The Separation of Fructose from Carbohydrate Mixtures by Chromatographic Techniques

A Thesis Submitted

by

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Dedicated to:

My Family and My Friends

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Chromatography is used extensively in the chemical industry as an analytical tool but in the last decade has been adopted for large scale separation of organic mixtures.

In this thesis a review is given of the general chromatographic theory, the factors affecting the performance of chromatographic columns and aspects of scale up of the chromatographic process. Also included is a review of methods available for the production of high fructose syrup and the processes in operation for enriching the fructose content in the syrup. Various industrial scale chromatographic processes, currently in operation, have been outlined.

The description and operation of a liquid-solid chromatographic refiner (SCCR) is described. Counter current operation was simulated by sequencing a system of inlet and outlet port functions around ten, 108 mm internal diameter x 650 mm long, stainless steel columns packed with a calcium charged zerolit SRC 14 resin (150-300 μm size range). This equipment was surrounded by a constant temperature enclosure.

This research, for the first time, operated the same liquid solid chromatographic refiner in the batch and semi-continuous mode and performed a comparison of the two modes of operation in terms of product quality and throughput. Approximately twice the throughput has been achieved by operating the equipment in the semi-continuous mode.

For the continuous operation, methods have been investigated to increase the throughput and the fructose concentration in the fructose rich product. The maximum throughput of sugar for 50% w/v binary equi-concentration glucose fructose feedstock was 2.1 kg/hr with a bulk fructose concentration of 7.6% w/v at 70% purity. However when using Fisons feedstock, containing glucose, fructose and dextran, a maximum throughput of 2.94 kg/hr of sugar with a bulk fructose concentration of 16.3% w/v at 99.9% purity was achieved. In both cases a feed flow rate of 70 cm^3/min, eluent flow rate of 210 cm^3/min and a switch period of 15 minutes was used. Part of the fructose rich product collected over a switch period of 15 minutes was used as an eluent. This research has demonstrated, for the first time, that a fructose rich product containing 16.3% w/v fructose at 99.9% purity can be obtained from Fisons feedstock using SCCR equipment.

The effect of temperature on the batch and continuous operation has also been investigated.

Through lack of equilibrium distribution coefficient (K_d) data previous workers assumed K_d values to obtain a best fit between the simulated and experimental concentration profile of the SCCR6 unit. In this project, experiments have been performed with a batch stainless steel column (5 mm I.D. x 500 mm length) packed with zerolit SRC 14 resin (150-300 μm size) to investigate the effect of on column sugar concentrations, at ambient temperature, on the value of K_d. Results from these experiments have been used to replace the guessed values thereby enabling a more accurate test of the model to be determined. The batch operation of the equipment was also simulated and a theoretical comparison was made between the two modes of operation in terms of throughput and product quality. A reasonable agreement between the simulated and experimental results has been achieved in all cases.

Key Words: Chromatography, Production Scale, Glucose, Fructose, Dextran

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CHAPTER ONE

INTRODUCTION

The most popular use of sugar is in the food industry as a sweetener. The source of sugar varies with location, in tropical countries it is produced from sugar cane and in temperate zones from sugar beet. The most common sugar produced in large quantity is sucrose but since the late 1970's some countries have started manufacturing sugar from starch sources such as corn, maize or rice by means of enzymes. Although through a combined acid-enzyme process, a complete conversion of starch into glucose has been achieved, the product is only 70-75% as sweet as sucrose. Hence other means of increasing the sweetness of starch syrup has been sought.

As fructose is much sweeter than its isomer glucose, methods are being developed to obtain corn syrups containing sufficient fructose to increase the sweetness. Enzymatic isomerisation of glucose into fructose has been commercialised and a high fructose corn syrup containing 71% w/v solids of which 50% w/w was glucose, 42% fructose and a balance higher sacchrides has been produced. This syrup has a sweetness comparable to sucrose but has a lower selling price.

Due to the higher sweetness of fructose per unit weight (fructose in cold solution is 1.8 times as sweet as an equivalent amount of sucrose) (1), very high fructose content syrups are desired by industries for producing

low calorie foods and drinks.

The enriching process may be accomplished by the use of liquid-solid chromatography. Columns packed with ion-exchange resin, charged in the calcium form, separates or refines by the formation of a complex of calcium ions with fructose molecules. Thus if a mixture of glucose and fructose is passed through the column, the fructose is retarded and separation occurs.

Chromatography has proved to be one of the most useful separation techniques of recent times. In the Nobel-Prize winning paper of Martin and Synge (2) they introduced liquid-liquid chromatography. James and Martin (3) introduced gas-liquid chromatography in 1952 and predicted a rapid development of both gas-liquid and gas-solid forms of the technique. Within a decade gas-chromatography was firmly established as a powerful and versatile method of analysis.

Growth of the chromatographic process has been biased towards the batch mode, but recently methods have been developed using chromatography for production scale operation. Applications are found in the sugar industry in the separation of the two isomers, glucose and fructose by Boehringer-Mannheim (4), Finnsugar (5) and Sudzuker (6).

Complete separation, or total resolution, has to occur in batch chromatography if pure products are required; otherwise a recycle is necessary and the throughput is low. However, continuous chromatography requires only partial separation in order to yield

pure products. Three stages have taken place in the development of continuous chromatography. These were: moving bed, moving column and simulated moving bed, of which the latter one has been the most successful. This was because it eliminated both the difficulties of mechanical sealing and problems associated with solids handling (93).

The inherent problems of the moving bed design and the limited size of the moving column has activated research into development of a counter-current scheme through simulated packing movement. Barker and co-workers have evolved a continuous counter-current process. The first successful outcome was in 1974 by Barker and Deeble (7) consisting of twelve 76 mm diameter columns to separate halo-carbon mixtures to 99.9% purity.

In 1978 Barker and Ching (8) used liquid-solid chromatography for the separation of fructose from carbohydrate mixtures. The equipment consisted of ten 25.4 mm I.D. x 700 mm glass columns and produced a fructose product of 90% purity. One reason for this lack of total purity was considered to be the 9% inter-column hold up associated with this equipment. An improvement to this design was made by Barker and Chuah (9) who used twelve 25.4 ID x 650 mm stainless steel columns and reduced the inter-column hold-up to 7%. Further improvement was made by Barker and Gould (10) in using ten 108 mm x 650 mm stainless steel columns to reduce the inter-column hold-up to

less than 1% and obtain, under appropriate conditions a product containing 99.9% fructose and 99.9% glucose. Based on a literature survey this equipment is the only equipment in the world that can do this without any recycle. This equipment has been adopted for this research work.

Investigation into the chromatographic separation of fructose from carbohydrate mixtures has been carried out mainly in the semi-continuous mode at ambient temperature.

Previous workers, Ching (8), Chuah (9) and Gould (10), have constructed a mathematical model of the semi-continuous refiner (SCCR), based on the plate theory. One of the assumptions in this model is a constant value of the distribution coefficient. The distribution coefficient of a component is defined as the ratio of the concentration of that component in the stationary to mobile phase. In reality the value of this parameter varies with the on-column concentration of sugars.

The object of this project is by using various carbohydrate mixtures

(i) to study the behaviour of ten columns each of 10.8 cm diameter x 65 cm high in the batch mode;

(ii) to make an experimental comparison between the batch and continuous mode of operation of the SCCR unit in terms of throughput and separation;

(iii) to study the column performance at elevated temperature;

(iv) to study the variation of the distribution coefficients with on-column sugar concentrations;

(v) to formulate a mathematical model of the batch process and also to improve the existing mathematical model used by Gould (10) for the SCCR unit by taking into account the variation of the distribution coefficients with on-column sugar concentration;

(vi) to make a theoretical and experimental comparison of the batch and continuous processes in terms of throughput and quality of products.

CHAPTER TWO

LITERATURE SURVEY

2.1 SCOPE

This literature survey has to be brief and selective because much work has been carried out in the field of chromatography. The first part of this survey provides a general introduction to the basic concepts and terminology of chromatography followed by a review of the various theoretical models concerned with chromatographic zone spreading. The second part discusses the methods available for the separation of fructose from a mixture of carbohydrates. In the third part of the literature survey factors affecting the scale up of the chromatographic processes are discussed followed by a review of production scale chromatography applications.

2.2 INTRODUCTION TO CHROMATOGRAPHY

Chromatography is used extensively in the chemical industry as an analytical tool but in the last decade it has been increasingly used for large scale separations of organic mixtures with some column diameter up to 3 metres in use. Separation in chromatography is effected by the differential migration velocities of components resulting from the distribution of a component between a mobile and a stationary phase. Modern liquid chromatography can be classified into four main categories, depending on their mechanism

of retention, as follows:

(a) Adsorption Chromatography - Separation is effected by a physical or chemical association formed between the solute and the active sites of solid packing.

(b) Exclusion Chromatography - Separation results because of the difference in the size of the sample molecules. Those that are small enough are able to penetrate the porous matrix of the packing, whereas the larger components remain in the interstitial regions between the particles. Consequently, the largest components elute first and the smallest molecules last.

(c) Ion Exchange Chromatography - This involves a continuous reversible exchange of ions between electrolytes and the ion exchangers. Separation is achieved through a difference in the affinities of the solute ions for the resin.

(d) Partition Chromatography - This relies on the absorption of solutes by an inert solid support coated with a liquid stationary phase.

Some chromatographic separations are achieved by the simultaneous occurrence of two or three of the mechanisms mentioned above.

2.2.1 Modes of Chromatographic Operation

There are three basic modes of chromatographic operations, namely elution, frontal analysis and displacement.

(a) Displacement Chromatography

In this mode of chromatography the mobile phase is much more strongly retained by the stationary phase than the sample. The sample is then pushed through the bed by the advancing mobile phase. It provides much poorer separations than elution chromatography but greater sample loads can be applied to the bed.

(b) Frontal Chromatography

In frontal chromatography, the sample is introduced as a step change and is fed continuously onto the column, hence the sample forms part of the mobile phase. The components are selectively retarded with the formulation of fronts (see Fig. 2.1). The least retained component, A, is eluted first and then followed by a mixture A and B.

(c) Elution Chromatography

In elution chromatography a small quantity of the mixture is injected onto a column and the separation of components is achieved by its distribution between the mobile and stationary phases. Hence components migrate through the bed at different rates and cause quantitative and qualitative separation of the mixture. This mode of chromatography is the one most commonly practised (see Fig. 2.2).

2.2.2 Definitions and Terminology

A chromatogram may be generally regarded as the solute concentration vs. time profile measured by the detector from the introduction of the solute to its

FIG. 2.1 FRONTAL ANALYSIS FOR A BINARY SYSTEM

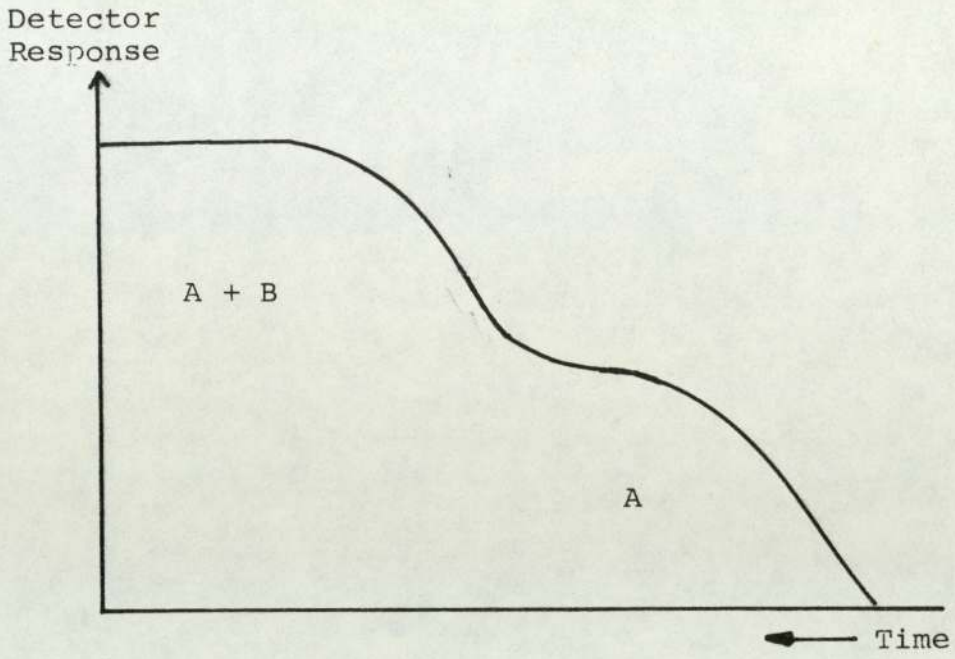
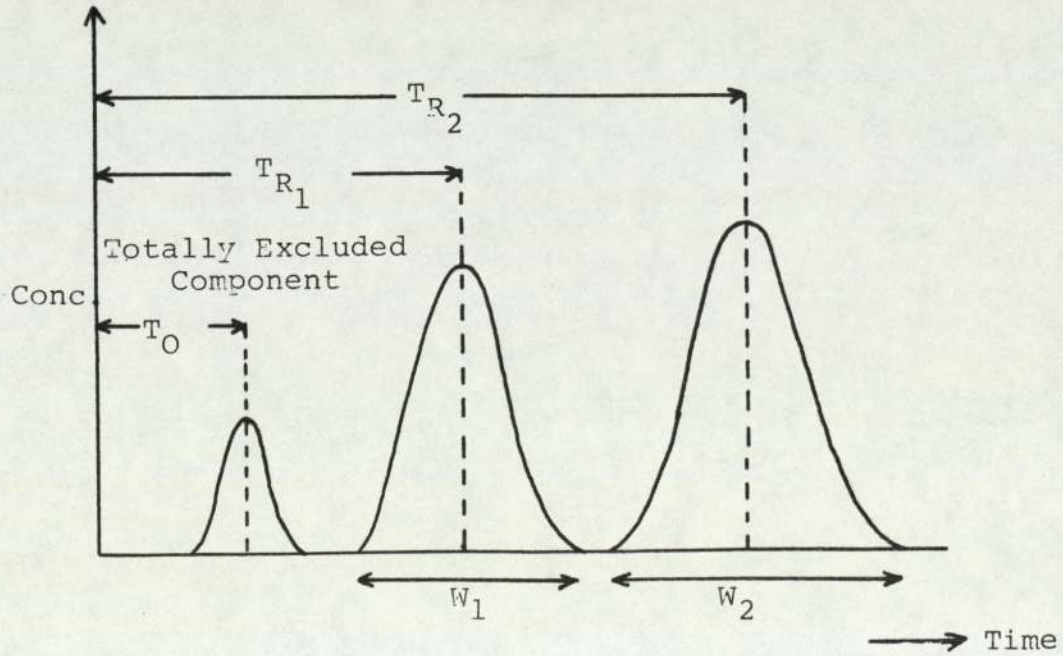


FIG. 2.2 A TYPICAL CHROMATOGRAM



emergence at the outlet from the column. The important parameters obtainable from a chromatogram are:

The retention time:- defined as the average time a molecule takes to travel the length of the column and is measured to the mid-point of the symmetrical breakthrough curve t_{RO}, t_{R1}, t_{R2} (see Fig. 2.2). This is a function of the velocity of the mobile phase.

