RESOLUTION OF CARBOHYDRATE MIXTURES BY CONTINUOUS CHROMATOGRAPHIC REFINING TECHNIQUES

A Thesis Submitted for the Degree of
Doctor of Philosophy
by

CHEN HENG, CHUAH

Department of Chemical Engineering
University of Aston in Birmingham

September 1980

TO,

ANITA LOW, MY FAMILY

AND MY FRIENDS

ACKNOWLEDGEMENT

The Author is indebted to the following:

Professor G.V. Jeffreys and the Department of Chemical Engineering for making available the facilities for research.

Professor P.E. Barker, who supervised the work, for his advice, guidance and encouragement, and for the opportunity to complete his research.

Mr. Alsop and the Pharmaceutical Division of the Fisons Company for the co-operation and providing me with a Scholarship for research.

Dr. S. Holding and fellow members in the Separation and Purification Research Group for many invaluable discussions.

Mr. N. Roberts and other members of the Departmental technical staff.

RESOLUTION OF CARBOHYDRATE MIXTURES BY CONTINUOUS CHROMATOGRAPHIC REFINING TECHNIQUES

CHENG HENG, CHUAH

SEPTEMBER, 1980

A Thesis Submitted for the Degree of Philosophy

SUMMARY

A review is given of the general chromatographic theory, the factors affecting the performance of chromatographic columns and the development of the chromatographic technique. Also included is a review of the industrial sources of fructose and a description of several industrial chromatographic processes.

A reconstruction of the semi-continuous chromatographic refiner (SCCR4) was performed. The SCCR4 unit now has twelve 2.54 cm (I.D.) x 70.5 cm stainless steel columns, a temperature enclosure and a new timer-control. It has more flexibility than previously and can be operated at liquid pressure of up to 1.68×10^3 kNm^{-2} (250 psi) at 80°C. Counter-current operation was simulated by sequencing a system of inlet and outlet ports around the twelve columns.

Experiments with a batch glass column (1.14cm I.D.) packed with a calcium charged zerolit SRC 14 resin (150-300 μm size range) were performed to determine the packed column characteristic and the effects of temperature and flowrate on the equilibrium distribution coefficient and the plate efficiency. Batch experiments were also conducted with the 2.54 cm I.D. stainless steel columns. Results from these experiments provided chromatographic data for selecting run parameters for the continuous operation of the SCCR4 unit, and in the simulation model.

Continuous operation of the SCCR4 unit was performed using seven different flow arrangements to find the best operating conditions for the highest sugar throughput, product purity and solids concentration in the outgoing product. Separation of a 50% (w/v) glucose-fructose mixture was achieved, giving 90% (w/w) fructose rich (FR) and glucose rich (GR) products and a solid concentration of 2.5% (w/w) and 7.8% (w/w) respectively at a carbohydrate throughput of 75 gms/hour. Separation of a 70% (w/v) fructose rich, dextran mixture yielded a 95% (w/w) dextran free, FR product having a solid concentration of 8.9% (w/w). The carbohydrate throughput was 126 gms/hr. A 600 hours life test with a Fisons feed containing dextran, glucose and fructose was completed without noticeable deterioration in the performance of the chromatographic packing. Ions in the Fisons feed were monitored in the product by using atomic absorption spectrometer techniques.

Improvements to the theoretical model to simulate the operation of the SCCR4 unit were made. Liquid hold-up in the SCCR4 unit and its effect on the performance was identified and allowed for in the model. The model was extended to cover multi-component systems and any number of columns. Due to data limitations the model could not be fully tested, but within the limits of the data, some general points of agreement between the experimental and simulated data were obtained

KEY WORDS

FRUCTOSE, GLUCOSE, DEXTRAN, CONTINUOUS, COUNTER-CURRENT, CHROMATOGRAPHY

CONTENTS

LIST OF FIGURES

LIST OF TABLES

C H A P T E R O N E

INTRODUCTION

1. INTRODUCTION

World production of sugar varies and is very much dependent on the success of the harvest of the sugar producing crops; sugar beet in the temperate countries and sugar cane in the tropical countries in the world. Most common of the sugars produced in large quantity is sucrose, but since the late 1970's interest has been focused on the production of monosaccharides from corn starch by enzymatic conversion and from sucrose by hydrolysis inversion.

In the United Kingdom, being a member of the European Economic Community (EEC), the production of sugar is strictly controlled by a commission of the EEC in order to protect the sugar beet industries in its member countries. A levy has been imposed on the import of sugar cane from the developing countries as well as that manufactured from corn starch from outside the EEC.

Since 1974, when the price of sugar rose several fold, an expansion programme to increase the production of sugar from sugar beet was encouraged by the EEC commission in anticipation of increasing demand.

The British Sugar Corporation, which controls the sugar beet industry in Britain, undertook a large expansion programme to increase production from 600,000 tons to 1.25 million tons by 1980. The 1979 figure stands at 925,000 tons. A meeting of the EEC commission earlier in the year admitted that it had

over estimated the demand for sugar. The sugar demand in Europe has actually been falling since 1974 and there is a sugar surplus in Europe with no profitable market elsewhere.

British annual output of sugar stands at 2.4 million tons in 1979; approximately 0.95 million tons from the British Sugar Corporation and 1.2 million tons from Tate and Lyle Ltd. and the rest produced by smaller independent companies[28].

The overall market for sugar for the food industries does not justify expansion of the sugar industry.

However, in view of the ever increasing demands for fuel and chemicals by the growing world population and also the escalating price of basic energy source such as crude oil, the future may offer a profitable avenue for the use of sugar as a potential feedstock for the chemical industries and through the production of alcohol as an energy source.

Lester R. Brown[29], a director of the worldwatch institute for the United Nations Environmental Programme and the George Gund Foundation in the United States, published a report emphasizing the potential flexibility of using agricultural techniques to convert agricultural products to fuels and chemicals to supplement crude oil.

It was said[29], 'Sugar cane is among the most efficient converter of solar energy to carbohydrates;

carbohydrates are potentially a flexible feedstock for the fuels and chemical industries'.

The use of sugar in this way offers an exciting and profitable future if uncertainties in the production of the 'energy' crops can be overcome. The use of sugar in the food industries can be more 'efficient' if it is used more specifically, like fructose as a sweetener. This would allow full use of the surplus sugar in other ways.

Fructose is the sweetest of all the natural sugars. In cold solution, it is twice as sweet as an equivalent amount of sucrose.

Acid hydrolysis of sucrose or enzymatic conversion of corn starch produces a 50-50% (w/w) fructose-glucose mixture which needs an enriching process to obtain a fructose rich product. Commercially, 50% (w/w) concentrated solution of sucrose or corn starch has been successfully converted.

Fructose is an isomer of glucose, that is to say it is similar in molecular size but differs in molecular structure. Conventional means for separating fructose from glucose are difficult and expensive to apply. However, the past decade has seen large scale ion-exchange chromatographic processes being applied successfully to separate fructose from glucose. It was understood that the processes were operated in a batch mode. The fundamental mechanism of retention involved

was the formation of complexes between the calcium ions and the fructose molecules.

Notable processes in operation today are commissioned by the Colonial Sugar Refining Company[34] and the Boehringer Mannheim Company[35].

Despite the use of repeated injections and recycling of a fraction of the product, batch chromatography tends not to use the entire bed length efficiently, consequently it has limited throughput.

However, in the continuous cross-current and the continuous counter-current designs, they have been shown to use the entire bed length efficiently and to have more resolving power. The solutes need only be partially resolved in a section of the total bed length to achieve high purity products.

Cross current flow schemes worked well on the small scale but proved to be difficult to implement on a large scale[61].

In the counter-current flow scheme, the mobile phase and the stationary phase are simulated to flow in opposite directions. Separation of the solutes is achieved by selective adsorption of a component by the stationary phase. High purity products are obtained at the mobile phase port and the stationary phase port. Feed is usually introduced into the middle of the separating section.

At the University of Aston in Birmingham, active

participation by Barker and co-workers (17-27) in chromatographic research has produced semi-continuous counter current chromatographic refiner in various forms; namely gas-liquid, liquid-liquid and solid-liquid. Successful separation of isomeric hydrocarbon mixtures and fractionation of polymeric mixture such as dextran have been achieved. More recently, a fructose rich product has been obtained from a 50-50% (w/w) fructose-glucose mixture by ion-exchange (liquid-solid) chromatography.

The Pharmaceutical Division of Fisons Limited has a dextran plant which produces approximately 7.6 million metric tons per annum of fructose rich by-product (5.0% (w/w) solid). The composition of the by-product is, 68.0% (w/w) fructose, 9.0% (w/w) glucose, 22.0% (w/w) dextran and 2.0% (w/w) maltose and reducing sugars, in total-sugar content.

It was decided, as part of the research to attempt a recovery of dextran free, fructose rich product from a 70% (w/w) the semi-continuous counter-current chromatographic technique.

This research program is aimed at:

(i) improving the original semi-continous chromatographic refiner (SCCR4) constructed by Dr. C.B. Ching[24].

(ii) finding the 'good' operating conditions of the improved unit using a 50% (w/w) solution of 50-50% (w/w) glucose-fructose. Different

experimental parameters and flow schemes to be investigated.

(iii) investigating the possibility of obtaining a dextran-free, fructose rich product by this technique. An artificial Fisons feed (70% (w/w) solid) consisting of 69% (w/w) fructose, 9% (w/w) glucose and 22% (w/w) dextran 5 in total sugar, to be used initially.

(iv) studying the performance of the calcium charged zerolit 225 resin columns by using the actual fructose rich by-product from the dextran product.

(v) finding an alternative feed source of fructose such as hydrolysed sucrose for supplementing the actual dextran contaminated feed from the dextran plant.

(vi) improving the basic theory of SCCR4 operation as written by Dr. C.B. Ching[24].

(vii) improving the mathematical model developed by Dr. C.B. Ching to incorporate the effect of inter-column hold-up. Finally, to adapt the computer model for a twelve column unit and a three component system, and compare simulated and experimental results.

C H A P T E R T W O

BASIC CHROMATOGRAPHIC TERMINOLOGY AND THEORY

2. BASIC CHROMATOGRAPHIC TERMINOLOGY AND THEORY

2.1 SCOPE

Interest in chromatography is very strong and reports on the advancement of the technique are plentiful and cover a wide variety of topics, in both the academic and the industrial worlds.

Early work of Martin and Sygne[45] provided the definitive basis of chromatography; Giddings[44], later improved the theory which was recognised as a very important advancement in chromatography. Similarly Snyder[46], then Knox[48] updated the theory and further extended its application to high speed liquid chromatography. In addition, there are many papers and texts published annually with more detailed treatment of the theroy but geared specifically towards selected topics.

In this literature survey, because of space limitation, it is necessary to select and restrict the work of earlier workers in the field.

It was decided to divide the literature survey into three sections which formed three chapters in this thesis.

The first section of the review is concerned with the basic concept and terminology of liquid chromatography. This is then followed by a survey of the chemi-adsorption chromatographic separation of fructose from carbohydrates. The final part of the survey consists of a review of production scale chromatography.

2.2 TYPES OF LIQUID CHROMATOGRAPHY

Liquid chromatography is a process for separating liquids involving the passage of liquids through an adsorbing medium. It is usually categorised according to the mechanism of retention, such as:

(i) Ion exchange chromatography (Ligand exchange)

(ii) Exclusion chromatography

(iii) Partition chromatography

(iv) Adsorption chromatography

Ion exchange chromatography refers to the technique in which the retention mechanism involves the formation of complexes between the cations on the stationary phase and the solute molecules. Ions are continuously exchanged between the solute and the charged stationary phase.

In exclusion chromatography, separation of the sample components is achieved by virtue of their molecular size; very large molecules cannot penetrate the pores of the packing and are eluted first in a volume equal to the voids in the column; very small molecules can penetrate into the pores of the packings and are last to be eluted; molecules between these two sizes are eluted at volumes between the two limits.

Partition chromatography relies on the adsorption of solutes by an inert solid support coated with a liquid stationary phase.

Finally, with adsorption chromatography, the retention mechanism depends on the association of the solute and the active sites of the stationary phase. The association can be physical or chemical.

Ligand exchange chromatography is a form of adsorption chromatography whose retention mechanism relies on the association of the solute with a suitably charged ion-exchanger on the stationary phase; although the mechanism does not involve the exchange of ions.

2.3 BASIC THEORIES AND DEFINITIONS

In addition to the different modes of chromatography previously described in Section (2.2), chromatography may be further classified into frontal analysis, displacement and elution.

In frontal analysis, the sample is introduced as a step change, being fed continuously onto the column and so the sample constitutes the mobile phase. The components are selectively retarded with the formulation of fronts. The least retained component A, is eluted first and then followed by the mixture A and B. In displacement chromatography the mobile phase is more strongly retained by the stationary phase than the sample. The sample is therefore moved through the bed by the advancing mobile phase. Both modes of chromatography cannot achieve complete separation of the products but they do have advantages which

circumstances may favour their application.

In elution chromatography, a sample is injected on to a column; development of component bands occurs as the sample components migrate down the packed bed. The result as traced by a detector is a chromatogram as in figure (2.1). Elution chromatography is the only mode that can result in a quantitative and qualitative separation of a mixture.

If a very small sample size is used (a linear distribution isotherm), the concentration profiles of the products are symmetrical and Gaussian. The time of elution of the peak maximum can be related to the distribution coefficient. The elution time or retention time is a function of the elution velocity of the mobile phase; the product of the two parameters yield the elution volume, V_R. The volume is the total volume of mobile phase required to elute a sample from the column. A fundamental retention equation for the gel permeation chromatography as developed by Kirkland[47] and Simpson[37] is as follows:

$$V_R = V_m + K_D V_s \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (2.1)$$

where

V_R = elution volume of a component

V_m = total volume of the mobile phase in the column
= void + pore volumes

V_s = volume of stationary phase (resin's solid matrix)

K_D = equilibrium distribution coefficient

$$= \frac{\text{concentration of solute in stationary phase}}{\text{concentration of solute in liquid phase}}$$

$V_m = t_o.F$ where F = mobile phase flowrate

t_o = retention time of a non-retarded component, Figure (2.1)

Another useful term is

$$K' = \frac{K_D V_s}{V_m} = \frac{\text{amount of solute in stationary phase}}{\text{amount of solute in mobile phase}} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (2.2)$$

Equation (2.) can be rearranged as:

$$t_R = t_o(1 + K') \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (2.3)$$

which relates the fundamental parameter time to the equilibrium distribution coefficient K'.

2.3.1 RESOLUTION

The separation between two adjacent bands is called the resolution R_s, and is defined as the distance between the peak maxima divided by the peak width in the same units. That is

$$R_s = \frac{2(V_{R2} - V_{R1})}{(W_1 + W_2)} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (2.4)$$

or $$R_s = \frac{2(t_{R2} - t_{R1})}{(W_1 + W_2)} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (2.5)$$

A resolution of R_s = 1.0 is considered to be satisfactory, an R_s value equal to 1.5 and above is considered a good separation factor, and on the contrary, a R_s value of 0.8 or less, separation is

FIG.2.1 A TYPICAL CHROMATOGRAM

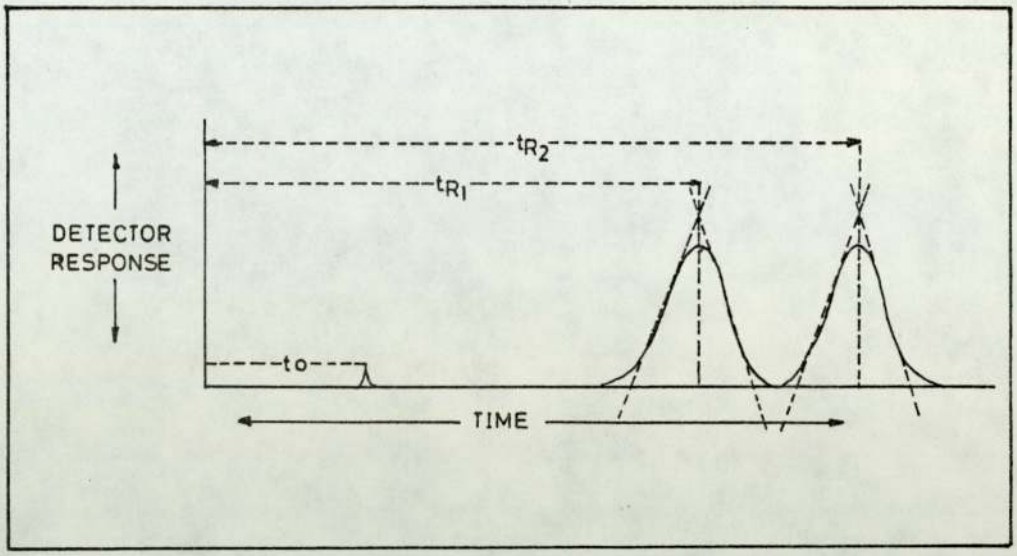
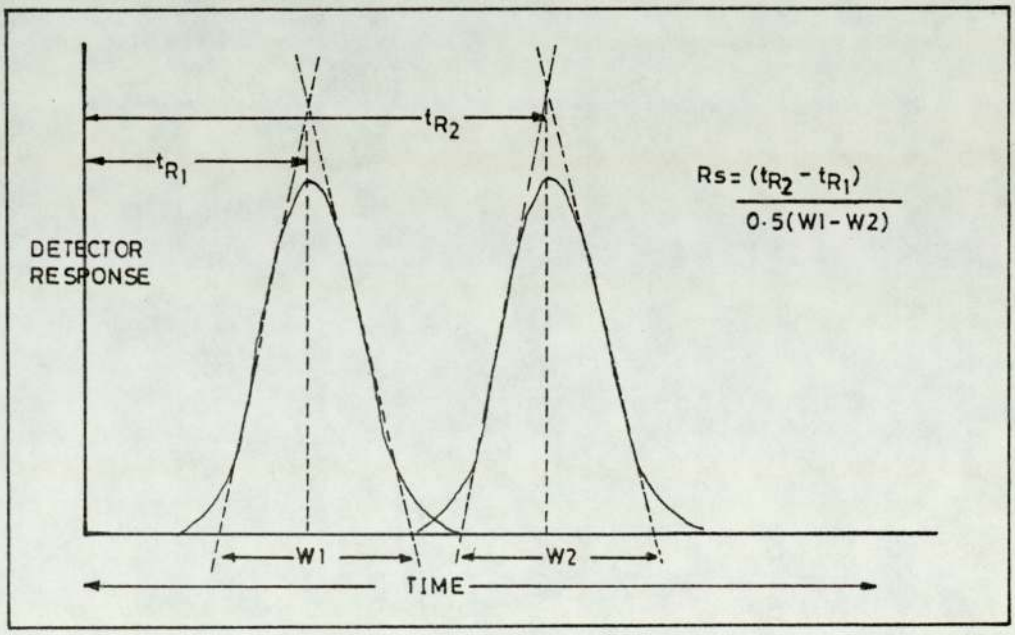


FIG.2.2 CHROMATOGRAM DEMONSTRATING FEATURES OF THE PEAKS FOR THE RESOLUTION FACTOR



considered unsatisfactory in normal chromatographic practice, Figure (2.2).

Purnell[48] showed that more information may be extracted about the factors controlling resolution, by transforming the simple equation to incorporate equilibrium distribution coefficients and column dispersion factor.

$$R_s = \frac{1}{4}\{\frac{\alpha-1}{\alpha}\}\{\frac{K_2}{1+K_2}\}(N)^{\frac{1}{2}} \quad \ldots\ldots\ldots\ldots\ldots\ldots (2.6)$$

where

N = number of theoretical plates

$\alpha = \frac{K_2}{K_1} = \frac{K_{D2}}{K_{D1}}$ = relative retention

K_{D_2} = distribution coefficient for the more retarded component

K_{D_1} = distribution coefficient for the less retarded component

K_2, K_1 are the capacity factors

2.4 THEORY OF ZONE SPREADING

The development of chromatographic bands as the solute proceeds in the column is dependent on its thermodynamic and column dynamic equilibria. It is the latter which determines the width of the solute zones and which theories of chromatography attempt to define. Efforts by various researchers have succeeded in demonstrating the dependence of zone spreading on various factors. However, a perfect quantitative

relationship linking both has yet to be developed.

2.4.1 THE THEORETICAL PLATE CONCEPT

The success of the theoretical plate model in describing a distillation process prompted Martin and Synge[45] to formulate and test a similar model for chromatography.

A chromatographic column is assumed to consist of a number of layers of chromatographic media each of whch is equivalent to one theoretical plate; the height of such a layer is called the height equivalent to one theoretical plate, H.E.T.P. The solution issuing from each plate is assumed to be in equilibrium with the mean concentration of solute in the stationary phase throughout the plate. It is assumed that the diffusion of solute from one pack to another is negligible and that the mobile phase flow is discontinuous, consisting of stepwise additions of volumes of the mobile phase equal to the mobile phase volume per plate. Further assumptions include that at equilibrium, the distribution ratio of one solute between the two phases must be independent both of the absolute value of its concentration and of the presence of other solutes.

From the assumption above, it was thought that a single solute band would spread into a Gaussian distribution curve. The degree of spreading of this solute band is qualified by the second moment, or the

variance of the curve.

A parameter used to characterise the efficiency of the chromatographic column is the plate height:

$$H = \frac{d\ \sigma_z^2}{d\ Z} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (2.7)$$

where

σ_z^2 = length based second moment

Z = distance along a column of length L

Martin and Synge also observed the dependence of H.E.T.P. (H) on the mobile phase velocity (u) and the particle diameter (d_p)

$$H = f(u, d_p^2) \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (2.8)$$

Furthermore, as the longitudinal diffusion from plate to plate becomes relatively more significant at reduced flowrate, they emphasised that for any given separation there is an optimum mobile phase flowrate.

Glueckauf[27] extended the model into a continuous one by reducing the plate volume to an infinitessimally small value. The concentration profile exhibits a Poisson distribution and could, if the number of plates, N, is large enough (>100), be approximated to a Gaussian distribution. The standard deviation (σ) of a Guassian distribution is given by:

$$\sigma(H.L_m)^{\frac{1}{2}} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (2.9)$$

where H is the plate height and L_m is the distance migrated.

Rearranging equation (2.9)

$$H = \frac{\sigma^2}{L_m} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (2.10)$$

Equation (2.9) shows that H varies directly with σ^2, i.e. the variance of the distribution and important statistical property of σ^2 is that it is additive and hence various independent contributions can be assumed.

i.e. $\sigma^2 = \sigma_1^2 + \sigma_2^2 + \sigma_3^2 + \ldots$ ..... (2.11)

Hence the H.E.T.P. can be expressed as:

$$H = \Sigma_i \frac{\sigma_i^2}{L_m} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (2.12)$$

As such, various contributions to the plate height may be determined independently and summed to give an overall value for H.

The most significant deviation of the plate model concept from real column processes rests on the assumption of plate wide equilibrium. In actual situations, equilibrium is only reached at the peak maximum point. In addition, the plate model fails to account for the contributions of molecular structure, sorption phenomenon, temperature, molecular distribution and flow pattern towards zone spreading. However, the plate height is a useful and widely accepted parameter for the characterization of zone spreading and column efficiency.

2.4.2 ZONE SPREADING RATE THEORY

2.4.2.1 VAN DEEMTER THEORY

Lapidus and Amundson[50] provided the foundation for a mathematical model which included mass transfer and longitudinal diffusion terms for the Van Deemter model. This model was extended by Van Deemter, Zuiderweg and Klinkenberg[51] to include contributions from axial diffusion and finite rates of mass transfer. The form of their equation is as follows:

$$H = A + \frac{B}{V} + C_m'V + C_s'V \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (2.13)$$

where

A = eddy diffusion term

B = longitudinal diffusion term

C_m', C_s' = resistance to mass transfer in the mobile and stationary phase, respectively

2.4.2.2 RANDOM WALK THEORY

Giddings and co-workers[52-58] conducted an extensive investigation into the mechanism of zone spreading and details are fully documented in his well known text[44]. With his random walk approach, he attempted to explain and correlate various individual molecular processes occurring in a chromatographic column. The final form of the equation is as follows:

$$H = A + B/u + C_s.u + C_m.u \quad \ldots\ldots\ldots\ldots\ldots \quad (2.14)$$

which is of a similar form to the Van Deemeter

equation (2.13) except for the addition of a mobile phase mass transfer resistance term. Implicit in equation (2.14) is the assumption that individual contributions to plate height, H are independent and additive.

Giddings, on recognising the close relationship between eddy diffusion and flow inequalities, proposed a 'Coupling Theory' in which the resistance to mass transfer in the mobile phase and the eddy diffusion term are coupled. The simplified form of the equation is:

$$H = \frac{B}{u} + C_s u + \{\frac{1}{A} + \frac{1}{C_m . v}\}^{-1} \quad \ldots\ldots\ldots\ldots\ldots \quad (2.15)$$

The total value of the contribution to H of the coupled term is always less than that obtained from either of the component parts (figure 2.3); however, the equation (2.15) has been used by many workers in chromatography for the prediction of plate height.

2.4.3 GENERALISED NON-EQUILIBRIUM THEORY

Giddings[44] also developed a more vigorous theory 'the Generalised Non-equilibrium Theory', and claimed the true equilibrium between two phases exists at the centre of the zone. The stationary phase concentration lags behind its equilibrium value, whilst the mobile phase concentration is ahead of its equilibrium value as indicated by figure (2.4). Slow mass transfer rates between the two phases account for the non-equilibrium situation. Giddings[44] discusses quantitatively the

FIG.2.3 COMPARISON BETWEEN CLASSICAL AND COUPLED EQUATION FOR PLATE HEIGHT

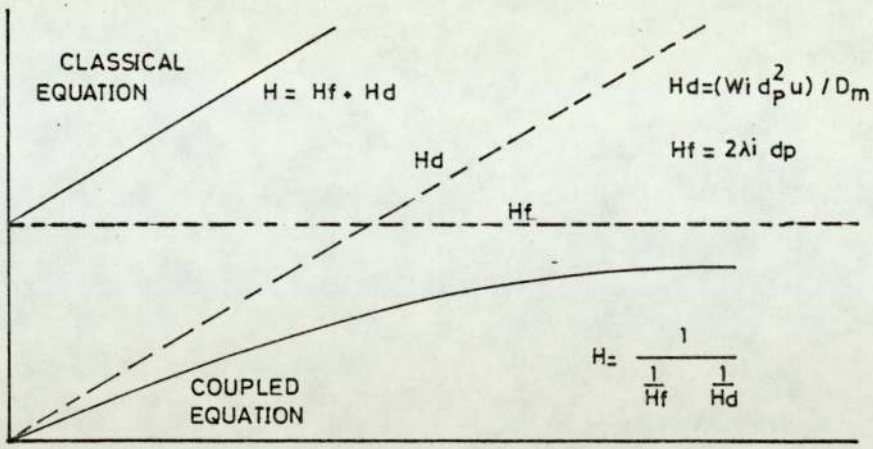
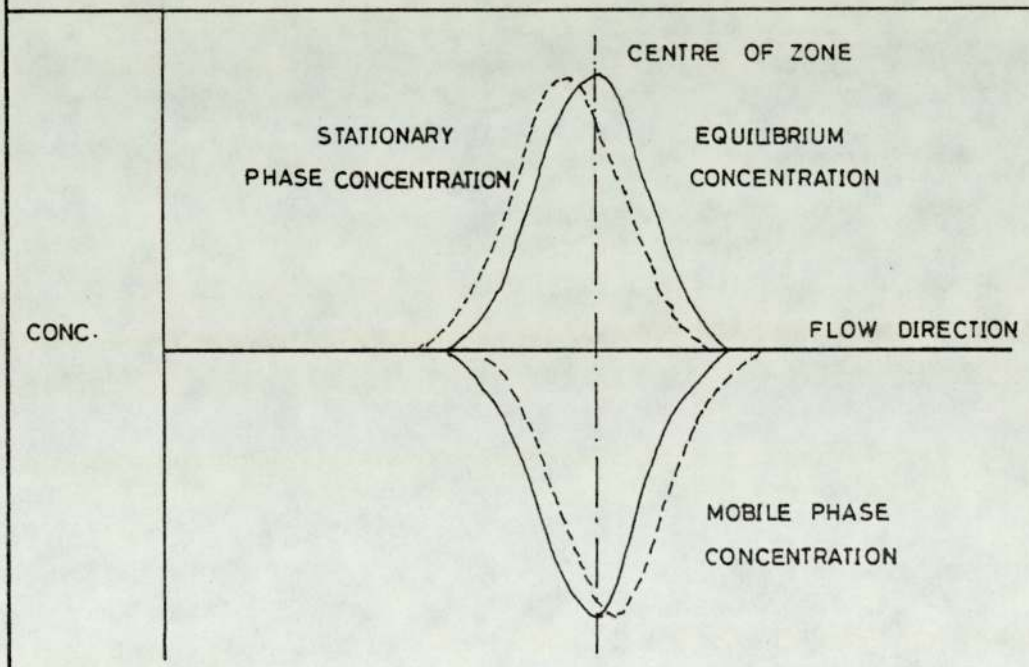


FIG.2.4 COMPARISON BETWEEN ACTUAL EQUILIBRIUM ZONE CONCENTRATION PROFILE



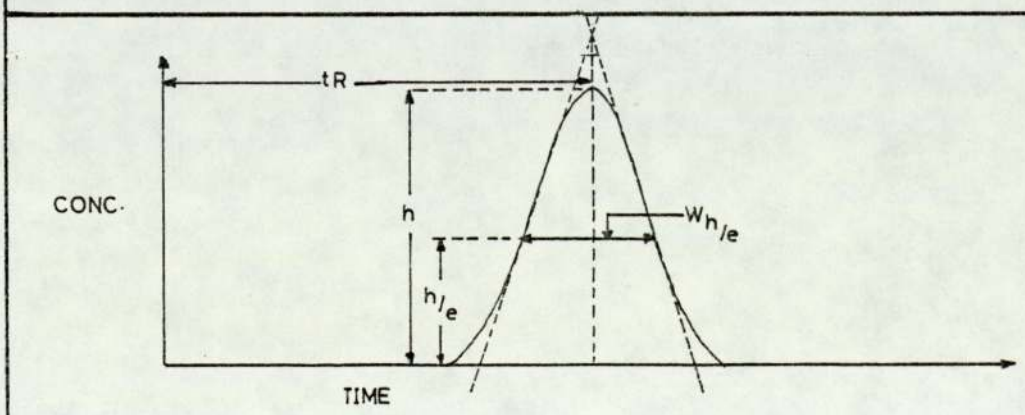


FIG.2.5 RELATIONSHIP BETWEEN PLATE EFFICIENCY AND PEAK CHARACTERISTIC

mass transfer processes in a variety of systems.

2.4.4 GENERAL STATISTICAL METHOD FOR RELATING PLATE EFFICIENCY TO THE PEAK CHARACTERISTIC

For a Gausian shaped peak, figure (2,5) shows the relationships between peak width and the standard deviation.

If it is assumed that the solute band is applied to the head of the column as a very narrow band, small in relation to the eluting band, then during the passage of this band through the chromatographic bed individual molecules are subjected to a variety of different restraints, so that the overall migration velocity of the band is $V_{band} \pm \Delta V$, where V_{band} is the migration velocity of the centre of the band.

This deviation from the mean velocity of the band arises through the different path lengths followed by various molecules during their passage through the column.

The width of the band is a measure of the column efficiency or number of theoretical plates, N.

Thus $$N = \left\{\frac{t_{R_i}}{\sigma_i}\right\}^2$$

where t_{R_i} is the time required to elute the band centre and σ_i^2 is the variance of the band in time units. A more convenient way of representing the standard deviation is the peak width taken at a fixed

height, Glueckanf[49] uses

$$N = 8 \left\{ \frac{t_{Ri}}{W_{h/e}} \right\}^2$$

where $W_{h/e}$ = width of the peak-band at a height of h/e.

C H A P T E R T H R E E

SEPARATION OF FRUCTOSE FROM CARBOHYDRATES BY CHEMICAL ADSORPTION METHODS

3. RECOVERY OF FRUCTOSE BY CHROMATOGRAPHIC TECHNIQUES

In this Chapter, the commercial sources and the chromatographic technique for preparing fructose will be reviewed.

3.1 COMMERCIAL SOURCES OF FRUCTOSE

3.1.1 HYDROLYSIS OF SUCROSE WITH MINERAL ACID

The most widely used source for preparing fructose in the period of 1950-60's, was by the use of invert syrup from sucrose. Sucrose, which contains molecules of fructose and glucose, was hydrolysed at elevated temperature with mineral acid. The final product contained 42-44% (w/w) fructose, 52-56% (w/w) glucose and 3% (w/w) oligosaccharides. The major source of sucrose is from sugar cane and sugar beet.

3.1.2 ISOMERISATION OF GLUCOSE USING IMMOBILISED ENZYMES

As early as 1895, Bruyn and Van Eckenstein[69], discovered that glucose could be converted to fructose in a process known today as isomerisation. The process involved the use of an alkaline catalyst on the glucose at elevated temperature in a reactor. From 1944 onwards, numerous patents were granted describing in detail isomerization processes using sodium hydroxide and ion-exchange resins. Amongst these workers,

Scallet and co-workers[70-71], Ikazaki[75] and Suzuki[76-77] contributed prominently. Others, namely, Parish[78], Tsao[79] and Barker, S.A.[80] used a less expensive catalyst such as insoluble alumina catalysed organic bases and organic acid derivatives. Reported conversions varied from 45% to 80%.

However, no industrial process was reported to have been built using the methods described above. The reason being due to the generally low conversion yields and the accompanying colour, ash and by-products. Glucose was also an expensive raw material to use which made the processes commercially unattractive.

In 1957, Marshall and Kooi[81] reported the discovery of an enzyme which functioned as a catalyst for the conversion of glucose to fructose. A patent[82] was granted in 1960. The enzyme was xylose isomerase which was obtained from the organism, pseudomonas hydrophilia. This organism did not produce any isomerase in the absence of xylose, but in the presence of asernate or fluoride in the feed mixture, it increased the yield of fructose; presumably by inhibiting certain unspecified side reactions. The presence of these toxic materials and the unavailability of a cheap source of xylose made this an unsuitable process for producing food products.

However, investigations along this line were further pursued by many other workers, notably the Japanese workers, Tsumura[83,84] worked with

streptomyces phaeochromogenes, Watake and Yoshimura (Kobe University)[85-89], with Escherichia intermedia, Yamanaka (Kagawa University)[90-92], with Lactobacillus Brevis, Danno[93-97], with Bacillus Coagulans and Takasaki[98] with various streptomyces. In 1971, Takasaki and Tanabe were granted a patent[99] which proposed the use of a special strain of streptomyces on xylan rather than xylose to produce the enzyme, glucose isomerases. Xylan was readily available from various sources, such as cereal bran and corn cobs. Furthermore, this particular strain of streptomyces did not require arsenate or fluoride. Later, Takasaki[100] outlined in detail a proposed commercial isomerization process in which heat-treated streptomyces cells, which contained the enzyme, could be used directly on the glucose substrate. The steptomyces cells could be recovered after the reaction and re-used in the subsequent batch reaction. Alternatively, the cells could be used continuously in a column. The Takasaki and co-workers proposal provided a commercially feasible glucose isomerisation process for obtaining a fructose-rich syrup.

Indeed, in 1974, Newton and Wardrip[101] of the Clinton Corn Processing Company, a subsidiary of Standard Brand Incorporated, reported the first commercial process in the United States for manufacturing a fructose rich corn syrup. The process used the basic technique derived by Takasaki and Tanabe as described

in their patent[99].

The enzyme used was obtained from steptomyces sp. ATcc 21175, cell free, and immobilised on DEAE cellulose as described in a patent to Thompson, Johnson and Lloyd[102]. The Clinton process was reported to have the following advantages over Takasaki's heat treated cells:

(i) Cellular material from the fermentation broth was removed and was not part of the immobilised enzyme product.

(ii) Immobilised enzyme product could be washed to remove soluble components.

(iii) Recovery of fermenter activity in immobilised form was good; up to 90%.

(iv) High enzyme activity loadings per gram dry substance product were obtained.

(v) Immobilised enzyme product minimises pressure drop problems when used in isomerisation reactors.

Detailed description of a possible isomerisation reactor system has been disclosed by Lloyd[103]. Numerous patents connected with the Clinton process has been taken up by different workers as disclosed by Sieman[60], in a paper presented at a meeting of the American Chemical Society, Chicago, Illinois, 1976.

Elsewhere, Nova Co.[107] in Denmark, developed a new source of immobilised enzyme, called Sweetzyme. The enzyme glucose isomerase was from a special strain of the Bacillus Coagulon cells.

The sweetzyme was produced in particles of different physical forms such as spheres, cylinder and flakes using a special immobilisation technique. The physical forms of the sweetzyme was designed for use in batch reactors and also continuously operated reactors.

In the United Kingdom, the Imperial Chemical Industries (ICI) also produced enzymes for isomerising glucose, but did not participate in manufacturing the fructose rich corn syrup; although it was known ICI did sponsor some research projects along this line.

Today, large continuous processes for producing fructose rich corn syrup from cheap starch sources are in evidence in Koog an Zoon in the Netherlands, Aalsf in Belgium, Saragossa in Spain, and at Greenwich in the United Kingdom. Reports indicated that the maize used was supplied by Brazil, South Africa, the United States of America, Rumania and Yugoslavia.

The latest investment for a fructose rich corn product process was by the Albion Sugar Company (a subsidiary of Koninklijke Sholten-Honig NV of Amsterdam) at Tilbury-on-Thames, in the United Kingdom. The project was started in 1974 and in 1978 it was ready to be commissioned, but the plant was not started up due to a levy imposed by the EEC on fructose from starch sources[105]. In 1979, this levy was declared to be illegal although so far as is known, the Tilbury plant has still not started up.

The Tilbury plant was designed to produce about 100,000 tonne per annum of the fructose rich product. The product would have been a water-white, odourless, rather viscous liquid of 71% solids; consisting of 42% (w/w) of fructose, 55% (w/w) of glucose and 3% (w/w) of oligosaccharides.

3.1.3 CONTINUOUS HYDROLYSIS OF SUCROSE USING ION-EXCHANGE RESIN

In a patent granted to the Boehringer Maunheim Company[35] in 1967, it was disclosed that sucrose was completely inverted to equal fractions of fructose and glucose after passing through a hydrogen charged ion-exchange bed, at a temperature of 60°C. The ion-exchnage resin used was a sulphonated polystyrene with 4% divinyl-benzene cross-linkage, and was marketed under the name of Dowex 5WX4.

It was also found that when the resin was charged with calcium chloride at room temperature, it still retained 1-30% of the free and group. When a slug of sucrose feed was passed through a suitable bed length of resin, hydrolysis of the sucrose and separation of the fructose from the glucose took place in the column. Pure glucose emerged initially from the column, followed by a mixture of glucose and fructose, and then finally pure fructose. A detailed description of the preparative scale batch process will be provided in Section (3.3.1).

Between 1969-73, Lauer and co-workers[108-110] were granted three U.S. patents. The first was for a process for inverting sucrose and separating the fructose-glucose products in the same column. The resin used was Dowex 5 WX4 in the calcium charged form. The inversion and separation temperature was 60°C. The second patent was for a polarimeter-refractometer automatic monitoring technique for continuous monitoring of the products from the column. The third patent was for a process which used two columns, the first column for the hydrolysis of sucrose and a second longer column for the separation of fructose from glucose. The analyser system mentioned above was used continuously at the outlet of the first column to divert impurities to waste storage and sugars to the second column where separation took place.

3.2 THE DEVELOPMENT OF THE CHROMATOGRAPHIC TECHNIQUE

3.2.1 INTRODUCTION

The earliest reports of the use of an ion-exchange resin as a chromatographic adsorbant appear to be by Samuelson and Sjostrom[111]. In their experiments, a bisulphate form of an anion resin was used to adsorb monosaccharides at high ethanol concentration. Separation of the monosacchorides was achieved by elution at a lower ethanol concentration. At about the same time Wheaton and Bauman[112] reported on an ion exclusion process whereby non-ionic materials were retarded at

different rates when passing through a resin bed such as Dowex 50; a strong cation exchanger but in the alkali salt form.

In 1962, Sargent[113] of the Dow Company (supplier of Dowex resins) was granted a patent for separating fructose from dextran by using the exclusion chromatographic technique. The resins used were of the alkaline salt form of a cation exchanger and quanternary ammonium anion-exchanger. Elutions were with water.

In the same year, Serbia[114] and Leferve[115-116] described processes for separating fructose from glucose using only water for elution. Serbia passed the glucose-fructose mixture through a calcium charged cation ion-exchanger in a column. While Leferve suggested the use of the barium-strotium salt of a similar resin and the silver salt form of Dowex 50W-X4.

Mountfort[117], in 1965 patented a system which used recycling and switching steps to obtain more concentrated glucose and fructose products. The resin used was of the alkali salt form of the cation exchanger, Dowex 50W-X4. Preferred operating conditions appeared to include resin of 1200-1500 μm (35-70 mesh) size, a 4% divinylbenzene cross-linking level, 60°C temperature and a flow rate of 2.0 m^3/m^2 of resin cross-sectional area per hour.

Later, in 1967 the Boehringer Maunhein Company was granted a British patent[35] for a process for obtaining pure fructose and glucose. It was discovered

that when the Dowex 50W-X4 resin was charged with calcium chloride solution at room temperature, between 1-3% of the free acid ions were still retained. When a mixture of invert solution containing fructose, glucose and sucrose was passed through the mixed bed, all the sucrose was hydrolysed and the products contained only fructose and glucose. The operating temperature was at 60°C. A similar result was achieved when 50% (w/w) concentrated sucrose feed was passed through the mixed bed.

The discovery was significant, for it offered a cost-saving and an attractive process for obtaining pure fructose and glucose at that time. The products obtained did not colour, and contained no ash or polymerial products.

Later, in the same year, a pamphlet[121] published by BMA disclosed that several large preparative plants were under construction. The BMA plants used the Boehringer invention and were built under a licence granted by the Boehringer Mannheim Company. The BMA process will be described in the next section (3.3.1).

About the same time, the Colonial Sugar Refining Company was granted a British patent[34] for a new process for the separation of fructose and glucose from a syrup containing them. In their patent, a 1.8m resin bed length (no mention of column diameter) was used. A calcium charged, Dowex 50W cation exchanger was used. The resin had a 4% divinylbenzene cross-

linkage and a particle size range of 420-120 μm. Invert sugar syrup was used as the feed.

Both the processes by the BMA and the Colonial Sugar Refining Company were operated in the batch mode. A batch feed injection technique was used and the intermediate fractions containing fructose and glucose were recycled.

Further research by Jones and Walls[118,119] discovered that a barium charged Dowex 50Wx8% (200-400 mesh) could also separate monosaccharides. In their work, 70 x 2.2 cm I.D. columns were used. Other group I and II metal ions in the chemical table were also used to charge the Dowex 50W resin.

In 1974, Takasaki[120] used the bisulphite form of an anion exchanger, Dowex 1-X4 for separating fructose and glucose. In contrast to the cation resin system the fructose was retarded less and was eluted first. In a series of experiments, Takasaki illustrated that the separation between fructose and glucose improved by elevating the temperature; a complete separation of fructose and glucose was achieved at 60°C. Water was used as the eluting solvent.

Kubota[122] in 1975, separated fructose from a dextran mixture produced by an enzymic or a fermentation reaction from sucrose. The mixture was passed through an anion exchanger containing quanternary ammonium salt, -OH type and eluted with water.

Much of the work reviewed so far used organic based cation or anion exchangers charged with different ions as the chromatographic adsorbent. Also, in most inventions, water was used as the eluting solvent.

However, in 1977, Odawara[123] disclosed a method of separating fructose from a sugar mixture using crystalline alumino-silicate, called zeolite. X and Y types (manufacturer classification) of zeolite were used. In his experiments, both types of zeolite were charged with all the metal ions from group I and II of the chemical table. It was found that a barium, calcium and strontium charged bed gave the best separation of the sugars at the temperature range of 10-50°C. Amongst the three, the barium charged bed of the Y-form had the best resolving power. It was also found that the pore size of the pellet form adsorbent must be between 5Å and 16Å for effective separation to take place. The size of the particle used was between 350 μm and 450 μm (40 and 30 mesh).

Two years later Odawara and co-workers[124] followed up their invention with another patent. They disclosed that by using eleven interconnected sections in a loop and moving a set of ports at a fixed time period, a continuous counter current movement between the desorbant and adsorbant was simulated. (Note Odawara and co-workers were not the first to use this sort of flow arrangement). Each section consisted of a 2.5 cm I.D. x 1.5 m long stainless steel column.

Barium zeolite in the form of Y-type was packed into the column to a height 1.35m from the bottom. The particle size was 0.5 mm. Copper particles having the size of 0.5 were also packed into each column in the remaining vacant space; that was to a height of 0.15m from the top of the zeolite layer.

It was claimed that when a 7% (w/w) concentrated feed mixture was fed into the system, a 1% (w/w) concentrated 100% (w/w) pure fructose extract was obtained continuously. The feed rate was 1.5 kg/hr and a 1.0% (w/w) of sugar mixture was introduced continuously at room temperature into the system at a flowrate of 8.5 kg/hr. The water rate was 2.9 kg/hr.

Two months later than the Japanese contingent in 1977, Neuzil and Priegnitz[125] were granted a patent for a process for separating a ketose from an aldose by selective adsorption. The process was a small batch unit, where the X-zeolite was used as the chromatographic adsorbent. The X-zeolite was charged with one or more cations at the exchangeable cationic sites. Sodium, caesium, barium calcium, potassium, magnesium and strontium were used as the active cationic exchanger. The best separation of fructose and glucose from a mixture was found to be the strontium charged X-zeolite, followed by a barium-strontium charged bed. No preparations were achieved with calcium, caesium and magnesium charged X-zeolites.

The experiments were conducted with a 1.14 cm I.D. by 2.3 m long stainless steel column at a temperature range of between 50-70^{o}C. Water was used as the eluting solvent.

In the same year, the U.O.P. Incorporated announced their Sarex process[127] for porducing high purity fructose syrup. The process was a direct development of their Parex and Sorbex[128] processes for separating hydrocarbon. Both the processes effectiveness and efficiency had been proved in several large-scale industrial operations with hydrocarbon streams since 1964.

The Sarex process was a continuous counter-current fluid-solid chromatographic system, in which the actual movement of the solid was simulated by moving parts. A very complex rotary valve was used to switch the various streams into and out of the system.

Details of the process were published in two papers [127,128] in 1977, but since then no further news of the process being brought into production has been reported.

Other prominent workers in research for a continuous separation system for preparing fructose were Isikawa[129] with his pseudo-moving bed system in 1976, Lui, S.H.[130] with his parametric pump system.

A more detailed review of the continuous counter-current chromatograhic technique will be provided in Chapter Four.

3.3 BATCH PROCESSES IN OPERATION TODAY

3.3.1 THE B.M.A. PROCESS

Shortly after the disclosure of the Boehringer patent, the BMA started construction on several plants under licence from the Boehringer Mannheim GmbH.

In the pamphlet published by BMA[121], it was stated that both crystallised fructose or syrup with a 70% dry substance of pure fructose could be achieved by their plant through various stages of filtration and evaporation.

The BMA plant could be separated into three main sections namely:

(i) the feed preparation and purification section,
(ii) the hydrolysis and separation section, and
(iii) the product collection, concentration and storage section.

A flow scheme of the plant is illustrated in Figure (3.1).

In the feed handling and purification section, the sucrose was taken from the silo and fed to an intermediate bunker by means of a worm-screw conveyor, from which it was fed by means of dosing equipment into a dissolving apparatus. Deionised water and sugar-containing intermediate component group (II), recycled from the separating plant, served as a dissolving agent. The prepared sugar syrup was subjected to a filtration, or with filtering agents as alluvial filtration. The filtrate was then passed through

various columns of different resins for demineralising. The demineralised sucrose was stored in the intermediate tanks and was then fed periodically to the separating column via the heat exchanger. Immediately after the sugar solution had been transferred to the component separating columns, the demineralising resins were washed out with water. Elution water was then fed to the separation column via the same heat exchanger.

In the separation section, the sucrose was separated into the two monosaccharides and the product was divided into four main fractions, Figure (3.2).

(i) Intermediate component group (I) - rich in glucose but contaminated with fructose

(ii) Glucose rich group

(iii) Intermediate component group (II) - rich in fructose but contaminated with glucose

(iv) Fructose-rich group

In the product collection, concentration and storage, the glucose-rich fraction and the intermediate component - group (I) were pumped into the same container pending to be fed to a continuous two-stage evaporating plant and, under vacuum, concentrated to a glucose syrup of 50% (w/w). However, the fructose-rich fraction and the intermediate component group (II) were collected in separate containers. Subsequently, the fructose-rich fraction, with a furctose purity in excess of 96%, was concentrated in a two-stage evaporation plant to a syrup of 70% dry substance. The

FIG. 3.1 SCHEMATIC DIAGRAM OF THE B.M.A. PROCESS

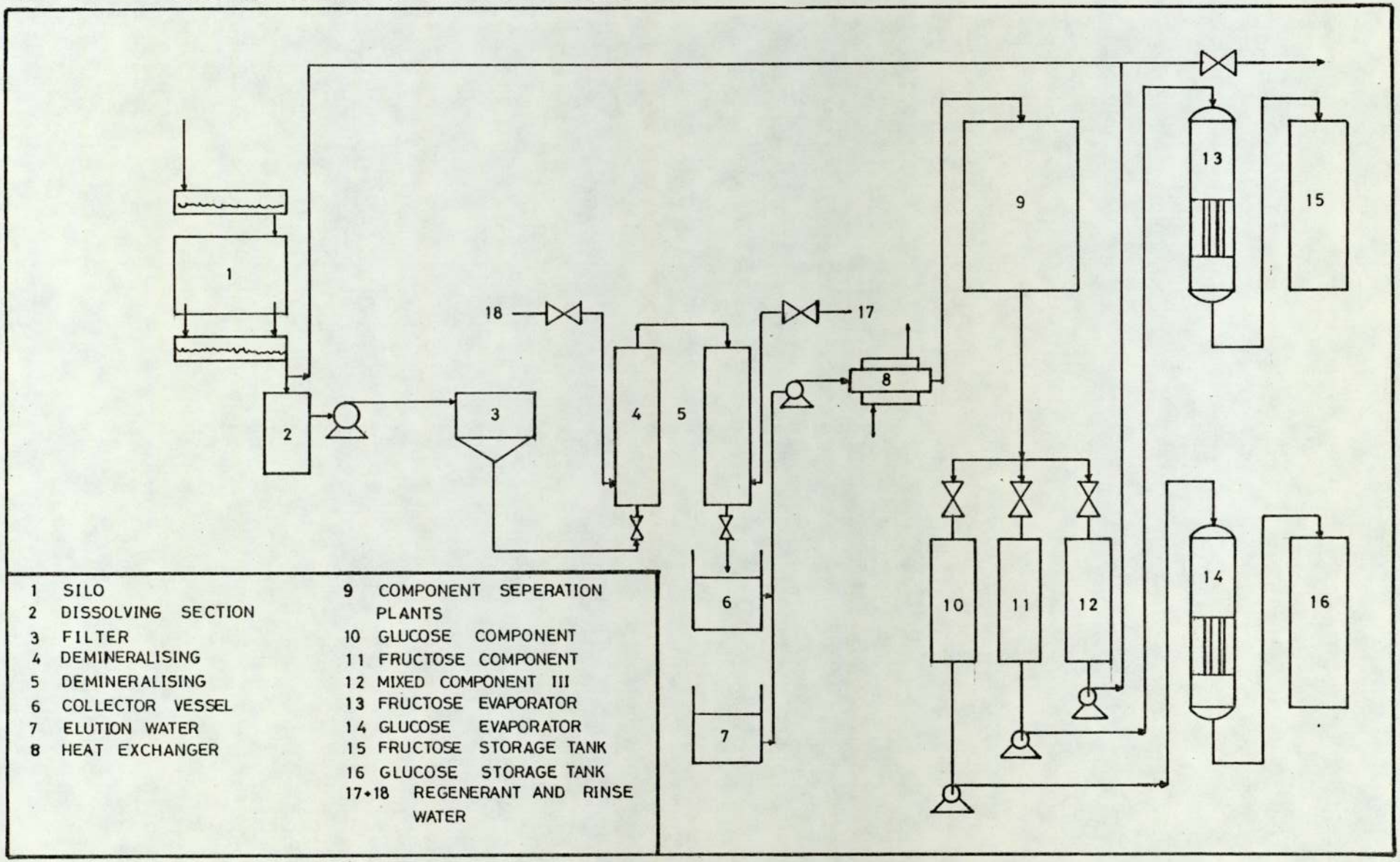
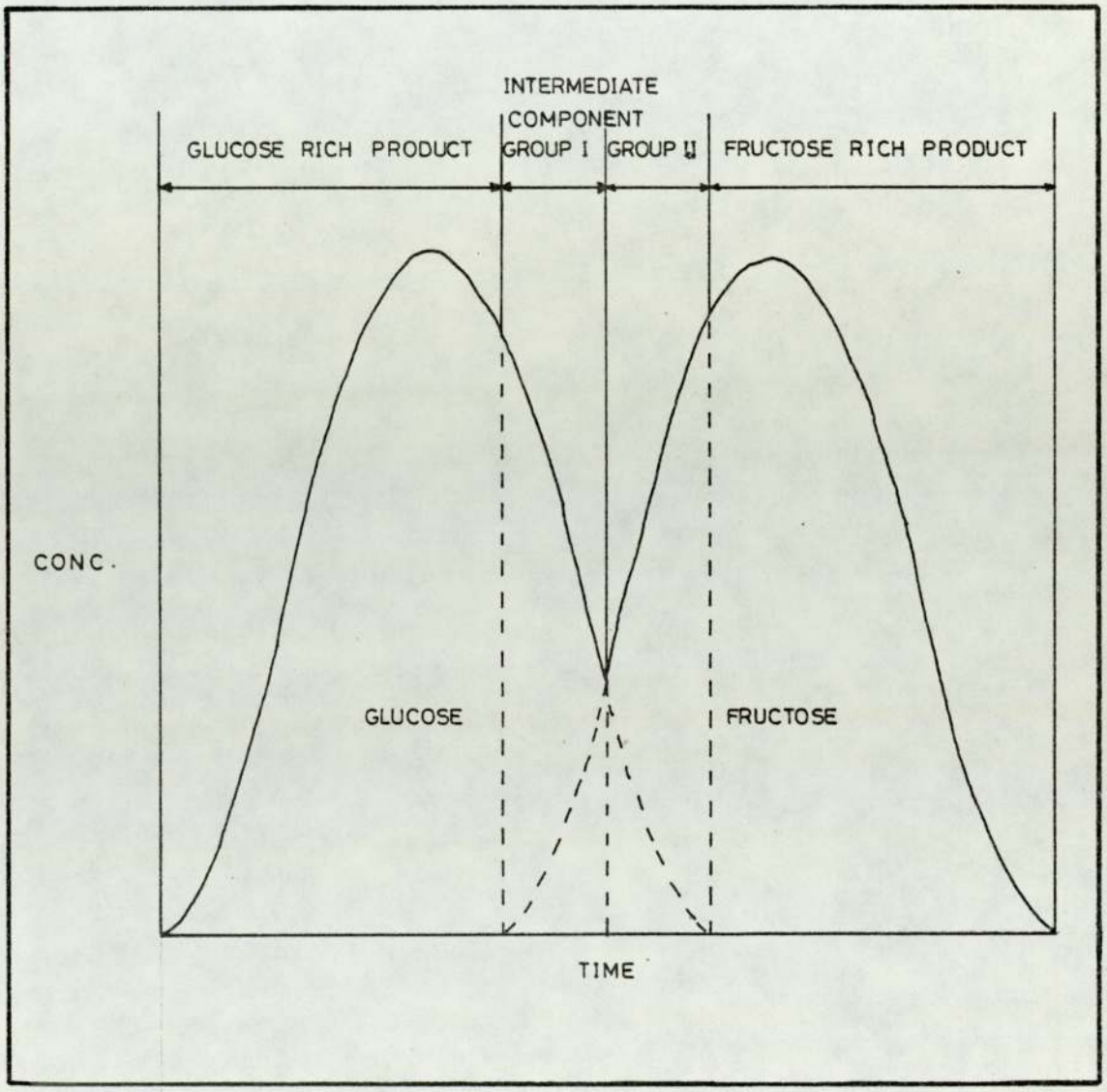


FIG. 3.2 CHROMATOGRAM ILLUTRATING THE B.M.A PROCESS PRODUCT FRACTIONATION



resulting syrup was then subjected to a carbonisation process for decolourising purposes. After the purification, the warm fructose syrup was put through a final safety filtration stage, cooled off in the heat exchanger to the storage temperature and pumped to the storage tanks which were installed with air conditioning and exterior heating facilities. The fructose processing of the 70% (w/w) syrup to fructose crystals was carried out by using methanol as a total crystallization from water.

The intermediate component group (II) was recycled back to the mixing tank for dissolving the fresh sucrose. In the event that liquid sugar was used as the raw material, the recycle (II) could be concentrated in a separate evaporator plant.

3.3.2 THE COLONIAL SUGAR REFINING COMPANY PROCESS[34]

The process used a calcium charged sulphonated polystyrene cation resin, with 4% divinylbenzene cross-link, Dowex 50W. Particle size of 420-120 µm was used and a total bed length of 1.8m was reported (no mention of column diameter). Invert sugar syrup was used as the feed.

The process included the recycling of certain fractions of product and could be identified in four main steps. Firstly, predetermined volumes of the feed syrup and water were sequentially admitted to the column with the control of various valves. At the start

of the operation the column was half filled with a water immersed resin bed. The water level was lowered to the upper surface of the resin and the syrup was fed to the top of the column. Elution water was then introduced into the column just before the syrup level dropped to the upper surface of the resin. The second step was the sequential separation of the effluent from the column into various fractions:

(i) a dilute solution of glucose

(ii) a concentrated glucose-rich solution

(iii) recycle (I) consisting of concentrated glucose-rich solution but highly contaminated with fructose

(iv) recycle (II) consisting of concentrated fructose-rich solution highly contaminated with glucose

(v) a concentrated fructose-rich solution

(vi) dilute fructose-rich solution

The next step was the re-admitting sequentially of recycle (I), recycle (II), the additional feed and elution water to the column. The final step was the repeat of step two and three in a cyclic manner.

The total product outlet flowrate was reported to be approximately 0.195 m^3 h^{-1} m^{-2} of resin bed. As stated in the patent, in spite of the fact that a greater separation of fructose and glucose could be achieved at ambient temperature (20°C) than at elevated temperature (60°C), the latter was preferred. This was related to the fact that concentrated syrups were

viscous and slow moving at low temperature and their dilution entailed increased evaporation costs. Hence, all the storage tanks containing feed syrups were equipped with heating devices. The operating column was also lagged to minimise heat loss. There were two sets of results presented in the patent with each representing a different fresh syrup to total feed ratio.

In the first one, in which a ratio of 1:4.68 was chosen, the effluent analysis was as follows: the concentrated glucose rich fraction had a total solids concentration of 24% (w/w), of which 78% was glucose and 22% (w/w) was fructose; the concentrated fructose-rich fraction had a total solids concentration of 29% (w/w), of which 82% was fructose and 18% was glucose; and the dilute solutions had a total solids concentration of 1% (w/w) containing almost all fructose.

In the second set of results, a fresh syrup to total feed charge ratio of 1:6 was used. The product analysis was as follows: the concentrated glucose-rich fraction had a total solids concentration of 23% (w/w), of which 75% was glucose and 25% was fructose. The concentrated fructose-rich fraction had a total solids concentration of 24% (w/w), of which 95% was fructose and 5% was glucose; the loss in the dilute solutions, being mainly fructose, was equivalent to a solid concentration of 2% (w/w).

The amount of recycle was shown to effect the purity of the products and so far a given volume of resin bed and elution water, increasing the fresh syrup quantity would lead to a poorer resolution.

The process was automated. However, as the raw feed employed in this process was invert sugar, a preliminary hydrolysis step was required.

C H A P T E R F O U R

SCALE-UP CHROMATOGRAPHY

4. SCALE UP EFFECTS AND CONTINUOUS CHROMATOGRAPHIC TECHNIQUE

The resolving power inherent in analytical chromatographic column prompted many workers into trying to develop large chromatographic columns for separating mixtures on a preparative scale. But like so many situations in chemical engineering operations, scaling up of the equipment often causes the departure of the actual situation away from the theoretical one found in the small scale apparatus. It is often found in practice that large processes do not perform as well as the processes on the pilot scale. In most cases, additional factors are brought into the theoretical equations which allow for the scal-up effects. Hence, included in the following sections is a survey of such factors. As studies on continuous chromatographic processes are extremely limited, findings for batch chromatographic processes are employed as a practical guideline to highlight the most important factors on scale-up.

4.1 FACTOR AFFECTING SCALE-UP

4.1.1 FLOW DYNAMICS IN PACKED COLUMNS

Giddings[53], in his random walk approach as outlined in Section (2.4.2.2) indicates five mechanisms by which velocity inequalities may occur in packed columns. Of these the transcolumn term is of particular

importance for production chromatography when large diameter columns are used. This is because substantial velocity differences often occur between the central and outer regions of large diameter columns due to effects associated with the column wall. To account for such uneveness in flow velocity, an extra term H_c, is incorporated into the Van Deemter plate height equation (2.13).

$$H = (A + B/u + C_m u + C_s u) + H_c \quad \ldots\ldots\ldots\ldots \quad (4.1)$$

Giddings[56] used his non-equilibrium theory to evaluate a plate height contribution, based on a parabolic velocity profile, and found close agreement with his experimental results for 0.6 cm and 5.1 cm diameter columns[58]. The contribution may be expressed as:

$$H_c = G_2 \frac{r_{cu}^2}{(96.\gamma'.D_m)} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (4.2)$$

G_2 = constant

Huyten[131] extended the study to columns with a 7.5 cm diameter, similar observations being made by Friscone[132]. A similar expression to equation (4.1) was obtained by Higgin and Smith[133] and Rijiners[134]. In contrast, Hupe[135] and Volkov[136] have observed maximum zone velocities at the centre of their packed column. This was attributed to the fact that the higher packed density in the central sections of a column leads to faster mass transfer rates. Bayer, Hupe and Mack[137] based their derivation on this observation

and obtained an empirical expression for H_c as:

$$H_c = 2.83 \frac{r_c^{0.58}}{u^{1.86}} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (4.3)$$

which gave good experimental agreement for columns between 1.3 and 10.2 cm diameter. The band spreading caused by the non-uniform velocity profile can be reduced by lateral diffusion. Littlewood[138] and Sie and Rijinders[139] described the lateral diffusion as being composed of molecular diffusion (γD_m) and 'convective' diffusion ($\alpha' d_p u$) arising from repeated mixing and separation of mobile phase streams. They obtained

$$H_c = \frac{0.5 I' d_c^2 u}{\gamma D_m + \alpha' d_p u} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (4.4)$$

α = constant for packing geometry

I = complicated double definite integral of the velocity profile gradient[140]

d_c = internal column diameter

All of these expressions, however, predict a fall-off in efficiency with increased diameter; differing only in degree. Pretorius and de Clerk[141] suspected these correlations and maintained that the 'wall effect' and the particle to column diameter ratio were the factors governing the velocity profile. The resultant profile they developed was of a 'w' shape with maximum velocity being experienced several particle diameters into the bed; the plate height expression was found to be

$$H_c = \frac{M' . d_c^2 . u}{2 . d_r . d_p} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (4.5)$$

d_r = radial diffusion coefficient

where

$$M = \frac{1}{100} \exp.\left(\frac{-d_c}{10d_p}\right) \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (4.6)$$

This indicates that the plate height increases with d_c at constant $\frac{d_p}{d_c}$, reaches a maximum at $\frac{d_p}{d_c} = 0.5$, and then decreases with increasing d_c. The results of Spencer and Kucharski[142] and Knox[32] give support to the above hypothesis. This effect could be due to the fact that if the column diameter is so large that radial equilibrium is not achieved, the plate height becomes independent of diameter[53,56]. This 'infinite diameter' effect was discussed by Knox and Parcher[143], who considered that adverse wall effects could be overcome by choosing a column of sufficient diameter that the sample was eluted before the solute had time to diffuse to the wall. The authors also suggest a technique whereby only the central portion of the eluted solute band is removed.

To summarise, the effect of column diameter on operating efficiency is still a debatable subject. However, the majority opinion indicates a loss of efficiency when columns are scaled to the production level.

4.1.2 FINITE CONCENTRATION EFFECTS

Feed concentration and band width are closely linked variables, and an increase in either leads to

a marked reduction of the column efficiency in terms of the number of theoretical plates[144,145]. Thus, in analytical chromatography the column size is so small that the chromatographic process is conducted essentially at infinite dilution. In contrast, the large sample sizes used in preparative or production scale chromatography create finite solute concentrations in the column which in term change the shape of the eluted peak and separation process, requiring a major change of the basic chromatographic theories discussed in Chapter (2).

At finite solute concentration, the chromatographic behaviour is affected by an adsorption isotherm effect. This effect assumes that, if the partition coefficient is a function of solute concentration, i.e. non-linear isotherm, then the elution volume is given by[146]

$$V_R = V_m + V_s.(\frac{\partial q}{\partial c}) \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (4.7)$$

V_R = retention volume of component

V_m = column mobile phase volume

q = solute concentration in stationary phase

c = solute concentration in mobile phase

V_s = column stationary phase volume

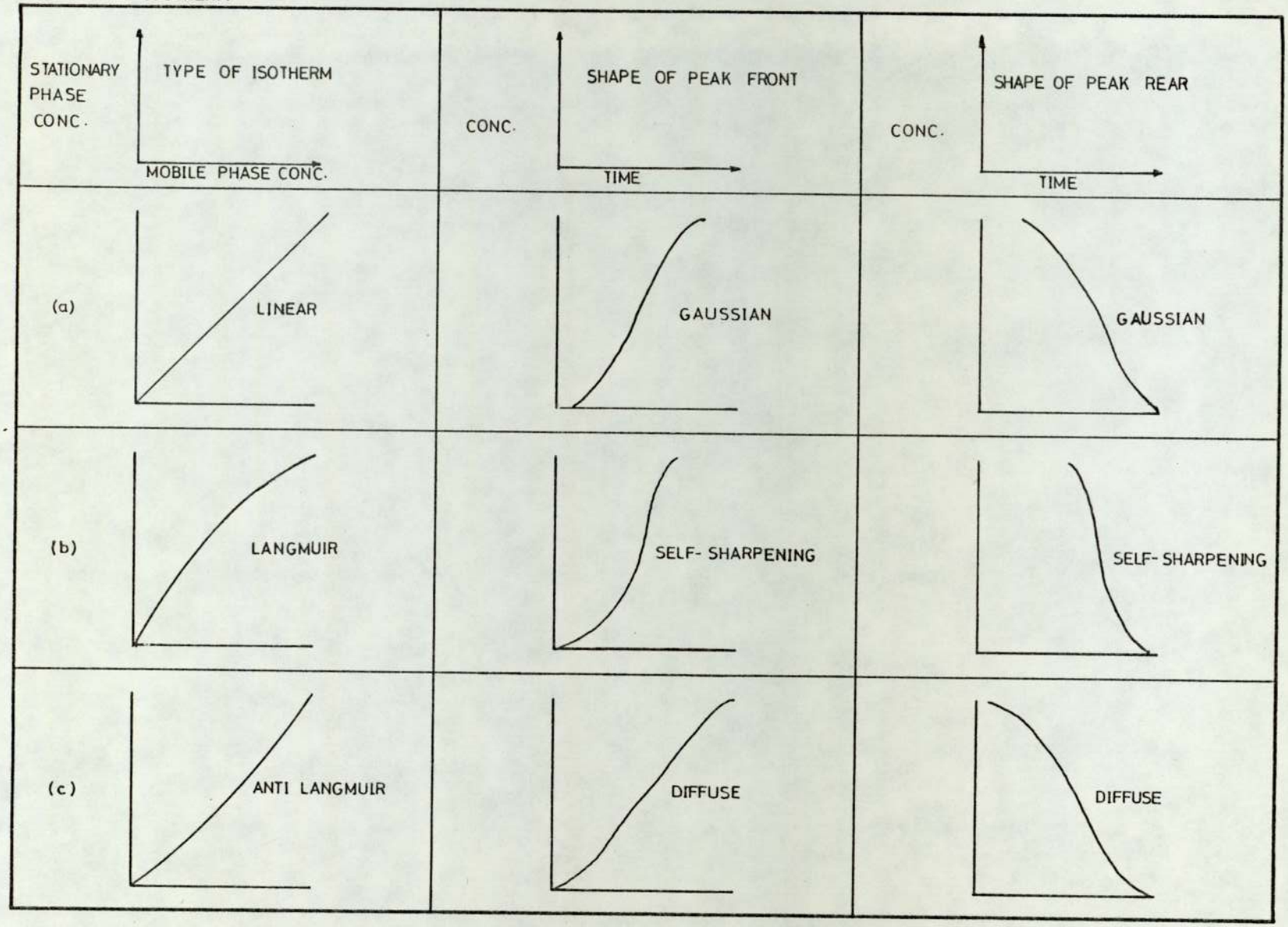
It is also assumed for the case of a linear adsorption isotherm that the fundamental retention equation for a chromatographic system is:

$$V_R = V_m + KV_s \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (4.8)$$

K = equilibrium partition coefficient

Figure (4.1) shows the effect of the three most common types of isotherm on the shape of the solute peak. For the Langmuir isotherm, in Figure 4.1(b) the partition coefficient decreases with increasing concentration, resulting in a lower elution volume. The eluted band has a sharpened leading edge and a diffuse trailing edge. In contrast for anti-Langmuir types, Figure 4.1(c), the partition coefficient increases with increasing concentration, resulting in a higher elution volume. This produces a diffuse front and sharpened trailing edge. The vast majority of chromatographic systems exhibit non-linear isotherms. Operation in the linear region requires an extra column length to compensate for the decrease in resolution. However, in production scale operations, it is unlikely that all of the solutes need to be separated completely from one another, and usually a certain degree of contamination can be tolerated. Consequently, a maximum feed throughput is the desire of most industrial processes so that by increasing the feed concentration, the corresponding liquid volume that has to be handled is reduced. Finally, an increase in feed concentration will undoubtedly lead to an increase in viscosity and pressure drop. Hence, the maximum feed concentration limit is usually governed by the permissible process pressure drop, and it is a common practice in industries to operate large scale chromatographic columns at elevated temperatures.

FIG. 4.1 THE RELATIONSHIP BETWEEN THE SOLUTE ZONE BOUNDARY CONCENTRATION PROFILE AND THE TYPE OF DISTRIBUTION ISOTHERM



4.1.3 EFFECT OF COLUMN LENGTH

An increase in column length will lead to a better resolution, but also increase the elution time. From Section (2.3.2) Purnell[48] suggested that the number of theoretical plates required to separate two peak centres by 6σ can be calculated as follows:

$$M_{Req} = 36\{\frac{\alpha}{\alpha-1}\}^2 \{\frac{1+k_2'}{k_2'}\}^2 \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (4.9)$$

k_2' refers to the capacity of the most retarded component

$\alpha = \frac{k_2'}{k_1'}$ = relative retention factor

Equation (4.9) shows that if $\alpha = 1$, an infinite number of plates is required for the separation. As α becomes larger, the corresponding column length (theoretical plates) needed is reduced. Similarly, the magnitude of k_2' also affects the plate's requirements. These illustrate, in elution chromatography, that the column length is solely dictated by the thermodynamics of the system.

For operations outside the elution mode, a similar direct dependence of the number of plates on the thermodynamics of the system has been shown and discussed by Conder and Purnell[147,148].

For separation involving a very difficult system, that is when α is very close to unity and when k_2' is very small, it is common practice in industries to incorporate a recycling process.

4.1.4 EFFECT OF THE MOBILE PHASE VELOCITY

The higher the velocity of the mobile phase, the less efficient a chromatographic column becomes in operation. Hence, in order to maintain the same degree of resolution, it requires extra column length. But an extra long column is not practical since it will have a high pressure drop and it will be very expensive to fabricate and to pack with a chromatographic medium. Usually, in large scale operations, a maximum mobile phase velocity may be used providing the resultant separation is acceptable, and also that the pressure drop across the packed bed is not too large.

4.2 PRACTICAL SOLUTION TO THE SCALE-UP PROBLEM

4.2.1 METHODS OF PACKING

Poor packing methods very often result in having low efficiencies in large diameter chromatographic columns. Many workers have sought to achieve a packing technique giving both high and reproducible column efficiencies.

In liquid chromatography, two main types of packing methods, namely dry and slurry technique, have been used to achieve more uniform and densely packed columns. Studies of dry packing have been carried out using adsorbants[149] for small particles in small diameter columns. With larger diameter columns, a slurry

packing technique is often preferred. This is the technique adopted for the SCCR4 unit. A detailed discussion will be provided in Chapter (5).

To summarise, a gain in efficiency with careful packing of chromatographic columns is possible, but opinions differ on the best packing technique to use. More comprehensive reviews about packing methods may be found in the literature[150].

4.2.2 REPEATED FEED INJECTIONS

In batch chromatography, only a small section of the packed bed is being used for separating a small sample. Therefore, to maximise column utilization, a repetitive way of sample feeding has been commonly employed. This involves the introduction of subsequent charges of feed into the column at controlled time intervals. The sequence and rate of injection is extremely critical if excessive overlapping is to be avoided. Considerable work has been carried out in this area. Two different approaches have been developed based on repetitive injection. The first where the eluted profiles are completely resolved and successive injections do not overlap, and the second technique in which the solute bands are allowed to overlap and the central impure portion is 'cut out' and recycled[150]. Gordon[151], indicated that a significant gain in throughput may be obtained by the latest 'cut-out' method

when high purity products are required. Conder, in his review[148] has reported that it is always preferable to overlap the component bands rather than to avoid the need for cutting by increasing column length and resolution, and that the optimum recovery value exists at 60% of the injected sample. The remaining contaminated 40% is recycled.

4.2.3 THE USE OF FLOW DISTRIBUTORS

The use of a flow distributor in a large diameter column at the inlet enhances radial mixing of the mobile phase. This leads to a more uniform profile and well developed solute bands. Musser and Spark[152] investigated the performance of inlet cones and their results indicated that wide angle cones (60^{o}-90^{o}) packed with inert material to about 80% of their volume, provide the most efficient means of distribution. Huyten[131] reported similar findings, and established that if chromatographic packing was used in the inlet and exit cones, column efficiency was improved.

Gould[153] in his research found a good distribution of liquid across the cross-section of a 10.16 cm diameter column when a perforated plate was used at the inlet distributor. Even solute concentrations were found at various points across the diameter of the column.

