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The Development and Applications of Preparative-Scale Continuous Chromatography

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Abstract

The scaling up of continuous chromatography to production scale is considered. The various continuous countercurrent and crosscurrent chromatographic techniques have been reviewed and judged according to their merits. The latest developments on a preparative/production scale semicontinuous chromatographic refiner (SCCR), consisting of 12 columns each of 5.4 cm i.d. × 75 cm long and packed with calcium charged resin, are reported. When the production of high fructrose corn syrup was carried out using industrial barley syrup, product throughputs of 32.3 kg sugar solids/m^3 resin/h were obtained, the fructose-rich product purity was over 90% with a concentration of 12.96% w/v, and glucose-rich product contained only 6.69% fructose and had a concentration of 25.4% w/v. The computer simulation of the SCCR's operation is reported, and a good fit with experimental data was obtained.

INTRODUCTION

Chromatography can be defined as the unit operation where the separation of solutes occurs due to their differential migration rates through a system of two phases, the mobile and the stationary phase. Chromatography has gained extensive recognition and applications as a powerful analytical tool. Over the last 20 years or so, its separating capabilities have been appreciated by industry, and a number of alternative production scale processes have been developed and have found applications in the sugar, petrochemical, and essential oil industries.

Although the chromatographic processes are low energy intensive, offer practically no heat generation, and possess very high separation efficiency, they have not yet made the great industrial impact that might be expected from these benefits. This is attributed to the conservatism of the chemical and biochemical industries to employ new, novel techniques.

It is believed that most of the major industrial establishments are now involved or show an increased interest in chromatographic developments, and it is now only a matter of time before we will see many more large-scale applications of chromatography. This belief has arisen from the great secrecy associated with the development of this separation process.

Production-scale chromatography already enjoys important applications in the desugarization of molasses, the production of high fructose corn syrups (HFCS), and other applications described later. Barker and co-workers, among others, have been involved with the scaling-up and development of various batch and continuous chromatographic configurations over the last 25 years (*1–5*). A brief review of the various chromatographic systems and some of their applications are now given with special emphasis on the development of the semicontinuous chromatographic refiner (SCCR) systems which are believed to offer a promising scaling-up potential.

CONTINUOUS CHROMATOGRAPHY

The large-scale development of chromatographic processes was biased toward the batch mode during the 1960s and 70s, although recently a number of alternative continuous systems have been introduced. The term "continuous" refers to any configuration which employs the continuous introduction of the feed stream to be separated and differs in design from the traditional batch column.

A comparison of the solute concentration profiles obtained from a binary mixture being separated by (a) a batch process and (b) a countercurrent continuous process is shown in Fig. 1.

The continuous chromatographic systems fully utilize the available mass transfer area, offer constant product quality, and usually do not require any product recycling, thus resulting in higher throughputs for a given quantity of packing. They fall into two broad categories, the crosscurrent and countercurrent flow processes, defined according to the relative movements of the mobile and "stationary" phases.

Some of the continuous configurations judged to offer scaling-up

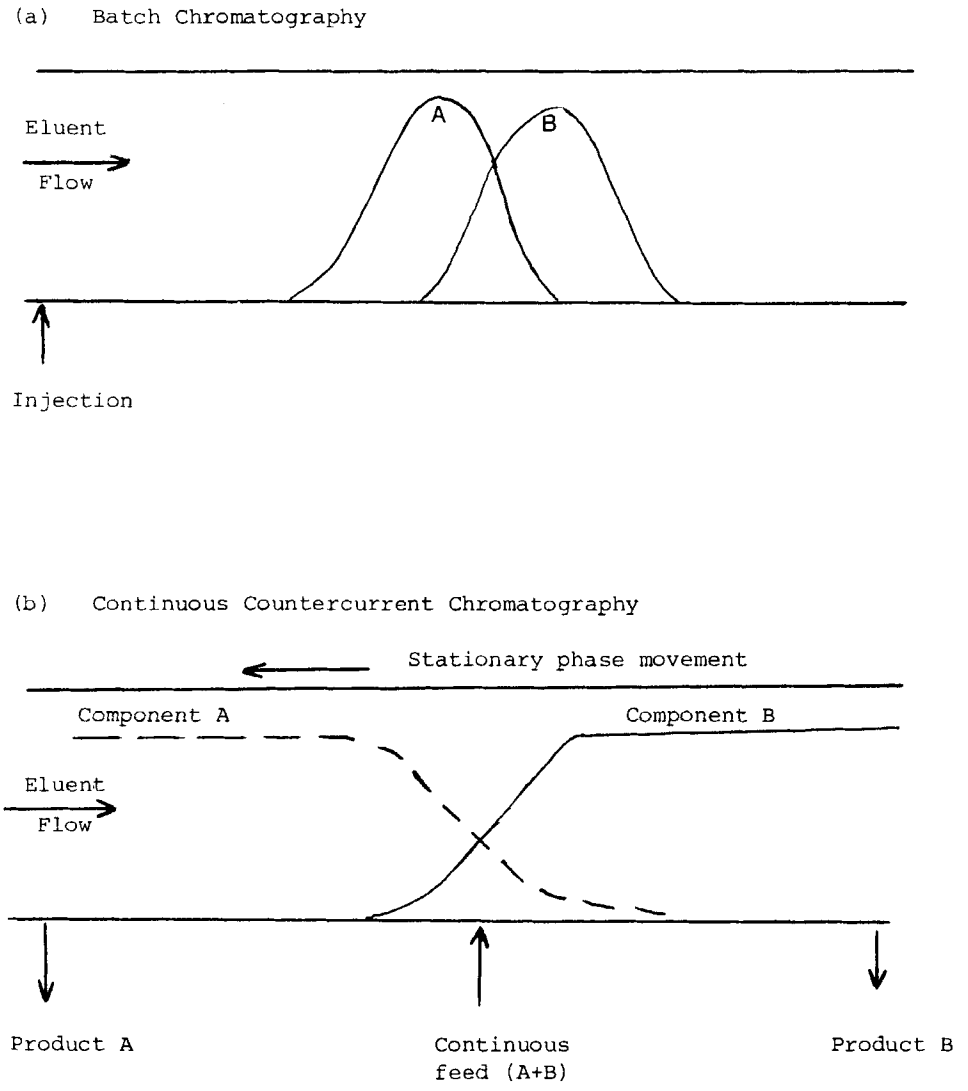


FIG. 1. Solute concentration profiles of a binary mixture (A and B).

potential are reviewed below, and their relative merits and shortcomings are commented upon.