The retention volume:- defined as the volume of the mobile phase that must pass through the column for the elution of a given component. The value for this is obtained by multiplying the retention time by the mobile phase flow rate.

The distribution coefficient:- The fundamental retention equation for a chromatographic process (11) 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 component, (m^3)

V_M = total volume of the mobile phase in the column, (m^3)

V_S = volume of the stationary phase
= volume of the solid matrix + pore, (m^3)

K_d = equilibrium distribution coefficient

$$= \frac{\text{concentration of solute in the stationary phase}}{\text{concentration of solute in the mobile phase}} \quad \ldots\ldots\ldots\ldots\ldots \quad (2.1a)$$

Capacity factor:- The capacity factor k' is defined as:

$$k' = K_d \frac{V_S}{V_M} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (2.2)$$

combining equation (2.1) and (2.2) gives

$$V_R = V_M(1 + k') \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (2.3)$$

$$\text{or} \quad k' = \frac{V_R - V_M}{V_M} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (2.4)$$

Resolution:- This measures the degree of separation and maybe obtained from

$$R_S = \frac{2(V_{R_2} - V_{R_1})}{(W_{1_V} + W_{2_V})} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (2.5)$$

$$\text{or} \quad R_S = \frac{2(t_{R_2} - t_{R_1})}{(W_{1_t} + W_{2_t})}$$

where

R_S = resolution

V_{R_1}, V_{R_2} = retention volumes of components

W_{1_V}, W_{2_V} = peak width at base in volumetric units

t_{R_1}, t_{R_2} = retention time of components

W_{1_t}, W_{2_t} = peak width at base in units of time

The larger the value of R_S, the better the operation. A value of R_S equal to 1.5 or above is considered a good separation factor and a value of 0.8 or less is considered unsatisfactory.

Purnell (12) developed a relationship between resolution and the fundamental parameters:

$$R_S = \tfrac{1}{4}\left(\frac{\alpha-1}{\alpha}\right)\left(\frac{k_2'}{1+k_2'}\right)(N^{\frac{1}{2}}) \quad \ldots\ldots\ldots\ldots\ldots\ldots (2.6)$$

where $\alpha = \frac{K_{d2}}{K_{d1}}$ = Ratio of equilibrium distribution coefficients

k_2' = Capacity factor of the most retarded component

N = Number of theoretical plates in the column

2.2.3 Theory of Band Broadening

Separations in elution chromatography can be measured by

(i) the distance between the adjacent peak centres and is related to the thermodynamic equilibrium of the process, and

(ii) the shape of the peaks and is dependent upon the column dynamics.

It is latter that is predicted by the theories discussed below:

2.2.3.1 The Theoretical Plate Concept

The concept of the theoretical plate was originally introduced into distillation theory in an attempt to find a quantitative method of expressing the efficiency of a distillation column. Martin and Synge (2) introduced a similar concept for chromatographic columns. They suggested that a chromatographic column could be considered to consist of a number of layers of packing, each of which was equivalent to a theoretical plate (HETP).

To simplify the mathematical modelling of such a complicated system the following assumptions were made.

(a) The distribution coefficient K_d, is constant throughout the column and is independent of concentration.

(b) Equilibration of the solute between phases is rapid compared with the rate of travel of the mobile phase.

(c) Diffusion along the length of the column in any phase is negligible.

(d) The column can be considered to consist of a number of identical volume elements, in each of which equilibration occurs.

(e) The flow of mobile phase can be regarded as discontinuous, that is, it consists of a stepwise addition of a volume of mobile phase, each equal to the free volume per plate.

Using the assumptions above, the model predicts a Gaussian distribution curve as a result of the spread of a single solute band. The degree of spreading of this curve is measured by means of its variance σ^2. The plate height is then defined by

$$H = \frac{d\sigma_z^2}{dz} \quad \text{..... (2.7)}$$

where H = plate height (m)

σ_z^2 = variance of Gaussian curve (m^2)

z = distance along the column length L (m)

Dependence of the HETP (height equivalent to a theoretical plate) on mobile phase flow rate, particle diameter and the longitudinal diffusion, the effect of which is enhanced at the reduced flow rate, was also reported by Martin and Synge (2).

2.2.3.2 The Continuous Model

A modification to the previous model by Martin and Synge (2) was made by Gluekauf (16). He converted the discrete plate model into a continuous one by reducing

the volume of the plate to an infinitessimally small value. The predicted concentration profile exhibited a Poisson distribution which became a Gaussian distribution when the total number of plates in the system exceeded 100.

The most significant error with the plate model arises from the assumption of plate wide equilibrium. In reality the equilibrium is only reached at plate maximum. The plate model also fails to take into account the effect of molecular structure, sorption phenomena, temperature, molecular distribution and flow pattern towards zone broadening, but it is useful for characterisation of zone spreading and column efficiency.

2.2.4 Band Broadening Rate Theory

There are two main headings under this section.

2.2.4.1 The Simplified Van Deemter Equation

Lapidson and Amundson (13) proposed a model to define HETP for gas chromatography, this was later modified by Deemter, Zuiderweg and Klinkenberg (14).

$$H = A + \frac{B}{u} + C_s u \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (2.8)$$

where H = height equivalent to a plate

A = the eddy diffusion term = $2\lambda d_p$

B = the longitudinal diffusion term = $2\gamma D_m$

C_s = the stationary phase mass transfer term

$$\frac{8K_d'^2}{\pi^2(1+K')^2 D_s}$$

u = the mobile phase velocity

and λ = packing characterisation term for eddy diffusivity such that $E = \lambda u d_p$

d_p = mean particle diameter

γ = labyrinth factor to allow for the torous flow path

D_m = mobile phase molecular diffusivity ($m^2 s^{-1}$)

D_s = stationary phase molecular diffusivity ($m^2 s^{-1}$)

d = thickness of stationary phase liquid film (m)

u = interstitial mobile phase velocity (ms^{-1})

$K' = \frac{F_m}{D_m} K_d$ = mass distribution coefficient

K_d = distribution coefficient

F_m = fractional volume of mobile phase

F_s = fractional volume of stationary phase

Van Deemter introduced a further term ($C_m u$) to allow for resistance to mass transfer in the mobile phase. A graphical presentation of equation (2.8) is shown in Fig. (2.3a). In gas chromatography, the gas phase longitudinal diffusion term becomes significant at low velocities and at high velocities the stationary phase resistance to mass transfer term ($C_s u$) becomes controlling.

Fig. (2.3b) illustrates a similar graph for liquid chromatography and shows how the shape differs from that of gas chromatography. The major reason being that the longitudinal diffusion coefficients in liquid are 10^4-10^5 times smaller than those in gases and hence contribute negligible effect towards zone spreading.

FIG. 2.3a GRAPHICAL PRESENTATION OF VAN DEEMTER EQUATION

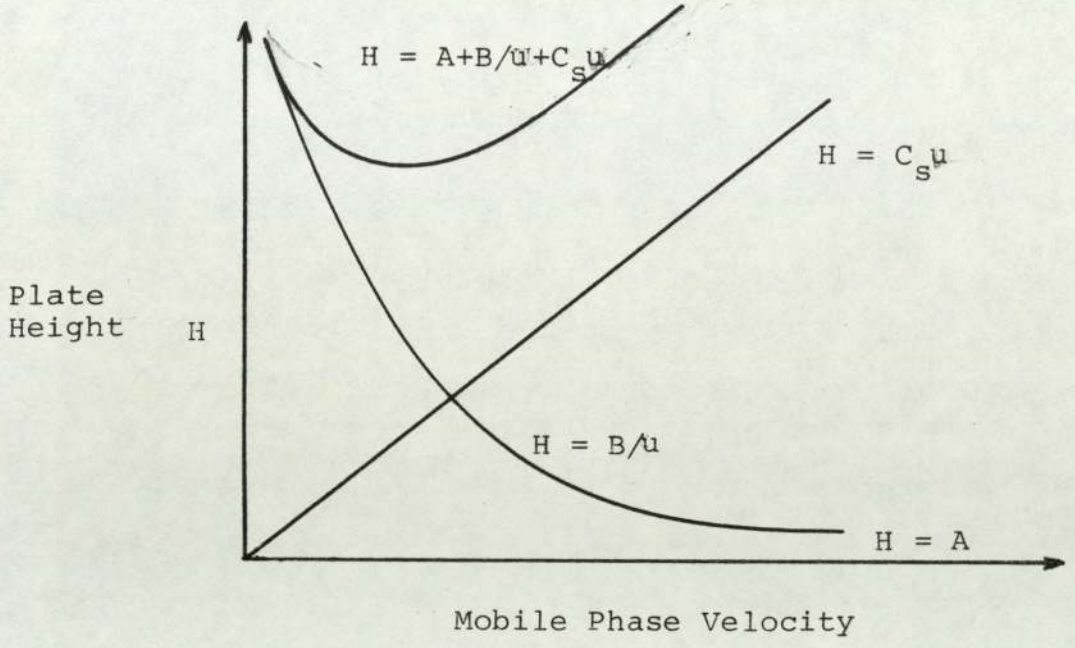
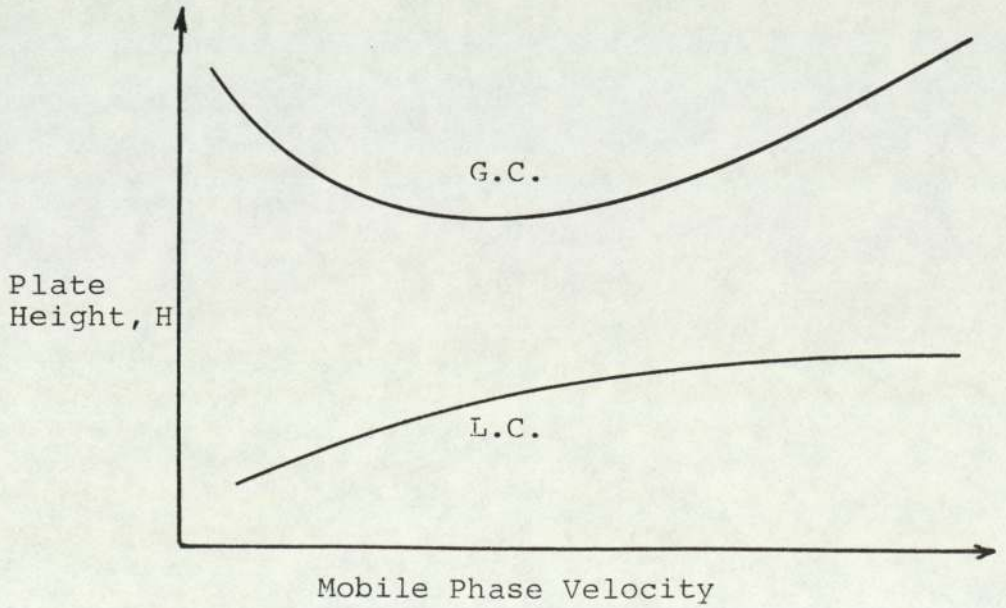


FIG. 2.3b COMPARISON OF THE CHROMATOGRAPHIC PLATE HEIGHT CURVES FOR GAS CHROMATOGRAPHY AND LIQUID CHROMATOGRAPHY



2.2.4.2 Random Walk Theory

Giddings and co-workers (15) proposed a 'coupling theory' relating eddy diffusion and flow inequalities. The final expression couples the eddy diffusion and resistance to mass transfer in the mobile phase to yield:

$$H = \frac{B}{u} + C_s u + \left(\frac{1}{A} + \frac{1}{C_m u}\right)^{-1} \quad \ldots\ldots\ldots\ldots\ldots\ldots (2.9)$$

The total value of the contribution to H of the coupled term is always less than that obtained from either of the component parts, Fig. (2.4); however the equation 2.9 has been used by many workers in chromatography for the prediction of plate height.

2.2.4.3 Generalised Non-Equilibrium Theory

Giddings (15) claimed that true equilibrium between two phases only exists at the centre of the zone as shown in Fig. (2.5). The stationary phase concentration has a lag in its equilibrium value, whilst the mobile phase concentration will always be ahead of its equilibrium concentration. The main cause for such a non-equilibrium situation is caused by a slow rate of mass transfer between the two phases. A quantitative discussion of mass transfer processes in a variety of systems has been presented by Giddings (15).

FIG. 2.4 COMPARISON BETWEEN CLASSICAL AND COUPLED EQUATION FOR PLATE HEIGHT

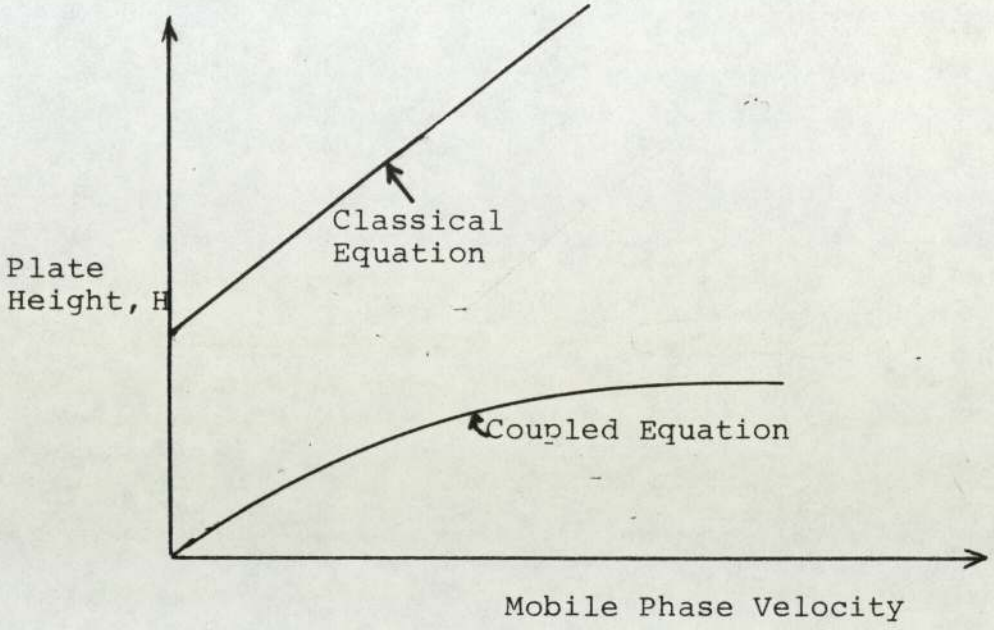
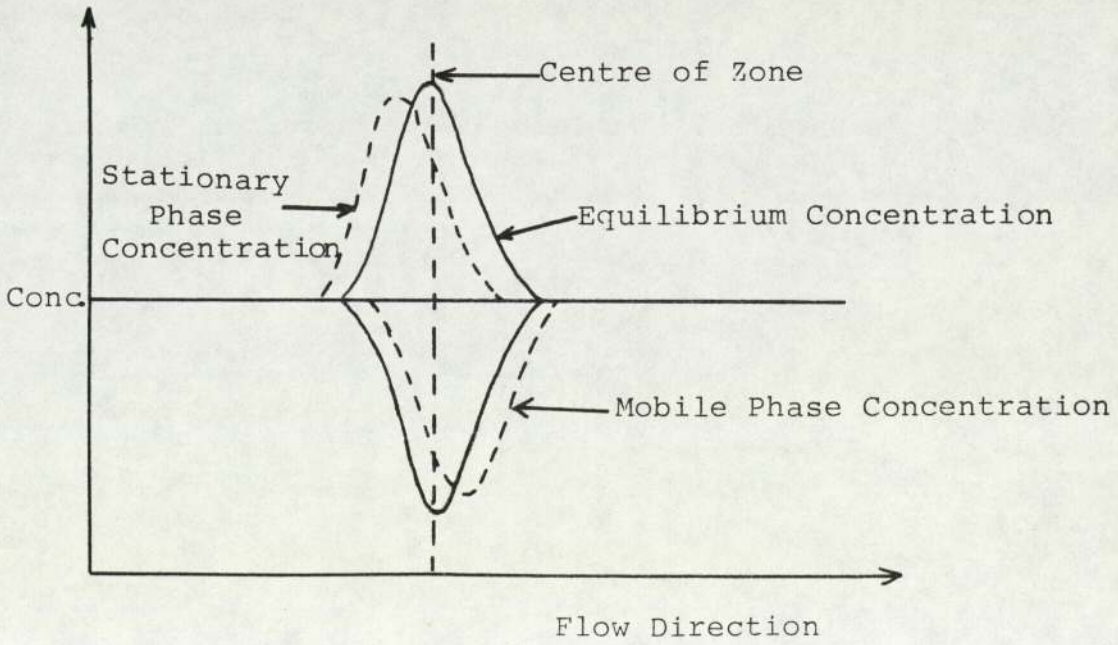


