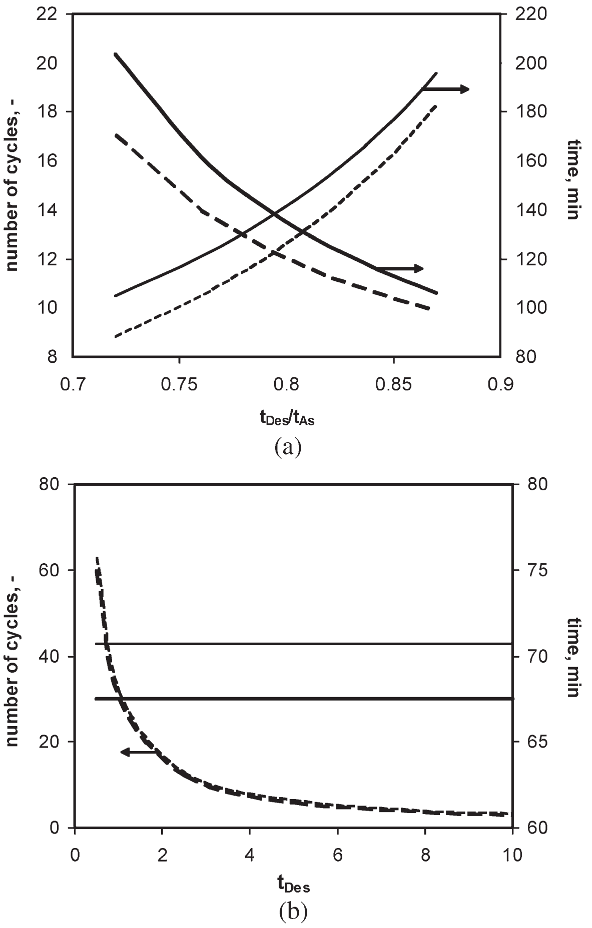
sCPC is cyclic process, which operates in a cyclic steady state (CSS). For the construction of the separation region, presented in Figure 3a, the feed and mobile phase flow rates during the descending and ascending step were preset (see Table 2). Therefore, the productivity and the solvent (mobile phase) consumption in CSS will be equal for any (t_{Des}, t_{As}) pair inside the region of complete separation. The only



(a) (b)

Figure 3. Region of complete separation presented in t_{As} vs. t_{Des} plot.

The region of compete separation is the area enclosed by the thick line. The flow rates and components distribution constants are given in Table 2. (a) Region of complete separation with the constraints on the operating parameters (Eqs. 20–23) presented by dashed lines; (b) region of complete separation with line $\overline{ab}$: $t_{Des} = 5$ and line $\overline{cd}$: $t_{Des}/t_{As} = 0.8$.



(a)

(b)

Figure 4. (a) Number of cycles (and time until CSS) vs. t_{Des}/t_{As}, for t_{Des} = 5 min. (b) Number of cycles (and time until CSS) vs. t_{Des}, for t_{Des}/t_{As} = 0.8.

Thin lines: Product 1 (Component A); thick lines Product 2 (Component B). Interval of complete separation: 0.72 < t_{Des}/t_{As} < 0.87. The parameters used in the calculation are listed in Table 2

parameter that could differ from case to case is the time needed to reach CSS. This time determines the amount of solvent needed until the unit reaches CSS.

Under the assumptions of the equilibrium theory, the time to CSS is approached by the time a component needs to pass the distance between the feed introduction and the product collection point (equal to the length of one sCPC column). This time can be different for both products (i.e., components). The number of cycles that should be carried out from the feed start up until the concentration front of the component reaches the product collection point can be calculated from the distance the component passes during one cycle in direction to the product collection point. For Component A, which is collected in descending step in Product 1 at the beginning of Column 1, this distance is

$$x_{A,1,Des} - x_{A,1,As} = \Delta x_A \tag{26}$$

and for Component B, collected in ascending step in Product 2 at the end of Column 2, the same distance is

$$x_{B,2,As} - x_{B,2,Des} = \Delta x_B \tag{27}$$

The number of cycles needed until the concentration front of Component k reaches its product collection point, N_k, can be calculated using the following equation

$$N_k = \frac{L_c}{\Delta x_k} \tag{28}$$

The time corresponding to this number of cycles can be calculated as the product of the number of the cycles and the duration of one cycle

$$t_k = N_k(t_{Des} + t_{As}) \tag{29}$$

In systems with significant dispersion effects the time needed to reach CSS will be longer than the one calculated by Eqs. 26–29. However, the above type of calculations can be used to evaluate the influence of the t_{Des}/t_{As} ratio, and the range of the absolute values of t_{Des} and t_{As} on the solvent consumption up to CSS.