4.2.4 THE USE OF A BAFFLE

Besides the use of inlet cones, the adverse effect of the velocity inequalities across the cross-section of the column can be minimised by remixing the solute stream at intervals along the column.

In 1966, Baddour[154] used baffles fixed at various intervals along the column to achieve remixing of the solute stream. Figure (4.2) is self explanatory. When baffles were arranged in a 'disc and doughnut' system, an improved efficiency in his 5.08 cm column was reported.

A similar baffle system was used by Abcor Incorporated, Massachusetts[155] and an improved efficiency of large diameter columns was also reported.

4.3 CONTINUOUS CHROMATOGRAPHY

In continuous chromatography, the introduction of the feed and the withdrawal of the extract and raffinate streams, into and from the system is performed continuously. Maximum use of the entire bed length for separation is achieved by this method. In figure (4.3) the concentration profiles of a repeated batch operation (4.3a) and a continuous counter-current operation (4.3b) demonstrate the point.

Co-current and cross-current continuous chromatographic flow schemes have been extensively investigated

FIG. 4.2 BADDOUR S DISC AND DOUGHNUT FLOW DISTRIBUTING DESIGN

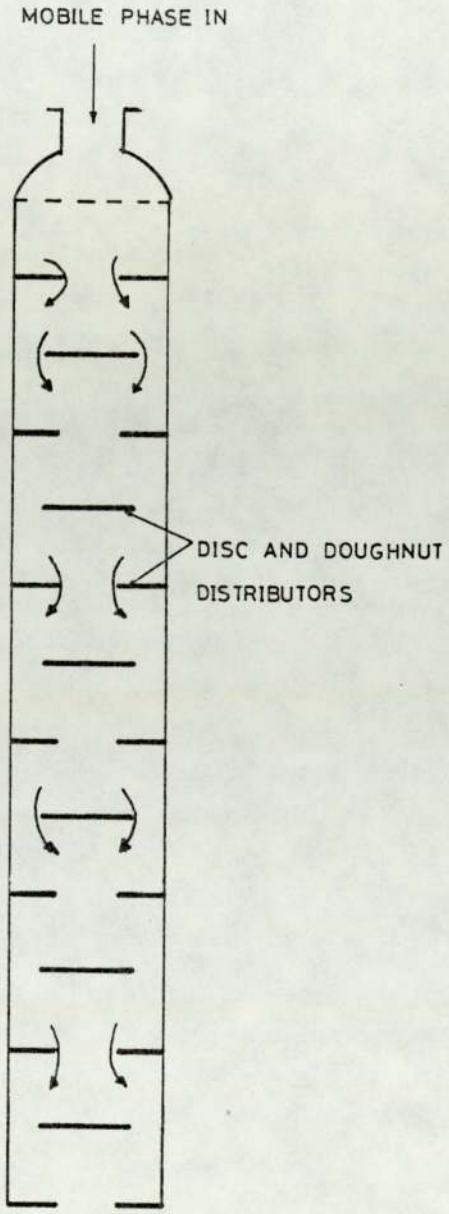
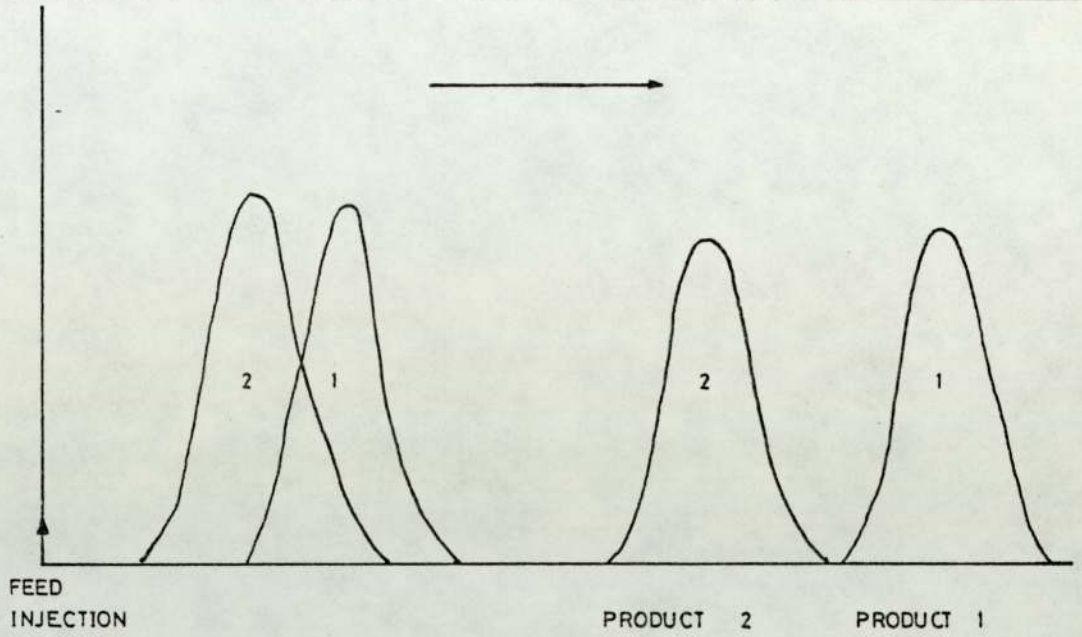
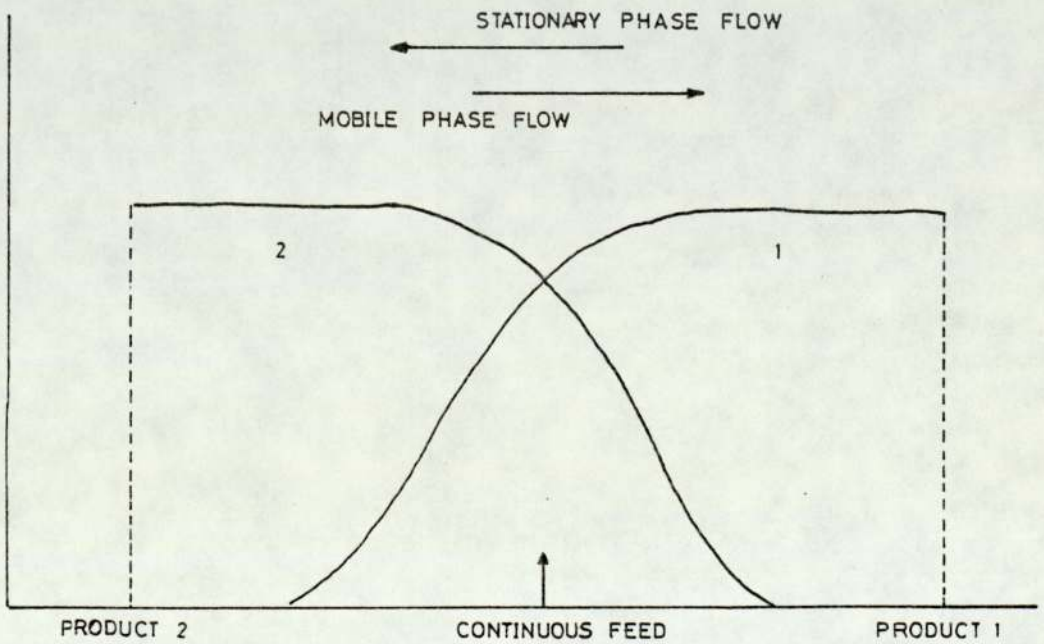


FIG. 4.3 CHROMATOGRAPHIC CONCENTRATION PROFILES FOR THE SEPARATION OF A BINARY MIXTURE

A REPEATED BATCH CO-CURRENT OPERATION



B CONTINUOUS COUNTER CURRENT OPERATION



by many workers in the past two decades; but both proved to be difficult to implement on a large scale. A detail survey of both the flow schemes has been reviewed by Ellison[21] and Ching[24] in their Ph.D. theses.

4.3.1 COUNTER CURRENT FLOW SCHEME

With this flow scheme, the adsorbent and the desorbent move in opposing directions. This flow movement can be achieved in three ways, namely

(i) moving bed

(ii) moving columns

and (iii) simulated moving bed (moving parts)

4.3.1.1 MOVING BED SYSTEM

In this system, the counter-current movement is achieved by having the packing move downwards under gravity against the mobile phase. An example of this system was used by Barker and co-workers[1-4,7]. A vertical brass column of 2.5 cm diameter was fed with solvent-coated solid support from a hopper. The solids flowed under gravity and the rate of flow was controlled by a rotating table at the column base. Vibration of the column wall ensured steady flow of packing. The feed mixture was introduced somewhere near the middle of the column. The relative flowrates

of the phases (packing and the carrier gas) could be adjusted to let the strongly adsorbed feed component travel with the packing into the heated stripping section, to be removed at the product 2 off take. The least strongly adsorbed component was removed at the product 1 port.

Barker and co-workers successfully used this equipment to achieve the separation of several binary mixtures involving benzene, cyclohexane and methyly-cyclohexane with air as a carrier gas and operating the separation section at ambient temperature. High separated product purities were obtained at throughputs of up to 30 $cm^3 h^{-1}$. Various other moving bed schemes have been reported on smaller diameter units[156-161]. The Philips Petroleum Co.[162] report the construction of a unit of 15 cm diameter and 2.6 m long for the separation of a 30% cyclohexane and 70% benzene mixture at 225 cm^3 min^{-1}.

An industrial unit has been developed by the Union Oil Company, Los Angeles, California, using activated carbon adsorbent, flowing down through a stream of hydrogen gases[163,164] but the process has subsequently proved uneconomic with the development of low temperature distillation[165].

To summarise, moving bed systems have the following advantages:

(i) Handling of large quantities of solid packing

(ii) Attrition of packing

(iii) Mobile phase velocity limited by minimum fluidization velocity of the packings

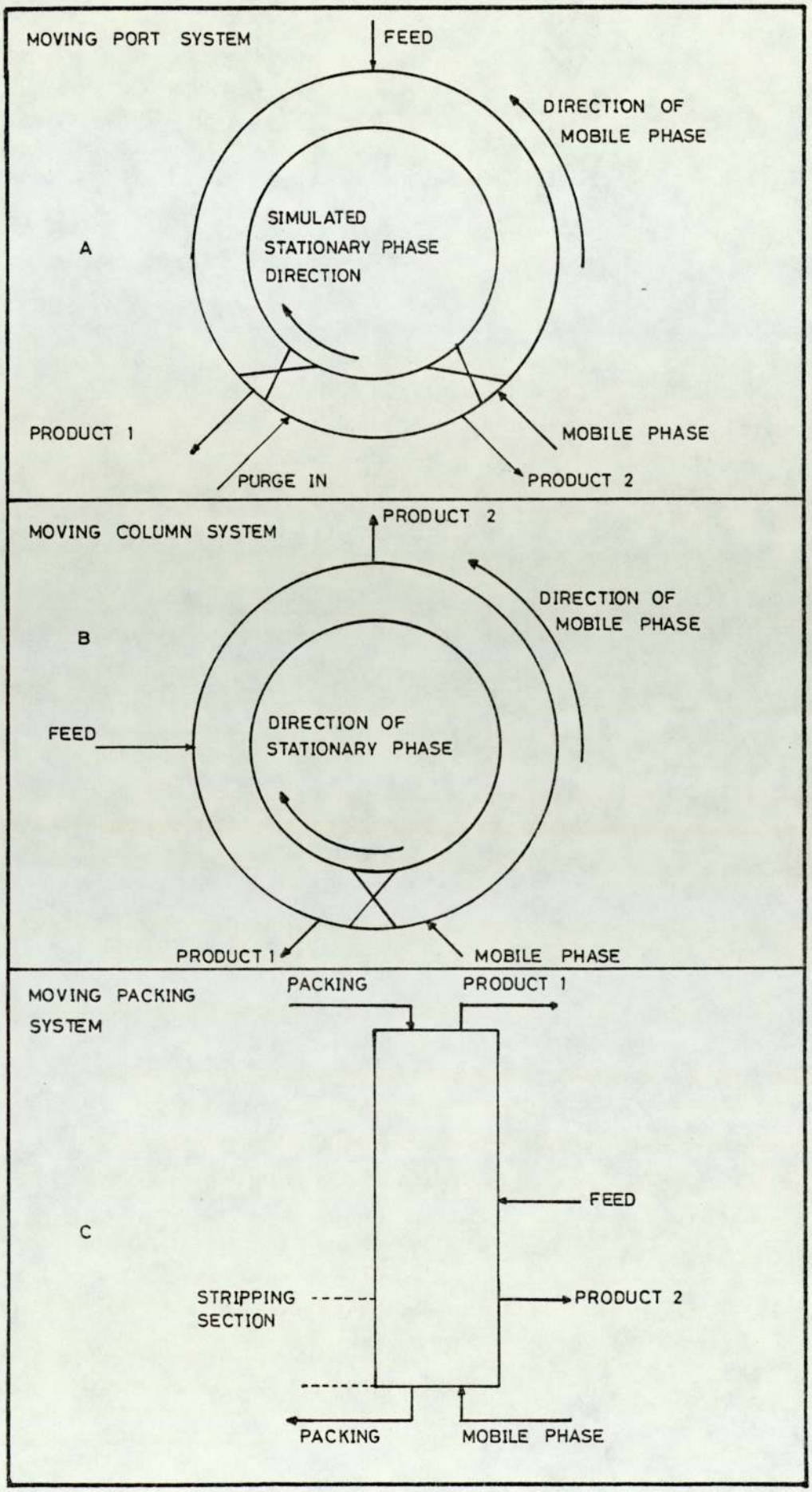
(iv) Back mixing and low uneven packed densities result in low column efficiency

4.3.1.2 MOVING COLUMN SYSTEMS

To overcome the problems mentioned above, a moving column system was proposed. The system involves the rotation of a circular column past fixed inlet and outlet ports in the opposite direction to the mobile phase flow, figure (4.4). Many novel mechanical designs were proposed, notable ones were Pinchler[166], Gulf Research and Development Corporation[167], Luft[168] and Glasser[169]. In their designs, the carrier gas flow rates within the column were controlled by pressure drop. Barker[9] overcame the restrictions by placing camloperated locks between the carrier gas inlet port and the product 1 off-take. As the gas flow was unidirectional, the length of the packed column stripping section was kept to a minimum.

Further development of the design continued, Barker and Huntington[6-8] constructed a prototype unit. Details and performance of the prototype unit has appeared in several publications[6-8]. Following the successful development of the prototype unit, Barker, in collaboration with Universal Fisher Group, Limited[170], constructed a new compact carrier chromatograph. The machine consisted of a cylinder

FIG. 4.4 COUNTER CURRENT SYSTEMS



net of 44, 2.5 cm diameter by 22.8 cm long stainless steel tubes linked alternatively at top and bottom to give a closed loop. The tube bundle rotated at speeds between 0.2 and 2.0 r.p.h. The transfer of gas between tubes was controlled by cam operated poppet valves.

Detailed experimental performance and result were reviewed in several publications[10-12]. One of the disadvantages of compact circular chromatography is the difficulty of sealing at high temperature.

4.3.1.3 SIMULATED MOVING BED SYSTEM

The problems and the difficulties experienced with the moving bed and moving column systems led to the development of the simulated moving bed system. In this system, the bed was fixed, and as the word 'simulated' implies the bed was made to move by periodically sequencing a set of ports around a closed loop bed system.

Szepesy and co-workers[174] proposed a scheme figure (4.5a) using a switching valve centrally mounted on a rotary P.T.F.E. disc. Rotation of the valve altered the relative position of the inlet and outlet ports to a series of stationary columns.

The Universal Oil Products[125-128] disclosed their Sarex process which also used a rotating valve for separating fructose and glucose from a carbohydrate mixture containing them. The process was a direct

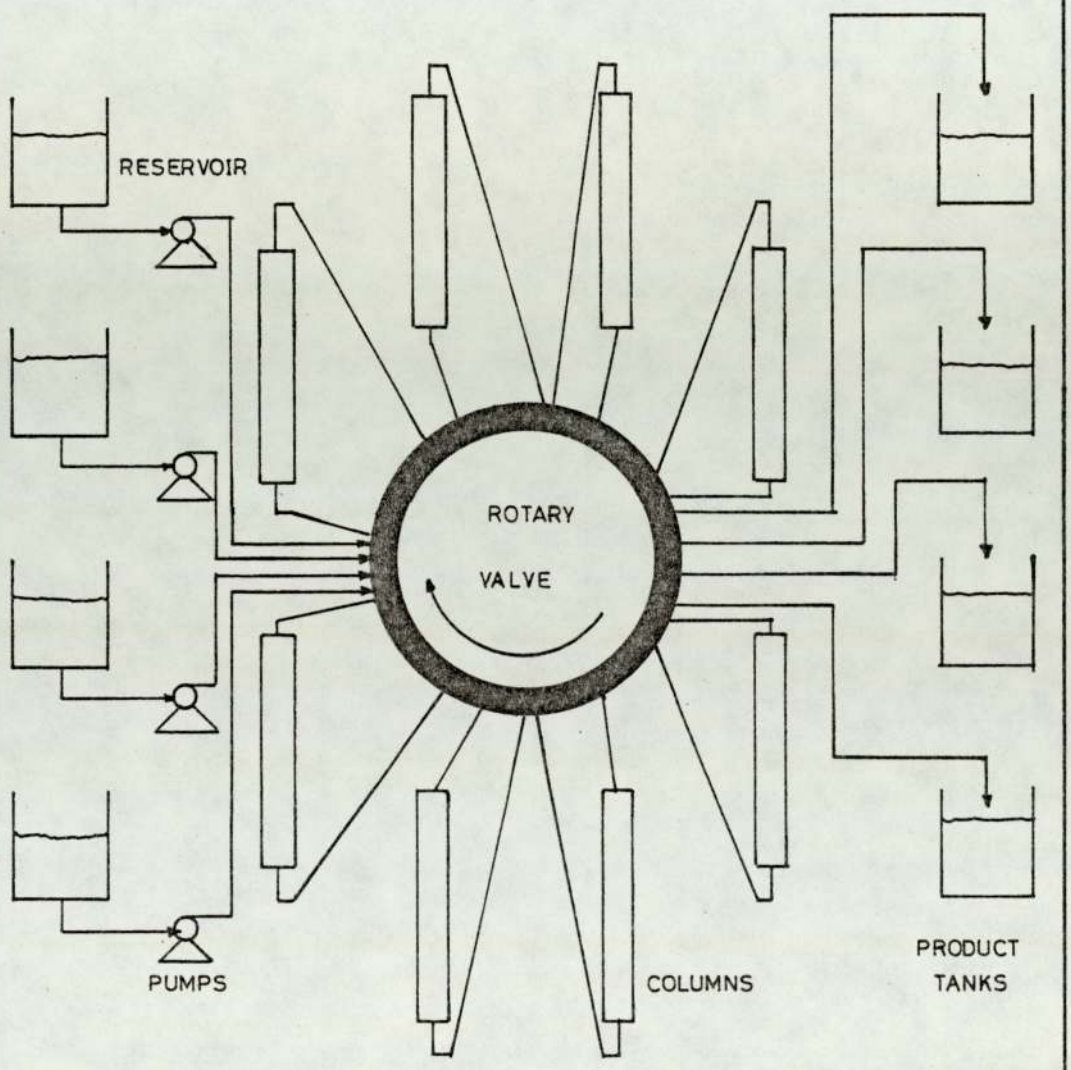


FIG. 4.5 a CONTINUOUS COUNTER CURRENT SCHEME.

SZEPESEY 'S SCHEME

development of the well proven Parex and Sorbex processes used for separating hydrocarbons in the oil industries. Figure (4.5b) illustrates the flow scheme of the Sarex process.

Barker and Deeble[18-20] disclosed a design for a novel process where all moving ports except for the closing and opening of seven valves, were eliminated. Counter-current movement of both phases was simulated using solenoid or pneumatically operated valves. In their equipment, twelve 7.6 cm diameter, 0.61 m long vertical columns were connected together to form a closed loop. Six valves were assigned to each column to control the flow of fluid into and out of the system and between columns. Successful results were achieved with this unit and a second unit was constructed with facilities for the study of high temperature gas-liquid chromatographic separations involving liable material[25].

In the liquid-liquid chromatographic studies, Barker and Ellison[21], Holding[172], England[26] developed similar units for fractionating dextran polymers. The projects were sponsored by the Pharmaceutical Division of the Fisons Company, based in Holmes Chapel, Cheshire, England. The outcome of the projects was successful and at present, work is still continuing along similar lines.

In the area of liquid-solid chromatography, a similar flow system was used by Barker and Ching[24], for separating glucose and fructose from a mixture

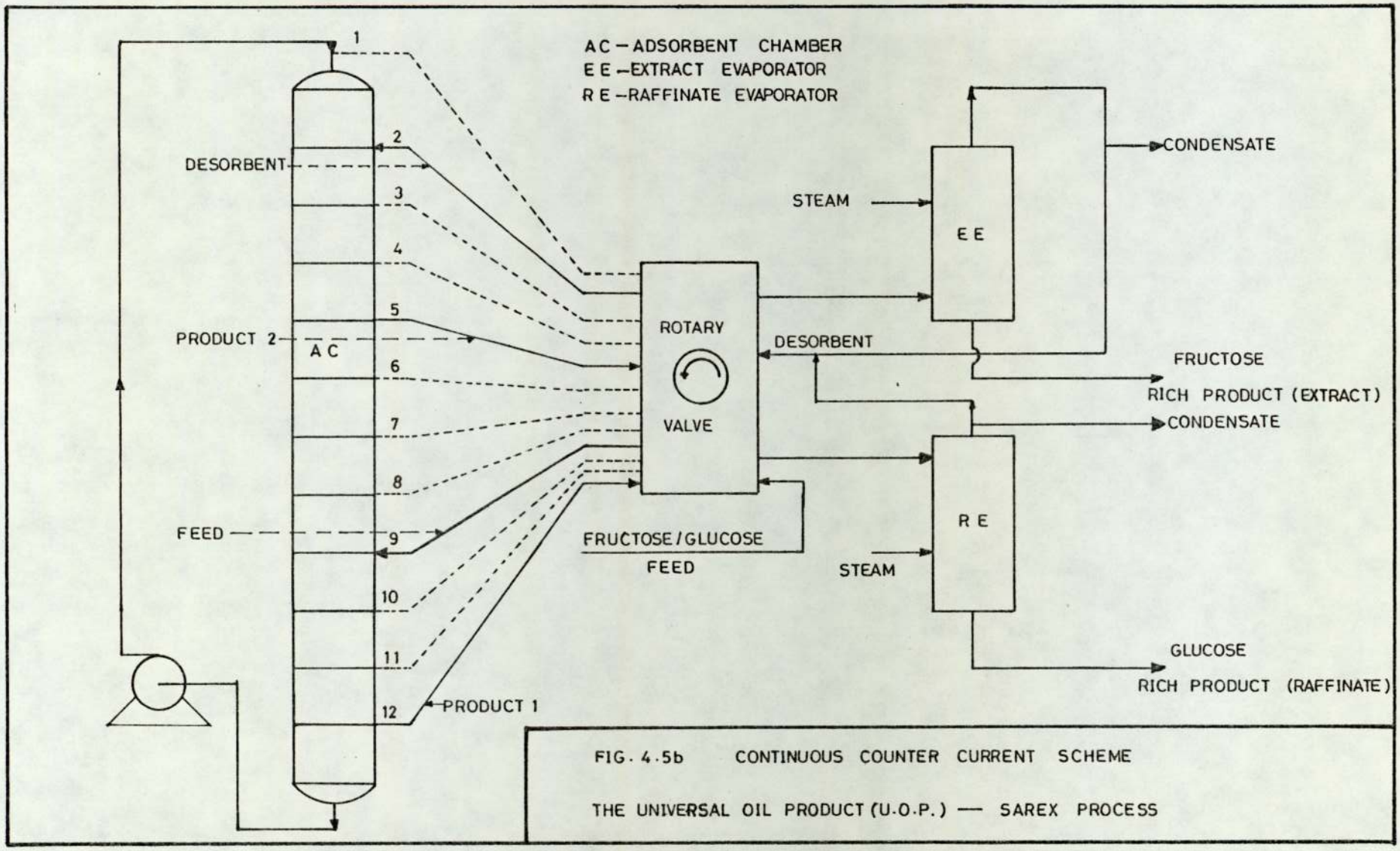


FIG. 4.5b CONTINUOUS COUNTER CURRENT SCHEME

THE UNIVERSAL OIL PRODUCT (U.O.P.) — SAREX PROCESS

containing both the sugars. Their system consisted of ten 2.5 cm glass columns, each packed with a calcium charged organic adsorbent. Sequencing of the valves to simulate the counter-current movement of the bed was performed by a mechanical cam-unit. Successful results were achieved, and 90% (w/w) pure fructose rich and glucose rich products were obtained from a 50% (w/w) concentrated feed mixture containing equal proportions of each of the sugars.

This project uses the operating principles formulated by Barker and Deeble[17-20] and Ching[24] for the separation of fructose from a dextran contaminated carbohydrate mixture.

C H A P T E R F I V E

ANALYTICAL EQUIPMENT AND TECHNIQUES

5.1 ANALYTICAL EQUIPMENT

The equipment used for this purpose must be precise, reliable and fast, and preferably also reasonably priced and easy to maintain.

It must also be ideal, very sensitive and very specific to the responses of each of the carbohydrate species, exhibited by virtue of their properties or through chemical reactions with the specific reagents.

Such equipment is available in the Chemical Engineering Department at the University of Aston in the form of a Technicon Auto-Analyser, a Bio-Rad high pressure liquid chromatographic column (H.P.L.C.) and an Atomic Absorption Spectroscopy Unit.

5.1.1 THE TECHNICON AUTO-ANALYSER

This equipment was marketed by Technicon Ltd. It was effectively a continuous colourmetric analyser. It consisted basically of a peristatic pump, an oil heater, a colourimeter and a chart recorder.

In operation, the sample and reagents were reacted in the mixing coil at the required temperature. Heat was provided by recirculating water around the mixing coil. Back-mixing along the line was minimised by introducing air bubbles between each volume of the sample-reagent mixture.

Coloured chromophores were formed from the sample-reagent reaction(s). The density of the chromophores was detected by a special filter which was recorded as optical density level on the chart recorder. The density of chromophores varied with the carbohydrates in the solution.

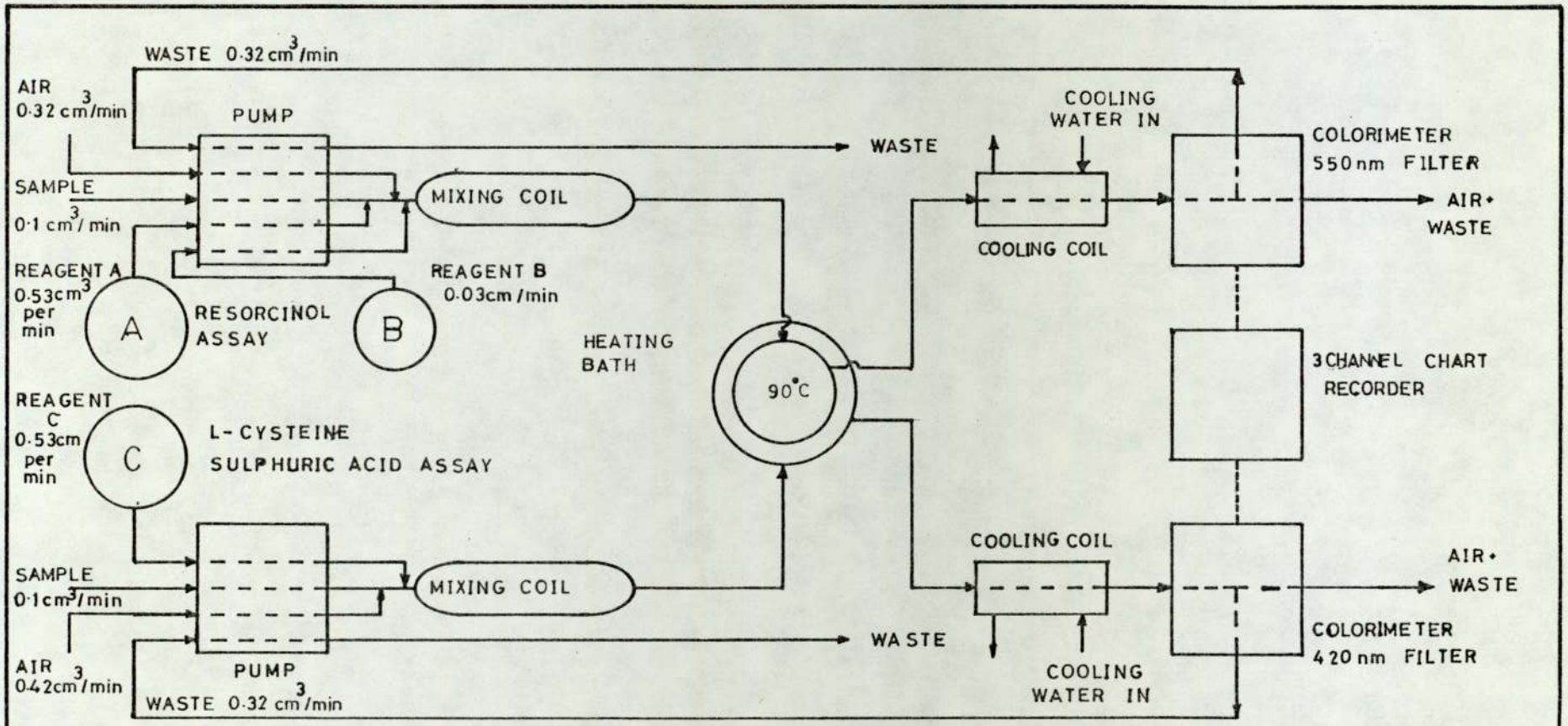
The flowrates were monitored by means of standard bore poly-vinyl chloride tubes and viton rubber acid resistance tubes. The tubes were supplied by Technicon Ltd and U.K. Laboratory Supplies Ltd. The range of flowrates available was from 0.1 cm^3/min to 4.0 cm^3/min.

The auto-analyser was used in two modes throughout the research programme; namely in the qualitative mode to determine the columns and packing characteristics; and in the quantitative mode to determine the quantity of carbohydrates in the products and the feed from the experiments with the S.C.C.R.4 unit.

5.1.1.1 CYSTEINE HYDROCHLORIDE - SULPHURIC ASSAY (Responsive to all carbohydrates)

Figure (5.1) shows the general arrangement for the use of the cysteine-sulphuric assay on the auto-analyser.

The composition of the assay was a 0.07 v/v solution of biochemical grade, L-cysteine hydrochloride (B.D.H., Poole, England) in 86.0% v/v 'analar' sulphuric acid[62].



KEY : A- RESORCINOL REAGENT B- ACETAL REAGENT C- L-CYSTEINE SULPHURIC ACID REAGENT

FIG. 5.1 RESORCINOL / L-CYSTEINE SULPHURIC ACID ASSAYS

The reaction temperature was 98°C and the wavelength of the filter was 420 nms. The flowrates were as indicated in Figure 5.1. The colour of the chromophore was yellow.

5.1.1.2 RESORCINOL ASSAY

(Chosen to be responsive to fructose only)

Two reagents A and B were used as shown in Figure (5.1).

The composition of reagent A was 0.005% resorcinol solution in 1.0 litre of 36.5% concentrated hydrochloric acid (analar grade - B.D.H., Poole, England)[63].

Reagent B contained 0.05% v/v of 1-1 diethoxyethane in distilled water.

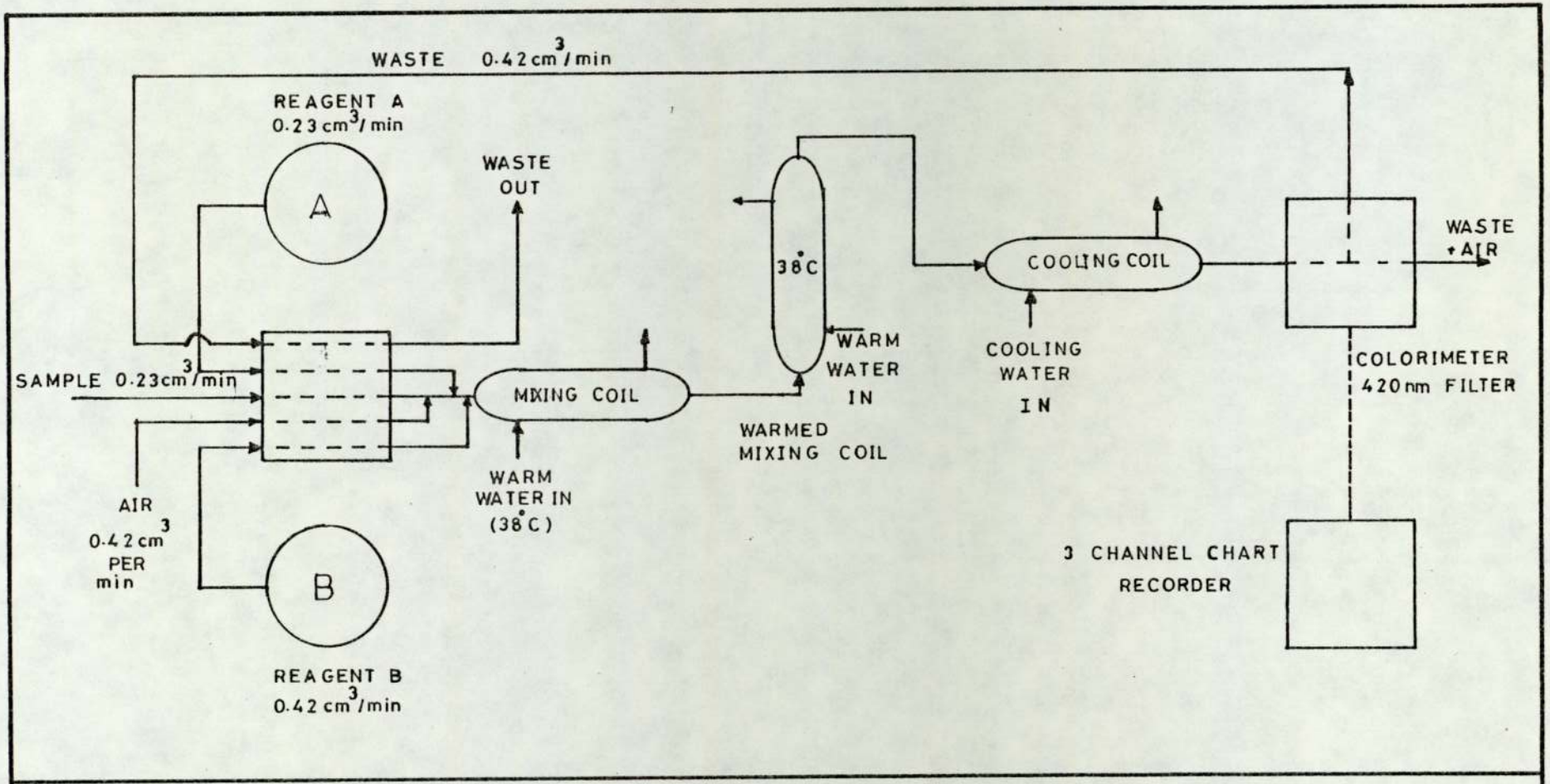
The reaction took place at 98°C and this optical density of the chromophores was determined with a 550 nm filter. The colour of the chromophore was pink.

5.1.1.3 ENZYME ASSAY

(Chosen to be responsive to glucose only)

Two reagents A and B were used as shown in Figure (5.2).

The composition of reagent A was made up of 25.0 mgms of glucose oxidase in a 25 cm^3 of tris-buffer solution. The final volume was made up to 250 cm^3 with distilled water.



KEY- A GLUCOSE OXIDASE B AZINO-DI-(3ETHYL-BENZTHIAZOLINE SULPHONATE)+PEROXIDASE

FIG. 5.2 GLUCOSE OXIDASE ASSAY / ENZYME PEROXIDASE ASSAY

Reagent B contained 50.0 mgms of 2.2-azino-di-(3-ethyl-benzihiazoline-sulphonate (6)), (A.B.T.S.) and 50 mgms of peroxidase (grade II) in 50.0 cm^3 of tris-buffer solution. The solution was made up to a final volume of 500 cm^3.

The tris buffer solution[64] was made by dissolving 30.2 gms of tris (hydroxymethyl)-methylamine in 200 cm^3 of 1.0N hydrochloric acid. The mixture was dissolved to a final volume of 500 cm^3.

The reaction temperature was 40°C and a filter of 420 nm was used to determine the optical density. The chromophores colour was green.

5.1.2 THE BIO-RAD-COLUMN (H.P.L.C. COlumn)

(For all carbohydrates including monosaccharides)

This was a high pressure liquid chromatographic (H.P.L.C.) column packed with a calcium charged Aminex HPX-87 organic resin having a particle size of 10 μm.

The column was of stainless steel construction with a dimension of 250 mm (length) by 7.8 mm (diameter). Recommended working pressure was not to exceed 100 bars.

The manufacturer recommended that the column be run at 85°C with the reservoir temperature of at least 60°C, and guaranteed an efficiency of at least 900 plates per meter.

The layout of the analytical system was as shown in Figure (5.3). Eluent, distilled water was moved

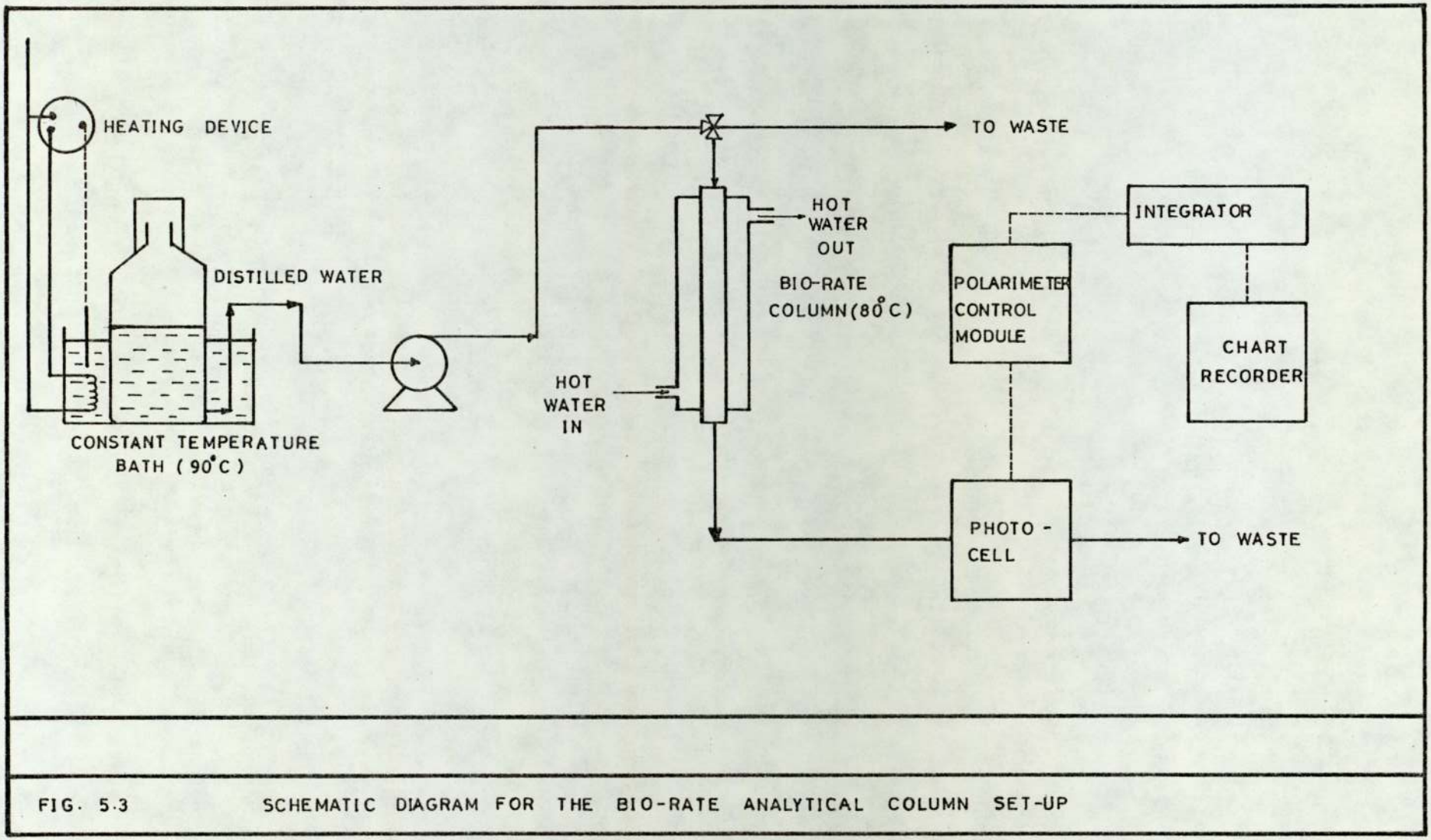


FIG. 5.3 SCHEMATIC DIAGRAM FOR THE BIO-RATE ANALYTICAL COLUMN SET-UP

from the reservoir through a filter before the pump. After the pump the eluent was pumped through the column via a two-way sample valve of stainless steel construction which allowed the eluent to pass through directly into the column or through the sample coil (volume 24.0 µls).

The mixture after emerging from the bio-rad column enters the cell of the Jobling refractometer which measures the intensity. The mixture was then directed to the waste reservoir.

The flowrate of the mobile phase was monitored by measuring the weight of the waste accumulated over a thirty minute period and then the appropriate conversion factor was used to calculate the rate in cm^3 per minute. The flowrates used ranged from 0.15 cm^3/min to 0.20 cm^3/min at an indicated pressure of approximately 55 bars.

The bio-rad column was kept warm at 85°C by recirculating water. The water heater-circulator was supplied by Tercam Ltd.

The eluent reservoir was heated in a water bath maintained at above 70°C.

Electrically, the refractometer was linked to a Jobling refractometer control module and a Servoscribe 1s, potentiometric chart recorder. The sensitivity of the chart recorder was set at 10 millivolts.

Detection of the concentration of the solute in the solution was by comparing the extent of refraction

of two beams of light passing through two thin layer cells; one containing the sample and the other containing the pure carrier solvent. The operation was continuous and the signal recorded in the chart, seen as chromatograms.

Later, a Hewlett-Packett, 3373B Integrator was incorporated into the system, linking the control module and the chart-recorder. The sensitivity of the recorder was further increased to 1 millivolt by a built-in unit inside the integrator. The function of the integrator will be explained later in the Chapter (Section 5.2.2.1).

5.1.3 THE ATOMIC ABSORPTION UNIT

This piece of equipment works on the principle of energy emitted by excited electrons jumping from a higher quantum shell into one which was lower in the atomic-sphere. The energy emitted was in the visible light spectrum and had a definite range of wavelength. This was a characteristic of the atom when excited by heat.

The equipment was marketed by Laboratory Instrument Ltd.

In operation, a high 'energised' flame (oxy-acetylene) provided the energy to excite the electrons in the ions present in the sample. A photo-source emitting a ray of light at a specific range of wavelengths specific to

a particular ion was passed through the flame longitudinally. Energy was adsorped by the ion responsive to that particular photo-source and the intensity of the photo-beam incidented on a receiving photo-cell was recorded. The actual concentration of the ions in the sample was found by comparing with a standard solution.

Special lamps were used for detecting sodium, calcium, lead, iron and copper.

5.1.4 GLASS COLUMNS FOR QUALITATIVE WORK

Figures (5.4) and (5.5) show the glass column arrangement and the general flow diagram of the equipment. The set up was used qualitatively to study the characteristic of the calcium charged resins. Different temperature and flowrate were used.

The glass column had an inner diameter of 1.14 cm and it was 70.0 cm long. Calcium charged Zerolit 225 SRC 14 resin was packed into the column to a height of 65.0 cm. The bed was supported by a small pad of glass wool.

On top of the column a 2.0 mm bore stainless steel tube inserted through a rubber bung provided the entrance of the eluent to the column.

At the bottom end, a poly-vinyl chloride tube was connected to a T-piece, where the sample was split into two streams; one going to the waste reservoir and the other to the Technicon auto-analyser.

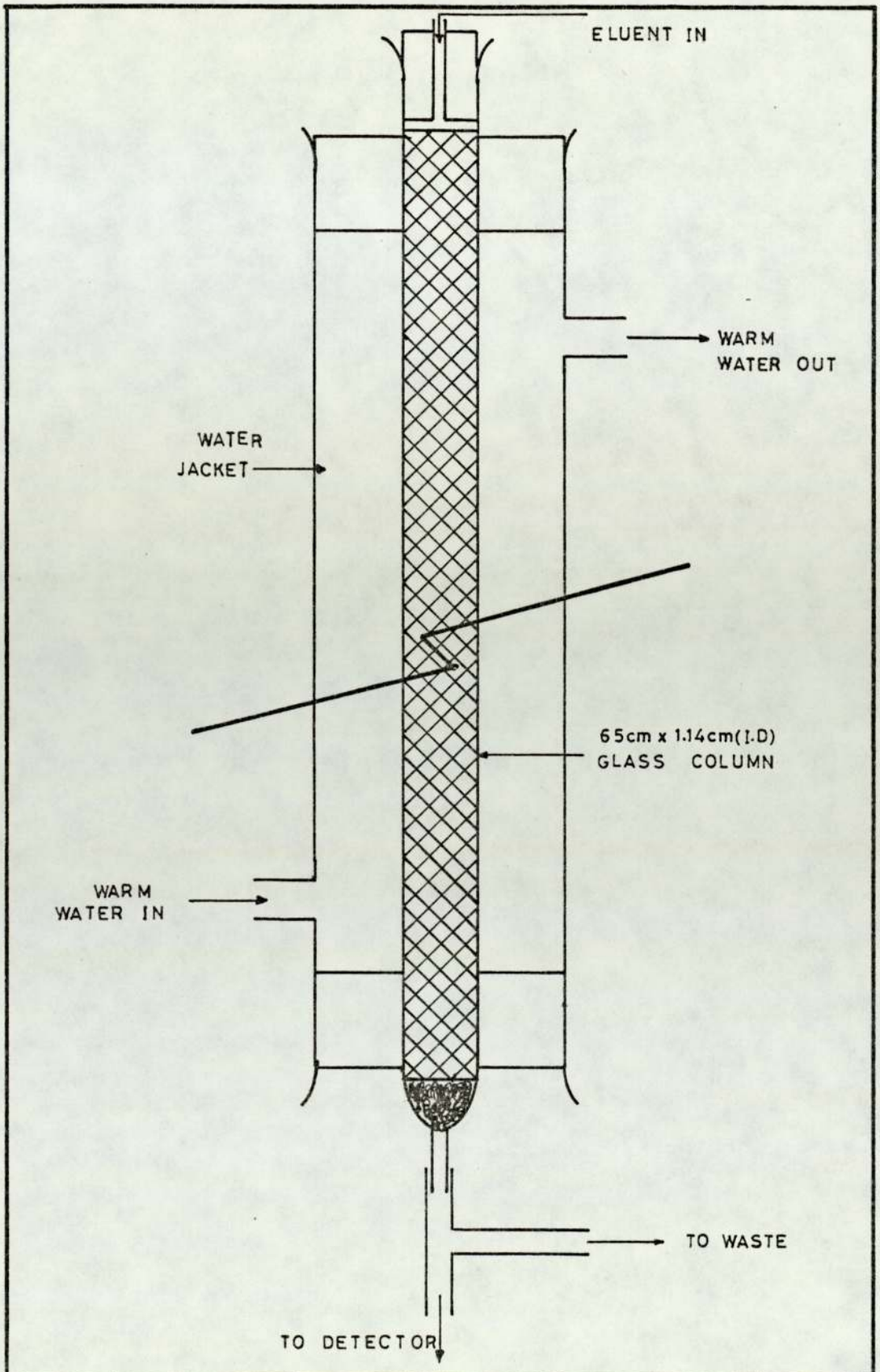


FIG. 5.4 1.14cm. GLASS COLUMN FOR BATCH ANALYSIS OF THE RESIN

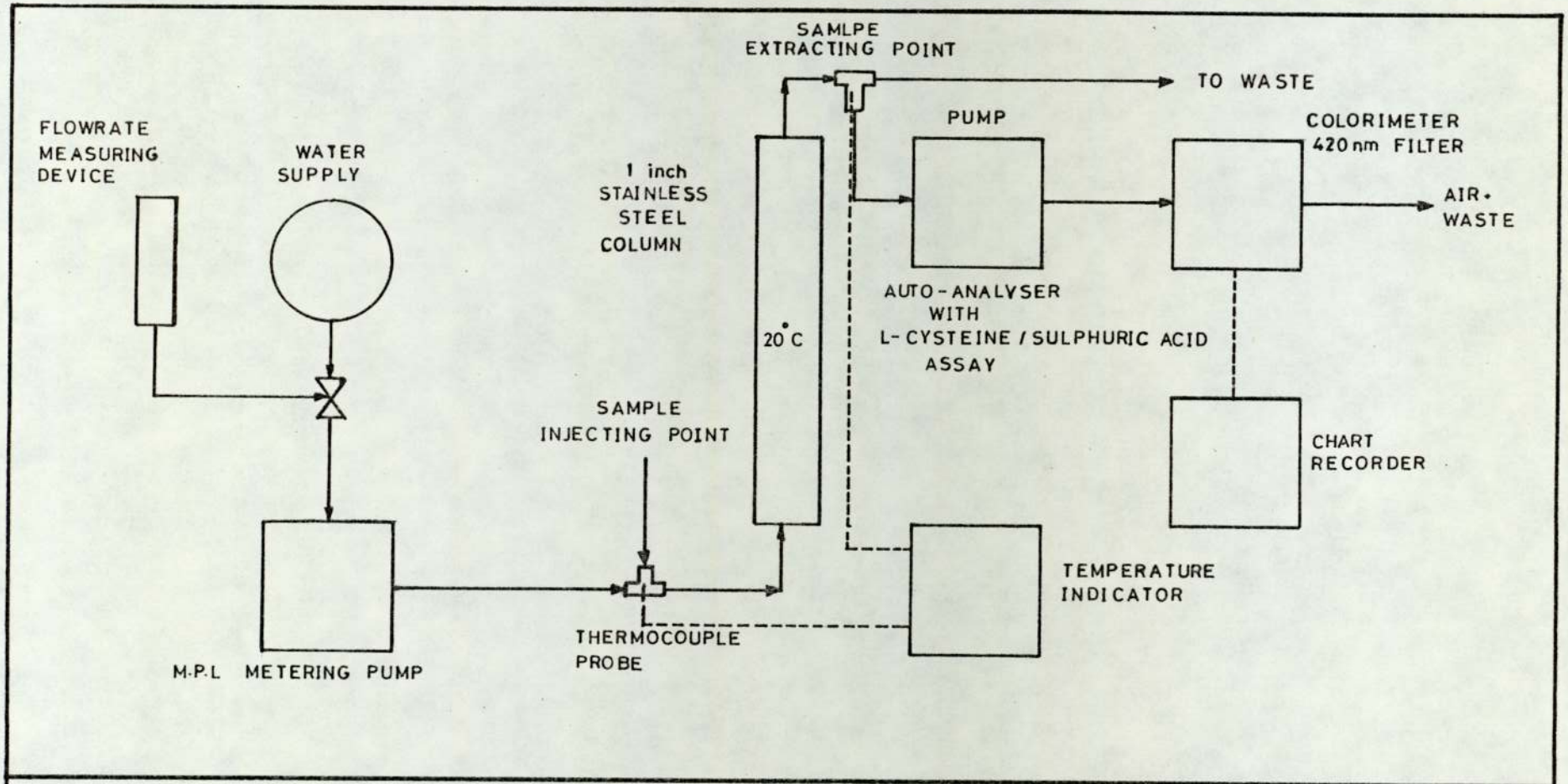


FIG. 5.5 ARRANGEMENT OF EQUIPMENT FOR COMPARING THE ONE INCH STAINLESS STEEL COLUMNS

The glass-column was lagged with a water jacket, where the temperature was kept constant by recirculating the water through an immersion heater. A constant water jacket temperature of up to 85°C ± 0.5°C was achieved as claimed by the manufacturer, Tercam Ltd.

5.2 ANALYTICAL TECHNIQUES AND PROCEDURES

5.2.1 TECHNICON AUTO-ANALYSER

5.2.1.1 QUALITATIVE WORK WITH THE GLASS COLUMN

The aim of this part of the research was to investigate the behaviour of the calcium charged zerolit 225 SRC14 resin under conditions likely to be used in the main pilot unit, as well as to obtain the basic information which characterised the zerolit 225 SRC14 resin.

5.2.1.1.1 COLUMN PACKING TECHNIQUE

A slurry packing technique was used to pack the glass column with the zerolit resin.

A very thick slurry containing the resin was thoroughly agitated in the container before pouring it into the glass column. This minimised the segregation of the particles according to size due to the terminal velocity effect under gravity.

When the column was filled, the outlet connection was opened to allow water to be drained off the column.

The outlet connection was opened and shut by means of a clip on a soft P.V.C. tube section.

Fresh water was introduced from the top to replace the water drained off from the column. A tap and turn procedure was used to encourage the bed to settle quickly. The precedure was performed in a random fashion.

When the bed had settled, further resin was introduced until the bed height reached the required level. The bung was replaced on top of the column leaving a small liquid gap between it and the resin bed surface.

The eluent line was replaced and the bed was purged of any remaining impurities for at least two hours.

At the end of the two hours period, the bed level was replenished until the height of the bed was returned to its required level, that was 66.0 cm. The column was ready for use. Figure (5.5) shows in detail the glass column used in the experiment.

5.2.1.1.2 SAMPLE LOADING

A standard procedure was adopted for this operation in order to achieve the consistency needed for comparison purpose.

A standard volume of 250 μm^3 of sample with a concentration of 1000 mgm per cm^3 was introduced onto

the bed surface by means of a micropipette. Following this, 250 μdm^3 of deionised water was introduced to the bed surface. The outlet clip was then opened to allow the sample into the bed. As soon as the liquid level reached the bed surface, the outlet clip was closed and an extra 500 μdm^3 of deionised water was introduced. The rubber bung was replaced, allowing a small liquid gap to be present between it and the bed surface.

The eluent line was then fitted to the stainless steel tube inserted through the rubber bung. The bed was then eluted at the required flowrate.

5.2.1.1.3 GENERAL MEASUREMENTS

The mobile phase flowrate was fixed by the standard bore P.V.C. tube used on the manifold of the peristaltic pump. However, the actual flowrate was measured by collecting the mobile phase at the outlet of the column.

This operation took place over a fixed period of time in which the weight of the mobile phase was determined. The volumetric flowrate was obtained by using the density factor.

A cysteine-sulphuric assay was used with the auto-analyser for detecting the constituents of the sample emerging from the glass column. The signal from the colourimeter was converted to a chromatogram on the

chart recorder from which the elution volume, distribution coefficient and column efficiency were obtained.

Dextran 5 (nominal molecular range of 5000 dactons) glucose and fructose samples were eluted at different temperatures and flowrates, 20° to 60°C and 0.1 to 1.5 mls per minute respectively.

5.2.1.2 QUALITATIVE WORK WITH THE TWELVE STAINLESS STEEL UNIT

Twelve stainless steel columns of 2.54 cm I.D. were packed with the calcium charged zerolit 225 SRC14 resin, each to an appropriate height of 66.0 cm.

The technique used was of the slurry method similar in procedure to that used to pack the glass column. Each column was subjected to four hours of compression by pumping deionised water through at a constant flowrate. At the end of the compression period the inlet end of the column was dismantled and the bed replenished with fresh resin until the height was 66.0 cm.

Each of the packed columns was used for determining the characteristics, namely distribution coefficient and column plate efficiency. Sample of dextran 5, glucose and fructose were used. The sample volume was 2.0 cm^3 and the concentration was 1000 µgm per cm^3. Cysteine-sulphuric assay was used with the auto analyser.

In addition, column number 12 was selected for its high plate efficiency for a separate study at

different volumetric flowrates.

5.2.1.3 QUANTITATIVE ANALYSIS OF THE PRODUCTS

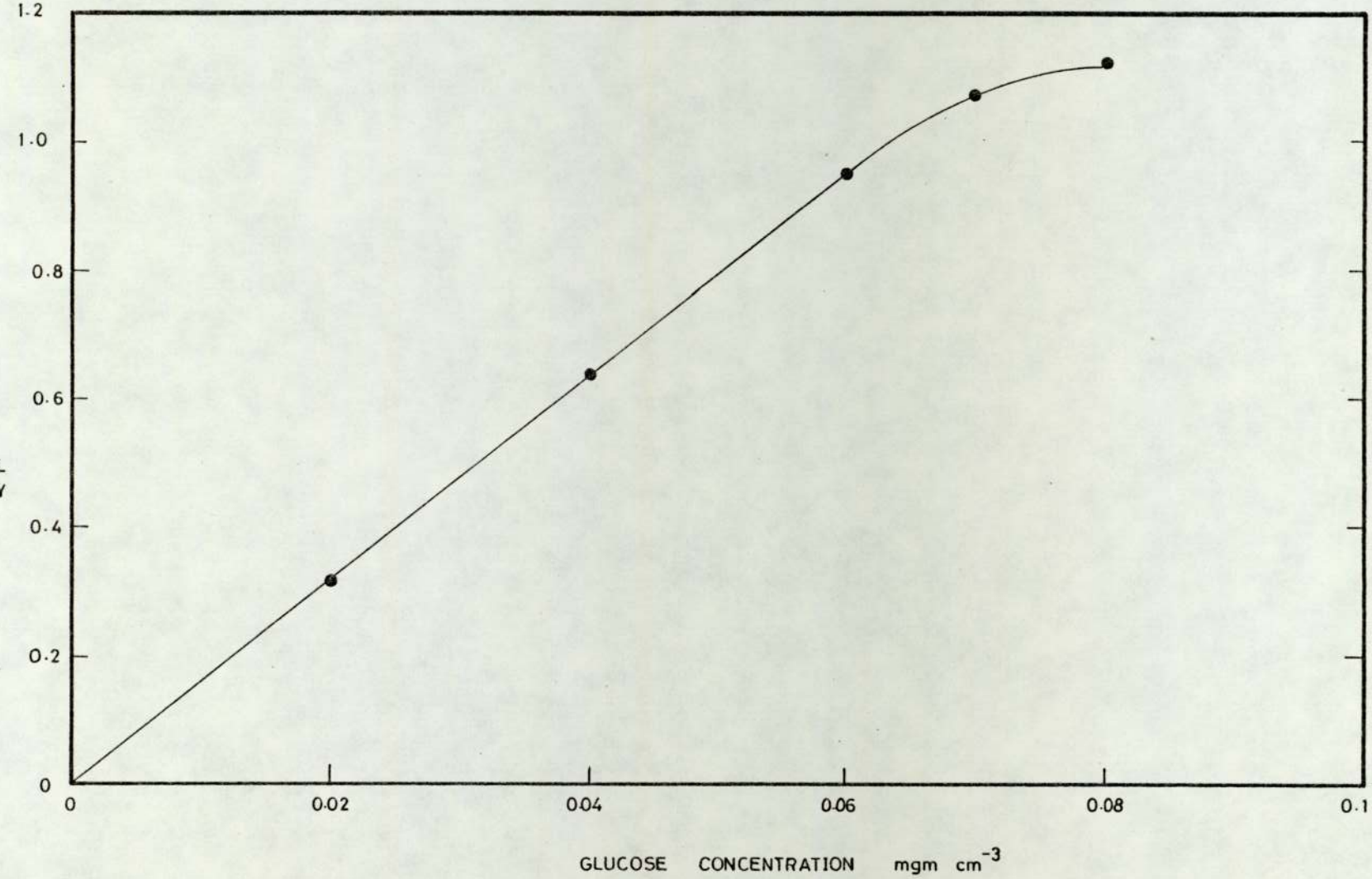
The working of the Technicon auto-analyser was described previously in Section (5.1.1) and the contents of the reagents in Sections (5.1.1.1), (5.1.1.2) and (5.1.1.3).

Samples to be analysed from a typical experiment with the SCCR4 were the feed, the two products and the twelve column purge contents. A complete experiment usually contained not less than six cycles; each cycle consisting of twelve switches round the column. At the end of each cycle two bulk samples of the fructose rich product and the glucose rich product were obtained.

Each of these samples was to be analysed for its carbohydrate content. Appropriate assays were used namely cysteine-sulphuric assay for total carbohydrate, resorcinol assay for fructose and enzyme assay for glucose.

Freshly made standards of concentration 10, 20 and 40 μgm per cm^3 for dextran, glucose and fructose were first put through the auto-analyser. The optical densities for each set of concentrations for each of the carbohydrates were recorded. Their values were plotted to obtain three calibration curves for dextran, glucose and fructose. This procedure was repeated at the end of the analysis for cross-checking with the

FIG. 5.6 CALIBRATION CURVE FOR THE CYSTEINE / SULPHURIC ASSAY



first set.

It was found that for concentrations above 70 µgm per cm^3, the relationship between the optical density and the concentration was non-linear. Therefore, it was necessary to dilute all the samples so that the concentration was within the linear range, Figure (5.6).

The auto-analyser was a very sensitive equipment; it detected solutes at concentration of less than 1 ppm.

The total time usually required to analyse a sample was about twenty minutes.

5.2.2 THE BIO-RAD COLUMN AND THE JOBLING REFRACTOMETER ANALYTICAL SYSTEM

This system was a later addition to the research group's analytical equipments.

It was used principally for analysing the quantitative content of the products from the SCCR4 experiments.

The concentration of the components in the products were obtained by comparing with standard solutions of the individual pure component at a given concentration level.

A Hewlett-Packett integrator was incorporated to calculate the area under the chromatogram recorded on the chart. The area of the chromatogram of a component from the product was compared to the area of

the chromatogram for the pure component of a known concentration.

By an appropriate conversion factor the concentrations of all the components in the products were obtained.

C H A P T E R S I X

THE SEMI-CONTINUOUS CHROMATOGRAPHIC REFINER - SCCR4

6.1 INTRODUCTION

The successful operations of both the continuous gas-liquid chromatographic process by Barker and Deeble[17-20] and the liquid-liquid chromatographic process by Barker, Hatt and Ellison[23], prompted Barker and Ching[24] to undertake the study of liquid-solid chromatographic process using a similar flow scheme.

The task undertaken by Barker and Ching was to design, build and commission a continuous chromatographic process in the ion-exchange mode to separate fructose from glucose.

A pilot unit was successfully designed and commissioned and the designated name was the Semi-Continuous Chromatographic Refiner MK.4 (S.C.C.R.4). A group of experiments were conducted with a glucose-fructose feedstock at various concentrations and flowrates, and at different temperatures to study the performances of the refiner. A computer programme was also compiled to simulate the system concentration profile.

The primary objective of the research was to improve the original refiner and to use it to recover fructose from glucose/dextran contaminated feedstock, as well as to search for the optimum operating parameters for the maximum recovery of fructose.

The original pilot unit had ten glass columns of

2.54 cm I.D. packed with calcium charged zerolit 225 SRC14 resin with 8% divinyl-benzene cross-linkage on an organic base. The packed bed height of each column was approximately 65.0 cm. A more detailed description of the apparatus is available in Ching's thesis[24].

6.1.1 PRINCIPLE OF OPERATION OF THE S.C.C.R.4 EQUIPMENT

Figures (6.1) and (6.4) illustrate the operation of the S.C.C.R.4 machine for separation of a binary feed mixture. A mixture of component 1 and 2 is fed into the system at port D. The less strongly adsorbed component (component 1) is preferentially moved with the mobile phase fluid towards product 1 offtake port A. A section of the closed loop column is isolated by locks T and TT; an independent purge fluid stream enters at port E and exits with the more strongly absorbed component (component 2) from port B. Figure (6.1a) represents the distribution of the two components within the system soon after 'start up'. In Figure (6.1b), all the port functions have been advanced one position in a direction co-current to the direction of mobile phase flow. This port advancement results in a simulated movement of the packed column in a direction counter-current to the direction of the mobile phase flow. The rate of advancing the ports must be less than the velocity of the less strongly adsorbed component through the packing, but greater than that of the more strongly adsorbed component. As such,

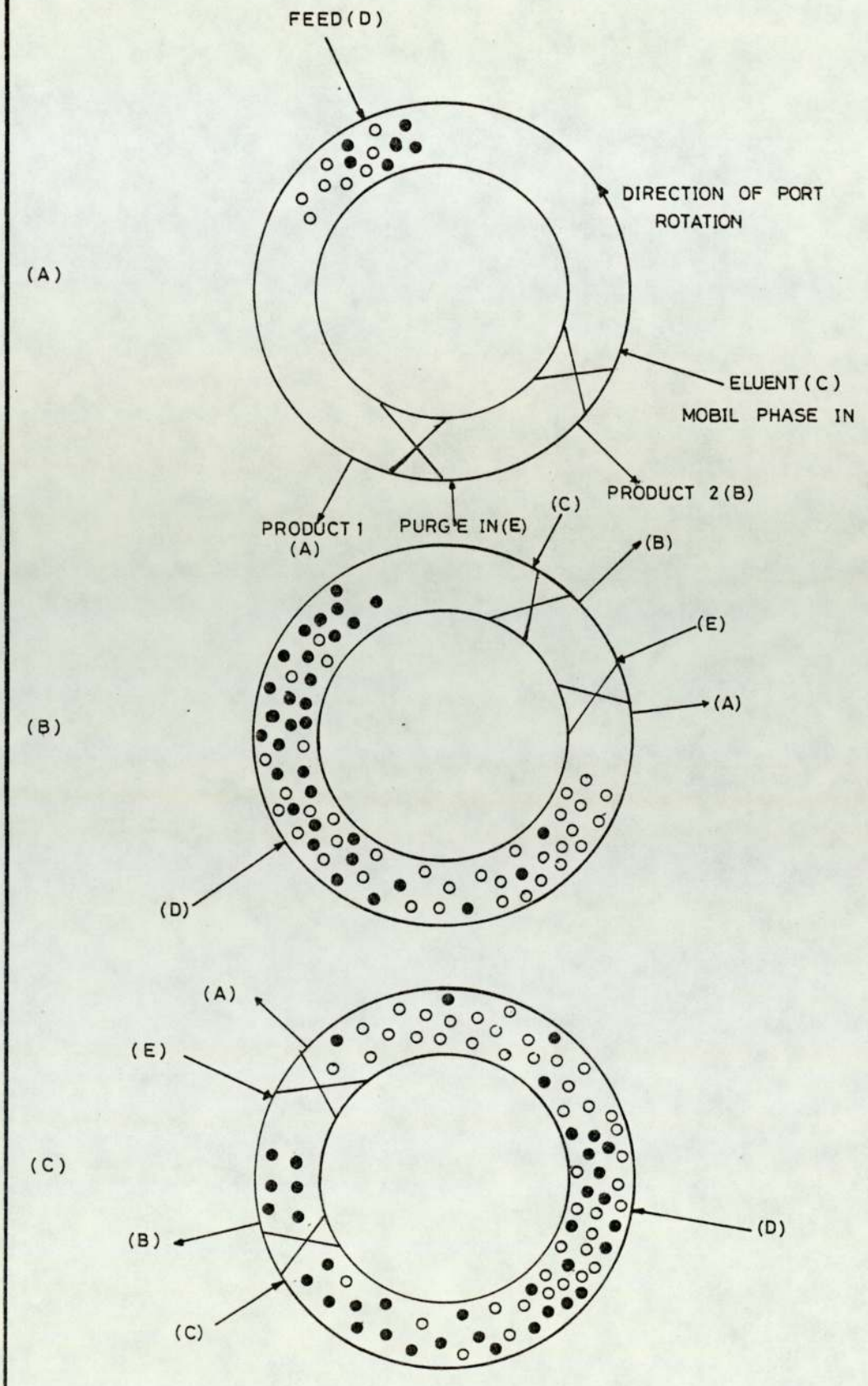
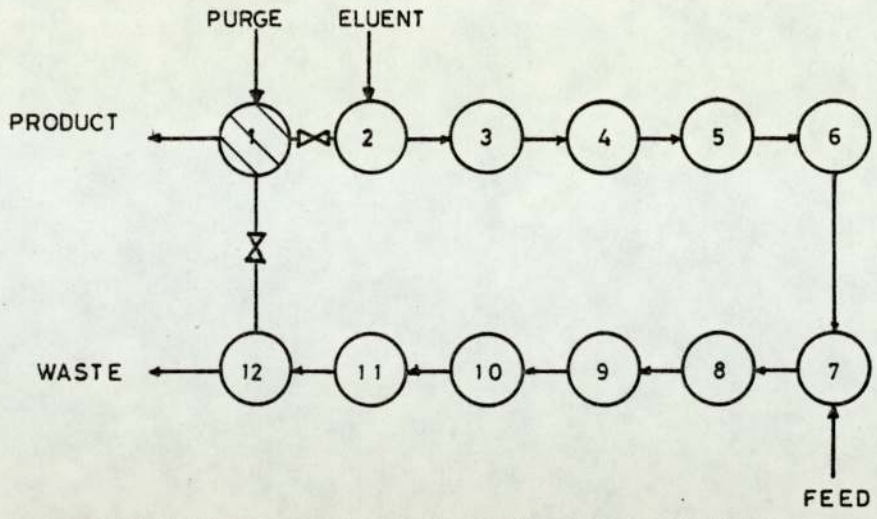
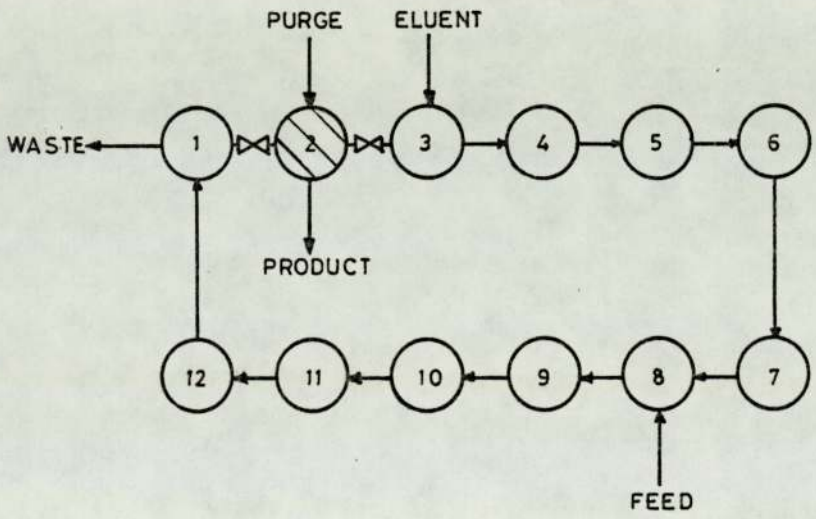


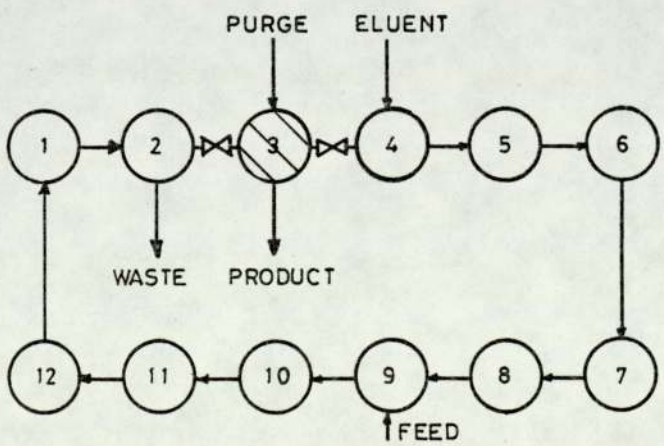
FIG. 6.1 PRINCIPLE OF OPERATION OF SCCR 4 UNIT



SWITCH ONE : COLUMN 1 - ISOLATED COLUMNS 2 TO 12 - FRACTIONATING



SWITCH TWO: COLUMN 2 ISOLATED COLUMNS 3 TO 1 FRACTIONATING



SWITCH THREE COLUMN 3 ISOLATED COLUMNS 4 TO 2 FRACTIONATING

FIG. 6.4 DIAGRAMS SHOWING SEQUENCES OF OPERATION OF THE S.C.C.R.4

component 2 is being retained preferentially on the resin bed while component 1 is emerging from port A. The last diagram (c) of Figure (6.1) shows the fully established operating conditions of the unit.

From Figure (6.1), it may be seen that seven valves need to be opened or closed simultaneously, namely the feed inlet, the mobile phase inlet, the product 1 outlet, the purge fluid inlet and outlet and two column isolation locks. Based on the above principle, a liquid solid chromatographic separation unit with separate vertical columns was built. A more detailed description of the twelve column unit is provided in the chapter.

6.1.2 RECONSTRUCTION OF THE ORIGINAL S.C.C.R.4 UNIT

Initially, a number of exploratory experiments were performed with Dr. Ching's unit, with the ten glass columns (2.54cm I.X.), so as to become familiar with the operational procedure and to test the possibilities of recovering fructose from a glucose/dextran contaminated feedstock (70% sugar solids in solution) as porduced by Fisons Pharmaceutical Limited.