FIG. 2.5 COMPARISON BETWEEN ACTUAL AND EQUILIBRIUM COMPONENT CONCENTRATION PROFILES FOR NORMAL ELUTION CHROMATOGRAPHY



2.2.5 A Direct Measurement of the Number of Theoretical Plates

If the solute is introduced at the beginning of the column as a small narrow band, an approximate Gaussian concentration profile is obtained at the outlet due to band broadening. The width of the band measures the efficiency of the column. Gluekauf (16) related the number of theoretical plates to the elution time and the width of the peak at a height of peak maxima divided by e (see Fig. 2.6).

$$N = 8\left(\frac{t_{Ri}}{W_{h/e}}\right)^2 \quad \ldots\ldots\ldots \qquad (2.10)$$

where

N_i = Number of theoretical plates in the column

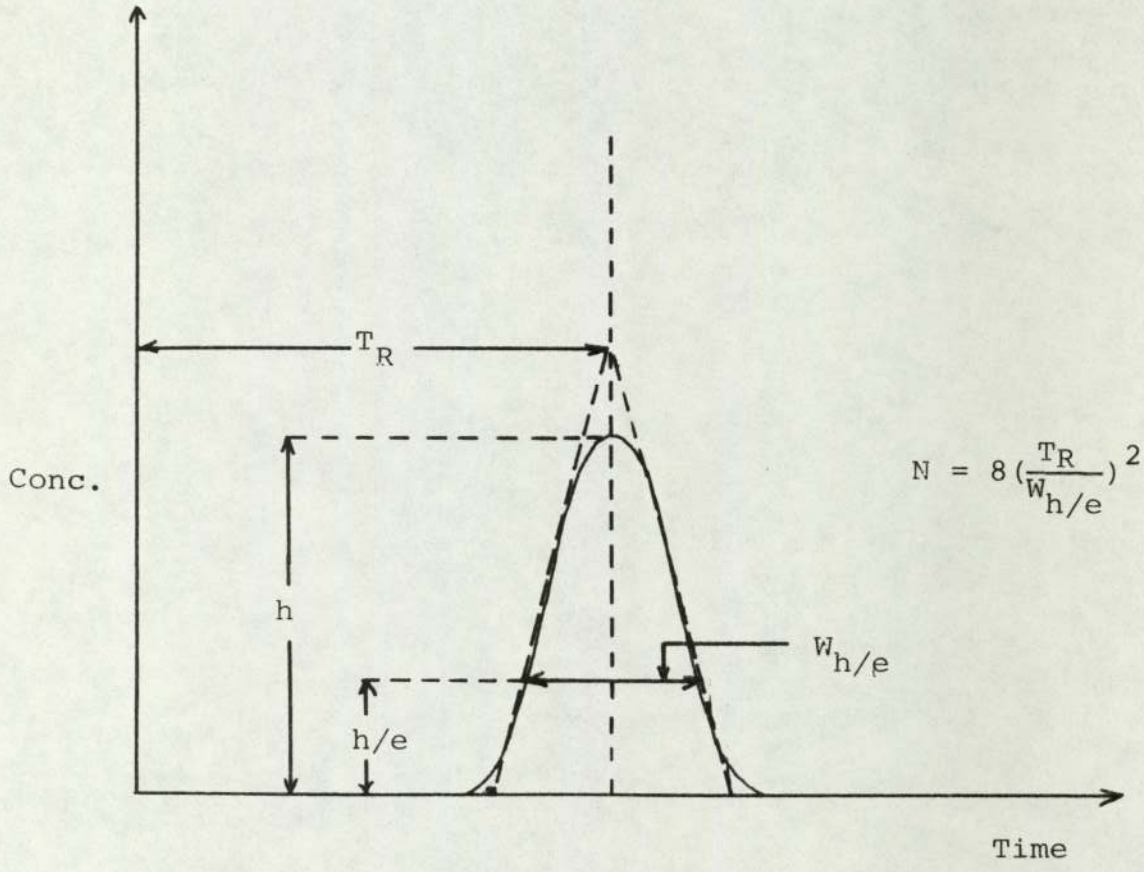
t_{Ri} = Retention time of component i (s)

$W_{h/e}$ = Width of the band at a height h/e (s)

2.3 SCALING UP OF THE CHROMATOGRAPHIC COLUMNS

Chromatography is normally practised in the laboratory as an analytical tool. Its application in separations at the production-scale level is possible if the factors affecting scale up are identified and accounted for. As studies on continuous chromatographic processes are very limited, findings for batch chromatographic processes are employed as a practical guideline to highlight the important aspects of scale up.

FIG. 2.6 RELATIONSHIP BETWEEN NUMBER OF PLATES AND PEAK CHARACTERISTICS



2.3.1 Factors Affecting Scale Up

2.3.1.1 Flow Patterns in Large Diameter Columns

The uneven velocity profile results from a deterioration in packing efficiency in large diameter columns. The overall effect is to decrease the plate height. This has been taken into account by introducing an additional term H_c in the van Deemter equation (2.8)

$$H = A + \frac{B}{u} + C_s.u + H_c$$

Giddings (76) expressed the parabolic profile as:

$$H_c = G \frac{r_c^2.u}{\gamma.D_m} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (2.11)$$

where

G = constant

r_c = column radius

u = mobile phase velocity

γ = radial Labrynth factor

D_m = diffusivity of solute in mobile phase

This correlation is found to give good agreement with experimental results obtained for 0.6 cm to 5.1 cm diameter columns (17) and also a 7.5 cm column (18).

Bayer, Hupe and Mack (19) assumed a concave profile and expressed it as

$$H_c = 2.83 \left\{\frac{r_c^{0.58}}{u^{1.886}}\right\} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (2.12)$$

This gave a good experimental agreement for columns from 1.3 cm to 10.2 cm diameter.

Pretorious and de Clerk (20) suggested a W shape profile and suggested the value of H_c as

$$H_c = \frac{1}{100} \text{Exp}\left(-\frac{d_c}{10 d_p}\right) \cdot \frac{d_c^2 . u}{2 D_r . d_p} \quad \ldots\ldots\ldots\ldots (2.13)$$

where

d_c = column diameter

u = mobile phase velocity

D_r = radial diffusivity of solute

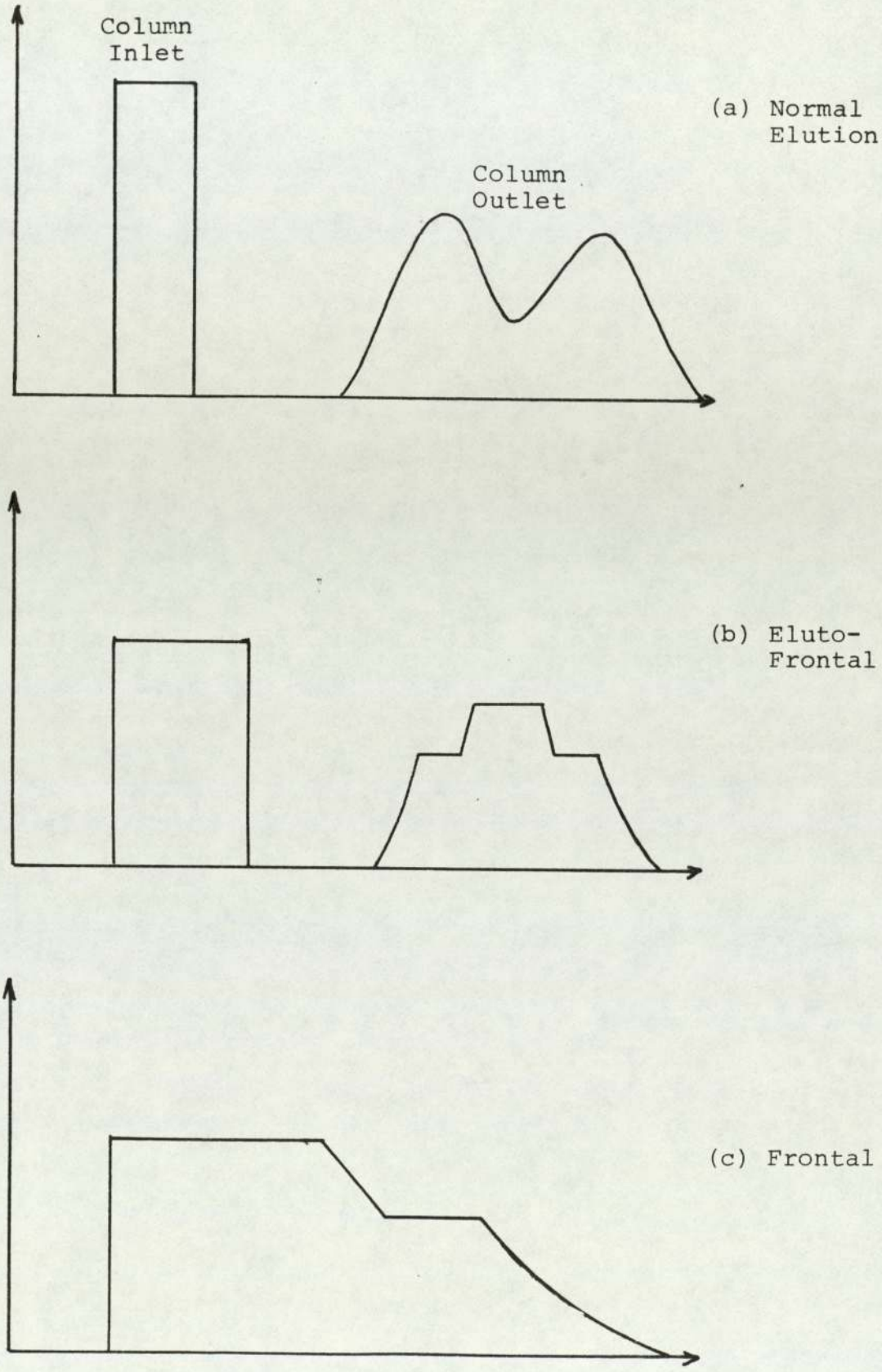
d_p = average particle diameter

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

2.3.1.2 Effect of Increased Sample Size

In ideal elution chromatography, a small sample of feed, spreading over a narrow inlet band, is eluted from a column. This produces a Gaussian outlet profile, the width of which is independent of the inlet band width. Van Deemter (14) and Gluekauf (16) suggested that if the ratio of the feed inlet band and the product outlet band increases above ¼ the Gaussian distribution profile will be altered. If the ratio is further increased, eventually the outlet profile will have the shape as shown in Fig. 2.7b. Such a mode of operation is called eluto-frontal. Finally a continuous input of feed will produce a plateau profile led by a multi-stepped front boundary (Fig. 2.7c). This mode of operation is called frontal analysis.

FIG. 2.7 ILLUSTRATION OF THE OPERATING MODES OF CHROMATOGRAPHY



Conder and Purnell (21,22) set the following conditions for the various modes of operation

$\theta < \frac{1}{2}$ Elution

$\frac{1}{2} < \theta < 6$ Overload elution

$\theta > 6$ Eluto frontal

where $\theta = \frac{N_f}{\sqrt{N}}$

N_f = number of plates occupied by the feed inlet band

N = total number of plates in the column

Conder and Purnell (21) reported that the eluto-frontal mode of operation offers the same degree of separation as the elution mode, but with at least six times increase in throughput at only a three fold increase in column length.

The increase in sample size leads to a drop in column efficiency. However, this is compensated for by a more complete utilisation of packing.

2.3.1.3 Effect of Concentration

In the models produced by Van Deemter (14) and Giddings (15) a linear absorption isotherm is assumed, i.e. the distribution of solute between the two phases is independent of solute concentration. In reality as concentration increases a deviation from ideality occurs. Helfferich (23) redefined the retention volume equation (Eqn. 2.1) to account for this.

$$V_R = V_m + V_s \frac{\partial q}{\partial c} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (2.14)$$

where

q = concentration of solute in the stationary phase

c = concentration of solute in the mobile phase

The curve representing this function which applies at constant temperature is the absorption isotherm. Three main types of isotherms may be classified by their different effects on column performance. Vermulen (24) describes favourable and unfavourable isotherms for resolution. A decreasing function of c is a favourable or Langmuir isotherm (Fig. 2.8a) and an increasing function of c is an unfavourable or antilangmuir isotherm (Fig. 2.8b). The intermediate or linear isotherm is represented by a dashed line.

When a 'Langmuir' isotherm is studied both the retention volume and the K_d decrease with an increase in solute concentration, with an 'Antilangmuir' isotherm both parameters decrease. Operation in non-linear region requires extra column length to compensate for the decrease in resolution. In production scale operation a degree of contamination of products is tolerated for an increase in the throughput gained by higher feed concentration. This will however be accompanied by an increase in viscosity and thus higher pressure drop. A compromise is often reached after an economic assessment.

