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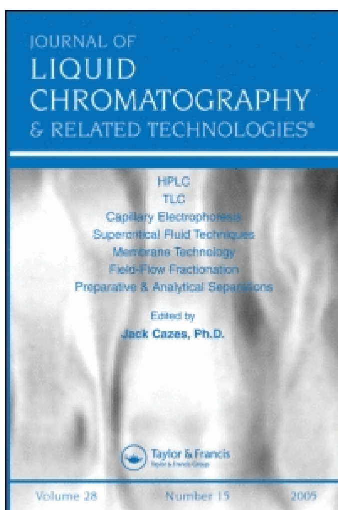

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MOVING BED CHROMATOGRAPHY

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MOVING BED CHROMATOGRAPHY

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ABSTRACT

Moving bed chromatography, and simulated moving bed chromatography has been known for over 50 years, but has recently become important in the isolation of pure substances where the components are very similar, as in the case of enantiomers and in the isolation of substances which would be difficult or impossible by other means. The first example of moving bed chromatography was in the separation of pure acetylene from methane oxidation products, reported in 1956. Subsequently, in 1958, the separation of pure benzene from coal gas was described using gas liquid chromatography and a moving bed system.

The movement of solely the chromatographic packing proved difficult to control and an alternative method using circular columns with moving ports to simulate the moving bed proved to be partially successful. Eventually, the circular columns were replaced by a group of static packed columns connected in series by a rotary valve that simulated a moving bed. This device proved very successful and was developed further, the disc valve eventually being replaced by low dead volume unit valves under computer control. Today, effective simulated moving bed chromatographic systems are becoming available, but it is still left to the

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operator to determine the optimum operating conditions, and that can often be difficult and tedious.

INTRODUCTION

The enthusiasm that has been shown in the recent literature for the different modes of continuous chromatography was evoked by the need to employ liquid chromatography for preparative purposes. As moving bed chromatography is a continuous form of chromatography, it would be the most efficient form of chromatography for preparative work. The concept of the moving bed, or simulated moving bed, chromatography was originally established using gas chromatography. Consequently, it would be appropriate to consider the early work on moving bed chromatography to establish the principle involved and explain the equipment that has been developed.

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The concept of Moving Bed Chromatography is almost as old as gas chromatography itself. An effective commercial unit for the continuous separation of pure acetylene from a hydrocarbon/carbon dioxide gas mixture, using the moving bed technique, was described in 1956 by Freund et al.[1] In addition, much of the experimental work had been carried out a number of years earlier but, unfortunately, the work was described in the then not-readily-available, Hungarian scientific literature.

Continuous moving bed chromatography is basically simple in concept, but more difficult in practice, particularly in LC. Consider the diagram of a column in Figure 1, where the packing moves at a velocity, (v), to the left and the flow of mobile phase, (Q), to the right.

If the retention volume of a solute placed on the column is (V_r), then the retention time, (to), is given by

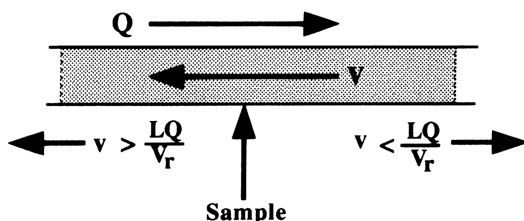

Figure 1. Moving bed chromatography.

$$t_0 = \frac{V_r}{Q}$$

Now, the velocity of the solute band along the column, (v), will be the ratio of the column length (L) to the retention time

$$\text{thus,} \quad v = \frac{L}{t_r} = \frac{LQ}{V_r}$$

Now, if $\frac{LQ}{V_r} > v$, then the solute will move through the column in the direction of the flow of mobile phase and will be eluted in the normal manner, albeit with an extended elution time. However, if $\frac{LQ}{V_r} < v$, then, the solute will move with the stationary and packing, counter current to the mobile phase flow, and be eluted (contained in the packing) at the other end of the column. Thus, if there are two solutes, (S1) and (S2), injected continuously onto the column, having retention volumes (Vr(1)) and (Vr(2)), respectively, then if

$$\left(\frac{LQ}{V_{r(1)}} < v\right) \text{and} \left(\frac{LQ}{V_{r(2)}} > v\right)$$

one solute, (S2), will be eluted with the mobile phase at one end of the column and the other, (S1), will be eluted in the stationary phase on the support at the other end of the column. The apparatus used in moving bed, or simulated moving bed, chromatography may become far more complex and, in the case of LC, very complex, but the basic principles given above will apply to all moving bed continuous chromatography systems.