Crosscurrent Continuous Chromatography

In crosscurrent systems the mobile phase moves almost perpendicularly to the direction of the "stationary" phase. This configuration was first suggested by Martin (*6*) who proposed the use of a packed annulus rotating past a fixed inlet point. The mobile phase is introduced continuously at the top of the annulus and leaves at the bottom. The components travel in helical paths around the annulus at different angles according to their relative affinities for the "stationary" phase and are eluted at different points from the bottom of the packing, with the strongly retarded components traveling along a longer helical path. Theoretically, this arrangement can provide continuous separation of a multicomponent mixture. A number of small systems have been constructed (*7, 8*), but further development is needed to bring this type of processing to the tonnage scale.

Continuous Countercurrent Chromatography

A number of countercurrent processes have been developed and can be classified according to the principle they employ to obtain the countercurrent movement of the two phases.

Moving Bed Systems

In moving bed systems, the packing flows under gravity countercurrent to a stream of mobile phase flowing upward in a column. When the feed mixture is introduced into the center of the column, the least strongly absorbed component is carried upward and exits from the top, and the retarded component is carried with the packing and is stripped at the bottom column outlet. Moving bed systems (*9, 10*) were the results of the first attempts in the 1950s and 1960s to achieve a continuous countercurrent movement but they have been found to suffer from the following disadvantages:

Difficulties in achieving packing flow control
Low mass transfer efficiencies due to uneven column packing

Packing attrition due to the increased shear forces, and packing entrainment in the stationary phase recycling system

Relatively low mobile phase velocities to prevent fluidization of the chromatographic bed

Moving Column Systems

To overcome the above problems, various alternative schemes have been proposed which employ a circular array of parallel columns interconnected to each other. The system rotates past fixed inlet and outlet ports. A number of such systems have been developed and there has been considerable success in the analytical field (*1, 2, 11*). Scaling-up, however, is difficult because as with the annular cross-flow systems there are difficulties in achieving a reliable seal between the static ports and the moving columns.

Moving Feed Point Systems

This technique is an intermediate development between conventional batch and simulated countercurrent systems. Wankat and Oritz (*12*) used such a process to separate dextran 2000 from cobalt chloride in water. The system consisted of a series of fixed columns. The mobile phase was pumped continuously through the inlet in the top column and the feed was introduced as a long pulse. The first feed pulse was introduced into the first column, then after a predetermined time period into the second column, and so on. The switching period was chosen so that the average velocity of the feed ports advancement was between the migration velocities of the least and the most strongly adsorbed components. This technique has been found to be more efficient than the batch processes, but less than the simulated countercurrent systems, since it utilizes only part of the available packing at any time.

Simulated Moving Bed Systems

These systems offer the greatest scaling-up potential since they make better use of the available mass transfer area, and are therefore capable of achieving better separation efficiencies and throughputs. Also, they are free of the mechanical difficulties associated with the moving bed, moving column, and crosscurrent systems. They consist of a number of

static interlinked columns or compartments, and the countercurrent movement is effectively achieved by sequentially moving the inlet and outlet ports in the direction of the mobile phase.

There are two main approaches. The Sorbex technique, Universal Oil Products, USA (*13*, *14*), and the Semi-Continuous-Chromatographic-Refiners (SCCR), Department of Chemical Engineering, Aston University, UK (*5*, *15*).

In a typical Sorbex process the stationary phase is packed into a number of compartments in a static vertical column. Each compartment is connected to a specially designed rotary valve operating on the principle of a multiport stopcock. This technique has been applied for over 15 years in hydrocarbon separations. Because of its design, extra care must be taken to overcome the problems associated with packing compressibility. It requires a very precise design of the main rotary valve and does not offer the flexibility of repacking part of the system.

Experience gained during the employment of some of the above chromatographic techniques, the unreliability of large flat face moving seals, and the awareness of the limitations associated with the various alternative techniques mentioned above led Barker and co-workers to develop an alternative technique to simulate the countercurrent movement of the two phases. They developed the "moving port" multicolumn semicontinuous chromatographic refiners (SCCR's) whereby all moving parts were eliminated by using valves of proven commercial reliability. The systems have been scaled up to total lengths of over 7.5 m and column diameters of 10.8 cm (*16*).

SOME INDUSTRIAL CHROMATOGRAPHIC SEPARATION PROCESSES

The Finnish Sugar Engineering Company, Finland, has achieved much in terms of large-scale batch chromatographic separations in the carbohydrate field. Seven columns of 3.6 m diameter × 12 m high have been used for the desugarization of molasses at a throughput of 60,000 ton/year (*17*). Elf-Aquainte, France (*18*), markets six preparative gas chromatographs using 10 mm to 500 mm diameter batch columns. It also markets liquid batch chromatographs of up to 30 cm diameter which are used in the pharmaceutical, fine chemicals, fragrance and flavors, and biotechnology industries.

Universal Oil Products (UOP) has developed simulated moving bed processes and over 40 plants are believed to operate worldwide using the Sorbex principle, with a total capacity of over 3.5×10^6 tons/year.

Other companies such as Abcor Inc and Illinois Water Treatment Co. (USA) have also contributed to the scaling up of chromatographic processes, although Abcor is understood to be no longer active in this field.

Crosscurrent chromatography has been employed to a great extent on the analytical scale, and several workers (*8*) have built small scale units. The Oak Ridge National Chemical Division, Tennessee, USA (*7*), has had the most notable success in applying this principle to the separation of metal ions in solution. Barker and co-workers at Aston, in cooperation with British Sugar plc, have constructed a 30 cm diameter × 1.5 m high annular chromatograph for carbohydrate separations.