It was soon found that the pilot unit had limitations, as the maximum pressure drop was rated at approximately 700 kNm^{-2} as specified by Jobling Ltd., the manufacturer of the Q.V.F. glass columns. The heat provided to the columns was by heating tapes

FIG. 6.2 PHOTOGRAPH OF THE ORIGINAL S.C.C.R. 4 UNIT CONSTRUCTED BY Dr. C. B. CHING


SMOKING
PNEUMATIC CONTROL
SYSTEM

FIG. 6.3a THE IMPROVE SCCR 4 UNIT CONSTRUCTED FOR THIS RESEARCH

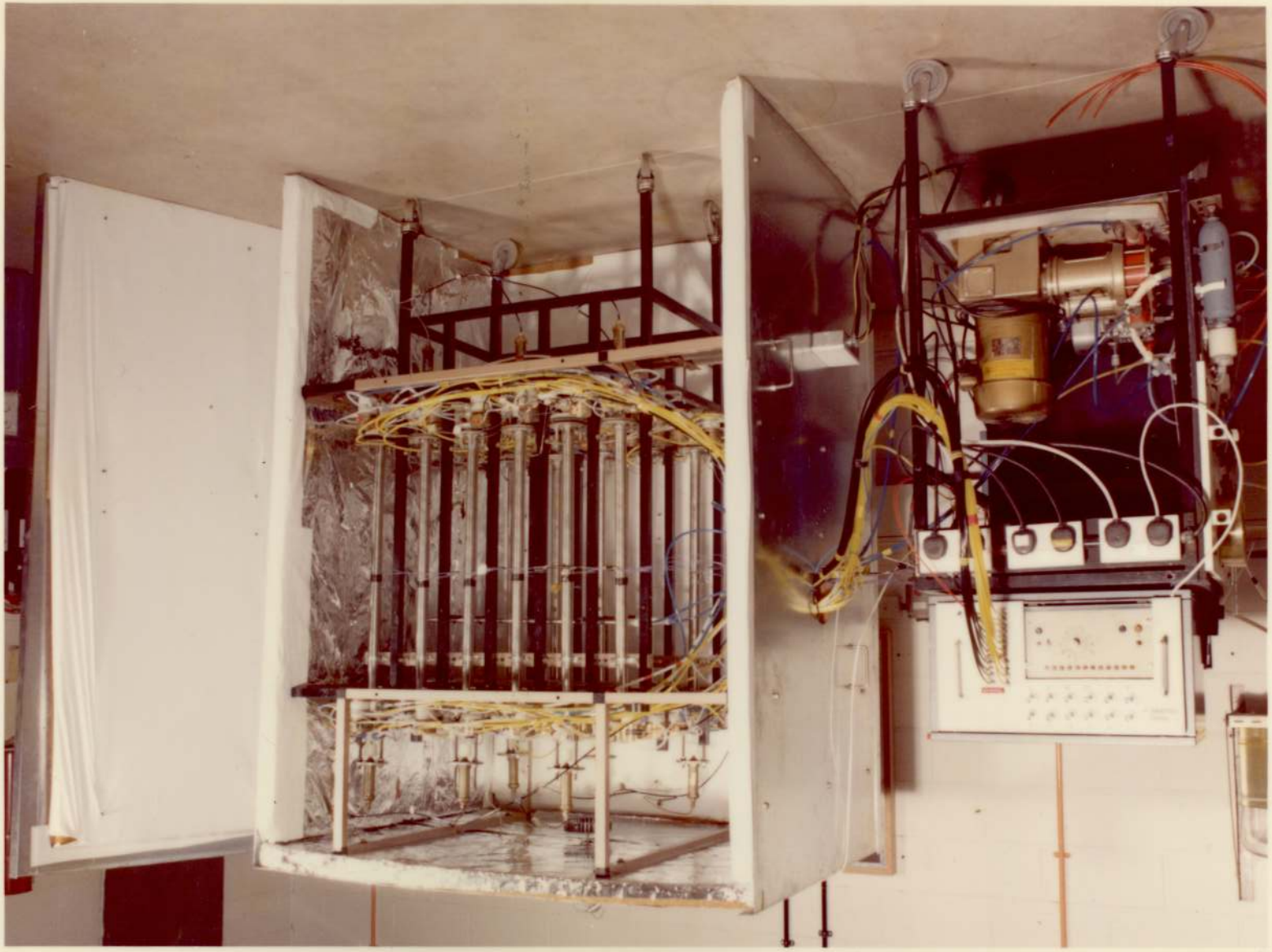
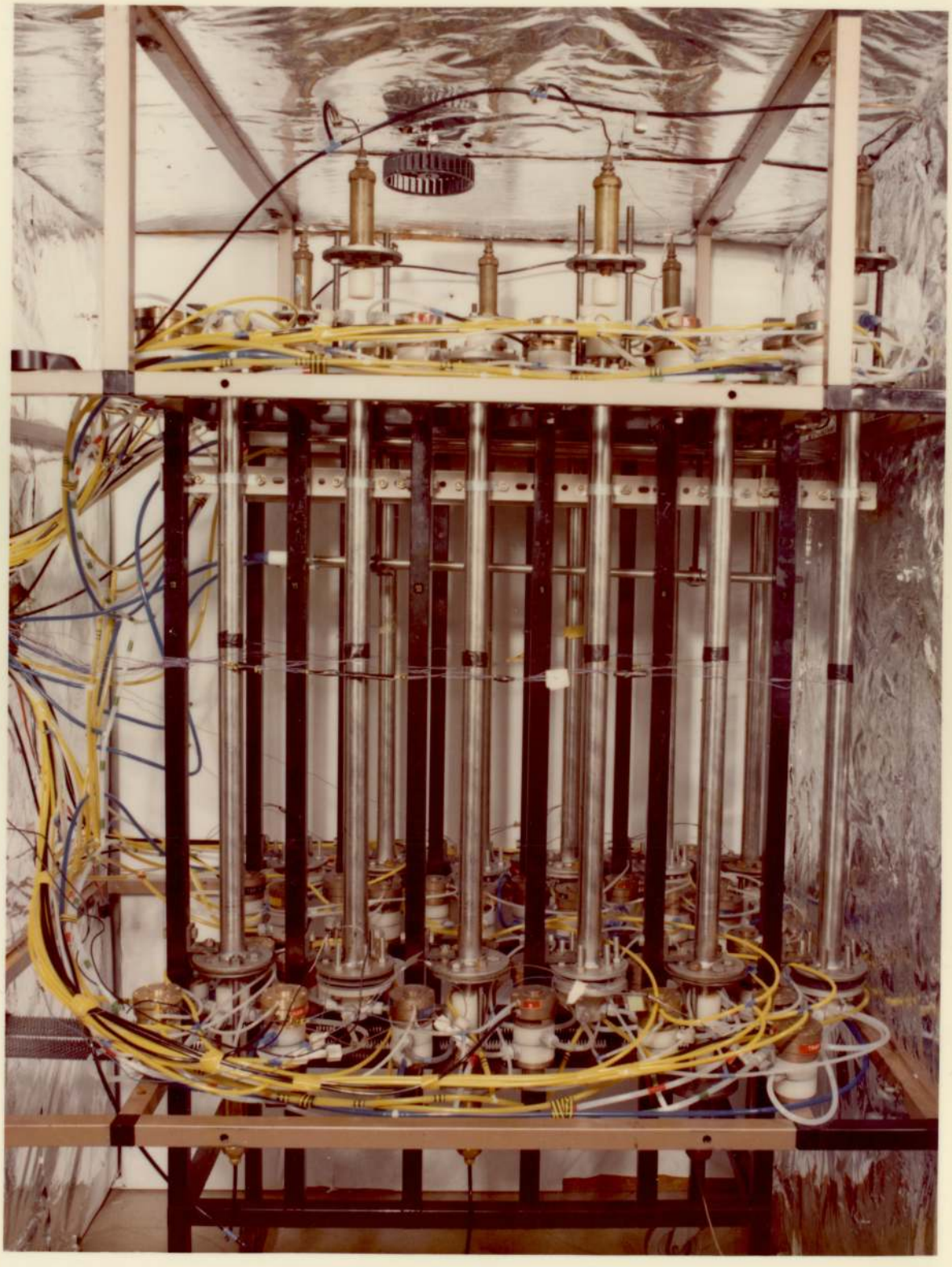
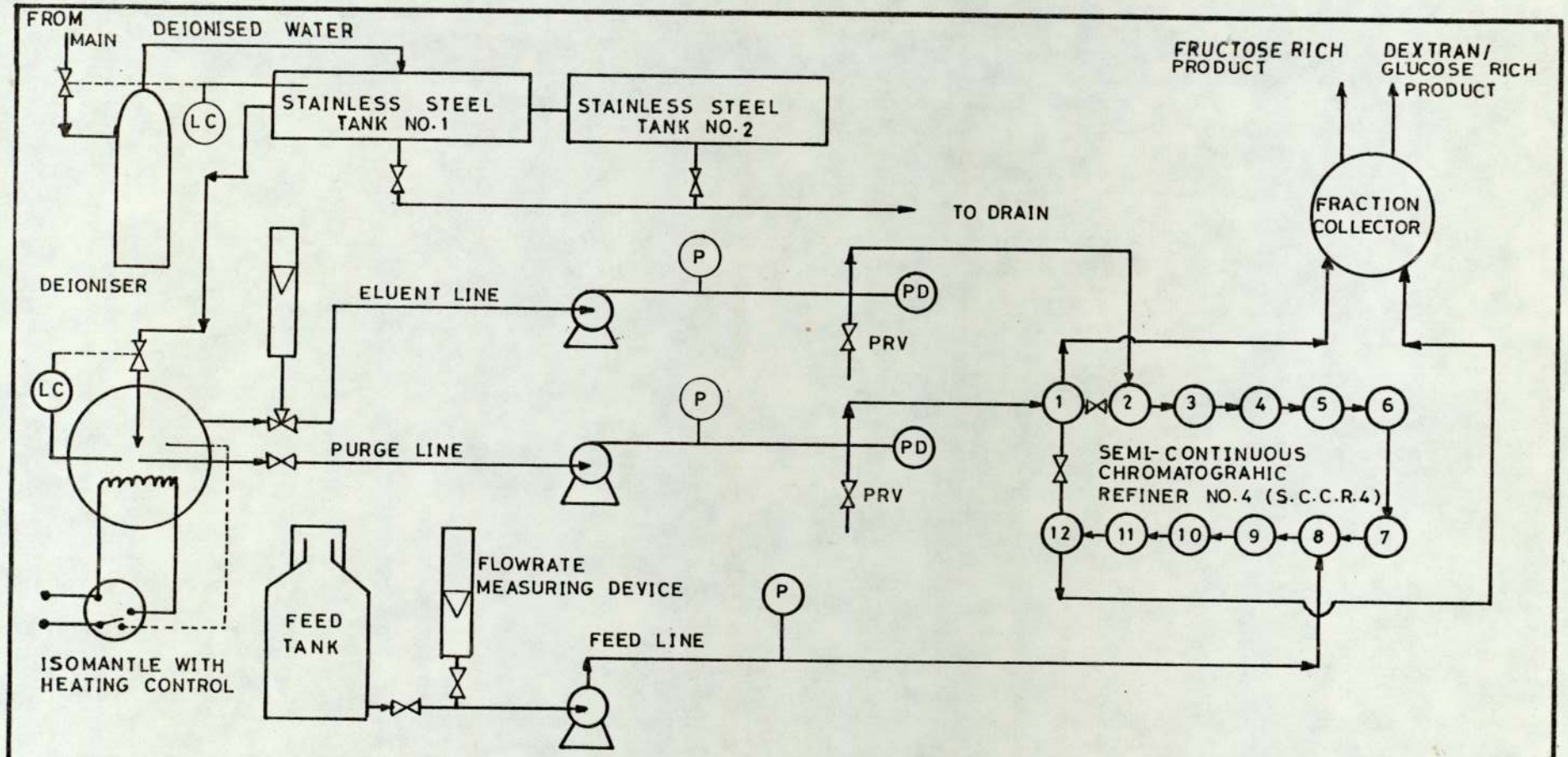


FIG. 6.3b PHOTOGRAPH OF THE SEPARATION SECTION OF THE S.C.C.R.4. UNIT





KEY: P-PRESSURE INDICATOR PD-PULSATION DAMPENER PVR-PRESSURE RELIEF VALVE LC-LEVEL CONTROLLER

FIG.6.3c SCHEMATIC DIAGRAM OF THE SEQUENTIAL CONTINUOUS CHROMATOGRAPHIC REFINER(S.C.C.R. 4)

strapped around each glass column which did not give an even distribution of temperature.

Plans were finalised to improve the original unit as described in the next sections.

6.1.3 GENERAL DESCRIPTION OF THE S.C.C.R.4

The S.C.C.R.4 unit consisted primarily of two assemblies, namely the pneumatic and the liquid process networks. Figure (6.2) shows an overall view of the S.C.C.R.4 built by Dr. Ching, and Figures (6.3a), (6.3b) and (6.3c) of the improved S.C.C.R.4 unit.

The separation section consisted of twelve stainless steel columns of 2.54 cm I.D. mounted in two parallel rows of six columns on a mobile support. On the inlet side of a column were fixed four pneumatic poppet valves controlling the feed, eluent, purge and the transfer from the previous column, whilst on the outlet side two similar valves controlled the fructose rich product (F.R.P) and glucose rich product (G.R.P) streams. A column was isolated by closing the two adjacent transfer valves as seen in Figure (6.4). The inlet and outlet lines were arranged in a ring distribution network connected respectively to the pumps and the product collecting device for the system.

6.2 THE LIQUID PROCESS NETWORK

This section deals only with the liquid process devices used in the SCCR4 unit, and follows a logical trace of the liquids from the reservoirs throughout the separation section and to the collection points. Figure (6.3) outlines the general flow schemes of the liquid network.

6.2.1 THE LIQUID RESERVOIRS

6.2.1.1 THE ELUENT AND PURGE RESERVOIRS

The mobile phase was Birmingham town's water which has passed through a Portcell deionizer into two stainless steel tanks of capacity approximately $9x10^{-1}m^3$ each. The tanks were connected together and had a Fisons pressure-level controller which could electrically switch off a solenoid valve on the feed water pipe after the deioniser.

The water from the tank was distributed to four points in the laboratory servicing four pilot units (including the SCCR4) and to the drain via a 5.1 cm diameter plastic pipe for rapid draining.

On the SCCR4 system, a plastic tanks with a capacity of $120x10^3cm^3$ was added to service the unit independently as the water requirement was small. From the tank the water flowed into a $60x10^3cm^3$ isomantle where it was heated. In the isomantle, a

Fisons pressure-sensitive level controller (similar to the unit used on the main stainless steel tanks) was used to control the water input from the tank by a solenoid valve on the inlet line.

The purge and eluent water flowed from the iso-mantle, thorugh a pre-heater and into the separation section.

6.2.1.2 THE FEED RESERVOIR

The feed reservoir was a $2 \times 10^{-2} m^3$ glass aspirator.

6.2.2 THE PUMP

Two multi-head pumps were used for the eluent, feed and the purge flows. Both pumps were supplied by Metering Pumps Ltd of Ealing, London.

A series II MPL micrometering pump, with dual heads rating at 10 cm^3 per minute and 20 cm^3 per minute, was used to pump the feed and eluent.

The purge water was pumped by a K-series metering pump with two heads of different types, namely a positive displacement piston head to give a high pressure but low flowrate, and a diaphragm head for low pressure and high flowrate. Flowrate ratings were 0.0 to 50.0 cm^3 per minute and 0 to 2000 cm^3 per minute respectively. Both were of a rigid plastic construction.

6.2.3 THE SEPARATION SECTION

The separation section consisted of twelve columns in two parallel rows of six columns. The columns were of stainless steel (type 316) construction having an inner diameter of approximately 2.54 cm. Each column was packed with the calcium charged zerolit 225 SRC14 resin (150-300 μm) with 8.0% divinyl-benzene cross-linkage on an organic base. Each column was packed by a slurry packing technique as described in Section (5.2.1.1.1). The height of the packed bed was approximately 66.5 cm.

6.2.3.1 THE INLET ASSEMBLY

The liquid inlet assembly was a dynamic one (Figure 6.5) and consisted of two polypropylene heads connected by a stainless steel shaft.

The upper head had four inlet channels with 6.34 mm Festo joints combined together into a common shaft. The main channel had a bore diameter of 3.0 mm.

The stainless steel shaft had a bore diameter of 6.35 mm but was filled with a nylon tube having a bore diameter of 3.0 mm. The shaft was 10.0 cm long and thread at both ends to accommodate the two polypropylene heads.

The lower head was essentially a liquid flow distributor which had a small dead volume covered by

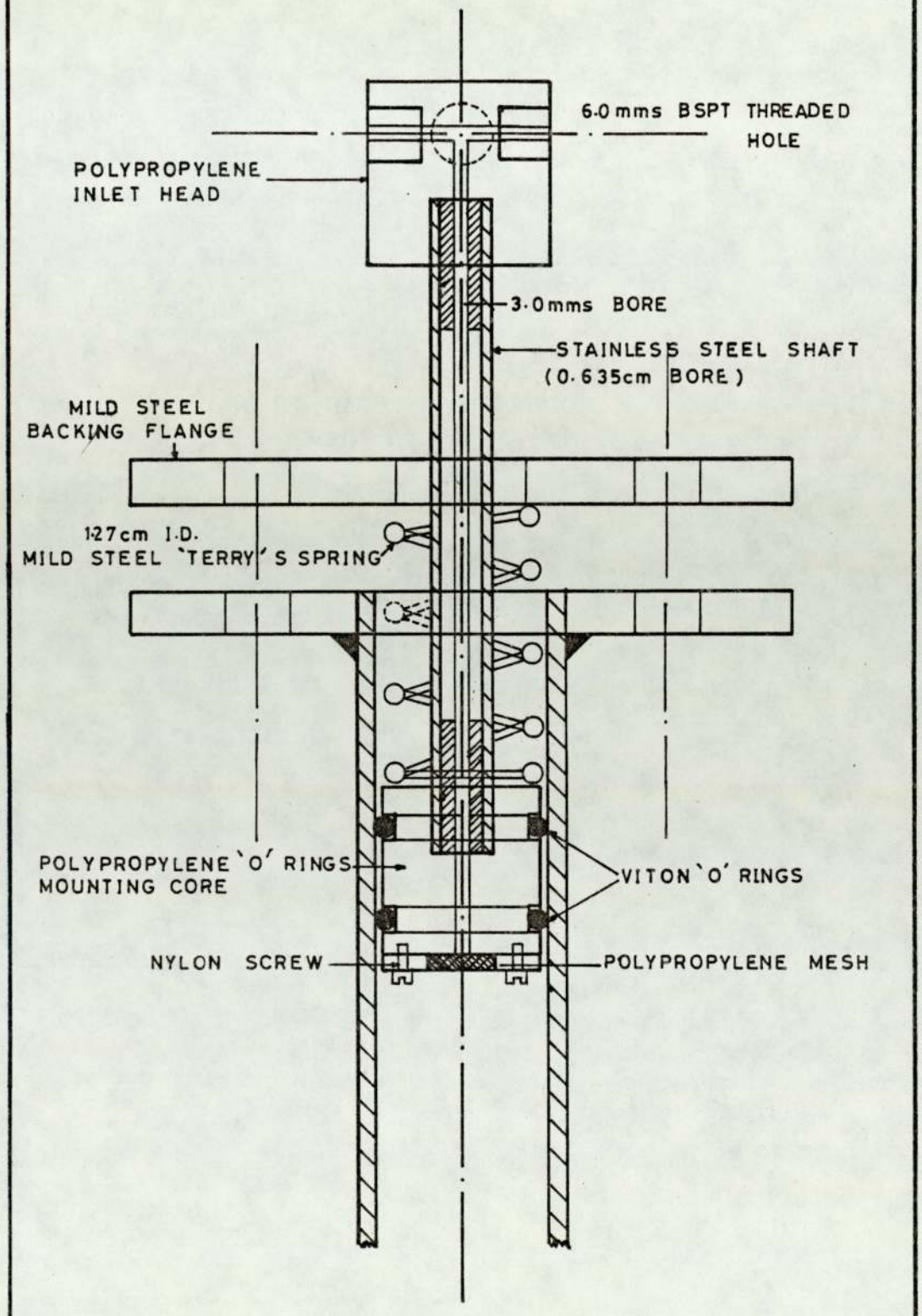


FIG. 6.5 DETAIL DRAWING OF THE INLET ASSEMBLY

propylene mesh. Two standard Dowty 'O' rings to fit a 'turn-down' diameter of 2.64 cm of the steel column were incorporated such that the head was able to move freely in the column at the same time sealing the liquid inside. The 'turn down' section of the column had a depth of 12.0 cm.

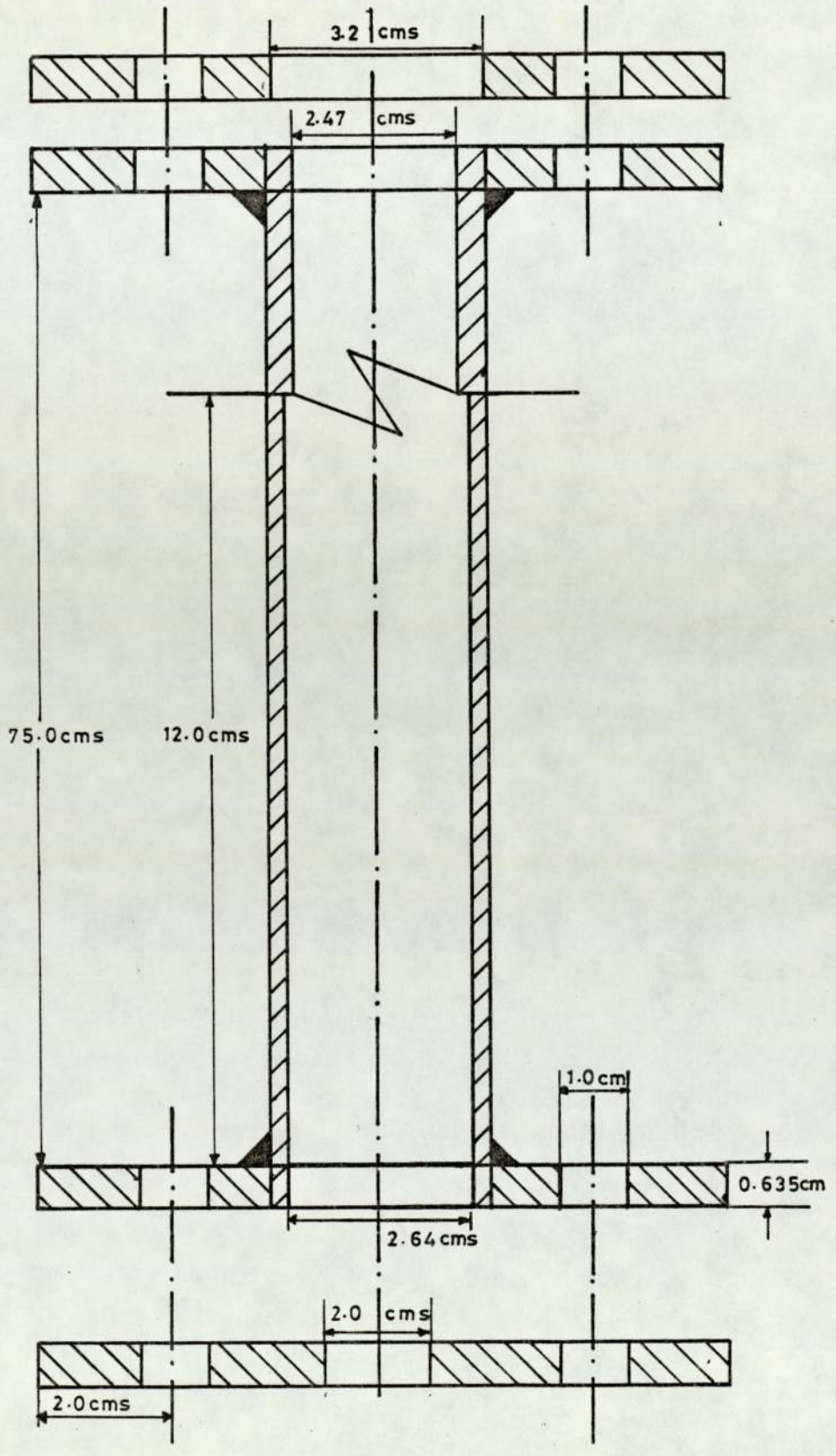
Around the stainless steel shaft and between the 6.35 mm thick mild steel backing flange and the distributor head was a Terry's spring of inner diameter 1.27 cm. The spring was custom made to fit the assembly and was made of 2.0 mm diameter mild steel wire. The height was 8.0 cm. At a reduced height of 5.5 cm by compression, the spring exerted a hydraulic pressure of approximately 300 kNm^{-2} on a constant volume of water in the column.

The whole assembly is held together as shown in Figure (6.5).

6.2.3.2 THE COLUMN

The column was fabricated from a seamless stainless steel (type 316) of a nominal bore diameter of 2.47 cm.

Figure (6.6) shows a detailed drawing of the fabricated column. On the inlet side of the column, the diameter of bore was turned down to 2.64 cm to accommodate the standard 'Dowty' rings on the lower head of the inlet assembly (Section 6.2.3.1). The



KEY 1.0 inch = 2.54 cm.

FIG. 6.6 DETAIL DRAWING OF THE 2.54cm. STAINLESS STEEL COLUMN

depth of the turned down section was 12.0 cm and the total column length was 75.0 cm.

At both the ends two mild steel flanges were welded which will accommodate the inlet and outlet assemblies.

6.2.3.3 THE OUTLET ASSEMBLY

Figure (6.7) shows a detailed diagram of the outlet assembly. The assembly consisted of two parts, namely the resin bed support disc and the liquid collecting head.

The bed support disc was made of polypropylene material with a 2.47 cm diameter meshed section corresponding to the diameter of the steel column. It was made by sandwiching two pieces of nylon mesh between two polypropylene plastic disc and then welding them together. The nylon mesh was supplied by Henry Simon Limited, Stockport and had two size ratings, one of 150 μm to retain the packing in the column and the other one of 1500 μm for support.

The outlet head resembled a 'top-hat' and was essentially a liquid collecting device. It had a funnel-shape cavity of diameter similar to the meshed diameter (2.47 cm) of the bed support disc. The cavity was linked to three outlets with Festo joints by a 3.0 mm channel.

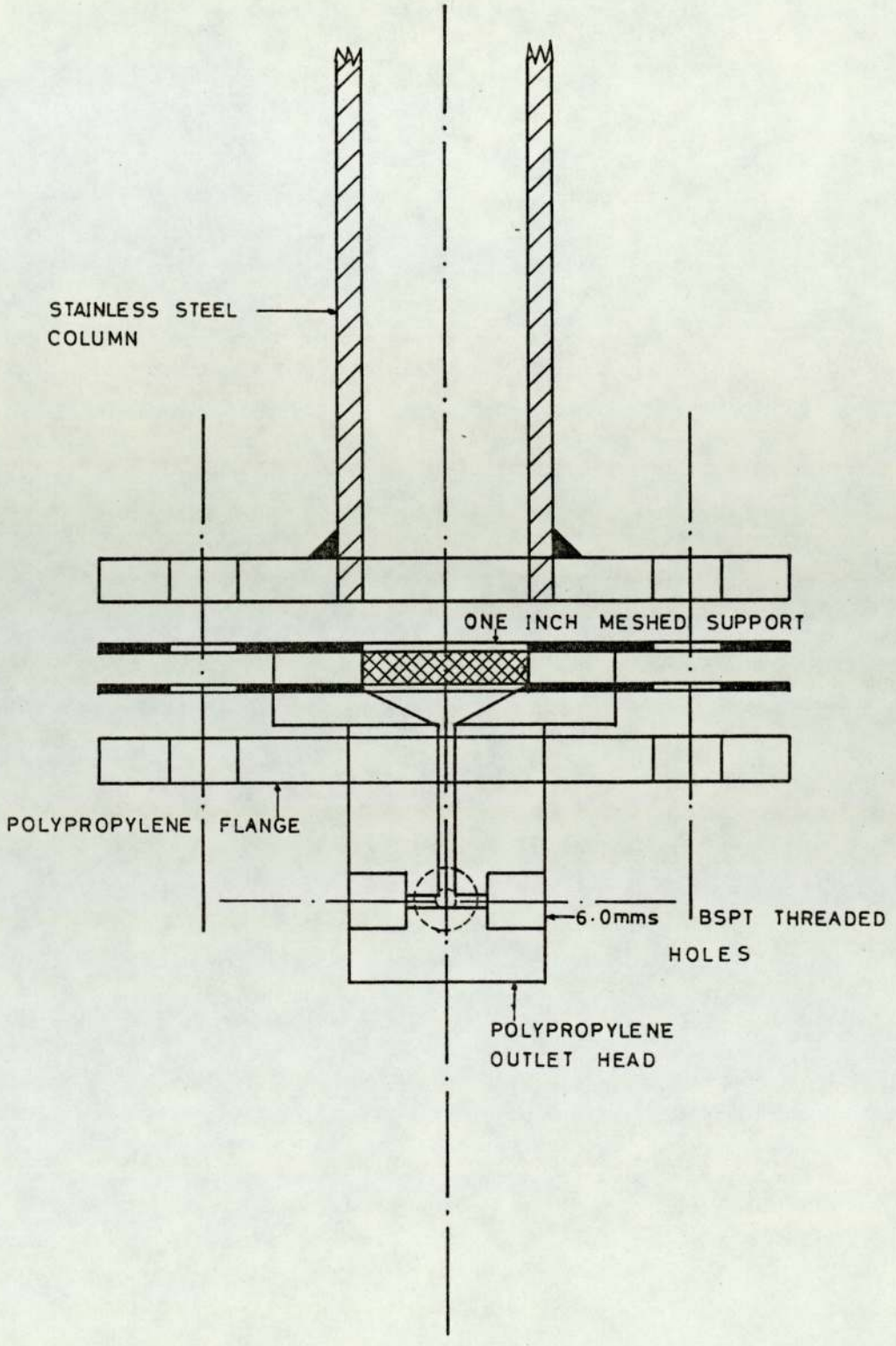


FIG. 6.7 DETAIL DRAWING OF THE OUTLET ASSEMBLY

The whole assembly was held together by a polypropylene backing flange and sealed by two layers of viton rubber gaskets as shown in Figure (6.7).

6.2.3.4 THE VALVE

A detailed description will be provided in Section (6.3.2).

6.2.3.5 THE LIQUID LINES

Past experience of working at temperatures up to $60^{o}C$ showed that the polypropylene tube used became soft and ruptured.

6.2.3.6 PRODUCT COLLECTION

The two product streams from the SCCR4 unit were collected in plastic containers of 6, 10 and $80x10^{-3}m^{3}$ capacity. Switching of the product streams from one container to the next was achieved using the fraction collector. The operating principle consisted of moving the product outlet lines at set time intervals from delivering to one pair of collecting vessels to delivering to the next pair. The fraction collector was designed to function automatically through the drive of one electric motor. However, during the course of this research, it was operated manually to collect a bulk sample per cycle.

6.2.3.7 FLOWRATES AND PRESSURE MEASURING DEVICES

The eluent and feed inlet flowrates were measured using 25 cm^3 glass burrettes. The flowrates were checked again by measuring the flowrate of the glucose rich product; which should be the sum of the two input flowrates.

The purge flowrate was measured by the outlet stream, i.e. the fructose rich product stream. This was sufficient as this was a single stream passing through one isolated column.

The inlet pressures for the three streams were monitored by using three Bourdon gauges installed between the pumps and the columns.

The eluent and feed pressure gauges had a range of 0 to 2100 kNm^{-2} and that of the purge, 0.0 to 1400 kNm^{-2}.

The gauges were supplied by Mackey and Bailey Ltd of Birmingham.

6.2.3.8 PRESSURE RELIEF DEVICES

Three Hoke relief valves were fitted to the eluent, feed and purge process lines. The eluent and feed lines were st to a limit of 1040 kNm^{-2} pressure to protect the Festo joints.

The purge line relief valve was set at 275 kNm^{-2}

to protect the diaphragm of the k-series pump as recommended by the manufacturer. The pressure drop across a column would not normally exceed the 275 kNm^{-2} level unless a flowrate of a

6.3 THE PNEUMATIC NETWORK

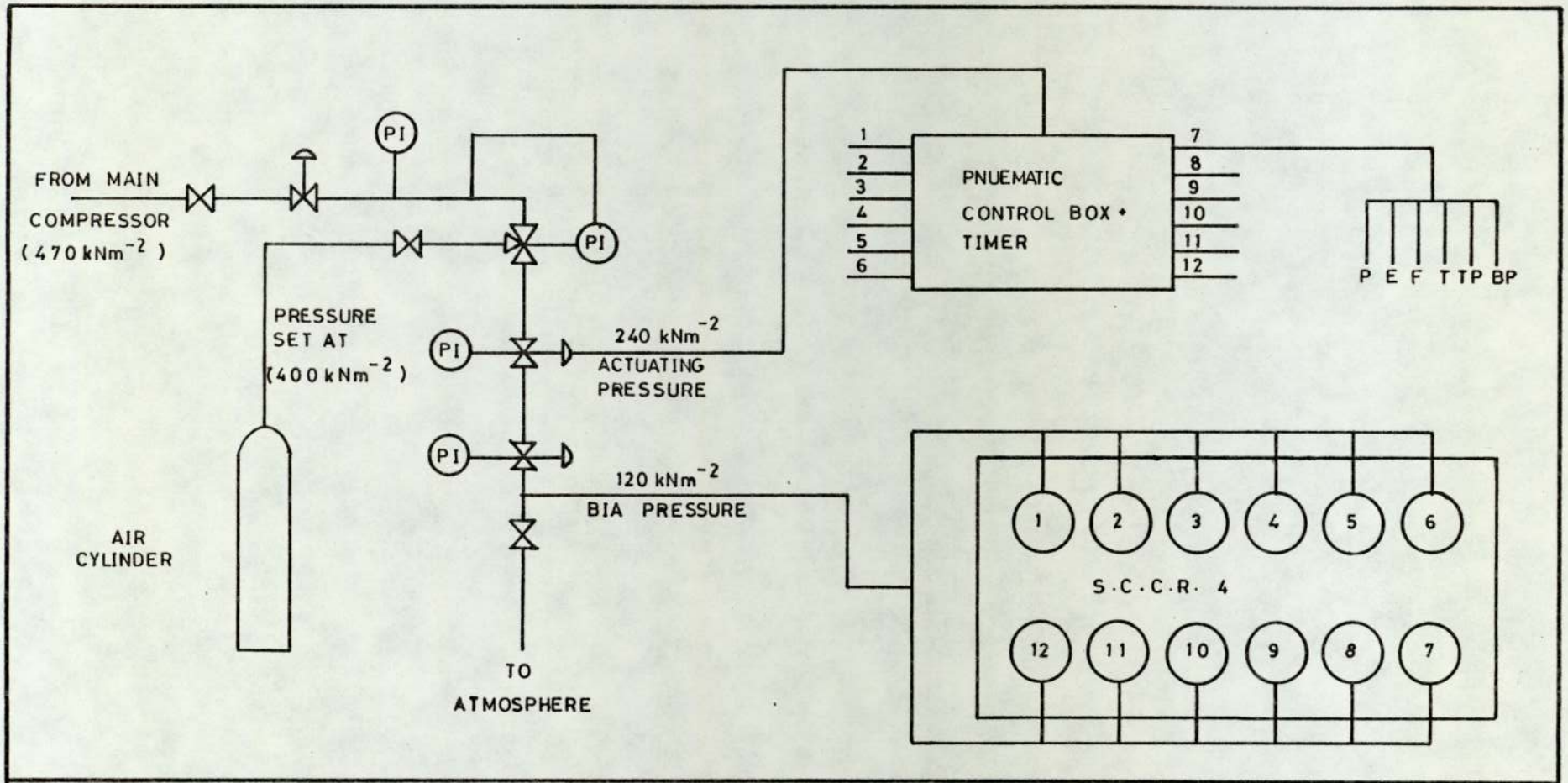
This section deals with the pneumatic control, the pneumatic devices and the safety devices incorporated to protect the system. Figure (6.8) shows the overall network.

6.3.1 THE PNEUMATIC SUPPLY

The main air supply came from the Departmental air compressor which maintained a constant pressure output of 620 kNm^{-2}. A switch valve which operated on a differential pressure principle was incorporated as a safety device. The valve will automatically cut in to an air bottle reserve when the air pressure on the main line falls below 480 kNm^{-2}.

The air leaving the switch valve is splitted into two streams, namely the actuating and bias streams. The air pressure in these streams were regulated at 550 kNm^{-2} and 240 kNm^{-2} respectively.

The bias line was linked directly to the valves and pressure was applied continuously throughout the



P - PURGE E - ELUENT F - FEED T - TRANSFER TP - GLUCOSE RICH STREAM BP - FRUCTOSE RICH STREAM

FIG. 6.8 SCHEMATIC DIAGRAM OF THE PNUEMATIC NETWORK

entire operation. The actuating air lead to a central control unit which in turn activated the appropriate valves in each sequence.

6.3.2 THE PNEUMATIC POPPET VALVES

The pneumatic poppet valves were previously developed by Barker and co-workers[20,21] and consultancy on the mechanical design was sought from Dr. Jones of the University of Birmingham. Fabrication of the valves were contracted to Aston Technical Services Limited. Figure (6.9) shows a photograph of a complete valve and its parts.

In the following sections, the term "bias pressure" refers to the air pressure applied constantly during operation to maintain the valve to be open or closed. The "actuating pressure" refers to that pressure required to close or open the appropriate valves during a particular sequence. The net difference of the two is referred to as the "differential pressure".

The pneumatically operated poppet valve incorporated in the SCCR4 unit consists primarily of a pneumatic section and a process fluid section. The pneumatic section is fabricated from brass and consists of lower and upper chambers. The two chambers are held together by six 4BA screws with a neoprene diaphragm sandwiched in between. Air can be separately introduced into or exhausted from individual chambers.

The process fluid section also consists of two sections and is made from polypropylene, a plastic which is resistant to most corrosive solvents. Process fluid enters the valve from the lower port and after flowing past the poppet, leaves the valve by the upper port, or vice versa. Closure of the valve is achieved by movement of the poppet upwards against the edge of the central core of the upper plastic section using an air pressure below the diaphragm. A viton gasket is placed between the two plastic sections of the valve to prevent the leakage of process fluid to the surroundings. The poppet is linked to the diaphragm of the pneumatic chamber by a specially designed stem, one end of which is permanently attached to the poppet and the other is guided through the central hole of the diaphragm where it is locked in position by a nut and washer. Three 'O' rings are positioned along the stem for sealing purposes. The first 'O' ring (Figure 6.10$^{(16)}$) is situated on the top of the poppet and under the thrust of a metal ring (Figure 6.10$^{(13)}$) and a screw type expander (Figure 6.10$^{(11)}$), prevents fluid leakage into the pneumatic chambers. The second 'O' ring (Figure 6.10$^{(15)}$) is located in a recess in the body of the lower pneumatic chamber and serves as a seal against air leakage through the stem. Finally, to prevent air escaping from a pneumatic chamber to the other through the centre hold, a third 'O' ring is placed (Figure 6.10$^{(14)}$ under the stem's lock nut and washer, and on top of the diaphragm. The entire valve is held together

FIG. 6.9 PHOTOGRAPH OF THE PNEUMATIC POPPET VALVE

ITEM NUMBER	PART NAME	MATERIAL
1	DIAPHRAGM CHAMBER - UPPER	BRASS
2	DIAPHRAGM	NEOPRENE
3	BODY GASKET	VITON
4	DIAPHRAGM CHAMBER - LOWER	BRASS
5	DIAPHRAGM BACKING PLATE	BRASS
6	SEALING RING WASHER	BRASS
7	BODY	POLYPROPYLENE
8	INLET CHAMBER	POLYPROPYLENE
9	MOUNTING PLATE	BRASS
10	POPPET	P.T.F.E. GLASS FILLED
11	ADJUSTING NUT FOR THE POPPET	BRASS
12	VALVE STEM	BRASS
13	THRUST WASHER	BRASS
14	O RING BS 007	NEOPRENE
15	O RING BS 008	NEOPRENE
16	O RING BS 110	NEOPRENE
17	4 BA CAP SCREW	BRASS
18	2 BA CHESSHEAD SCREW	BRASS
19	4 BA HEX. SCREW	BRASS

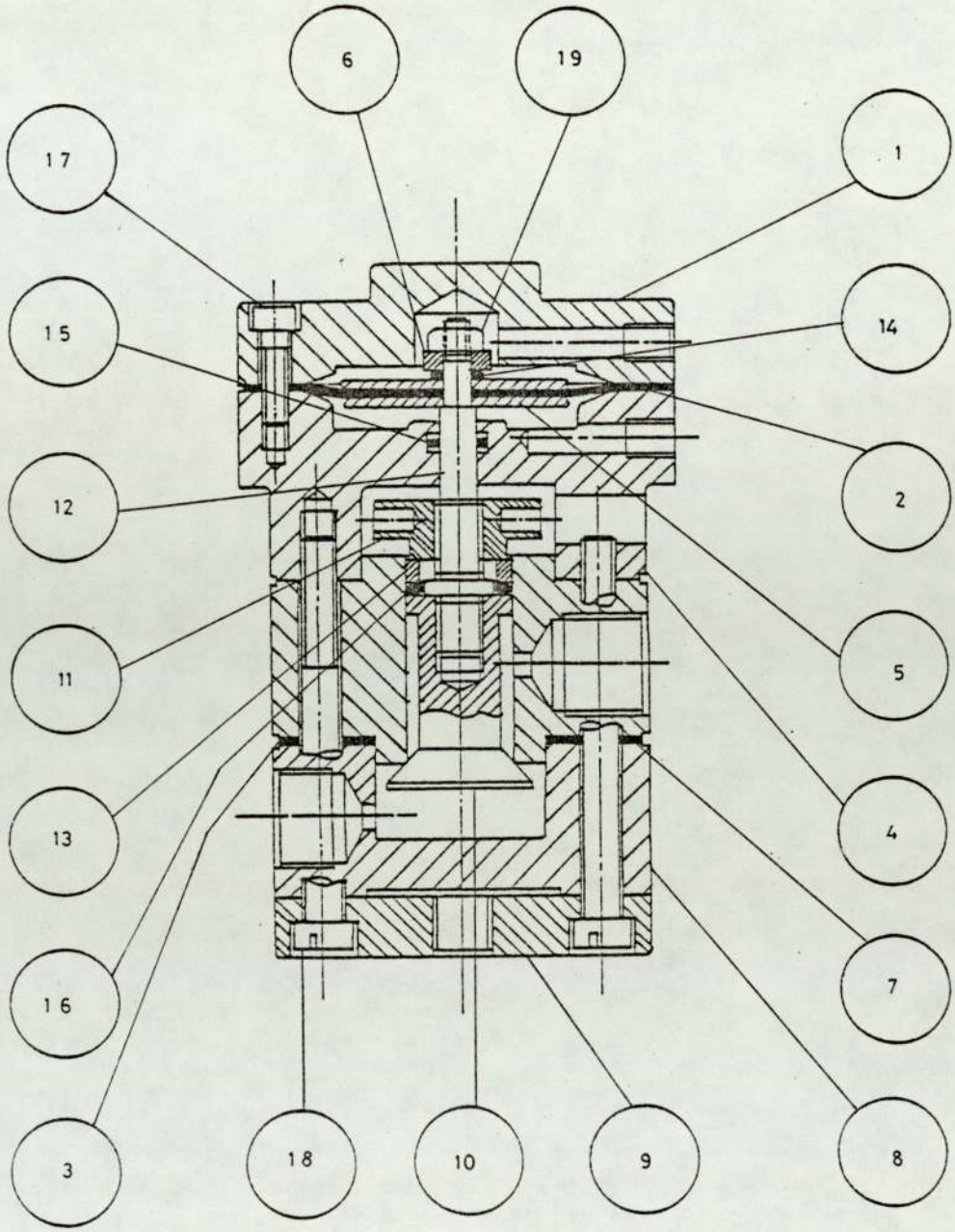


FIG. 6.10 DRAWING OF THE PNEUMATIC VALVE

by four 6.25 cm screws. The opening of the valve depends upon the introduction of air into the upper pneumatic chamber thereby closing the valve. The poppet (figure 6.10[10]) is fabricated from glass loaded Telfon.

With a bias and actuating pressure of 240 kNm^{-2} and 550 kNm^{-2} respectively, the valve can seal and open against a process differential pressure of up to 700 kNm^{-2} in both forward and backward direction. Under such conditions, the valve has been continuously tested for five hundred hours. No leakage was observed and the neoprene diaphragm showed no sign of rupture. As such, this design was considered to have satisfied the selection criterion and a total of sixty valves were fabricated. Later an extra fifteen valves were ordered to permit two more columns to be added to the 10 column-unit.

The valves remained reliable and showed no sign of deterioration in performance.

6.3.3 THE CONTROL SYSTEM

The control system worked on the basis that all the valves controlling the liquid into and out of the columns were closed until activated to open. The working of the valve has been described in section (6.3.2).

The foundation of the control mechanism was built on twelve solenoid valves which was activated

individually by a rotating cam-mechanism. The numbering of the solenoid valves was set corresponding to the twelve columns such that each solenoid valve would directly activate the transfer valves to isolate its corresponding column. The twelve solenoid valves were linked to twelve double return valves which activated the appropriate feed, eluent, purge input valves and the fructose rich and glucose rich output valves.

A digital timer was incorporated into the cam-unit which controlled the rotating mechanism which in turn opened and shut the solenoid valve at a fixed time period. An example now follows.

Solenoid valve number 1 was activated - it activated transfer valves numbers 12 and 1 to isolate column 1; from the solenoid valve to the double-return valves five valves were activated, namely the feed valve into column 8, the eluent valve into column 2, the purge valve into column 1 and the fructose rich valve out of column 1 and glucose rich valve out of column 12. Table (6.1) and Figure (6.4) show the sequence in tabulated and diagramatic forms.

The timer was set at a fix period, and at the end of the period a signal was triggered and set the cam-unit to rotate by thirty degrees. The next set of valves were then activated.

Later on in the research, a much more sophisticated control unit was used in place of the original one to give more flexibility in the investigation of the

TABLE 6.1 SEQUENCES OF VALVE SETTINGS

NUMBERS	VALVES							
SEQUENTS	TRANSFER	TRANSFER	PURGE	F.R.P	FEED	ELUENT	G.P.R	SEQUENTS
1	1	12	1	1	8	2	12	1
2	2	1	2	2	9	3	1	2
3	3	2	3	3	10	4	2	3
4	4	3	4	4	11	5	3	4
5	5	4	5	5	12	6	4	5
6	6	5	6	6	1	7	5	6
7	7	6	7	7	2	8	6	7
8	8	7	8	8	3	9	7	8
9	9	8	9	9	4	10	8	9
10	10	9	10	10	5	11	9	10
11	11	10	11	11	6	12	10	11
12	12	11	12	12	7	1	11	12

FIG. 6.11 CONTROL PNEUMATIC NETWORK

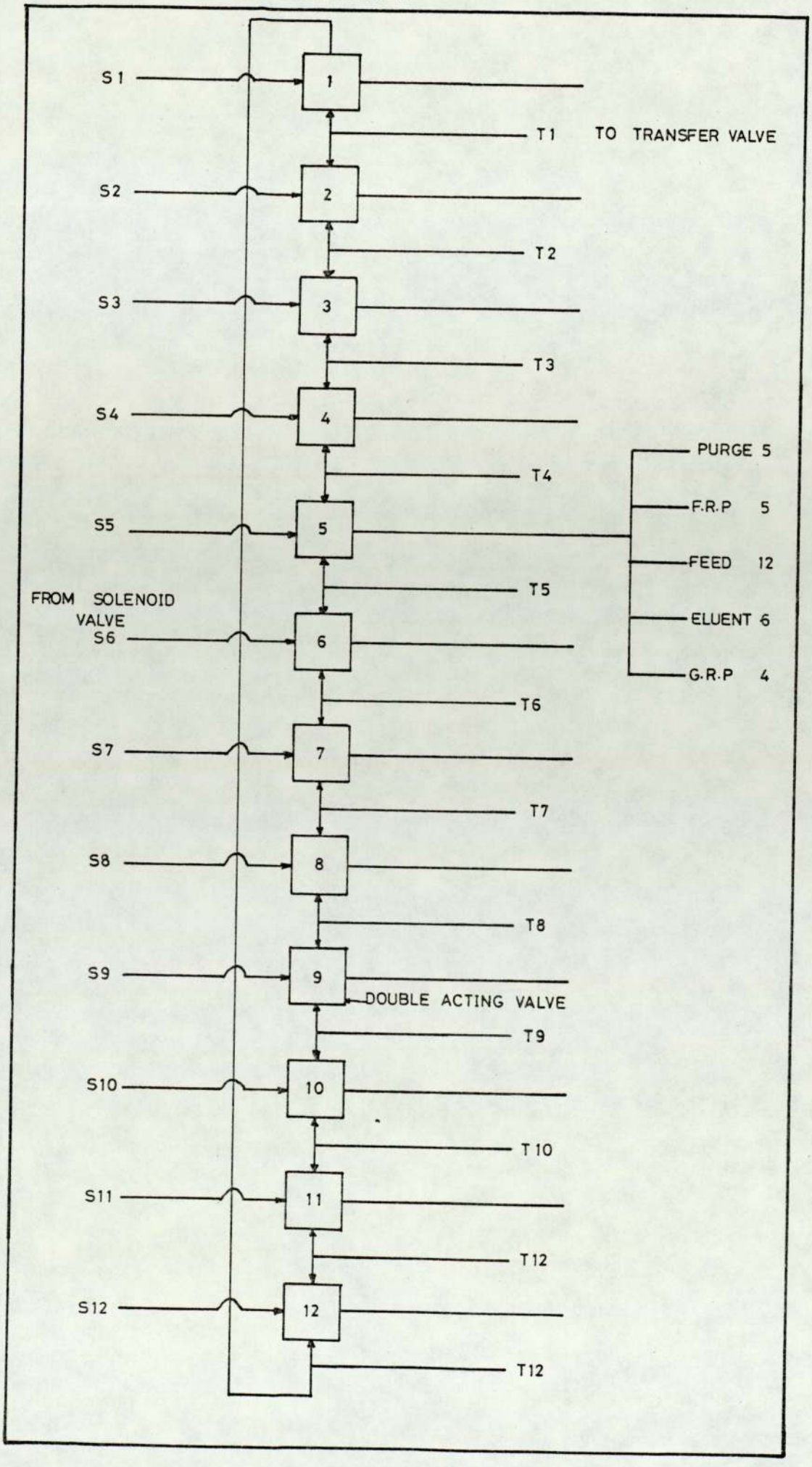
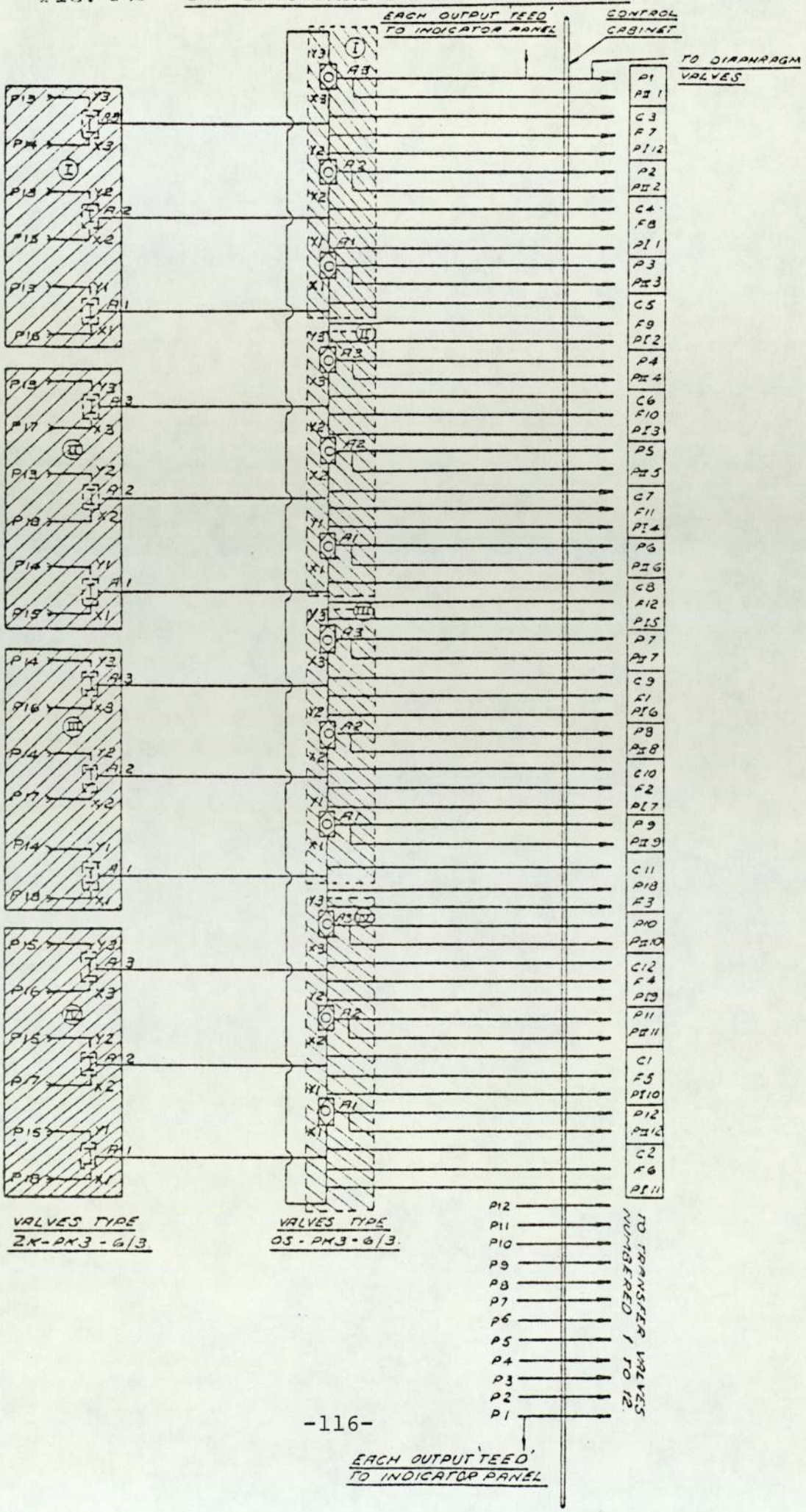


FIG. 6.12 THE SECONDARY PNEUMATIC CIRCUIT



different flow schemes for optimal throughput studies. Figures (6.11) and (6.12) show the flowchart of the original and modified control unit.

6.3.4 THE SAFETY DEVICES

Two safety devices were incorporated into the pneumatic network, namely a relief valve and a switch valve.

The relief valve was installed on the main air line leading to the SCCR4 unit and the limit set at 700 kNm^{-2}.

The switch valve was actually a differential pressure device which was connected to an air bottle set at 480 kNm^{-2}. A feedback from the main air line, normally used to operate the SCCR4 unit was linked with the valve in an opposing chamber.

In an event of failure, if the air compressor stopped, the pressure in the main air falls. As soon as the pressure fell below 480 kNm^{-2}, the switch valve switched the air supply from the main compressor to the air bottle. The air bottle was able to sustain enough pressure for the pilot unit to continue work for at least three hours.

6.4 THE TEMPERATURE MONITORING NETWORK

An elaborate temperature monitoring system was available on the SCCR4 unit.

It consisted of an intricate network of thermocouples and sensors strategically placed on the pilot unit. The feedback was an electrical signal displayed as millivolt potential on a digital indicator.

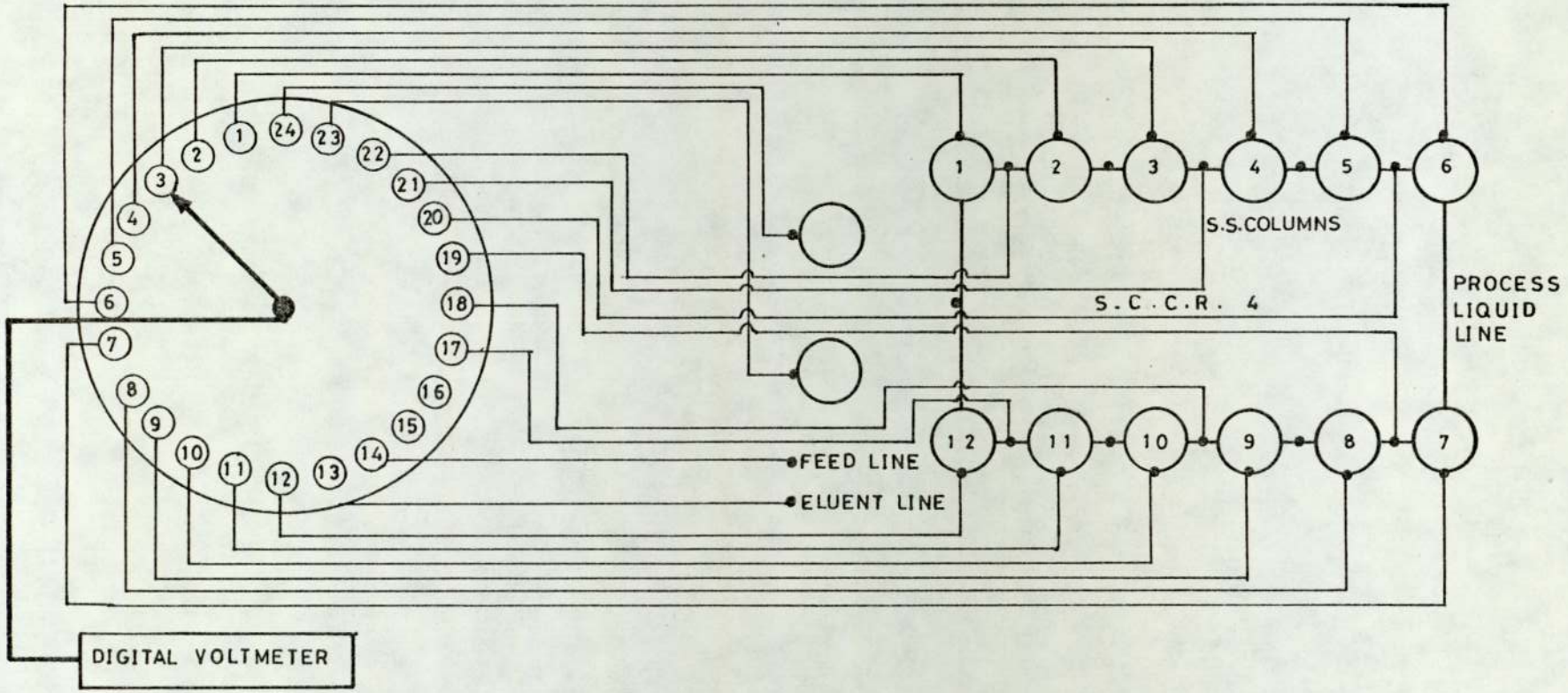
A total of twenty-two nickel-chrome thermocouples were placed on the mid-section of the twelve stainless steel columns, in between the transfer lines, the inlet lines for the eluent, feed and purge and on the mid-section of two pre-heating columns for the feed and eluent.

All the twenty-two thermocouples were linked to a twenty-four point selector unit which was linked to the digital indicator.

The unit used an ice reference as the datum level. Figure (6.13) shows the network of thermocouples and its control.

6.5 THE HEATING DEVICES AND CONTROLS

Since the reconstruction of the original unit, a more refined heating system was built in to the pilot unit; the heating tapes on the columns were replaced by a constant temperature enclosure with some fibre glass lagging over the separation section.



KEY: • THERMOCOUPLE POINTS

FIG. 6.13 SCHEMATIC DIAGRAM OF THE THERMOCOUPLE NETWORK

The pre-heater for the feed before entering the separation section was replaced by a glass column (2.54 cm I.D.) with heating tapes linked to a fine control unit. A similar pre-heated column was also installed for the eluent.

The sections to follow describe briefly all these heating devices and controls as more detailed descriptions are available from C.B. Ching[24] and manufacturer manuals[65-71].

6.5.1 THE ISOMANTLE

The isomantle was a $60 \times 10^3 cm^3$ aspirator jacketed with two electric heaters, one of 5.0 kW (the booster) and inside a glass protrusion which went beneath the liquid level, two-thirds distant from the centre. The thermostat was set at $65^{\circ}C$ and linked to the 2.0 kW heater.

A Fisons pressure-sensitive liquid level controller was used to maintain the level, however there was a level lag between activating and deactivating the level controller. This had the effect of a volume lag and hence temperature variation due to the heat required to bring the temperature of that volume to the set point. The variation was as much as $\pm 5^{\circ}C$ on $65^{\circ}C$, observed throughout the course of the experiment.

6.5.2 THE PRE-HEATERS FOR THE ELUENT AND FEED

These were glass columns (2.54 cm I.D.) from the original pilot unit wrapped with tape heaters adapted as heating columns. The tape heaters were linked to a fine temperature controller built by M. Lea, Chemical Engineering Department, Aston University[68].

These pre-heated columns were fitted to help the viscous liquid feed to move along the process line before entering the heated enclosure.

6.5.3 THE CONSTANT TEMPERATURE ENCLOSURE

This was effectively a box structure built over the separation section. Its dimensions were 200 cm high, 140 cm long and 140 cm wide.

It was constructed from five slabs of galvanised steel sheets and lagged with 50.0 mm thickness glass fibre pads. The pads were held into place by screws onto the main structural support of the separation section.

The corners were covered by overlapping steel sheets to minimise heat lost.

The heater was a U-shaped fin device supplied by Eltron Ltd of Ealing, London and it had a power output of 5.0 kW.

Temperature was measured by a nickel-chrome thermocouple linked to a proportional digital

controller supplied by Diamond Control Ltd, East Anglia.

An air temperature of up to 80°C was possible inside the enclosure, with variation of less than 1°C recorded on the twelve columns.

C H A P T E R S E V E N

DETERMINATION OF THE CHARACTERISTIC OF THE CONVERTED ZEROLIT RESIN IN THE PACKED COLUMN

7.1 INTRODUCTION

The SCCR4 unit used a calcium-hydrogen charged zerolit 225 SRC 14 resin as a chromatographic adsorbant.

The selection of this resin was based on past successful work by Ching and Barker[24] in their research on the separation glucose and fructose mixtures. It was also based on the lower price of the zerolit resin as compared to other very much more expensive resins; a large quantity of the resin was also required for a similar larger 10.16 cm diameter unit being built in the laboratory. Other resins considered were amberlite CG-120, Dowex 5WX4, Lewatit-SP120 and zerolit macroporous types.

The original purchased form of the zerolit 225 SRC14 resin was sodium charged. Conversion to the calcium hydrogen charged forms was performed in the laboratory by first displacing the sodium ions with hydrogen free ions and then subsequently displacing the hydrogen ions by calcium ions. It was reported[35, 108-110] that at room temperature between 1-30% of the hydrogen free ions were still retained after treatment of the resin.

Sixteen batches in equal volume of the resin (360 cm^3) were extracted from the main bulk by means of a sample-splitting device. Fourteen of the sixteen batches were subject to the conversion treatment to

the calcium-hydrogen forms; detailed procedure for the treatment was published by the manufacturer[176] and Ching[24]. The remaining two batches were dried and sieve analysed.

This chapter will review the experiments and the findings of the characteristic of the converted zerolit resin and its physical property.

7.2 EXPERIMENT WITH THE CALCIUM CHARGED ZEROLIT RESIN PACKED IN AN ANALYTICAL GLASS COLUMN AND A 2.54 cm I.D. STAINLESS STEEL COLUMN

7.2.1 EXPERIMENT WITH THE CALCIUM CHARGED ZEROLIT RESIN PACKED IN A GLASS COLUMN

The aim of these experiments was to acquire the basic information regarding the performance of the converted resin under various temperature and elution rates.

The performances of the resin were evaluated by the effects of the conditions on the equilibrium factor and the on-column dispersion represented by the distribution coefficients and the height equivalent of a theoretical plate (HETP).

The basic parameters involved were the elution volumes of dextran 5, glucose and fructose for the determination of the distribution coefficients; and the retention time and peak height for the column efficiency.

7.2.1.1 DETERMINATION OF THE COEFFICIENTS OF DISTRIBUTION

From the model of J.J. Kirkland[47], it was established that the fundamental retention equation for a chromatographic process was

$$V_R = V_m + K_D V_s \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (7.1)$$

Rearranging equation (7.1), the distribution coefficient, K_D, becomes a function of the elution volumes.

$$K_D = \frac{V_R - V_m}{V_s} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (7.2)$$

where

V_R = retention volume of the component

V_m = total volume of mobile phase in the column
= void volume

V_s = volume of solid stationary phase (the resin's solid matrix

For a matrix containing a very large molecular size specie and two isomeric species passing through a calcium charged packed bed in a column, two modes of chromatography must be considered, namely gel permeation and chemi-adsorption; the former affecting separation between Dextran 5 (the large molecules) and glucose and fructose (isomeric-species), and the latter affecting separation between glucose and fructose by chemical complexing.

In practice, Dextran 5 would emerge initially, followed by glucose and finally fructose from a calcium charged packed bed, when a sample containing the three carbohydrates was eluted.

By definition,

K_d = equilibrium distribution coefficient

$$= \frac{\text{amount of solute in the stationary phase}}{\text{amount of solute in the mobile phase}}$$

and applying the definition to a dextran, glucose and fructose mixture: glucose which was retained by diffusing into the pores of the resin beads had a K_{dg} value represented by

K_{dg} = equilibrium coefficient of distribution of glucose

$$= \frac{V_g - V_d}{V_t - V_d} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (7.3)$$

Fructose which was retained by diffusing into the pores of the resin beads, as well as by calcium complexing reaction had a K_{df} value represented by

K_{df} = equilibrium coefficient of distribution of fructose

$$= \frac{V_f - V_d}{V_T - V_d} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (7.4)$$

V_f = elution volume of fructose

V_g = elution volume of glucose

V_d = elution volume of dextran

V_T = total volume of the column without the packing

$$V_m = V_d$$

$$V_s = V_T - V_m$$

hence

$$V_s = V_T - V_d$$

Equations (7.3) and (7.4) must also apply when a binary mixture of fructose and glucose was used.

7.2.1.2 DETERMINATION OF ON-COLUMN DISPERSION

This was evaluated by the column efficiency, i.e. number of theoretical plates per column. The values were calculated from the chromatograms obtained for dextran, glucose and fructose. For a Gaussian Peak

$$N = 8\left(\frac{t_R}{W_{h'/e}}\right)^2 \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (7.5)$$

t_R = Peak retention time of the component

$W_{h'/e}$ = width of the component peak at the height of h/e

h = height of the component peak

The corresponding H.E.T.P. values were

$$H.E.T.P. = \ell/N$$

where ℓ = length of packed column section

TABLE. 7.1 GLASS COLUMN - ANALYTICAL APPROACH TO CHROMATOGRAPHY

EFFECT OF TEMPERATURE ON COLUMN EFFICIENCY AND THE DISTRIBUTION COEFFICIENTS

TEMPERATURE	ELUTION VOLUMES			NUMBER OF PLATES			DISTRIBUTION COEFFICIENTS Kd	
	DEXTRAN	GLUCOSE	FRUCTOSE	DEXTRAN	GLUCOSE	FRUCTOSE	GLUCOSE $Kd = \frac{Vg - Vd}{Vt - Vd}$	FRUCTOSE $Kd = \frac{Vf - Vd}{Vt - Vd}$
°C	mls	mls	mls	plates	plates	plates		
25	33.08	44.63	63.53	435	147	107	0.332	0.875
33	33.60	46.20	61.95	412	204	131	0.368	0.827
40	34.13	46.20	61.95	433	245	188	0.358	0.825
50	34.13	47.25	59.85	390	248	226	0.389	0.762
65	33.60	44.63	56.70	425	274	257	0.322	0.674

GLASS COLUMN - 1.14 cms. (INNER DIAMETER) ; BED HEIGHT - 66.5 cms.

SAMPLE SIZE 250 µls. CONCENTRATION 1000 ugms./ml

ELUTING RATE 0.42 mls/min

7.2.1.3 EXPERIMENT PROCEDURE

7.2.1.3.1 EFFECTS OF TEMPERATURE ON THE DISTRIBUTION COEFFICIENTS AND THE COLUMN EFFICIENCIES

A 250 µl sample containing Dextran 5, having a concentration of 1000 µgms/ml (p.p.m.) was eluted through the glass column packed with the calcium charged zerolit 225 SRC 14 resin. A constant elution rate of 0.42 cm^3/min was used and the water jacket temperature was 25°C.

Separate samples of glucose and fructose were eluted through the column at similar conditions.

The procedure was repeated at water jacket temperatures of 33°C, 40°C, 50°C and 65°C.

Tables (7.1) and (7.3a) show the variation of the distribution coefficients of glucose and fructose and on column dispersions represented by the height equivalent of a theoretical plate (H.E.T.P.) with temperature.

7.3.1.3.2 EFFECTS OF FLOWRATE ON THE DISTRIBUTION COEFFICIENTS AND THE COLUMN EFFICIENCIES

A 250 µl sample containing Dextran 5, having a concentration of 1000 µgms/ml (p.p.m.) was eluted through a glass column packed with calcium charged resin. The water jacket temperature was kept constant at 20°C and the elution rate was 0.1 cm^3/min.

Separate samples of glucose and fructose were

also eluted through the column under similar conditions.

The procedure was repeated at elution rates of 0.1, 0.42, 0.60, 0.83, 1.40, 1.60 and 2.04 cm^3/min.

Tables (7.2) and (7.3b) show the variation of the distribution coefficients for glucose and fructose and the on-column dispersions of dextran 5, glucose and fructose, represented by the height equivalent of a theoretical plates (H.E.T.P.) with different eluent flowrates.

7.2.1.4 RESULTS AND DISCUSSIONS

7.2.1.4.1 EFFECT OF TEMPERATURE ON H.E.T.P. AND Kds

It was found that at a higher jacket temperature around the column the plate efficiency of the packed column improved when dextran 5, glucose and fructose were passed through it.

As shown in Table (7.1) and (7.3a), and Figure (7.1), it appeared that fructose was the most sensitive to the temperature, the H.E.T.P. value decreasing from 0.62 cm at 25°C, to 0.322 cm at 65°C. This increase in plate efficiency was possibly due to the increased rates of diffusion and complexing with the calcium ions on the active site around and in the pores of the resin bed.

Since glucose and fructose were isomers, the differences in the H.E.T.P. values with temperature was due mainly to the complexing effect of fructose with

TABLE 7.2 GLASS COLUMN- ANALYTICAL APPROACH TO CHROMATOGRAPHY

EFFECTS OF FLOWRATE ON COLUMN EFFICIENCY AND THE DISTRIBUTION COEFFICIENTS

ELUENT FLOWRATES mls/min	ELUTION VOLUME			NUMBER OF PLATES			DISTRIBUTION COEFFICIENTS Kd	
	DEXTRAN mls	GLUCOSE mls	FRUCTOSE mls	DEXTRAN plates	GLUCOSE plates	FRUCTOSE plates	GLUCOSE $Kd=\frac{Vg}{Vt}\frac{Vd}{Vd}$	FRUCTOSE $Kd=\frac{Vf}{Vt}\frac{Vd}{Vd}$
0.10	30.75	41.75	60.75	803	275	105	0.290	0.808
0.42	31.50	39.90	58.27	429	130	86	0.231	0.735
0.60	31.50	40.50	57.75	254	110	60	0.247	0.722
0.83	31.25	40.46	57.14	208	89	48	0.252	0.712
1.40	33.25	43.75	56.00	138	61	32	0.303	0.657
1.60	32.83	42.00	55.55	126	56	25	0.262	0.648
2.04	32.83	40.40	55.55	116	45	22	0.216	0.648

GLASS COLUMN 1.14 cm. (INNER DIAMETER: BED HEIGHT - 66.5 cm

SAMPLE SIZE 250 µl CONCENTRATION 1000 µgm/ml

TEMPERATURE 20°C

TABLE 7.3a GLASS COLUMN ANALYTICAL APPROACH TO CHROMATOGRAPHY

EFFECTS OF TEMPERATURE ON THE H.E.T.P. AND Kds

TEMPERATURE °C	HEIGHT EQUIVALENT OF A THEORETICAL PLATE (H.E.T.P.)			DISTRIBUTION COEFFICIENTS Kds	
	DEXTRAN plates	GLUCOSE plates	FRUCTOSE plates	GLUCOSE $Kd = \frac{Vg - Vd}{Vt - Vd}$	FRUCTOSE $Kd = \frac{Vf - Vd}{Vt - Vd}$
25	0.153	0.452	0.621	0.332	0.875
33	0.161	0.326	0.507	0.368	0.827
40	0.154	0.271	0.354	0.358	0.825
50	0.171	0.268	0.294	0.389	0.762
65	0.156	0.243	0.259	0.322	0.672

TABLE 7.3b

EFFECTS OF ELUENT FLOWRATE ON THE H.E.T.P. AND Kds

FLOWRATES ml/min	HEIGHT EQUIVALENT OF A THEORETICAL PLATE (H.E.T.P.)			DISTRIBUTION COEFFICIENTS Kds	
	DEXTRAN plates	GLUCOSE plates	FRUCTOSE plates	GLUCOSE $Kd = \frac{Vg - Vd}{Vt - Vd}$	FRUCTOSE $Kd = \frac{Vf - Vd}{Vt - Vd}$
0.10	0.083	0.453	0.621	0.290	0.808
0.42	0.155	0.512	0.772	0.231	0.735
0.60	0.262	0.604	1.108	0.247	0.722
0.83	0.319	0.747	1.385	0.252	0.712
1.40	0.480	1.090	2.293	0.303	0.657
1.60	0.527	1.188	2.660	0.262	0.648
2.04	0.573	1.478	3.023	0.216	0.648

the calcium ions.

Dextran, which was a polymeric chain of glucose of many thousands, did not have the capability of penetrating the pores of the resins is merely slipped through the interstitial space between the beads. The effects of temperature was confined to the resistance of flow of the dextran through the void in between the resin beads under dilute conditions. In Figure (7.1), it showed that the H.E.T.P. value of dextran 5 remained approximately constant at 0.16 cm.

The coefficient of distribution of fructose, kd_f decreased from 0.875 to 0.672 as the temperature around the packed column increased from 25°C to 65°C. This indicated that, at a higher temperature, less fructose was being retained on the stationary phase, as most of it was carried along with the mobile phase. This undesirable effect was aggrevated by the reduced bonding strength between the fructose and the calcium ions on the active sites, see Figure (7.2).

As with the glucose, the distribution coefficient, kd_g, taken with respect to the dextran, did not appear to be affected by temperature. It remained approximately constant at 0.38. Thos was so because glucose was only slightly retained by the packing, through diffusion of glucose molecules into the pores. Besides most of the glucose was carried along in the mobile phase.

FIG. 7.1 GLASS COLUMN (1.14 cms I.D.)