THE CONTINUOUS MOVING BED PROCESS FOR THE ISOLATION OF PURE ACETYLENE USING GAS SOLID CHROMATOGRAPHY

The process for the isolation of pure acetylene, described by Freund et al.,[1] in 1956, is depicted in Figure 2. The development of the technique arose from a need from the petroleum industry to isolate pure acetylene from the gaseous product from methane oxidation. The gaseous end-product produced during the partial oxidation of methane contains 8-9% of acetylene, 4-5% of carbon dioxide, 4-5% of methane, 25% of carbon monoxide, and about 50% of hydrogen.

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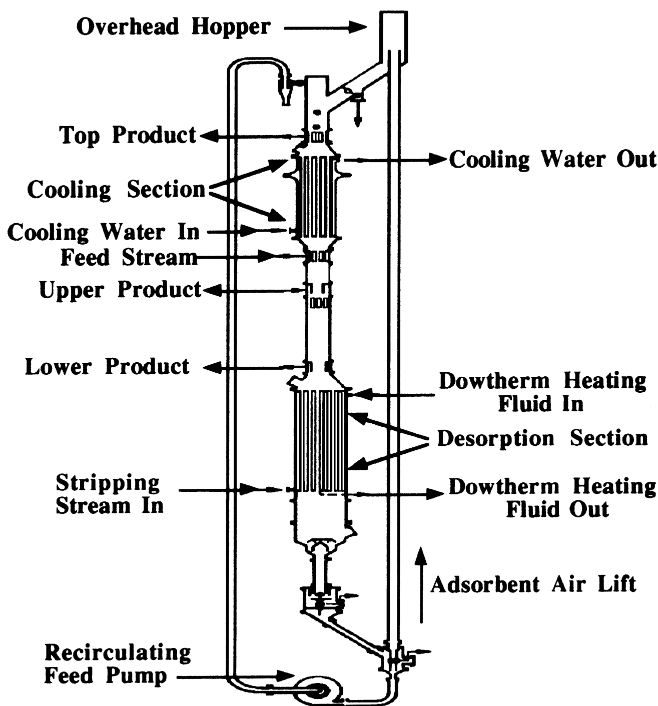

Figure 2. Apparatus for the continuous extraction of pure acetylene from a gaseous hydrocarbon mixture by continuous adsorption chromatography.

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The apparatus was designed to separate the acetylene, in relatively pure state, directly from the mixture. Using active carbon as an adsorbent, the acetylene and carbon dioxide are first removed from the mixture and the remaining methane, carbon monoxide, and hydrogen pass out of the adsorber at the top, as a top-product. The carbon dioxide is then removed as an upper product by part of a stripping gas flow, leaving pure acetylene adsorbed on the carbon to pass down into a stripping section where the acetylene is regenerated.

The continuous chromatograph comprised basically of four sections. The upper section is a heat exchanger comprising a water coil that reduces the temperature of the active carbon, fed from the desorber by the recycling system, to a temperature that will allow the carbon to strongly adsorb the acetylene and weakly adsorb carbon dioxide. The adsorption takes place in the second section.

The lighter gases are eluted at the top of the adsorber (top-product in Figure 2). The cooled adsorbent, containing carbon dioxide and acetylene, passes down into a chamber heated with Dowtherm heat exchanging fluid. The carbon dioxide is first desorbed into part of a stream of stripping gas and collected as the upper product (Figure 2). Moving further into the heat exchanger and, consequently, at a higher temperature, the acetylene is desorbed and collected as the lower product (Figure 1). The acetylene produced had a purity of better than 98%. Considering the limited knowledge available on chromatography, and the equipment limitations, this process and plant design was, indeed, an impressive achievement at that time.

This report, presented at the Symposium on Vapour Phase Chromatography in London in 1956, stimulated a number of workers in the field of gas chromatography to develop the process further, However, at that time, liquid chromatography was still a laboratory novelty about which there was limited knowledge and understanding; as a consequence, further developments of the technique still utilized gas chromatography columns. In the symposium held in Amsterdam in 1958, Scott[2] described the first application of the moving bed technique using gas liquid chromatography as opposed to gas solid chromatography.