PRINCIPLE OF OPERATION OF THE SCCR SYSTEM

A schematic representation of the operating principle is shown in Fig. 2 where the whole system is illustrated as a closed loop. The mixture to be separated is fed continuously at Port F, and the mobile phase (usually deionized water) flows continuously through Port M. The less strongly adsorbed Component B moves preferentially with the mobile phase toward the product offtake P1. A section of the loop is isolated at any time by the two Valves V1 and V2, and an independent purge fluid stream (usually deionized water) enters at Port PU, strips the adsorbed Component A, and exits from Port P2. Figure 2(a) shows the component distribution within the system soon after "start up." In Fig. 2(b) all the port functions have been advanced by one position in the direction of the mobile phase flow. This port advancement results in a simulated movement of the stationary phase countercurrent to the direction of the mobile phase. To achieve separation and hence two enriched products, the rate of port advancement must be greater than the migration velocity of Component A through the bed and lower than the migration velocity of B (see Fig. 2c). The frequency with which this port advancement occurs represents the "switch time." The countercurrent mode of operation is shown in Fig. 3.

The SCCR7 system used for the work reported in this paper consisted of twelve 5.4 cm i.d. × 75 cm long stainless steel columns connected at the top and bottom to form a closed loop (*19*). Six pneumatic poppet valves were associated with each column, the feed, eluent, and purge inlet valves, the top product valves, and the transfer valve to the next column. Figure 3(a) represents the first switch period where Column 1 is isolated and purged to give the product rich in A. Feed and eluent enter Columns 7 and 2, respectively, and the product rich in B is eluted from Column 12.

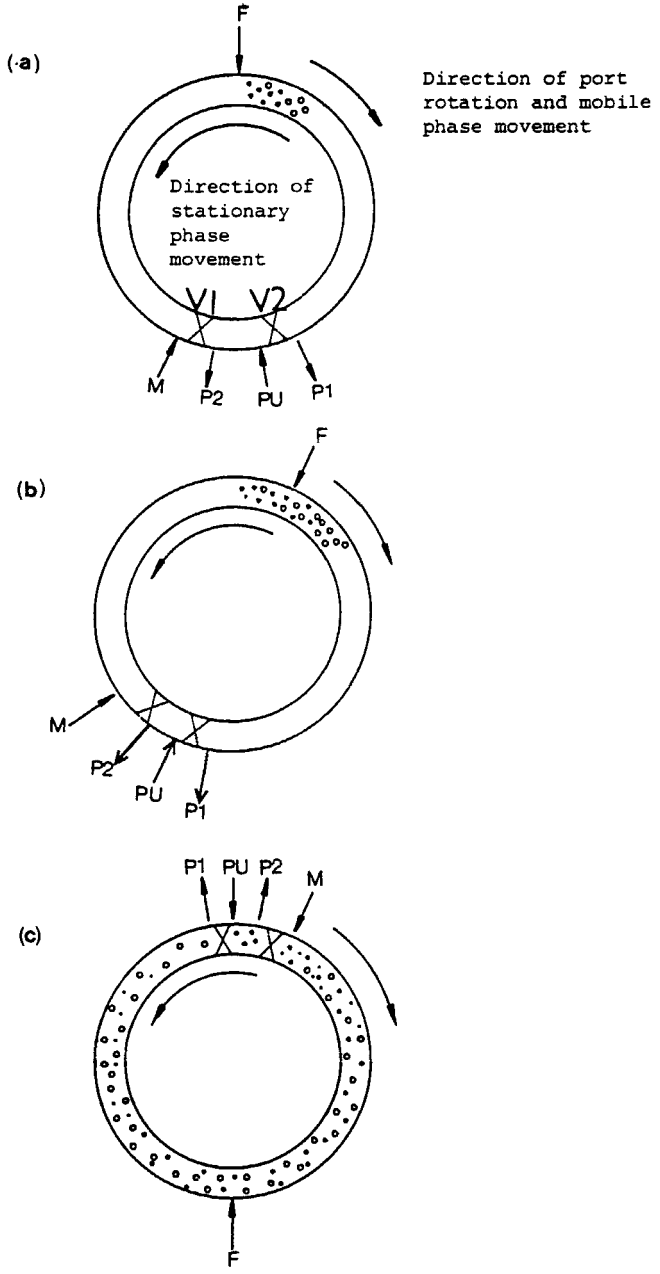


FIG. 2. Principle of operation of the SCCR system. M = mobile phase inlet; PU = purge inlet; F = feed inlet; P1 = glucose-rich product; P2 = fructose-rich product; V1, V2 = transfer valves; (•) fructose; (○) glucose.