From a point of view of unit operation, another important issue is the duration of the cycle steps (i.e., the cycle). Short steps lead to extensive exploitation of the valves and less stable unit operation.

Another important aspect, which deserves attention, is the product concentration profile at the product collection point in each step. In CSS, at the beginning of each step, the component collected in that step would be at a certain distance from the product collection point. Namely, at the beginning of the descending step the Component A would be positioned at a distance $x_{A,1,As}$ from the product collection point (left end of Column 1, in Figure 1b) and at the beginning of ascending step Component B would be positioned at a distance $x_{B,2,Des}$ from the product collection point in this step (right end of Column 2, in Figure 1a). Therefore, in each mode, in the first part of the step only the mobile phase would be collected at the respective product collection point. The duration of this part of the step would be $x_{A,1,As} \times F_{L,1}$ in descending step and $x_{B,2,Des} \times F_{U,2}$ in ascending step. This means that diluted products would be obtained, if the product streams are collected during the whole step. In practice, an UV detector placed at each of the product collection point could be used to identify the exact time when the component elutes from the column and to start with the collection of product stream. The mobile phase coming out from the column during the first part of each step can be collected in a separate reservoir and reused.

Selection of the descending and ascending step times

To screen the (t_{Des}, t_{As}) region of the complete separation and give an answer to the most obvious question, that is, which (t_{Des}, t_{As}) should be used, we have defined two lines inside this region, presented in Figure 3b:

- line $\overline{ab}$ that corresponds to a constant value of the descending step time t_{Des} = 5 and different ascending step times;
- line $\overline{cd}$ that corresponds to a constant value of the t_{Des}/t_{As} ratio, $t_{Des}/t_{As} = 0.8$.

For different (t_{Des}, t_{As}) values along these two lines, the number of cycles and time needed until the sCPC unit achieves CSS was calculated using Eqs. 26–29 together with Eqs. 16–19.

In Figure 4a, the number of cycles and time needed to arrive at CSS for Product 1 (pure Component A) and

Product 2 (pure Component B) for different t_{Des}/t_{As} ratio along the $\overline{ab}$ line are presented. For a t_{Des}/t_{As} value close to the lower or to the upper limit of the allowed t_{Des}/t_{As} interval the time needed to reach CSS for one of the product streams is very long. This leads to a higher solvent consumption before the unit enters into CSS operation. Therefore, when both products are desired, t_{Des}/t_{As} value in the middle of the allowed interval should be used.

Along the $\overline{cd}$ line the t_{Des}/t_{As} ratio is constant, while the absolute values of the descending and ascending step times increase. As shown in Figure 4b, with the increase of the absolute values of t_{Des}, and consequently t_{As}, the number of cycles needed to reach CSS for both products decreases. The time needed to achieve CSS operation for each component is equal for all (t_{Des}, t_{As}) along the $\overline{cd}$ line. In terms of hydrodynamic equilibration in the chambers of the sCPC columns after the switch from one to another step (descending to ascending step and vice versa), it would be recommended to use longer step times. This choice is also favorable concerning the valves usage.

Validation of the approach and test of its robustness

To validate the proposed approach and test its applicability for a selection of the sCPC operating parameters for systems in which the dispersion and mass transfer effects cannot be neglected, the unit operation was simulated for (t_{Des}, t_{As}) along the $\overline{ab}$ line presented in Figure 3b. The sCPC unit operation was simulated with the developed cell model (Eqs. 1–11) using different number of cells per column. The other model parameters used in the simulations are presented in Table 2.

Under typical operating conditions (flow rate and centrifugal force), the number of theoretical plates in a standard hydrostatic type of CCC column is in a range between 50 and 2000.[23,34] Our simulation study has shown that for the selected column size (see Table 2) the dispersion and mass transfer effects are negligible, when the cell number per column is higher than 1000.