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THE CONTINUOUS MOVING BED PROCESS FOR THE ISOLATION OF PURE BENZENE FROM COAL GAS USING CONTINUOUS GAS LIQUID CHROMATOGRAPHY

Domestic gas in the 1950s was derived from the pyrolysis of coal during the production of coke, and contained a number of aromatic hydrocarbons including significant quantities of benzene and toluene and some xylenes. The aromatic hydrocarbons were extracted from coal gas and the accompanying product, coke, was used in the production of iron and for domestic heating. The addition of aromatic hydrocarbons to petroleum fractions, as an alternative to tetra-ethyl-lead, raised the octane rating of the fuel to a level suitable for use with high compression-ratio internal combustion engines. It follows that the direct extraction of pure benzene from coal gas at that time had significant commercial interest. The apparatus Scott[3] used in the extraction of pure benzene from coal gas is shown in Figure 3.

The packing consisted of ground fire brick (30-60 B.S. Mesh) coated with 30% w/w Carbowax 2000. The temperature of the extraction section was about 15°C, the benzene stripping section 70°C ,and the final stripping section 120°C. The efficient operation of the system hinged on the accurate control of the pressures at each inlet and outlet.

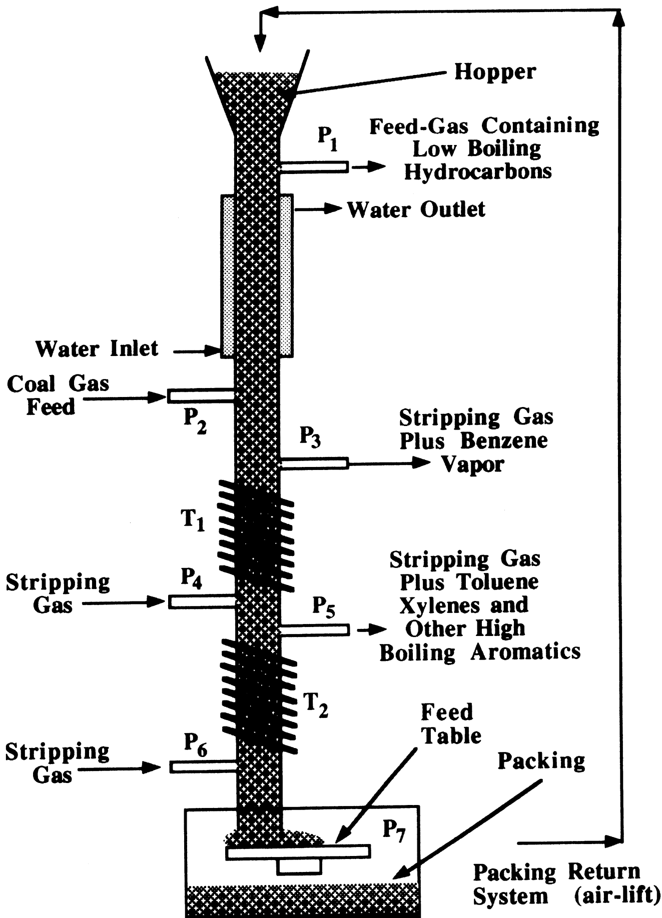

Figure 3. Apparatus for isolating pure benzene from coal gas using a continuous chromatographic procedure.

Assuming (P1) is atmospheric, the flow had to be adjusted to ensure that

P2 = P3.

This prevented feed gas from passing down the column. Similarly, it was required that

P4 = P5.

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This ensured that none of the high-boiling hydrocarbons could pass up the column and contaminate the gas that stripped the benzene from the packing.

In addition, it was required that

P4 > P3.

This condition provided the necessary flow required to strip the benzene from the packing but not remove the toluene and other higher boiling hydrocarbons. The optimum flow varied with the temperature of the benzene stripping section; the lower the stripping temperature, the higher the necessary flow rate would be.

It was also necessary to ensure that

P6 = P7.

This condition prevented any downward flow of gas to the bottom of the column and, thus, avoided loss of high boiling material.

Finally, to provide the necessary flow to strip all the high-boiling hydrocarbons from the packing,

P6 > P5.

This pressure difference must also be adjusted to ensure that all the high boiling materials are removed and will also depend on the stripping temperature; again, the higher the stripping temperature, the lower the optimum flow rate will be and, thus, the smaller the pressure difference. This apparatus was reported to provide benzene, directly from coal gas, having a purity better than 99.8% w/w. Chromatograms of the different fractions are shown in Figure 4.