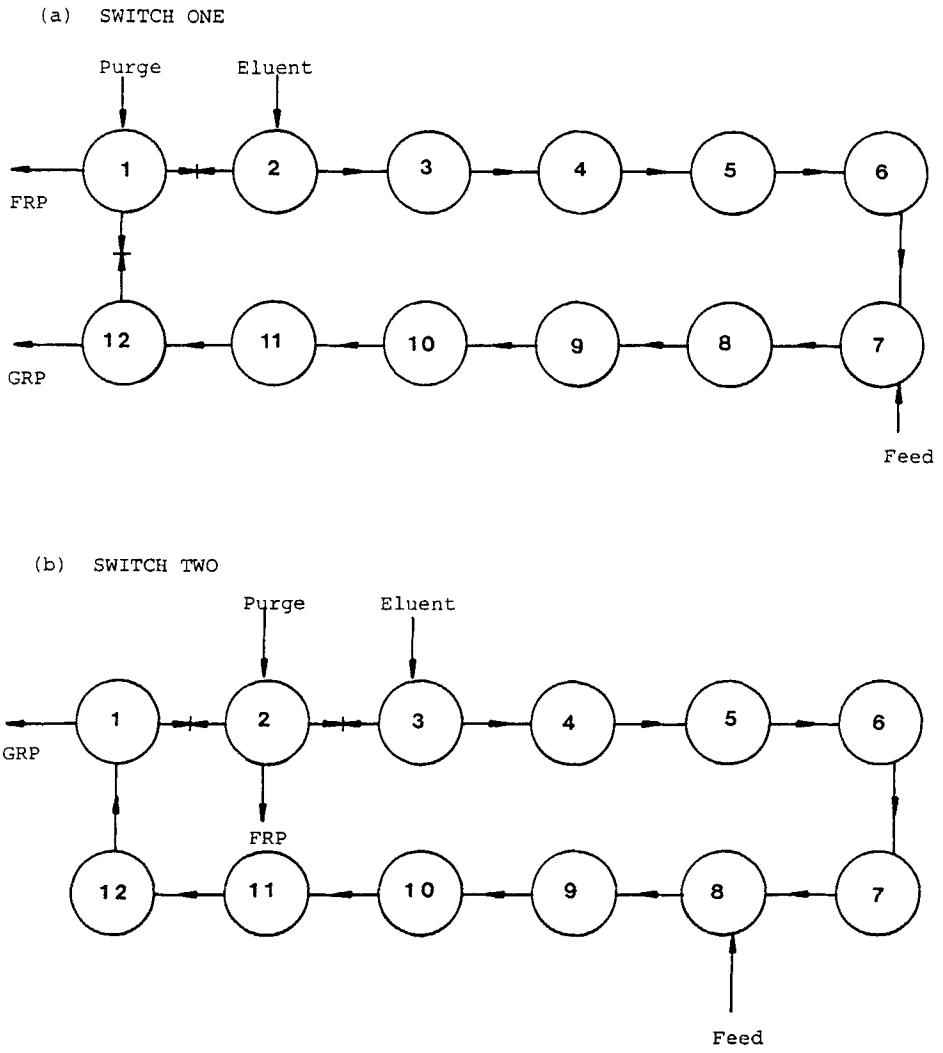


FIG. 3. Sequential operation of the SCCR7 system. FRP = fructose-rich product; GRP = glucose-rich product.

In the next switch period (Fig. 3b) all ports are advanced by one position and so on. After twelve such advancements a "cycle" is completed. After approximately six cycles the concentration profiles in the system become reproducible and a "pseudo-equilibrium" state is reached. Typically in the example given the columns were packed with a crosslinked polystyrene resin in the Ca^{2+} form. The fructose forms a chemical complex with the Ca^{2+} ions and is preferentially retarded.

A THEORETICAL APPROACH TO THE SCCR PRINCIPLE

An idealized model can be constructed relating mobile and stationary phase flow rates and component separation. A material balance on the less retarded component, Component B, about the feed point (Fig. 4) gives

$$L_2 f_B = L_e y_B + P x_B \tag{1}$$

For a B molecule to move preferentially with the mobile phase:

$$L_e y_B > P x_B \tag{2}$$

Rearranging,

$$L_e/P > x_B/y_B \tag{3}$$

and since by definition the distribution coefficient of B is

$$Kd_B = x_B/y_B \tag{4}$$

Substituting Eq. (4) into Eq. (3):

$$L_e/P > Kd_B \tag{5}$$

Similarly, for Component A to move with the stationary phase,

$$L_e/P < Kd_A \tag{6}$$

The theoretical limits of mobile and stationary phase to give separation of the two components are obtained by combining Eqs. (5) and (6), i.e.,

$$Kd_B < L_e/P < Kd_A \tag{7}$$

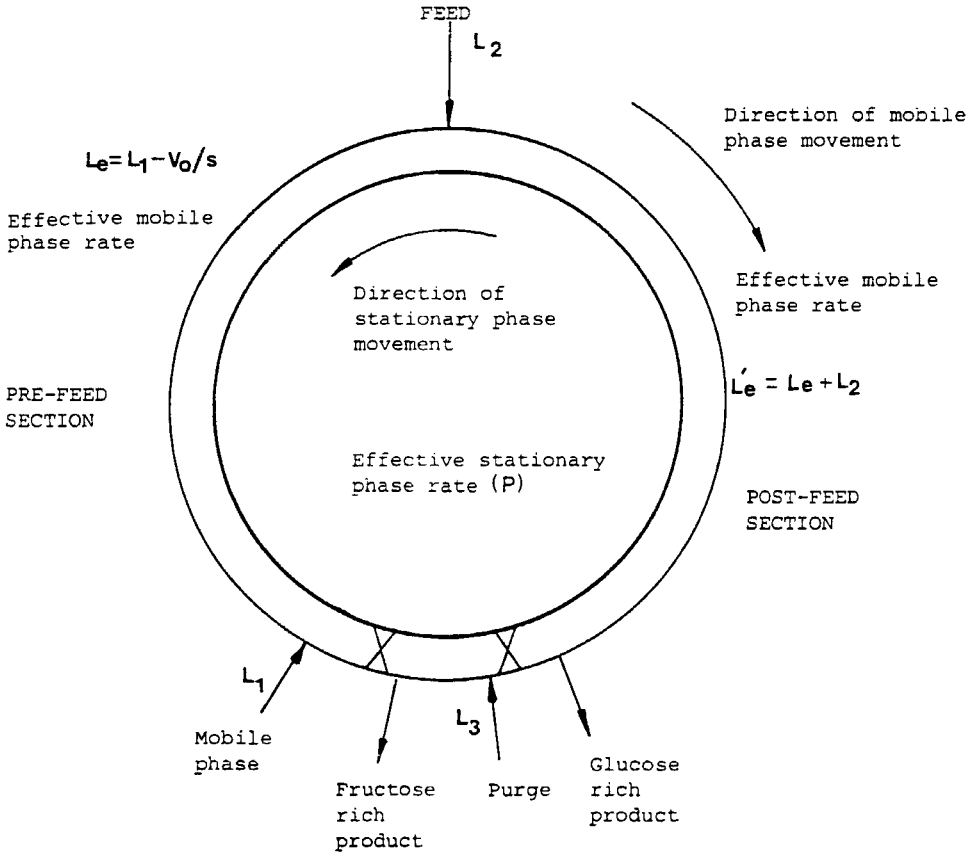


FIG. 4. Diagrammatic representation of the semicontinuous principle of operation.