In Figure 5, the purity of Products 1 and 2 in CSS along the $\overline{ab}$ line, obtained with 50, 200, and 500 cells per sCPC column is presented. For 1000 cells per column the t_{Des}/t_{As}, interval of complete separation is equivalent to the interval calculated using Eq. 24 (results not presented in Figure 5). With the decrease of the number of cells per column the t_{Des}/t_{As} interval in which a complete separation is attained shrinks. For a column with 50 cells completely pure products cannot be obtained. This kind of result was expected, because the influence of the axial dispersion and mass transfer was neglected in the derivation of the operating parameters restrictions. In practice, the concentration profile dispersion issues can be taken into account by selecting a value for t_{Des}/t_{As} far enough away from the limiting values of the allowed t_{Des}/t_{As} interval. For systems with significant dispersion effects the lower and upper value of t_{Des}/t_{As} interval should be corrected by using a safety factor. Another possible approach to ensure high product purities would be to select t_{Des}/t_{As} value at the middle of the allowed interval.

Conclusions

The sCPC is a cyclic liquid–liquid chromatographic separation technology by which a feed stream is continuously separated into two products, which are alternately collected during the two steps of the process cycle.

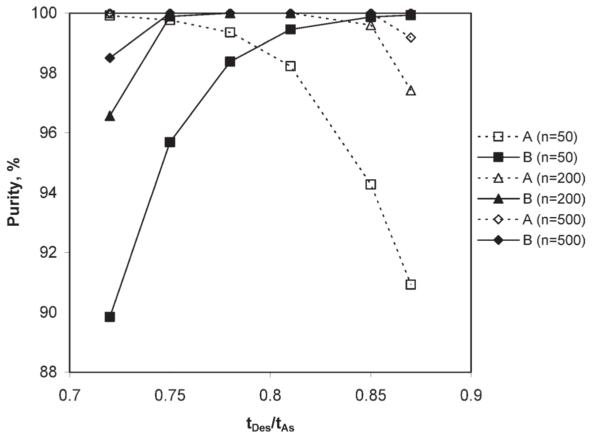


Figure 5. Simulated purity of Product 1 (Component A) and Product 2 (Component B) in the t_{Des}/t_{As} interval of complete separation using different number of cells per sCPC column: 50, 200, and 500.

Closed symbols: Product 1 (Component A), open symbols Product 2 (Component B). $t_{Des} = 5$ min, interval of complete separation: $0.72 < t_{Des}/t_{As} < 0.87$, model parameters used in the simulation are listed in Table 2.

Based on the assumption of instantaneous solutes partitioning between the two liquid phases, a set of constrains on the sCPC unit operating parameters, that is, feed flow rate, mobile phase flow rate in descending and ascending step and time duration of these two modes, was derived. It is described how the derived constraints can be used to select preliminary operating parameters of a sCPC unit for a complete separation of a binary feed mixture.

In the proposed approach, the distribution constants of the feed components, feed flow rate and mobile phase flow rate in descending and ascending step, are used as input information. They should be acquired/selected by a preliminary experimental equilibrium and hydrodynamics studies. The output information is an interval of the ratio of the descending and ascending mode time in which complete separation of the binary feed mixture is possible. The theoretical analysis that has been carried out has shown that (1) it is better to select a value for the ratio of the descending and ascending step time in the middle of the interval of complete separation, and (2) to attain this ratio, the descending and ascending step time duration should be selected from the range near to their maximum possible values. Using these recommendations the influence of the dispersion and mass transfer on the product purities will be considered and minimized, the solvent consumption until the achievement of the CSS will be reduced, hydrodynamically more stable sCPC unit operation will be achieved, and its valves life time will be extended.

It is worth mentioning that the approach proposed in this work was successfully validated experimentally in our laboratory.[31]

Notation

c = concentration, kg/m^3
F = flow rate, m^3/s
K = distribution constant
n = number of cells per column
N = number of cycles

L = column length, m
t = time, s
V = volume, m^3

Subscripts and superscripts

1 = Column 1
2 = Column 2
A = Component A
As = ascending step
B = Component B
C = column
CSS = cyclic steady state
Des = descending step
F = feed
i = number of cell
in = inlet concentration
j = number of column
k = Component k
L = lower phase
U = upper phase

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