FIG. 2.8a LANGMUIR 'FAVOURABLE' ISOTHERM

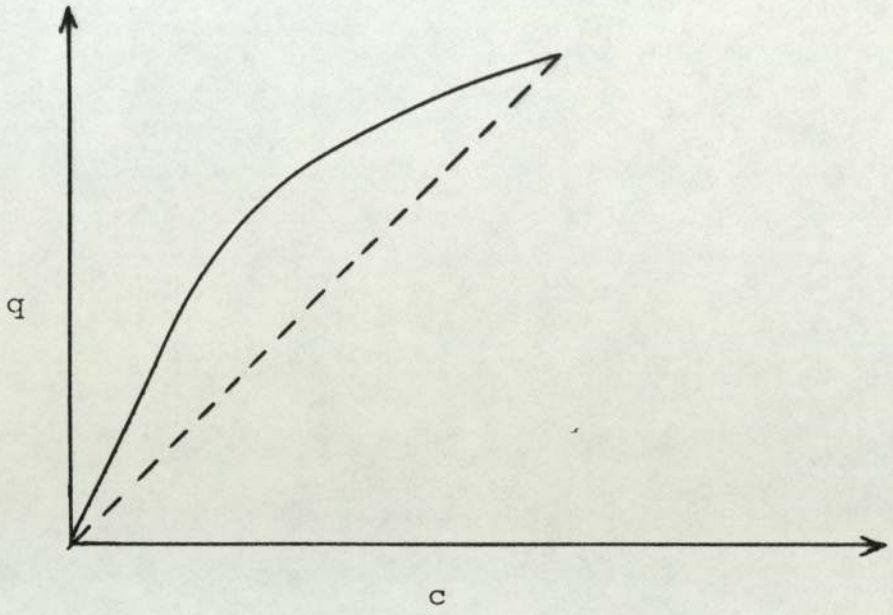
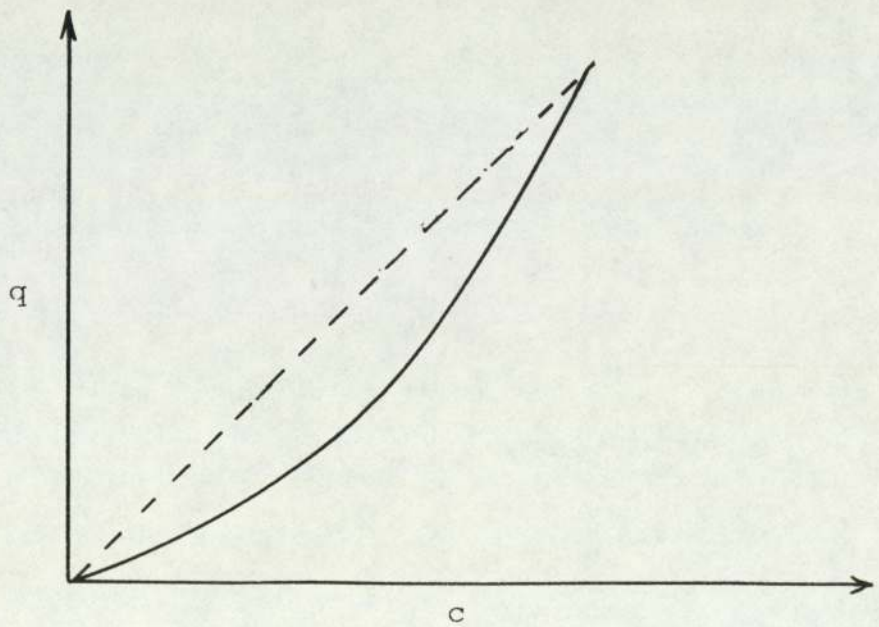


FIG. 2.8b 'ANTILANGMUIR' UNFAVOURABLE ISOTHERM



2.3.1.4 Effect of Mobile Phase Velocity and Column Length

In production scale chromatographic equipment throughput plays an important part. Increase in throughput can be achieved by increasing the velocity of the mobile phase. This reduces the residence time and increases the plate height as the column's ability to resolve two or more components decreases. A longer column is required to maintain the same degree of resolution. This in turn results in a longer elution time. Generally a compromise is reached between throughput and product purity in conjunction with pressure drop and pumping energy.

2.4 PRACTICAL SOLUTION TO PRODUCTION SCALE CHROMATOGRAPHY

2.4.1 Column Packing Technique

A poor packing technique very often results in low efficiencies in large diameter chromatographic columns. An efficient packing technique to obtain high and reproducible column efficiency is desirable.

Various techniques have been used to achieve these aims. Two basic methods used are dry packing and slurry or wet packing. In gas chromatography, Higgins and Smith (25) studied several methods of dry packing and produced most favourable HETP values. The fluidisation technique of Guillemin (26) produced a very high initial efficiency but beds packed by this technique are very prone to collapse. Bayer (19) introduced mechanical tapping and vibration to improve efficiencies, but the classical "shake-turn-pressure" method developed

by Verzele (27) produced a good repeatability with dry packing.

Slurry techniques include bulk pouring, pouring with external vibration, pouring under vacuum and reservoir packing. The formation of a packed bed occurs by sedimentation of a thick suspension. In such a suspension, particles do not behave individually according to Stoke's law but interact with each other and the inter-particle fluid. Thus they tend to flow downwards as a unit in some places forcing less concentrated suspension upwards. Thus segregation occurs. The best method of slurry packing is often found by trial and error for the particular column diameter and packing. Gould (10) found that pouring slurry under vacuum was most efficient and repeatable for zerolit 225 resin used in the SCCR unit hence this packing technique has been adopted for this research.

2.4.2 The Use of Flow Distributors and Baffles

In large diameter columns, the velocity profile of the mobile phase varies considerably across the cross section of the column. The installation of flow distributors at the column inlet enhances radial mixing and consequently leads to a uniform velocity profile. Musser and Spark (28) investigated the performance of inlet cones in gas chromatography and found a significant increase in column efficiency. Other devices used have included perforated plates and screens.

Gould (10) in his research found a good distribution of liquid across the cross section of the 10.8 cm diameter column when a perforated plate was used as the inlet distributor. Even solute concentrations were found at various points across the diameter of the column.

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. Baddour (29) used a "disc and doughnut" arrangement with the disc of a smaller diameter than the column, forcing the mobile phase towards the column walls. When the fluid strikes the doughnut it is redistributed towards the central region. An improved efficiency of large diameter columns was reported by Abcor Inc., Massachusetts (30) using a similar baffle system.

2.4.3 The Use of a Repeated Feed Injection System

In batch chromatography, only a small section of the packed bed is being used for separating a small sample. To maximise column utilization, a repetitive way of sample injection has been commonly employed. This involves the introduction of subsequent charges of feed into the column at controlled time intervals. This interval is calculated such that the leading edge of an injected sample elutes from the column just as the trailing edge of the previous injected sample leaves the column. Thus the whole column length is being used for resolution at all times. Conder (31)

has performed a detailed study in this field.

2.4.4 Continuous Chromatography (93)

The use of a continuous system involves the continuous introduction of feed into the column and continuous removal of two products from the column in a manner similar to a distillation column. Most workers have attempted to move the stationary and mobile phase counter-current to each other. Fig. 2.9 illustrates the type of concentration profile which would result for the separation of a two component feed by the continuous counter-current chromatography.

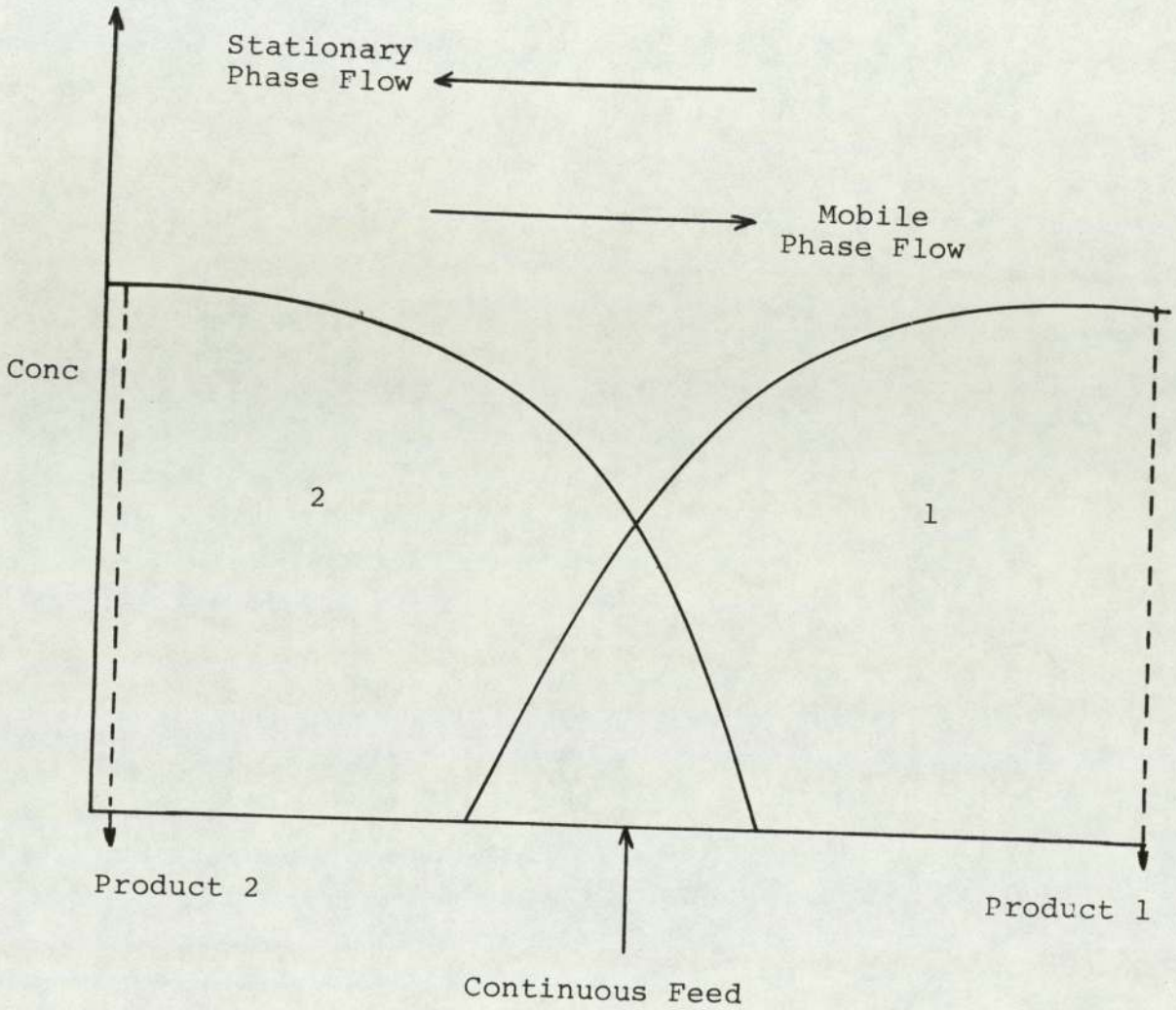
Many chromatographs have been designed to achieve the continuous separation. Three basic systems have been developed namely fixed bed, moving bed and simulated moving bed. The flow schemes are shown in Fig. 2.10.

2.4.4.1 Fixed Bed Operation (Fig. 2.10a)

Early work concentrated on GLC or GSC. Tiley (32-34) used a 2.5 cm column with a knitmesh packing. The liquid stationary phase flowed downward over the knitmesh packing against the mobile gas flowing upwards as shown in Fig. 2.10a. High product purities were obtained but low throughputs.

Extensive studies have been undertaken using pulsing technique by Wankat (35,36) and a survey of similar attempts are included in his review (36).

FIG. 2.9 CHROMATOGRAPHIC CONCENTRATION PROFILES OBTAINED FOR THE SEPARATION OF TWO COMPONENTS BY CONTINUOUS COUNTER-CURRENT OPERATION



2.4.4.2 Moving Bed System (Fig. 2.10b)

This group of developments may be divided into those in which the stationary phase physically moves counter-currently to the mobile phase and those in which the column of stationary phase is made to move in a counter current direction to the mobile phase. Useful contributions in this field of activity have been made by Barker (37,38), Schultz (39), Scott and Ti ley (32).

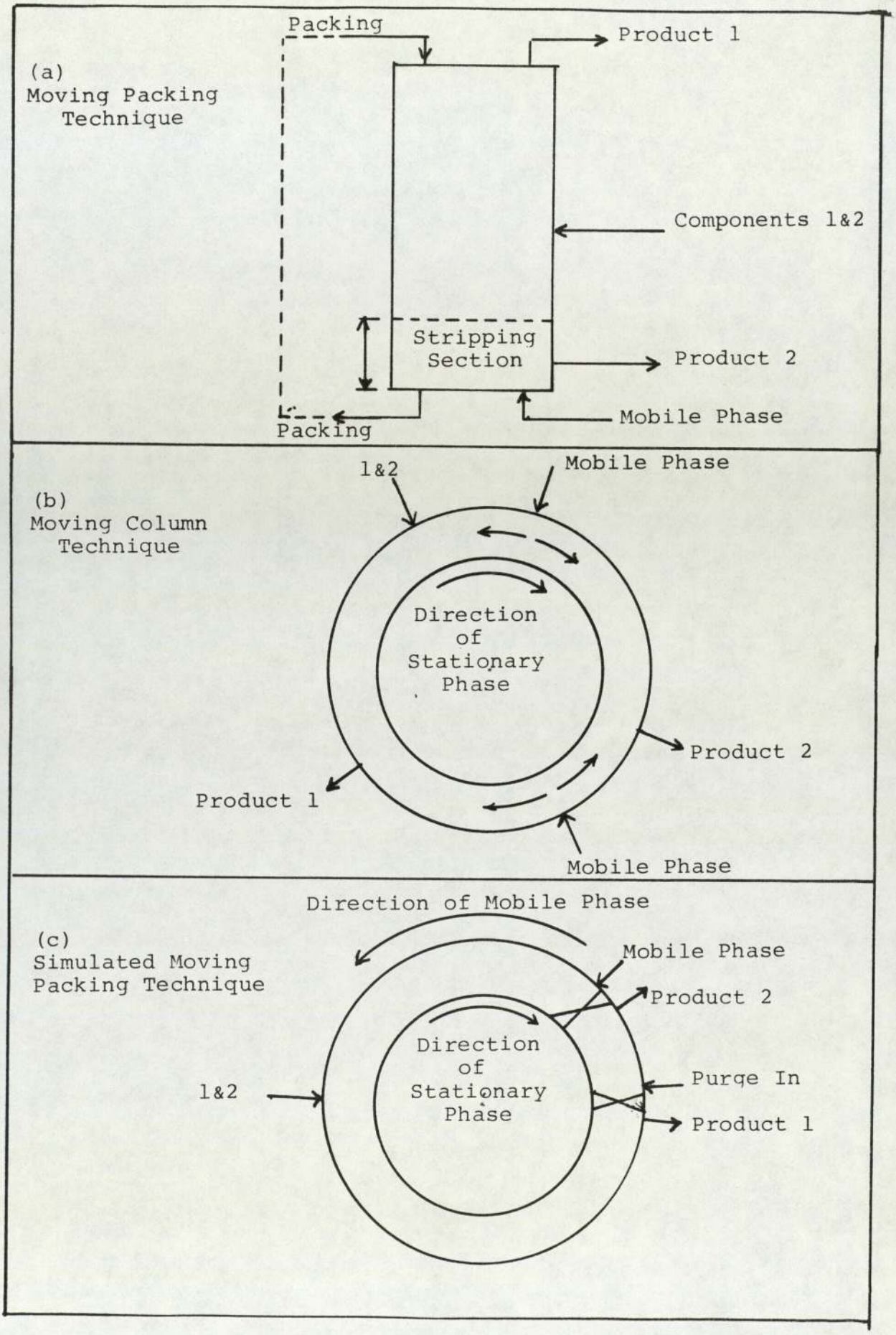
Moving bed systems had inherent disadvantages in that large quantities of solid packing needed to be physically moved, thus causing the attrition of particles. The flow rate of the mobile phase flow rate was also linked to a value below that of the minimum fluidising velocity of the particles. Physically as the bed moved down the column, packing characteristics varied and poor efficiency through backmixing often resulted.