As each column contains the eluent phase in the void volume, V_0, the effective mobile phase flow rate is reduced to

$$L_e = L_1 - (V_0/s) \tag{8}$$

Because of the feed flow rate L_2, the effective mobile phase rate in the postfeed section L'_e becomes

$$L'_e = L_e + L_2 = L_1 + L_2 - (V_0/s) \tag{9}$$

Therefore Eq. (7) becomes

$$Kd_B < L_e/P < L'_e/P < Kd_A \quad (10)$$

and this equation now gives the true theoretical limits for a separation to be obtained provided the chromatographic column is of sufficient length.

The purging flow rate L_3 in the isolated column is also governed by

$$L_3/P \gg Kd_A \quad (11)$$

A detailed theoretical approach for designing a SCCR system from the minimum of experimental data has been reported (*20*).

PREPARATIVE SCALE SEPARATIONS USING THE SCCR SYSTEM

The separation of carbohydrate mixtures and the production of high fructose corn syrups (HFCS) in particular is one of the major fields where chromatography has been applied. Although the first SCCR system was operating in the gas–liquid mode (*21*), the subsequent development of the SCCR systems were carried out in the liquid–liquid form using various carbohydrate multicomponent feedstocks. Size exclusion and ion-exchange principles have been employed in the development of the SCCR system. England and Vlachogiannis (*22*) used such an SCCR system consisting of 10 columns each of 5.4 cm i.d. × 70 cm long and operating with the size exclusion principle for polymer fractionation. The continuous fractionation of the macromolecular dextran was carried out.

In more recent work the ion-exchange principle was used where the columns were packed with crosslinked polystyrene resin in the calcium form. The fructose present in the feedstock forms a loose chemical complex with the Ca^{2+} ions and is retarded while the other carbohydrates travel with the mobile phase.

An alternative approach is to operate in the anion-exchange principle where strongly basic resins in the bisulfite form are used and the complex is now formed between the glucose and the anions. Glucose is the retarded component and fructose the component traveling with the mobile phase. Abusabah (*23*) employed this approach on a twelve column, 5.4 cm i.d. × 75 cm long SCCR system to separate glucose–fructose mixtures. The SCCR anion exchangers are capable of giving high fructose products of concentrations higher than the corresponding cationic SCCR's. Anion-exchange resins, however, are less stable, and in multicomponent carbohydrate separation the maximum obtainable fructose purity is lower because fructose is not eluted last from such a chromatographic system.

A number of feedstocks have been used ranging from synthetic equimolar glucose-fructose to industrial multicomponent mixtures. When a synthetic glucose-fructose feed was used at 18.6% w/v feed concentration (run: 18.6-9-30-30-20), both product purities were 99.9%.

In the latest work an industrial glucose isomerose syrup was used consisting of 52% glucose, 42% fructose, and 6% maltose and oligosaccharides. The objectives were to produce a 90% fructose-rich product and a glucose-rich product containing no more than 7% fructose at a feed throughput of at least 30 kg sugar solids/m^3 resin/h with products having total sugar solid concentrations of over 20% w/v. Because of the low fructose content of the feed and its multicomponent nature, the separation difficulty was increased. The results of some key experimental runs are summarized in Tables 1 and 2. Each run is defined with a set of five figures; for example, the set 54-13-39-24.5-60 corresponds to feed concentration (% w/v), feed flow rate (cm^3/min), eluent flow rate (cm^3/min), switch time (min), and operating temperature (°C), respectively. The following results refer mainly to the work carried out on the twelve 75 cm × 5.4 cm diameter column SCCR7 system unless it is stated otherwise. Calcium charged crosslinked polystyrene resins were used.

An examination of the criterion of separation (Relationship 10 and Eqs. 8 and 9) reveals that the switch time is one of the main operating parameters. As it is shown from Figs. 5, 6, and 7 (Runs 37-13-40-21-60, 36-13-40-23-60, and 37-13-40-25-60) and the corresponding results in Table 2, the switch time was found to be the controlling parameter, and its selection must be very accurate to obtain the specified separation (*24*). In fact, the equipment's performance was found to be sensitive to switch time variations as low as 10 s (Runs 45.7-13-39-24-60, 45.7-13-39-24.33-60, and 46-13-39-24.17-60).

The production throughput and hence the equipment's utilization increases by increasing the feed concentration. This, however, has a detrimental effect on the separation efficiency since the sugar concentration increases and leads eventually to an equipment overload. The drop in separation efficiency is a direct result of the increasing background sugar concentration on the distribution coefficients which has been described in Refs. *19* and *25*. As the feed concentration was increased (Runs 36-13-40-23-60, 46-13-39-24.17-60, and 66-14.6-40-25-60), the product purities were kept within specification by increasing appropriately the corresponding switch times. These feed concentration increases, however, resulted in an increasing deterioration of the product purities, i.e., as the concentration increased from 18.6 to 66% w/v the FRP purity decreased from 99.9 to 90.1% and the GRP fructose content increased from 0.1 to 6.9%. By comparing the ratio of switch time to feed concentration it is

TABLE 1
Operating Conditions for the Experimental Runs Carried Out on the SCCR7

Run code number	Switch time (min)	Average flow rates (cm^3/min)			Feed concentration (% w/v)	Feed fructose to glucose ratio	Throughput (sugar solids) (kg/h)
		Feed	Eluent	Purge			
18.6-9-30-30-20	30	9	30	75	18.6	42:58	0.100
37-13-40-21-60	21	13	40	80	37.0	43:52.4	0.288
36-13-40-23-60	23	13	40	80	36.02	42.2:52.1	0.281
37-13-40-25-60	25	13	40	80	37.0	43:52.3	0.288
45.7-13-39-24-60	24	13	39	80	45.72	41.2:52.5	0.357
45.7-13-39-24.33-60	24.33	13	39	80	45.72	41.2:52.5	0.357
46-13-39-24.17-60	24.17	13	39	80	46.0	41.8:52.5	0.359
54-13-39-24.5-60	24.5	13	39	80	54.0	42.09:52.0	0.421
66-14.6-40-25-60	25	14.6	40	70	66.0	42.1:52.0	0.578
66.3-14.6-40-26.5-60	26.5	14.6	40	60	66.3	42.0:52.1	0.581