H.E.T.P. VERSUS TEMPERATURE

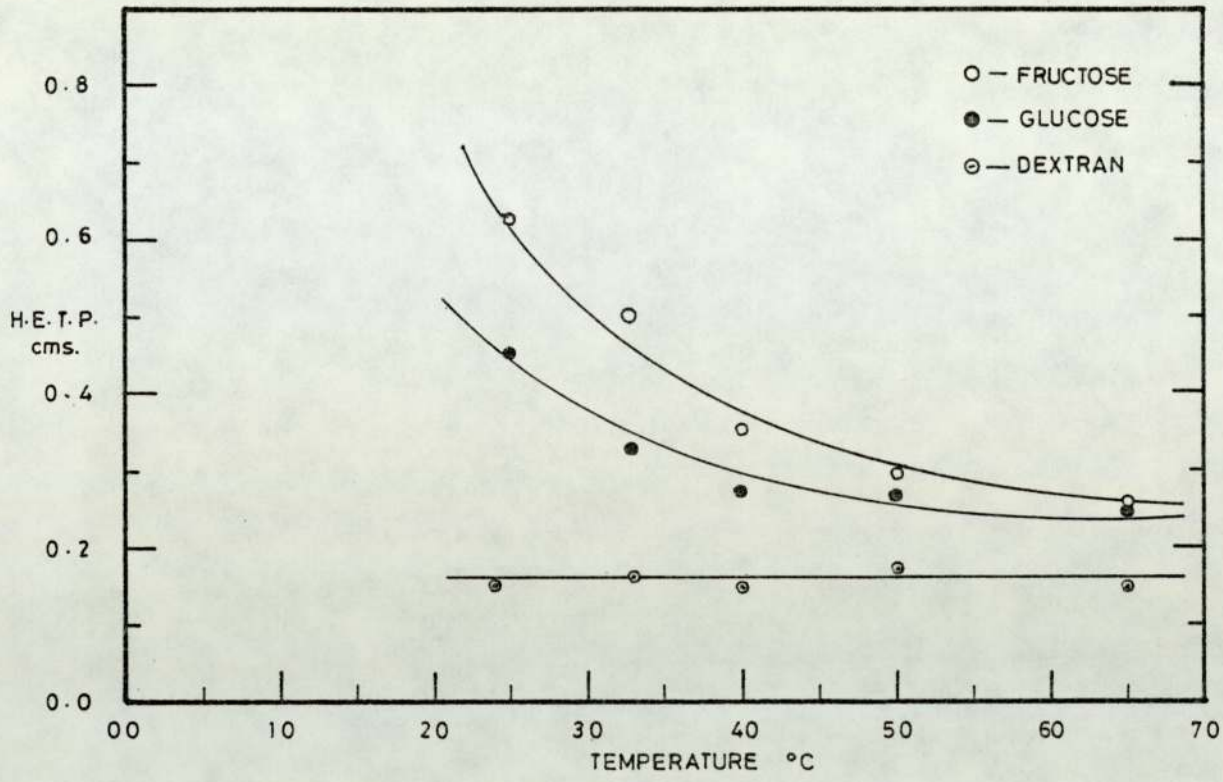
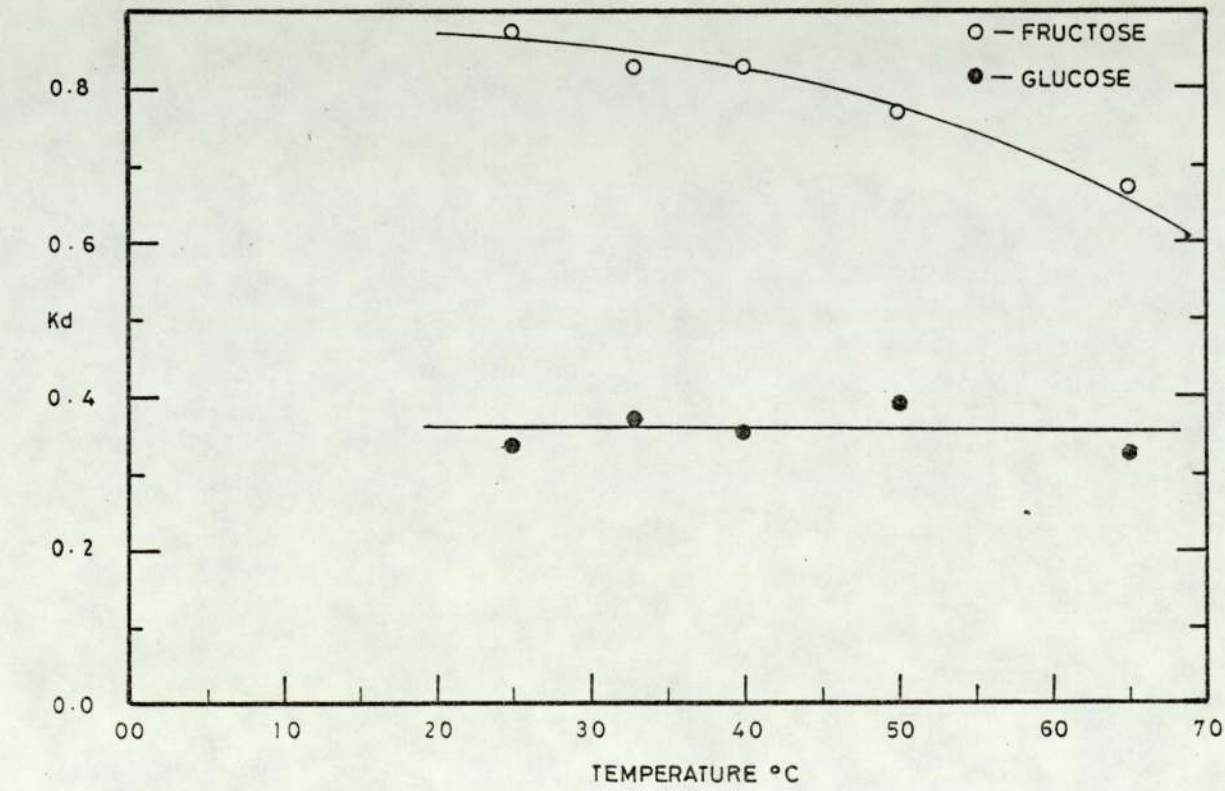


FIG. 7.2 DISTRIBUTION COEFFICIENTS VERSUS TEMPERATURE



7.2.1.4.2 EFFECTS OF FLOWRATE ON THE H.E.T.P. VALUES AND THE Kds

At an increased flowrate, longitudinal diffusion of the material dominated the distribution of the carbohydrate components. The plate efficiency for the dextran, the glucose and the fructose components decreased as seen in Tables (7.2) and (7.3b), and Figure (7.3).

Again, the effect of flowrate on the H.E.T.P. value of fructose was most apparent compared to the glucose and the dextran H.E.T.P. values. This happened because, at a high mobile phase flowrate, most of the fructose was carried along in the mobile phase. The retention of the fructose on the packed bed by complexing with the calcium ions was followed swiftly by the desorption of the fructose from the packed bed by the continuing fresh desorbent.

Similarly, the glucose and the dextran were mixed along the bed in the mobile phase.

The Kdf values decreased for the same reason stated above, figure (7.4).

Table (7.4) showed the characteristic of the fourteen batches converted to the calcium charged form for use in the SCCR4 unit. Table (7.5) tabulated the results obtained from the sieve analysis.

FIG 7.3 GLASS COLUMN (1·14 I.D.)
H.E.T.P. VERSUS FLOWRATE

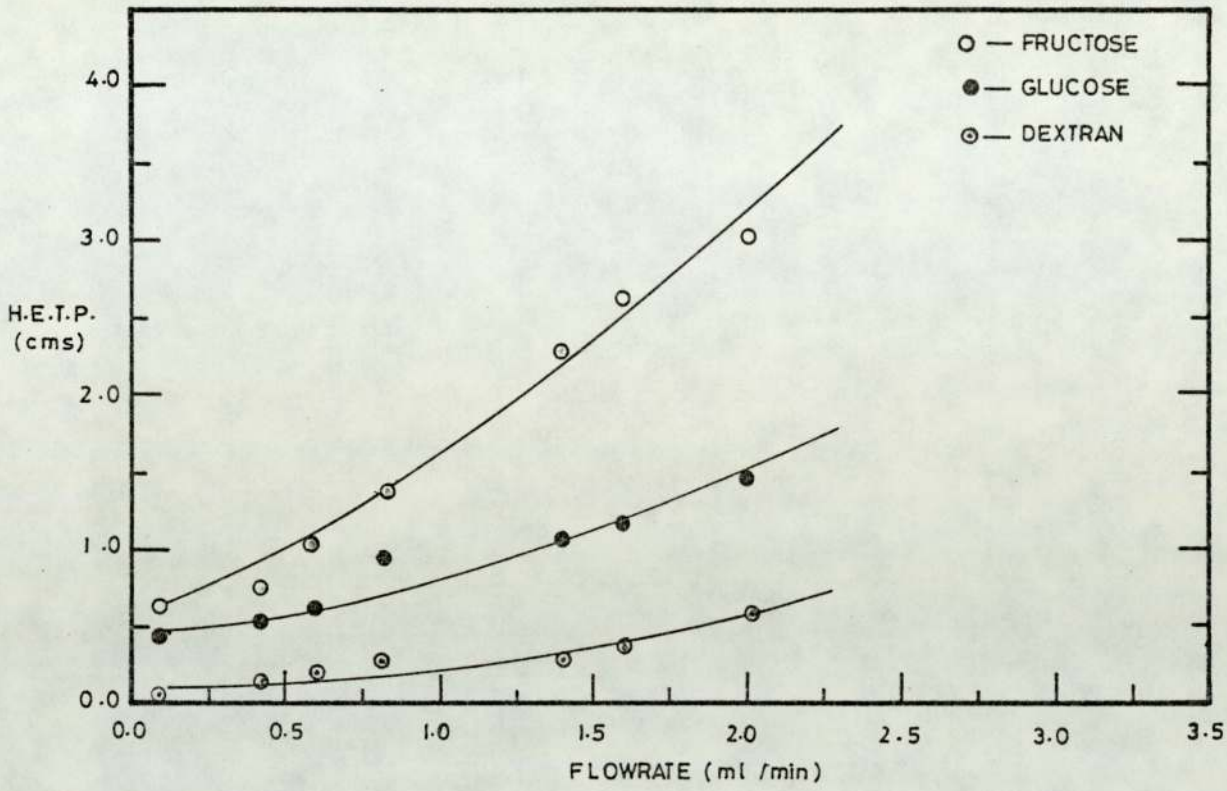


FIG. 7.4 DISTRIBUTION COEFFICIENTS VERSUS FLOWRATE

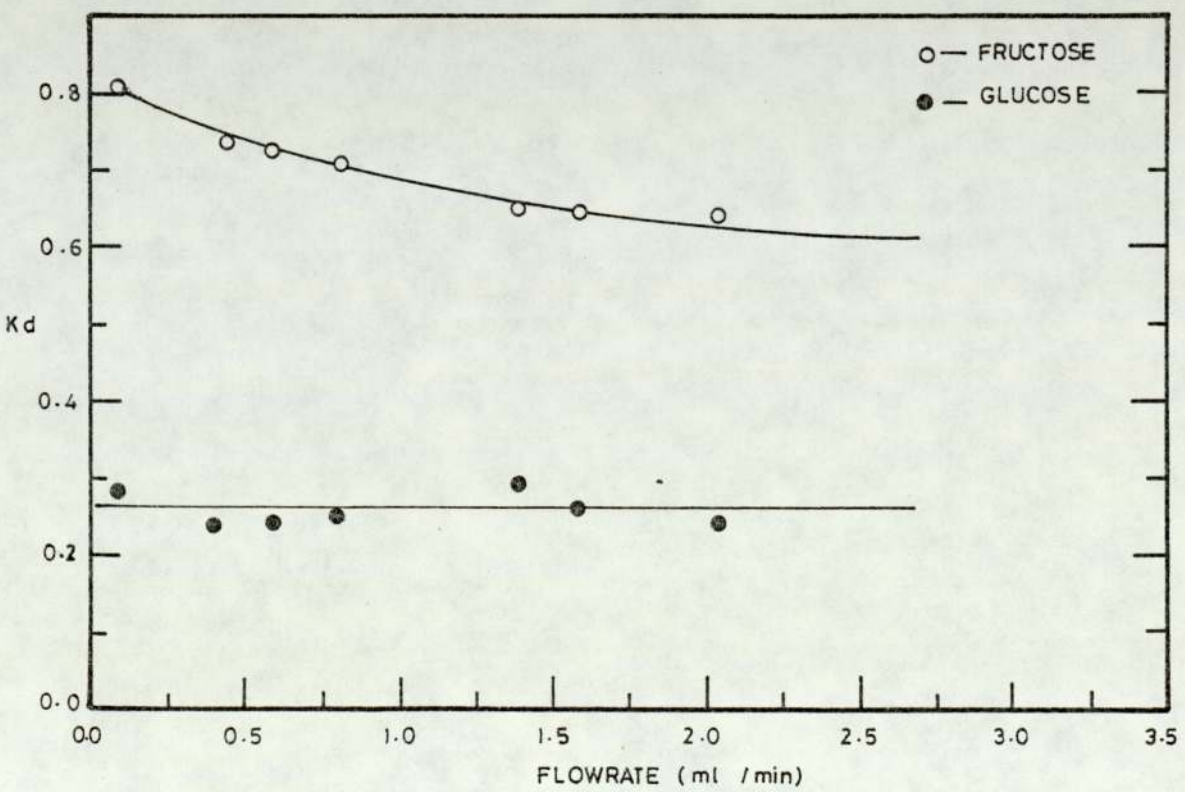


TABLE 7.4 PERFORMANCES OF THE RESIN BATCHES

BATCH NUMBERS	ELUTION VOLUMES		NUMBER OF PLATES		DISTRIBUTION COEFFICIENT $Kdg = \frac{Vf - Vg}{Vt - Vg}$	RESOLUTION TERM Rs.
	GLUCOSE Vg mls.	FRUCTOSE Vf mls.	GLUCOSE plates	FRUCTOSE plates		
1	44.10	66.15	135	99	0.990	0.960
2	41.47	60.37	149	140	0.776	1.080
3	39.90	59.33	112	80	0.749	0.925
4	40.43	60.38	120	106	0.801	0.980
5	40.43	58.28	130	86	0.717	0.893
6	40.95	60.38	123	99	0.780	0.980
7	42.53	60.90	146	84	0.806	0.870
8	43.58	62.48	165	117	0.830	0.97
9	41.48	59.33	158	105	0.733	1.095
10	42.00	60.90	137	146	0.810	1.030
11	42.00	60.90	157	111	0.776	0.990
12	42.00	60.90	160	111	0.776	0.980
13	42.53	61.43	163	122	0.810	0.990
14	43.58	63.00	180	113	0.870	1.040

EQUIPMENTS USED :- GLASS COLUMN 1.14 cms (I.D) X 65 cms BED HEIGTH

ELUTION RATE 0.42 mls per min

SAMPLE SIZE - 200.0 µl ; CONCENTRATION - 1000 µgms/ml

TABLE 7.5 SIEVE ANALYSIS OF TWO RESIN BATCHES

MICRONS	MESH NUMBERS	MASS FRACTION $\times 10^{-3}$	
		SAMPLE I	SAMPLE II
1204	14	0.570	0.560
355	44	1.100	1.100
295	52	2.900	2.780
251	60	8.300	7.800
210	72	17.000	15.600
180	85	679.000	658.000
150	100	212.000	224.000
125	120	53.000	53.000
105	150	18.300	22.000
89	170	6.300	10.560
75	200	—	—
64	240	—	—

7.2.2 EXPERIMENT WITH THE CALCIUM CHARGED ZEROLIT RESIN PACKED IN A 2.54 cm I.D. STAINLESS STEEL COLUMN

Table (7.7) and Figures (7.6) and (7.7) showed the effects of eluent flowrate on the H.E.T.P. and Kds values.

A decrease in column efficiency with respect to dextran glucose and fructose was observed, as indicated by the increase in H.E.T.P. values.

However, the values for the distribution coefficient for fructose were scattered about the value of 0.63. This could be largely due to the less well formed flow pattern and the back-mixing effect on a larger diameter column (2.54 cm I.D.) as compared to the glass column (1.14 cm I.D.).

THe distribution coefficient of glucose Kdg remained approximately constant at a value of 0.25.

Table (7.8) also shows the characteristic of the twelve stainless steel columns packed with the calcium charged zerolit 225 SRC 14 resin.

7.3 SUMMARY OF THE EXPERIMENTS

The effect of temperature on the performance of the zerolit resin was such as to cause an increase in the efficiency of the columns (both glass and stainless steel) but to decrease the distribution of the

TABLE 7.6 STAINLESS STEEL COLUMN

EFFECTS OF FLOWRATES ON COLUMN EFFICIENCY AND THE DISTRIBUTION COEFFICIENTS

FLOWRATES mls/min	ELUTION VOLUME			NUMBER OF PLATES			DISTRIBUTION COEFFICIENTS Kd	
	DEXTRAN mls	GLUCOSE mls	FRUCTOSE mls	DEXTRAN plates	GLUCOSE plates	FRUCTOSE plates	GLUCOSE $Kd = \frac{Vg - Vd}{Vt - Vd}$	FRUCTOSE $Kd = \frac{Vf - Vd}{Vt - Vd}$
2.02	114.25	159.07	227.25	91	67	44	0.218	0.549
2.49	114.00	168.80	225.00	84	55	38	0.266	0.684
3.49	122.75	174.50	261.75	82	51	42	0.262	0.705
4.79	119.75	167.65	245.49	60	42	33	0.239	0.628
6.41	136.21	176.27	264.41	49	34	21	0.218	0.697
7.13	114.25	160.43	240.64	41	29	17	0.224	0.614

STAINLESS STEEL COLUMN 2.45cms (INNER DIAMETER) BED HEIGHT 66.5 cms

SAMPLE SIZE 2.0 mls CONCENTRATION 1000 ugms/ml

TEMPERATURE 20 °C

TABLE 7.7 STAINLESS STEEL COLUMN (2.54 cms I.D.)

EFFECTS OF FLOWRATES ON H E T P AND THE DISTRIBUTION COEFFICIENTS

FLOWRATES mls/min	HEIGHT EQUIVALENT OF THEORITICAL PLATES (H.E.T.P.)			DISTRIBUTION COEFFICIENTS Kd	
	DEXTRAN cms	GLUCOSE cms	FRUCTOSE cms	GLUCOSE $Kd = \frac{Vg - Vd}{Vt - Vd}$	FRUCTOSE $Kd = \frac{Vf - Vd}{Vt - Vd}$
2.02	0.731	0.993	1.511	0.218	0.549
2.49	0.792	1.209	1.750	0.266	0.684
3.49	0.810	1.304	1.583	0.262	0.705
4.79	1.108	1.583	2.015	0.239	0.628
6.41	1.357	1.956	3.167	0.218	0.697
7.13	1.622	2.293	3.912	0.224	0.614

FIG. 7.5 FLOW DIAGRAM OF EXPERIMENTAL SET-UP

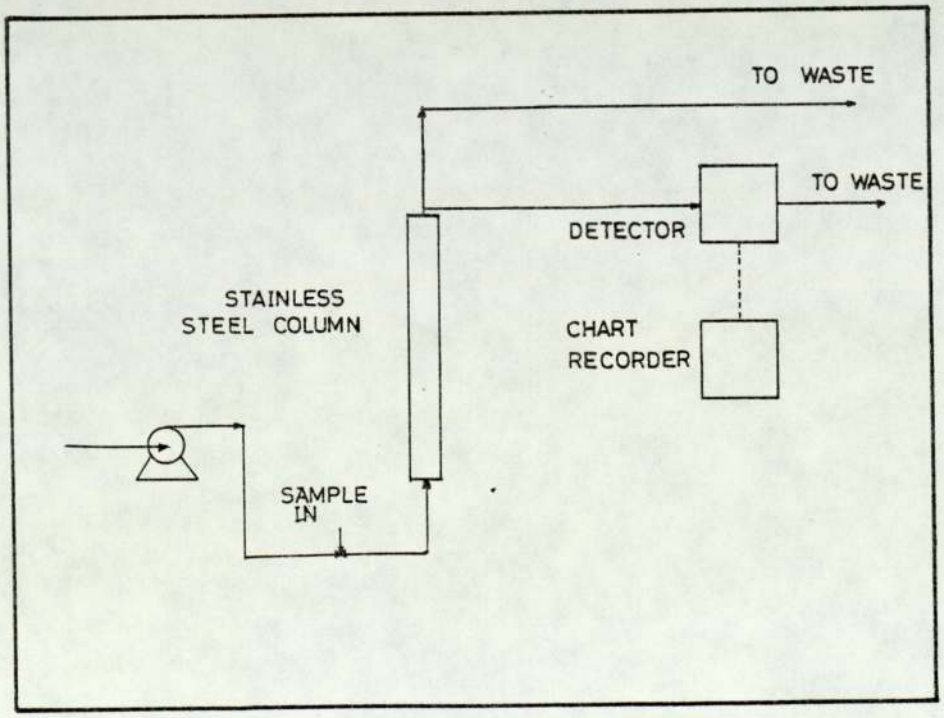


FIG. 7.6 STAINLESS STEEL COLUMN (2.54 cm I.D.)

H.E.T.P. VERSUS FLOWRATE

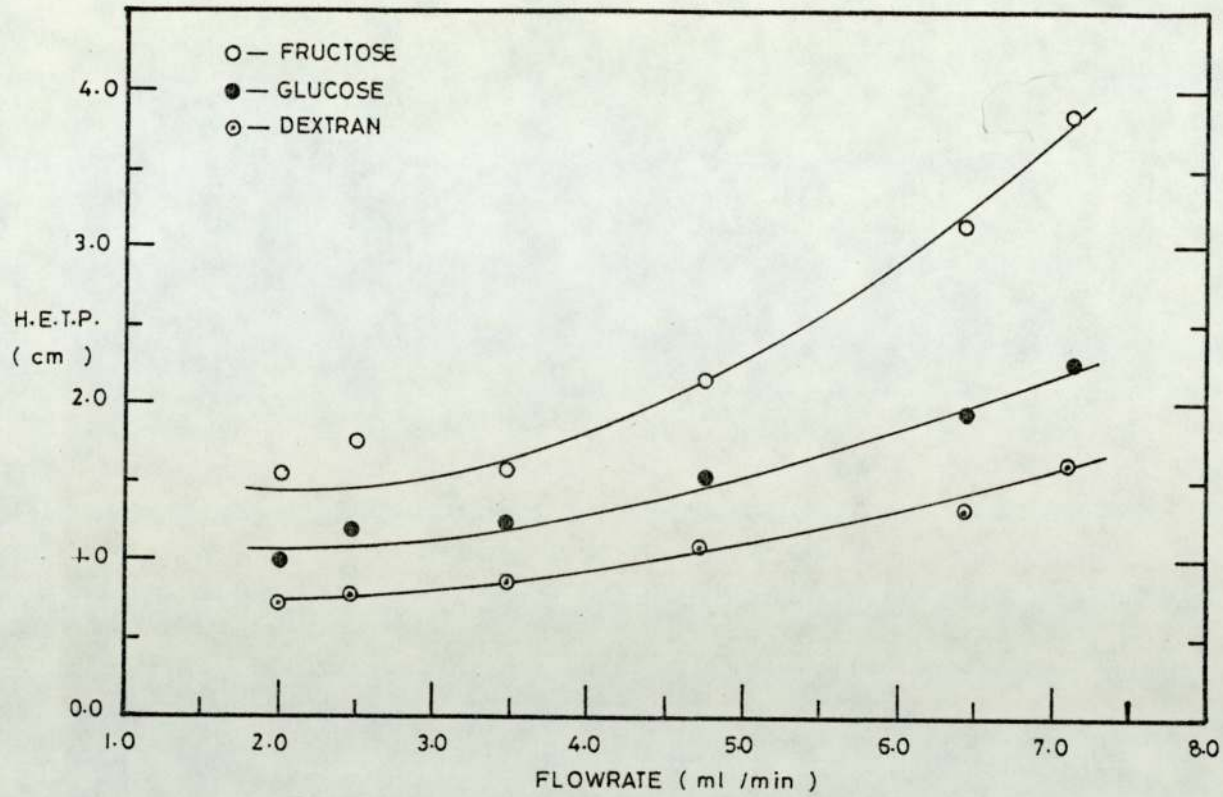


FIG. 7.7 DISTRIBUTION COEFFICIENTS VERSUS FLOWRATE

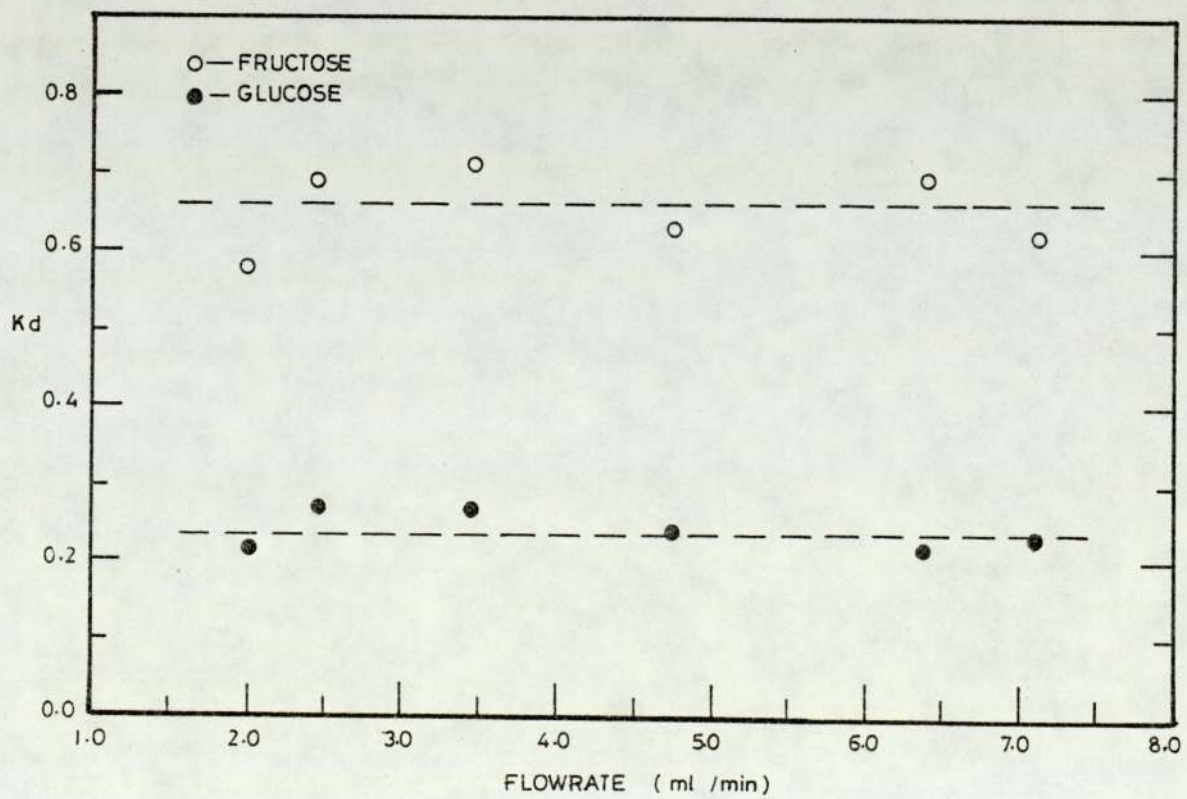


TABLE 7.8 COLUMN CHARACTERISTICS

COLUMN NOS.	ELUTION VOLUMES			NUMBER OF PLATES			HEIGTH EQUIVALENT OF THEORITICAL PLATE			DISTRIBUTION COEFFICIENTS	
	DEXTRAN mls	GLUCOSE mls	FRUCTOSE mls	DEXTRAN plates	GLUCOSE plates	FRUCTOSE plates	DEXTRAN cms	GLUCOSE cms	FRUCTOSE cms	GLUCOSE Kdg	FRUCTOSE Kdf
1	138.83	184.00	253.00	42	34	24	1.57	1.94	2.75	0.253	0.640
2	128.79	184.00	260.65	42	32	26	1.57	2.06	2.54	0.292	0.697
3	145.66	184.00	260.65	46	31	25	1.46	2.16	2.68	0.216	0.649
4	145.66	184.00	260.65	46	31	23	1.44	2.14	2.89	0.216	0.649
5	138.83	184.00	260.65	41	32	24	1.61	2.06	2.75	0.253	0.683
6	138.00	184.00	253.00	42	33	21	1.57	2.00	3.14	0.257	0.642
7	138.00	168.65	260.65	42	34	25	1.57	1.94	2.64	0.171	0.684
8	138.00	184.00	268.32	42	31	29	1.57	2.23	2.27	0.256	0.727
9	145.66	184.00	260.65	42	36	26	1.57	1.83	2.54	0.223	0.670
10	153.33	184.00	275.98	41	33	28	1.61	2.00	2.36	0.183	0.749
11	138.83	184.00	260.65	42	33	23	1.58	2.08	2.89	0.249	0.672
12	138.00	184.00	299.00	41	33	30	1.62	2.02	2.22	0.253	0.884

carbohydrates on the stationary phase and mobile phase, favouring the mobile phase at high temperatures. This effectively moved the fructose fraction closer to the glucose fraction with a result of greater overlapping of the two fractions. Dextran and glucose were less affected by the temperature.

The effects of increasing the eluent flowrate was deterimental to the performances of the resin in the glass and the stainless steel columns.

At a higher flowrate, the plate efficiency and the coefficient of distribution of the sugars decreased.

C H A P T E R E I G H T

CONTINUOUS OPERATION OF THE S.C.C.R.4 UNIT

8. CONTINUOUS OPERATION OF THE S.C.C.R.4 UNIT

It has been successfully demonstrated by Ching and Barker[24] that a ten column SCCR4 unit was able to separate a 50% (w/w) mixture containing equal portions of glucose and fructose into 90% plus pure products. A maximum throughput of 90 gms per hour of sugar was achieved at a recovery efficiency of better than 90%, for both the glucose and fructose. However, the highest concentration of solid in the fructose rich product contained only 0.2% (w/w) solid and approximately 8.0% (w/w) of solid in the glucose rich product.

Like many other chromatographic processes, the SCCR4 unit required a large volume of desorbent for the separation of the carbohydrates and for the purging off of the retained solute in the isolated section. The ratio of desorbent to feed used by Ching[24] in his work was as follows: 3 volumes of desorbent to 1 volume of feed in the separation section, and as much as 150 volumes of desorbent to 1 volume of feed in the purging section. The products obtained from the SCCR4 unit were low in solid concentration and would require several evaporation stages to concentrate the products to 70% (w/w) solutions. This excess volume of desorbent would entail a higher operating cost in the evaporating stages and an extra capital cost for fabricating the larger

equipment. It is therefore necessary to reduce the volume of the desorbent required both in the separation section and the purging section, if the SCCR4 unit is to be operated in an economically attractive process.

As mentioned in Chapter One, part of this research is devoted to the study of the operational mode of the improved SCCR4 unit. Included amongst the objectives are:

1. to find the best operating conditions under which a maximum throughput of sugar can be achieved, with
   (i) the highest concentration of solid in the products
   (ii) the highest purity in the fructose rich product
2. to obtain a dextran-free fructose rich product from a dextran contaminated feed
3. to find an alternative source of fructose such as hydrolysed sucrose to supplement the Fisons feed should this be necessary

In the following sections, the operating procedure for the SCCR4 unit will be initially outlined. This is followed by an experimental study on the SCCR4 unit using a 50% (w/w) solution of glucose/fructose. In this study various run parameters and different liquid flow arrangements will be used. Next, an artificial Fisons feed and a Fisons feed will be used on the SCCR4 unit in an attempt to obtain a dextran-free

fructose rich product. Finally, sucrose will be hydrolysed in a hydrogen charged ion exchange packed bed, and the inverted syrup separated in the SCCR4 unit.

8.1 PROCEDURE FOR THE OPERATION OF THE SCCR4 UNIT

Prior to each of the experimental runs, a check list of preparation had to be carried out. This consisted of feed-preparation, eluent storage and an equipment check.

8.1.1 FEED PREPARATION

All the artificial feed used in the experiment was prepared by dissolving calculated quantities of pure laboratory grade carbohydrates in warmed deionised water. The carbohydrates were glucose and fructose, supplied respectively by the B.D.H. Chemical Company and the Kinsley-Keith Company in 99.9% pure grade. Refined grade Dextran 5 was provided by the Pharmaceutical Division of Fisons Ltd, Holmes Chape, Cheshire.

Usually a 2×10^{-2} m^3 (20 litres) batch of feed was prepared; enough for a minimum of 60 hours continuous operation. The solid composition of the glucose/fructose and the artificial Fisons feeds were as follows.

Glucose/Fructose Feed	Artificial Fisons Feed
50% - fructose	69% fructose
50% - glucose	9% glucose
50%(w/w) solution	22% dextran
	70% (w/w) solution

A toxic preservative, sodium azide (NaN_3) was used to prevent micro-organism growth in the feed at a concentration of 0.02% w/v) as recommended by the Fisons Company. The feed was then stored in a 3.0×10^{-2} m^3 aspirator, after being thoroughly mixed to ensure that a homogeneous mixture was obtained.

Finally, the feed was usually prepared with in the 12 hours prior to the commencement of the run.

8.1.2 ELUENT PREPARATION

The eluent or desorbent was deionised water. The tap water from the Birmingham City supply was passed through a portacell deioniser and the effluent stored in a 1.2 m^3 plastic tank. Approximately, 4.0×10^{-2} m^3 of this deionised water was continuously heated in an isomantle at a temperature of $60^{o}C$. From the isomantle the eluent and the purge streams were withdrawn for use in the SCCR4 unit.

8.1.3 EQUIPMENT CHECK

8.1.3.1 PRESSURE TESTING

The SCCR4 unit was designed to work at a nominal pressure of 1.68×10^3 kNm^{-2}. Depending on the feed used, and its concentration, 'normal' working pressure did not exceed 1.02×10^3 kNm^{-2} (150 psi) at the highest pressured point in the unit, usually on the eluent line after the pump. The feed line pressure was normally half the eluent line pressure, and the purge line pressure was limited by a relief valve set at 272 kNm^{-2} (40 psi).

Pressure testing of the unit involved blocking off all the liquid outlets. Gradual pressure build up in the system was achieved by pumping liquid into the unit at low flowrates. Three stages of pressure testing were normally performed at 340 kNm^{-2} (50 psi), 680 kNm^{-2} (100 psi) and 1.02×10^3 kNm^{-2} (150 psi). At each of these pressure stages, the pressure in the unit was maintained and a leak check was carried out.

Leakages were usually from the plastic connections and the moving-part of the valves. These were easily cured by tightening and by replacing the defective parts.

8.1.3.2 FLOWRATE MEASUREMENT

Flowrates for the feed, the eluent and the purge streams were measured at the inlets to the pumps and checked by measuring the volume of liquids collected at the outlet. Care was taken to ensure that the outlet points were higher than the inlet points, to eliminate the effect of gravity on the liquid flowrate.

8.1.3.3 HEATING EQUIPMENT

When the experiment was to be carried out at an elevated temperature, the heating sources and the temperature sensing devices were checked. This was done by setting the temperature of the enclosure at the required level and allowing it to reach a steady state. Following this, the temperature of each of the twelve columns were measured by means of a thermo-couple placed on the mid-section of the column outside wall. The heating system was considered satisfactory if the columns temperature did not differ more than $2^{o}C$. Usually, a difference of $1^{o}C$ was detected across the twelve columns.

8.1.3.4 PNEUMATIC CONTROL

This has been the most reliable part of the unit, due mainly to the simplicity of the operating mechanism. Nevertheless, constant maintenance and inspection were

were carried out to ensure that it was in good working order. Amongst the equipment inspected were the timer, the rotating cam mechanism and the line connections.

8.1.4 START-UP PROCEDURE

Safety arrangements were made for the continuous operation of the departmental air compressor and the SCCR4 unit.

The heaters on the isomantle and in the enclosure were switched on and allowed to reach a steady level. When this had been achieved, the pumps were switched on and the SCCR4 unit was in full operation.

All the run parameters were pre-determined by methods which will be reviewed in detail in the later sections.

A pseudo-steady state was reached when the unit had been operating for three complete cycled, consisting of twelve switchings in each cycle. The period of each switch was set depending on the operating parameters; a switch period of between 30 minutes and 120 minutes was used.

8.1.5 SHUT-DOWN PROCEDURE

At the end of each experiment, the pumps were switched off to relieve the pressure in the system. This was performed at the end of each cycle and not

allowed to overlap into the next. Following this, the air and the electrics were switched off and the product outlet closed.

8.1.6 SAMPLE COLLECTION DURING A RUN

When the SCCR4 unit was operating at a pseudo-steady state, two samples were collected; a fructose rich product and a glucose or dextran rich product for each complete cycle. Collection of these samples began after three undisturbed cycles had been completed, as past experiments have shown that repeatable results were obtained from the poroducts collected after the first three cycles. Bulk samples for each cycle were collected in large containers.

At the end of the run, each column in the unit was isolated and purged with fresh water, the contents collected and analysed for the system profile.

8.1.7 ON-LINE SAMPLING

On-line sampling points were provided in between columns and on the feed line inlet.

8.2 EXPERIMENTAL STUDY OF THE SCCR4 UNIT WITH A GLUCOSE/FRUCTOSE FEED

In this study, the operational mode of the SCCR4 unit was investigated. A glucose/fructose feed was

used for the reason that, it would serve as a difficult test for the separating system, as glucose and fructose were isomers. Also it was a binary mixture which made it easier to monitor the distribution of the sugars across the separating section.

Various liquid flowrates, switch periods and flow configurations were investigated, and the objectives were:

(1) maximum throughput of sugar

(2) highest purity in the products

(3) highest solid concentration in the products

8.2.1 THEORETICAL METHOD FOR SELECTING THE RUN PARAMETERS

Barker and workers[1-5] had developed a theoretical method for selecting run parameters. In their method, the equilibrium distribution factors were related to a dimensionless ratio of the effective mobile phase flowrate and the stationary phase flowrate:

$$K_{d_1} < L/P < K_{d_2} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (8.1)$$

L = effective mobile phase flowrate

P = effective stationary phase flowrate

K_{d_1}, K_{d_2} = distribution coefficients of component 1 and component 2 respectively

The L/P factor was dependant of the eluent flowrate, the feed flowrate and the switch period. If one

of the independent variables was altered, such that the L/P ratio was computed to be equal or less than K_{d_1}; no separation was achieved, as component 1 and component 2 were left behind in the separating section. In the other extreme, that is it was equal or more than K_{d_2}, both component 1 and component 2 were eluted from the separating section. An L/P ratio in between the two limits gave a separation of the two components. Firm experimental evidences were reported by Barker and Lloyd [3-5] from their work with a gas-liquid chromatographic system.

More recently, this theoretical method has been used for selecting run parameters in a liquid-liquid and a liquid-solid chromatographic systems[21-23, 24, 26]. As a guide, it also proved to be as equally successful in selecting run parameters, as the results from Ellison's, Ching's and England's work[21-23, 24, 26] showed. However at higher concentration levels in the apparatus the K_d values are effected by concentration and since this effect has not been quantified we can only use equation 8.1 as an approximate guide.

Another approach towards the development of a basically similar theoretical method for selecting run parameters was as follows:

This method used the fundamental properties of the stainless-steel chromatographic column as found in the batch experiments reported in Chapter 7. Consider a slug of carbohydrate mixture containing dextran 5,

glucose and fructose being eluted through the calcium charged packed bed inside the column. Dextran 5 emerged initially, followed by glucose and then finally fructose. Figure (8.1) shows a typical chromatogram.

Suppose dextran has an elution volume of V_d, glucose V_g and fructose V_f. Overlapping of glucose and fructose occurred more severely than that between dextran and glucose. In order to separate fructose from glucose, the selected elution volume V, must have a value between V_g and V_f, hence

$$V_g < V < V_f \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (8.2)$$

$$V_g < L.t < V_f \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (8.3)$$

L = elution rate

t = retention time

but from equation (7.3) and (7.4)

$$K_{D_g} = \frac{V_g - V_d}{V_t - V_d} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (7.3)$$

$$K_{d_f} = \frac{V_f - V_d}{V_t - V_d} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (7.4)$$

$$V_g = K_{D_g}(V_t - V_d) + V_d \quad \ldots\ldots\ldots\ldots\ldots \quad (8.4)$$

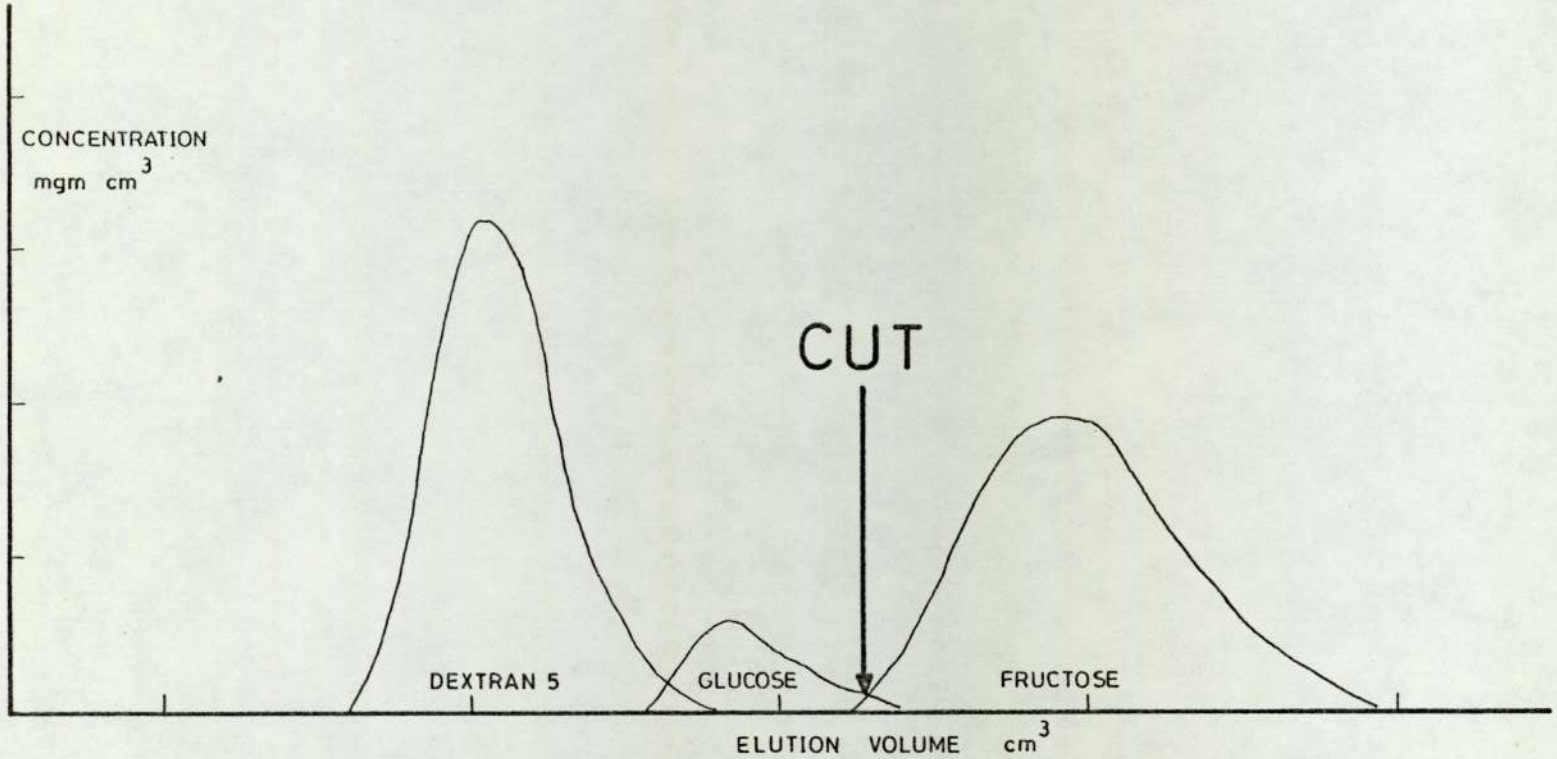
$$V_f = K_{D_f}(V_t - V_d) + V_d \quad \ldots\ldots\ldots\ldots\ldots \quad (8.5)$$

Substituting equation (8.4) and (8.5) into equation (8.3)

$$K_{D_g}(V_t - V_d) + V_d < L.t < K_{D_f}(V_t - V_d) + V_d \quad .. \quad (8.6)$$

$$K_{dg} + \frac{V_d}{(V_t - V_d)} < \frac{L.t}{(V_t - V_d)} < K_{d_f} + \frac{V_d}{(V_t - V_d)} \quad .. \quad (8.7)$$

FIG. 8.1 EXAMPLE OF A CHROMATOGRAM OF THE ARTIFICIAL FISONS FEED



Now $V_s = V_t - V_d$ ..... (8.8)

$$P = \frac{V_s}{t} = \frac{(V_t - V_d)}{t} \quad \text{..... (8.9)}$$

$$V_d = V_m \quad \text{..... (8.10)}$$

Substituting (8.9) and (8.10) into (8.7)

$$K_{d_g} + \frac{V_m}{(V_s)} < \frac{L}{P} < K_{d_f} + \frac{V_m}{V_s} \quad \text{..... (8.11)}$$

$$K_{d_g} + \frac{V_m \cdot t}{V_s \cdot t} < \frac{L}{P} < K_{d_f} + \frac{V_m \cdot t}{V_s \cdot t} \quad \text{..... (8.12)}$$

where

$L_m = \frac{V_m}{t}$ = actual mobile phase flowrate

rearranging equation (8.13)

$$K_{d_g} < \frac{L - L_m}{P} < K_{d_f} \quad \text{..... (8.14)}$$

or $K_{d_g} < \frac{L'}{P} < K_{d_f}$ ..... (8.15)

$L' = L - L_m$ = effective mobile phase flowrate

L = eluent flowrate

For a system, like the SCCR4, where there were two liquid entry ports, see figure (8.2)

$$K_{d_g} < \frac{L_1'}{P} < \frac{L_2'}{P} < K_{d_f} \quad \text{..... (8.16)}$$

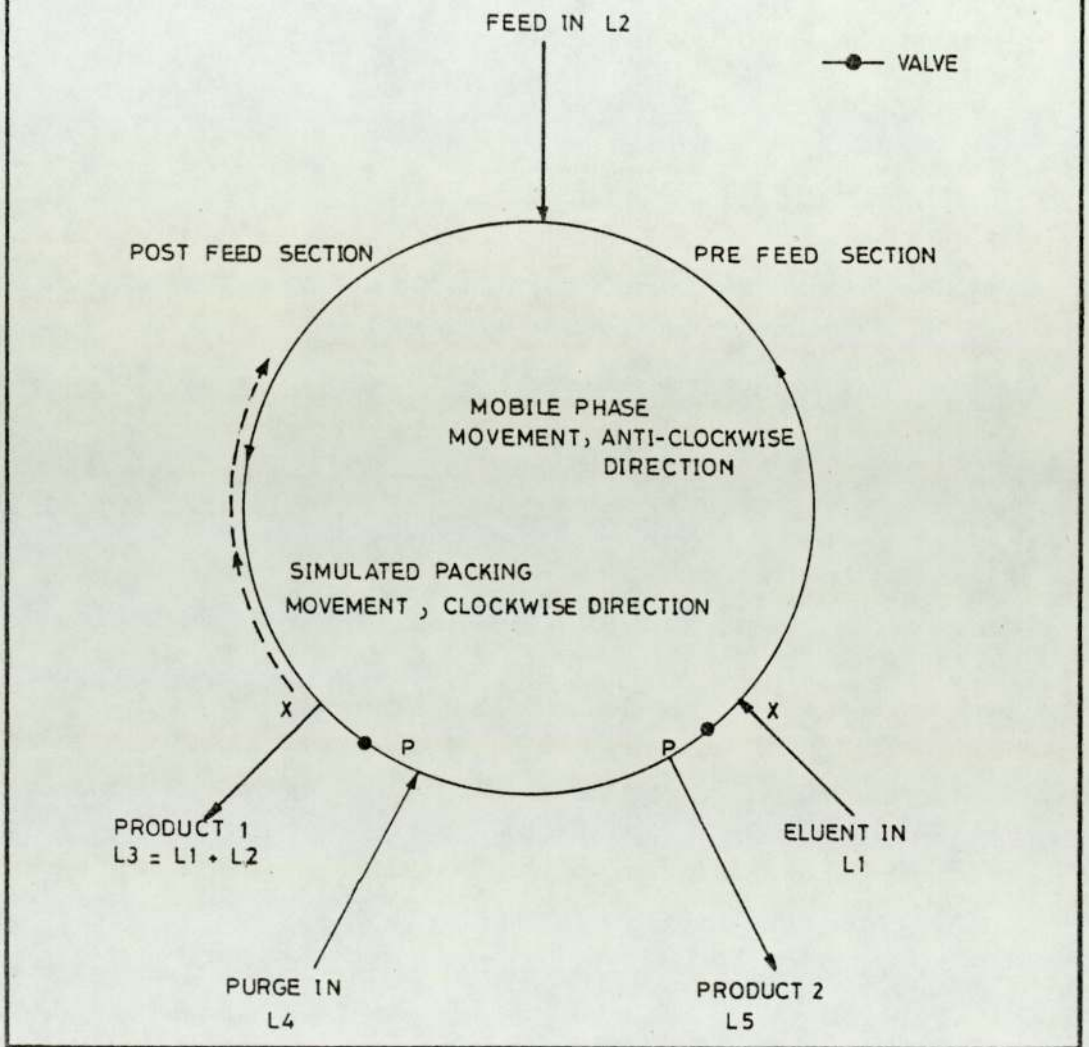
$L_1' = L_1 - L_m$ = effective mobile flowrate in the pre-feed section

$L_2' = L_2 - L_m$ = effective mobile flowrate in the post-feed section

For an insignificant feed flowrate as compared to eluent flowrate

$$K_{d_g} < \frac{L_1}{P} < K_{d_f} \quad \text{..... (8.17)}$$

FIG. 8.2 SCHEMATIC DIAGRAM OF THE S.C.C.R.4 UNIT



X-X SEPARATION SECTION P-P PURGE SECTION

PRODUCT 1 – GLUCOSE DEXTRAN RICH PRODUCT 2 - FRUCTOSE RICH

otherwise

$$K_{d_g} < \frac{L'mean}{P} < K_{d_f} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (8.18)$$

$$L'mean = \frac{(L_1' + L_2')}{2}$$

As found from the batch experiments with the stainless steel chromatographic column, the two limits were

$$K_{d_g}(0.15) < \frac{L'mean}{P} < K_{d_f}(0.66) \quad \ldots\ldots\ldots \quad (8.19)$$

or $V_g(180\ cm^3) < L.t(6x30)\ cm^3 < V_f(256\ cm^3)$ (8.20)

L = eluent flowrate (6 $cm^3 min^{-1}$)

t = switch period (30 min)

As seen in equation (8.19), the L/P ratio must not be less than a K_{d_g} value of 0.15 and not exceed a K_{d_f} value of 0.66. It must be emphasised that these K_{d_g} and K_{d_f} values were obtained under infinite dilution conditions and may not be true at higher concentration.

In equation (8.20), it suggested that a final volume of eluent in a switch period must be more than 180 cm^3, which was the elution volume of glucose. Hence, it followed that elution of glucose from the column occurred when the eluent volume exceeded 180 cm^3. Separation of glucose from fructose took place along the entire length of the 11-column separation section, even though each column (65 cm packed bed height) length was not long enough to resolve glucose and fructose into separate fractions.

The theoretical method as described by equations (8.19) and (8.20) was applied in the experiments for selecting run parameters. The independant variables, eluent rate and the switch period were altered in various experiments, but the total eluent volume per switch was kept approximately to 180 cm^3.

8.2.2 EXPERIMENTAL CONDITIONS

A total of six experiments were performed using a glucose-fructose mixture. Various conditions and flow-arrangements were used.

The assigned run number was as written

1 - 2 - 6 - 30 - 30

the first digit denoted the experiment number, the second and the third digits indicated the feed and eluent flowrates (cm^3/min) respectively. These were followed by the temperature (^oC) and the switch period indicators (minutes).

8.2.2.1 EFFECT OF VARYING FEED RATE

8.2.2.1.1 INTRODUCTION

This group of experiments used different feed flowrates of 2.0, 2.5 and 3.0 $cm^3\ min^{-1}$. The eluent flowrate was constant at 6 $cm^3 min^{-1}$, temperature at 30^oC and switch period at 30 minutes.

The object of this exercise was to find the highest throughput of a 50% (w/w) glucose-fructose mixture at which the SCCR4 unit could handle.

The features to note were as follows:

(i) fructose purity, % (w/w) in the fructose rich stream (F.R.S.)

(ii) glucose purity, % (w/w) in the glucose rich stream (G.R.S.)

(iii) fructose recovery, i.e. fructose recovered in the fructose rich stream with respect to the total fructose input, % (w/w)

(iv) solid concentration in the fructose rich stream and glucose rich streams

(v) the end-of-run system profiles

The feed used in these experiments consisted approximately of 25% (w/w) fructose nad 25% glucose in 50% (w/v) of solid. The desorbent used was deionised water.

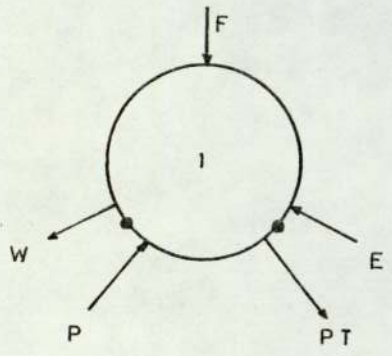
Flow arrangement (1) in Figure (8.3) was used in the three runs.

8.2.2.1.2 RESULT AND DISCUSSION

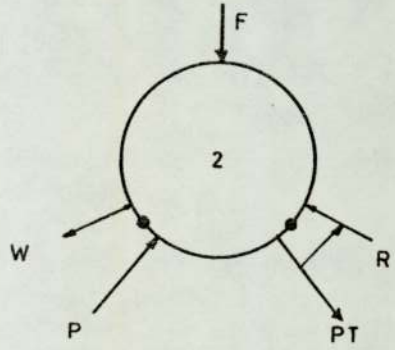
The conditions and the result of these three experiments were as tabulated in Table (8.1) and (8.2), the system profile in FIgure (8.4), (8.5) and (8.6).

The fructose purity in the fructose rich stream

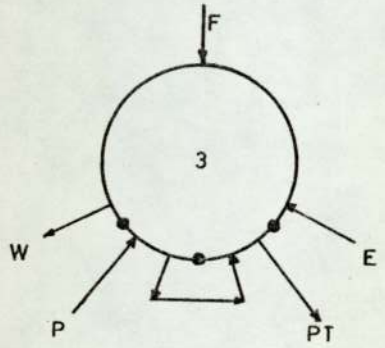
ONE COLUMN LOCKED - ONCE THROUGH ARRANGEMENT



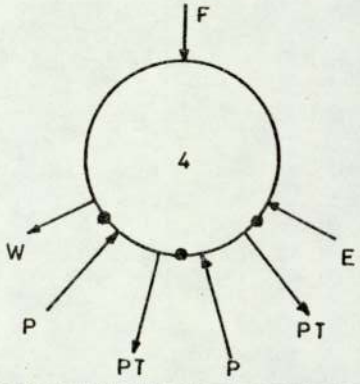
ONE COLUMN LOCKED - WITH RECYCLE - ONCE THROUGH ARRANGEMENT



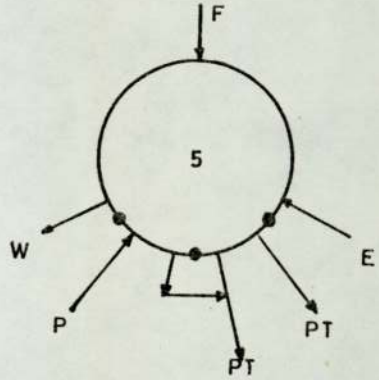
TWO COLUMNS LOCKED - IN SERIES - ONCE THROUGH ARRANGEMENT



TWO COLUMNS LOCKED - IN PARALLEL - ONCE THROUGH ARRANGEMENT



TWO COLUMNS LOCKED - IN SEMI PARALLEL - ONCE THROUGH ARRANGEMENT



TWO COLUMNS LOCKED - IN PARALLEL - WITH RECYCLE ARRANGEMENT

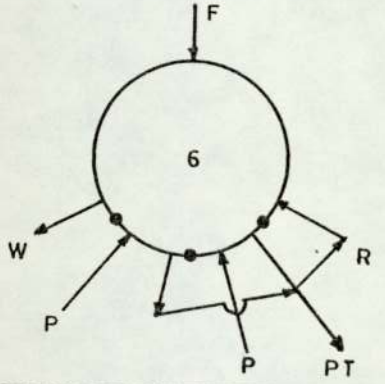


FIG. 8.3 —●— CLOSED VALVE F - FEED E - ELUENT P - PURGE PT - PRODUCT W - WASTE R - RECYCLE

DIFFERENT FLOW ARRANGEMENTS USED TO INVESTIGATE THE PERFORMANCES OF THE S.C.C.R. 4

was approximately 91.0% (w/w) in all the three runs.

The fructose recovery or recovery efficiency for run 1-2-6-30-30 and run 1-2.5-6-30-30 was approximately 90% (w/w), but for run 3-3-6-30-30, the recovery efficiency fell to approximately 84% (w/w) with respect to the total fructose input. This indicated that at 3.0 $cm^3 min^{-1}$, the SCCR4 unit was overloaded with sugars.

The glucose purity in the glucose rich stream (G.R.S.) was approximately 90% (w/w) for run 1-2-6-30-30 and 2-2.5-6-30-30. As for run 3-3-6-30-30 the glucose purity in the same stream decreased to approximately 86% (w/w). This happened because of the excess fructose eluted from the separating section due to the overloading of the SCCR4 unit with the sugars.

The solid concentration in the glucose rich stream increased with the increased feed rate, from 7.25% to 7.76% and 9.58% (w/w). In the fructose rich stream, the solid concentration in run 1-3-6-30-30 and 3-3-6-30-30 was approximately 0.21% (w/w), this was due to the excess purge water (300 cm^3 run^{-1}) used to elute the fructose off the isolated section of the bed length. The reason for the use of this excess purge water was as a precautionary measure to make certain that all the fructose and glucose was purged off the isolated section.

At the end of run 1-2-6-30-30, the column rich with fructose was isolated and then purged with 30 $cm^3 min^{-1}$ of water. Spot samples were taken at five minute

interval through a switch period of 30 minutes. The result of these experiment was as shown in Figure (8.8). It could be seen that almost all the fructose and glucose was purged off the column after fifteen minutes into the switch period. The volume of purge water used during the fifteen minute period corresponded to 450 cm^3.

These findings led to the reduction of the purge rate to 30 $cm^3 min^{-1}$ in the later run 2-2.5-6-30-30. The solid concentration in the fructose rich stream increased ten fold to 2.13% (w/w).

The system profiles for run 1-2-6-30-30 and 2-2.5-6-30-30, Figure (8.4) and (8.5) had different features.

1. The highest average fructose concentration in a column was 330 mg cm^{-3}.
2. The 'cross-over' point of the glucose profile and the fructose profile was at the position of the feed column.
3. Distinct separation of the fructose and the glucose components at both the pre-feed and the post-feed sections.
4. Accumulation of fructose in the post-feed section due to the hold-up volumes in the process line and the poppet valve.

The system profile of run 3-3-6-30-30 Figure (8.6) was not as developed as the other runs in the group. The heighest average fructose concentration in a column increased to 400 mg cm^{-3} and the 'cross-over'

TABLE 8.1 RUN CONDITIONS

RUN NUMBER	FLOWRATE			CONCENTRATION		SWITCH	ELUENT VOL.
	FEED	ELUENT	PURGE	FRUCTOSE	GLUCOSE	PERIOD	PER SWITCH
	$cm^3 min^{-1}$			$mg\ cm^{-3}$		min	cm^3/switch
1-2-6-30-30	2.0	6.0	300.0	260.0	260.0	30.0	180.0
2-2.5-6-30-30	2.5	6.0	30.0	270.0	260.0	30.0	180.0
3-3-6-30-30	3.0	6.0	300.0	270.0	260.0	30.0	180.0

TABLE 8.2 RESULTS

RUN NUMBER	F-RICH PRODUCT CONC.		G-RICH PRODUCT CONC.		F-RICH PRODUCT PURITY		G-RICH PRODUCT PURITY		SUGAR IN F-RICH STREAM		MASS BALANCE (OUT/IN)		SOLID IN STREAM	
	F	G	F	G	F	G	F	G	F	G	F	G	FRP	GRP
	$mg\ cm^{-3}$		$mg\ cm^{-3}$		%		%		%		%		%	
1-2-6-30-30	1.86	0.11	8.62	63.86	91.09	10.40	11.85	89.51	91.20	9.61	103.31	99.12	0.21	7.25
2-2.5-6-30-30	19.5	1.85	6.30	71.26	91.34	8.66	8.12	91.88	90.46	8.38	98.89	98.17	2.13	7.76
3-3-6-30-30	2.62	0.27	12.47	83.32	90.58	9.41	13.05	86.94	83.39	8.81	97.0	98.42	0.29	9.58

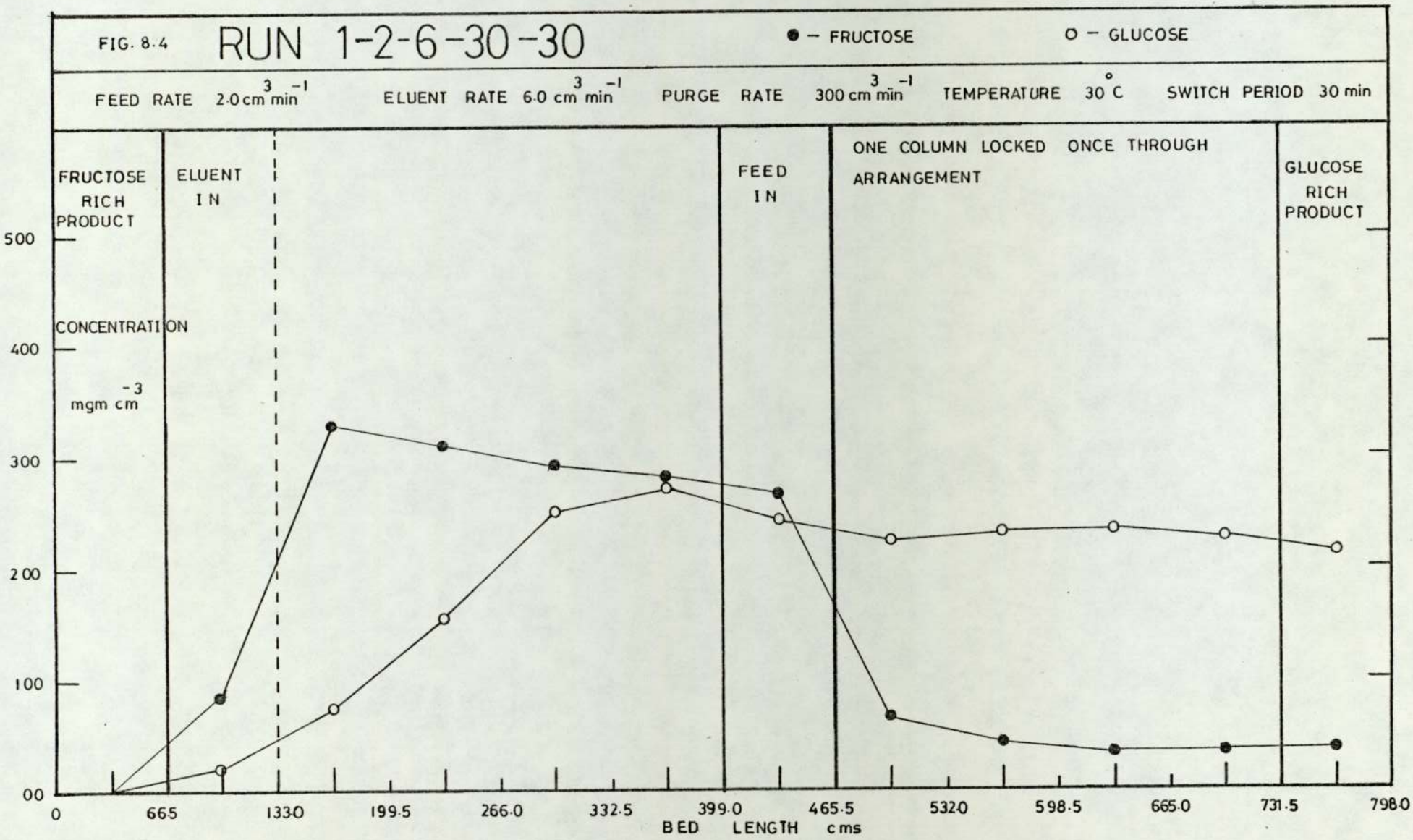


FIG. 8.4 RUN 1-2-6-30-30
● – FRUCTOSE
O – GLUCOSE
FEED RATE 2.0 cm³ min⁻¹
ELUENT RATE 6.0 cm³ min⁻¹
PURGE RATE 300 cm³ min⁻¹
TEMPERATURE 30 °C
SWITCH PERIOD 30 min
FRUCTOSE RICH PRODUCT
ELUENT IN
FEED IN
ONE COLUMN LOCKED ONCE THROUGH ARRANGEMENT
GLUCOSE RICH PRODUCT
CONCENTRATION
mgm cm⁻³
500
400
300
200
100
00
0
66.5
133.0
199.5
266.0
332.5
399.0
465.5
532.0
598.5
665.0
731.5
798.0
BED LENGTH cms

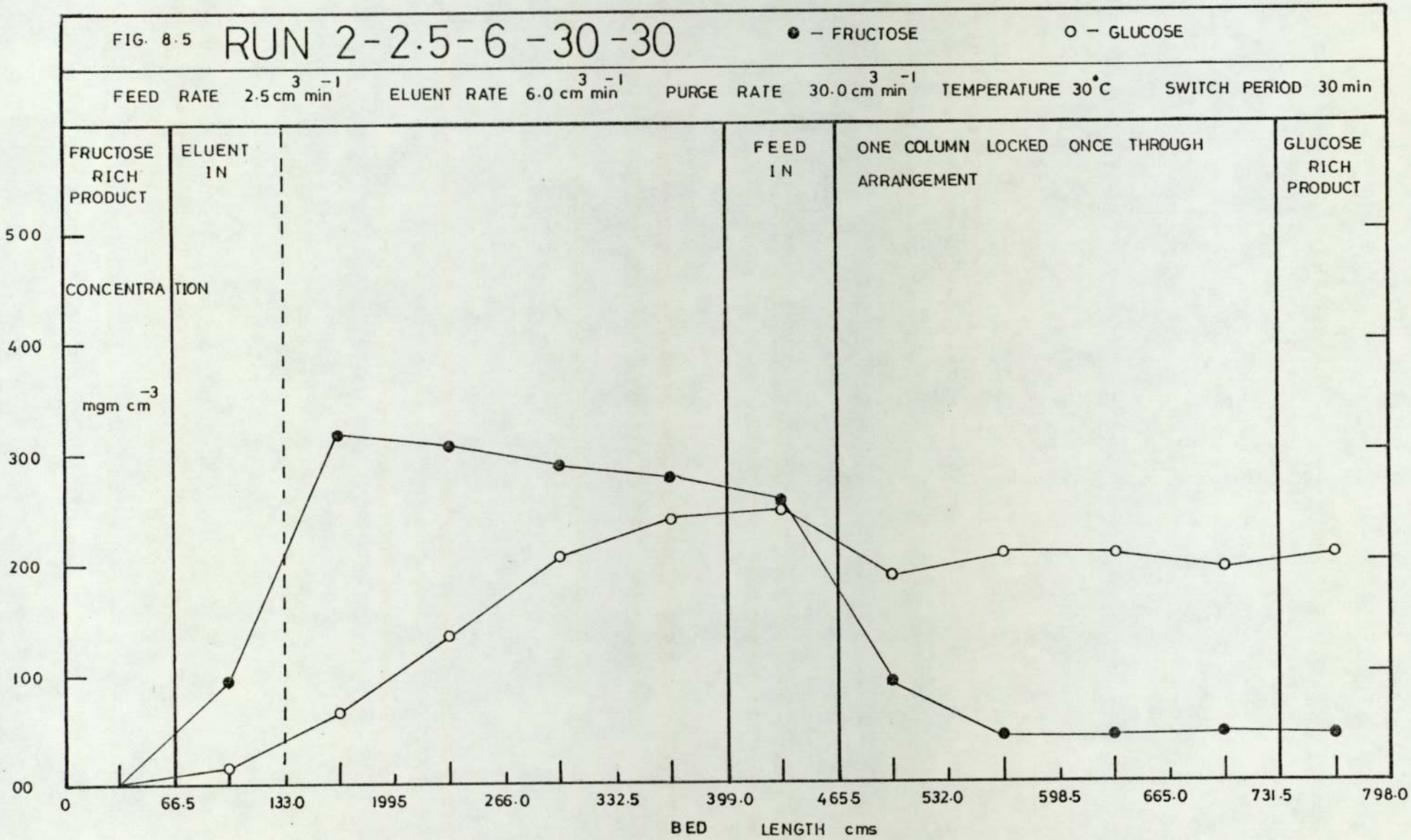


FIG. 8·5 RUN 2-2·5-6 -30 -30
● – FRUCTOSE
O – GLUCOSE
FEED RATE 2·5 cm³ min⁻¹
ELUENT RATE 6·0 cm³ min⁻¹
PURGE RATE 30·0 cm³ min⁻¹
TEMPERATURE 30°C
SWITCH PERIOD 30 min
FRUCTOSE RICH PRODUCT
ELUENT IN
FEED IN
ONE COLUMN LOCKED ONCE THROUGH ARRANGEMENT
GLUCOSE RICH PRODUCT
CONCENTRATION
mgm cm⁻³
500
400
300
200
100
00
0
66·5
133·0
199·5
266·0
332·5
399·0
465·5
532·0
598·5
665·0
731·5
798·0
BED LENGTH cms

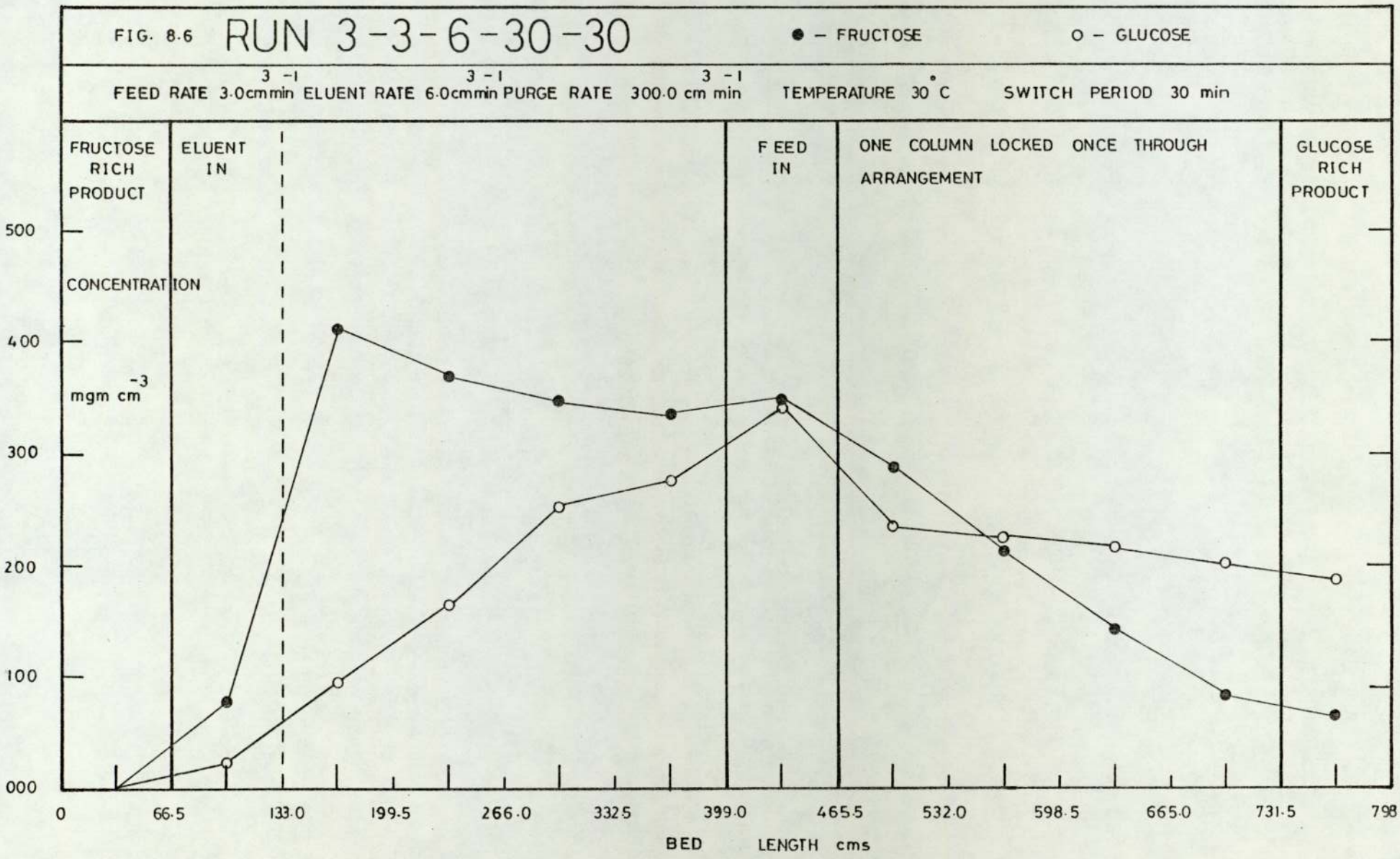


FIG. 8.6 RUN 3-3-6-30-30
● – FRUCTOSE
O – GLUCOSE
FEED RATE 3.0cm³min⁻¹ ELUENT RATE 6.0cm³min⁻¹ PURGE RATE 300.0 cm³ min⁻¹ TEMPERATURE 30° C SWITCH PERIOD 30 min
FRUCTOSE RICH PRODUCT
ELUENT IN
FEED IN
ONE COLUMN LOCKED ONCE THROUGH ARRANGEMENT
GLUCOSE RICH PRODUCT
CONCENTRATION
mgm cm⁻³
500
400
300
200
100
000
0
66.5
133.0
199.5
266.0
332.5
399.0
465.5
532.0
598.5
665.0
731.5
798
BED LENGTH cms

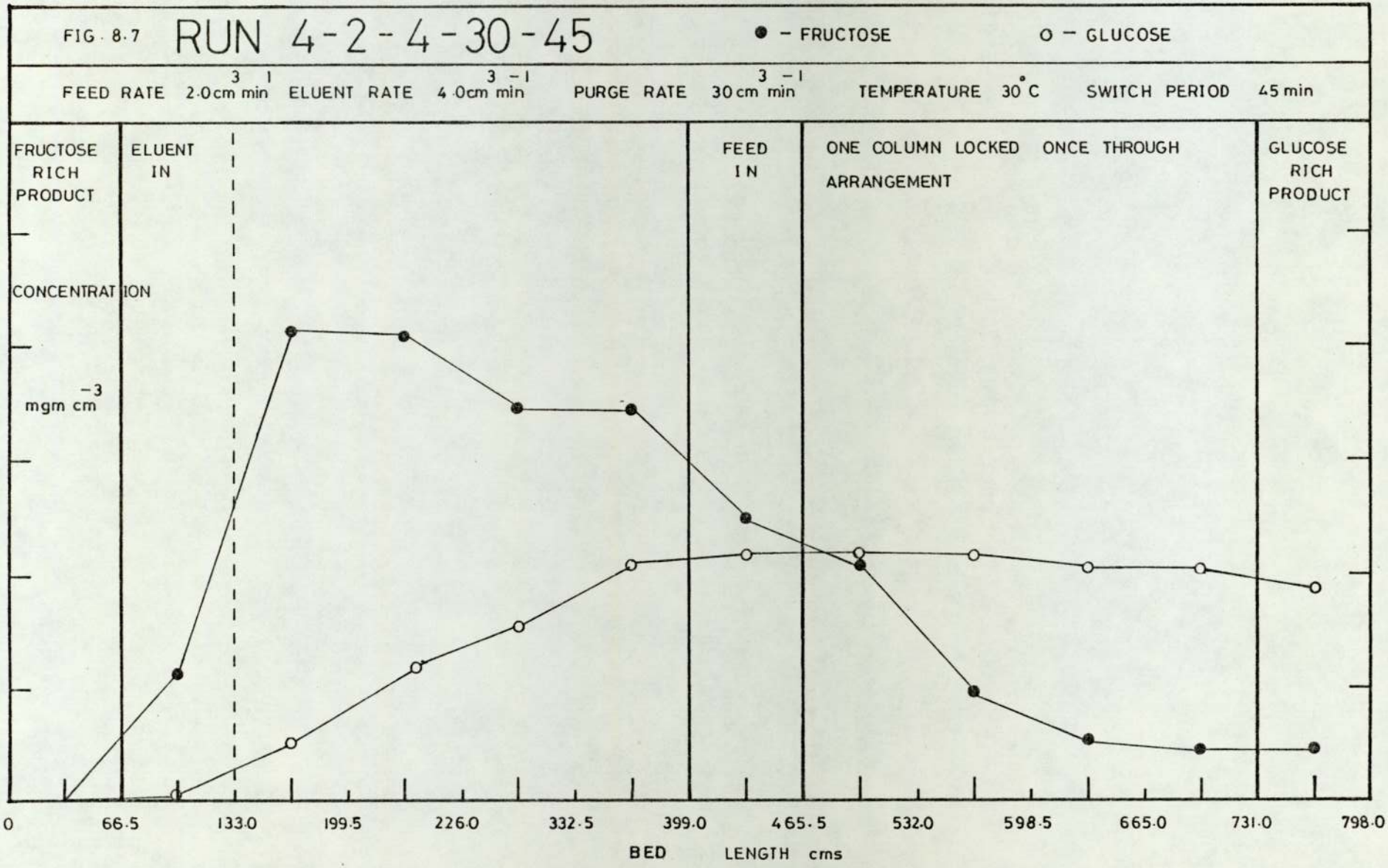


FIG. 8.7 RUN 4-2-4-30-45
● - FRUCTOSE
O - GLUCOSE
FEED RATE 2.0 cm³ min⁻¹ ELUENT RATE 4.0 cm³ min⁻¹ PURGE RATE 30 cm³ min⁻¹ TEMPERATURE 30°C SWITCH PERIOD 45 min
FRUCTOSE RICH PRODUCT
ELUENT IN
FEED IN
ONE COLUMN LOCKED ONCE THROUGH ARRANGEMENT
GLUCOSE RICH PRODUCT
CONCENTRATION
mgm cm⁻³
500
400
300
200
100
00
0
66.5
133.0
199.5
226.0
332.5
399.0
465.5
532.0
598.5
665.0
731.0
798.0
BED LENGTH cms

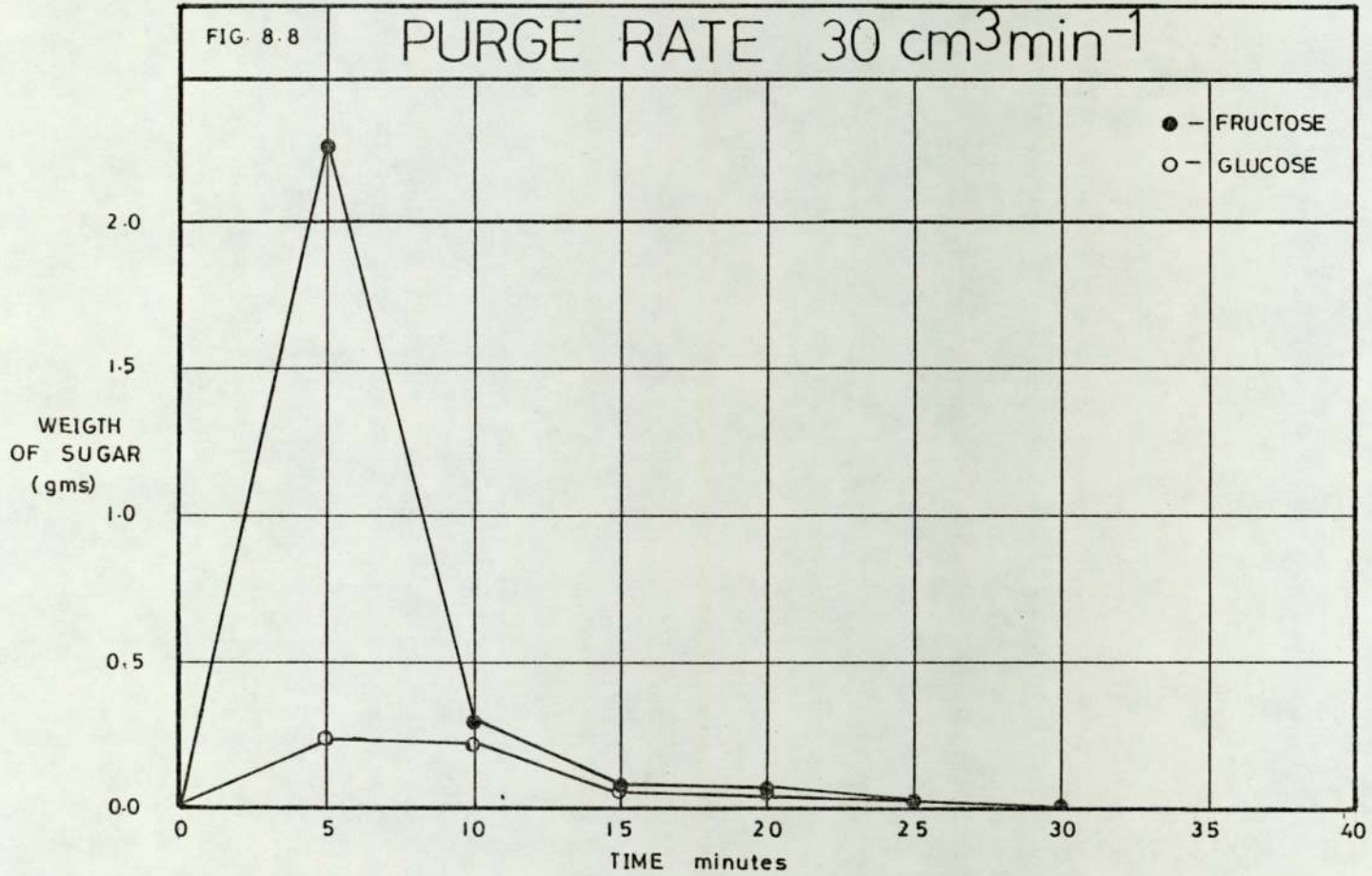


FIG. 8.8
PURGE RATE 30 cm3min-1
● – FRUCTOSE
○ – GLUCOSE
WEIGTH OF SUGAR (gms)
2.0
1.5
1.0
0.5
0.0
0
5
10
15
20
25
30
35
40
TIME minutes

point was shifted to two column lengths into the post feed section.