To avoid these problems the moving column system was developed. This involved the rotation of a series of columns past fixed inlet and outlet ports against the direction of the mobile phase flow. Barker (40,41), Pichler and Schultz (42), Luft (43), and Glasser (44) were some of the important workers in this field.

2.4.4.3 Simulated Moving Bed Counter Current System (Fig. 2.10c)

Moving seal problems incurred with the above system encouraged the development of a simulated moving bed design. Barker and Deeble (7) introduced a system whereby the counter-current movement is simulated by

FIG. 2.10 CONTINUOUS FLOW SCHEMES



opening and closing of inlet and outlet valves. Ching (8) used a similar flow scheme in constructing a liquid-solid chromatograph. The apparatus used in this research uses a similar flow schemes and will be discussed in detail later.

Szepsy (45) proposed a scheme in which a switching valve was centrally mounted on a rotary PTFE disc. Rotation of the valve altered the relative position of the inlet and outlet ports to a stationary series of columns. In such a manner counter-current column movement was simulated.

2.5 OPTIMISATION OF PRODUCTION SCALE BATCH CHROMATOGRAPHY

Craven (46) systematically developed the optimisation of GLC systems. Later Conder (47) studied the effect of various parameters and performed optimisation of a gas-liquid production scale gas chromatography for α/β pinene system. The effect of some of these parameters are discussed in turn.

2.5.1 The Effect of Feed Band Width, Recovery Ratio and Column Length

Conder (47) investigated the effect of these parameters on throughput per unit cost and suggested that an optimum value of 0.6 as the recovery ratio (defined as the ratio of useful product obtained to input feed). The feed band width and column length are calculated using appropriate equations published by Conder (47).

2.5.2 The Effect of Column Diameter

The column diameter chosen depends on the throughput desired and is not a parameter to be optimised. Conder (47) obtained Fig. 2.11 which shows the effect of scale up on product cost and indicates that it decreases rapidly at first with increasing scale of operation and more slowly when the scale is large.

2.5.3 The Effect of Carrier Velocity or Eluent Flowrate

Increase in carrier velocity has four principle effects:

(i) it increases HETP hence increases the necessary column length for the same resolution of components.

(ii) feed size can be increased in each batch in direct proportion to the rise in HETP.

(iii) it reduces the elution time in proportion to carrier velocity.

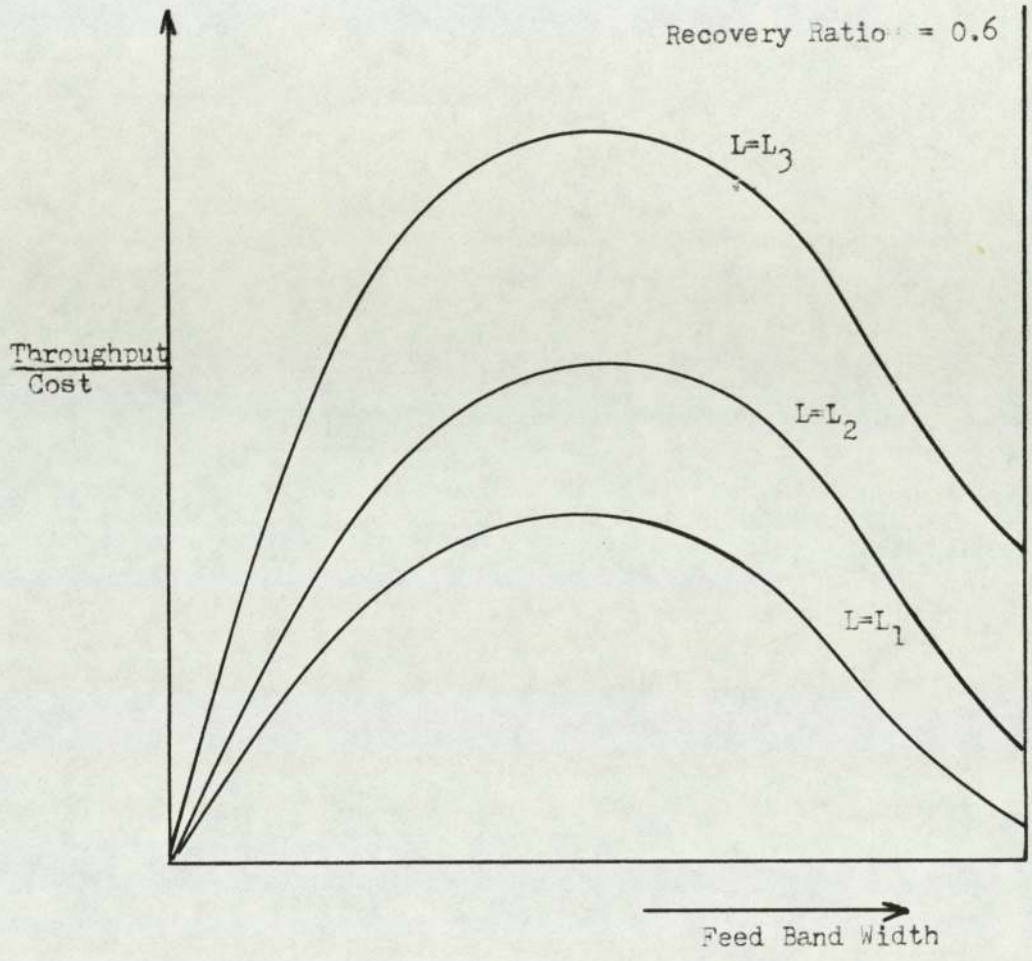
(iv) it increases the pressure drop in the column.

It is desirable to use the highest possible velocity because although it requires longer columns, it reduces the overall product cost by raising throughput as shown for GLC by Conder (47).

2.5.4 The Effect of Feed Concentration

Conder (47) suggested that the concentration of solute in both stationary and mobile phase of the column should be as high as possible to make overall efficient use of the stationary phase in the column.

FIG. 2.11 THE EFFECT OF COLUMN DIAMETER ON THROUGHPUT



2.5.5 The Nature of the Stationary Phase

The stationary phase should be one which, at the proposed operating temperature, is completely stable chemically.

Conder (47) has only performed the optimisation of gas-liquid chromatography system when considering optimisation of liquid-solid chromatograph, the effect of temperature has to be considered. The temperature reduces the viscosity of the mobile phase, easing the handling of the viscous liquids and reducing the pumping cost. This has to be balanced against the higher energy cost involved in heating of the input streams.

The other factors such as feed band width, recovery ratio, column length, column diameter, eluent velocity, feed concentration and the nature of stationary phase will all have the similar effects in liquid-solid chromatography as in gas-liquid chromatography because the mechanism of separation in both types of chromatography are identical, i.e. the separation is effected by the relative velocity of the components through a stationary phase.

2.6 SEPARATION OF FRUCTOSE FROM A MIXTURE OF CARBOHYDRATES

Crystalline fructose is 1.8 times sweeter than sucrose (48) in cold solution. Accordingly, fructose is fast becoming one of the most popular candidates for sweetening foods and beverages, its greater sweetening power making possible a significant reduction in the calorific intake of food or beverage by a consumer, A

number of synthetic sweeteners have been discarded as a result of causing carcinogenic activity in experimental animals, hence a purely 'natural' route to lower calorific intake offered by fructose sweetening has acquired even greater significance.

Traditionally sugar has been produced either from cane, grown in tropical and sub-tropical areas, or from beet, grown in more temperate zones such as the U.K., France and Belgium. However, since about 1957, the isomerisation of glucose to the sweeter fructose has been known to be possible, thus leading to a route from maize, potatoes or wheat flour to starch, to a glucose-fructose syrup, comparable in sweetness with sucrose.

2.6.1 Commercial Sources of High Fructose Syrup

Methods for producing high fructose syrup are classified into three main categories according to the raw materials:

(i) Hydrolysis of sucrose

(ii) Enzymatic conversion of corn starch

(iii) Hydrolysis of inulin, a polyfructosan

2.6.1.1 Hydrolysis of Sucrose

The hydraulic process is called sugar inversion and can be achieved by directly contacting the feed with mineral acids, or by passing the sugar through columns of cation exchange-resin charged to the H^+ form. In the former case, all the free acid ions in the hydrolysate have to be removed subsequently by an

anion exchanger.

As sucrose molecules consist of one molecule of glucose and one molecule of fructose, the product from an inversion process should contain an equal amount of both sugars. A complete inversion is difficult to obtain, and the resulting solution usually contains some residual disacchride. The purity of fructose in the syrup produced from such processes rarely exceeds 50%. Consequently, a further refining process is required to enrich the fructose content.

In a patent granted to Boehringer Mannheim Company of Germany (4) in 1967, it was disclosed that sucrose was completely inverted to glucose and fructose after passing through a hydrogen charged ion exchange resin bed at a temperature of 60°C.

By charging the resin with calcium chloride at room temperature it still kept 1-30% of the free hydrogen ions. When a slug of sucrose feed was passed through a suitable bed length of resin, hydrolysis of sucrose and separation of fructose from glucose took place simultaneously in the column. The separation was effected by formation of a complex between calcium ions and fructose. No strong complexing occurs between calcium ions and glucose.

Lauer and co-workers (49-51) were granted U.S. patents for inverting sucrose and separating the glucose-fructose mixtures in the same column which was packed with Dowex 5 WX4 in the calcium charged form. The inversion and separation temperature was 60°C.

2.6.1.2 Isomerisation of Glucose Using Immobilised Enzyme

In 1895 Bruyn and Van Eckenstein (52) converted glucose into fructose using an alkaline catalyst at elevated temperature. Developments have taken place since then to perform the isomerisation using sodium hydroxide and ion exchange resins. Some notable workers in this field were Okazaki (53) and Suzuki (54-55). Further improvements have been introduced by Parrish (56), Tsao (57), and Barker (58) who used a less expensive catalyst such as insoluble alumina catalysed organic bases and acids, reported conversion varied from 45% to 80%. Expensive raw material, low conversion yield and formation of ash and useless by-products made the industrial adaptation of the above processes commercially unattractive.

In 1957, Marshall and Kooi (59) discovered an enzyme, xylose isomerase, for conversion of glucose into fructose. Presence of arsenate and fluoride increased the yield of fructose. The presence of these toxic materials and the unavailability of a cheap source of xylose made this an unsuitable process for producing the food product.

Takasaki and Tanabe (60) porposed the use of xylan for the isomerisation process. Xylan was readily available from various sources, such as cereal bran and corn cobs. Furthermore this enzyme did not require arsenate or fluoride. Later Takasaki and co-workers (61) provided a commercially feasible glucose isomerisation

process for obtaining fructose rich syrup. Using this technique Newton and Wardrip (62) of the Clinton Corn Processing Company reported the first commercial process in the U.S.A. for manufacturing a fructose rich corn syrup.

Nova Company (63) in Denmark developed a new source of immobilised enzyme called sweetzyme which was designed for use in batch reactors and also continuously operated reactors.

Today, large continuous processes for producing fructose rich corn syrup from cheap starch sources are in evidence in Koong and Zoon in the Netherlands, Saragossa in Spain and at Greenwich in the United Kingdom.

2.6.1.3 Hydrolysis of Inulin, a Polyfructosan

Inulin is a polysacchride that exists in the roots of the compositae like Jerusalem artichoke, dandelion, and dahlia tubers. Its molecule is unbranched and consisted of about thirty D-fructofuranose units linked together. The breaking down of inulin into its monomers will produce an extremely high purity fructose syrup.

Plant geneticists and the chemists are investigating the technique for improving the crop yields of tubers, but little information is published. In a paper by Yasushi (64) of the Asaki Chemical Industry Company Limited, it was stated, based on laboratory work, that fructose can be produced from the inulin. An economic evaluation is required to assess the viability of adopting this process commercially.

2.6.2 Batch Processes in Operation Today

2.6.2.1 The Colonial Sugar Refining Co. Processes (65)

A patent was granted to the Company in 1967 for the separation of glucose and fructose. Dowex 50W, a sulphonated polystyrene cation resin, cross-linked with 4% divinylbenzene and having a particle size of 210-420 μm was reported to be a suitable packing. It was charged in the calcium form. This resin was able to hydrolyse and separate invert sugar into glucose and fructose fractions. Their 1.8 m length packed bed was operated in a co-current batch mode with various recycle fractions. From their published results (65) the fractions collected varied in concentration and purity. One fructose rich product had a concentration of 29% w/w solids of which 82% was fructose, another was 24% w/w solids of which 95% was fructose. The process was operated at 60°C which necessitated the lagging of all process lines, vessels and columns. The use of high temperature enabled to keep the viscosity of the syrup low enough so that reasonable pumping costs could be maintained.

2.6.2.2 The Boehringer Mannheim Process (4)

In 1967 the Boehringer Mannheim Company was granted a patent for a process from which glucose and fructose products could be obtained from sucrose or sucrose containing invert sugars. They used an ion exchange resin, Dowex 50W with 4% divinylbenzene crosslinkage, in six glass columns in series each 15 cm in diameter. A total separating length of 9 m was used.

The eluent was water and the preferred rate was reported to be 1-2 $cm^3 min^{-1} cm^{-2}$. The resin was charged at room temperature at a particular condition of pH, with calcium chloride solution to render it in the calcium form. This allowed the resin to retain 5-30% of its active sites in the hydrogen form. It is this property of the resin namely having free hydrogen ions which allows complete hydrolysis of the sucrose to take place in-situ. The calcium ions then retard the fructose by forming a complex and thus effect the separation.

This process uses deionised water as an eluent and operates at 60°C to keep the viscosity low. Two sets of results have been published. In the first set the feed was sucrose and in the second a mixture of glucose and fructose was used as the feed. The resultant concentration profiles are shown in Fig. 2.12. It is evident from Fig. 2.12 that no sucrose appears in the product, hence a total hydrolysis has been achieved. A repeated feed injection operation was adopted but a total separation was not achieved. The recycling of the mixture in the 'overlap' section was essential.

Chuah (9) using a semi-continuous chromatographic system with a pre-column packed with the Amberlite 1R-118 resin charged in the free hydrogen form performed both hydrolysis of sucrose and separation of fructose simultaneously. A complete inversion of sucrose and a 95% pure fructose rich product has been reported from a pure sucrose feed material.