It is seen that, in order to maintain the high purity of the major product (benzene), some benzene was allowed to be lost in the low boiling fraction and some was allowed to contaminate the high boiling fraction. The slip of some benzene into the high boiling fraction was necessary to ensure the elimination of thiophene from the benzene product; thiophene had very similar chromatographic properties, on the stationary phase, to those of benzene and eluted only slightly later than the main product.

The operation of the apparatus was difficult; the falling bed produced varying flow impedance along the column and, thus, the flow rates had to be continually adjusted during operation; this had to be carried out manually. Modern flow control systems might well render the system more practical, but

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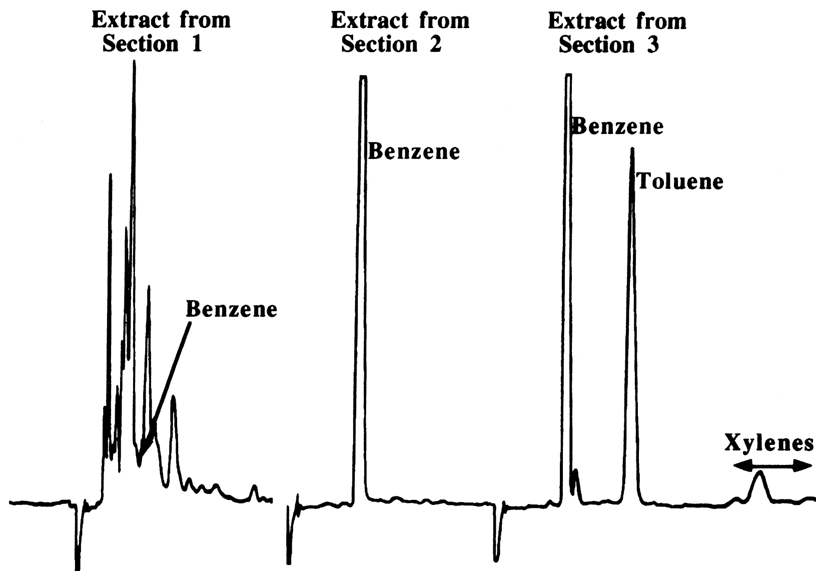

Figure 4. The extraction of pure benzene from coal gas by continuous extraction using a moving bed technique (ref. 3).

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sophisticated electronic flow controllers were not available in the 1950s and, so, the technique, as described above, was not developed further. This type of system, which incorporated a gravity-driven moving bed, would be extremely difficult, if not impossible, to operate with a liquid chromatography system using a liquid mobile phase.

CONTINUOUS CHROMATOGRAPHY WITH A CIRCULAR COLUMN

In an attempt to avoid changes in flow impedance, and to develop an apparatus that would be amenable to liquid chromatography, Barker[4,5] developed a circular column which, at the time, was to become affectionately known to his friends and colleagues as "Barker's bloody-great-wheel." This device was virtually a hybrid between a true falling bed continuous apparatus and a simulated moving bed, and was probably the first practical step towards the modern simulated moving bed chromatograph. A diagram depicting this wheel concept is shown in Figure 5.

The column took the form of a circular groove round the circumference of a very large wheel, vaguely resembling the driving wheel of a pacific steam

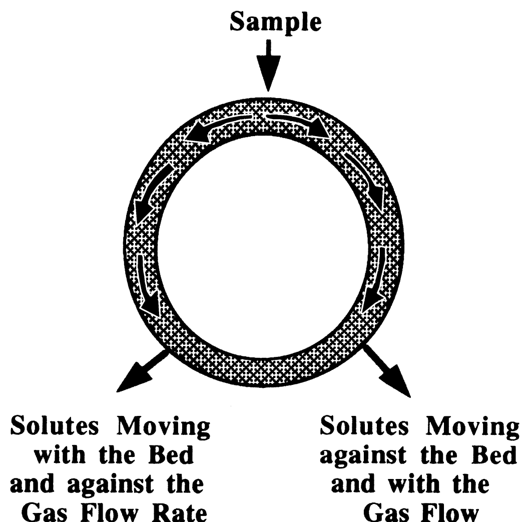

Figure 5. The circular simulated moving bed column.

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locomotive. The groove could be packed and covered by a circular plate that encaptured the packing and produced a circular column. There were regular and frequent apertures around the rim, covered by valve flaps that allowed gas access to and from the packing. The apertures remained closed until they were connected to one of the ports which occupied fixed positions at the periphery.