8.2.2.1.3 CONCLUSIONS

When a 3.0 cm^2m^{-1} of feed consisting of 50% (w/v) solid glucose-fructose was passed through the SCCR4 unit, an overloading situation was observed. The result was a greater loss of the fructose into the glucose rich stream.

The best operating conditions appeared to be as those used in run 2-2.5-6-30-30 Figure (8.5), where 2.5 cm^3min^{-1} was the best throughput rate attained, with a recovery efficiency of approximately 90%, and the purity of both the glucose and the fructose in the glucose rich stream and the fructose rich stream was approximately 91%.

Increasing the feedrate increased the solid concentration in the glucose rich stream. Reducing the purge flowrate through the isolated fructose rich section had increased the solid concentration in the fructose rich stream by ten fold to 2.13%.

The high average fructose concentration (400 mg cm^{-3}) in a column as shown in the system profile of run 3-3-6-30-30, indicated that the concentration in each column could be achieved if a longer switch period was used. Fructose lost could be reduced as well, if a more developed system profile was achieved.

In the post-feed section, it was found that a significant quantity of fructose was accumulated in the columns. This was found to be caused by the 'hold-up' volume in the process line between the columns and the poppet valves. Subsequent experiments performed by Gould[174] on the 10.16 cm I.D. unit (SCCR6), showed that similar 'hold-up' volumes in the unit did not have any detrimental effect on the performance. A more detailed discussion of this physical constraint will be provided in the next chapter.

8.2.2.2 EFFECT OF LENGTHENING THE SWITCH PERIOD

8.2.2.2.1 INTRODUCTION

In this group of experiments, different switch periods were used in each run; 30 minutes in run 1-2-6-30-30, 45 minutes in run 4-2-4-30-45 and 120 minutes in run 5-1.5-1.5-30-120. The eluent volume per switch period was kept constant at 180 cm^3 by altering the eluent flowrate accordingly.

The object of these experiments was to investigate the effect of a longer switch period on the separating power of the SCCR4 unit.

The features to note were

(1) The purity of the fructose product and the glucose product.

(2) The solid concentration in the fructose-rich stream and the glucose rich stream.

(3) The fructose recovery efficiency.

(4) The system profile.

8.2.2.2.2 RESULT AND DISCUSSION

The purity of the fructose product in the three runs remained at approximately 91.0%, this suggested that 180 cm^3 of eluent per switch period was required to achieve this purity level in the fructose product.

The glucose purity in the glucose rich stream varied from 86.94% in run 3-3-6-30-30, to 91.36% in run 4-2-4-30-45 and 75.19% in run 5-1.5-1.5-30-120.

In run 3-3-6-30-30 and 4-2-4-30-45, a similar ratio of feed to eluent, 1:2 was used and they differed only in the length of the switch period and the liquid flowrates. The eluent volume per switch period was constant at 180 cm^3. Yet run 4-2-4-30-45 had a better glucose purity in the glucose rich product than run 3-3-6-30-30. It was also found that run 4-2-4-30-45 had a better fructose recovery efficiency and a more developed system profile compared to those of run 3-3-6-30-30. (See Table (8.3) and (8.4), Figure (8.5) and (8.7)). The reason was simply that at a lower eluent flowrate a better plate efficiency and a better distribution of the fructose and the glucose in the system was achieved. Similar features were also seen in the batch chromatographic experiments in Chapter 7. The plate efficiency of the fructose and the glucose

TABLE 8.3 RUN CONDITIONS

RUN NUMBER	FLOWRATE			CONCENTRATION		SWITCH PERIOD	ELUENT VOL. PER SWITCH
	FEED	ELUENT	PURGE	FRUCTOSE	GLUCOSE		
	$cm^3 min^{-1}$			$mgm\ cm^{-3}$		min	cm^3/switch
3-3-6-30-30	3.0	6.0	300.0	260.0	260.0	30.0	180.0
4-2-4-30-45	2.0	6.0	30.0	260.0	250.0	45.0	180.0
5-1.5-1.5-30-120	1.5	1.5	5.0	237.0	240.0	120.0	180.0
5-1.75-1.5-30-120	1.75	1.5	5.0	237.0	240.0	120.0	180.0

TABLE 8.4 RESULTS

RUN NUMBER	F-RICH PRODUCT CONC.		G-RICH PRODUCT CONC.		F-RICH PRODUCT PURITY		G-RICH PRODUCT PURITY		SUGAR IN F-RICH STREAM		MASS BALANCE (OUT/IN)		SOLID IN STREAM	
	F	G	F	G	F	G	F	G	F	G	F	G	FRP	GRP
	$mgm\ cm^{-3}$		$mgm\ cm^{-3}$		%		%		%		%		%	
3-3-6-30-30	2.62	0.27	12.47	83.32	90.58	9.41	13.05	86.94	83.39	8.81	97.0	98.42	0.29	9.58
4-2-4-30-45	15.92	1.63	9.07	95.76	90.74	8.64	9.62	91.36	89.98	7.74	100.9	104.5	1.75	10.48
5-1.5-1.5-30-120	38.96	3.25	18.80	79.86	92.30	7.69	19.06	80.94	81.36	6.96	101.6	96.25	4.42	9.87
5-1.75-1.5-30-120	20.87	1.65	84.24	111.2	92.69	43.11	24.18	75.19	24.47	1.80	99.40	98.33	2.25	19.54

increased as the eluent flowrate was decreased. The equilibrium distribution coefficient of fructose also increased at a lower flowrate in the smaller diameter column (glass column 1.14 cm I.D.), suggesting that a better distribution of the fructose in the mobile phase and the stationary phase was achieved.

In run 5-1.5-1.5-30-120, the feed to eluent ratio was decreased to 1:1, while still maintaining the eluent volume per switch at 180 cm. Overloading of the separation section in the SCCR4 unit with the sugar occurred. Purity of the glucose in the glucose rich stream fell to 80.94% and the fructose recovery efficiency decreased to 81.46% compared to the recovery efficiency of run 4-2-4-30-45, 89%.

Run 5-1.5-1.5-30-120 also used different flow arrangements as shown in Figure (8.3).

(1) Figure (8.3.1), once-through, single column purged.
(2) Figure (8.3.4), once-through, double locked columns in a parallel purge scheme.
(3) Figure (8.3.5), once-through, double locked columns in a semi-parallel purge scheme.
(4) Figure (8.3.3), once through, double locked columns in a series purge scheme.

No significant difference in the overall performances of the SCCR4 unit was observed. Hence the best flow arrangement for the most effective use of the bed length of the SCCR4 unit was the arrangement (1), as seen in Figure (8.3).

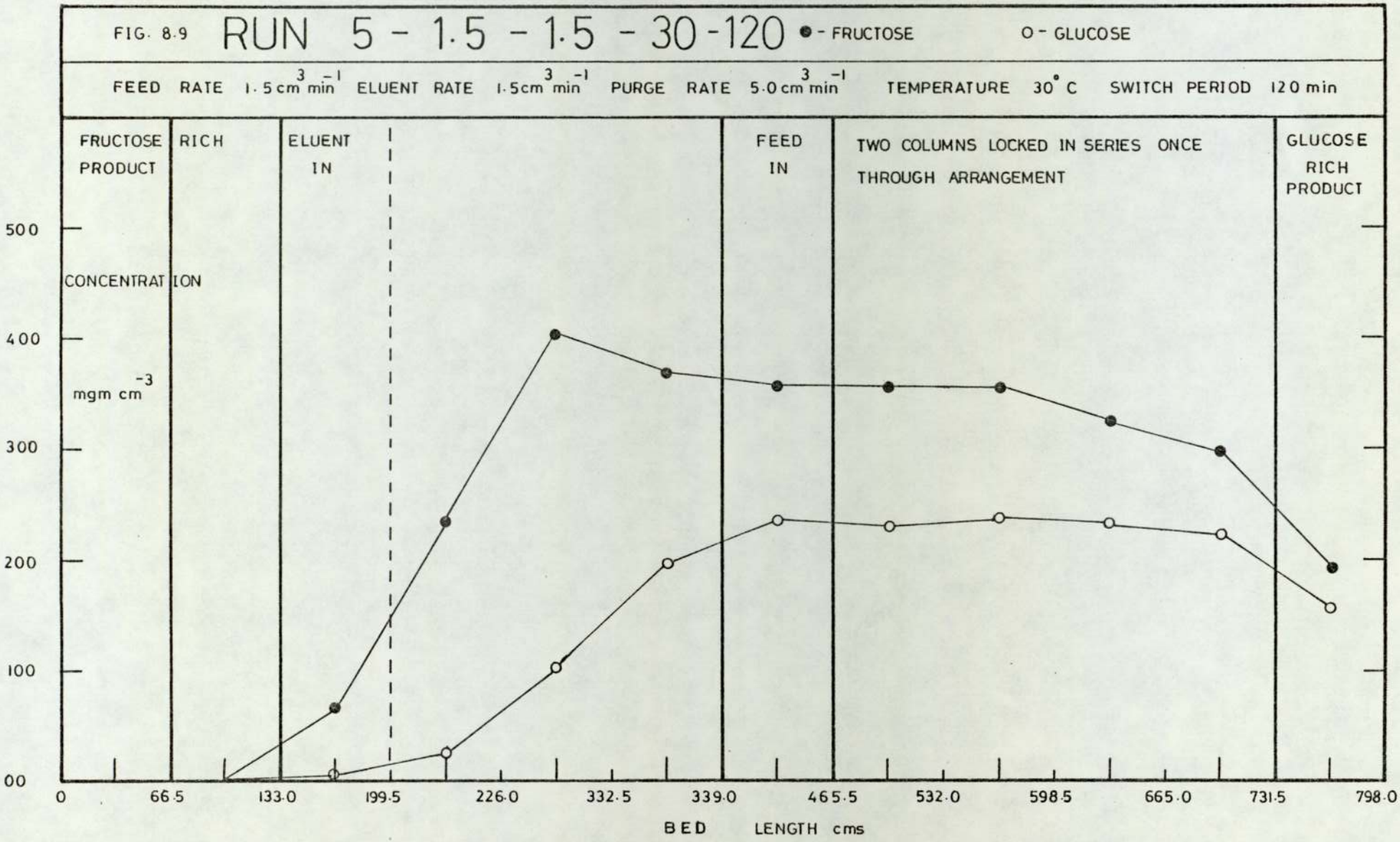


FIG. 8.9 RUN 5 - 1.5 - 1.5 - 30 - 120 ● - FRUCTOSE O - GLUCOSE
FEED RATE 1.5 cm³ min⁻¹ ELUENT RATE 1.5 cm³ min⁻¹ PURGE RATE 5.0 cm³ min⁻¹ TEMPERATURE 30° C SWITCH PERIOD 120 min
FRUCTOSE PRODUCT
RICH
ELUENT IN
FEED IN
TWO COLUMNS LOCKED IN SERIES ONCE THROUGH ARRANGEMENT
GLUCOSE RICH PRODUCT
CONCENTRATION
mgm cm⁻³
500
400
300
200
100
00
0
66.5
133.0
199.5
226.0
332.5
339.0
465.5
532.0
598.5
665.0
731.5
798.0
BED LENGTH cms

In run 5-1.5-1.5-30-120, the feed flowrate was also increased to 1.75 $cm^3 min^{-1}$ during the run. The conditions were 1.75:1.5, feed to eluent ratio, temperature of the enclosure 30°C and the switch period, 120 minutes. Four continuous cycles were completed.

As predicted, severe overloading of the columns in the separating section occurred. This was reflected by the fall of fructose recovery efficiency to 24.44% and the increase in the solid concentration of the glucose rich stream, 19.54% (w/w). Glucose purity in the glucose rich stream was 75.99%. The system profile, Figure (8.9) showed that fructose was accumulated in all the columns in the separation section.

8.2.2.2.3 CONCLUSION

At a longer switch period of 45 minutes and at a feed to eluent ratio of 1:2, the SCCR4 performed more efficiently than it did at a switch period of 30 minutes.

A better fructose recovery efficiency and a higher solid concentration were achieved in the products, at 89.98% and 10.48% (w/w) respectively.

Four flow arrangements were used and no significant improvement in the performances of the SCCR4 unit was observed. Under these circumstances, the best flow arrangement was the once-through, single column purge scheme, Figure (8.3-1).

When the feed to eluent ratio was decreased to 1:1 and 1.75:1.5, severe overloading of the columns in the separating section occurred. This resulted in a very poor fructose recovery efficiency and glucose purity in the glucose rich stream.

The fructose purity in the fructose rich stream remained at approximately 91.5% in all the experiments, when a constant eluent volume per switch of 180 cm^3 was used.

Pressure drop in the lines across the separation section increased with decreasing feed to eluent ratio, and the highest pressure drop recorded on the eluent line was just over 750 kNm^{-2} (110 lb in^{-2}).

Note, a significant quantity of the fructose was accumulated in the columns in the post-feed section, as observed in the previous run reported.

8.2.2.3 EFFECT OF RECYCLING PART OF THE FRUCTOSE RICH PRODUCT

8.2.2.3.1 INTRODUCTION

Run 6-2-6-30-30-R recycled a portion of the fructose rich product as the eluent. A 30 minutes switch period and a feed to eluent ratio of 1:3 were used. The temperature in the enclosure was maintained at 30°C. The flow arrangements investigated in this run were

(1) single lock column with recycle, figure (8.3 .2)

(2) double lock column, parallel purge scheme with recycle, figure (8.3.6)

Run 8-2-6-30-30 used the 'familiar' once-through, single column purge arrangement and similar run conditions.

The features to note were:

(1) the fructose purity in the fructose rich stream

(2) the solid concentration in the products

(3) the recovery efficiency of fructose in the fructose rich stream

8.2.2.3.2 RESULT AND DISCUSSION

The fructose purity in the fructose rich stream of run 6-2-6-30-30-R was 85.56% compared to 91.09% of run 8-2-6-30-30. The fall in the fructose product purity was due mainly to the 10% glucose present in the recycle effluent. It has been established earlier in the batch chromatographic experiment with the stainless steel column that, at least two columns length was required to separate a sample containing the glucose and the fructose.

The solid concentration in the fructose rich product of run 6-2-6-30-30-R increased to 4.14% compared to 2.26% of run 8-2-6-30-30.

TABLE 8.5 RUN CONDITIONS

RUN NUMBER	FLOWRATE			CONCENTRATION		SWITCH PERIOD	ELUENT VOL. PER SWITCH
	FEED	ELUENT	PURGE	FRUCTOSE	GLUCOSE		
	$cm^3 min^{-1}$			$mgm\ cm^{-3}$		min	cm^3/switch
6-2-6-30-30-R	2.0	6.0	30.0	240.0	250.0	30.0	180.0
8-2-6-30-30	2.0	6.0	30.0	250.0	240.0	30.0	180.0

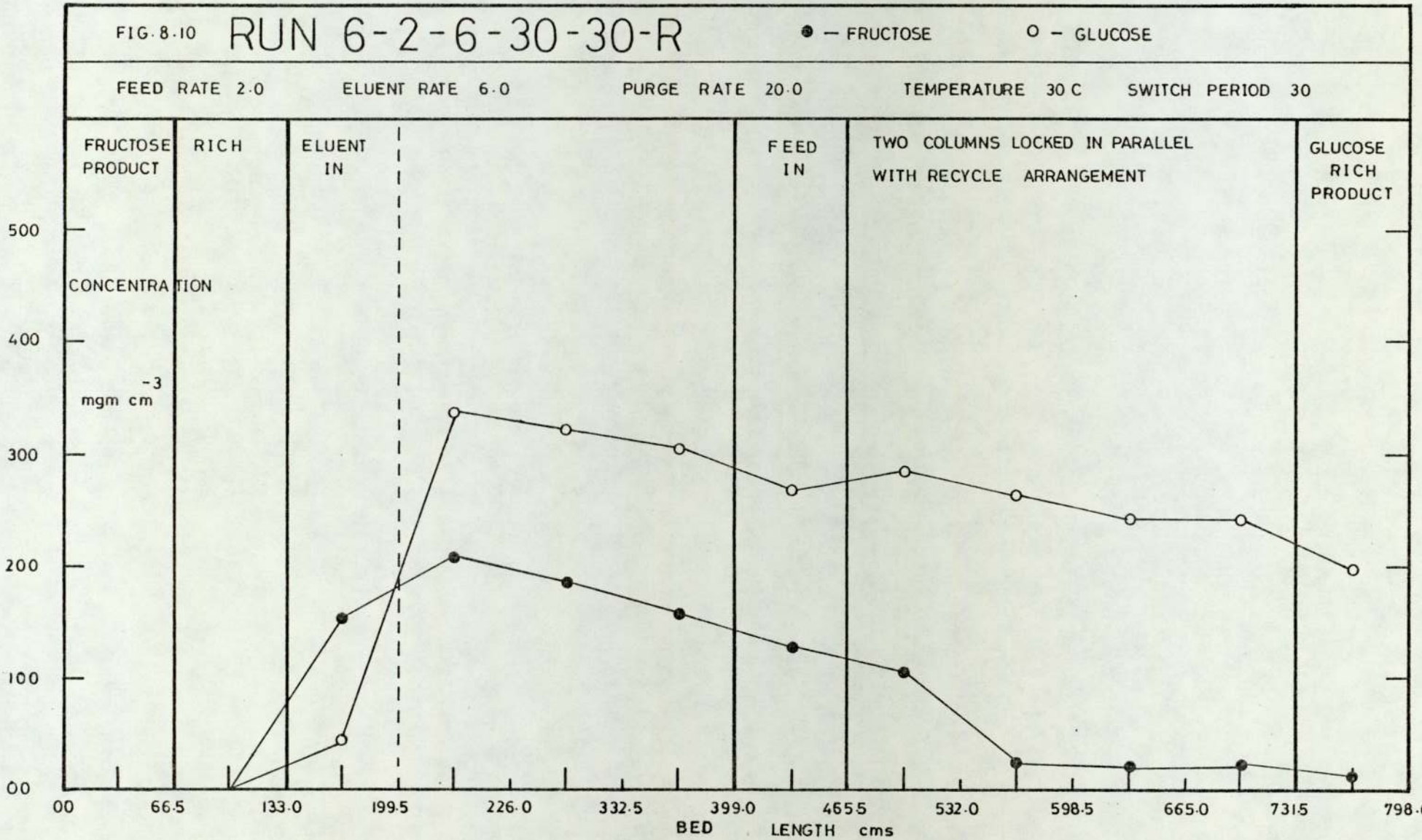
TABLE 8.6 RESULTS

RUN NUMBER	F-RICH PRODUCT CONC.		G-RICH PRODUCT CONC.		F-RICH PRODUCT PURITY		G-RICH PRODUCT PURITY		SUGAR IN F-RICH STREAM		MASS BALANCE (OUT/IN)		SOLID IN STREAM	
	F	G	F	G	F	G	F	G	F	G	F	G	FRP	GRP
	$mgm\ cm^{-3}$		$mgm\ cm^{-3}$		%		%		%		%		%	
6-2-6-30-30-R	35.79	5.57	3.35	49.51	85.56	13.46	6.34	93.69	96.34	21.85	100.23	99.04	4.14	5.28
8-2-6-30-30	19.2	3.80	7.46	53.46	92.04	14.96	11.76	87.71	91.30	17.32	101.78	99.30	2.26	6.20

The fructose recovery efficiency improved to 96.34% when recycling was used, compared to 91.3% in the once-through arrangement. See tables (8.5) and (8.6) and figures (8.10) and (8.12).

The system profile of run 6-2-6-30-30-R showed a high concentration of glucose in the entire length of the separation section, figure (8.10). The fructose concentration was low compared to those of run 8-2-6-30-30-R. Why the profile exhibited such a feature was not clear, but one possible reason was that fructose was accumulated in the column where the eluent normally entered the section, which was also the next column to be purged. The majority of the fructose input into the SCCR4 unit was recovered in the fructose rich product, and what was left in the separation section was unable to saturate the packing. Meanwhile, glucose which was introduced into the SCCR4 unit in the eluent, accumulated in both the mobile phase and the stationary phase along the entire length of the separation section. It was possible that by recycling, the fructose rich product had a deterimental effect on the retaining ability of the packings for fructose.

However, on the other hand, the glucose purity in the glucose rich stream increased to 93.69% compared to 87.71% of run 8-2-6-30-30.


FIG·8·10 RUN 6-2-6-30-30-R
● – FRUCTOSE
O – GLUCOSE
FEED RATE 2·0
ELUENT RATE 6·0
PURGE RATE 20·0
TEMPERATURE 30 C
SWITCH PERIOD 30
FRUCTOSE PRODUCT
RICH
ELUENT IN
FEED IN
TWO COLUMNS LOCKED IN PARALLEL WITH RECYCLE ARRANGEMENT
GLUCOSE RICH PRODUCT
CONCENTRATION
mgm cm -3
500
400
300
200
100
00
00
66·5
133·0
199·5
226·0
332·5
399·0
465·5
532·0
598·5
665·0
731·5
798·0
BED LENGTH cms

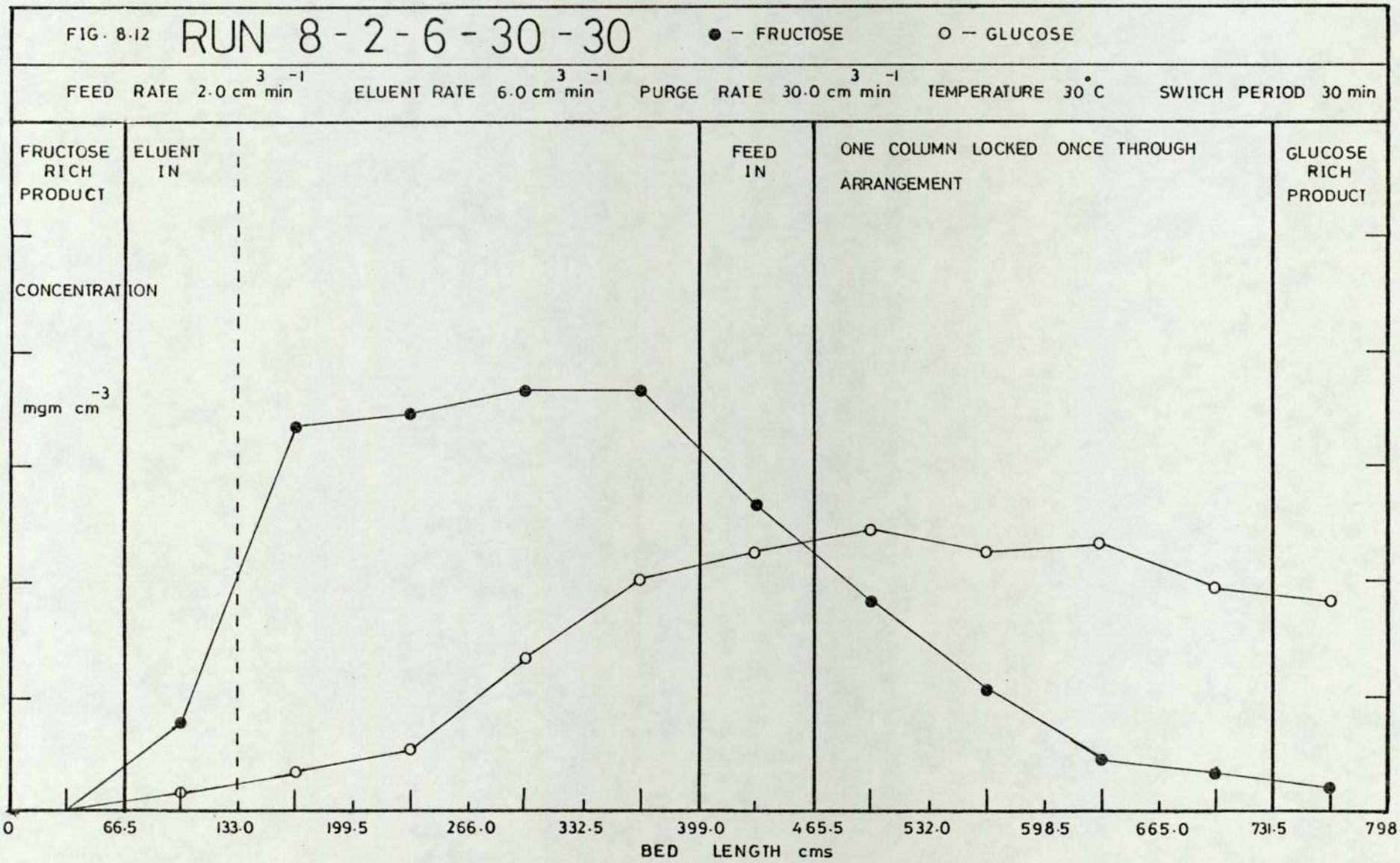


FIG. 8.12 RUN 8-2-6-30-30
● — FRUCTOSE
O — GLUCOSE
FEED RATE 2.0 cm³ min⁻¹
ELUENT RATE 6.0 cm³ min⁻¹
PURGE RATE 30.0 cm³ min⁻¹
TEMPERATURE 30°C
SWITCH PERIOD 30 min
FRUCTOSE RICH PRODUCT
ELUENT IN
FEED IN
ONE COLUMN LOCKED ONCE THROUGH ARRANGEMENT
GLUCOSE RICH PRODUCT
CONCENTRATION
mgm cm⁻³
500
400
300
200
100
0
0
66.5
133.0
199.5
266.0
332.5
399.0
465.5
532.0
598.5
665.0
731.5
798.0
BED LENGTH cms

8.2.2.3.3 CONCLUSIONS

It was clear from the results obtained above, that by recycling a portion of the fructose rich product, it had a detrimental effect on the fructose purity in the fructose rich product. But on the hand, the plus points for using the recycling arrangement had more advantageous features such as:

(1) increase in the fructose recovery efficiency
(2) increase in the solid concentration in the fructose rich product
(3) increased glucose purity in the glucose rich product
(4) decrease in the volume of water used, as the eluent was extracted from the purged fructose rich product

Therefore in conclusion, the use of the recycling arrangement would be favourable in situations which demanded less pure fructose product but purer glucose product, and when minimum use of desorbent was desired.

8.2.2.4 EXPERIMENTS TO TEST THE SENSITIVITY OF THE THEORETICAL GUIDE WITH A SMALL CHANGE OF SWITCH PERIOD

8.2.2.4.1 INTRODUCTION

These particular pair of experiments were performed mainly to test the theoretical method derived in

section (8.2.1), for selecting run parameters.

The switch period of run 1-2-6-30-30 was 30 minutes and of run 7-2-6-30-35, it was increased to 35 minutes. At a constant eluent flowrate of 6.0 cm^3m^{-1}, the eluent volumes per switch of run 1-2-6-30-30 and 7-2-6-30-35 were 180 cm^3 and 210 cm^3 respectively.

Referring to the theoretical relationship

$$V_g < L.t < V_f \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (8.20)$$

the following observations were expected when the eluent volume per switch period was increased from 180 cm^3 to 210 cm^3.

(1) higher purity level of fructose in the fructose rich product

(2) greater loss of fructose into the glucose rich stream, which would also lower the purity level of glucose in the glucose rich product

(3) decrease in solid concentration in the fructose rich product

The once-through, single column purge arrangement was used, and the feed to eluent ratio was 1:3. The temperature in the enclosure was maintained at 30°C, see figure (8.3-1) and table (8.7).

8.2.2.4.2 RESULT AND DISCUSSION

The fructose purity in the fructose rich stream increased slightly from 91.09% to 92.04%, for run

TABLE 8.7 RUN CONDITIONS

RUN NUMBER	FLOWRATE			CONCENTRATION		SWITCH PERIOD	ELUENT VOL. PER SWITCH
	FEED	ELUENT	PURGE	FRUCTOSE	GLUCOSE		
	$cm^3\ min^{-1}$			$mgm\ cm^{-3}$		min	cm^3/switch
1-2-6-30-30	2.0	6.0	300.0	260.0	260.0	30.0	180.0
7-2-6-30-35	2.0	6.0	300.0	270.0	260.0	35.0	210.0

TABLE 8.8 RESULTS

RUN NUMBER	F-RICH PRODUCT CONC.		G-RICH PRODUCT CONC.		F-RICH PRODUCT PURITY		G-RICH PRODUCT PURITY		SUGAR IN F-RICH STREAM		MASS BALANCE (OUT/IN)		SOLID IN STREAM	
	F	G	F	G	F	G	F	G	F	G	F	G	FRP	GRP
	$mgm\ cm^{-3}$		$mgm\ cm^{-3}$		%		%		%		%		%	
1-2-6-30-30	1.86	0.11	8.62	63.86	91.09	10.40	11.85	89.51	91.20	9.61	103.31	99.12	0.21	7.25
7-2-6-30-35	1.40	0.11	19.41	58.16	92.46	7.84	24.55	74.95	67.49	6.09	96.80	97.36	0.15	7.75

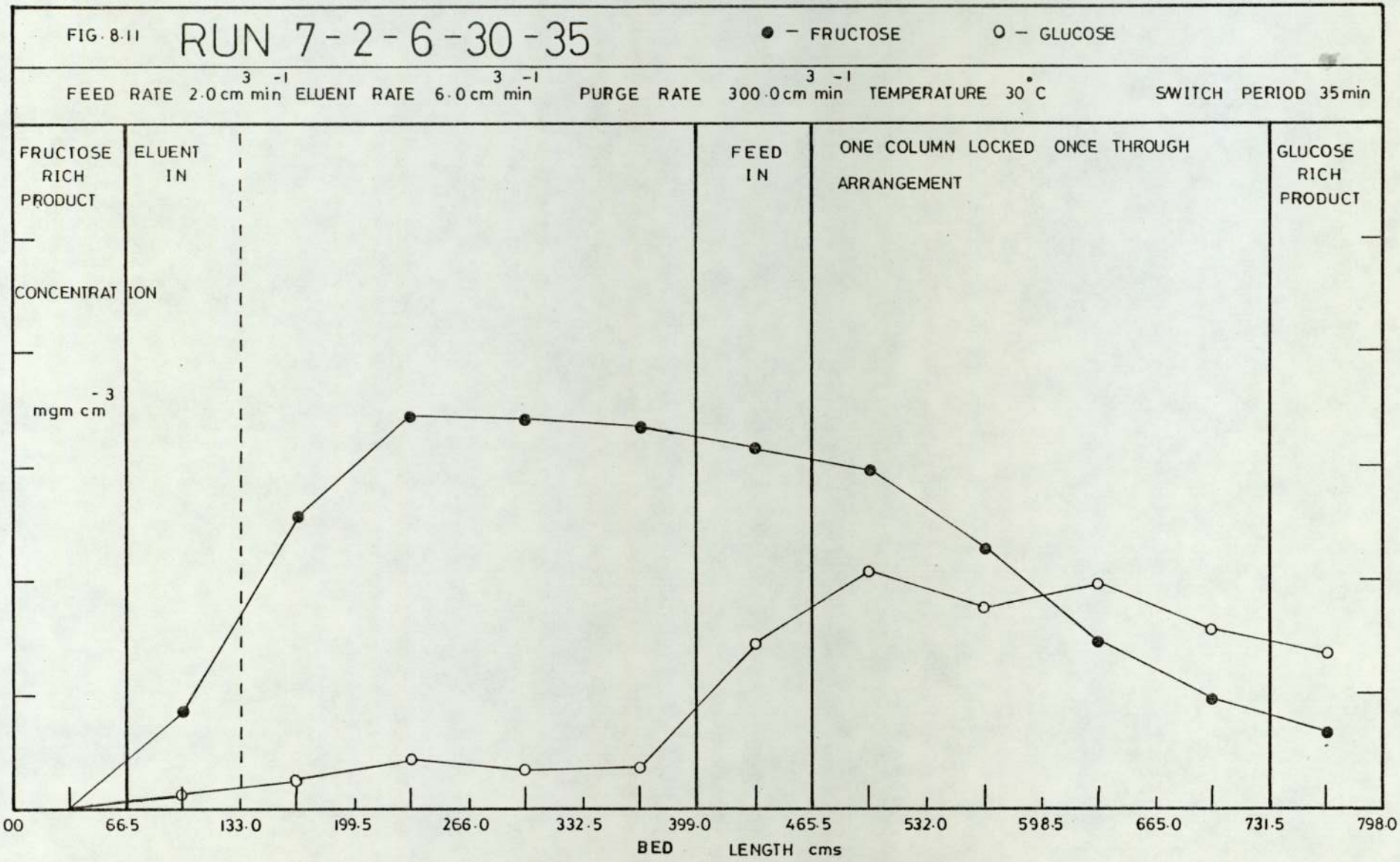


FIG. 8.11 RUN 7-2-6-30-35
● – FRUCTOSE
O – GLUCOSE
FEED RATE 2.0 cm³ min⁻¹ ELUENT RATE 6.0 cm³ min⁻¹ PURGE RATE 300.0 cm³ min⁻¹ TEMPERATURE 30° C SWITCH PERIOD 35 min
FRUCTOSE RICH PRODUCT
ELUENT IN
FEED IN
ONE COLUMN LOCKED ONCE THROUGH ARRANGEMENT
GLUCOSE RICH PRODUCT
CONCENTRATION
mgm cm⁻³
500
400
300
200
100
00
00
66.5
133.0
199.5
266.0
332.5
399.0
465.5
532.0
598.5
665.0
731.5
798.0
BED LENGTH cms

1-2-6-30-30 and run 7-2-6-30-35 respectively. See table (8.8).

The fructose recovery efficiency was 67.49% for run 7-2-6-30-35 compared to 91.2% for run 1-2-6-30-30.

The solid concentration in the fructose rich stream fell from 0.21% to 0.15% as in run 1-2-6-30-30 and 7-2-6-30-35 respectively.

The above results suggested when excess desorbent was used in run 7-2-6-30-35, less fructose was was retained on the packings, as more was washed along with the mobile phase.

An analogy of the situation could be seen in batch chromatography, when cutting of the separated fractions into two products took place. Best cutting point was obviously the 'valley' between the two component peaks. Prolonging or decreasing the cutting time caused the cut-point to shift into either of the separated fractions, resulting in contamination of one of the products.

8.2.2.4.3 CONCLUSION

By increasing the eluent volume per switch period to greater than the elution volume of the glucose, V_g (180 cm^3), it caused the fructose to travel with the mobile phase. This increased the fructose purity in the fructose rich product, but more fructose was lost into the glucose rich product. Hence, contamination of the glucose rich product occurred.

Finally, the results from this experiment demonstrated the sensitivity of the theoretical relationship to the switch period in the operation of the SCCR4 unit.

8.3 EXPERIMENTS WITH THE DEXTRAN CONTAMINATED FRUCTOSE RICH FEED - FISONS FEED

8.3.1 INTRODUCTION

In this study, the artificially produced Fisons feed and the actual commercially produced Fisons feed were used. The feed compositions were as follows:

ARTIFICIAL FISONS FEED	ACTUAL FISONS FEED
Fructose - 69% (w/w)	Fructose - 68%
Glucose - 9% (w/w)	Glucose - 8%
Dextran - 22% (w/w)	Dextran - 22%
70% (w/v) solid in solution	Reducing Sugars - 2% 70% (w/v) solid in solution with metal ions

A total of four runs were successfully performed, of which three runs were initially completed using the artificial Fisons feed. The final run used the actual Fisons feed, which contained metal ions of iron, copper, zead, lead and calcium, and insoluble debris. The final run in this group of experiments was also the last run of this research work. A life-test on the performances of the packings was carried out by monitoring the quantity of metal ions introduced into and withdrawn from the SCCR4 unit, in the feed and the products streams respectively. The metal ions were

detected by using the atomic absorption spectrometer. A total of 600 hours of semi-continuous operation (Monday to Friday) was completed for run 12-3-5.5-60-30.

Runs 9-2-6-30-30, 10-1.5-3-30-60, and 11-1.5-3-60-60 were also operated continuously and a minimum of eight cycles were completed in each run.

The objectives from this group of experiments were:

(1) to obtain a dextran-free fructose rich product
(2) to find the most suitable operating conditions for the highest feed throughput per hour
(3) to find the most suitable operating conditions whereby a high solid concentration in the fructose rich product could be achieved

and (4) to find the best operating conditions for the highest fructose recovery efficiency

8.3.2 RUNS WITH FISONS SYNTHETIC FEED

8.3.2.1 INTRODUCTION

The synthetic Fisons feed has been used in all the three runs making up this group of experiments.

Run 9-2-6-30-30 used a 1:3 feed to eluent ratio, a 20 $cm^3 min^{-1}$ of purge water rate and a 30 minute switch period. The temperature in the surroundings was maintained at $30^{o}C$.

Run 10-1.5-3.0-30-60 and 11-1.5-3.0-60-60 used a

1:3 feed to eluent ratio, a 10 $cm^3 min^{-1}$ of purge water and a 60 minutes switch period. The temperature in the enclosure for the former run was maintained at 30°C and at 60°C for the latter run.

The operating conditions in all these runs were selected with the knowledge acquired from the experiments with the glucose and fructose feed (Section 8.2).

The best operating conditions found in those experiments were, a 1:2 feed eluent ratio, a minimum of two empty column volumes of purge water per switch period (600 cm^3), a switch period of greater than 45 minutes and a once-through single column purge flow arrangement.

The features to note in this group of experiments were:

(1) the throughput of sugar per hour
(2) the purity of the fructose product
(3) the fructose recovery efficiency
(4) the solid concentration in the fructose rich product
(5) the system profile

8.3.2.2 RESULT AND DISCUSSION

The operation conditions and the results of the experiments were as shown in Tables (8.9) and (8.10), and the system profiles in Figure (8.13), (8.14) and (8.15).

TABLE 8.9 RUN CONDITIONS

RUN NUMBER	FLOWRATE			CONCENTRATIONS			SWITCH PERIOD	ELUENT VOL. PER SWITCH	TEMPERATURE OF ENCLOSURE
	FEED	ELUENT	PURGE	FRUCTOSE	GLUCOSE	DEXTRAN			
	$cm^3\ min^{-1}$			$mgm\ cm^{-3}$			min	cm^3/switch	°C
9-2-6-30-30	2.0	6.0	20.0	465.0	485	160.0	30.0	180.0	30.0
10-1.5-3-30-60	1.5	3.0	10.0	470.0	60.0	156.0	60.0	180.0	30.0
11-1.5-3-60-60	1.5	3.0	10.0	470.0	60.0	158.0	60.0	180.0	60.0

TABLE 8.10 RESULTS

RUN NUMBER	F-RICH PRODUCT CONC.			D-RICH PRODUCT CONC.			F-RICH PRODUCT PURITY			D-RICH PRODUCT PURITY			SUGAR IN F-RICH STREAM			MASS BALANCE (OUT/IN)			SOLID IN STREAM	
	F	G	D	F	G	D	F	G	D	F	G	D	F	G	D	F	G	D	FRP	DRP
	mgm cm			mgm cm			%			%			%			%			%	
9-2-6-30-30	60.3	2.98	0.01	6.15	10.06	56.9	94.5	4.78	0.00	10.33	17.02	72.60	95.71	36.42	0.00	100.51	100.00	101.27	6.40	7.31
10-1.5-6-30-60	67.25	3.04	0.07	9.97	15.18	49.26	94.23	4.77	0.00	13.43	20.44	66.12	92.34	30.06	0.00	98.96	99.17	99.78	7.14	7.44
11-1.5-6-60-60	61.50	2.75	0.2	27.60	16.31	50.16	94.00	4.80	0.00	29.37	17.33	53.29	80.61	25.78	0.00	98.00	98.69	99.05	6.55	9.41

Run 9-2-6-30-30 was initially performed using the more familiar operating conditions because of the artificial Fisons feed. The operating conditions were similar to those used in run 8-2-6-30-30 in the previous group of experiments using the glucose/fructose feed.

The fructose purity in the fructose rich product was 94.5% (w/w) and the rest consisting of glucose. No appreciable quantity of dextran was found.

The fructose recovery efficiency was 95.71% (w/w) and the solid concentration of the fructose rich product was 6.40% (w/w).

The sugar throughput per hour was 8.4 gms (solids)

The system profile, in Figure (8.13) showed that the distribution of the sugars were well developed. Fructose, which was the retained specie was accumulated mainly in the pre-feed section of the separating length and dropping sharply to the minimum level at the last but one column before the exit port for the dextran rich product.

Dextran and glucose were concentrated mainly in the post feed section, more of the former than the latter, as glucose was slightly retained by the packings in the column.

The system profile showed that the separating section was not fully loaded and suggested that more sugar could be processed.

Results from run 3-3-6-30-30, showed that a less well developed system profile was obtained when a 3 cm^3min^{-1} feed rate, 6 cm^3min^{-1} eluent rate and 30 minutes switch period was used. Overloading of the system occurred and resulted in a larger quantity of fructose lost to the glucose rich product. Therefore the only way to increase the sugar concentration in each column in the separating section was by lowering the feed to eluent ratio, from 1:3 to 1:2 and using a longer switch period of 60 minutes instead of 30 minutes.

The results from run 10-1.5-3.0-30-30 showed a slight decrease in fructose recovery efficiency, 92.3% compared to 95.7% for run 9-2-6-30-30. But the solid concentration in the fructose rich stream increased from 6.4% of run 9-2-6-30-30 to 7.14%. No dextran was detected in the fructose rich product.

The sugar throughput fell from 84 gms per hour to 63 gms per hour, but the sugar processed per cycle increased from 504 gms per hour of run 9-2-6-30-30 to 756 gms.

The benefits from increasing the switch period and using a lower feed to eluent ratio were mainly in increasing the solid concentration in the fructose product and the more efficient use of the separating medium in the system.

These were clearly seen in the system profile obtained at the end of the run, Figure (8.14).

The fructose concentration level in the pre-feed section almost doubled the concentration in run 9-2-6-30-30. The reason for this apparent high level of fructose concentration was because of the presence of fructose in the mobile phase and on the stationary phase. At a higher feed to eluent ratio of 1:3, most of the fructose was retained on the packings, and as seen in the system profile, figure (8.13), the separating section was not saturated with the fructose.

On the other end of the profile, the fructose concentration in the last column was higher and some loss of fructose into the dextran stream occurred, but the fructose recovery efficiency was at an acceptable level of 92.3%.

The fructose purity in the fructose rich stream was 94.23%. It was observed that a higher purity fructose product was obtained from separating the artificial Fisons feed as compared to the glucose/fructose feed, 91% pure fructose product. The reason was due to the quantity of glucose present in the feed. A larger quantity of glucose present caused greater overlapping between the two glucose and fructose fractions and greater contamination of the products. Likewise, in the artificial Fisons feed, less overlapping occurred between the fructose and the glucose fractions, as a smaller quantity of glucose was present in the feed.

After discussions with the Fisons Company representatives it was decided that it would be beneficial to

perform the separations at an elevated temperature of 60°C. The reasons given were that at an elevated temperature, the sugar solutions had less chances of microbial growth and thereby would not need preservatives to be added into the solution.

Run 11-1.5-3.0-60-60 had similar operating conditions to that of run 10-1.5-3.0-30-60, except that the enclosure temperature was maintained at 60°C.

Earlier experiments with the glass chromatographic column in the batch mode showed that the plate efficiency of the column with respect to each of the sugars increased with temperature, see Chapter Seven, Figure (7.1). But the equilibrium distribution coefficient K_d of the sugars decreased with elevated temperatures, Figure (7.2). Therefore, at an elevated temperature, a compensating effect was expected between the plate efficiency and the distribution of the material in the stationary and the mobile phases.

Fructose recovery efficiency in run 11-1.5-3.0-60-60 was lower at 80.61% compared to 92.3% of run 10-1.5-3.0-30-60. The fall in the recovery efficiency was mainly due to the effect of the temperature on the distribution of the sugar in the stationary phase and the mobile phase. The chemical and the mechanical contribution to this were the increased complexing rate between the fructose and the calcium present on the solid matrix, and the increase in the diffusion rate of the sugars into and out of the pores of the solid matrix containing

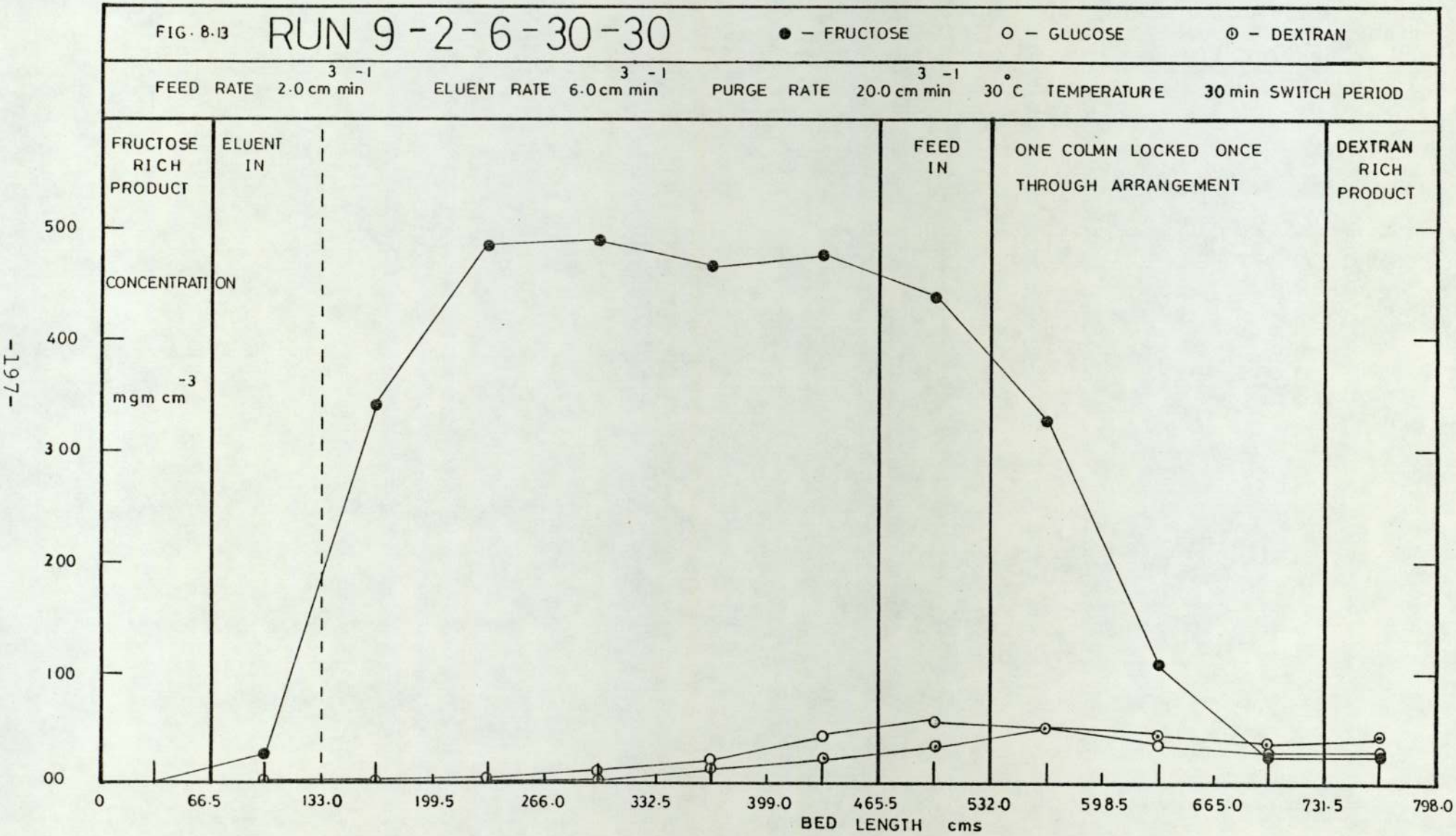
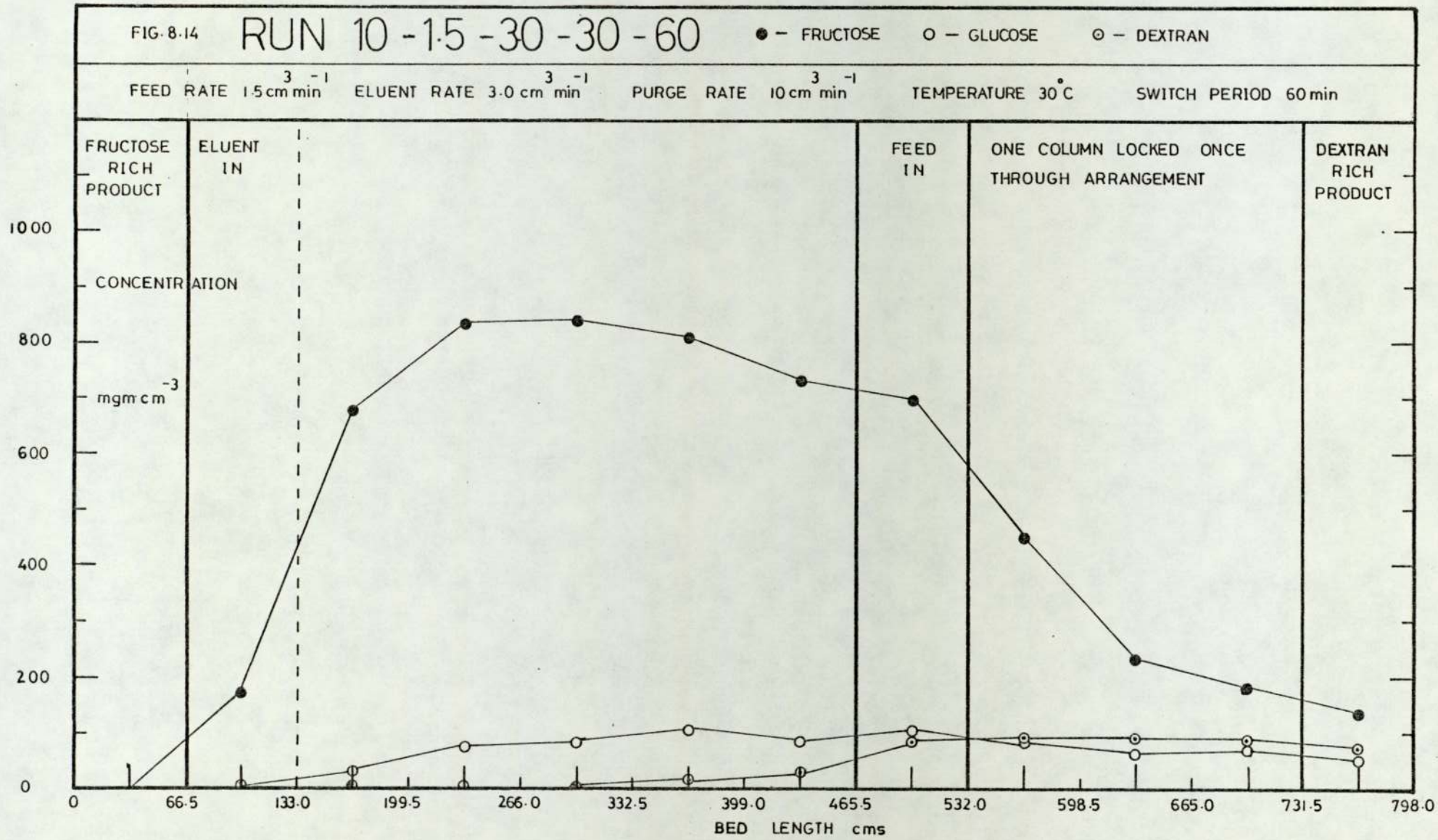


FIG. 8.13 RUN 9-2-6-30-30
● – FRUCTOSE
O – GLUCOSE
⊙ – DEXTRAN
FEED RATE 2.0 cm³ min⁻¹
ELUENT RATE 6.0 cm³ min⁻¹
PURGE RATE 20.0 cm³ min⁻¹
30 °C TEMPERATURE
30 min SWITCH PERIOD
FRUCTOSE RICH PRODUCT
ELUENT IN
FEED IN
ONE COLMN LOCKED ONCE THROUGH ARRANGEMENT
DEXTRAN RICH PRODUCT
CONCENTRATION
mgm cm⁻³
500
400
300
200
100
00
0
66.5
133.0
199.5
266.0
332.5
399.0
465.5
532.0
598.5
665.0
731.5
798.0
BED LENGTH cms


FIG·8·14 RUN 10 - 1·5 - 30 - 30 - 60
● – FRUCTOSE
O – GLUCOSE
⊙ – DEXTRAN
FEED RATE 1·5 cm³ min⁻¹
ELUENT RATE 3·0 cm³ min⁻¹
PURGE RATE 10 cm³ min⁻¹
TEMPERATURE 30°C
SWITCH PERIOD 60 min
FRUCTOSE RICH PRODUCT
ELUENT IN
FEED IN
ONE COLUMN LOCKED ONCE THROUGH ARRANGEMENT
DEXTRAN RICH PRODUCT
CONCENTRATION
mgm·cm⁻³
1000
800
600
400
200
0
0
66·5
133·0
199·5
266·0
332·5
399·0
465·5
532·0
598·5
665·0
731·5
798·0
BED LENGTH cms

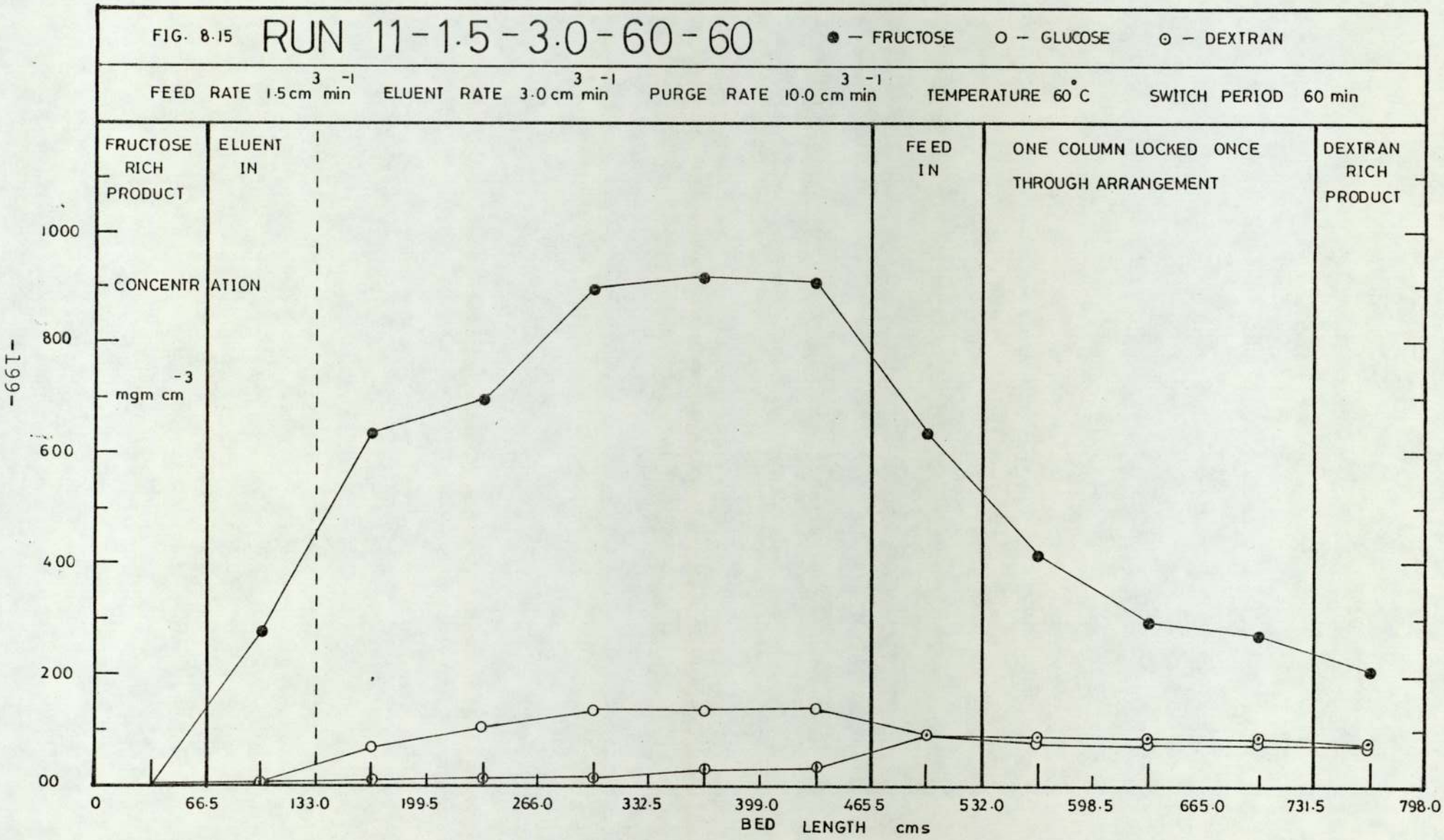


FIG. 8.15 RUN 11-1.5-3.0-60-60
● – FRUCTOSE
O – GLUCOSE
⊙ – DEXTRAN
FEED RATE 1.5 cm³ min⁻¹
ELUENT RATE 3.0 cm³ min⁻¹
PURGE RATE 10.0 cm³ min⁻¹
TEMPERATURE 60° C
SWITCH PERIOD 60 min
FRUCTOSE RICH PRODUCT
ELUENT IN
FEED IN
ONE COLUMN LOCKED ONCE THROUGH ARRANGEMENT
DEXTRAN RICH PRODUCT
CONCENTRATION
mgm cm⁻³
1000
800
600
400
200
00
0
66.5
133.0
199.5
266.0
332.5
399.0
465.5
532.0
598.5
665.0
731.5
798.0
BED LENGTH cms

the active sites.

Pressure drop in the eluent line and the feed line decreased by half when the run was performed at 60°C.

Purity of the fructose product remained at the 94% level, while the solid concentration in the fructose rich product fell to 6.55% (w/w). A small trace of dextran was detected in the fructose rich product but was considered to be of insignificant importance.

The system profile was similar to run 10-1.5-3.0-30-60, and only differed slightly by the higher concentration of the fructose in the columns in the pre-feed section, 910 mg cm^{-3}, as compared to 830 mg cm^{-3}. A slightly higher concentration of fructose was also detected in the last column in the post-feed section.

8.3.2.3 CONCLUSION

A dextran-free fructose rich product was achieved by separating a mixture of a dextran contaminated fructose-rich feed, in the SCCR4 unit.

A fructose rich product containing 94% fructose and 6% glucose was obtained and a solid concentration of 7.1% in the fructose rich product was achieved.

The quantity of sugar processed per cycle (12 hours) was 756 gms or 63 gms per hour.

A feed to eluent ratio of 1:2 was found to be the best at an enclosure temperature of 30°C or a ratio

0.75:2 at 60°C.

The flow arrangement used was the once-through single column purge scheme, Figure (8.3-1).

8.3.3 RUN WITH THE FISONS FEED

8.3.3.1 INTRODUCTION

As mentioned in Section (8.3.1), the Fisons feed contained known carbohydrates, metal ions and unknown substances (<2.0%). This run was performed as the last run in the research program where the risk of ruining the calcium charged packings was less important. See Figure (8.18).

A total of 600 hours of continuous operation was completed on the SCCR4 unit on a Monday to Friday basis. A life test to monitor the 'movement' of the metal ions was carried out by monitoring the quantity of the metal ions in the feed going into the unit and on the products obtained. Detection of the metal ions was achieved by using the Atomic Absorption Spectrometer. The metals under scrutiny were sodium, calcium, lead, copper, zinc and iron.

Three sets of operating conditions were used which were as follows:

(1) 2.0 $cm^3 min^{-1}$ of feed
6.0 $cm^3 min^{-1}$ of eluent
30.0 $cm^3 min^{-1}$ of purge
60°C temperature in the enclosure

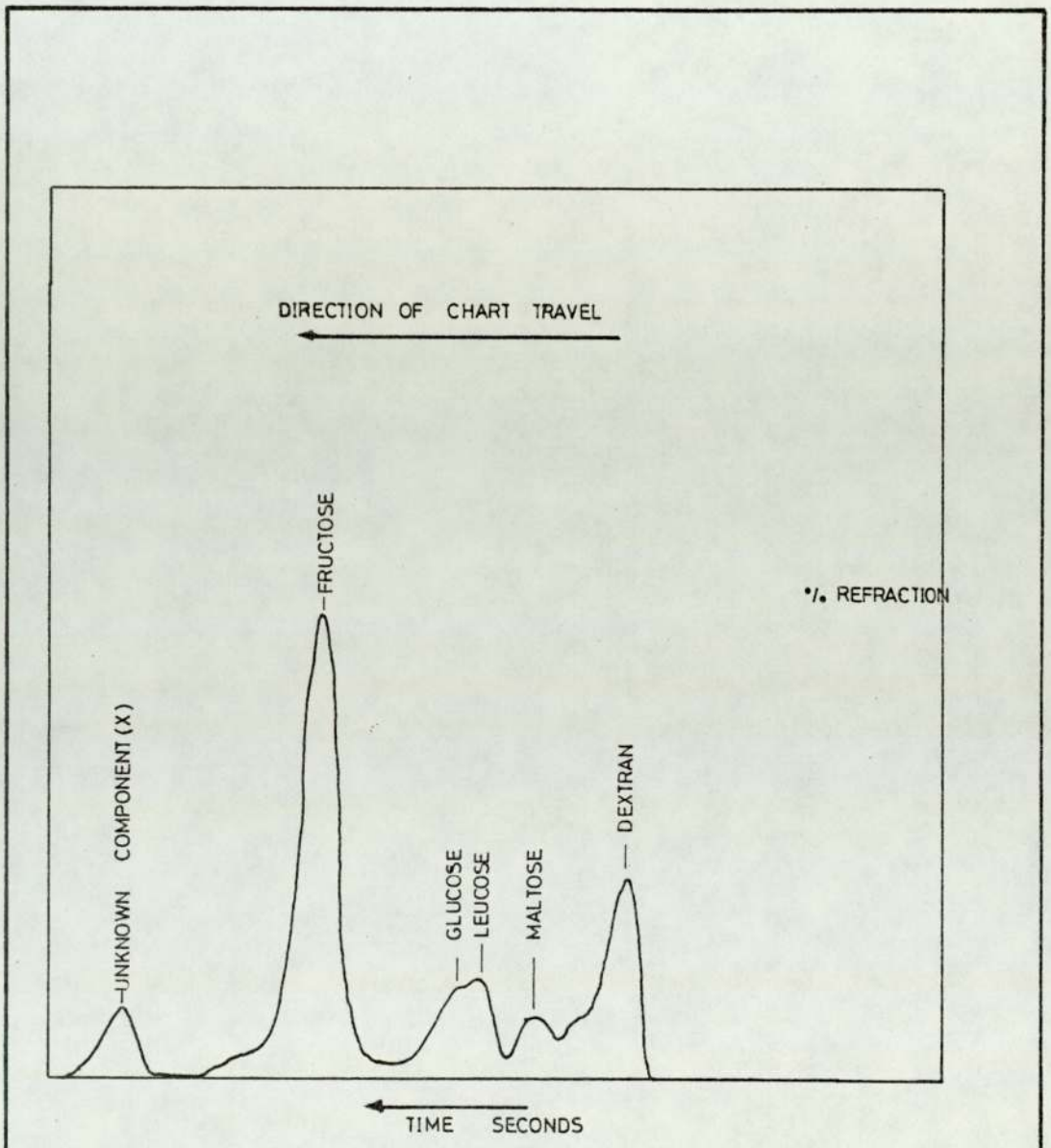


FIG. 8.18 TRAYING OF THE CHROMATOGRAM FOR THE FISONS FEED

(2) 2.5 cm^3min^{-1} of feed
6.0 cm^3min^{-1} of eluent
30.0 cm^3min^{-1} of purge
60°C temperature in the enclosure

(3) 3.0 cm^3min^{-1} of feed
5.5 cm^3min^{-1} of eluent
30.0 cm^3min^{-1} of purge
60°C temperature in the enclousre

Two flow arrangements were used.

(1) the once through single column purge (8.17-1)

(2) the once through single column lock with split purge streams, figure (8.17-2)

8.3.3.2 RESULT AND DISCUSSION

When a sample of the Fisons feed was passed through a Bio-Rad HPLC column, it was found that it contained in addition to the fructose, glucose and dextran, a small detectable quantity of maltose, leucrose and an unknown soluble material. The sucrose and the leucrose fractions emerged initially from the column before the fructose fraction, while the unknown fraction emerged last after the fructose. The quantity of the sucrose, the leucrose and the unknown material present in the total solid were 1.0%, 1.0% and 2% respectively.

Several attempts to identify the unknown fraction were carried out by spiking the feed samples with

FIG. 8.17-1 ONCE THROUGH SINGLE COLUMN PURGE ARRANGEMENT

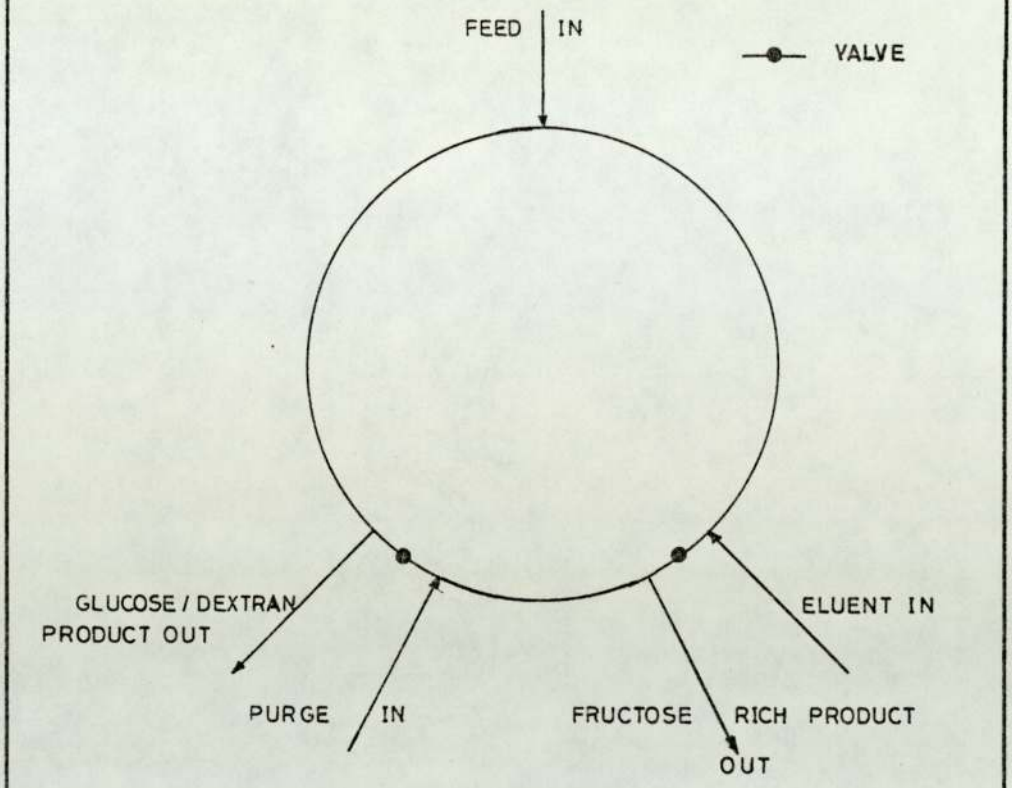
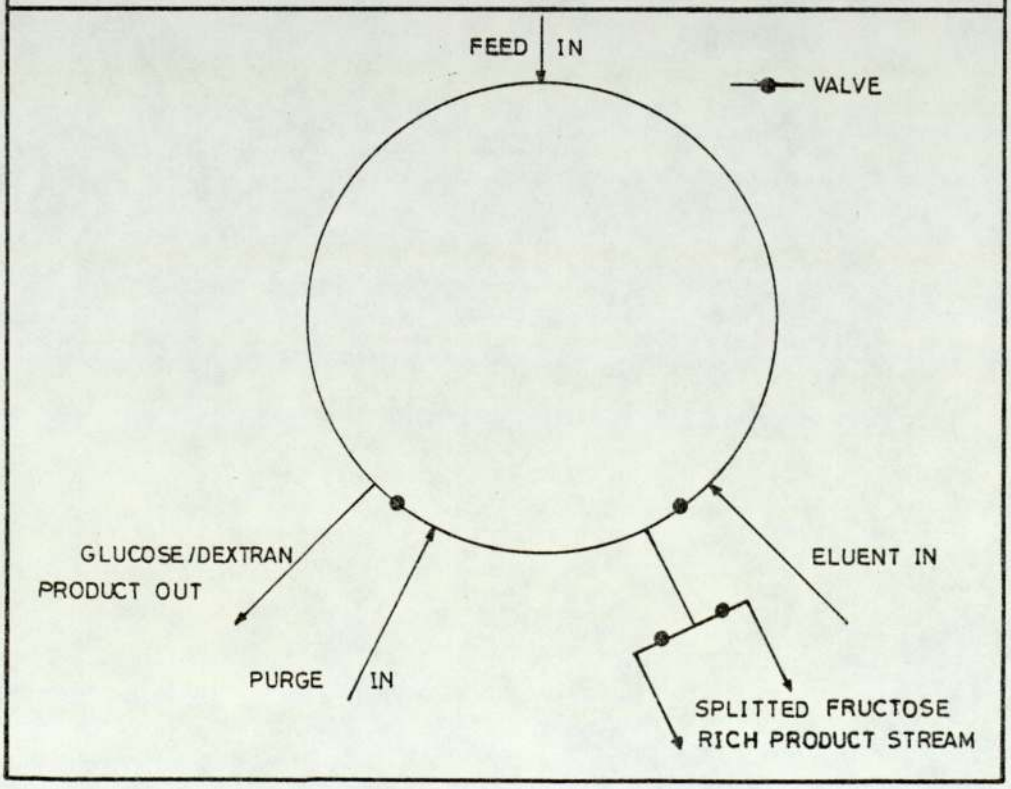


FIG. 8.17 2 ONCE THROUGH SINGLE COLUMN LOCKED WITH SPLITTED F.R.P. STREAM ARRANGEMENT



possible organic and inorganic compounds. The compounds used were methanol, ethanol, maltose, manose, sodium chloride, calcium chloride and sodium azide (preservative). None of the retention times of these compounds matched the unknown material. At the time of writing, analytical work was still being carried out in close co-operation with the Pharmaceutical Division of the Fisons Company, at Holmes Chapel, Cheshire, to identify the unknown material. The result of this finding should be published in the papers to follow this thesis.