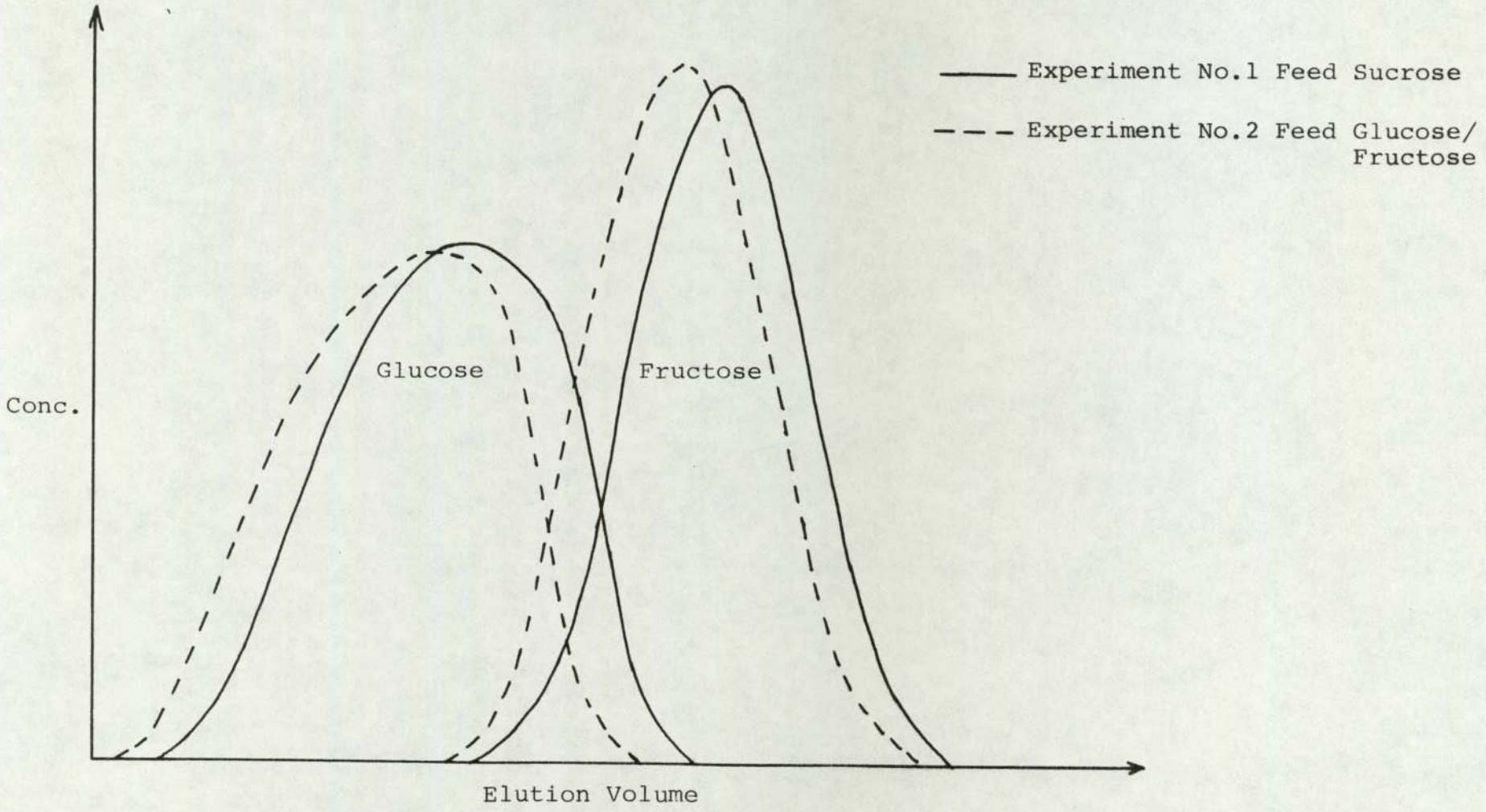


FIG. 2.12 RESULTS PUBLISHED IN THE BOEHRINGER PATENT

2.6.2.3 Other Batch Processes for Fructose Production

Newton and Wardrip (62) of the Clinton Corn Company reported the first industrial plant in operation in U.S.A. using sucrose as feed and inverting it by an enzyme, xylan. Albion Sugar Company (subsidiary of Koniklijke Sholten-Honig NV of Amsterdam) has invested in a plant in Tilbury-on-Thames producing high purity fructose. Other industrial scale plants have been started in the Netherlands, Belgium and Spain.

2.6.3 Continuous Processes in Operation Today

2.6.3.1 Sarex Process (66) (commercialised UOP Sorbex Process)

This is a continuous process for producing up to 90% pure fructose syrup. The feed containing 42% fructose in the high fructose corn syrup (HFCS) at 50% w/v dry solid is continuously charged to a single adsorption column via a distributing device known as a rotary valve. At the same time through different parts of the same rotary valve, desorbent water is passed. Extract (high-purity fructose) and raffinate (fructose-depleted glucose) streams are removed - each from different sections of the column and all on a continuous basis (see Fig. 2.13).

Products from the Sarex system have been diluted with desorbent water (to approximately 20 wt % dry solid) and require evaporation after ion exchange. A recovery of more than 90% of the fructose in the feed can be achieved in the extract. Enriched fructose

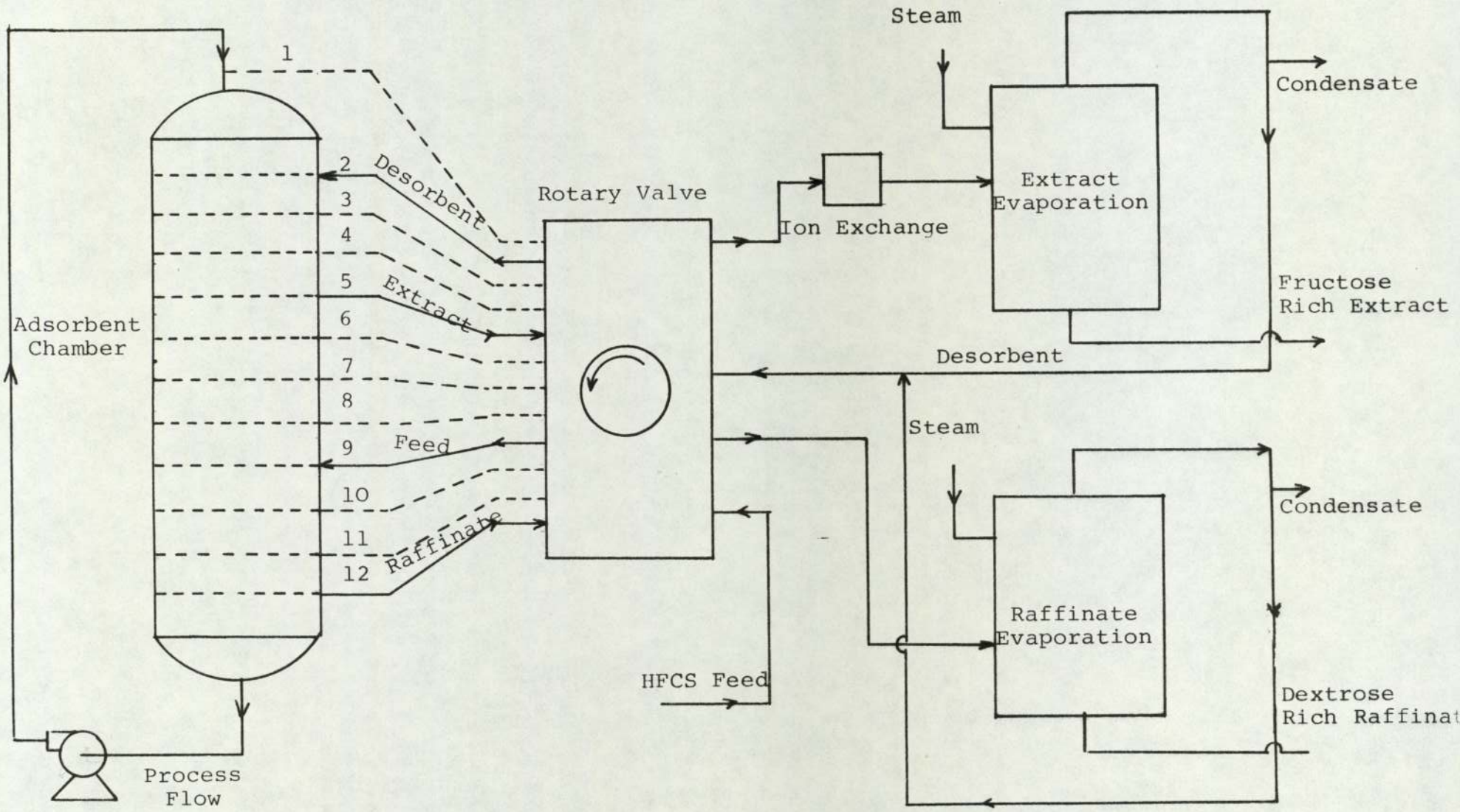


FIG. 2.13 SAREX PROCESS

syrup products of less than 90% fructose are produced by blending extract with 42% HFCS.

Details of the equipment size have not been published.

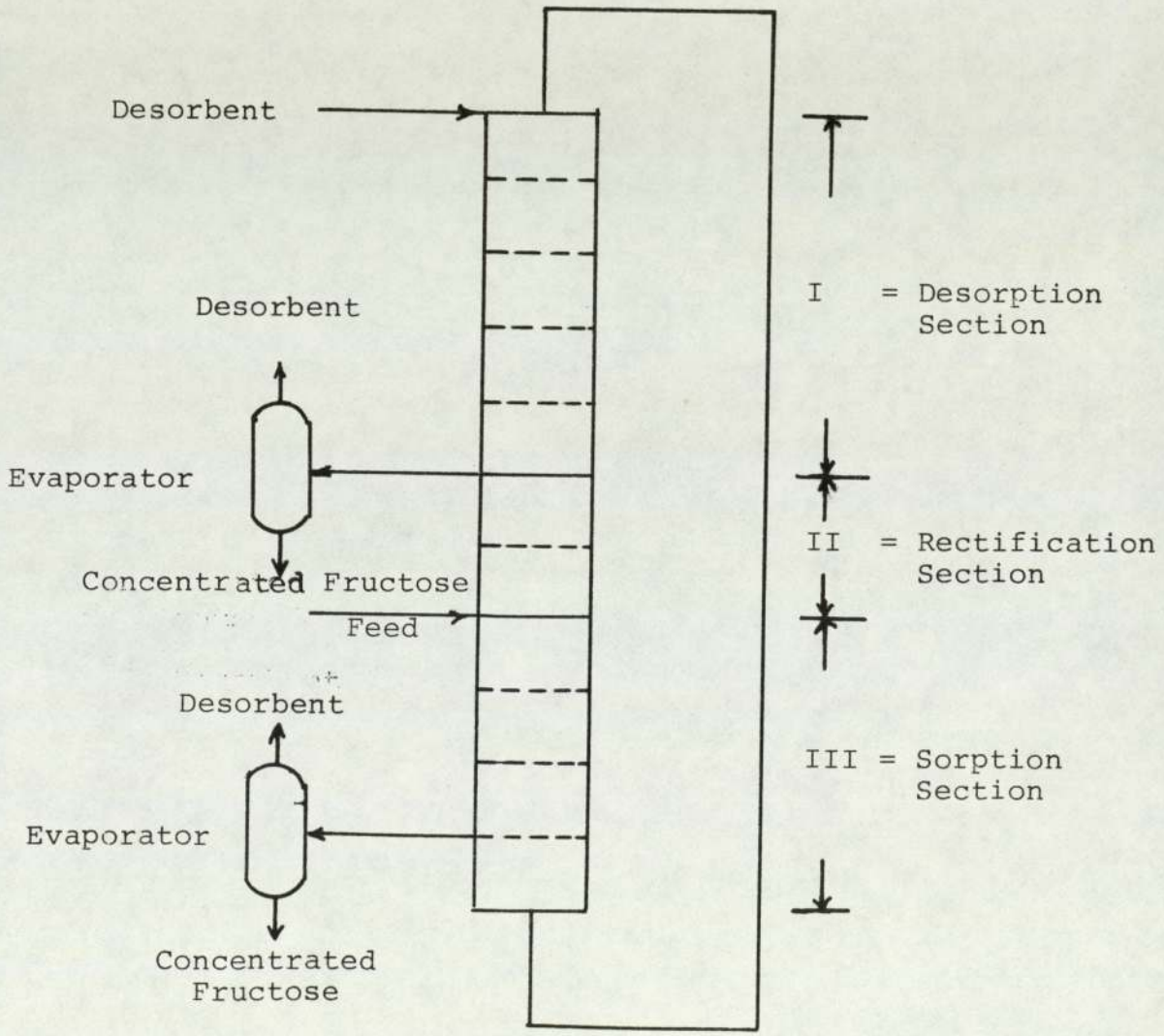
2.6.3.2 Odawara of Toray Industries Inc., Tokyo, Japan (67)

This is a continuous process for separating fructose from a mixture of glucose and fructose. Fructose is absorbed by the solid phase of crystalline zeolite. The liquid streams are allowed to flow through three serially and circularly inter-connected zones including a desorption zone, a rectification zone and a sorption zone. Water is introduced into the desorption zone and a portion of the desorption effluent comprising of fructose and water is removed as fructose rich product. Fig. 2.14 shows the flow scheme of the streams.

The equipment consisted of eleven columns of 25 mm internal diameter and 1.5 m length packed with barium zeolite to a height of 1.35 m each. All the columns were divided into three zones: desorption, rectification and sorption comprising of 5, 2 and 4 columns respectively. A total of 66 valves and a timing device was used to simulate continuous operation by advancement of entry and exit ports around the closed loop.

To this equipment a feed containing 7% w/v of solid sugar consisting of 57.5% glucose and 42.5% fructose was fed at 1.4 kg hr^{-1} and another aqueous solution of 1.0% w/v of sugar solids at room temperature was continuously fed as a reflux stream at a rate of

FIG. 2.14 ODAWARA OF TORAY INC., TOKYO, JAPAN PROCESS



8.5 kg hr^{-1}. Two products were continuously withdrawn. The raffinate effluent at 0.2 kg h^{-1} consisting of 45% w/v of sugar solids of which 3% was fructose, and the desorption effluent at 12.7 kg hr^{-1} containing 1% w/v of pure fructose.

2.6.4 Mechanism of Separation Used in this Research

Both the molecules of glucose and fructose are of identical size and weight, and would therefore be eluted at the same rate through a bed of porous type packing. However, if the mixture of glucose and fructose is passed through a bed of calcium charged cationic resins, fructose, due to its complex formation with calcium ions, is retarded and glucose will emerge first from the column.

Reviews of the research carried out by earlier workers on the metal complexing of fructose have been published by Von Lippman (68) and Vogel (69). However recently Angyal (70-75) has published a series of papers proposing a hypothesis for the complexing mechanism.

2.6.5 The Chemistry of Glucose and Fructose

Glucose in solution exists as four isomeric ring structures of which two are six membered rings referred to as glucopyranoses and the other two are five membered rings called glucofuranoses (Fig. 2.15). An equilibrium exists between these structures at all conditions.