The packed bed moved continuously in one direction relative to the ports as the wheel rotated, and the mobile phase moved in the opposite direction, thus simulating a moving bed system. It is clear that the flow is not continuous, but only occurs when the gas supply port coincides with one of the peripheral valves. Those solutes that traveled at a rate slower than the wheel velocity continued in the direction of the wheel movement; those that migrated faster than the wheel velocity moved with the mobile phase and in the opposite direction to the rotation of the wheel.

The two fractions were collected from the take-off ports and segments of the wheel could be heated or cooled, by heat exchangers, to adjust solute migration rate and facilitate regeneration and collection. Unfortunately, the wheel system only achieved moderate success due to problems with leaks past the sliding port valve surfaces on the wheel periphery. Again, modern valve technology might render the system more viable but, so far, no one has explored the technique using modern valve devices. As a result of its somewhat dubious suc-

cess with gas chromatographic separations Barker's wheel was never tried with liquid chromatography systems or, at least, only in a cursory manner. Nevertheless. the device stimulated the imagination of Hurrel[6] to produce the first truly simulated moving bed chromatograph.

THE SIMULATED MOVING BED CHROMATOGRAPHY COLUMN

The chromatographic apparatus described by Hurrel in the late 1960s was extremely practical and could be used as a simulated continuous moving bed liquid chromatography system. Hurrel's device was an ingenious extension of the large circular column devised by Barker. There are a number of significant advantages to the simulated moving bed over the actual moving bed system. Besides the technical simplicity of the simulated bed, there is, undoubtedly, a significant conservation of adsorbent and, as the mobile phase is recirculated, there is also considerable solvent economy. In addition, the columns can be packed individually, and far more efficiently, improving greatly the overall resolution of the system. Hurrel's system is shown diagramatically in Figure 6.

The circular column can be considered to be divided into a number of sections, in practice, each section being a short, packed, preparative column. In the original apparatus, the columns took the form of a slanting U and were individually packed using standard packing techniques (either for packed GC

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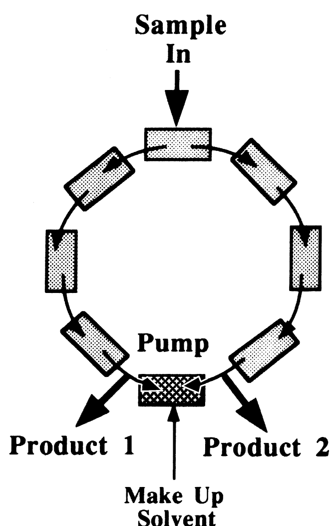

Figure 6. The multi-column simulated moving bed column.

columns or LC columns). The columns are connected in series by a large rotary disc valve.

The valve consisted of two thick steel discs, the upper containing connections to the different inlet and outlet ports, and the lower disc connections to the individual columns. The lower disc was also mounted on a steel frame that supported the columns, and the upper disc could be rotated, thus simulating the moving bed. The disc valve, although fairly complex, involving many sliding surfaces that had to be gas-tight and leak free, could be constructed relatively simply, particularly when compared with the fabrication difficulties involved in producing Barker's massive rotating wheel device. Using suitable surface grinders, the valve, though large, could be made leak proof and could even be constructed to tolerate the necessary high pressures used in liquid chromatography.

A diagram of the cross section of the disc valve with an attached column (that may be glass or metal depending on whether the columns are to be used for GC or LC) is shown in Figure 7.

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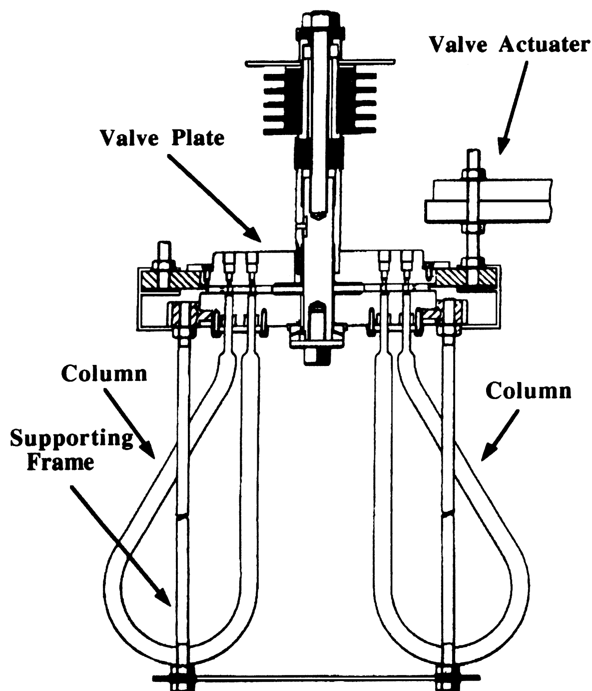

Figure 7. A cross section of the Hurrel disc valve system and columns.