In this thesis, the unknown material was considered separately and labelled as material, X.

When operating conditions (1) were used, a dextran free 99% fructose rich product was obtained. The recovery efficiency of the fructose fraction was approximately 91%. The solid concentration in the fructose rich product was 2.8% (w/w), and the sugar throughput per cycle was 504 gms per cycle. See Tables (8.13) and (8.14).

In operating conditions (2), the feed rate was increased to 2.5 $cm^3 min^{-1}$ thereby lowering the feed to eluent ratio to 1:2:4. All other operating conditions were similar to the one mentioned above.

The fructose purity in the furctose rich product remained at 99% and again, no appreciable quantity of dextran was detected. The fructose recovery efficiency was 90.41%. The solid concentration in the fructose

TABLE 8.11 RUN CONDITIONS

RUN NUMBER	FLOWRATE			CONCENTRATION		SWITCH PERIOD	ELUENT VOL. PER SWITCH	TEMPERATURE IN ENCLOSURE
	FEED	ELUENT	PURGE	FRUCTOSE	DEXTRAN + GLUCOSE			
	$cm^3 min^{-1}$			$mgm\ cm^{-3}$		min	cm^3/switch	°C
12-2-6-60-30	2.0	6.0	30.0	460.0	220.0	30.0	180.0	60.0
12-2.5-6-60-30	2.5	6.0	30.0	460.0	220.0	30.0	180.0	60.0
12-2.5-6-60-30	2.5	6.0	30.0 SPLITTED	460.0	220.0	30.0	180.0	60.0
12-3-5.5-60-30	3.0	5.5	30.0 SPLITTED	460.0	220.0	30.0	180.0	60.0

TABLE 8.12 RESULTS

RUN NUMBER	F-RICH PRODUCT CONC.		D-RICH PRODUCT CONC.		F-RICH PRODUCT PURITY		D-RICH PRODUCT PURITY		SUGAR IN F-RICH STREAM		MASS BALANCE (OUT/IN)		SOLID IN STREAM	
	F	D	F	D	F	D	F	D	F	D	F	D	FRP	DRP
	$mgm\ cm^{-3}$		$mgm\ cm^{-3}$		%		%		%		%		%	
12-2-6-60-30	28.0	0.0	12.16	70.16	99.0	0.0	14.76	85.23	90.68	0.0	102.90	100.87	2.80	8.23
12-2.5-6-60-30	30.8	0.0	9.76	81.90	99.0	0.0	10.65	89.35	90.41	0.0	101.50	97.20	3.08	9.17
12-2.5-6-60-30	48.6	0.0	11.82	80.97	99.0	0.0	12.74	87.26	90.16	0.0	102.03	97.0	4.86	9.28
12-3-6-60-30	76.33	4.92	5.2	92.14	93.94	6.05	5.34	94.65	92.39	8.52	96.1	101.43	8.12	9.73

rich product increased to 3.08% (w/w) as compared to 2.80% (w/w) of the previous cycles mentioned above.

At this point of the run, a new flow arrangement was proposed by Gould[174] who was exprimenting with a scaled-up version of the SCCR4 unit. The arrangement was the once through single purge column with split fructose rich product streams, see figure (8.17). As seen in the figure, the arrangement was basically similar to the once-through single column purge arrangement, except that the purge stream was split into two; each conveying to a separate container the purged product of the first half and the second half of the switch period. The switching of the two controlling pneumatic valves was performed by a timer snychronized to the SCCR4 timer.

The benefit of using this flow arrangement was in the solid concentration of the fructose rich product. It increased from 2.8% (w/w) in the original arrangement to 4.86% (w/w). The reason for this occurrence was that, at 30 $cm^3 min^{-1}$ of purge water rate, the majority of the sugar in the purged column was washed off in the first ten minutes of the switch period, see figure (8.7). This was further confirmed by Gould[174] during his research when a continuous automated polarimeter was used to trace the distribution of fructose and glucose in the fructose rich stream.

In operating conditions (3), the feed rate was further increased to 3 $cm^3 min^{-1}$ and the eluent rate was

decreased to 5.5 $cm^3 min^{-1}$. The feed to eluent ratio was lowered to 1:1.83. All the other conditions were similar to those in conditions (1) and (2) above. The once through, single purge column with split fructose rich product streams arrangement was used.

When a lower eluent rate was used, the fructose rich product consisted of 93.94% (w/w) fructose and 6.05% (w/w) dextran and glucose. This happened because of the eluent volume per switch period, 165 cm^3 being less than the 180 cm^3 stated in equation (8.20).

The fructose recovery efficiency increased to 92.39% from 90.41% in the previous sets of conditions (1,2). This indicated more sugar was retained in the columns in the separating section.

The solid concentration improved to 8.12% (w/w).

The run was terminated after 600 hours when feed was exhausted. The columns were purged off individually and the system profile was obtained, figure (8.16). The system profile was quite similar to that of run 9-2-6-30-30, figure (8.13), except for the higher concentration of the glucose and the dextran in the columns in the pre-feed section.

Finally, material x was detected only in the fructose rich product. Consultation with Barker [175], and Alsop and Gibbs of the Fisons Company[176], suggested that the material x was to be identified and that steps were to be taken to eliminate it during the feed treatment stage, before passing it through the

SCCR4 unit.

A life-test on the SCCR4 unit was carried out by monitoring the movement of the metal ions going into and out of the separating section. Table (8.13) showed the result from the atomic absorption spectrometer equipment. Sodium, calcium, lead, iron, zinc and copper were the ions under scrutiny.

Generally, the mass balance of the ions into and out of the SCCR4 unit did not balance, suggesting that they were being retained on the packings.

The large quantity of sodium ions detected was artificial, as the preservative used on the feed was sodium azide (concentration of 0.02% (w/v)). Consultation with Holding[172] and Forrester, J., Bio-Rad Company[177] indicated that sodium had no displacement effect on the calcium ions on the packings.

The calcium and the iron ions were present in the town water used in the dextran plant, as informed by Forrester, I., of the Fisons Company[178]. Again, both the ions were retained on the packing after the feed was passed through the SCCR4 unit. In the case of the calcium ions, retention of the ions was advantageous, as it recharged the packings in situ.

Zinc, lead and copper ions were present in a very small quantity, not detectable in the case of the latter two ions.

TABLE 8.13 ATOMIC ABSORPTION SPECTROMETER RESULTS

FRUCTOSE RICH PRODUCT

RUN 12 CYCLE	Na SODIUM ppm	Ca CALCIUM ppm	Pb LEAD ppm	Fe IRON ppm	Zn ZINC ppm	Cu COPPER ppm
4	2.1	10.0	< 0.001	1.8	0.1	< 0.001
12	2.0	10.0	"	1.6	0.01	"
16	2.1	2.5	"	1.6	0.2	"
27	2.2	2.7	"	2.2	0.2	"
32	2.4	2.7	"	1.7	0.0	"
64	2.2	2.4	"	4.1	0.1	"
86	2.0	2.8	"	4.5	0.2	"
92	1.9	2.4	"	4.5	0.2	"
100	2.3	3.2	"	4.3	0.15	"
GLUCOSE RICH PRODUCT						
4	300	10	"	1.2	0.2	"
12	320	12	"	3.0	1.7	"
16	315	26	"	2.1	0.2	"
27	300	25	"	3.0	0.4	"
32	330	27	"	2.6	0.3	"
64	330	19	"	2.1	0.1	"
86	340	20	"	2.7	0.2	"
92	310	21	"	2.4	0.25	"
100	327	20	"	2.2	0.2	"
FEED	1565	650	< 0.001	60.8	7.5	< 0.001

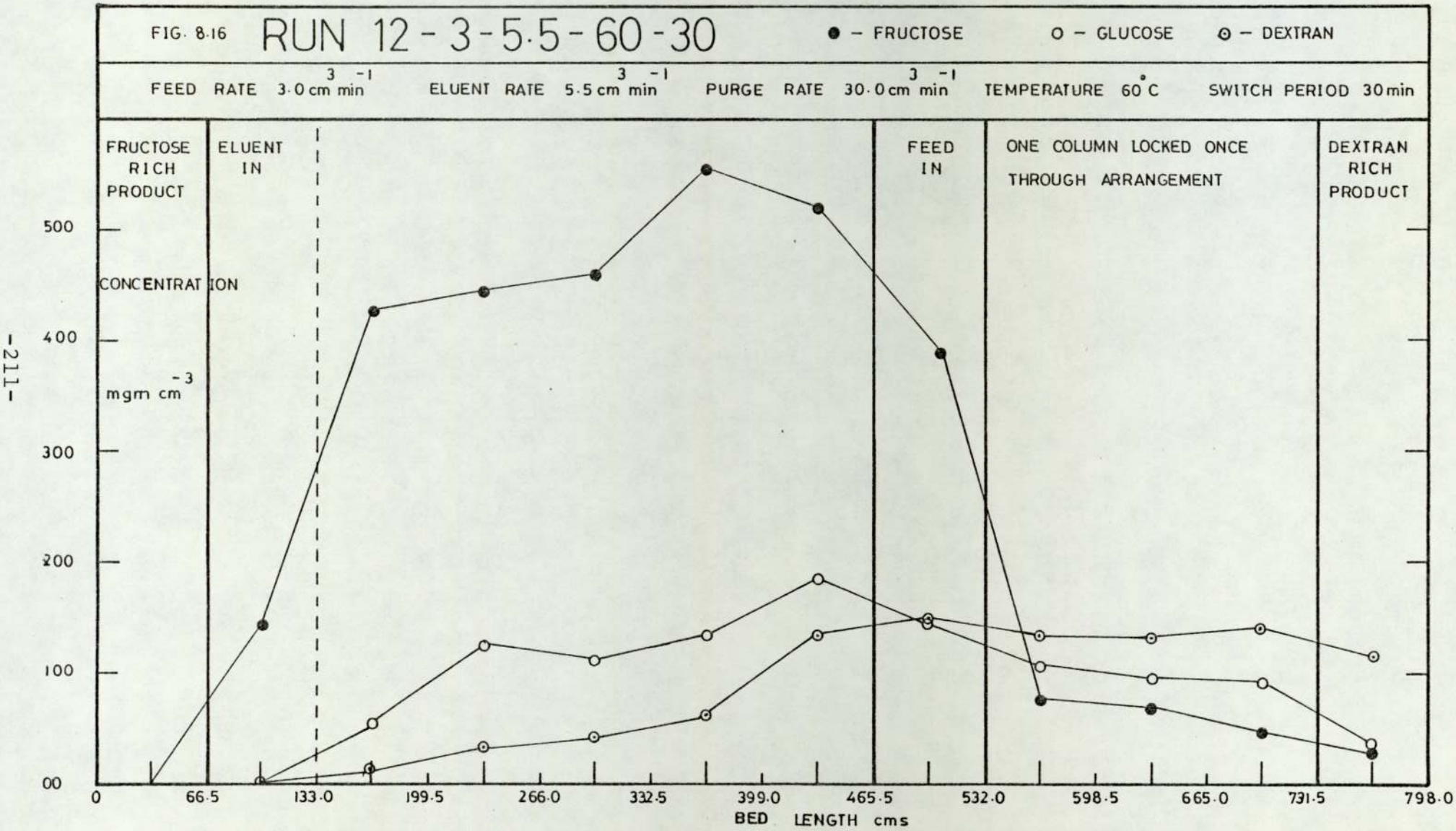


FIG. 8.16 RUN 12 - 3 - 5.5 - 60 - 30
● – FRUCTOSE
O – GLUCOSE
⊙ – DEXTRAN
FEED RATE 3.0 cm³ min⁻¹
ELUENT RATE 5.5 cm³ min⁻¹
PURGE RATE 30.0 cm³ min⁻¹
TEMPERATURE 60°C
SWITCH PERIOD 30 min
FRUCTOSE RICH PRODUCT
ELUENT IN
FEED IN
ONE COLUMN LOCKED ONCE THROUGH ARRANGEMENT
DEXTRAN RICH PRODUCT
CONCENTRATION
mgm cm⁻³
500
400
300
200
100
00
0
66.5
133.0
199.5
266.0
332.5
399.0
465.5
532.0
598.5
665.0
731.5
798.0
BED LENGTH cms

Finally, from the mechanical point of view, the SCCR4 unit operated smoothly when a short switch period of 30 minutes was used. Pressure drop was within the designed range, 340 kNm^{-2} (50 lb in^{-2}) and 1020 kNm^{-2} (150 lb in^{-2}), in all three sets of operating conditions. However, towards the last five cycles of the run, the pressure drop on the eluent line entering the separating section increased to 1100 kNm^{-2} (165 ib in^{-2}). It indicated that debris or insoluble dextran were accumulating in the columns. Deposits of solid were observed on the wall of the polystyrene tubes. Later analysis of the solid by dissolving in water at high temperature (100°C) and passing the solutiong through the Bio-Rad HPLC column, detected a small trace of dextran. Most of the solid remained in suspension in the solution. Pure crystalline dextran was difficult to dissolve in water[176], an experience gained in the Pharmaceutical Industry selling bottled clinical dextran products.

The fructose rich product obtained was visibly coloured, like caramel sugar solution, but it was expected that the colour could be removed by passing the product through a bed of activated carbon particles.

8.3.3.3 CONCLUSION

In addition to the sugars, fructose, glucose and dextran in the Fisons feed, sucrose, leucrose and

an unknown soluble material labelled, x were also detected. Through close co-operation and consultation with the sponsors, Fisons Company, it was decided that further work was to continue to identify material x, and that if possible, material x should be eliminated during the feed processing stage, before passing the feed through the SCCR4 unit.

An almost pure fructose rich product of 99% was obtained at a throughput of 630 gms per hour. The solid concentration in the fructose product was 4.86% but later cycles had improved the figure to 8.17%, when the new proposed once through single purge column with split fructose rich streams was used. Further improvement was thought possible with the use of recycling and by using a lower purge flowrate. From the limited range of experiments studied with the synthetic Fisons feed indicated that the best operating conditions were as follows:

(1) 1.5 $cm^3 min^{-1}$ feed flowrate
3.0 $cm^3 min^{-1}$ eluent flowrate
10.0 $cm^3 min^{-1}$ purge flowrate
30°C temperature in the enclosure
or 60°C as preferred by the Fisons Company

But when the Fisons feed was used the best operating conditions preferred were as follows:

(2) 2.5 $cm^3 min^{-1}$ feed flowrate
6.0 $cm^3 min^{-1}$ eluent flowrate
3.0 $cm^3 min^{-1}$ eluent flowrate
60°C temperature in the enclosure

The packing life-test indicated that metal ions were retained in the system, but no detrimental effect on the performance of the SCCR4 was observed.

Mechanically, the SCCR4 unit operated smoothly and blockages of lines could be easily removed by flushing with warm water after a period of continuous running. 500 hours was recommended for flushing and general maintenance. The packings seem to have a long and durable life, as the results of these experiments show.

8.4 EXPERIMENTS WITH THE SUCROSE FEED

The advancement in ion-exchanger resin technology has made it possible today to hydrolyse sucrose into a glucose/fructose mixture, by passing it through a hydrogen charged polystyrene based resin packed in a column. An elevated temperature around the column was essential for an almost complete hydrolysis inversion.

In this part of the research, a hydrogen charged amberlite 1R-118 resin was used in a pre-column for inverting the sucrose feed continuously. The amberlite resin was donated by the Rohm and Hass Company based in Croydon, England.

The inverted feed from the pre-column contained mainly glucose, 5.3% (w/w) and fructose, 44% (w/w), and approximately 3% (w/w) sucrose. The inversion temperature was 60^{o}C and the residence time of the sugar in the column was 90 minutes.

Combining the pre-column and the SCCR4 unit, a new continuous chromatographic process for producing a fructose-rich product from sucrose was developed.

8.4.1 EXPERIMENTS WITH THE PRE-COLUMN PACKED WITH THE AMBERLITE 1R-118 RESIN

A 2.54 cm (1.0 in) I.D. column was packed with the amberlite 1R-118. The resin was charged in the free hydrogen form and packed to a height of 65 cm. A fitting with a large hold-up was fitted at the outlet of the column to increase the time of the sugar passing through the packed bed, see figure (8.18).

A 50% (w/v) solution of sucrose was passed through the hydrogen charged packed bed continuously for 456 hours, at a flowrate of 2.0 $cm^3 min^{-1}$ and at an elevated temperature of 60°C. Table (8.14) shows the results of the experiment.

It was found that the composition of the inverted mixture varied through the length of the experiment. Glucose, 55%-66% (w/w) and fructose 38%-44% (w/w), and the remaining fraction containing approximately 3% (w/w) sucrose. The result showed an unexpectantly high glucose to fructose ratio, 1.3:1, in contrast to the 1:1 ratio expected, because one molecule of sucrose contained one molecule of glucose and one molecule of fructose. Through consultation with Burke and Vane[179] both distinguished workers in the ion-exchange technology in the sugar industry suggested that, at 60°C possible

FIG. 8.19a PHOTOGRAPH OF THE PRE-COLUMN

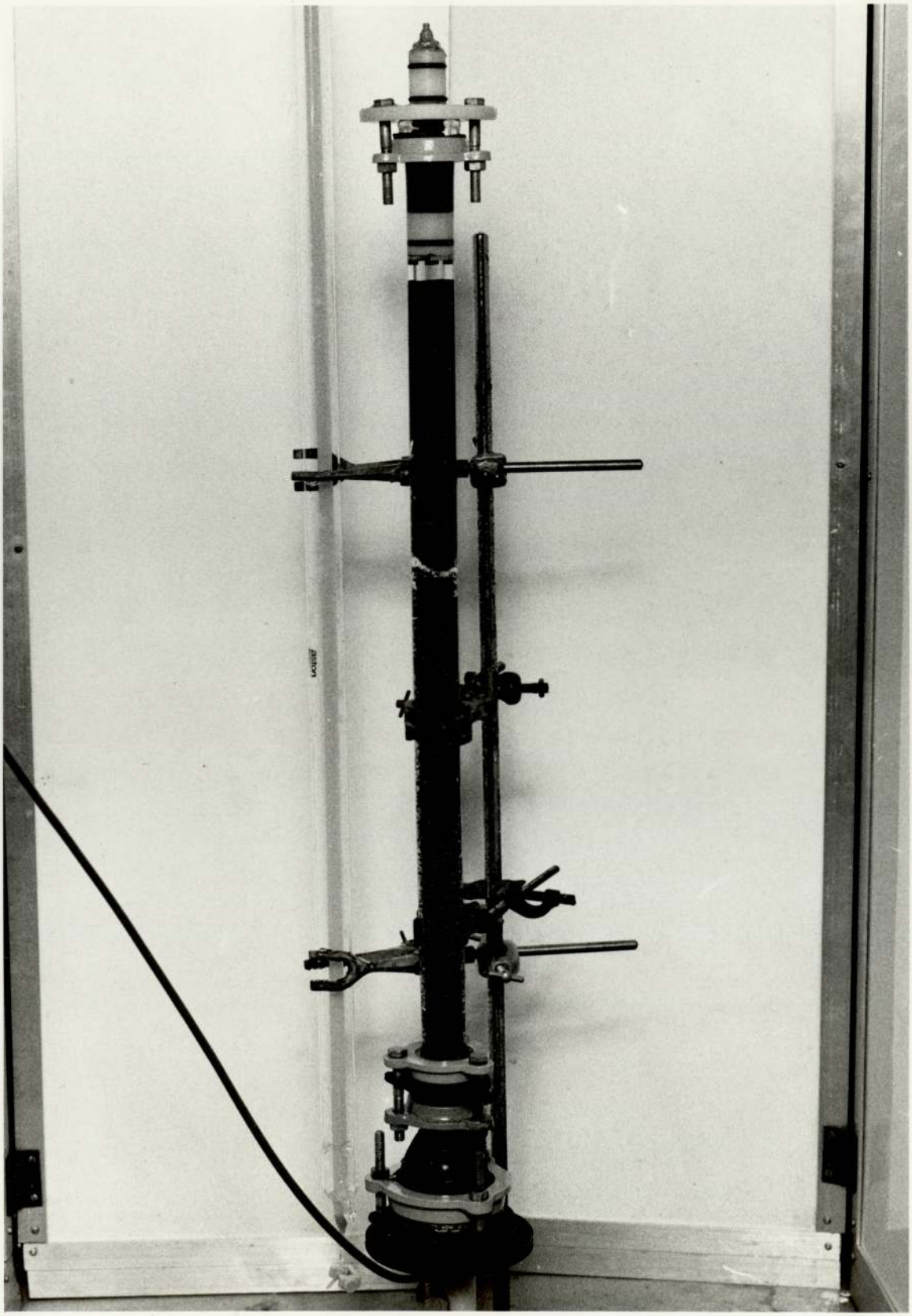


FIG. 8.19b PHOTOGRAPH OF THE PRE-COLUMN OUTLET

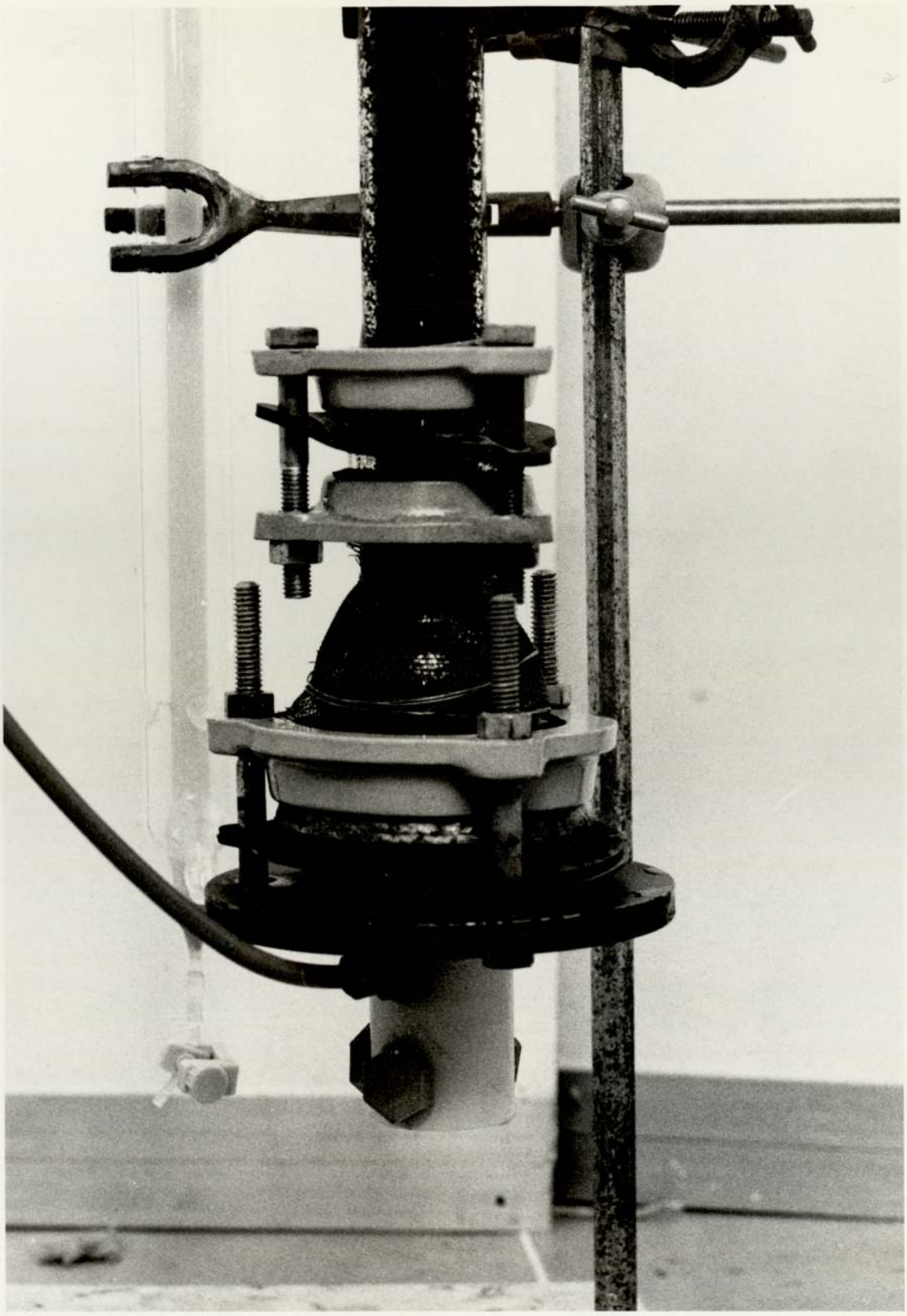


TABLE 8.14 SUCROSE INVERSION RESULTS.

NUMBER	HOUR	GLUCOSE %	FRUCTOSE %
1	24	59.87	41.13
2	48	61.50	38.50
3	72	56.49	43.50
4	96	59.80	40.19
5	144	57.05	42.95
6	216	55.80	44.10
7	336	58.37	41.63
8	360	56.83	43.16
9	456	55.07	44.94

FLOWRATE – 2.0 $cm^3 min^{-1}$ TEMPERATURE – 60 °C

CONCENTRATION FEED – 500.0 mgm cm^{-3}

BED – HYDROGEN FORM , AMBERLITE IR–118

degradation of the sugar took place after passing through the packed bed. The inverted syrup was honey coloured. It was possible that fructose was more sensitive to the conditions in the packed column, but the physical properties of fructose did not suggest it to be so.

The Boehringer patent claimed an equal proportion of the fructose and the glucose was obtained when the sucrose was passed through the hydrogen charged packed bed, but other owrkers had reported a similar proportion as found in this work of the fructose (42% (w/w)) and the glucose (55% (w/w)) in a paper published by Siedman[60].

Later a proposed inversion conditon for the pre-column was suggested by William and Bucke[180], from the record of their work with a similar type of resin.

The proposed conditions were a pH value of 4.5 in the feed solution, an elevated temperature of between 40-50^{o}C and a residence time of 60 minutes. These conditions were used in a later experiment but it was found that there was no significant change in the composition of the iverted syrup.

Nevertheless, the Amberlite 1R-118 resin did successfully invert 97% (w/w) of the sucrose feed.

8.4.2 EFFECTS OF TEMPERATURE AND SWITCH PERIOD ON THE SEPARATION OF THE INVERTED SYRUP IN THE SCCR4 UNIT

These three runs differed in several ways; run 13-2-6-60-30 used a 1:3 feed ratio, a 60 minutes switch period, and an enclosure temperature of 60°C. The feed was passed through the pre-column and directly into the SCCR4 unit, see table (8.15).

Run 14-2-6-30-30 used a 1:3 feed to eluent ratio, a 30 minutes switch period and an enclosure temperature of 30°C. The feed was prepared separately under the conditions proposed by Reid and Bucke[180], i.e. at a temperature of 45°C, residence time of 60 minutes and a pH 4.5 in the sucrose solution. The inverted syrup was stored and then fed into the SCCR4 unit.

Run 15-2-6-60-30 used a 1:3.2 feed to eluent ratio, a 30 minutes switch period and an enclosure temperature of 60°C. The sucrose feed was inverted in the pre-column and the inverted syrup fed directly into the SCCR4 unit.

The main objective of these experiments was to find an alternative feed source of fructose.

8.4.3 RESULT AND DISCUSSION

The operating conditions of the run 13-2-6.0-60-30 was the most favourable for separating a 50% (w/v) glucose/fructose mixture. But the result in Table (8.16)

TABLE 8.15 RUN CONDITIONS

RUN NUMBER	FLOWRATE			CONCENTRATION			SWITCH PERIOD	ELUENT VOL PER SWITCH	TEMPERATURE IN ENCLOSURE
	FEED	ELUENT	PURGE	FRUCTOSE	GLUCOSE	SUCROSE			
	$cm^3\ min^{-1}$			$mgm\ cm^{-3}$			min	cm^3/switch	°C
13-1.5-3-60-60	1.5	3.0	30.0	250.0	340.0	15.0	60.0	180.0	60.0
14-2-6-30-30	2.0	6.0	30.0	250.0	320.0	20.0	30.0	180.0	30.0
15-2-6.4-60-30	2.0	6.4	30.0	250.0	320.0	20.0	30.0	192.0	60.0

TABLE 8.16 RESULTS

RUN NUMBER	F-RICH PRODUCT CONC.		G-RICH PRODUCT CONC.			F-RICH PRODUCT PURITY		G-RICH PRODUCT PURITY			SUGAR IN F-RICH STREAM		MASS BALANCE (OUT/IN)		SOLID IN STREAM		INVERSION OF SUCROSE
	F	G	F	G	S	F	G	F	G	S	F	G	F	G	FRP	GRP	
	$mgm\ cm^{-3}$		$mgm\ cm^{-3}$			%		%			%		%		%		%
13-1.5-3-60-60	16.07	6.10	8.85	62.70	4.26	72.48	27.54	11.67	82.71	5.62	89.26	24.55	104.0	100.2	2.22	7.58	97.14
14-2-6-30-30	18.61	5.61	6.33	57.84	3.62	76.84	23.15	9.33	85.32	5.34	95.94	24.42	99.20	97.16	2.42	6.37	97.00
15-2-6.4-60-30	15.26	2.25	7.65	55.42	2.50	87.01	12.98	11.69	84.43	3.65	89.18	11.86	103.18	101.89	1.73	654	98.0

showed that the purity of the fructose in the fructose rich product was 72.5%. The fructose recovery efficiency was 89.26% and the solid concentration in the fructose rich product was 2.22% (w/w). The glucose purity in the glucose rich product was 82.71%.

The reason for the poor fructose purity in the fructose rich product was due to the higher percentage of the glucose present in the feed, see figure (8.20). Greater overlapping of the glucose into the fructose fraction occurred, hence the 'over-shadowing' effect.

Run 14-2-6-30-30 was performed at room temperature using the operating parameters similar to the run 8-2-6-30-30 for a 50-50% (w/w) glucose-fructose feed.

The fructose purity in the fructose rich product improved to 76.84% (w/w) as compared to run 13-2-6.0-60-30. The glucose purity in the glucose rich product improved to 90.86%. The fructose recovery efficiency improved to 95.94% as compared to 89.26% for run 13-1.5-3-60-50.

The improvement in the products quality was mainly due to the use of a lower sugar throughput, 360 gms per cycle compared to 540 gms per cycle of run 13-2-6-60-30, and the enclosure temperature at $30^{o}C$.

The solid concentration in the fructose rich product was 2.42%.

In the last run, the eluent flowrate was increased slightly to 6.4 $cm^3 min^{-1}$, hence the eluent volume per switch period was 192 cm^3 (>180 cm^3, V_g).

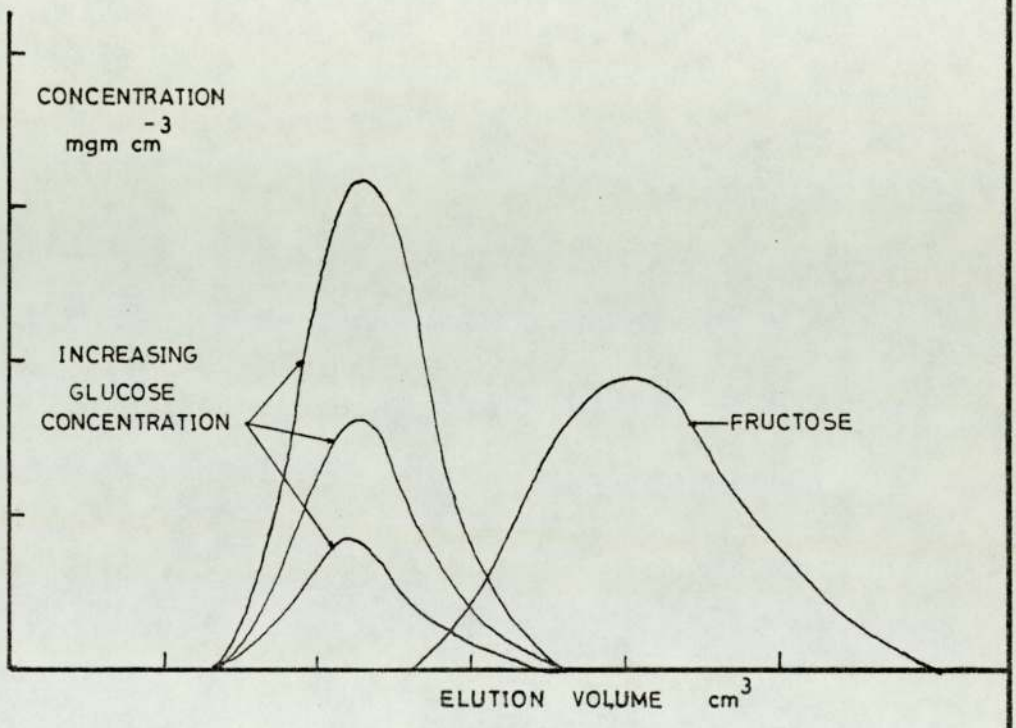


FIG. 8.20 ILLUSTRATION OF THE OVERLAPPING EFFECT CAUSE BY INCREASING THE GLUCOSE CONCENTRATION

The fructose purity in the fructose rich product improved to 87.01% compared to 76.84% or run 14-2-6-30-30.

The fructose recovery efficiency decreased to 89.18% and the solid concentration in the fructose rich product was 1.73% compared to 95.94% and 2.42% respectively of run 14-2-6-30-30. The glucose purity in the glucose rich product decreased to 84.43%.

Higher fructose purity was obtained due to the increased eluent flowrate from 6.0 to 6.4 cm^3min^{-1}, but fructose recovery efficiency and the solid concentration in the fructose rich product decreased, indicating that more sugars were being carried along in the mobile phase.

Also, higher temperatures tended to affect the retention of the fructose as shown in the batch analytical experiment in Chapter (7). Distribution of the fructose in the stationary phase and the mobile phase favoured the latter phase at elevated temperature.

The system profiles of run 13-2-6-60-30 and 14-2-6.0-30-30, figures (8.21) and (8.22) showed the difference in the shape of the profile at 60^oC in the enclosure and at room temperature. At 60^oC the concentration of the fructose component in each column was higher at approximately 65 mgm cm^{-3} compared to 23 mgm cm^{-3}, at room temperature. This feature supported the results obtained from the run as shown in Table (8.16), especially in the fructose recovery efficiency and the solid concentration in the fructose rich product.

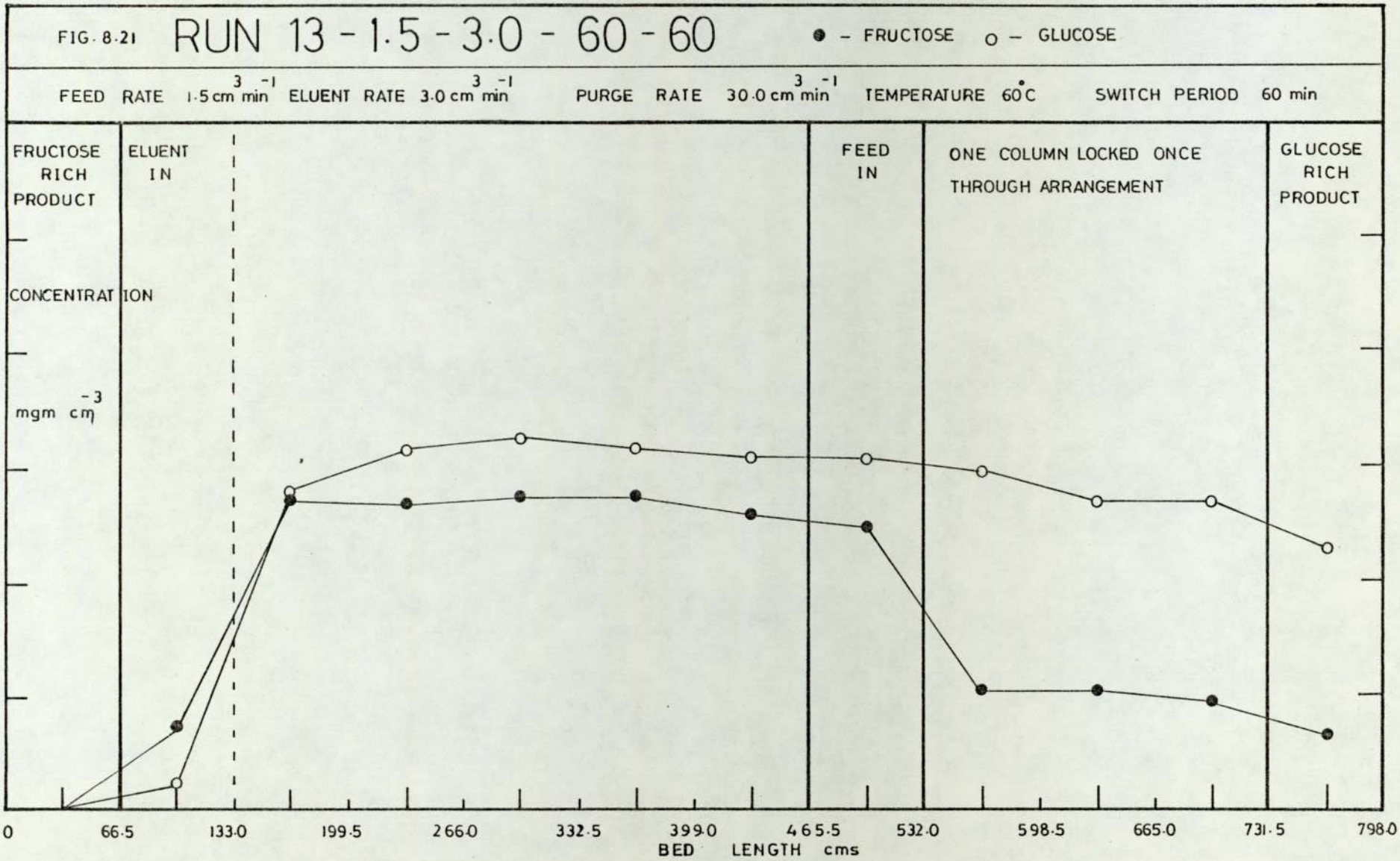


FIG. 8.21 RUN 13 - 1.5 - 3.0 - 60 - 60
● - FRUCTOSE o - GLUCOSE
FEED RATE 1.5 cm³ min⁻¹ ELUENT RATE 3.0 cm³ min⁻¹ PURGE RATE 30.0 cm³ min⁻¹ TEMPERATURE 60°C SWITCH PERIOD 60 min
FRUCTOSE RICH PRODUCT
ELUENT IN
FEED IN
ONE COLUMN LOCKED ONCE THROUGH ARRANGEMENT
GLUCOSE RICH PRODUCT
CONCENTRATION
mgm cm⁻³
500
400
300
200
100
00
0
66.5
133.0
199.5
266.0
332.5
399.0
465.5
532.0
598.5
665.0
731.5
798.0
BED LENGTH cms

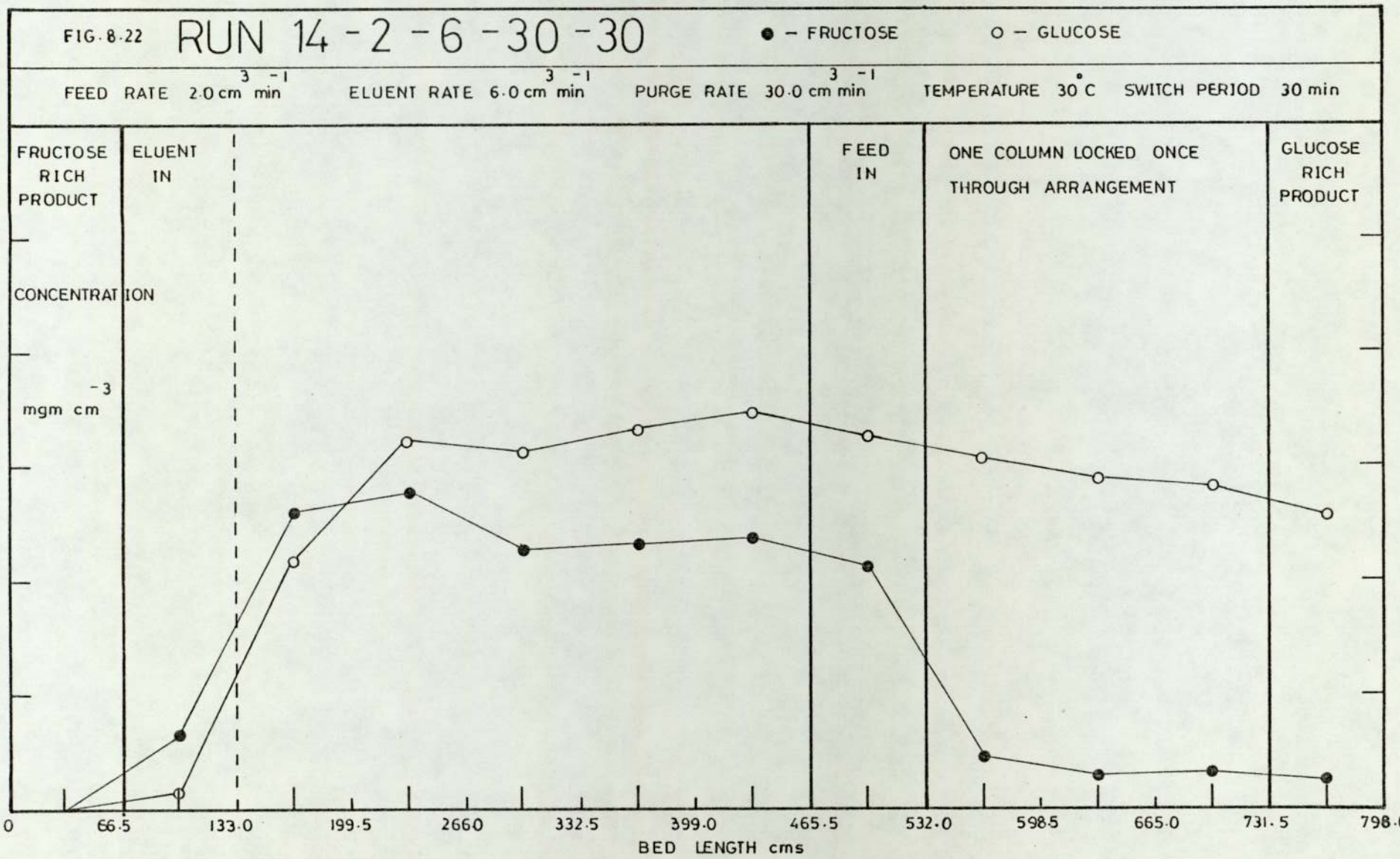
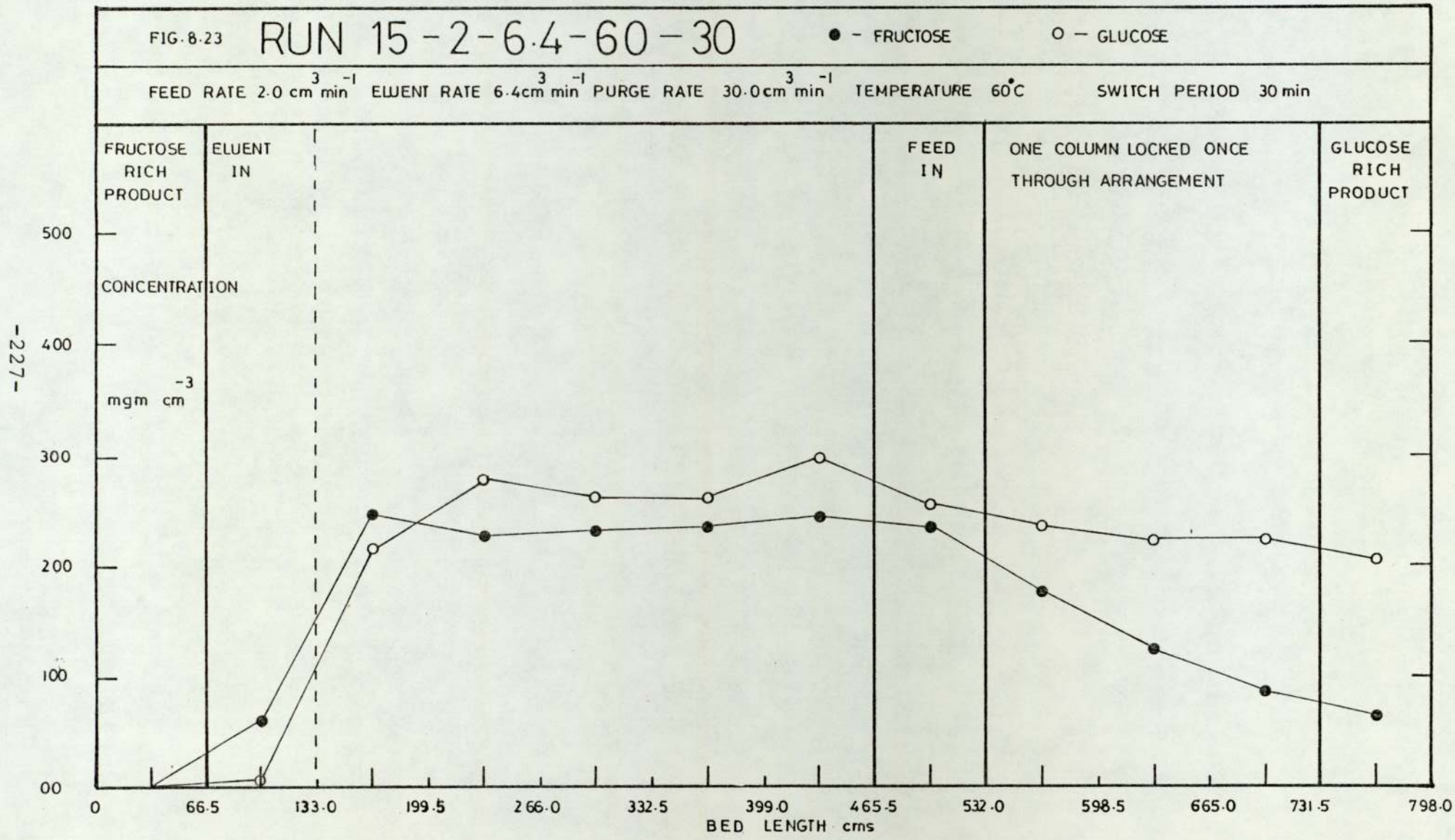


FIG. 8.22 RUN 14 - 2 - 6 - 30 - 30
● – FRUCTOSE
O – GLUCOSE
FEED RATE 2.0 cm³ min⁻¹
ELUENT RATE 6.0 cm³ min⁻¹
PURGE RATE 30.0 cm³ min⁻¹
TEMPERATURE 30°C
SWITCH PERIOD 30 min
FRUCTOSE RICH PRODUCT
ELUENT IN
FEED IN
ONE COLUMN LOCKED ONCE THROUGH ARRANGEMENT
GLUCOSE RICH PRODUCT
CONCENTRATION
mgm cm⁻³
500
400
300
200
100
00
0
66.5
133.0
199.5
266.0
332.5
399.0
465.5
532.0
598.5
665.0
731.5
798.0
BED LENGTH cms


FIG·8·23 RUN 15-2-6·4-60-30
● - FRUCTOSE
O - GLUCOSE
FEED RATE 2·0 cm³ min⁻¹ ELUENT RATE 6·4cm³ min⁻¹ PURGE RATE 30·0cm³ min⁻¹ TEMPERATURE 60°C SWITCH PERIOD 30 min
FRUCTOSE RICH PRODUCT
ELUENT IN
FEED IN
ONE COLUMN LOCKED ONCE THROUGH ARRANGEMENT
GLUCOSE RICH PRODUCT
CONCENTRATION
mgm cm⁻³
500
400
300
200
100
00
0
66·5
133·0
199·5
266·0
332·5
399·0
465·5
532·0
598·5
665·0
731·5
798·0
BED LENGTH cms

The system profiles of run 13-2-6-60-30 and 15-2-6.4-60-30 were similar as the operating conditions only differed slightly with the eluent flowrate, 6.0 cm^3min^{-1} and 6.4 cm^3min^{-1} respectively.

All the three system profiles, figures (8.21), (8.22) and (8.23) showed the overshadowing effect of the glucose component over the fructose component in the pre-feed section.

8.4.4 CONCLUSION

A 50% (w/v) feed solution of sucrose was successfully hydrolysed after passing through a hydrogen charged packed column. The inverted syrup contained 50% (w/v) solid, consisting of 55% (w/w) glucose, 42% (w/w) fructose and 3% sucrose. The residence time of the sugar in the column was 60 minutes and the temperature around the pre-column was 60°C.

Separation of the inverted syrup directly from the pre-column in the SCCR4 unit produced an 87% fructose rich product and an 84% glucose rich product.

The best operating conditions found were a feed to eluent ratio of 1:3.2, a switch period of 30 minutes and a temperature of 60°C in the enclosure. The flow arrangement used was the once through, single column purge type, figure (8.3-1).

The combined inverting and separating stages into a process for producing a fructose rich product and a

glucose rich product, from sucrose was possible and served our purpose in looking for an alternative fructose/glucose feed source for the larger unit (10.5 cm I.D. columns).

C H A P T E R N I N E

COMPUTER SIMULATION OF THE EXPERIMENTS PERFORMED THE SEMI CONTINUOUS CHROMATOGRAPHIC REFINER

9. COMPUTER SIMULATION OF THE EXPERIMENTS PERFORMED THE SEMI CONTINUOUS CHROMATOGRAPHIC REFINER

Notable works of theoretical modelling for the batch chromatographic technique has been developed by Martin and Synge (45), Giddings (44), Synder (46) and Kirkland (47). All their works have been documented in various textbooks and in papers published in a wide variety of journals. Chapter two in this thesis reviewed in brief, some of their more distinguished achievements.

In continuous chromatography, which is comparatively a new technique being developed as a separation process, publications of the work on the theoretical model are more limited. However, a short review of the work published in this particular subject will be outlined, which is then followed by a detailed discussion on the improvement to the modelling previously used by Dr. C.B. Ching (24).

Chosen experimental results from Dr. C.B. Ching (24), J.C. Gould (174) and from the present project will be simulated by computer. The theoretical modes adapted for this work was originally developed by Sunal (16) in his work on a gas/liquid chromatography system. The modes used a plate to plate calculations analogous multi-stage reactor design.

9.1 MODEL BASED ON THE 'EQUILIBRIUM STAGE OR PLATE' CONCEPT

Sciance and Crosser (181) proposed a model for a moving bed form of continuous chromatography, relating to the degree of separation, operating conditions and required column length for a binary feed mixture. On

an example in which the feed was introduced into the mid-section of the column, they proposed

$$\ln (U_{\not B})_A = \frac{0.5\ \ell K_A''}{u} (K_A - \Psi) \quad \ldots\ldots\ldots\ldots \quad (9.1)$$

$$\ln 1-(U_{\not B})_B = \frac{-0.5\ \ell K_B''}{u} (K_B - \Psi) \quad \ldots\ldots\ldots\ldots \quad (9.2)$$

A refers to the faster moving component

B refers to the slower moving component

$(U_{\not B})_A$ = Bottom/feed mass flowrate ratio of A

$(U_{\not B})_B$ = Tops/feed mass flowrate ratio of B

K'' = rate constant of desorption

u = average mobile phase velocity

Ψ = operating mobile phase/stationary phase velocity ratio

ℓ = required column length

Use of the above equations rests on knowing values of K_A'' and K_B''. As published values are scarce and the experimental procedures for their determination are difficult, the application of this model is very restricted.

Al-Madfai (12), used the randon walk approach developed by Giddings (44) and adopted it for predicting plate height in a continuous 'moving column' counter-current chromatography system. His proposed model is as follows

$$H = \frac{dp+2Dm}{U} + \frac{2\gamma_1\gamma_2}{(\gamma_1+\gamma_2)^2} \cdot \frac{(U+U_L)^2}{(U\gamma_2-U_2\gamma_1} \quad \ldots\ldots\ldots\ldots\ldots \quad (9.3)$$

where γ_1 = Rate of transfer of molecules from gas to liquid

γ_2 = Rate of transfer of molecules from liquid to gas

U_L = Stationary phase velocity

Al-Nadfai (12 also related the number of theoretical plates required to resolve a binary system employing a static column, N, to N_{CC}, the number of plate required by a continuous chromatographic column to achieve the same separation

$$\frac{N_{CC}}{N} = 3\ (\alpha-1) \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (9.4)$$

N_{CC} = Number of counter-current theoretical plates

N = Number of co-current theoretical plates (static column)

Details of his work are available in various publications (10-12).

Barker and Huntingdon (7) adopted the theory of stagewise liquid/liquid extraction given by Alder (1 & 2) to develop a relationship between product purity, the number of equilibrium stages and the difficulty of separation

$$\log \frac{\Psi_R}{\Psi_S} = \log \frac{K_B}{K_A} + \frac{2}{N_{CC}} \left\{ \log \frac{(1-E_A)}{f_A} + \log \frac{E_B}{f_B} \right\} \quad \ldots\ldots \quad (9.5)$$

where Ψ_R, Ψ_S = the ratio of mobile phase/stationary phase flowrate in the 'rectifying' and 'stripping' sections respectively

E_A, E_B = the mass production rates of components A and B in the top product.

f_A, f_B = the mass feedrate of components A and B to the column

K_A, K_B = Partition coefficients for the components A and B.

Using this relationship (9.6), they obtained H.E.T.P. values of approximately 5 cm. when separating benzene and cyclohexane on the circular, moving-column unit.

9.2 MODES BASED ON THE TRANSFER UNIT CONCEPT

Barker and Lloyd (4) employed the transfer unit concept of Chilton and Colburn in their treatment of the counter-current gas/liquid chromatographic process. The following relationships between the number of transfer units for the rectifying and stripping sections, and the run parameters were derived:

$$(N_{OG})_R = \frac{1}{V_6/(K_O V_2 - 1)} \ln \frac{E_i/K_O V_L - C_1(V_6/K_O V_2 - 1)}{E_i/K_O V_L - C_2(V_6/K_O V_2 - 1)} \quad \ldots \quad (9.6)$$

$$(N_{OG})_S = \frac{1}{(1-V_6(K_O V_2)} \ln \frac{E_{ii}/K_O V_L - C_1(1-V_6/K_O V_2}{E_{ii}/K_O V_L - C_2(1-V_6/K_O V_2} \quad \ldots \quad (9.7)$$

$$Z = H_{OG} \cdot N_{OG} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (9.8)$$

$$H_{OG} = G_{ii}/K_{Gi}$$

where

$(N_{O6})_R, (N_{O6})_S$ = the number of overall gas phase transfer units in the 'rectifying' and 'stripping' sections respectively.

E_i, E_{ii} = the mass flowrate of solute leaving in Product i and Product ii streams respectively.

C_1, C_2 = Gas phase solute concentration at points 1,2 in the column

V_6, V_L = the gas and liquid volumetric flowrates

K_O = Partition coefficient.

Experimental studies on a 2.5 cm. diameter vertical moving-bed column with benzene, cyclo-hexane and methylchyclohexane as solutes and polyoxyethylene 400 diricinoleate as the solvent phase, was conducted by Barker and Lloyd (4). Their results indicated that the main resistance to mass transfer was in the gas phase. Furthermore, a first order relationship was found between the solvent (stationary) phase flowrate and the logarithm of H_{O6}.

9.3 THE MATHEMATICAL MODEL USED FOR SIMULATING THE SCCR4 EXPERIMENTS

Sunal (16), originally introduced the plate to plate model concept into the gas/liquid chromatographic system in which he was simulating. The unit he used, was of

a compact circular continuous counter-current chromatographic type.

Deeble (2), subsequently improved Sunal's model and adopted it to simulate the operation of the SCCRI, gas-liquid chromatograohic unit. Detailed results of his achievement were published in several papers and his thesis (17-20). Further improvements for the gas-liquid chromatographic model were made by Bell (183).

Following Deeble, Ching (24) revised the model and applied it to simulate the operation of the SCCR4, liquid-solid chromatographic unit. In it, Ching achieved a generally good agreement between the experimental and the simulated results. Details of his work were published in his thesis (24).

In this project, the model used by Ching will be improved and adapted for use in a multi-component, twelve-column system.

9.3.1 The Theoretical Development of the Plate to Plate Model

This model is based on the theoretical plate concept. It is assumed that each plate has a volume consisting of the stationary phase and a volume consisting of the mobile phase (void and pore volumes). A stream of a flowrate Q passing through the plate, having an initial concentration of C_{n-1}, and a concentration of C_n after leaving it.

A mass balance over the plate gave, (refer to figure 9.1)

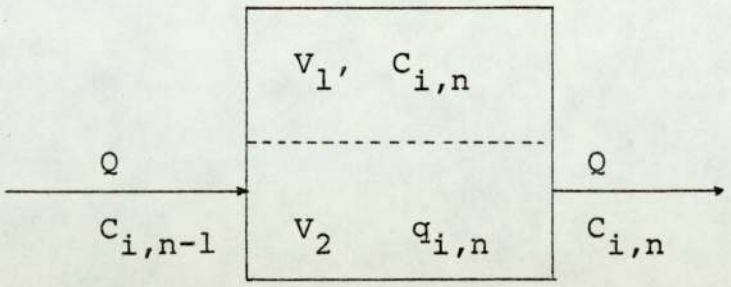


fig (9.1)

$$Q_i C_{n-1} = QC_{i,n} + \frac{V_1 \, d \, C_{iyn}}{dt} + V_2 \frac{dqi,n}{dt} \quad \ldots\ldots\ldots (9.9)$$

Q = mobile phase volumetric flowrate

C = solate concentration in the mobile phase

q = solute concentration in the stationary phase

V_1 = Volume of mobile phase in a plate

V_2 = Volume of stationary phase in a plate

n = the number of the plate

i = the number of the component in the system, fructose, glucose, dextran, ...

Substituting $Kd_i = \frac{qi,n}{C_{i,n}}$, Kd_i = the distribution coefficient of a component,

$$Q \, C_{i,n-1} = QC_{i,n} + (V_1 + Kd_i V_2) \, d \, \frac{C_{i,n}}{dt} \quad \ldots\ldots (9.10)$$

Now, providing the time increment t is sufficiently small to allow C_{n-1} to be considered constant, integration of

equation 9.10 yields

$$C_{i,n} = C_{i,n-1}\left(1-e^{\frac{-Q.\Delta t}{(V_1+V_2Kd_i)}}\right) + C^{o}_{i,n}\, e^{\frac{-Q.\Delta t}{(V_1+V_2Kd_i)}} \quad \ldots (9.11)$$

Where C_n^{o} = initial concentration of the solute in plate, n.

The first term on the right-hand side of equation (9.11) represents the contribution to C_n from the (n-1)th plate to the nth plate, while the second turn represented the contribution from material present on nth plate at the beginning of the time increment.

For a feed plate, a mass balance yielded a similar equation,

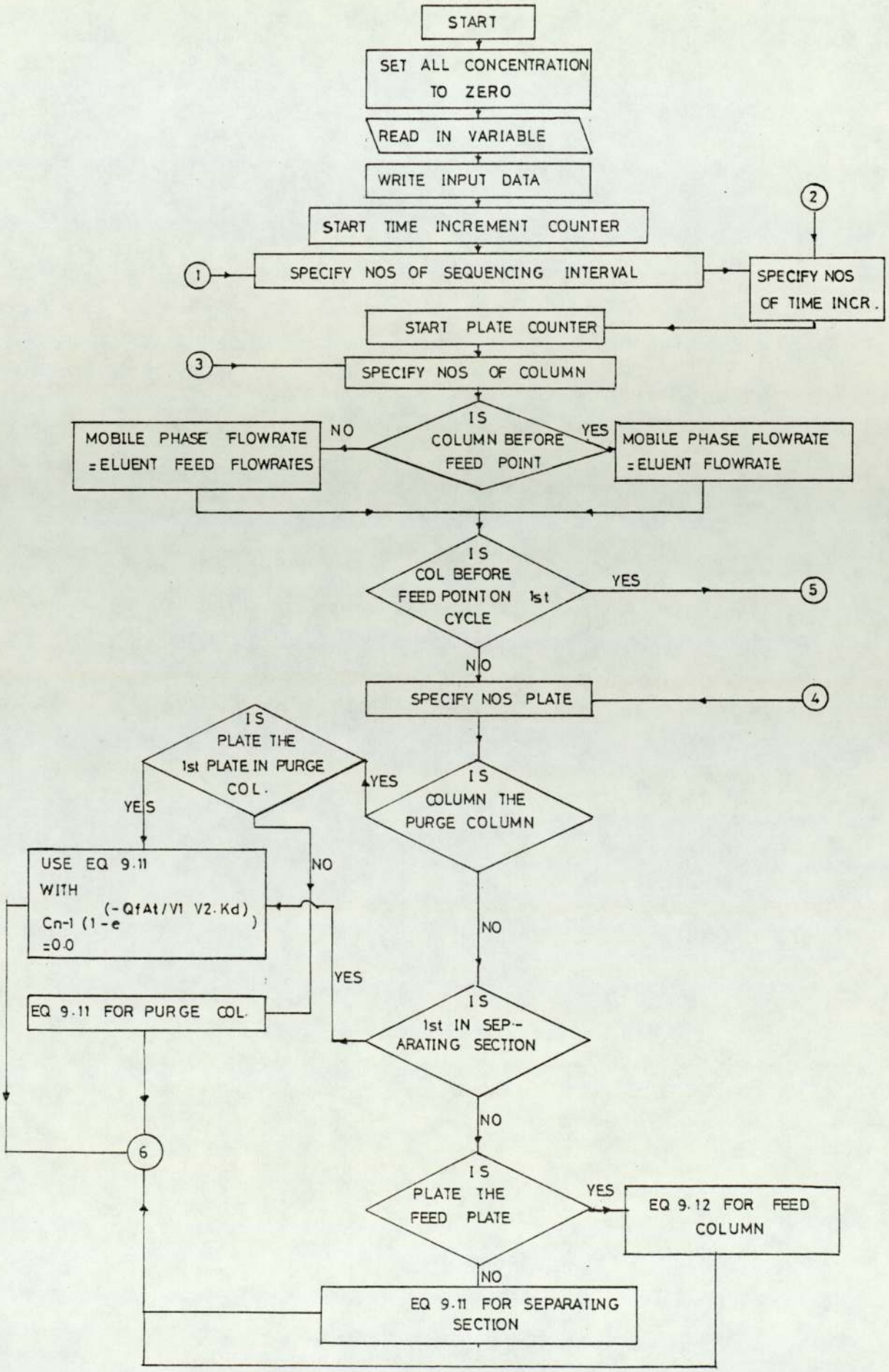
$$C_{i,n} = \left|\frac{QC_{n-1} + F_{(i,f)}}{Q+F}\right| \left|1 - e^{\frac{-(Q+F)\Delta t}{(V_1+V_2Kd_i)}}\right| + Co\, e^{\frac{-(Q+F)\Delta t}{(V_1+V_2Kd_i)}} \quad \ldots (9.12)$$

Where F, c = feed volumetric flowrate and concentration.

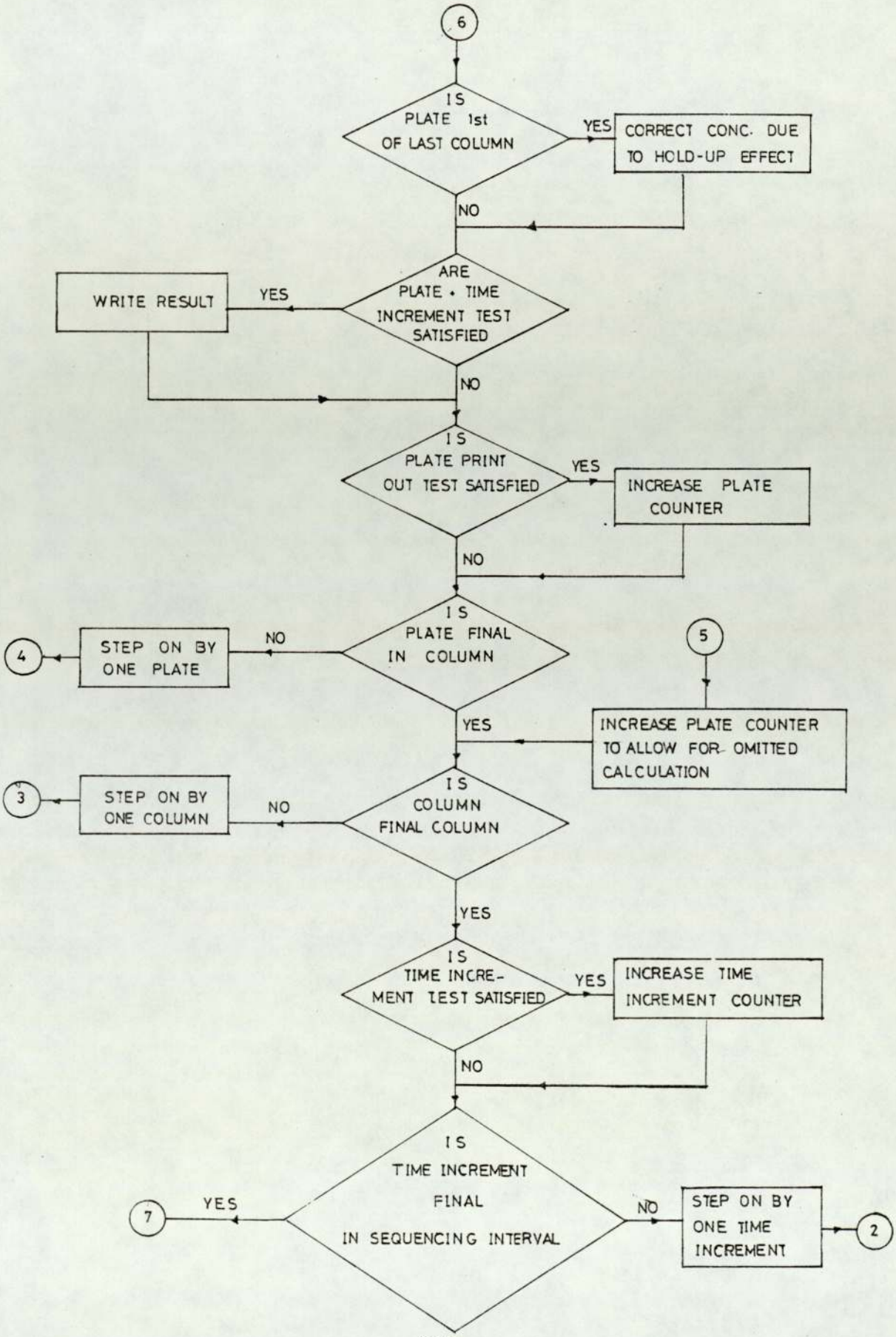
The sequencing action of the SCCR4 was simulated by stepping the system profile backwards, by one column, at the end of a sequencing interval. A flow chart for the program listing and a print-out results are provided in the appendices, I, II and III. A flowchart is provided in Fig. (9.2)

9.3.2. <u>The Objectives Of This Exercise</u>

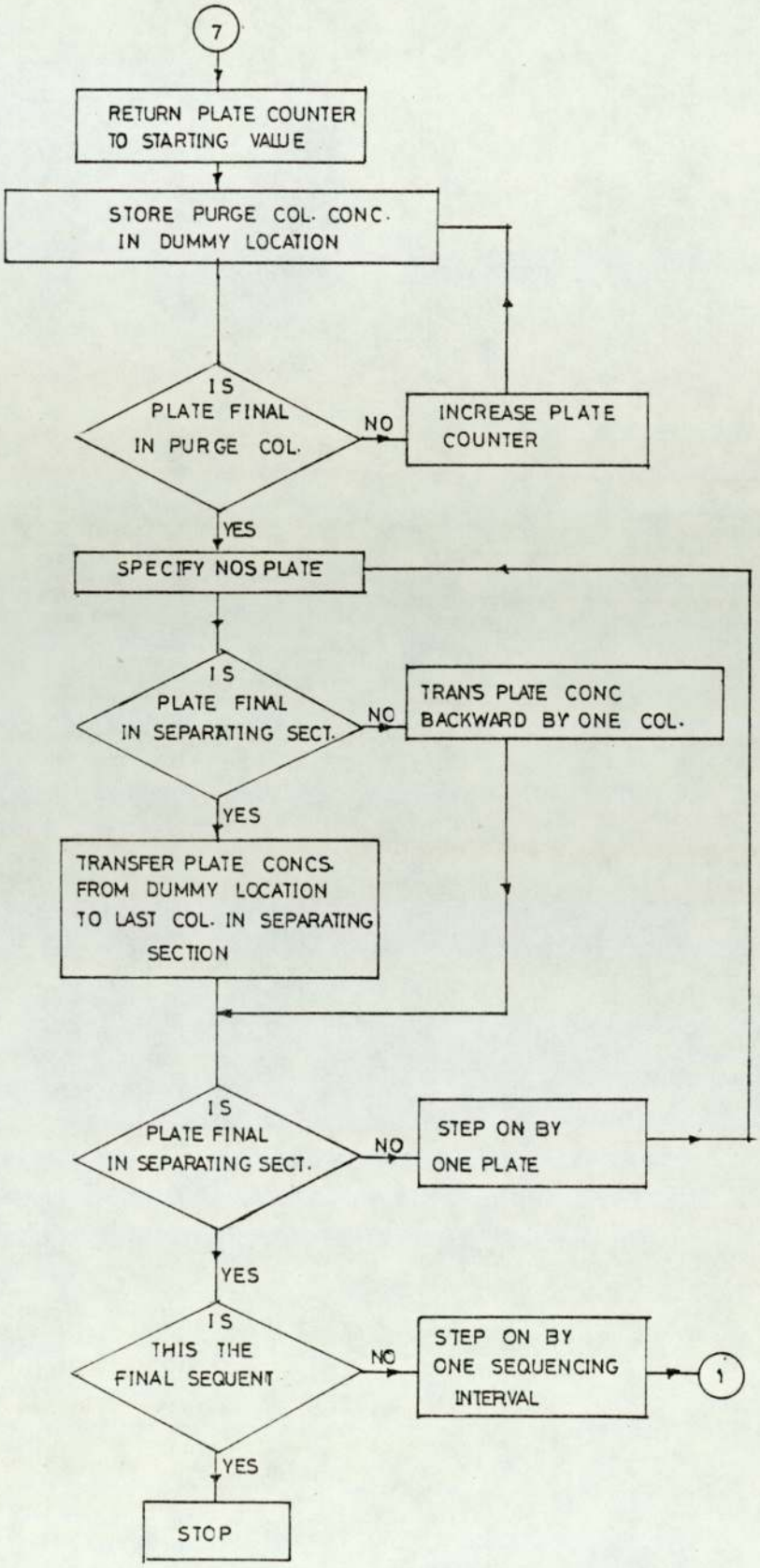
FIG. 9.2 COMPUTER FLOW CHART FOR THE SIMULATION MODEL



CONTINUE.....


6
IS PLATE 1st OF LAST COLUMN
YES
CORRECT CONC. DUE TO HOLD-UP EFFECT
NO
ARE PLATE + TIME INCREMENT TEST SATISFIED
YES
WRITE RESULT
NO
IS PLATE PRINT OUT TEST SATISFIED
YES
INCREASE PLATE COUNTER
NO
IS PLATE FINAL IN COLUMN
NO
STEP ON BY ONE PLATE
4
5
YES
INCREASE PLATE COUNTER TO ALLOW FOR OMITTED CALCULATION
IS COLUMN FINAL COLUMN
NO
STEP ON BY ONE COLUMN
3
YES
IS TIME INCREMENT TEST SATISFIED
YES
INCREASE TIME INCREMENT COUNTER
NO
IS TIME INCREMENT FINAL IN SEQUENCING INTERVAL
YES
7
NO
STEP ON BY ONE TIME INCREMENT
2

CONTINUE.....