TABLE 2
Experimental Results Obtained from the SCCR7

	Glucose-rich product					Fructose-rich product				
				Impurities (%)					Impurities (%)	
Run code number	Glucose purity (%)	Percent of glucose in feed recovered	Total product concentration (% w/v)	Fructose	Maltose + OS[a]	Fructose purity (%)	Percent of fructose in feed recovered	Total product concentration (% w/v)	Glucose	Maltose + OS[a]
18.6-9-30-30-20	99.9	97.1	2.12	0.1	—	99.9	98.4	0.93	0.1	—
37-13-40-21-60	89.7	99	2.27	—	11.3	70.6	115.4[b]	3.56	29.4	—
36-13-40-23-60	83.04	88.1	4.49	5.49	11.46	92.4	77.1	1.69	7.6	—
37-13-40-25-60	71.6	113[b]	8.12	22.5	5.9	100	56.6	1.2	—	—
45.7-13-39-24-60	83.3	74.2	4.76	2.4	14.3	89.5	81.5	2.30	10.5	—
45.7-13-39-24.33-60	77.24	88.6	5.84	11.76	10.98	95.37	80.2	2.08	4.62	—
46-13-39-24.17-60	80.84	83.1	5.17	6.1	13.06	91.78	82.8	2.19	8.22	—
54-13-39-24.5-60	81.11	86.58	6.94	6.35	12.54	91.35	88.61	3.12	8.65	—
66-14.6-40-25-60	82.9	94.13	11.6	6.4	10.7	90.07	90.72	5.84	9.93	—

[a]OS = oligosaccharides.
[b]Value too high due to an analytical inaccuracy.

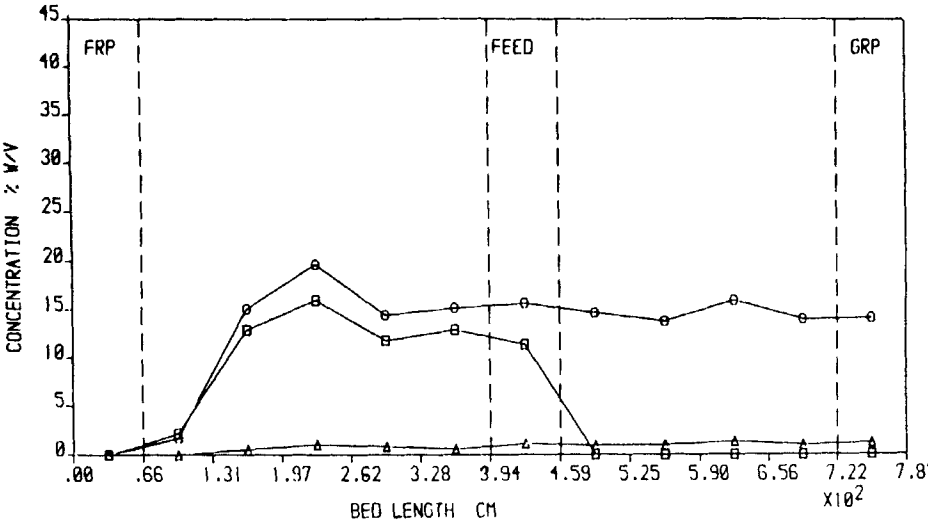


FIG. 5. On-column concentration profile for Run 37-13-40-21-60. (□) Fructose; (○) glucose; (△) maltose and oligosaccharides. Cycle 7.

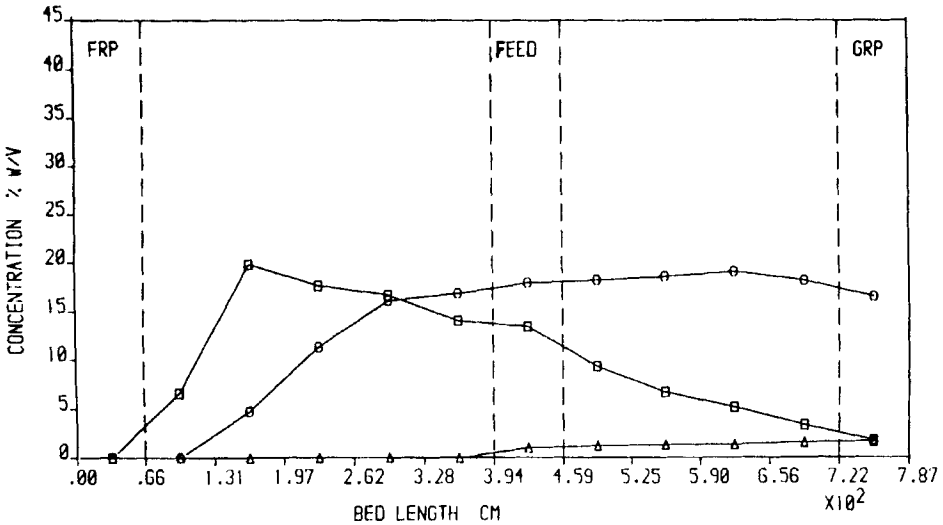


FIG. 6. On-column concentration profile for Run 36-13-40-23-60. (□) Fructose; (○) glucose; (△) maltose and oligosaccharides. Cycle 7.

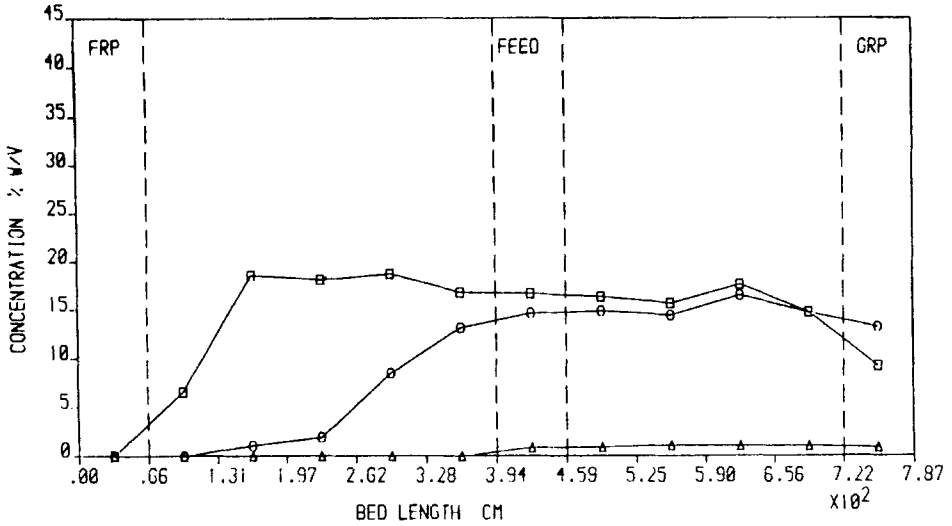


FIG. 7. On-column concentration profile for Run 37-13-40-25-60. (□) Fructose; (○) glucose; (△) maltose and oligosaccharides. Cycle 7.

apparent that at 45% w/v a "critical" feed concentration is reached, after which the operation is carried out at overloaded conditions.