The columns are packed individually, employing standard packing procedures appropriate for either GC or LC. The system also allows ready replacement of columns; contaminated or damaged columns can be unpacked and reused if required. The unusual oblique column shape allows the overall system to be relatively compact but, at the same time, have a reasonably high loading capacity.

Most contemporary simulated moving bed systems used for preparative chromatography are based on the Hurrel device. However, they all work on the same principle, and the simple theory given for the actual moving bed system will apply, albeit in a slightly modified form. The apparatus of Hurrel was originally made available commercially, but the company was relatively small and was eventually taken over by a large corporation that used the device exclusively for its own products. However, in due course, other companies took over the development and manufacture of simulated moving bed equipment and devices are again becoming commercially available.

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The more recent simulated moving bed devices are depicted in a somewhat different manner, as shown in Figure 8, and can be oriented in a number of different ways, although they are all are basically the same as the Hurrel system.

Referring to Figure 8, the mobile phase is depicted as passing through several static columns, each containing the stationary phase which may be some coated support, silica gel, or a bonded phase. There are, in a similar manner, a number of different valved ports: the mobile phase inlet, the sample feed, a number of take-off outlets, and one for the return of the mobile phase.

In the example given in Figure 8, there is a central feed port and two take-off ports. These ports can, by appropriate valve programming, be connected

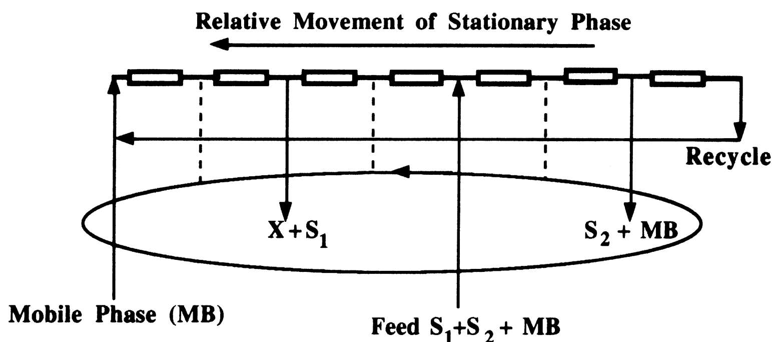

Figure 8. The simulated moving bed chromatography system.

sequentially to link each column to its neighbor. In modern systems, disc valves are no longer used and have been replaced with individual low dead volume valves with low volume connecting conduits, and valve programming is now under the control of a computer. The apparent counter current movement of the stationary phase, relative to the mobile phase, is achieved by valve switching, which simulates the rotation of the ports between each column.

In fact, the same sequential procedure as that in the original Hurrel system is simulated and, by appropriate valving, the columns are, in effect, made to appear to move instead of the packing. Part of the feed moves with the mobile phase and is collected by a small take-off flow in front of the feed port (S_2 + solvent). The other solute, the more retained component of the sample, accumulates in a column on the other side of the feed port and is collected by another small take-off flow behind the feed port (S_1 + solvent). This particular system produces two products and, thus, lends itself specifically to the separation of samples such as enantiomeric pairs or other geometric isomers, pure products with a trace level of a single contaminating substance, and the separation of chemically similar compounds. However, for the efficient isolation of components with high purity yields, the stationary phase capacity for the two enantiomers must be fairly large and, thus, the phase system must be carefully selected. The technique has been successfully used to isolate a number of single enantiomer drugs.[7-9]

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Unfortunately, the design and operation of simulated moving bed systems is still considered highly proprietary and its is often difficult to obtain operating details for a particular application. Thus, after having obtained suitable equipment, the chromatographer is usually left with the difficult challenge of finding the optimum operating conditions for the specific application in mind. However, the basic principles, as outlined in this review will be a good guide to initial optimization experiments. Data on the separation obtained from an analytical column, using the same phase system can also help in identifying the best operating conditions.

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