7
RETURN PLATE COUNTER TO STARTING VALUE
STORE PURGE COL. CONC. IN DUMMY LOCATION
IS PLATE FINAL IN PURGE COL.
NO
INCREASE PLATE COUNTER
YES
SPECIFY NOS PLATE
IS PLATE FINAL IN SEPARATING SECT.
NO
TRANS PLATE CONC BACKWARD BY ONE COL.
YES
TRANSFER PLATE CONCS. FROM DUMMY LOCATION TO LAST COL. IN SEPARATING SECTION
IS PLATE FINAL IN SEPARATING SECT.
NO
STEP ON BY ONE PLATE
YES
IS THIS THE FINAL SEQUENT
NO
STEP ON BY ONE SEQUENCING INTERVAL
1
YES
STOP

9.3.2.1 Improvement on Ching's Model

A close examination of Ching's simulation of the experimental results (24) suggested that, further improvement on the model was possible. The two most obvious areas in which improvement could be achieved were; firstly, redefining the mechanism of separation in the operation of the equipment. Ching considered that only one chromatographic mode was operating in the SCCR4 system, that was, chemi-adsorption chromotography. He proposed that glucose was not retained at all by the absorbent and the distribution coefficient of glucose, Kdg equalled zero. The distribution coefficient of fructose Kdf, was determined experimentally with respect to glucose as the completely eluted component. This was not accurate as the packing used in the SCCR4 unit did retain glucose in the pores. The elution volumes fround experimentally of a very large molecule such as dextran (112 cm^3) and of glucose (184 cm^3) provided the evidence to justify this claim, (refer to chapter 7 for further reading). In other words, glucose had a Kdg value of approximately 0.15, and fructose a Kdf value of approximately 0.62; and that two modes of chromatography were operating in the SCCR4 unit, namely gel permeation chromatography and chemi-adsorption chromatography.

Secondly, a hold-up liquid volume having a high fructose concentration was present and had a detrimental effect on the performance of the SCCR4 unit. The hold-up liquid volume consisted of the liquid volume in the transfer lines

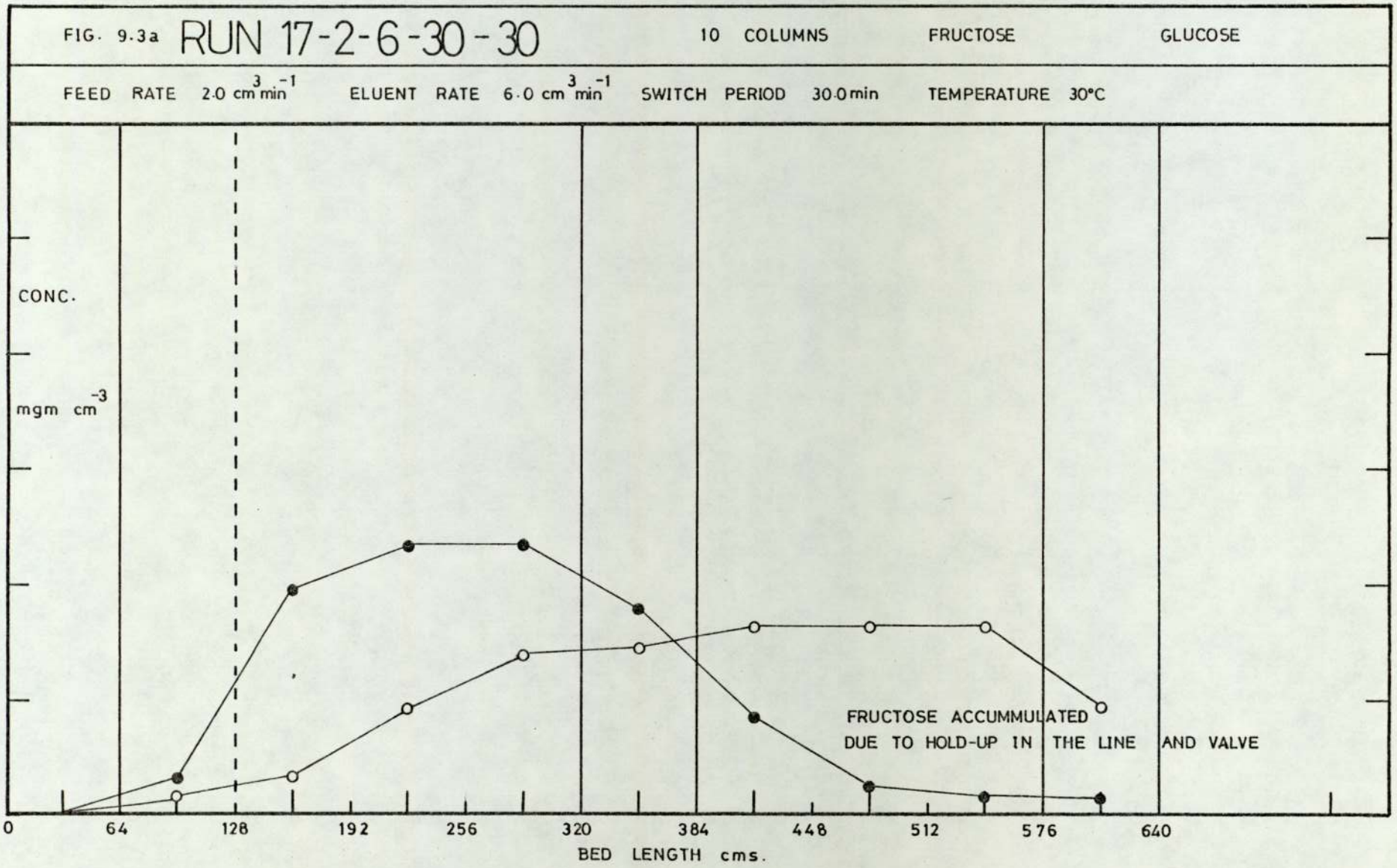


FIG. 9.3a RUN 17-2-6-30-30
10 COLUMNS
FRUCTOSE
GLUCOSE
FEED RATE 2·0 cm³ min⁻¹
ELUENT RATE 6·0 cm³ min⁻¹
SWITCH PERIOD 30·0 min
TEMPERATURE 30°C
CONC.
mgm cm⁻³
500
400
300
200
100
0
0
64
128
192
256
320
384
448
512
576
640
BED LENGTH cms.
FRUCTOSE ACCUMMULATED
DUE TO HOLD-UP IN THE LINE AND VALVE

and the liquid volume in the transfer poppet valve. The effect of this hold-up liquid volume on the performance of the SCCR4 unit can best be illustrated in several diagrams in figure (9.3).

Figure (9.3a) shows a system profile for a run 17-2-6-30-30 performed by Ching (24); notice the presence of fructose in all the volumes in the post feed section. This fructose was present in the 'dead' liquid volumes in the transfer lines and the transfer valves between the isolated column and the eluted column, X, and the isolated column and the last column in the post-feed section, Y, figure (9.3b). In the next switch, the fructose rich liquid in the section Y, entered the last column of the post-feed section, and the X section assumed the position of the Y section of the previous switch, figure (9.3c). The fructose entering the last column in the post feed section was partly retained in the column in the switch period. This occurred in every switch period and the fructose concentration in the columns in the post-feed section gradually built up until a pseudo-steady state was reached, then it remained approximately constant. During the experiment, this was detected by the gradual increase in the percentage solid of fructose in the glucose rich produce of the earlier cycles.

Other improvements carried out were mainly to the computer programme namely:

FIG. 9.3b DIGRAM ILLUSTRATING THE EFFECT OF LIQUID HOLD UP IN THE SCCR4 UNIT

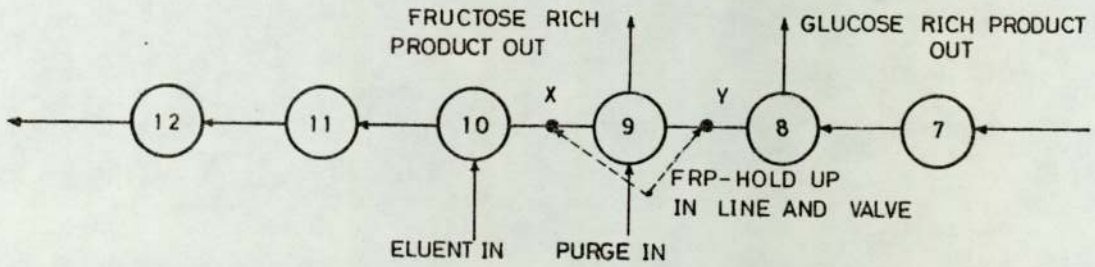
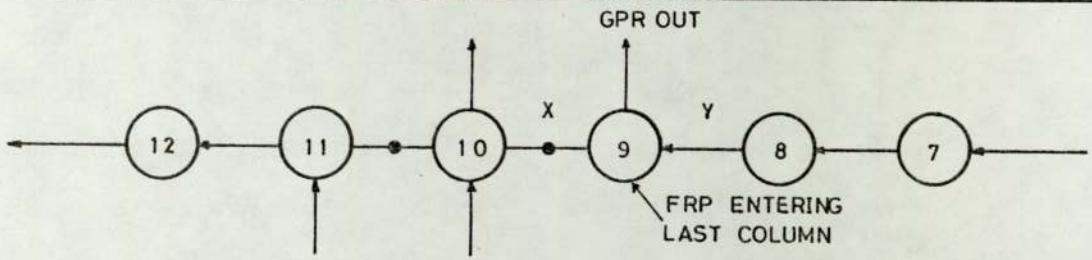


FIG 9.3c



(i) extending the programme to include a third component for the simulation of the system profile.

(ii) extending the programme for a 12-column system.

(iii) removing an artifical limit incorporated by the previous worker (24), for excluding all the material entering the pre-feed columns in the first five switches calculation. New evidence was provided by Gould (174) from his work with a 10.25 cms I.D. column unit, to suggest that the limit did not apply in practise.

(iv) altering the structure of the programme to allow for more flexible application.

9.3.2.2 Simulation of Experiments

As a means of testing the improved computer programme for simulating the system profile, it was decided that selected results from Ching (24), from Gould (174) and from this research were to be simulated.

It has been mentioned earlier in this chapter (section 9.3.2.1) that a hold-up liquid volume in the transfer line and valves of the SCCR4 unit, had a detrimental effect on the performance, in that fructose was accumulated in the volumes in the post-feed section.

In order to allow for this, the initial concentration on the first plate on the last column $C^{o}_{i,n}$, was equated to

the concentration on the last plate on the eluted column, hence equation (9.11) for that plate became,

$$C_{i,n} = C_{i,n-1}\left(1-e^{\frac{-Q\Delta t}{V_1+V_2Kd_i}}\right) + C^{o}_{i,n-m} \cdot e^{\frac{-Q\Delta t}{(V_1+V_2Kd_i)}} \; H/V_m \ldots \quad (9.13)$$

Where

m = 140 or 180 for the 10 column unit and 12 column unit respectively

H = the hold-up volume

V_m = the mobile phase volume

In the 10.50 cms (4 ins) I.D. column unit, SCCR6, of Gould (174) experimental results showed that the liquid hold-up volume in transfer line and valves did not have any significant effect on the performance. The results from the SCCR6 unit provided an adequate test of the use of equation (9.13), when the H/V_m term was very small.

9.3.3 Selection of Results for Simulation

Table (9.1 a,b,c), shows that summary of the results used in the simulation work.

The results selected from the three sources were based on parameters in which there was a common ground to enable the results to be compared. The parameters were, the feed to eluent ratios, the number of carbohydrate components

TABLE 9.1a SUMMARY OF CONDITIONS USED IN THE EXPERIMENTS AND SIMULATION WORK

EXPERIMENTAL

RUN NUMBER	FEED CONC.			FLOWRATES			DISTRIBUTION COEFFICIENTS			TEMP. OF SURROUND.	SWITCH PERIOD	RESEARCHER
	F	G	D	FEED	ELUENT	PURGE	Kdf	Kdg	Kdd			
	mgm cm^{-3}			cm min^{-1}						°C	min	
16-1-6-30-30	250	240	00	1	6	300	-	-	-	30	30	CHING C.
17-2-6-30-30	250	240	00	2	6	300	-	-	-	30	30	"
18-3-6-30-30	250	240	00	3	6	300	-	-	-	30	30	"
25-2-6-30-30	10	10	00	2.4	6	300	-	-	-	30	30	"
SIMULATION												
16-1-6-30-30	250	230	00	1	6	300	0.60	0.11	00	30	30	CHUAH C.
17-2-6-30-30	250	230	00	2	6	300	0.60	0.15	00	30	30	"
18-3-6-30-30	250	230	00	3	6	300	0.60	0.15	00	30	30	"
25-2.4-6-30-30	10	10	00	2.4	6	300	0.60	0.1	00	30	30	"

TABLE 9.1 b SUMMARY OF CONDITIONS USED IN THE EXPERIMENTS AND SIMULATION WORK

RUN NUMBER	FEED CONC.			FLOWRATES			DISTRIBUTION COEFFICIENTS			TEMP. OF SURROUND.	SWITCH PERIOD	RESEARCHER	
	F	G	D	FEED	ELUENT	PURGE	Kdf	Kdg	Kdd				
	mgm cm^{-3}			cm^3 min						°C	min		
19-36-108-30-30	100	100	00	36	108	540	-	-	-	30	30	GOULD J.	EXPERIMENTAL
20-45-108-30-30	100	100	00	45	108	540	-	-	-	30	30	"	
21-54-108-30-30	100	100	00	54	108	540	-	-	-	30	30	"	
22-36-108-30-30	200	200	00	36	108	540	-	-	-	30	30	"	
23-36-108-30-30	300	300	00	36	108	540	-	-	-	30	30	"	
24-36-108-30-30	483	63	162	36	108	540	-	-	-	30	30	"	
19-36-108-30-30	100	100	00	36	108	540	0.57	0.07	-	30	30	CHUAH C.	SIMULATED
20-45-108-30-30	100	100	00	45	108	540	0.57	0.17	-	30	30	"	
21-54-108-30-30	100	100	00	54	108	540	0.55	0.20	-	30	30	"	
22-36-108-30-30	200	200	00	36	108	540	0.60	0.30	-	30	30	"	
23-36-108-30-30	300	300	00	36	108	540	0.60	0.30	-	30	30	"	
24-36-108-30-30	483	63	154	36	108	540	0.57	0.27	00	30	30	"	

TABLE 9.1c SUMMARY OF CONDITIONS USED IN THE EXPERIMENTS AND SIMULATION WORK

EXPERIMENTAL

RUN NUMBER	FEED CONC.			FLOWRATES			DISTRIBUTION COEFFICIENTS			TEMP. OF SURROUND	SWITCH PERIOD	RESEARCHER
	F	G	D	FEED	ELUENT	PURGE	Kdf	Kdg	Kdd			
	mgm cm^{-3}			cm min^{-1}						°C	min	
1-2-6-30-30	260	260	00	2	6	300	-	-	-	30	30	CHUAH C.
2-2.5-6-30-30	270	260	00	2.5	6	300	-	-	-	30	30	"
3-3-6-30-30	270	260	00	3	6	300	-	-	-	30	30	"
9-2-6-30-30	465	485	160	2	6	20	-	-	-	30	30	"
14-2-6-30-30	250	320	00	2	6	30	-	-	-	30	30	"
SIMULATED												
1-2-6-30-30	250	240	00	2	6	300	0.59	0.22	00	30	30	CHUAH C.
2-2.5-6-30-30	250	240	00	2.5	6	300	0.57	0.21	00	30	30	"
3-3-6-30-30	250	240	00	3	6	300	0.60	0.23	00	30	30	"
9-2-6-30-30	483	63	154	2	6	20	0.57	0.20	00	30	30	"
14-2-6-30-30	250	300	00	2	6	30	0.61	0.31	00	30	30	"

used in the system, the concetration of the feed and the number of columns, the temperature of the surroundings and the switch period. Table (9.1) is self explanatory. In addition, the results obtained by Dr C.B. Ching (24) using a 2% (w/v) feed concentration was included, enabling comparison to be made with the simulated results of dilute conditions. It must be made clear, that the equilibrium coefficient of distribution for glucose and fructose, Kdg and Kdf respectively, were evaluated at infinite dilution conditions, (see chapter 7).

The effect of concentration of the carbohydrate in the chromatographic column on the equilibrium coefficeint of distribution Kd, was being investigated by Dr. S. Holding (172) by fractionating dextran in a glucose rich mobile phase. Research work should be extended in the near future to include fructose being eluted with a glucose rich mobile phase and vice versa.

Therefore, until the data from the research mentioned above is available, the theoretical model as used in this research cannot be fully tested. However, improvements to the model have been carried out and experimental results obtained by two other independent research workers, namely Dr C.B. Ching (24) and J.C. Gould (178) will be simulated.

9.3.4 Result and Discussion

The simulation model required a long computer time and a large memory core, which was not available in the

ICL 1904S model at the University of Aston. Instead, the North-West Regional Computer CDCI 7600, at the University of Manchester was used, through a line linked between the Universities.

A summary of the experiments to be simulated is provided in table (9.1ai) and in table (9.1aii) the conditions used in the simulation runs. The results of the simulation runs are shown in figures (9.4-9.16) and the print-outs in appendix (II).

Generally, a good agreement between the experimental and the simulated results was achieved, in particular the glucose profile. The liquid hold-up term incorporated into the programme allowed for the accumulation of the fructose in the columns in the post-feed section. The extension of the programme to include dextran and the two extra columns has made it more felxible with 'built-in' statements to accept n number of components and m number of columns.

However, there were still two shortcomings which needed further development, and one of those was the fructose profile; particularly the concentration of the fructose in the columns in the pre-feed section. In practice, much higher frucrose in the concentrations were found in the columns in the pre-feed section, as compared to the simulated fructose concentration in the same columns. The simulated fructose concentration in these columns only equalled the fructose

concentration in the feed, where else the experimental ones went beyond the feed concentration level. The explanation for this difference was due mainly to fructose being washed from the first eluted column into the next column, and from the next column into the one after it. Hence, fructose was present in both the mobile phase and the stationary phase, which gave the apparent higher concentration; since the average concentration of the column was calculated with respect to the liquid volumn (void and pore volumes) in the column. The experimental results of all the system profiles showed that a lower fructose concentration was found in the first eluted column in the pre-feed section, as compared to the sumulated system profile for the same column.

The other shortcoming was the long and expensive computer time required to simulate the system profile. Recently, England (26) adapted a computing technique used in simulating a distillation process in his work on the fractionation of dextran using a similar SCCR unit. An attempt to use this technique to simulate the experiments of this research was unsuccessful, as the results generated diverged into very large numbers and oscillated. This happened when a thirty minute switch time was used. However, England (26) has shown that this technique was applicable with a 7½ minutes switch period, and it would warrant a detailed investigation in the future.

Finally, a recommendation from Dr Ching (24) regarding the use of a numerical technique to solve the differential equation (9.14)

$$Q\,C_{i,n-1} = Q\,C_{i,n} + \frac{V_i dC_{i,n}}{d} + V_2\,K_d\,\frac{dC_{i,n}}{dt} + C_n\,\frac{dK_d}{dt} \qquad (9.14)$$

$$\frac{dq_{i,n}}{dt} = K_d\,\frac{dC_{i,n}}{dt} + C_n\,\frac{dKd_i}{dt},$$

as Kd_i is dependent on $C_{i,n}$

was not investigated as no relationship between the k_d and the $C_{i,n}$ was available and also because an investigation into this particular area was being carried out by Dr Holding (172). Publication of his work on the fractionation of dextran with a glucose-rich mobile phase is expected in the near future. It is expected that an investigation in this area will be extended to the fructose and glucose system.

9.3.4.1 Ching's experimental runs

Simulation of Ching's experimental runs, 16-1-6-30-30, 17-2-6-30-30, 18-3-6-30-30 and run 25-2-6-30-30 were successfully achieved, as seen in figures (9.4-9.6). 5.5% (v/v) liquid hold-up was introduced into the calculation and it agreed with the experimental results in all cases. The coefficient of distribution of fructose, kdf was 0.6, and that of glucose ranged from 0.10 to 0.15. The coefficient of

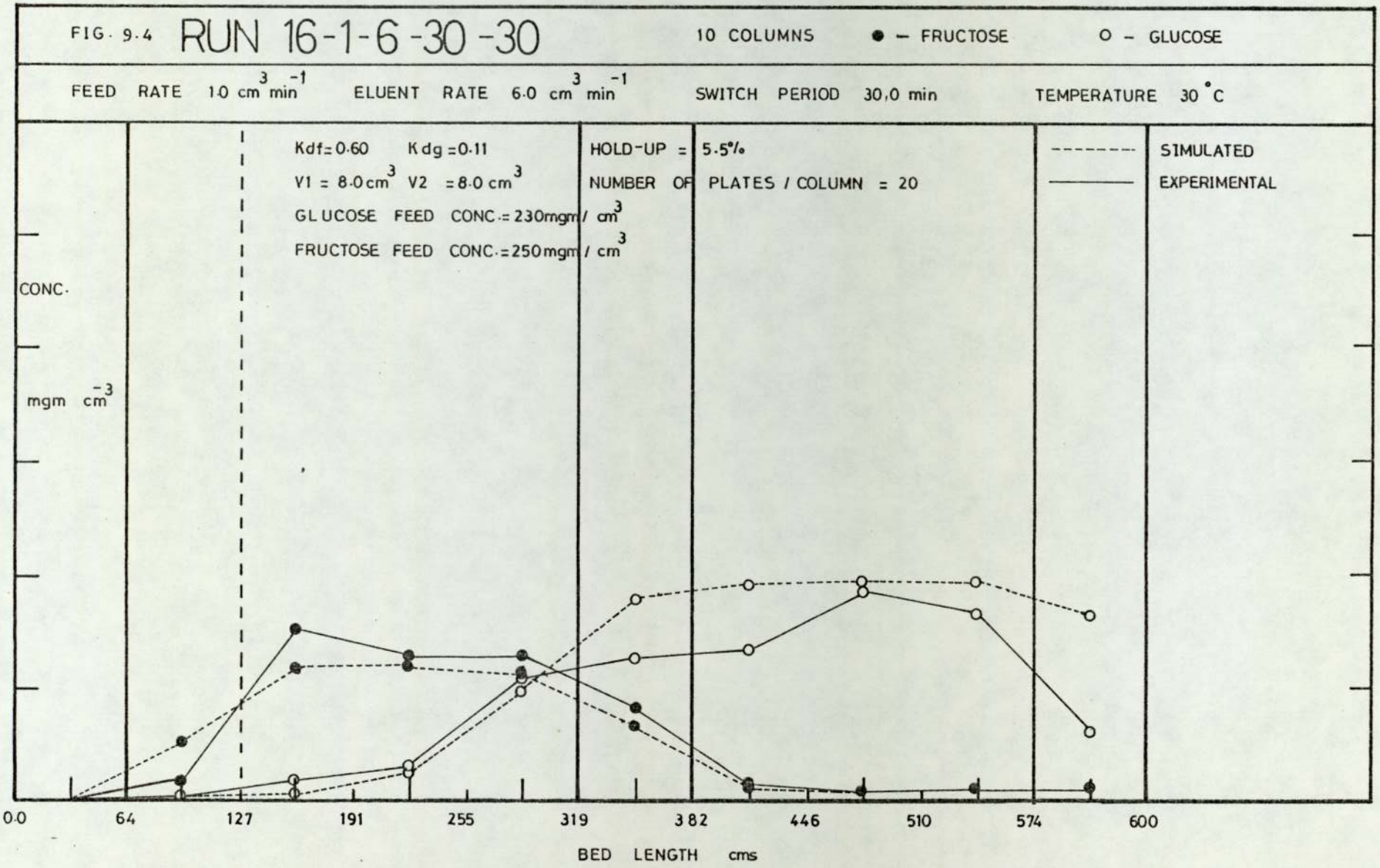


FIG. 9.4 RUN 16-1-6-30-30
10 COLUMNS
● – FRUCTOSE
O – GLUCOSE
FEED RATE 1.0 cm³ min⁻¹
ELUENT RATE 6.0 cm³ min⁻¹
SWITCH PERIOD 30.0 min
TEMPERATURE 30 °C
Kdf = 0.60 Kdg = 0.11
V1 = 8.0 cm³ V2 = 8.0 cm³
GLUCOSE FEED CONC. = 230 mgm / cm³
FRUCTOSE FEED CONC. = 250 mgm / cm³
HOLD-UP = 5.5%
NUMBER OF PLATES / COLUMN = 20
SIMULATED
EXPERIMENTAL
CONC.
mgm cm⁻³
500
400
300
200
100
0
0.0
64
127
191
255
319
382
446
510
574
600
BED LENGTH cms

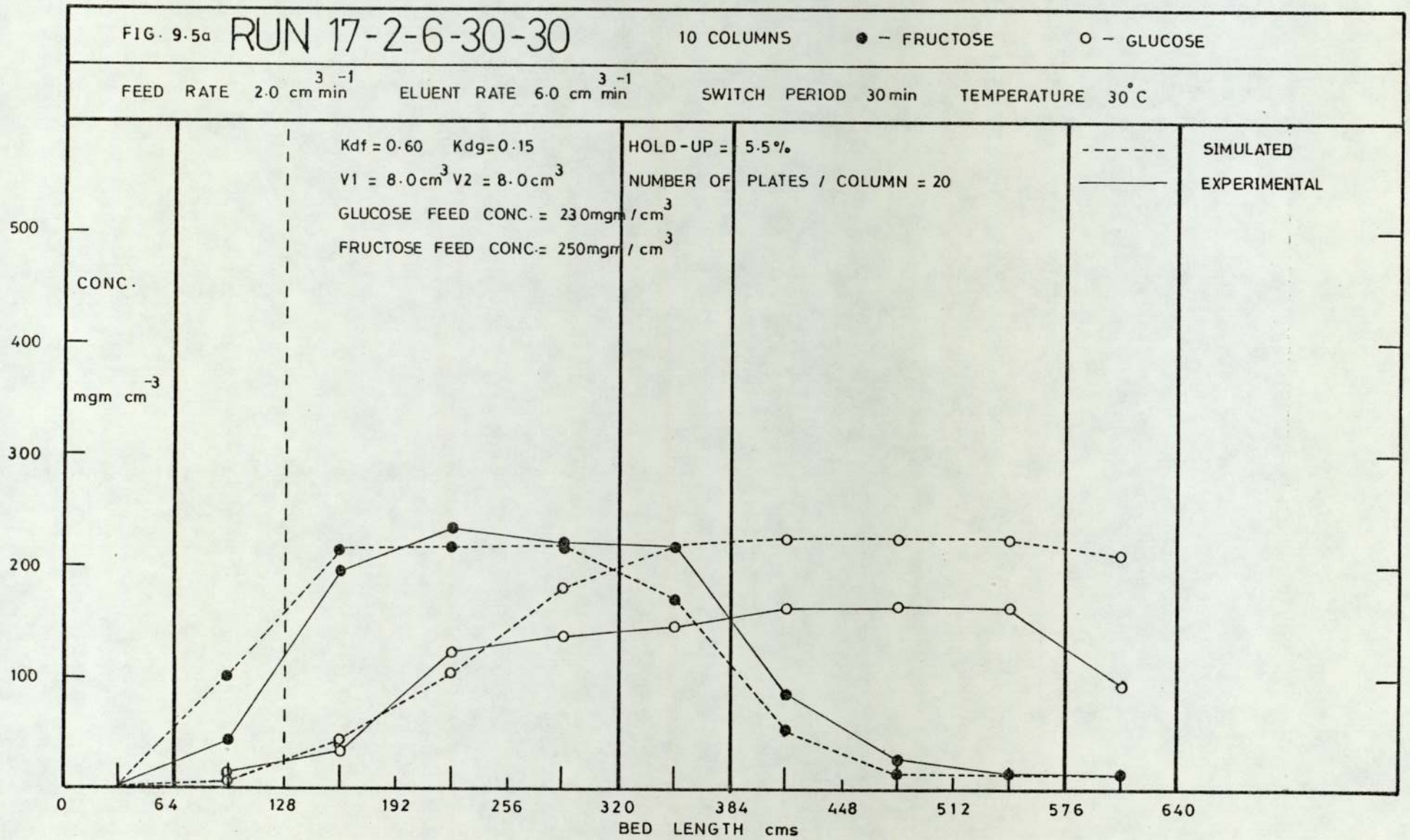


FIG. 9.5a RUN 17-2-6-30-30
10 COLUMNS
● – FRUCTOSE
○ – GLUCOSE
FEED RATE 2.0 cm³ min⁻¹
ELUENT RATE 6.0 cm³ min⁻¹
SWITCH PERIOD 30 min
TEMPERATURE 30°C
Kdf = 0.60 Kdg = 0.15
V1 = 8.0 cm³ V2 = 8.0 cm³
GLUCOSE FEED CONC. = 230 mgm / cm³
FRUCTOSE FEED CONC. = 250 mgm / cm³
HOLD-UP = 5.5 %
NUMBER OF PLATES / COLUMN = 20
SIMULATED
EXPERIMENTAL
CONC.
mgm cm⁻³
500
400
300
200
100
0
64
128
192
256
320
384
448
512
576
640
BED LENGTH cms

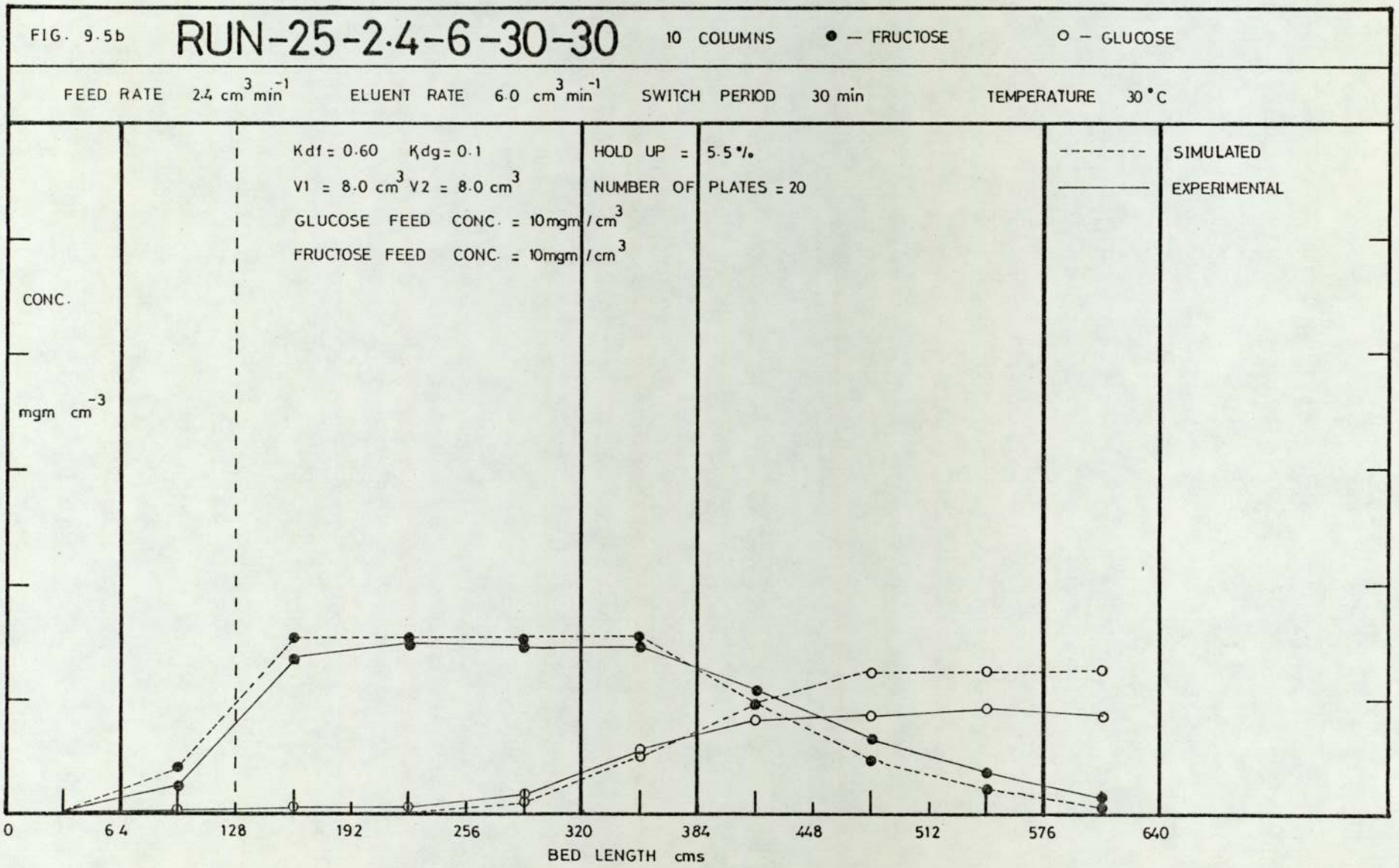


FIG. 9.5b
RUN-25-2.4-6-30-30
10 COLUMNS
● — FRUCTOSE
○ — GLUCOSE
FEED RATE 2.4 cm³ min⁻¹
ELUENT RATE 6.0 cm³ min⁻¹
SWITCH PERIOD 30 min
TEMPERATURE 30 °C
Kdf = 0.60 Kdg = 0.1
V1 = 8.0 cm³ V2 = 8.0 cm³
GLUCOSE FEED CONC. = 10mgm / cm³
FRUCTOSE FEED CONC. = 10mgm / cm³
HOLD UP = 5.5 %
NUMBER OF PLATES = 20
SIMULATED
EXPERIMENTAL
CONC.
mgm cm⁻³
25
20
15
10
5
0
0
64
128
192
256
320
384
448
512
576
640
BED LENGTH cms

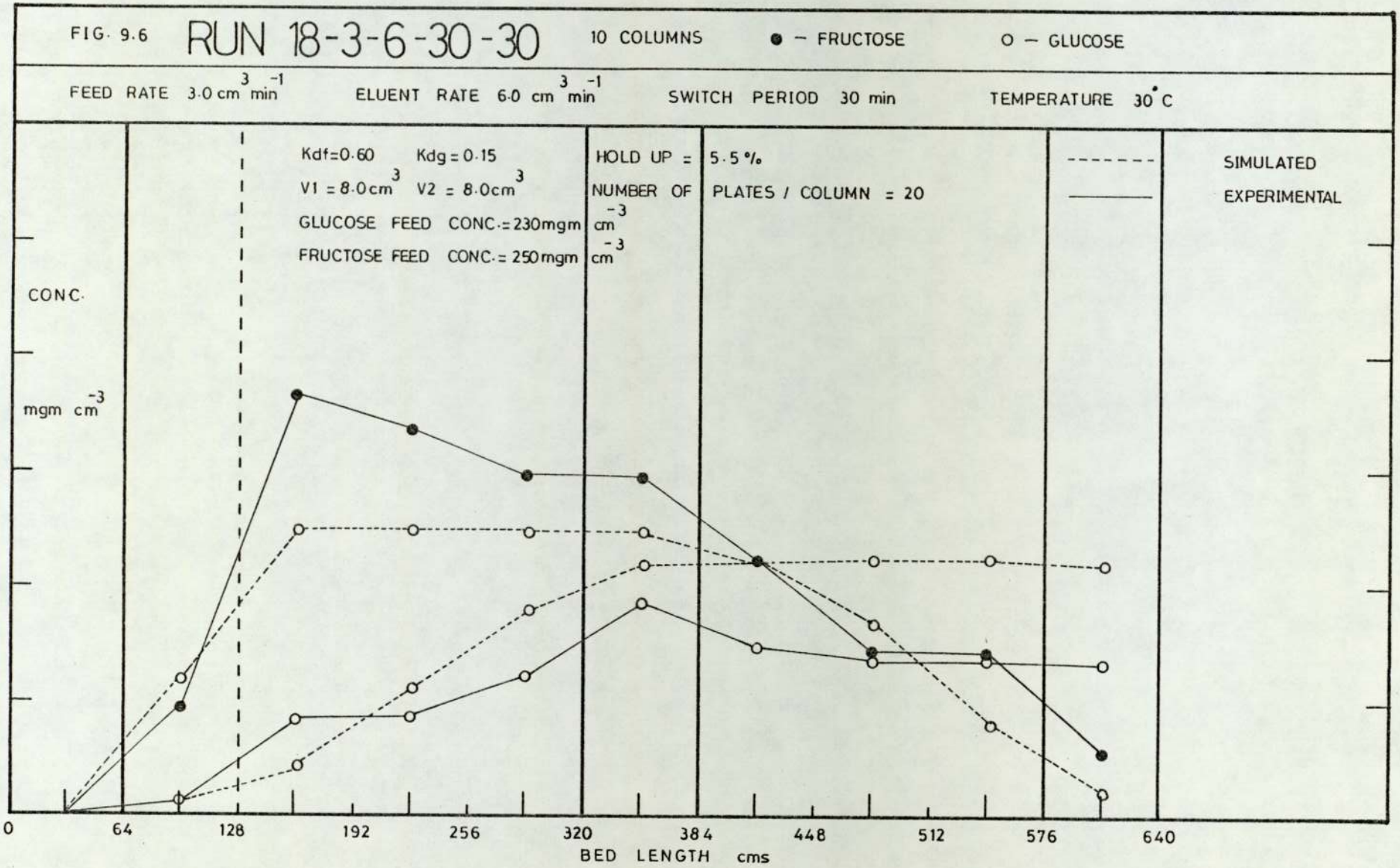


FIG. 9.6 RUN 18-3-6-30-30
10 COLUMNS
● — FRUCTOSE
O — GLUCOSE
FEED RATE 3.0 cm³ min⁻¹
ELUENT RATE 6.0 cm³ min⁻¹
SWITCH PERIOD 30 min
TEMPERATURE 30° C
Kdf=0.60 Kdg = 0.15
V1 = 8.0cm³ V2 = 8.0cm³
GLUCOSE FEED CONC.= 230mgm cm⁻³
FRUCTOSE FEED CONC.= 250mgm cm⁻³
HOLD UP = 5.5 %
NUMBER OF PLATES / COLUMN = 20
SIMULATED
EXPERIMENTAL
CONC.
mgm cm⁻³
0
100
200
300
400
500
0
64
128
192
256
320
384
448
512
576
640
BED LENGTH cms

distribution for glucose varied with different run conditions as seen in table (9.1a).

A much closer agreement between the simulated and the experimental results was found when the feed concentration was 2.0% as in run 25-2-6-30-30; as it approaches to infinite dilution conditions used when evaluating the values of the equilibrium distribution coefficients, Kd (see chapter 7).

However, at the other extreme, that is, at a feed to eluent rates of 1:2, run 18-3-6-30-30, more difficulties were experienced in simulating the experimental results due to the less well developed system profile.

9.3.4.2. Gould's results

A good agreement between the simulated and the experimental system profile was achieved with this group of experiments. The liquid hold-up used in the programme was approximately 0.5% (v/v) and the distribution coefficeints of fructose, Kdf was 0.55 and of glucose, Kdg, ranged between 0.07 and 0.20.

See Figures (9.7 - 9.12).

It was found that the performance of the 10.50 cm. (4 inches) I.D. column, SCCR unit approached the theoretical one as simulated by the plate to plate model. This was probably due to the negligible liquid hold-up volume as compared to the total liquid volume in each column, and the

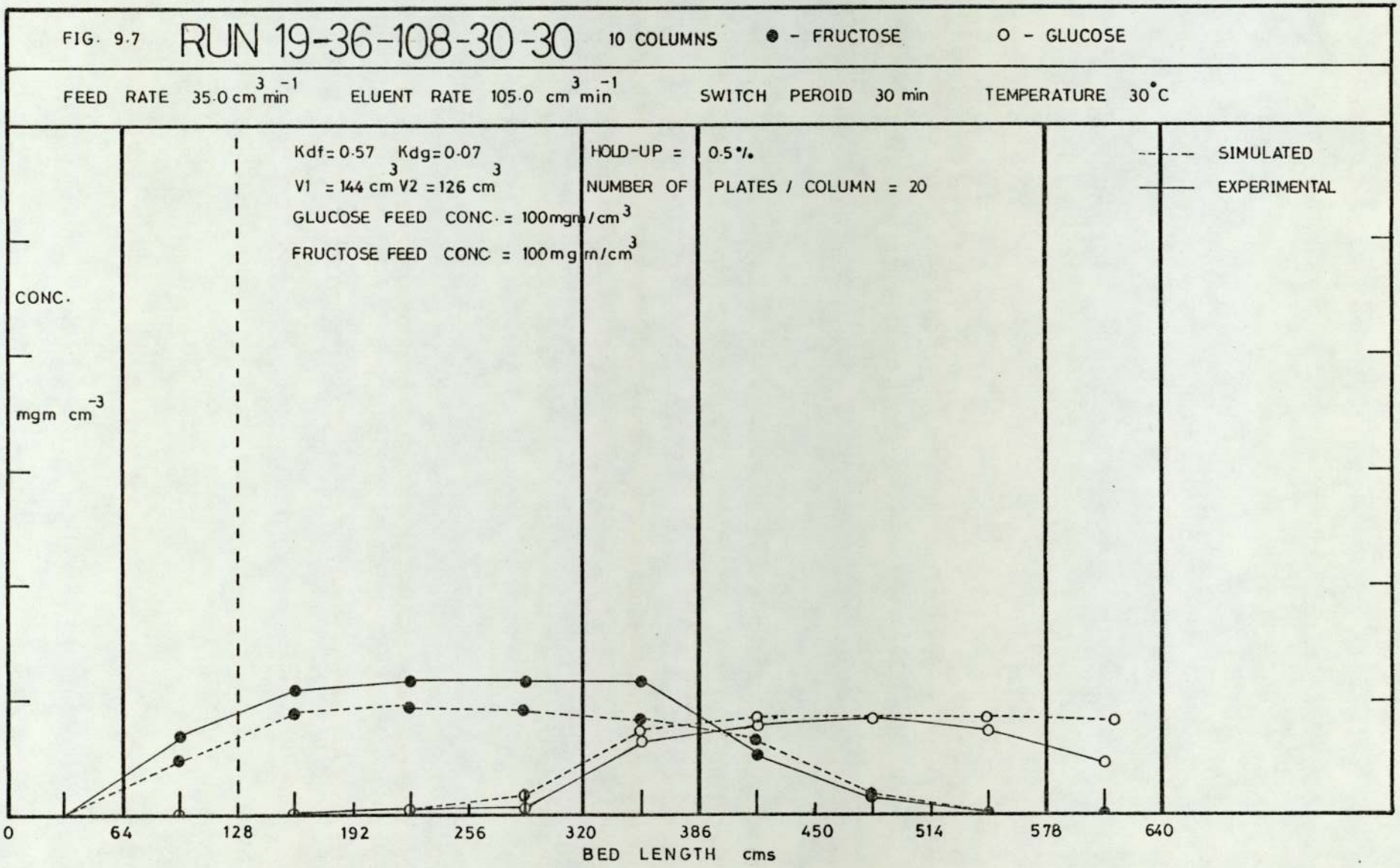


FIG. 9.7 RUN 19-36-108-30-30 10 COLUMNS ● - FRUCTOSE O - GLUCOSE
FEED RATE 35.0 cm3 min-1 ELUENT RATE 105.0 cm3 min-1 SWITCH PEROID 30 min TEMPERATURE 30°C
Kdf = 0.57 Kdg = 0.07
V1 = 144 cm3 V2 = 126 cm3
GLUCOSE FEED CONC. = 100mgm/cm3
FRUCTOSE FEED CONC = 100mgm/cm3
HOLD-UP = 0.5%
NUMBER OF PLATES / COLUMN = 20
SIMULATED
EXPERIMENTAL
CONC.
mgm cm-3
500
400
300
200
100
0
0
64
128
192
256
320
386
450
514
578
640
BED LENGTH cms

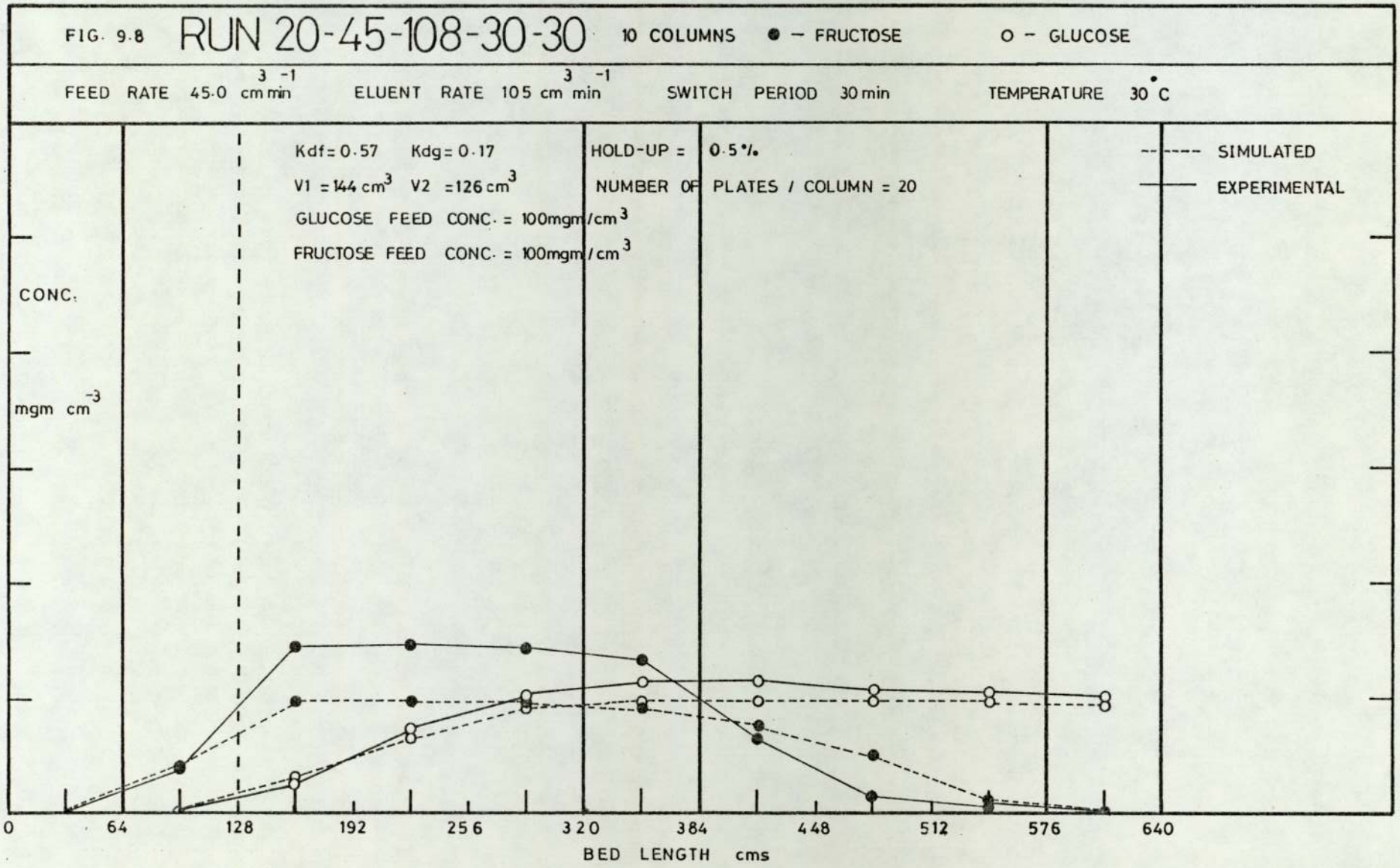


FIG. 9.8 RUN 20-45-108-30-30 10 COLUMNS ● – FRUCTOSE O – GLUCOSE
FEED RATE 45.0 cm³ min⁻¹ ELUENT RATE 105 cm³ min⁻¹ SWITCH PERIOD 30 min TEMPERATURE 30 °C
Kdf = 0.57 Kdg = 0.17
V1 = 144 cm³ V2 = 126 cm³
GLUCOSE FEED CONC. = 100mgm/cm³
FRUCTOSE FEED CONC. = 100mgm/cm³
HOLD-UP = 0.5 %
NUMBER OF PLATES / COLUMN = 20
SIMULATED
EXPERIMENTAL
CONC.
mgm cm⁻³
500
400
300
200
100
0
0
64
128
192
256
320
384
448
512
576
640
BED LENGTH cms

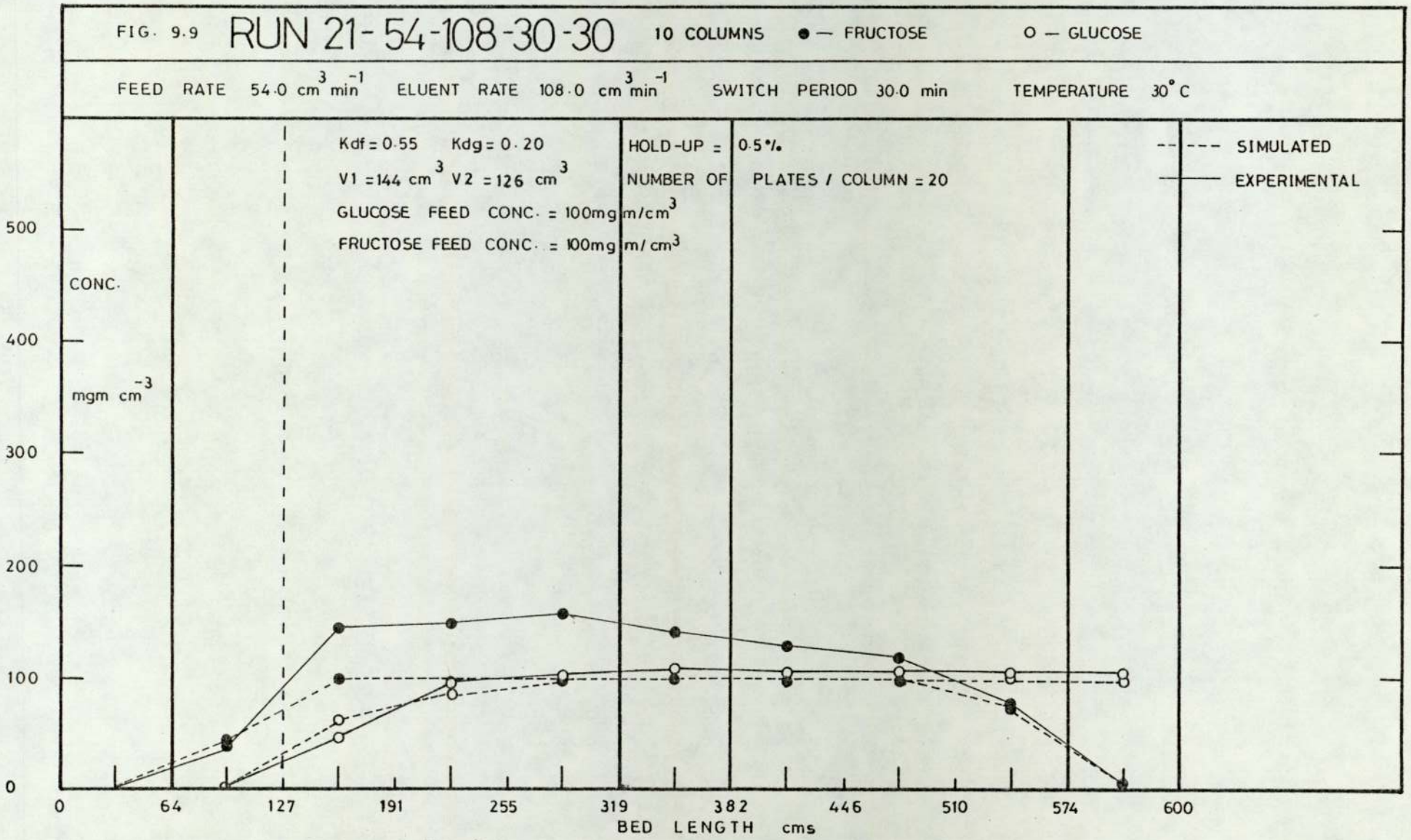


FIG. 9.9 RUN 21-54-108-30-30 10 COLUMNS ● — FRUCTOSE O — GLUCOSE
FEED RATE 54.0 cm3 min-1 ELUENT RATE 108.0 cm3 min-1 SWITCH PERIOD 30.0 min TEMPERATURE 30° C
Kdf = 0.55 Kdg = 0.20
V1 = 144 cm3 V2 = 126 cm3
GLUCOSE FEED CONC. = 100mg m/cm3
FRUCTOSE FEED CONC. = 100mg m/cm3
HOLD-UP = 0.5%
NUMBER OF PLATES / COLUMN = 20
SIMULATED
EXPERIMENTAL
CONC.
mgm cm-3
500
400
300
200
100
0
0
64
127
191
255
319
382
446
510
574
600
BED LENGTH cms

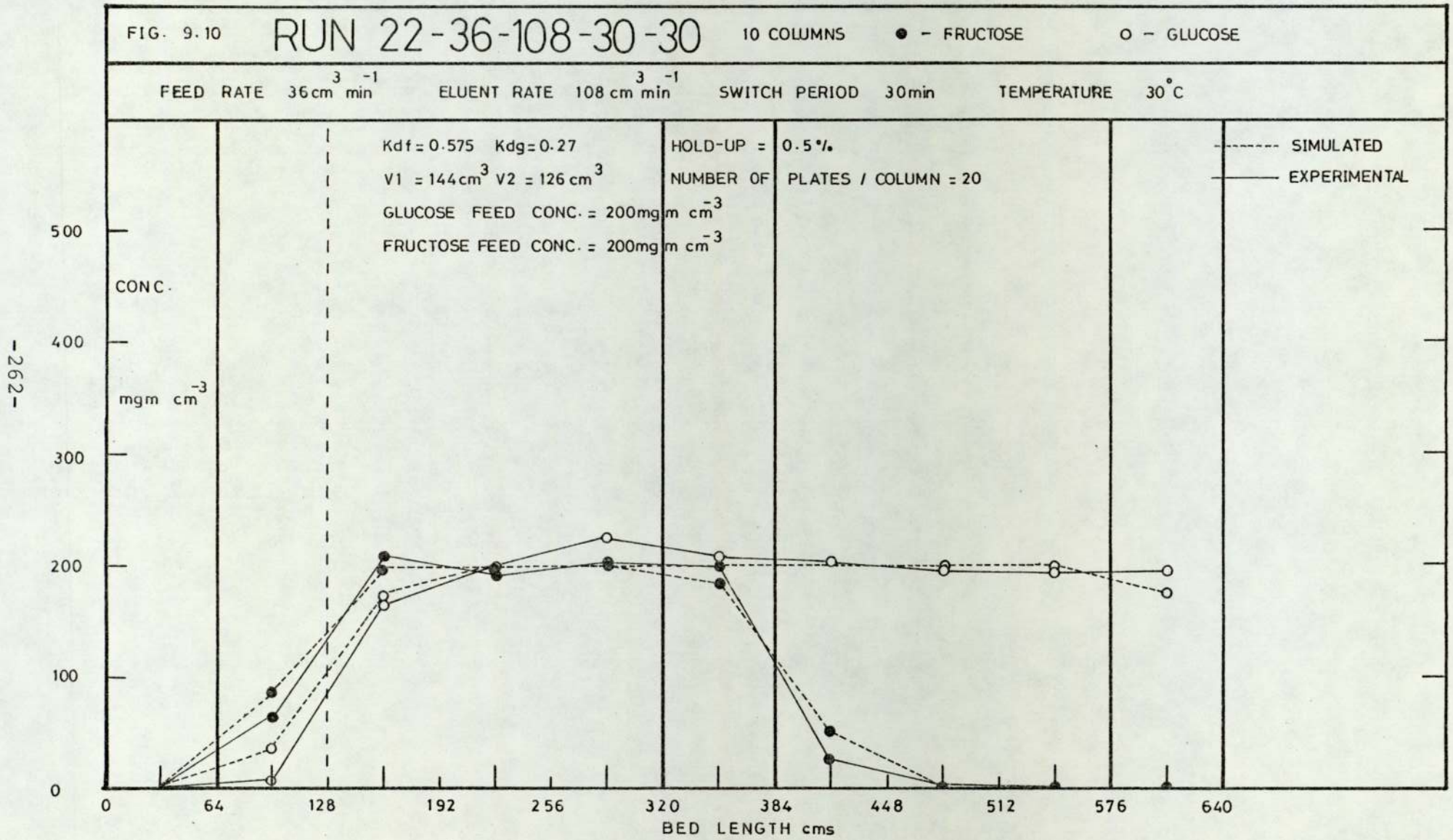


FIG. 9.10
RUN 22-36-108-30-30
10 COLUMNS
● - FRUCTOSE
○ - GLUCOSE
FEED RATE 36 cm³ min⁻¹
ELUENT RATE 108 cm³ min⁻¹
SWITCH PERIOD 30 min
TEMPERATURE 30°C
Kdf = 0.575 Kdg = 0.27
V1 = 144 cm³ V2 = 126 cm³
GLUCOSE FEED CONC. = 200 mgm cm⁻³
FRUCTOSE FEED CONC. = 200 mgm cm⁻³
HOLD-UP = 0.5 %
NUMBER OF PLATES / COLUMN = 20
SIMULATED
EXPERIMENTAL
CONC.
mgm cm⁻³
0
100
200
300
400
500
0
64
128
192
256
320
384
448
512
576
640
BED LENGTH cms

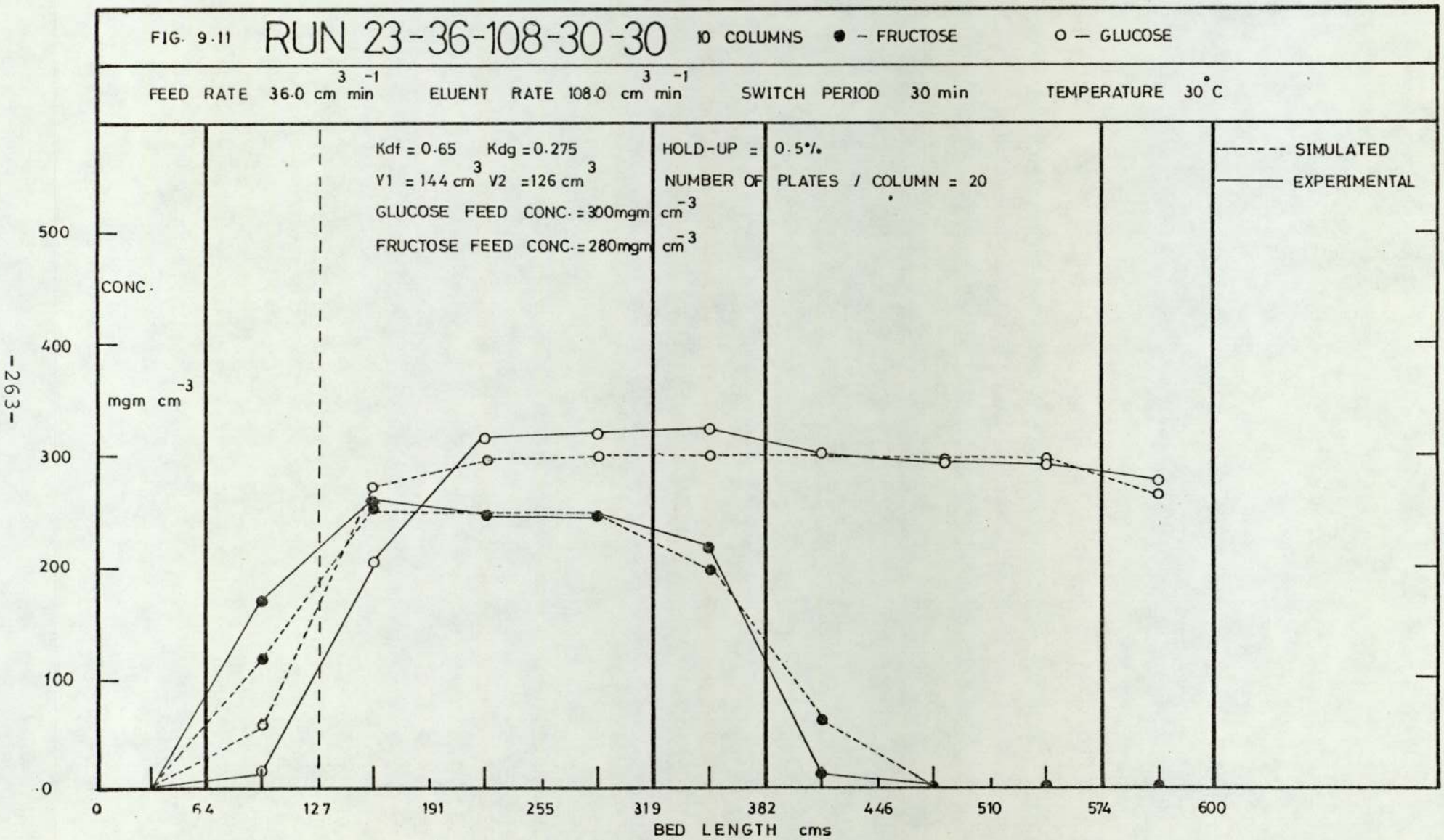


FIG. 9.11 RUN 23-36-108-30-30 10 COLUMNS ● – FRUCTOSE O — GLUCOSE
FEED RATE 36.0 cm³ min⁻¹ ELUENT RATE 108.0 cm³ min⁻¹ SWITCH PERIOD 30 min TEMPERATURE 30°C
Kdf = 0.65 Kdg = 0.275
V1 = 144 cm³ V2 = 126 cm³
GLUCOSE FEED CONC. = 300mgm cm⁻³
FRUCTOSE FEED CONC. = 280mgm cm⁻³
HOLD-UP = 0.5%
NUMBER OF PLATES / COLUMN = 20
SIMULATED
EXPERIMENTAL
CONC.
mgm cm⁻³
500
400
300
200
100
0
0
64
127
191
255
319
382
446
510
574
600
BED LENGTH cms

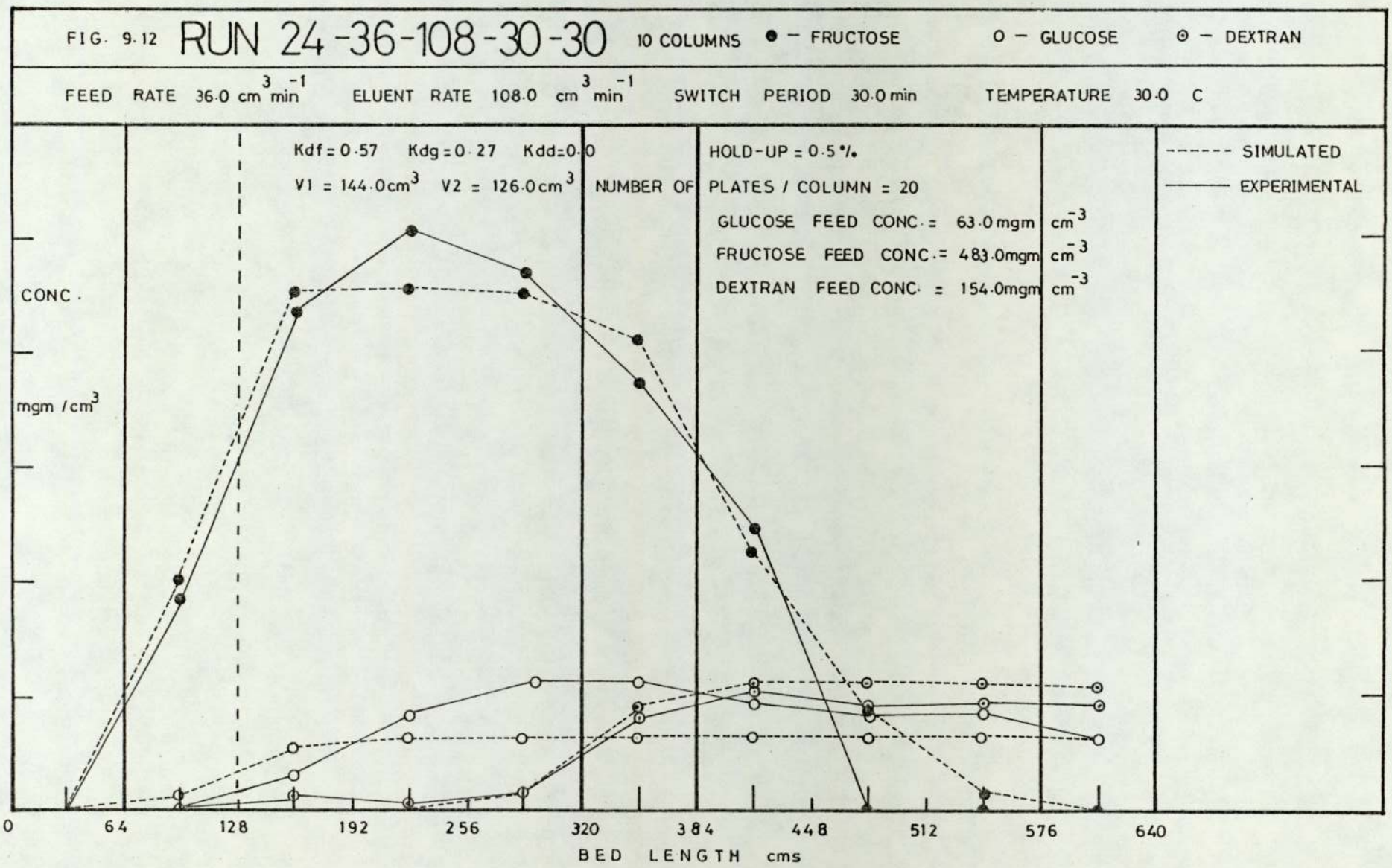


FIG. 9.12 RUN 24-36-108-30-30 10 COLUMNS ● – FRUCTOSE O – GLUCOSE ⊙ – DEXTRAN
FEED RATE 36.0 cm3 min-1 ELUENT RATE 108.0 cm3 min-1 SWITCH PERIOD 30.0 min TEMPERATURE 30.0 C
Kdf = 0.57 Kdg = 0.27 Kdd=0.0
V1 = 144.0cm3 V2 = 126.0cm3 NUMBER OF
HOLD-UP = 0.5 %
PLATES / COLUMN = 20
GLUCOSE FEED CONC. = 63.0 mgm cm-3
FRUCTOSE FEED CONC. = 483.0mgm cm-3
DEXTRAN FEED CONC. = 154.0mgm cm-3
SIMULATED
EXPERIMENTAL
CONC.
mgm /cm3
500
400
300
200
100
0
0
64
128
192
256
320
384
448
512
576
640
BED LENGTH cms

smaller column diameter to height ratio (d/h); 10.5:65 for the 10.5 cm I.D. column unit and 2.54:66.5 for the SCCR4 unit (2.54 cm. I.D.)

9.3.4.3 Results from this project

A generally good agreement between the simulated and experimental results was obtained. The liquid hold-up was 10% (v/v), and the distribution coefficient of fructose, Kdf, ranged between 0.55 and 0.60 and of glucose, Kdg, ranged between 0.2 and 0.3.

It should be noted that only experiments with a switch period of 30 minutes were used in this exercise. The reason was simply that the 60 minutes switch period meant that the core space and the computer time would be twice as large.