In most of the experiments the eluent to feed ratio was maintained at 3 to 1, except for Run 66-14.6-40-25-60 where it was reduced to 2.74 to 1. By reducing this eluent to feed ratio and also the purge flow rate, the product concentrations increase but at the expense of the separation efficiency. The minimum recommended eluent to feed ratio is 2.75 to 1 and purge to eluent ratio 1.5 to 1.

By increasing the feed concentration and flow rate the product concentrations will be increased but at the expense of product purities. When an effluent of a Dextran plant (Fisons Pharmaceuticals plc, Cheshire, UK), containing over 68% fructose, was used on a 10 column (10.8 cm i.d. × 75 cm long) SCCR system, the maximum throughput obtained was 39.5 kg solids/m^3 resin/h (*26*).

Operating the SCCR7 at the conditions of Run 66-14.6-40-25-60, a throughput of 0.578 kg/h of sugar solids or 32.1 kg sugar solids/m^3 resin/h was achieved; the bulk GRP contained 6.4% fructose and had a concentration of 11.6% w/v, and the FRP was over 90% and had a concentration of 5.84% w/v. An analysis of the GRP and FRP elution products over a switch has shown that most of the glucose in the GRP is eluted approximately over the second half of the switch and the fructose

contaminant over the first half. During the elution of the FRP, however, the fructose is eluted over the first half of the switch and the glucose present toward the end of the switch. Therefore, by splitting the FRP and GRP elutions into two and collecting the two splits separately, the product concentrations will be increased and the purities of the concentrated fractions will also be improved. When this technique was applied on Run 66-14.6-40-25-60, the FRP purity increased to 94.8% and the concentration of the concentrated FRP split to 11.29% w/v, where over 95.7% of the fructose entering the system was recovered (Tables 1, 3, and 4). The concentration of the concentrated GRP was increased to 22.65% w/v, over 94.2% of the glucose entering the system was recovered, while the fructose content was less than 4.5%.

In the above experiment the dilute and contaminanted GRP and FRP splits were discarded. To minimize the eluent requirements, however, and recover all the sugar solids entering the system, these splits could be recycled as eluent and purge water. This approach was followed in Run 66.3-14.6-40-26.5-60 (Tables, 1, 5, and 6) and the FRP concentration increased to almost 13% w/v and the GRP to 25.4% w/v. Over 84% of the glucose in the feed was recovered in the GRP and its fructose content was 6.69%. The FRP fructose recovery was 87.8% and the product was over 90% pure. An examination of the results shows that the selection of the right splitting periods is critical and also that the product purities were affected due to the mixing together of the dilute GRP and FRP splits. It is therefore recommended to use only the dilute FRP fraction for purging and the dilute GRP fraction for diluting the industrial feedstock to the required concentration levels. The FRP product concentration could be increased further if the fructose concentration in the eluent entry column is kept artificially high. It is therefore proposed that only the very concentrated FRP fraction is retained and the rest is recycled in the purge and eluent streams. This will reduce the fructose recovery per pass but it should increase the product concentration to the specified level. An economic evaluation should determine the exact lengths of the collection and recycling periods.

COMPUTER SIMULATION OF THE SEMICONTINUOUS OPERATION OF THE SCCR7

The equilibrium stage or plate model was employed in the computer simulation. The system's length is considered to consist of a number of theoretical plates, each containing a volume of mobile phase and a volume of stationary phase. The mobile phase leaving each plate is

TABLE 3
Results of Run 66-14.6-40-25-60 when Product Splitting Was Employed on the GRP[a]

4 to 16.5 min collection					16.5 to 4 min collection				
Glucose purity (%)	Percent of glucose in feed recovered	Total product concentration (% w/v)	Impurities (%)		Glucose purity (%)	Percent of glucose in feed recovered	Total product concentration (% w/v)	Impurities (%)	
			F	M + OS				F	M + OS
47.2	1.97	0.87	26.4	26.4	84.83	94.23	22.56	4.49	10.67

[a]F = fructose, M = maltose, OS = oligosaccharides.

TABLE 4
Results of Run 66-14.6-40-25-60 when Product Splitting Was Employed on the FRP[a]

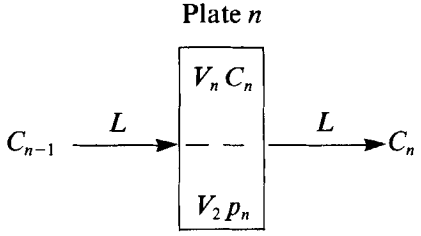
0 to 12.5 min collection					12.5 to 25 min collection				
Fructose purity (%)	Percent of fructose in feed recovered	Total product concentration (% w/v)	Impurities (%)		Fructose purity (%)	Percent of fructose in feed recovered	Total product concentration (% w/v)	Impurities (%)	
			G	M + OS				G	M + OS
94.8	95.78	11.29	5.2	—	75.6	2.82	0.45	24.4	—

[a]G = glucose, M = maltose, OS = oligosaccharides.