FIG. 2.15 FORMS OF GLUCOSE IN SOLUTION

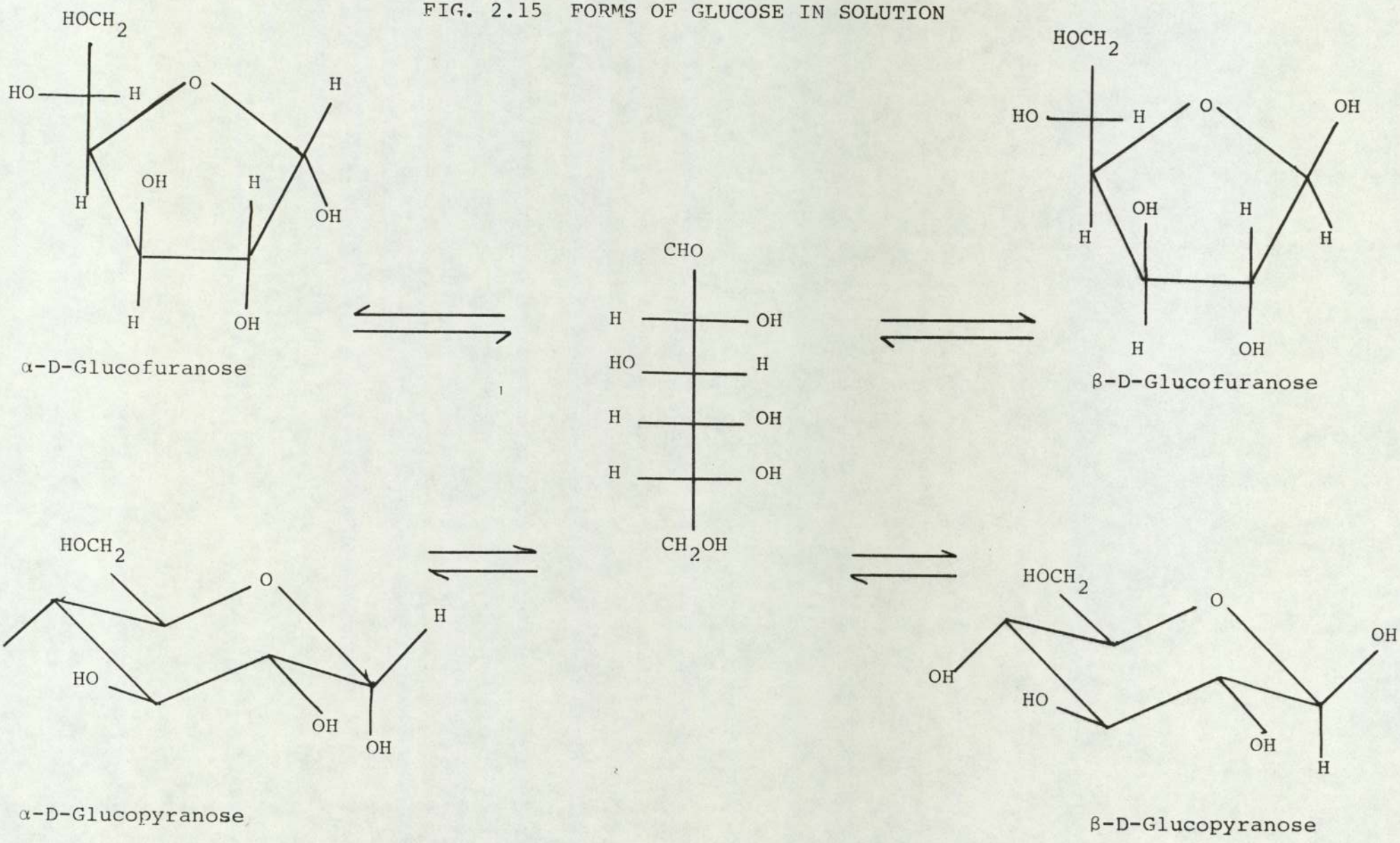
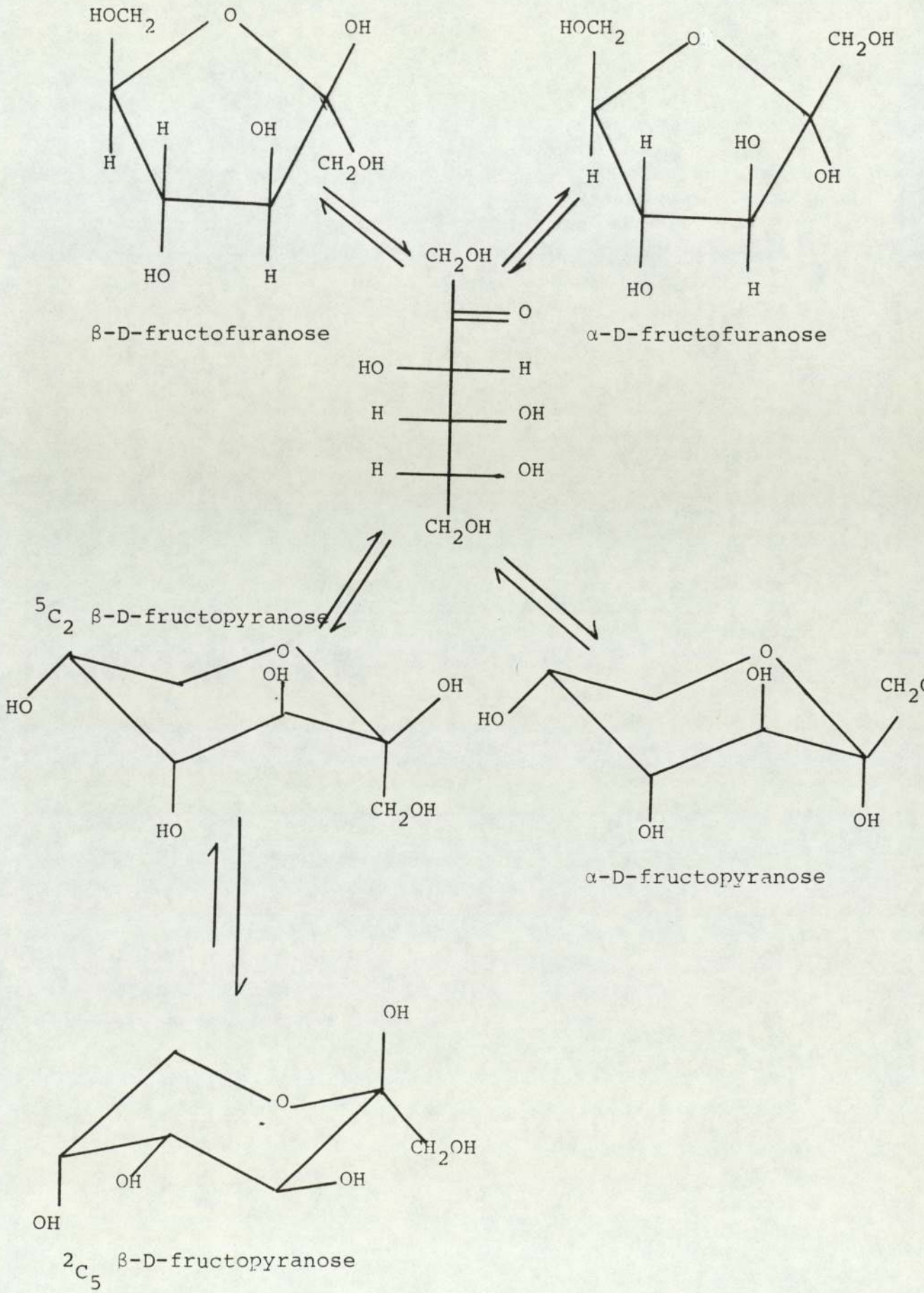


FIG. 2.16 FORMS OF FRUCTOSE IN SOLUTION



Angyal (70) in his hypothesis suggested that for a successful complex formation, a sequence of eq-ax-eq-ax arrangement of oxygen atoms on adjacent carbon atoms is desirable. This is not exhibited in any of the glucose isomers. The abbreviation "eq' stands for equotarial which means that the oxygen atoms lie in a plane horizontal to a carbon atom, whereas "ax" means axial when the oxygen atom lies vertical to the carbon atom.

In solution fructose exists in five isomeric forms of the ring structures being shown in Fig. 2.16. An equilibrium exists between the two forms of the β-D fructofuranose. The equilibrium arises from the variation in the "chair" shape of the ring in relation to the equatorial or axial position of the CH_2OH group. These are referred to as the $5C_2$ and $2C_5$ fructopyranose and describe the ring structure as viewed from a certain position. It is the $2C_5$ form which exhibits the sterically favourable form of the ring, the eq-ax-eq-ax arrangement of the oxygen atom for complexing to occur.

2.7 OTHER PRODUCTION SCALE CHROMATOGRAPHS IN OPERATION TODAY

In Section 2.6, the production scale chromatographs producing high fructose syrup are mentioned. In this section a brief account of other commercial scale chromatographs are included.

2.7.1 The Finsugar Molasses Desugarisation Process (5)

Since March 1975, the Finnsugar plant is believed to be the largest batch chromatographic molasses separation plant in the world. The equipment consists of a column of 270 cm in diameter packed with 300-600 cm high resin bed. The resin used is sulphonated polystyrene strong cation exchanger, cross-linked with 4-8% divinyl benzene, of mean particle size 0.35-0.60 mm. The feed consists of 25-45 kg of molasses DS as a 30-40% water solution per m^3 of resin. A recovery of up to 95% of sugar in the molasses is reported. The product containing sugar content in the desugarised fraction of 5-25% of DS and a purity of 92% is obtained.

2.7.2 The Zudsucker Process for Sugar Recovery from Molasses (6)

The Zudsucker process for molasses sugar recovery depends on the separation of the components of molasses from one another with the help of liquid distribution chromatography. The stationary phase used comprises of a strongly acidic cation exchanger resin with about 4% cross linkage ('Lewatit TSW 40 of Bayer AG, Leverkusen) in the Ca^{++} form whereas water which has been decarbonated or made alkaline with calcium oxide is used as the mobile phase. The working conditions are a temperature of $90^{o}C$ and a linear flow rate of 3.4 cm min^{-1}. The chromatographic column has an overall length of 18 metres, a diameter of 1 metre and a resin content of 13.4 m^3. By feeding the column with 0.06 bed volumes

of molasses with 50% dry matter and a purity of 60%, a product containing 10-11% dry matter of 90% purity is obtained. A recovery of up to 95% of the sugar in the molasses is reported.

2.7.3 Elf Process for the Separation of Component by Gas-Liquid Chromatography (77)

Three sizes of batch GLC separation equipment are available:

1. a laboratory unit with a production of 10-100 g h^{-1} of substance (40 mm diameter columns)
2. a pilot plant unit with a capacity of 10T/year (125 mm diameter columns)
3. a test loop with 300 mm diameter columns producing 20-100T/year of substance

The substances to be treated have to have boiling points between 0 and 200-250°C. In the near future, the equipment handling 10,000T/year (3-5 m diameter columns) is expected to appear to economically handle substances having boiling points within -200°C to +300°C.

The load is injected in bursts (preset flow and time) into the carrier gas. The mixture passes into an evaporator and then into the chromatographic column where the different constituents of the feed separate. A system of valves controlled by a programming clock directs the column's effluents to the appropriate reservoir.

Some examples of Elf equipment in industrial operations are:

1. 40 cm diameter x 1.5 m long GC column to treat flavour chemicals such as terpene derivatives at a rate of 130t/year by Glidden Organics in Jacksonville, Florida (78-81).
2. A production scale GC unit to separate iso and normal paraffins handling 100,000t/year of feed is being built in Donges, France. It was due to start in 1982, but no further reports on its progress has been reported. The unit can handle a range of materials from C_4 to C_{10} producing paraffins ranging from 80 to 99.8% pure (82,83)

2.7.4 Molex, Parex and Olex Processes (Commercialised, UOP Sorbex Process)

Molex, parex and olex (84), all three are commercialised Sorbex processes and work on a continuous basis as shown in Fig. 2.13 and explained in Section 2.6.3.1.

Molex process (85) uses a 5A zeolite as a molecular sieve to extract normal paraffins from kerosine. The pilot plant extraction of a wide boiling range feedstock C_{10} to C_{23} has been investigated. A total of 93.5% of the normal paraffins were extracted at a purity of 99.5%. Typical commercial performance in a kerosine range stock is 97% extraction at 98.7% purity.

Olex process (85) is used for the separation of olefins from unreacted paraffins. A mixture containing 9% olefins has been injected to extract 93.9% olefins

at 95.2% purity.

The Parex Process (85) for the separation of p-xylene from a C_8 aromatic extract or from C_8 catalytic reformate, is in worldwide use. From a feed containing 11.7% p-xylene, a recovery of 96.7% at 99.5% purity was achieved.

2.7.5 Abcor Production Scale Chromatographic Columns

Abcor Inc., Cambridge, Massachusetts (USA) and Boehringer and Sohne (Germany) have designed a stainless steel pilot plant (86) to be as versatile as possible. The two systems available namely GC50 and GC100 contain two 300 cm long columns each of diameter 15 cm and 30 cm respectively. The GC50 is designed so that it can accommodate one 300 cm x 30 cm column instead of two 300 cm x 15 cm columns. Boehringer is operating a 25 cm diameter column for a commercial preparation of a drug intermediate (87). The company has also developed a control unit suitable for use with production scale liquid chromatography. Developed during Abcor's work on gas chromatography, the unit can be programmed to control the operation during unattended operation by sensing peaks and fronts and so making the required product cuts and feed injections.

Abcor and Boehringer columns have used a packing material of aluminas, silicas and ion exchange resins. A cross linked polystyrene resin from Rohm and Haas is also suitable. A Swedish firm Pharmacia Fine Chemicals sells a cross-linked dextran polymer gel trade-named

Sephadex with wide application. Pharmacia has been promoting the sale of sephadex by using production size chromatographic columns of 180 cm diameter for the separation of milk protein from whey.

Further development in production scale chromatography by Abcor Inc (88) has led to a 120 cm diameter x 300 cm high GC unit for the separation of alpha and beta pinenes. It is projected that the unit will separate 100T/year of crude alpha and beta pinene.

Abcor has also developed a GC and LC process (89) for the separation of m-xylene from p-xylene. The GC process consists of two 430 cm in diameter x 430 cm long columns being operated with alternate feed injection. The LC process uses two alternative fed columns of 370 cm diameter and 780 cm high.

2.7.6 Other Processes (90)

Oak Ridge National Laboratory's Chemical Division Tenn) research division have produced a system for production scale continuous liquid chromatography which is ready for commercialisation. The unit offers particular advantages for the continuous separation of components having close distribution coefficients; the process employs an annular bed of sorbent resin that rotates slowly (e.g. $90^{o}\ h^{-1}$) about a vertical axis . The mixture to be separated enters under pressure at a stationary point above the top of the annulus. Because of varying retention times for the components, they trace about a helical path of differing pitches

as they descend through the bed. Accordingly a given component can be drawn off into a collector (under the annulus) that has been placed at the appropriate angular distance from the feed point.

The preparative LC system 500 (99) sold by Water Accociates Inc. (Milford, Mass. USA) can purify 20 or more grams of material in a run lasting from 5 to 30 minutes, depending on the difficulty of the separation. The system features a column with capacity for 350 g of adsorbent. Two types of packings are available: standard silica and a modified version with a hydrophobic surface. The two are said to be effective over a range of polar and non-polar compounds.