The inclusion of two extra columns into the original 10 columns in the SCCR4 unit, appeared to have increased the average concentration of fructose and glucose in each column. This was clearly seen in the average concentration in the column as found in run 18-2-6-30-30, by Ching (24) and run 1-2-6-30-30 of the present research, figure (9.5) and figure (9.13) respectively. The reason for this is thought to be due mainly to the increase residence time of the carbohydrates in the system, which also explains why the fructose concentration in the columns in the pre-feed section was higher than the simulated. (Note, similar results were

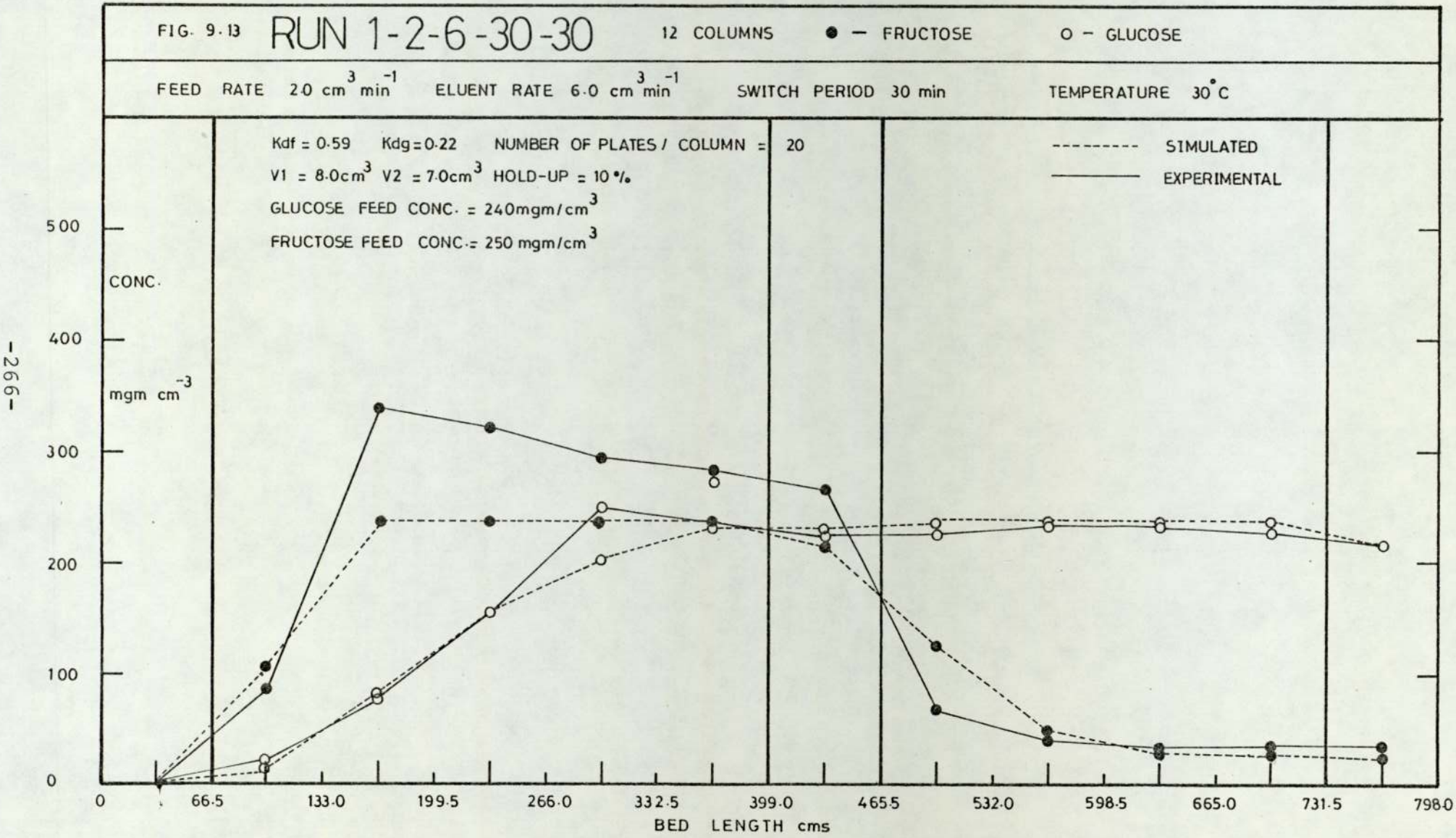


FIG. 9.13 RUN 1-2-6-30-30
12 COLUMNS
● — FRUCTOSE
O — GLUCOSE
FEED RATE 2.0 cm³ min⁻¹
ELUENT RATE 6.0 cm³ min⁻¹
SWITCH PERIOD 30 min
TEMPERATURE 30°C
Kdf = 0.59 Kdg = 0.22 NUMBER OF PLATES / COLUMN = 20
V1 = 8.0cm³ V2 = 7.0cm³ HOLD-UP = 10 %
GLUCOSE FEED CONC. = 240mgm/cm³
FRUCTOSE FEED CONC. = 250 mgm/cm³
SIMULATED
EXPERIMENTAL
CONC.
mgm cm⁻³
500
400
300
200
100
0
0
66.5
133.0
199.5
266.0
332.5
399.0
465.5
532.0
598.5
665.0
731.5
798.0
BED LENGTH cms

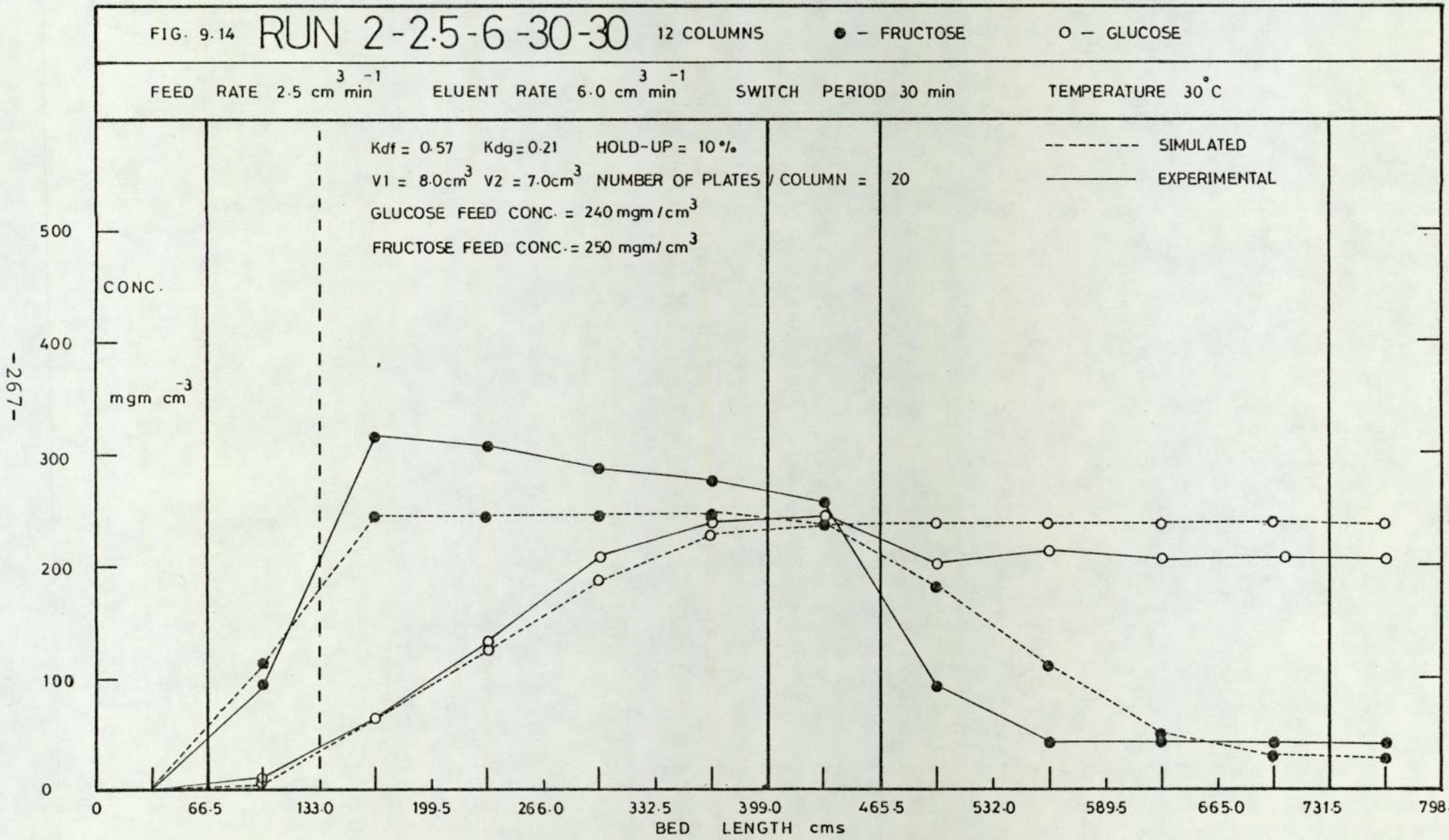


FIG. 9.14 RUN 2-2.5-6-30-30 12 COLUMNS ● – FRUCTOSE O – GLUCOSE
FEED RATE 2.5 cm³ min⁻¹ ELUENT RATE 6.0 cm³ min⁻¹ SWITCH PERIOD 30 min TEMPERATURE 30°C
Kdf = 0.57 Kdg = 0.21 HOLD-UP = 10 %
V1 = 8.0cm³ V2 = 7.0cm³ NUMBER OF PLATES / COLUMN = 20
GLUCOSE FEED CONC. = 240 mgm / cm³
FRUCTOSE FEED CONC. = 250 mgm / cm³
SIMULATED
EXPERIMENTAL
CONC.
mgm cm⁻³
500
400
300
200
100
0
0
66.5
133.0
199.5
266.0
332.5
399.0
465.5
532.0
589.5
665.0
731.5
798.0
BED LENGTH cms

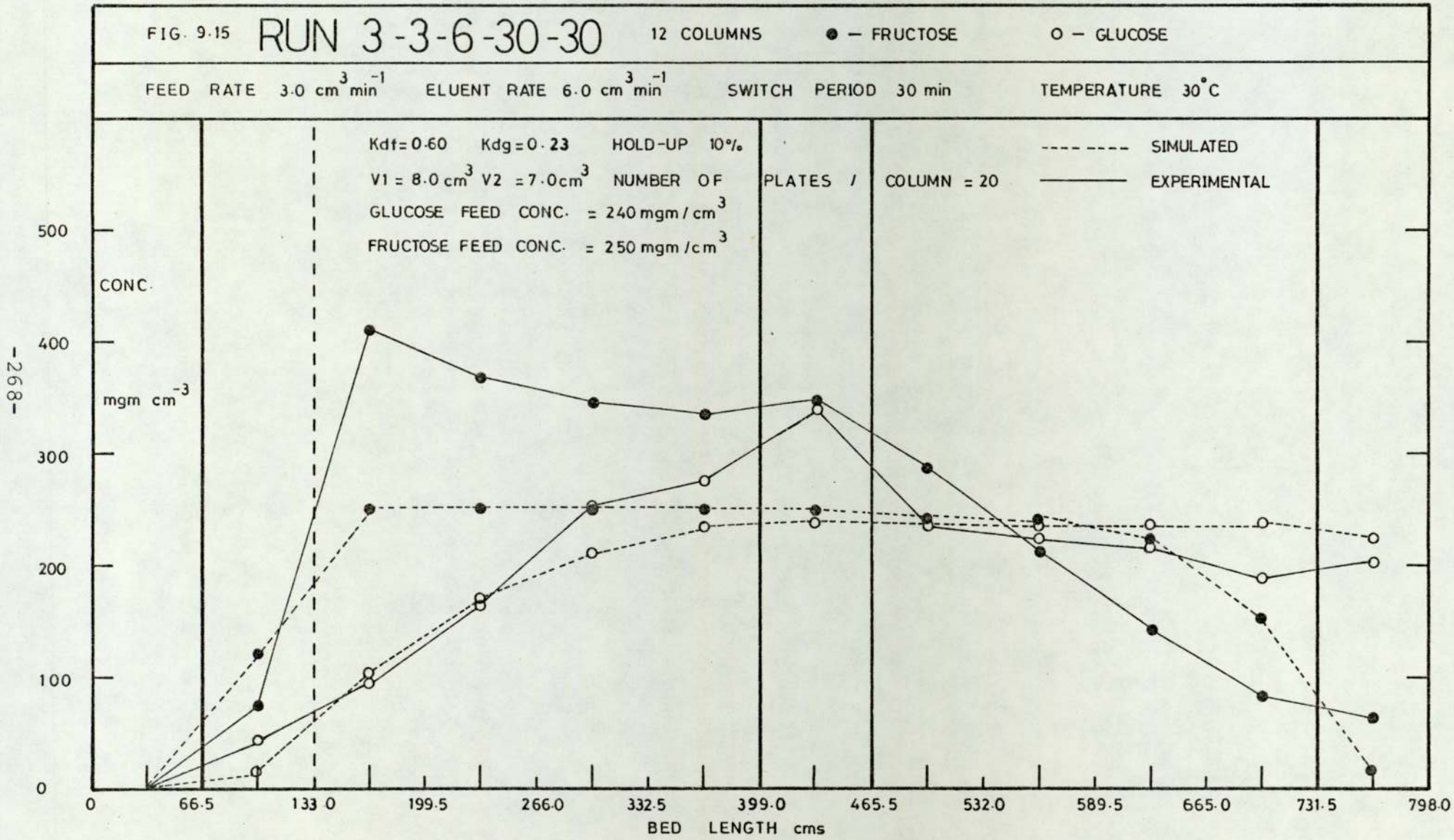


FIG. 9.15 RUN 3-3-6-30-30
12 COLUMNS
● — FRUCTOSE
O — GLUCOSE
FEED RATE 3.0 cm³ min⁻¹
ELUENT RATE 6.0 cm³ min⁻¹
SWITCH PERIOD 30 min
TEMPERATURE 30°C
Kdf = 0.60 Kdg = 0.23 HOLD-UP 10%
V1 = 8.0 cm³ V2 = 7.0 cm³ NUMBER OF PLATES / COLUMN = 20
GLUCOSE FEED CONC. = 240 mgm / cm³
FRUCTOSE FEED CONC. = 250 mgm / cm³
SIMULATED
EXPERIMENTAL
CONC.
mgm cm⁻³
0
100
200
300
400
500
0
66.5
133.0
199.5
266.0
332.5
399.0
465.5
532.0
589.5
665.0
731.5
798.0
BED LENGTH cms

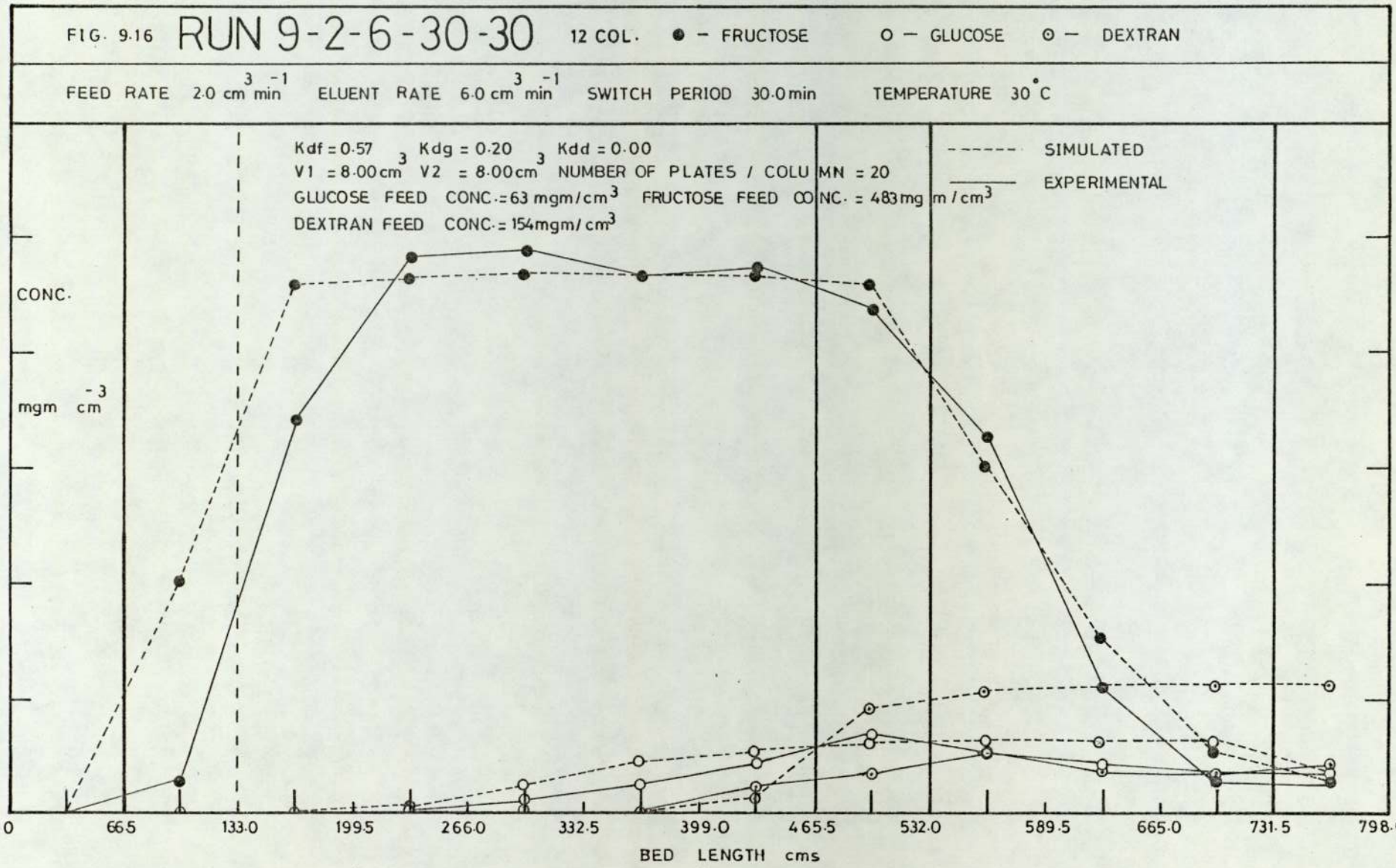


FIG. 9.16 RUN 9-2-6-30-30 12 COL. ● — FRUCTOSE O — GLUCOSE ⊙ — DEXTRAN
FEED RATE 2.0 cm3 min-1 ELUENT RATE 6.0 cm3 min-1 SWITCH PERIOD 30.0 min TEMPERATURE 30 °C
Kdf = 0.57 Kdg = 0.20 Kdd = 0.00
V1 = 8.00 cm3 V2 = 8.00 cm3 NUMBER OF PLATES / COLUMN = 20
GLUCOSE FEED CONC. = 63 mgm/cm3 FRUCTOSE FEED CONC. = 483 mgm/cm3
DEXTRAN FEED CONC. = 154 mgm/cm3
SIMULATED
EXPERIMENTAL
CONC.
mgm cm-3
500
400
300
200
100
0.0
0
66.5
133.0
199.5
266.0
332.5
399.0
465.5
532.0
589.5
665.0
731.5
798.0
BED LENGTH cms

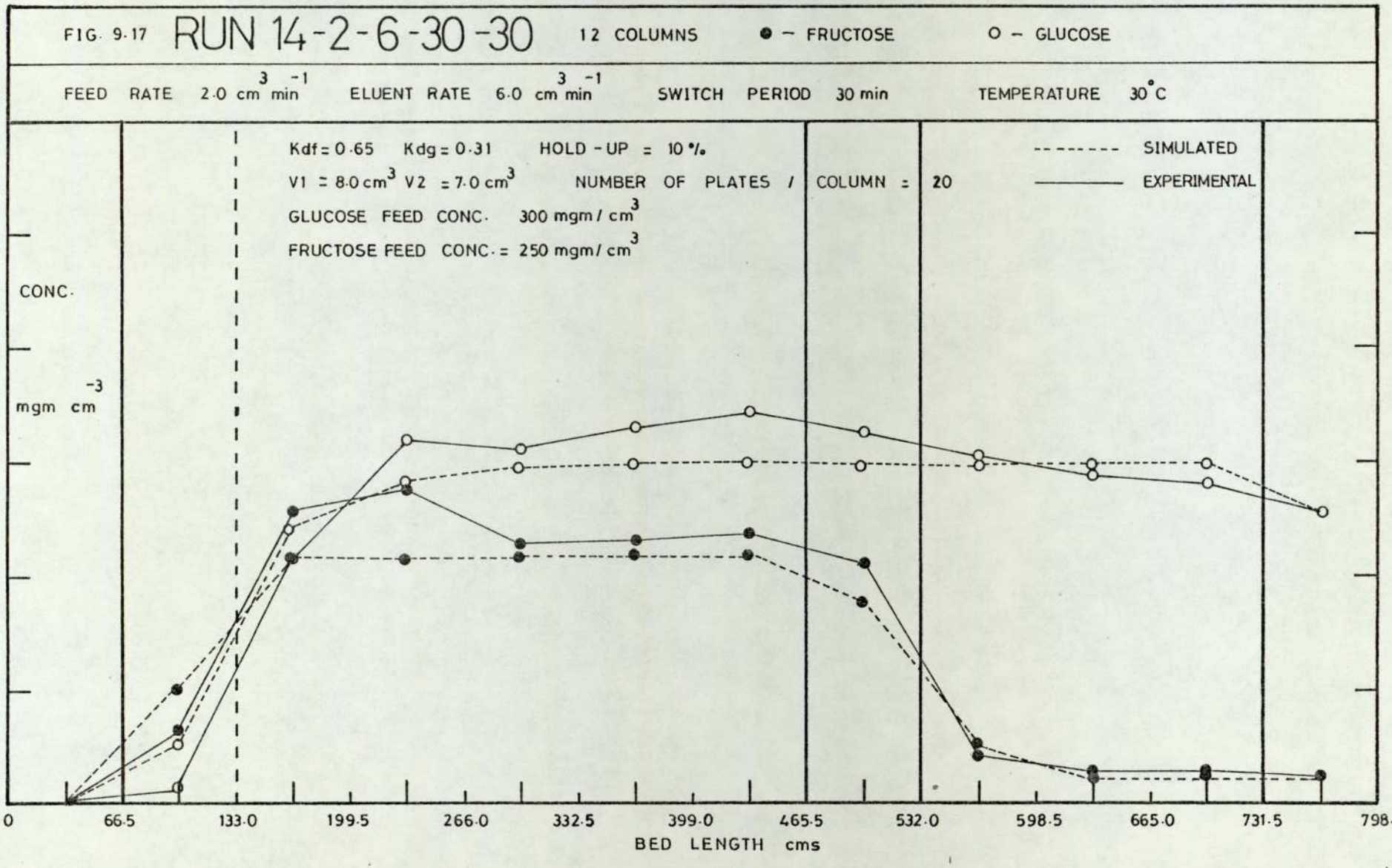


FIG. 9.17 RUN 14-2-6-30-30 12 COLUMNS ● – FRUCTOSE O – GLUCOSE
FEED RATE 2.0 cm³ min⁻¹ ELUENT RATE 6.0 cm³ min⁻¹ SWITCH PERIOD 30 min TEMPERATURE 30°C
Kdf = 0.65 Kdg = 0.31 HOLD - UP = 10 %
V1 = 8.0 cm³ V2 = 7.0 cm³ NUMBER OF PLATES / COLUMN = 20
GLUCOSE FEED CONC. 300 mgm / cm³
FRUCTOSE FEED CONC. = 250 mgm / cm³
SIMULATED
EXPERIMENTAL
CONC.
mgm cm⁻³
500
400
300
200
100
0
0
66.5
133.0
199.5
266.0
332.5
399.0
465.5
532.0
598.5
665.0
731.5
798.0
BED LENGTH cms

also found in the 10.50 cm. I.D. column unit built by Gould (174)).

9.3.5. Conclusion

Improvements to the plate to plate model first used by Ching for simulating the operation of the SCCR4 unit has been achieved. The programme was extended to accept a multi-components system and to include the two extra columns added to the original ten columns on the SCCR4 unit.

A liquid hold-up volume was identified in the transfer line and the transfer valves which had a detrimental effect on the performance of the SCCR4 unit. As a result, a mathematical term was incorporated into the plate to plate model to allow for this effect on the simulated operations. The results obtained were in good agreement with the experimental.

The SCCR4 unit operated in two chromatographic modes, namely, gel permeation chromatography and chemi-adsorption chromatography. Experimental proof of this observation was achieved from the work performed with the batch analytical column, as reported in chapter (7). Notice of this phenomenon gave a better understanding in the distribution of the various components on the mobile and the stationary phases. This was essential as the plate to plate model was based on the distribution of the components on the packing media.

It was also seen that, the simulated and the experimental system profiles were closest in agreement when the experiment was conducted with a 2% (w/v) feed concentration and that, Kds of the sugar components seems to be dependent on the concentration of the sugar in the system.

Two areas in which the model could be improved further were identified, namely, the concentration level of the fructose in the profile and the program modifications to reduce the large core space and computer job unit required to run the simulation. Suggestions for these improvements have been passed on the Gould (172) for further investigation.

Finally, it was believed that a better understanding of the operation of the SCCR4 unit was achieved through this simulation exercise.

C H A P T E R T E N

CONCLUSION AND RECOMMENDATION FOR FUTURE WORK

10. CONCLUSION AND RECOMMENDATION FOR FUTURE WORK

10.1 CONCLUSIONS

As stated at the beginning of this thesis, this research project was aimed at recovering fructose from a dextran contaminated mixture by using a semi-continuous chromatographic refiner. It was also stated that this research project was aimed at studying the performance of the SCCR4 unit originally built by Ching (24).

All the objectives set out at the beginning of this research project were successfully achieved.

10.1.1 OBJECTIVE I:- RECONSTRUCTION OF THE SCCR4 UNIT

The SCCR4 unit was improved by replacing the ten, 2.54 cms (1 in.) I.D. columns with twelve stainless steel columns of similar dimensions. A constant temperature enclosure was constructed over the separation section of the unit, such that it was capable operating at a constant temperature of up to $80 \pm 1^{o}C$. The timer was replaced with a more sophisticated, flexible unit which enable many flow arrangements to be operated on the SCCR4 unit.

The SCCR4 unit was able to operate to a pressure of 1.68×10^{3} KNm^{-2} (250 p.s.i.) and a temperature of $80^{o}C$.

10.1.2 OBJECTIVE II:- BEST OPERATING CONDITIONS OF THE SCCR4 UNIT FOR THE SEPARATION OF FRUCTOSE FROM THE CARBOHYDRATE MIXTURE.

An extensive experimental programme was carried out to studying the performance of the SCCR4 unit. The results obtained suggested that the best operating conditions for

i) highest products throughput were

a) 2.5 cm^3 min^{-1} of feed

b) 6.0 cm^3 min^{-1} of eluent

c) 30.0 cm^3 min^{-1} of purge

d) once through single column purge flow arrangement

e) feed, 50% (W/V) solid, fructose/glucose mixture

f) switch period of 30 minutes

ii) high concentrated product and minimum water requirement

a) 1.5 cm^3 min^{-1} of feed

b) 3.0 cm^3 min^{-1} of eluent

c) 20 cm^3 min^{-1} of purge

d) once through single column purge flow arrangement

e) feed, 50% (W/V) solid fructose/glucose mixture

f) switch period of 60 minutes.

In addition to this achievement, a liquid hold-up volume in the transfer line and transfer values was found to have a detrimental effect on the performance of the SCCR4 unit. This effect was identified and steps were taken to minimise the hold-up volume. Experiments reported by Gould (147) indicated that this effect was apparent only in the 2.54 cms (1 in) I.D. column unit only. The hold-up volume was calculated to be approximately 10.0% (W/V) of the total liquid volume in each column (void and pore volumes).

Finally, 90% (W/V) pure fructose-rich and glucose rich products were obtained at a maximum sugar throughput

of 75 gms per hour.

The highest solid concentration in the fructose rich product obtained was, 4.14% (W/V) solid when recycling of a portion of the fructose rich product was used. The highest solid concentration in the glucose product obtained was, 9.85% (W/V) solid when a feed throughput of 90 gm per hour was used.

10.1.3 OBJECTIVES III and IV:- RECOVERY OF A DEXTRAN-FREE FRUCTOSE-RICH PRODUCT FROM THE ARTIFICIAL FISONS FEED AND THE ACTUAL FISONS FEED.

A 95% (W/V) pure dextran-free fructose rich product was achieved when both types of feed were used

The best operating conditions for processing the artificial Fisons feed were:-

a) 1.5 cm^3 min^{-1} of feed
b) 3.0 cm^3 min^{-1} of eluent
c) 30.0 cm^3 min^{-1} of purge
d) switch period of 60 minutes
e) once through single column purge flow arrangement
f) temperature of enclosure at 30°C

As for the actual Fisons feed, the best conditions were

a) 2.5 cm^3 min^{-1} of feed
b) 6.0 cm^3 min^{-1} of eluent
c) 15 x 15 cm^3 min^{-1} of purge (split stream)
d) switch period of 30 minutes
e) once through single column locked with fructose product stream
f) stream temperature of enclosure at 60°C.

Finally an unknown component, labelled X, was found in the actual Fisons feed. This component, X was retained more strongly than the fructose component, when passed through a calcium charged chromatographic bed, hence contaminating the fructose rich product. Attempts to identify the component X are still being performed in collaboration with the Pharmaceutical Division of the Fisons Company in Holmes Chapel, Cheshire. The removal of the component X, will have to be undertaken at the feed preparation stage.

10.1.4 OBJECTIVE V: AN ALTERNATIVE SOURCE OF FRUCTOSE.

Sucrose was successful hydrolysed to give a 55% glucose, 42% fructose and 3% sucrose mixture after passing through a hydrogen charged Amberlite 1R-118 resin.

The best inverting conditions found were,

a) $60^{o}C$ enclosure temperature ($45^{o}C$ was recommended by Burke, of Tate and Lyle Sugar Refining Company (180))

b) a residence time of greater than 60 minutes

c) feed flowrate of 2 $cm^{3}\ min^{-1}$

Finally, the inverted syrup was successfully separated in the SCCR4 unit giving an 88% (W/W) pure fructose rich product.

10.1.5 OBJECTIVES VI and VII: IMPROVEMENT OF THE BASIC THEORY OF OPERATION OF THE SCCR4 UNIT AND THE MATHEMATICAL MODELLING OF THE SYSTEM PROFILE.

Through experiments with the batch analytical columns, it was possible to show that the SCCR4 unit operated with two chromatographic modes namely, gel-permeation chromatography and chemi-adsorption chromatography.

Identification of these phenomena of the SCCR4 unit enabled the plate to plate model to be modified and used to simulated the system profile with very good agreements.

A hold-up volume term was incorporated in the model as well, and the simulated results again showed good agreement with the experimental.

Finally, superficial improvement was made to the computer programme such that it now can accept a multi-component system, as well as m. number of columns.

In conclusion, all the objectives set at the beginning of this research project have been achieved. It was felt that the semi-continuous chromatographic refining technique had a great potential and would be widely used in the near future, but first more research fund must be made available to continue the development of this commercially attractive system. Also, application of this technique as a separation process on a large scale need not be restricted to the Food and the Pharmaceutical Industries, instead its application in the hydrocarbon and chemical processing industries should be encouraged.

10.2 RECOMMENDATION FOR FUTURE WORK

The research on this method of separation is on the verge of a breakthrough into becoming an attractive commercial process. Therefore, a positive attitude must be adopted now and steps to be taken to ensure that the advantages are not lost. Recommendations for future work are:-

1) to find another packing which has a greater resolving power for fructose and its isomers. It is suggested that the search for this new packing be concentrated on the inorganic material, in particular the compounds of alumino-silicate.

2) to find the best flow-arrangement in which minimum water is required for the separation. A once through single column locked with split fructose rich stream was used in this research which doubled the concentration of the fructose rich product to approximately (10% W/W) solid. Part of the fructose rich stream could be recycled as the eluent and with the right 'split-period', it is expected that the concentration of the fructose rich product could be increased.

3) to modify the plate-to-plate model to account for the fructose present in the mobile phase and the stationary phase, in the columns in the pre-feed section. The modification only requires a conversion factor to calculate the weight of fructose in each column. This suggestion has been passed on to Gould (174) who is developing this model to simulate his work.

4) to investigate the effect of the column diameter to height ratio, $^{d}/_{h}$, on the performance of the semi-continuous chromatographic refiner. It was felt that the $^{d}/_{h}$ ratio was too small in the SCCR4 unit, such that the effect of the liquid slipping along

the column wall might be significant to the performance of the unit. In fact, a better performance was achieved by Gould (174) on the 10.5 cm (4 ins) I.D. column SCCR unit as compared to the SCCR4 unit (2.54 cm I.D. column). Suggestion in this area is to investigate the performance of 30.5 cms (1 foot) I.D. by 182.88 cms (6 feet) columns and use the result to compare with the smaller units.

5) to incorporate sensors and automatic control on to the SCCR4 unit such that the entire operation can be controlled by computer. This will make the process more efficient and less labour intensive, and hence less costly to operate.

6) a detail cost study on the feasibility of constructing a large-scale preparative process for obtaining fructose and glucose using sucrose as the feed.

A P P E N D I X I

```
      MASTER ANITA
      PROGRAM PROFILE(INPUT,OUTPUT,TAPE1=INPUT,TAPE2=OUTPUT)
      DIMENSION G(1500),F(1500),AG(150),AF(150),V1(10),V2(10),CFLOW(5)
     1,FFLOW(5),SFLOW(5),FFEED(10),GFEED(10),DFEED(10),D(1500),AD(150)
      REAL KD1,KD2,KD3,KD12,KD22
      READ(1,31)(V1(J),V2(J),J=1,1)
      READ(1,32)(CFLOW(I),FFLOW(I)LSFLOW(I),I=1,1)
      READ(1,111)(GFEED(IJ),FFEED(IJ),DFEED(IJ),IJ=1,2)
      READ(1,4)NFEED,NNBED,KTOTAL,KKINK,KKTYPE,NNTYPE,NP
      READ(1,5)KD1,KD2,KD3,KD12,KD22
      READ(1,6)H,VM
      READ(1,33) DT
      DO 711 IJ=1,2
      DO 1 NN=1,1500
      G(NN)=0.0
      F(NN)=0.0
      D(NN)=0.0
    1 CONTINUE
      DO 2 NN=1,150
      AG(NN)=0.0
      AF(NN)=0.0
      AD(NN)=0.0
    2 CONTINUE
      WRITE(2,210) CFLOW(I)
      WRITE(2,211) SFLOW(I)
      WRITE(2,212)@FFLOW(I)
      WRITE(2,213) V1(J)
      WRITE(2,214) V2(J)
      WRITE(2,215) NFEED
      WRITE(2,216) NNBED
      WRITE(2,217) KTOTAL
      WRITE(2,218) KKINK
      WRITE(2,219) KKTYPE
      WRITE(2,220) NNTYPE
      WRITE(2,221) GFEED(IJ)
      WRITE(2,222) FFEED(IN)
      WRITE(2,224) DFEED(IJ)
      WRITE(2,223) DT
      WRITE(2,225) KD1,KD2,KD3
      WRITE(2,226) KD12,KD22
      WRITE(2,227) H,VM
      NNTOT=NNBED*NP
      NNNINE=NNBED*(NP-1)+1
      NNFEED=(NFEED-1)*NNBED+1
      WRITE(2,12)
      KKSUM=1
      DO 100 K=1,KTOTAL
      ISTKK=KKINK*(K-1)+1
      LSTKK=KKINK*K
      DO 200 KK=ISTKK,LSTKK
      NNSUM=1
      DO 300 N=1,NP
      IF(N.LE.(NFEED-1)) GO TO 1700
      GO TO 1701
1700  KD1=KD1
      KD2=KD2
```

```
1701  IF(N.LE.(NFEED-1))CFLOWC=CFLOW(I)
      IF(N.GE.NFEED) GO TO 1702
      GO TO 1703
1702  KD1=KD12
      KD2=KD22
1703  IF(N.GE.NFEED)CFLOWC=CFLOW(I)+FFLOW(I)
      IF(K.GE.2) GO TO 508
      IF (N.LE.(NFEED-K)) GO TO 500
508   NNFST=NNBED*(N-1)+1
      NNLST=NNBED*N
      DO 400 NN=NNFST,NNLST
      IF(N.EQ.1) GO TO 80
      IF((N.EQ.2).AND.(NN.EQ.NNFST)) GO TO 40
      IF(NN.EQ.NNFEED) GO TO 50
      GO TO 60
 40   G(NN-1)=0.00
      F(NN-1)=0.00
      D(NN-1)=0.0
      GO TO 70
 50   A=CFLOWC*DT
      IF(G(NN/1).LT.0.1E-10)G(NN-1)=0.0
      IF(F(NN-1).LT.0.1E-10)F(NN-1)=0.0
      IF(D(NN-1).LT.0.1E-10)D(NN-1)0.0
      RR=EXP(-A/(V1(J)+V2(J)*KD1))
      SS=EXP(-A/(V1(J)+V2(J)*KD2))
      TT=EXP(-A/(V1(J)+V2(J)*KD3))
      G(NN)=(1.0-RR)*((CFLOW(I)*G(NN-1)+FFLOW(I)*GFEED(IJ))/
     1 CFLOWC)+RR*G(NN)
      F(NN)=(1.0-SS)*((CFLOW(I)*F(NN-1)+FFLOW(I)*FFEED(IJ))/
     1 CFLOWC)+SS*F(NN)
      D(NN)=(1.0-TT)*((CFLOW(I)*D(NN-1)+FFLOW(I)*DFEED(IJ))/
     1 CFLOWC)+TT*D(NN)
      GO TO 150
 60   IF(G(NN-1).LT.0.1E-10)G(NN-1)=0.0
      IF(F(NN-1).LT.0.1E-10)F(NN-1)=0.0
      IF(D(NN-1).LT.0.1E-10)D(NN-1)=0.0
 70   A=CFLOWC*DT
      RR=EXP(-A/(V1(J)+V2(J)*KD1))
      SS=EXP(-A/(V1(J)+V2(J)*KD2))
      TT=EXP(-A/(V1(J)+V2(J)*KD3))
      IF (K.EQ.(KTOTAL-1)) GO TO 153
      IF (NN.EQ.(NNBED* (NP+1)+1)) GO TO 152
153   G(NN)=(1.0-RR)*(G(NN-1))+RR*G(NN)
      F(NN)=(1.0-SS)*(F(NN-1Y)+SS*F(NN)
      D(NN)=(1.0-TT)*(D(NN-1))+TT *D(NN)
      GO TO 150
 152  F(NN)=(1.0-SS)*(F(NN-1))+SS*F(NN-((NP-3)*20)).H/VM
      G(NN)=(1.0-RR)*(G(NN-1))+RR*G(NN)
      D(NN)=(1.0-TT)*(D(NN-1))+TT *D(NN)
151   GO TO 150
 80   IF(NN.EQ.NNFST) GO TO 90
      IF(G(NN-1).LT.0.1E-10)G(NN-1)=0.0
      IF(F(NN-1).LT.0.1E-10)F(NN-1)=0.0
      IF(D(NN-1).LT.0.1E-10)D(NN-1)=0.0
      GO TO 95
 90   G(NN-1)=0.0
```

```
      F(NN-1)=0.0
      D(NN-1)=0.0
   95 A=SFLOW(I)*DT
      RR=EXP(-A/(V1(J)+V2(J)*AD1))
      SS=EXP(-A/(V1(J)+V2(J)*AD2))
      TT=EXP(-A/(V1(J)/V2(J)*JD3))
      G(NN)=(1.0-RR)*(G(NN-1))+RR*G(NN)
      F(NN)=(1.0-SS1*(F(NN-1))+SS*F6NN)
      D(NN)=(1.0-TT)*(D(NN-1))+TT *D(NN)
  150 IF((NN.EQ.(NNTYPE*NNSUM)).AND.(KK.EQ.(KKTYPE*KKSUM)).AND.
     1 (K.EQ.KTOTAL)) GO TO 160
      GO TO 170
  160 WRITE(2,161)K,KK,N,NN,G(NN),F(NN),D(NN)
  170 IF(NN.EQ.(NNTYPE*NNSUM))NNSUM=NNSUM+1
  400 CONTINUE
      GO TO 300
  500 NNSUM=NNSUM+NNBED/NNTYPE
  300 CONTINUE
      IF(KK.EQ.(KKTYPE*KKSUM)) GO TO 180
      GO TO 200
  180 KKSUM=KKSUM+1
  200 CONTINUE
      IF(K.EQ.KTOTAL) GO TO 131
      GO TO 132
  131 WRITE(2,190)
      WRITE(2,12)
  132 DO 1500 NN=1,NNBED
      AG(NN)=G(NN)
      AF(NN)=F(NN)
      AD(NN)=D(NN)
 1500 CONTINUE
      DO 2000 NN=1,NNTOT
      IF(NN.GE.NNMINE) GO TO 2010
      NNADJ=NN+NNBED
      G(NN)=G(NNADJ)
      F(NN)=F(NNADJ)
      D(NN)=D(NNADJ)
      GO TO 2000
 2010 NNADJ=NN+1-NNMINE
      G(NN)=AG(NNADJ)
      F(NN)=AF(NNADJ)
      D(NN)=AD(NNADJ)
 2000 CONTINUE
  100 CONTINUE
  711 CONTINUE
   31 FORMAT(2F10.5)
   32 FORMAT(3F10.5)
    4 FORMAT(714)
    5 FORMAT(5F10.5)
    6 FORMAT(2F10.5)
   33 FORMAT(F10.5)
  210 FORMAT( 1H, 7HCFLOW= ,F5.3/)
  211 FORMAT( 1H,7HSFLOW= ,F5.3/)
  212 FORMAT( 1H, 7HFFLOW= ,F5.3/)
  213 FORMAT( 1H, 4HV1= ,F8.3/)
```

```
214    FORMAT( 1H, 4HV2= ,F8.3/)
215    FORMAT( 1H, 7HNFEED= ,I2/)
216    FORMAT( 1H, 7HNNBED= ,I3/)
217    FORMAT( 1H, 8HKTOTAL= ,I3/)
218    FORMAT( 1H, 7HKKINK= ,I4/)
219    FORMAT( 1H, 8HKKTYPE= ,I3/)
220    FORMAT( 1H, 8HNNTYPE= ,I3/)
221    FORMAT( 1H, 7HGFEED= ,E13.6/)
222    FORMAT( 1H, 7HFFEED= ,E13.6/)
224    FORMAT(1H,7HDFEED= ,E13.6/)
223    FORMAT( 1H, 4HDT= ,F10.5/)
225    FORMAT(1H,5HKD1= ,F10.5,5X,5HKD2= ,F10.5,5X,5HKD3= ,F10.5/)
226    FORMAT(1H,6HKD12= ,F10.8,5X,6HKD22= ,F10.8/)
227    FORMAT(1H,3HH= ,F10.5,5X,4HVM= 8F 0.51)
 111   FORMAT(3F10.5)
  12   FORMAT(1H ,10X,1HK,12X,2HKK,13X,1HN,11X,2HNN,7X,14HGLUCOSE CONC.
     1 ,5X,15HFRUCTOSE CONC.  ,5X,14HDEXTRAN CONC.  )
 161   FORMAT(1HO,10X,12,10X,15,10X,12,10X,14,5X,F12.8,5XF12.8,5X,F12.
     1 8)
 190   FORMAT(1H1,23HNEXT SWITCHING INTERVAL)
       STOP
       END
```

APPENDIX II

```
** MFY (SN/121) SCOPE V2.1 CY512B ( 07/05/80 ) ****          22/07/80      80204

UNIVERSITY OF MANCHESTER REGIONAL COMPUTER CENTRE  (7600-MAX USER SCM = 160K, LCM = 354K)

HH.MM.SS CPU SECOND ORIGIN
            15.07.04 22JUL80 EB2 4S G3 MARK 8.63K   PR=1 JOB :EAKXX      .JF2PR05
16.09.54 00000.009 MFY.     -JF2PR05,P1000,TD1000.
16.09.54 00000.010 JOB.     -ACCOUNT (EAKXX     )
16.09.54 00000.011 LOD.     -FTN.
16.10.00 00000.475 USR.           .456 CP SECONDS COMPILATION TIME
16.10.00 00000.475 JOB.     -LDSET(MAP=B/ZZZZMP,PRESET=NGINF)
16.10.00 00000.476 LOD.     -LGO(PL=1000)
16.10.01 00000.626 MFY.        LD610 - FLS REQUIRED TO LOAD - 0013162 OU.COG
16.10.01 00000.627 MFY.        LD603 - EXECUTION INITIATED 05.EXP
16.10.01 00000.627 USR.       FORTRAN LIBRARY 498A          05/10/79
16.38.02 00684.560 USR.          STOP
16.38.02 00684.560 USR.         683.923 CP SECONDS EXECUTION TIME
16.38.02 00684.564 MFY.         RM770 - MAXIMUM ACTIVE FILES                    5
16.38.02 00684.564 MFY.         RM771 - OPEN/CLOSE CALLS                       23
16.38.02 00684.564 MFY.         RM772 - DATA TRANSFER CALLS                 2,921
16.38.02 00684.564 MFY.         RM773 - CONTROL/POSITIONING CALLS              16
16.38.02 00684.565 MFY.         RM774 - BM DATA TRANSFER CALLS                254
16.38.02 00684.565 MFY.         RM775 - BM CONTROL/POSITIONING CALLS           53
16.38.02 00684.565 MFY.         RM776 - QUEUE MANAGER CALLS                    58
16.38.02 00684.565 MFY.         RM777 - RECALL CALLS                           50
16.38.02 00684.566 MFY.         SCM              5 262,948  KWS
16.38.02 00684.566 MFY.         I/O                  0,014  MW
16.38.02 00684.566 MFY.         RMS                  0,011  MWS
16.38.02 00684.567 MFY.         USER               684,097  SEC
16.38.02 00684.567 MFY.         JOB                684,568  SEC
16.38.02 00684.567 MFY.         JM166 - MAXIMUM USER SCM          47000B WORDS
16.38.02 00684.567 MFY.         JM167 - MAXIMUM USER LCM             0B WORDS
16.38.02 00684.568 MFY.         JM170 - MAXIMUM JS+IO LCM          628 BUFFERS
16.38.02 00684.568 MFY.         SC050 - 000233 SC/LC SWAPS
16.38.02 00684.568 MFY.         COST OF JOB            274  UNITS
16.38.02 00684.569 MFY.         BUDGET EXCEEDED BY     188  UNITS
```

```
                SCOPE  2  LOAD  MAP

 PROGRAM  WILL BE ENTERED AT  PROFILE     (   156)


                BLOCK           ADDRESS     LENGTH       FILE

                PROFILE           110       13201        LGO
                 /STP,END/      13311           1     SL=SYSTEMA
                 /FCL.C,/       13312          30     SL=SYSTEMA
                 /Q8,IO,/       13342         240     SL=SYSTEMA
                Q2NTRY=         13602          20     SL=SYSTEMA
                COMIO=          13622          10     SL=SYSTEMA
                FECMSK=         13632          41     SL=SYSTEMA
                FEIFST=         13673           3     SL=SYSTEMA
                FLTIN=          13676         156     SL=SYSTEMA
                FLTOUT=         14054         315     SL=SYSTEMA
                FMTAP=          14371         377     SL=SYSTEMA
                FORSYS=         14770         422     SL=SYSTEMA
                FORUTL=         15412          45     SL=SYSTEMA
                GETFIT=         15457          54     SL=SYSTEMA
                INCOM=          15533         144     SL=SYSTEMA
                INPC=           15677         173     SL=SYSTEMA
                KODER=          16072         476     SL=SYSTEMA
                KRAKER=         16570         454     SL=SYSTEMA
                OUTC=           17244         155     SL=SYSTEMA
                OUTCOM=         17421         204     SL=SYSTEMA
                ERRCAP=         17625         321     SL=SYSTEMA
                FERCAP=         20146         171     SL=SYSTEMA
                EXP             20337           6     SL=SYSTEMA
                EXP,            20345          73     SL=SYSTEMA
                EXP.MSG         20440          16     SL=SYSTEMA
                SYSAID=         20456           1     SL=SYSTEMA
                SYS=1ST         20457          65     SL=SYSTEMA
  CFLOW= 1.800

  SFLOW= 9.000

  FFLOW=  .600

  V1=  144.000

  V2=  126.000

  NFEED=  6

  NNBED=  20

  KTOTAL=  60

  KKINK=  900

  KKTYPE= 900

  NNTYPE=  10

  GFEED=   .630000E-01

  FFEED=   .483000E+00

  DFEED=   .154000E+00

  DT=    2.00000
```

.27000000 KD22= .60000000

.00050 VM= 184.00000

K	KK	N	NN	GLUCOSE CONC.	FRUCTOSE CONC.	DEXTRAN CONC.
60	54000	1	10	0.00000000	0.00000000	0.00000000
60	54000	1	20	0.00000000	0.00000000	0.00000000
60	54000	2	30	.00038589	.03171591	0.00000000
60	54000	2	40	.02297481	.38848955	.00000000
60	54000	3	50	.05077074	.45115582	.00000006
60	54000	3	60	.05861548	.45220782	.00000089
60	54000	4	70	.06119395	.45271113	.00001214
60	54000	4	80	.06227512	.45317960	.00016424
60	54000	5	90	.06274888	.45358182	.00222058
60	54000	5	100	.06293515	.45119717	.02559562
60	54000	6	110	.06298139	.44410500	.08770806
60	54000	6	120	.06298820	.38396229	.10686042
60	54000	7	130	.06298685	.27407529	.11282087
60	54000	7	140	.06298364	.18170764	.11243297
60	54000	8	150	.06297961	.11268431	.11249381
60	54000	8	160	.06297448	.06395466	.11248743
60	54000	9	170	.06296785	.03048662	.11248767
60	54000	9	180	.06295523	.00870201	.11248773
60	54000	10	190	.06266963	.00002547	.11248630
60	54000	10	200	.05027641	.00000143	.11022789

A P P E N D I X III

RUN NUMBER \ COLUMN NUMBER	CONCENTRATION OF SUGAR IN EACH COLUMN (mgm cm^{-3})																					
	1		2		3		4		5		6		7		8		9		10		11	
	G	F	G	F	G	F	G	F	G	F	G	F	G	F	G	F	G	F	G	F	G	F
1-2-6-30-30	21.76	85.82	75.98	329.76	156.55	310.35	250.86	293.86	271.43	281.95	221.92	267.80	224.06	68.83	230.00	40.22	233.01	32.44	228.64	34.16	217.22	38.33
2-2.5-6-30-30	14.20	95.84	63.85	313.36	136.04	307.58	208.75	289.94	239.51	277.14	243.85	256.86	180.95	90.47	213.34	40.72	208.44	40.98	191.19	45.19	207.46	42.76
3-3-6-30-30	42.65	74.15	92.72	410.50	163.07	369.34	251.20	348.68	276.30	335.31	346.55	349.52	236.06	288.52	223.78	210.22	213.66	140.33	189.84	81.36	201.27	63.44
4-2-4-30-45	3.86	110.67	50.59	411.34	118.68	408.37	153.83	347.30	204.65	342.64	218.22	249.78	216.80	208.84	212.09	96.67	203.00	51.26	202.48	44.83	186.76	50.12
5-1.5-1.5-30-120	-	-	7.90	67.67	24.87	232.05	101.00	401.86	198.93	369.52	237.39	335.76	230.73	334.02	239.81	337.62	231.03	320.87	224.96	298.42	157.75	191.55
6-2-6-30-30-R	-	-	40.53	151.00	337.49	208.72	320.90	184.05	304.27	158.86	263.06	126.27	286.23	103.32	262.99	34.81	240.01	20.26	242.64	20.99	198.18	12.25
7-2-6-30-35	13.87	87.59	24.33	255.54	46.14	340.03	31.57	239.08	33.20	253.39	163.70	313.39	209.93	293.89	173.40	227.58	198.20	146.86	157.17	94.09	129.59	65.97
8 2-6-30-30	19.19	78.89	32.68	180.21	53.55	345.84	135.57	365.50	201.28	368.60	225.78	263.37	244.84	188.66	224.40	105.60	234.96	49.07	197.78	32.00	183.87	20.43

TABLE 1a DETAIL OF SYSTEM PROFILE OF THE SCCR 4 UNIT OBTAINED IN THIS RESEARCH

RUN NUMBER \ COLUMN NUMBER	CONCENTRATION OF SUGAR IN EACH COLUMN (mgm cm^{-3})																					
	1		2		3		4		5		6		7		8		9		10		11	
	G	F	G	F	G	F	G	F	G	F	G	F	G	F	G	F	G	F	G	F	G	F
9-2-6-30-30	0.0	26.80	0.0	340.41	3.39	482.44	11.60	489.59	20.64	463.92	42.18	472.39	34.68	438.20	51.48	326.64	43.66	109.76	36.90	28.36	33.09	28.39
10-1.5-3-30-60	3.46	173.25	34.45	676.69	75.70	825.71	84.05	832.11	105.21	809.27	90.24	730.13	85.46	694.02	82.46	447.28	64.22	231.33	70.55	183.30	56.10	138.93
11-1.5-3-60-60	5.77	273.67	60.96	628.04	100.04	691.95	132.69	896.64	138.88	919.74	138.26	910.25	88.27	637.76	78.39	412.14	73.05	293.93	78.18	264.15	73.40	205.78
12-3-5.5-60-30	0.0	141.63	53.31	426.82	125.14	441.35	112.76	459.39	136.28	553.22	186.32	519.95	148.88	389.50	106.74	77.25	97.86	67.13	96.79	48.13	37.80	28.05
24-36-108-30-30	0.0	182.22	30.00	435.00	81.94	505.50	111.11	469.44	111.11	372.22	90.83	147.78	83.09	0.00	87.78	0.00	65.83	0.00	-	-	-	-

TABLE 1b DETAIL OF SYSTEM PROFILE OF THE SCCR UNITS OBTAINED BY J.C.GOULD AND IN THIS RESEARCH

RUN NUMBER \ COLUMN NUMBER	CONCENTRATION OF SUGAR IN EACH COLUMN (mgm cm^{-3})										
	1	2	3	4	5	6	7	8	9	10	11
	D	D	D	D	D	D	D	D	D	D	D
9-2-6-30-30	0.00	0.00	2.40	1.57	1.32	23.79	69.97	51.20	39.51	39.82	44.72
10-1.5-3-30-60	2.11	1.40	4.31	6.67	18.66	33.17	104.08	91.22	94.07	93.34	71.79
11-1.5-3-60-60	0.52	7.06	10.86	16.36	24.09	39.71	92.98	89.97	85.43	84.87	76.18
12-3-55-60-30	0.00	13.03	32.26	42.76	62.79	135.52	146.89	138.00	131.90	141.46	116.89
24-36-108-30-30	0.00	14.70	6.94	16.40	81.11	103.33	91.66	96.39	91.67	-	-

TABLE 1c DETAILS OF SYSTEM PROFILE OF THE SCCR UNITS OBTAINED J C GOULD AND IN THIS RESEARCH

RUN NUMBER \ COLUMN NUMBER	CONCENTRATION OF SUGAR IN EACH COLUMN (mgm cm^{-3})																					
	1		2		3		4		5		6		7		8		9		10		11	
	G	F	G	F	G	F	G	F	G	F	G	F	G	F	G	F	G	F	G	F	G	F
13-1.5-3-60-60	26.79	74.65	278.46	270.63	314.64	268.45	322.44	272.81	314.31	272.81	306.79	259.30	303.80	248.26	295.40	102.04	269.40	102.02	268.39	91.79	237.40	63.48
14-2-6-30-30	17.61	64.58	217.43	259.89	320.10	277.36	310.54	225.82	330.68	230.46	343.73	238.40	324.18	210.41	305.53	43.98	288.96	29.91	280.07	31.85	255.48	23.84
15-2-6.4-60-30	9.18	61.17	216.98	247.33	279.58	228.86	261.94	230.39	260.23	235.48	297.09	243.86	253.83	252.02	233.84	176.23	221.66	124.87	222.22	86.53	206.17	62.40

TABLE 1d DETAILS OF SYSTEM PROFILE OBTAINED IN THE RESEARCH

RUN NUMBER \ COLUMN NUMBER	CONCENTRATION OF SUGAR IN EACH COLUMN (mg cm^{-3})																			
	1		2		3		4		5		6		7		8		9		10	
	G	F	G	F	G	F	G	F	G	F	G	F	G	F	G	F	G	F	G	F
16-1-6-30-30	-	-	5.13	19.40	19.12	150.39	30.39	129.67	109.16	128.18	125.58	81.04	132.34	15.45	184.09	9.33	167.21	11.56	61.56	11.29
17-2-6-30-30	-	-	15.32	30.71	31.10	197.53	123.57	232.98	139.81	220.13	147.92	176.23	163.57	85.52	149.61	26.29	160.06	16.28	94.48	15.39
18-3-6-30-30	-	-	11.23	92.88	82.21	363.96	83.05	334.28	120.13	296.36	189.41	297.79	148.64	220.71	136.36	142.21	138.51	140.58	132.34	57.47

TABLE 2 DETAILS OF SYSTEM PROFILE OF THE SCCR UNIT OBTAINED C.B.CHING (24)
PERMISSION FROM PROFFESOR P.E.BARKER

RUN NUMBER \ COLUMN NUMBER	CONCENTRATION OF SUGAR IN EACH COLUMN (mg cm^{-3})																			
	1		2		3		4		5		6		7		8		9		10	
	G	F	G	F	G	F	G	F	G	F	G	F	G	F	G	F	G	F	G	F
19 - 36 - 108 - 30 - 30	-	-	0.0	69.17	0.0	108.50	1.15	116.11	5.83	50.00	63.33	10.55	79.17	0.0	81.39	0.0	71.39	0.0	46.67	0.0
20 - 45 - 108 - 30 - 30	-	-	0.0	39.17	27.78	143.89	75.00	147.22	102.78	144.44	113.39	133.33	116.67	64.44	108.33	13.89	105.56	1.39	102.77	0.0
21 - 54 - 108 - 30 - 30	-	-	0.0	38.61	47.50	144.72	94.44	149.44	109.44	158.60	110.27	140.28	106.94	129.44	106.11	119.44	105.56	76.60	105.80	6.94
22 - 36 - 108 - 30 - 30	-	-	8.89	61.94	161.38	206.67	199.44	188.89	212.78	202.50	204.72	198.61	201.39	22.78	192.50	0.0	191.66	0.0	195.00	0.0
23 - 36 - 108 - 30 - 30	-	-	18.33	69.72	218.83	257.50	316.90	247.22	319.40	245.50	322.78	215.55	300.00	11.28	291.66	0.0	291.67	0.0	277.78	0.0

TABLE 3 DETAILS OF SYSTEM PROFILE OF THE SCCR UNIT OBTAINED BY J.C. GOULD (174)
PERMISSION FROM PROFFESOR P.E.BARKER

N O M E N C L A T U R E

NOMENCLATURE

A	Eddy diffusion mass transfer resistance terms in Van Deemter equation
B	Axial diffusion mass transfer resistance term in Van Deemter equation
C_S	Stationary phase mass transfer resistance term in Van Deemter equation
C_M	Mobile phase mass transfer resistance term in Van Deemter equation
C	Solute concentration in mobile phase
C_1, C_2	Gas phase solute concentration at point 1,2 in the column, in Barker and Lloyd's H.T.U. model
C^o	Initial concentration of solute in plate n used in SCCR4 simulation model
d	Dextran
D	Diffusion coefficient
dp	Mean particle diameter
dc	Diameter of column
E_A, E_B	The mass production rates of components A and B in the top products employed by Barker and Huntington relationship between product purity, number of plates and difficulty of separation
Ei,Ei	Mass flowrate of solute leaving in product i and product ii streams respectively in Barker and Lloyd's H.T.U. model
f	feed
F	Fructose
fA,fo	The mass feedrate of components A and B to the column employed in Barker and Huntington's relationship

Fj	Creed flowrate used in the simulation study of the SCCR4 unit
G	Glucose
H	Plate height
H.E.T.P.	Height Equivalent to a Theoretical Plate
Kd	Equilibium distribution coefficient
K'	Capacity factor
k"	Rate constant of desorption
K_A,K_B	Partition coefficient for components A and B used by Barker and Huntington equation
Ko	Partition coefficient for a component in Barker and Lloyd's H.T.U. Model
Lm	Distance migrated in the Random Walk model
l	length of packed bed
L	Effective mobile phase flowrate in the SCCR4 unit
n	nth number of plate
N	Number of theoretical plates
Noc	Number of counter-current theoretical plates
$(NO_G)s$, $(NO_G)R$	Number of overall gas phase transfer units in the stripping and rectifying sections respectively in Barker and Lloyd's H.T.U. model.
P	Stationary phase flowrate in SCCR4 unit
Q	Mobile phase flowrate used in the SCCR4 model
R_S	Resolution term
R	Inaction of time of solute in the mobile phase
t	time
tr	retention time of a component
to	retention time of a non-retained component

U	Mobile phase linear velocity
$(U_2)A$, $(U_2)B$	Mass flowrate ratio of component A and B used in the equilibrium stage model of Sciance and Crosser
U_L	Stationary phase velocity
V_R	Elution volume of a component
V_M	Total volume of the mobile phase in a SCCR4 column
V_S	Volume of stationary phase in a SCCR4 column
V	Volume of fluid flowing in time, t.
Vi	Pore volume
Vo	Void volume (elution volume of dextran)
V_G, V_L	The gas and liquid volumetric flowrates in Barker and Lloyd's H.T.U. model
V_1, V_2	Volume of mobile and stationary phase respectively in a theoretical plate used in the SCCR4 simulation model
W	Solute band width of a component
$W_{h/c}$	Peak width of i/e of peak height used to calculate N
~~Z~~	Distance along column of length L

Greek Symbols

σ	Standard Deviation
λ	Packing characterisation term for eddy diffisivity
α	Relative retention factor
α'	Constant for packing geometry
γ'	Labyrinth factor to allow for the torous flow path

γ_1, γ_2 Rate of transfer of molecules from gas to liquid and from liquid to gas in Al-Medfai S model

Ψ Operation mobile phase/stationary phase velocity ratio

Ψ_R, Ψ_S The ratio of mobile phase/stationary phase flowrate in the rectifying and stripping sections used in Barker and Huntington's equation.

LIST OF SYMBOLS FOR THE

SIMULATION PROGRAM

G	GLUCOSE CONCENTRATION	gms cm^{-3}
F	FRUCTOSE "	" "
V1	VOLUME OF MOBILE PHASE PER THEORETICAL PLATE	cm^3
V2	" STATIONARY " " " "	"
CFLOW	MOBILE PHASE FLOWRATE	$cm^3 min^{-1}$
FFLOW	FEED FLOWRATE	" "
SFLOW	PURGE "	" "
Kd1	DISTRIBUTION COEFFICIENT OF GLUCOSE	
Kd2	" " " FRUCTOSE	
DT	LENGTH OF TIME INCREMENT	sec
GFEED	GLUCOSE CONCENTRATION IN FEED	gms cm^{-3}
FFEED	FRUCTOSE " " "	" "
NNBED	NUMBER OF PLATE PER COLUMN	
KTOTAL	NUMBER OF SEQUENCES	
KKINK	NUMBER OF TIME INCREMENT IN A SEQUENCE	
KKTYPE	NUMBER OF TIME INCREMENTS BETWEEN PRINT OUT	
NNTYPE	" " PLATE " " " "	
NN	COUNTER FOR OF PLATES	
N	" " " COLUMN	
NNTOT	NUMBER OF FINAL PLATE IN SEPARATING SECTION OR TOTAL NUMBER OF PLATES	

NNNINE	FIRST PLATE IN LAST COLUMN OF SEPARATING SECTION	
NNFEED	NUMBER OF FEED PLATE	
KKSUM	TIME INCREMENT COUNTER USED FOR PRINT OUT CONDITION	
K	COUNTER FOR NUMBER OF SEQUENCING INTERVALS	
ISTKK	FIRST TIME INCREMENT IN SEQUENCING INTERVAL	
LSTKK	LAST " " " " "	
KK	COUNTER FOR NUMBER OF TIME INCREMENTS	
NNSUM	COUNTER FOR PLATE PRINT OUT	
CFLOWC	POST FEED MOBILE PHASE FLOWRATE	$cm^3 min^{-1}$
NNFST	FIRST PLATE IN THE COLUMN	
NNLST	LAST " " " "	
HM	HOLD UP VOLUME	cm^3
VM	VOID VOLUME	"

REFERENCES

1. Critcher, D. and Barker, P.E., Chem.Eng.Sci., 13, 82 (1960).

2. Critcher, D., Ph.D. Thesis, University of Birmingham, 1963.

3. Lloyd, D. and Barker, P.E., Symposium on the Less Common Means of Separation, 1963, Institute Chem.Eng., London, 1964, p.68.

4. Lloyd, D., Ph.D. Thesis, University of Birmingham, (1963).

5. Lloyd, D. and Barker, P.E., U.S. Patent 3,338,031.

6. Huntington, D.H. and Barker, P.E., J. Gas Chromatog., 4, 59, (1965).

7. Huntington, D.H., Ph.D. Thesis, University of Birmingham, (1967).

8. Huntington, D.H. and Barker, P.E., Dechema Monograph, 62, 153, (1969).

9. Barker, P.E. and Universal Fisher Eng. Co. Ltd., British Application 33630/65, 43629/65, 5764/68, 44375/68.

10. Al-Madfai, S. and Barker, P.E., J. Chromatog. Sci., 7, 425, (1969).

11. Al-Madfai, S. and barker, P.E., Proc. 5th International Symposium on Advances in Chromatography, Las Vegas, 1969, Preston Technical Abstracts Co., Evanston, Illinois, 1969, p.123.

12. A-Madfai, S., Ph.D. Thesis, University of Birmingham, (1969).

13. Barker, P.E., "Preparative Gas Chromatography", A. Zlakis, Ed., Wiley-Interscience, London, 1971, p.325.

14. Hatt, B.W., Ph.D. Thesis, University of Birmingham, (1970).

15. Barker, P.E., Barker,S.A., Hatt, B.W. and Somers, P.J., Chem. and Proc.Eng., 52(1), 64, (1981).

16. Sunal, A.B., Ph.D. Thesis, University of Aston in Birmingham, 1973.

17. Deeble, R.E. and Barker, P.E., paper presented at the Symposium on Less Common Means of Separation, Inst.Chem.Eng., London, 1972.

18. Deeble, R.E. and Barker, P.E., Anal.Chem., 45, 1121, (1973).

19. Deeble, R.E. and Barker, P.E., British Patent, Appl. 27786/72, and U.S. Patent Appl. 368,584.

20. Deeble, R.E., Ph.D. Thesis, University of Aston in Birmingham, (1974).

21. Ellison, J.F., Ph.D. Thesis, University of Aston in Birmingham, (1976).

22. Williams, A.N., Ph.D. Thesis, University of Aston in Birmingham, (1976).

23. Ellison, F.J., Hatt, B.W. and Barker, P.E., 'Chromatography of Synthetic and Biological Polymers', Vol.1, pp.218-238, 1977.

24. Ching, C.B., Ph.D. Thesis, University of Aston in Birmingham, (1978).

25. Liodakis, Ph.D. Thesis, University of Aston in Birmingham, (1978).

26. England, K.E., Ph.D. Thesis, University of Aston in Birmingham, 1979.

27. Howari, M.I., Ph.D. Thesis, University of Aston in Birmingham, 1980.

28. B.B.C., The Risk Business, 'Mr. Cube Fight Back', 16th April, 1980.

29. Brown, L.R., Guardian, 10th April, 1980.

30. Tswett, Trav.Soc.Mat. Varsovia, No.6, 14 (1963).

31. Marshall, R. and Kooi, E., Science 125-648 (1957).

32. Knox, J.H., "Advances in Gas Chromatography", A. Zlatkis and L. Ettre, Eds., Preston Technical Abstracts Co., Illinois, 1966.

33. Hollenberg, W.C.J., Netherland Patent 6,504,333.

34. The Colonial Sugar Refining Co., Brit. Pat. 1,083,500, September, 1967.

35. Boehringer, C.F. and Soehme GmbH; British Patent 1,085,696, Oct.1967.

36. Bristow, P.A., Liquid Chromatography in Practice, ICI (Pharmaceutical Division), Macclesfield, U.K.

37. Simpson, 'Practical High Performance Liquid Chromatography'.

38. Angyal, S.J., Inst.J.Chem., 1972, 25, pp.1957-66.

39. Angyal, S.J., and Evan, M.E., Carbohydrate Research, 25, (1972), 43-48.

40. Angyal, S.J., Greeves, D. and Mills, J.A., Aust. J.Chem., 1974, 27, 1447-56.

41. Angyal, S.J. and Hickman, R.J., Australian J. Chem., 1975, 29, 1279-87.

42. Angyal, S.J., Bodkin, C.L. and Parrish, F.W., Aust.J.Chem., 1975, 28, 1541-9.

43. Angyal, S.J., Journal of Pure Applied Chem., 1973, 35, 131-146.

44. Giddings, J.C., 'Dynamics of Chromatography, pt.1, E. Arnold (London) and Dekker, M. (New York), 1965, ISBN 8247 12250.

45. Martin, A.J.P. and Synge, R.L.M., Biochem J., 35, 1358, (1941).

46. Snyder, L.R., Principles of Adsorption Chromatography, Dekker, M., New York, 1967.

47. Kirkland, J.J. Ed., 'Modern Practice of Liquid Chromatography', J.Willey, New York, 1971, lSBNO 47 48878 X.

48. Purnell, J.H., J.Chem.Soc., 1268 (1960).

49. Gluekauf, E., Trans.Faraday Soc., 51, 34, (1955).

50. Lapidus, L. and amundson, N.R., J.Phys.Chem., 56, 984 (1952).

51. Van Deemter, J.J., Zuiderweg, F.J. and Klinkenberg, A., Chem.Eng.Sci, 5, 271, (1956).

52. Giddings, J.C. Mainwaring, W.A. and Myers, M.N., Science, 154, 146, (1966).

53. Grubner, O., 'Advances in Chromatography Vol.6', R.A. Keller and Giddings J.C. Eds., Marcel Dekker Inc., New York, 1968, p.173.

54. Giddings, J.C., J.Chem.Ed., 35, 588, (1958).

55. Giddings, J.C., G. Gas Chromatog., 1(1), 12, (1963).

56. E. Kucera, J. Chromatogr., 19, 237, (1965).

57. Giddings, J.C., J. Gas Chromatog., 1(4), 38, (1963).

58. Giddings, J.C. and Jensen, G.E., J. Gas Chromatography, 2(9), 290, (1964).

59. Neuzil, R.W., Priegnitz, J.W., U.S. Patent 4,024,331, May 17th, 1977.

60. Seidman, M., "Developments in Food Carbohydrates - 1", Birch and Shallenberger, Applied Science, 1977.

61. Ishikawa, H., Japan Kokai 7,851, 179, 10th May, 1978.

62. Holding, S.H., Ph.D. Thesis, 1975.

63. Ching, C.B., Private Communication.

64. Zerolit Limited, London Road, Iselworth, Middlesex, England.

65. Hotfoil Company - Heating Element Manual.

66. Diamond H Control, Temperature Control Manual.

67. Eltron Company, Croydon, London, Heater Manual.

68. M. Lea, Private Communication, University of Aston in Birmingham.

69. Bruyn, L. and Van Eckenstein, A. (1895) Rec. Tran-Chim. 14, 203.

70. Scallet, B.L. and Ethrenthal, I., (1966), U.S. Patent 3,285, 776.

71. Scallet, B.L. and Ethrenthal, I., (1967), U.S. 3,305,395.

72. Scallet, B.L. and Ethrenthal, I., (1968), U.S. 3,383,245.

73. Katz, E., Ethrenthal I. and Scallet, B.L. (1972), U.S. 3,684,574.

74. Katz, E., Ethrenthal, I. and Scallet, B.L., (1972), U.S. 3,690,948.

75. Okazaki, K., Kohino, S., Yamatsu, I., Sugiyama, K. and Ueyama, S., (1971), U.S. 3,558,355.

76. Suzuki, S., Kainuma, K. and Tadolora, K., (1968), Nippon, Nogei, Kagaku Kaishi, 42, 173.

77. Suzuki, S., Kainuma, K. and Yamato, K., (1968), Nippon Nogei Kagaku, Kaishi, 42, 243.

78. Parrish, F.W. (1969), U.S. 3,431,253.

79. Tsao, G.T., Reid, T.H., Hiller, F.L. and Hubbard, L.H. (1969), U.S. 3,432,345.

80. Barker, S.A., Somers, P.J. and Hatt, B.W., (1975), U.S. 3,875,140.

81. Marshall, R.O, and Kooi, E.R., Science 125-648, (1957).

82. Marshall, R.O. and Kooi, E.R., U.S. Patent 2,950,228, (1960).

83. Tsumara, N. and Sato, T. (1960), Agri.Chem.Soc., Japan, 24, 326.

84. Tsumara, N., Sokakura, N., Ishikawa, M. and Sato, T. (1965), Hakko Kyoskashi 23, 516.

85. Natake, M. and Yoshimura, S. (1963), Agri.Biol.Chem. 27, 342.

86. Natake, M. and Yoshimura, S., (1964), Agri.Biol.Chem. 28, 505.

87. Natake, M. and Yoshimura, S., (1964), Agri.Biol.Chem. 28, 510.

88. Natake, M. (1966), Agri.Biol.Chem., 32, 303.

89. Natake, M., (1968), Agri.Biol.Chem., 32, 303.

90. Yamanaka, K., (1963), Agri.Biol.Chem., 27, 265.

91. Yamanaka, K., (1963), Agri.Biol.Chem., 27, 271.

92. Yamanaka, K., (1968), Biochem.Biophys.Acta., 151(3), 670.

93. Yashimura, S., Danno, G. and Natake, M., (1966), Agri.Biol.Chem., 30, 1015.

94. Yashimura, S., Danno, G. and Natake, M., (1967), Agri.Biol.Chem., 31, 284.

95. Danno, G., (1970), Agri.Biol.Chem., 34, 1658.

96. Danno, G., (1970), Agr.Biol.Chem., 34, 1795.

97. Danno, G. (1970), Agri.Bio.Chem., 34, 1805.

98. Takasaki, Y. (1966), Agri.Biol.Chem., 30, 1247.

99. Takasaki, Y. and Tanabe, O., U.S. 3,616,221.

100. Takasaki, Y., Fermentation Advances, Academic Press, New York, p.561 (1969).

101. Newton, A. and Wardrip, (1974), In Symposium : 'Sweetners, High-Fructose Corn Syrup', (G.E. Inglett, Ed), Ch.8, AVI, New York.

102. Thompson, M.N., Johnson, R.A. and Lloyd, N.E., (1972), U.S. 3,788,945.

103. Lloyd, N.E., Lewis, L.T., Logan, R.M. and Patel, D.N., (1972), U.S. 3,694,314.

104. Birch and Shallenberger, 'Development in Food Carbohydrates-1', Applied Science, 1977.

105. Albion Sugar Co. Ltd., Fructose-Glucose Syrups Plants, The Chemical Engineer, June 1976.

106. Heave, D., Process Biochemistry, June, 1974.

107. Zittan, L., Poulson, P.B. and Hummingsen, St.H. (1975), Die Starke 27, 236.

108. Lauer, K., Weber, M. and Stoeck, C. (1969), U.S. 3,483,031.

109. Lauer, K., Springler, H., Wallach, K.E. and Stoeck, G., (1972), U.S. 3,694,158.

110. Lauer, K., Budka, H.G. and Stoeck, G., (1974), U.S. 3,785,864.

111. Samuelson, O. and Sjostrom, E., (1952), Swensk Kem. Tidski, 64, 305.

112. Wheaton, R.M. and Bauman, W.C. (1953), New York, Acad.Sci. 57, 159.

113. Sargent, R.N., 63 2nd Eng.Chem.Process, 1, 57.

114. Serbia, G.R. (1962), U.S. 3,044,904.

115. Lefevre, L.J., (1962), U.S. 3,044,905.

116. Leferve, L.J., (1972), U.S. 3,044,906.

117. Mountfort, C.B., Cortis-Jones, B. and Wickham, R.T. (1968), U.S. 3,416,961.

118. Jones, J.K.N. and Walls, R.A., Can. J. Chem. (1969), 38, 2290.

119. Jones, J.K.N., Walls, R.A. and Pittet, A.O., Can. J. Chem., 1960, 38, 2285-9.

120. Takasaki, Y., (1974), U.S. 3,806,363.

121. BMA Process Pamphlet by Boehringer Vlannheim GmbH, 1968.

122. Kubota, T. and Tatuki, R., (1972), U.S. 3,666,647.

123. Odawara, H., Naguchi, Y. and Ohno, M., U.S. 4,014,711, 29th March 1977.

124. Odawara, H., Yamazaki, T. and Kanaoka, M., U.S. 4,157,267.

125. Neuzil, R. and Priegnitz, J., U.S. 4,024,331, 17th May 1977.

126. Bieser, J. and Rosset, A., (1977), Die Storke 29, Jabrg. Nr 11, S. 392-397.

127. Broughton, D., Biesser, H.J., Berg, R.C., Sucrerie Belge Sugar Ind. Abstr., (1977), 96(5), 155-62.

128. Brougthen, Chem.Eng.Prog., 64, 60, 1968.

129. Tsikawa, H., Tanabe, H., Shioda, K., Japan Kokai 7851, 179, 10th May 1978.

130. Lui, S.H., Lloyd, N.E. (Standard Brands), U.S. 4,096,036, 20th June 1978.

131. Huyten, F.H., Van Beersan, W. and G.W.A. Rijinders, "Gas Chromatography 1960", Scott, R.P.W. Ed., Butterworths, London, 1960, p.224.

132. Friscone, G.J., J. Chromatogr., 6, 97, 1961.

133. Higgin, G.M.C. and Smith, J.F., "Gas Chromatography", A. Gold Ed., p.94, 1965.

134. Rijinders, G.W.A., 'Advances in Chromatography", Vol.3, Marcel Dekker, Ed. New York, p.215,1966.

135. Hupe, K.P., Busch, U. and Winder, K., J. Chromatogr. Sci., 7, 1, 1969.

136. Volkov, S.A., Zel, V.Y., K.I. Sakodynskii and F. Ya. Fvolov, J. Chromatogr., 77, 97, 1973.

137. Bayer, E., Hupe, K.P. and Mack, H., Anal Chem. 35, 492, 1963.

138. Littlewood, A.B., Anal.Chem., 38, 2, 1966.

139. Sie, S.T. and Rijinder, G.W.A., Anal.Chem.Acta., 38, 3, 1967.

140. Aris, A., Proc. Roy. Soc. Ser. A., 252, 538, 1959.

141. Pretorius, V. and de Clark, K., "Preparative Gas Chromatography', Zalkis, A. and V. Pretorius, Eds., Wiley-Interscience, London, p.1, 1971.

142. Spencer, S.F. and Kucharski, Facts and Methods, 7 (4), 8, 1966.

143. Knox, J. and Parcher, J.F., Anal.Chem., 41, 1599, 1959.

144. Verzele, M., J. Chromatogr., 15, 482, 1964.

145. Verzele, M., Planta. Medica. Suppl., 38, 1967.

146. Helferich, F., J.Chem.Educ., 41, 410, 1964.

147. Conder, J.R. and Purnell, J.H., Trans. Farad. Soc., 64, 13, 1968.

148. Conder, J.R. and Purnell, J.H., Trans. Farad. Soc., 65, 824, 1969.

149. Synder, L.R., Anal.Chem., 39, 698, (1967).

150. Spencer, S.F. and de Clark, K., 'Preparative Gas Chromatography', Zalkis, A., and Prectorius, V. Eds., Wiley-Interscience, London, p1, 1971.

151. Gordon, J.M., Kring, G.J. and V. Pretorius, J., Gas Chromatogr., 2, 285, 1964.

152. Musser, W.N. and Sparke, R.E., J. Chromatographic Sci., 9, 116, (1971).

153. Gould, J.C. - private communication, Ph.D. research on scale-up chromatographic refiner, 1980.

154. Baddour, R.F., Method and Apparatus for Chromatographic Separations, U.S. 3,250,058, 1966.

155. Timmins, R.S., Mir, L. and Ryan, J.M., Chem.Eng., 76, 170 (1969).

156. Fitch, G.R., Probert, M.E. and Tiley, P.F., J.Chem.Soc., 4875, 1962.

157. Pritchard, D.W., Probert, M.W. and Tiley, P.F., Chem.Eng.Sci., 26, 2063, 1971.

158. Scott, R.P.W., "Gas Chromatography", D.H. Desty, Ed. Butterworths, London, p.189, 1958.

159. Schultz, H., "Gas Chromatography", M. Van Swaay, Ed., Butterworths, London, p.225, 1963.

160. Clayer, A., Agneray, L., Vanderbussche, G. and Bruni, M., Anal.Chem., 236, 250, 1968.

161. Clayer, A., Agneray, L., Vandenbussche, G., and Patel, P., Anal.Chem., 236, 240, 1968.

162. U.S. Patent, 2,869,672, (1958).

163. Berg, C., Chem.Eng.Progr., 47, 585, 1951.

164. Sussman, M.V., Chem.Tech., 6 April, 260, 1976.

165. Benenati, R.F. and C.B. Brosilow, 1962, Polytechnic Institute Brooklyn, New York, New York.

166. Pichler, H. and Schultz, H., Brennstoff. Chem., 39, 48, 1958.

167. Gulf Oil, U.S. 2,893,995 (1959).

168. Luft, U.S. 3,016,107, (1962).

169. Glasser, D., "Gas Chromatography", A.B. Littlewood, Ed., Inst. of Petroleum, London, p.119, (1967).

170. Guillemin, C.L., J.Chromatogr., 30, 222, (1967).

171. Szepesy, L., Sebestyen, S.Z., Feher, I. and Nagy, Z., J. Chromatogr., 108, 285, 1975.

172. Holding, S. and Barker, P.E., Paper to be published, University of Aston in Birmingham, 1980.

173. Zerolit Treatment Procedure, B.D.H. Catalogue.

174. Gould, J.C., Private Communication (198), Fisons Reports.

175. Barker, P.E., Meeting with Sponsor, 18th June 1980.

176. Alsop and Gibbs - private communication, 18th June 1980.

177. Forrester, J. - Bio-Rad - correspondence, 1980.

178. Forrester, I. - Fisons, Analysis of Feed.

179. William, J.C., Bucke, C. and Vane, G.W., private conversation, Tate-Lyle Company, 1980.

180. William, J.C., private correspondence, 1980, Tate-Lyle Company.

181. Sciance, C.T. and Crosser, O.K., A.I. Chem. Eng. Journal, 12(1), 100, 1966.

182. Alder, L., 'Liquid-Liquid Extraction', Elsevier, Amsterdam, 1959.

183. William, A., paper to be published, 1980.