TABLE 5
GRP Results after Recycling the Dilute Fraction, Run 66.3-14.6-40-26.5-60. Collection Period from 18.25 to 5 min

Glucose purity (%)	Percent of glucose in feed recovered	Total product concentrated (% w/v)	Impurities (%)	
			F	M + OS
86.22	84.1	25.4	6.69	7.19

considered to be at equilibrium with the stationary phase in the plate. Therefore, considering a mobile phase flow rate, L, passing through a plate n having an initial solute concentration of C_n, the conditions around the plate n may be represented by



A mass balance over the plate n for the solute gives

$$LC_{n-1} = LC_n + V_1 \frac{dC_n}{dt} + V_2 \frac{dp_n}{dt} \tag{12}$$

TABLE 6
FRP Results after Recycling the Dilute Fraction Run 66.3-14.6-40-26.5-60. Collection Period from 0 to 13.25 min

Fructose purity (%)	Percent of fructose in feed recovered	Total product concentrated (% w/v)	Impurities (%)	
			G	M + OS
90.2	87.8	12.96	8.87	0.93

Equilibrium on the plate is represented by the distribution coefficient Kd, where by definition

$$Kd = p_n/C_n \tag{13}$$

Hence:

$$LC_{n-1} = LC_n + (V_1 + V_2Kd)\frac{dC_n}{dt} \tag{14}$$

This equation can be integrated provided Δt is sufficiently small to allow C_{n-1} to be considered constant to give

$$C_n = C_{n-1}\left[1 - \exp\left(\frac{-L\Delta t}{V_1 + V_2Kd}\right)\right] + C_n^0 \exp\left(\frac{-L\Delta t}{V_1 + V_2Kd}\right) \tag{15}$$

For multicomponent feedstocks, similar concentration profile equations can be derived for each component by assuming no interaction between the components. When this equation is applied for the postfeed section, it is modified to account for the component feed concentration C_f and feed flow rate F, hence the term C_{n-1} is replaced by the ratio

$$\frac{LC_{n-1} + FC_f}{L + F} \tag{16}$$

The model predicts the solute concentration in the mobile phase leaving each theoretical plate over a small time increment Δt, and the calculations are repeated over the total number of increments. When this predetermined total number of increments, which is equal to the switch period, has been reached, the sequencing countercurrent action is simulated by stepping the concentration calculations by one column. When this approach has been carried out over the total predetermined number of cycles, the concentrations of the various components in each column are calculated and printed. A plot of these concentrations corresponds to the purging concentration profile.

The model is particularly flexible and can be applied easily to any SCCR system of any configuration. The effects of background concentration, liquid flow rates, and temperature on the distribution coefficients have also been incorporated in the program. Figure 8 shows a typical concentration profile (i.e., Run 54-13-39-24.5-60). The solid lines represent the experimentally obtained results while the broken lines represent the

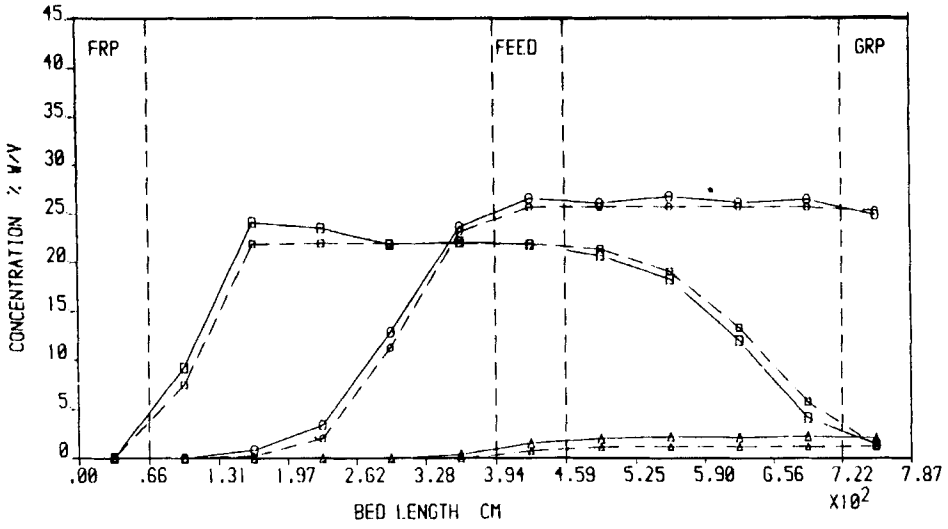


FIG. 8. Concentration profiles for Run 54-13-39-24.5-60. (□) Fructose; (○) glucose; (△) maltose and oligosaccharides; (——) experimental profiles; (- -) simulated profiles.

results obtained from the simulation program. The accuracy of the computer program is illustrated by the good agreement obtained.

CONCLUSIONS

The experimental results have shown that the semicontinuous chromatographic refiners can be used effectively as separators to give products meeting the strictest of industrial specifications. When used in the separation of industrial barley syrups as throughputs of 32.3 kg sugar solids/m^3 resin/h, FRP purities of over 90% were obtained at 12.96% w/v product concentrations. The GRP contained less than 6.69% fructose and had a concentration of 25.4% w/v.

It is believed that all the main chromatographic separators mentioned here, including the batch, will be used increasingly in industry in the future not only for carbohydrate and biotechnological applications but as an alternative to other more traditional energy-intensive separation processes.

SYMBOLS

C	solute concentration in the mobile phase (g/cm^3)
C^0	initial concentration of solute in the plate (g/cm^3)
C_f	feed concentration (g/cm^3)
F	fructose rich product
f_i	component i concentration in feed (g/cm^3)
GRP	glucose rich product
HFCS	high fructose corn syrup
Kd_i	distribution coefficient of component i
L	mobile phase flow rate (cm^3/min)
L_1	eluent flow rate (cm^3/min)
L_2	feed flow rate (cm^3/min)
L_3	purge flow rate (cm^3/min)
L_e	mobile phase flow rate (cm^3/min)
P	stationary phase effective flow rate (cm^3/min)
p	solute concentration in the stationary phase (g/cm^3)
s	switch time (min)
SCCR	semicontinuous chromatographic refiner
V_0	void volume (cm^3)
V_1	mobile phase plate volume (cm^3)
V_2	stationary phase plate volume (cm^3)
x_i	component i concentration in the mobile phase (g/cm^3)
y_i	component i concentration in the stationary phase (g/cm^3)

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