Another LC system Prep 100 (99) is manufactured by Jobin-Yvon (Longjumeau) in France and marketed in the USA by instruments S.A. The system consists of a 10.8 cm diameter column packed with a number of commercially available adsorbents including silica, alumina, cellulose and a variety of bonded phase packing. The column holds about 1.7 kg of adsorbent. Nitrogen pressure rather than a pump drives the sample through the column. The adsorbent is compressed up to 180 psi by a porous stainless steel piston. Overall the system can handle about three times the throughput of a Prep 500 but takes a proportionately greater amount of time to perform the purification step.

CHAPTER THREE

MEASUREMENT OF THE DISTRIBUTION COEFFICIENTS, K_d

3.1 INTRODUCTION

In equation 2.1a, the distribution coefficient has been defined. Within an analytical chromatographic column, the feed sample is so small, approximately 20 µl compared to the column volume of about 10 cm^3 that the elution can be considered to take place at infinite dilution. In preparative and production chromatography a feed volume as high as 25% of the total column volume is used. This produces a considerably high on-column sugar concentration and causes an effect on the distribution coefficient of the components.

The significance of the variation in the distribution coefficient is particularly important in the mathematical modelling of the chromatographic system. Gould (10) and Chuah (9), while simulating the chromatographic process, found it necessary to change the value of the distribution coefficient of components to fit the simulated results with the experimental results. This chapter investigates the effect of on-column sugar concentrations on the distribution coefficients in order to improve the mathematical modelling of the system and hence obtain a better fit to the experimental data.

3.2 EQUIPMENT

A relatively simple chromatographic system was used for measuring the distribution coefficients,

consisting of a pump, sample introduction device, a column, detector and recorder. All results were obtained by manual measurement of the chromatograms. An illustration of the arrangement for the chromatographic system is shown in Fig. 3.1.

The refractometer was placed as close as possible to the column outlet to minimise any extra-column dispersion.

3.2.1 Eluent and Sample Delivery System

Solutions of glucose and fructose were used individually as eluent. The concentration of sugar ranging 10-50% w/v; 0.02% w/v of sodium azide was added to the eluent sugar solution to prevent biological growth. The eluent was fed to the column by a micro-pump supplied by Metering Pumps Ltd. of Ealing. Samples were applied using sample injection valves supplied by Spectroscopic Accessory Co., Kent. All the samples were filtered before being injected on to the column using a syringe filter (supplied by Millipore, London) that was fitted with a 0.46 μm cellulose acetate and nitrate mixed disposable filter.

3.2.2 The Column

A jacketed stainless steel column of 0.5 cm I.D. x 50 cm length, packed with zerolit SRC 14 (150-300 μm) with 4% DVB cross-linking charged in the calcium form, and pressure sealed at both ends was used for this set of experiments. As the packing had to remain wet, a

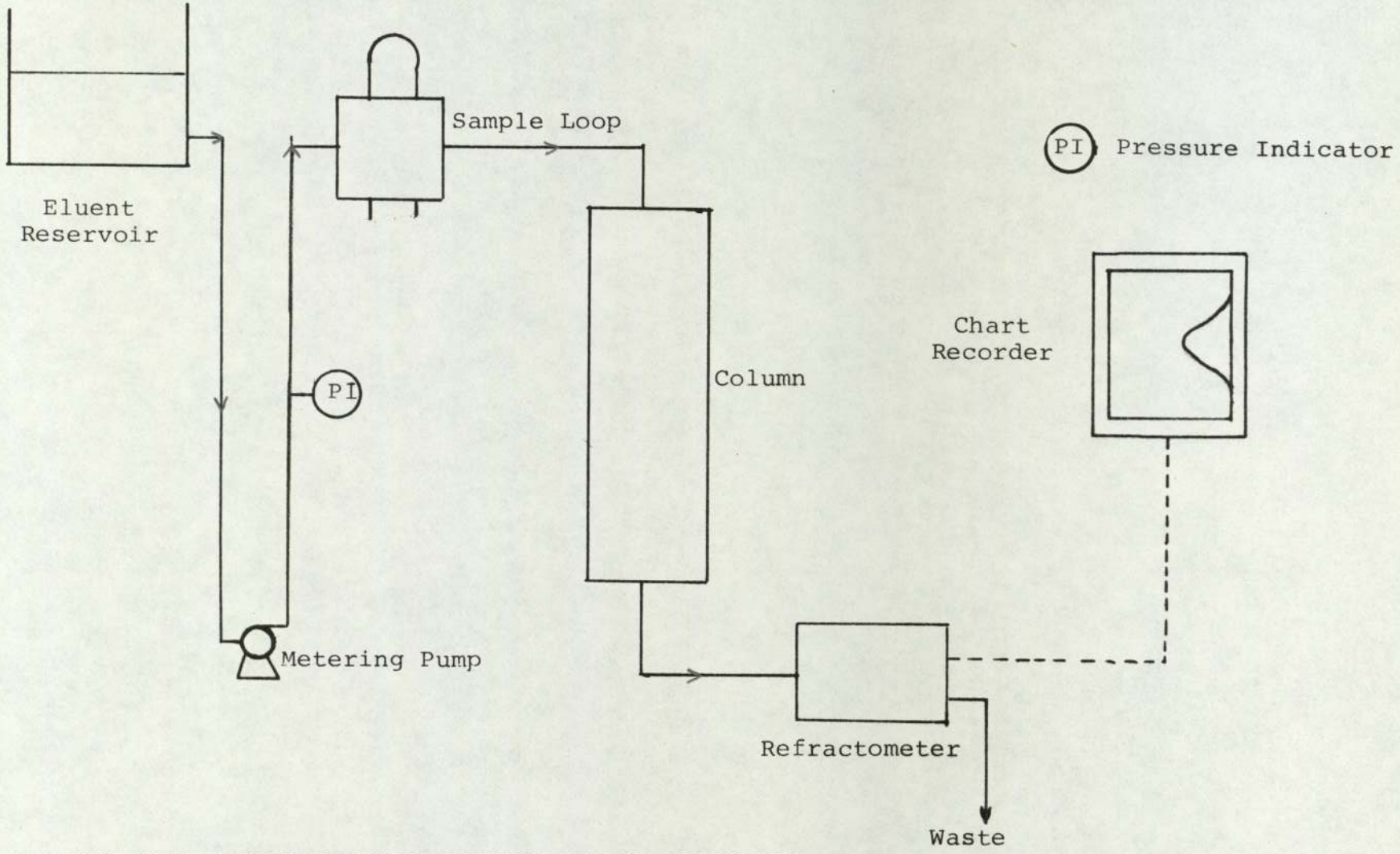


FIG. 3.1 SCHEMATIC ARRANGEMENT OF THE EQUIPMENT

slurry packing technique was necessary. The slurry containing resin to water ratio of approximately 1:1 was poured into the column to which a vacuum was applied. The column had a mechanical seal at both ends.

3.2.3 Sample Detection

The eluate from the column passed into a differential refractometer model 1107LJ supplied by Laboratory Data Control of Stone. Its mode of operation was to compare the refractive index of the outlet stream from the column with that of the pure eluent. The resulting change in the eluate concentration was registered on a flat bed recorder (Smith Ltd., Cricklewood, London, Venture Servoscribe Type 2). From the resulting chromatograms the K_d values could be calculated.

3.3 EXPERIMENTAL TECHNIQUES

The general analytical procedure for the analysis of the samples is outlined below.

3.3.1 Sample Preparation

The sample was prepared by dissolving a known amount of sugar in the eluent sugar solution. Three sample solutions were prepared for each experiment.

(i) 10 g of dextran dissolved in eluent* to make 100 cm^3 of sample;

(ii) 10 g of glucose dissolved in eluent* to make 100 cm^3 of sample;

(iii) 10 g of fructose dissolved in eluent* to make 100 cm^3 of sample.

* The eluents used are as defined in Section 3.3.5.

3.3.2 Sample Loading

The filtered sample was injected into a six port sample injection valve fitted with a constant volume sample loop. When the sample was injected on to the column the movement of the chart paper was simultaneously started. The chart paper speed was set at 1 cm per minute.

3.3.3 Verification of Column Parameters

The measurement of the elution volumes depended upon an accurate and precise measurement of the eluent flowrate. This was performed by weighing the eluent collected in a known time period. A frequent checking on the flowrate was essential. The void volume was taken to be the elution volume of dextran. The elution volume of glucose and fructose were also obtained by appropriate chromatographs.

3.3.4 Determination of Distribution Coefficient Values

The fundamental retention equation for a solute in chromatography is defined (11) as:

$$V_R = V_m + K_d V_s \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (3.1)$$

where V_R = Retention volume of a component

V_m = Volume of mobile phase in the column

= volume of void + pore

V_s = Volume of stationary phase in the column

= total column volume - void volume

K_d = partition coefficient

K_d is defined as

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

From equation 3.1 the K_d can be defined as a function of the retention volume of a solute

$$K_d = \frac{V_R - V_m}{V_s} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (3.2)$$

Consequently the distribution coefficient of glucose may be defined as

$$K_{dg} = \frac{V_g - V_d}{V_T - V_d} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (3.3)$$

where V_T = Total column volume

V_d = Mobile phase volume or void volume V_o

and for fructose

$$K_{df} = \frac{V_f - V_d}{V_T - V_d}$$

3.3.5 Experimental Procedure

The measurement of the distribution coefficient was performed with three different types of eluent.

(i) Various glucose solution within the concentration range of 0-50% w/v;

(ii) Various fructose solution within the concentration range 0-50% w/v;

(iii) Various dextran solution within the concentration range 0-20% w/v.

Three chromatograms per eluent were run: dextran, glucose and fructose.

In the 10.8 cm diameter column the operating flow rate was 1.15 cm^3 per cm^2 cross-sectional area. The flowrate per unit area in 0.5 cm I.D. column was kept approximately the same.

The reference and the sample cell in the refractometer was filled with the eluent to be used, the cell was balanced and the position of the pen was marked on the chart recorder. The sample cell was then connected to the outlet of the column. The eluent was pumped through the column until the cell was balanced again and the pen reached the marked position. When a steady base line had been established on the chart recorder, the sample (as described in 3.3.1) was injected through the sample valve. The peak was shown on the chart recorder as the sugar was eluted. All the chromatograms produced were analysed and the information obtained shown in Table 3.1, 3.2 and 3.3.

Glucose Concentration % w/v	Eluent Flow-Rate $cm^3 min^{-1}$	Dextran		Glucose		Fructose		Distribution Coefficient	
		Elution Time (min)	Elution Volume (cm^3)	Elution Time (min)	Elution Volume (cm^3)	Elution Time (min)	Elution Volume (cm^3)	K_{dg}	K_{df}
0	.25	33.8	8.45	39.50	9.875	52.0	13.07	.12	.38
10	.25	35.95	8.98	45.05	11.26	54.5	13.63	.196	.40
20	.26	34.25	8.91	48.15	12.50	57.0	14.82	.3	.51
30	.27	33.70	9.10	47.65	12.86	57.25	15.50	.33	.56
40	.29	35.40	10.26	51.30	14.87	58.10	16.80	.45	.63
50	.3	34.70	10.40	51.70	15.50	57.95	17.40	.50	.69

TABLE 3.1 RESULTS WITH GLUCOSE SOLUTION AS ELUENT

Fructose Concentration % w/v	Eluent Flow-Rate $cm^3 min^{-1}$	Dextran		Glucose		Fructose		Distribution Coefficient	
		Elution Time (min)	Elution Volume (cm^3)	Elution Time (min)	Elution Volume (cm^3)	Elution Time (min)	Elution Volume (cm^3)	K_{dg}	K_{df}
0	.25	33.8	8.45	39.5	9.875	52.0	13.07	.12	.38
10	.25	34.8	8.70	42.27	10.56	53.90	13.48	.16	.40
20	.284	31.8	9.03	39.20	11.13	48.80	13.86	.18	.42
30	.284	32.9	9.35	40.90	11.62	50.60	14.37	.20	.45
40	.29	36.7	10.60	44.50	12.90	51.40	14.91	.23	.43
50	.3	33.8	10.14	42.20	12.66	50.00	14.96	.24	.46

TABLE 3.2 RESULTS WITH FRUCTOSE SOLUTION AS ELUENT

Dextran Concentration % w/v	Eluent Flow-Rate $cm^3 min^{-1}$	Dextran		Glucose		Fructose		Distribution Coefficient	
		Elution Time (min)	Elution Volume (cm^3)	Elution Time (min)	Elution Volume (cm^3)	Elution Time (min)	Elution Volume (cm3)	K_{dg}	K_{df}
0	.25	33.8	8.45	39.5	9.875	52	13.07	.12	.38
5	.26	33.55	8.723	42.6	11.076	57.4	14.924	.19	.52
10	.27	34.5	9.315	43.1	11.637	58.4	15.768	.21	.57
20	.27	34.25	9.248	45.95	12.407	60.4	16.308	.28	.62

TABLE 3.3 RESULTS WITH DEXTRAN SOLUTION AS ELUENT

3.4 RESULTS AND DISCUSSION

A method known as 'simple linear regression' was adopted to analyse statistically the experimental data obtained. This is shown in Appendix 1. The regression line (the best fit straight line) for individual solutions, together with the correlation coefficients and the results from the confidence limits and the tests of significance are presented in Table 3.4.

The regression line has been represented graphically together with the data points in Figs. 3.2-3.7.

From the experimental results the following observations can be made.

(i) Comparing the distribution coefficients in dextran, glucose and fructose medium, the distribution coefficient increased most rapidly in dextran medium.

(ii) The distribution coefficient of glucose and fructose increased more rapidly with glucose solution than with fructose.

The distribution coefficient is defined as the ratio of concentration of a component in the stationary phase to that in the mobile phase. The mechanism by which a component is retained in the stationary phase contributes significantly to the variation in the partition coefficient. The dextran molecules cannot be retained in the stationary phase because the molecules are too large to enter the pores, the glucose molecules however are small enough to enter the pores and can be retained by the stationary phase. The retention of

Eluent Medium	Component	Correlation Equation for the Component	Correlation Coeff.	Confidence Level	Significance of Correlation
Glucose	Glucose	$K_{dg} = 0.77\ C_g + 0.1237$	.992	>99.5%	Significant Correlation
	Fructose	$K_{df} = 0.65\ C_g + 0.3648$	.991	>99.5%	Significant Correlation
Fructose	Glucose	$K_{dg} = 0.24\ C_f + .129$	.987	>99.5%	Significant Correlation
	Fructose	$K_{df} = 0.15\ C_f + .386$	.923	>99.5%	Significant Correlation
Dextran	Glucose	$K_{dg} = 0.7\ C_d + 0.143$	.95	>97.5%	Significant Correlation
	Fructose	$K_{df} = 1.1\ C_d + 0.426$	.91	>97.5%	Significant Correlation

TABLE 3.4 STATISTICAL ANALYSIS OF EXPERIMENTAL DATA

where C_g, C_d, C_f are concentration in w/v fraction

i.e. $C_g = \frac{\text{weight of glucose}}{\text{volume of solution}}$

FIG. 3.2 VARIATION OF DISTRIBUTION COEFFICIENT OF GLUCOSE WITH GLUCOSE CONCENTRATION AT AMBIENT TEMPERATURE

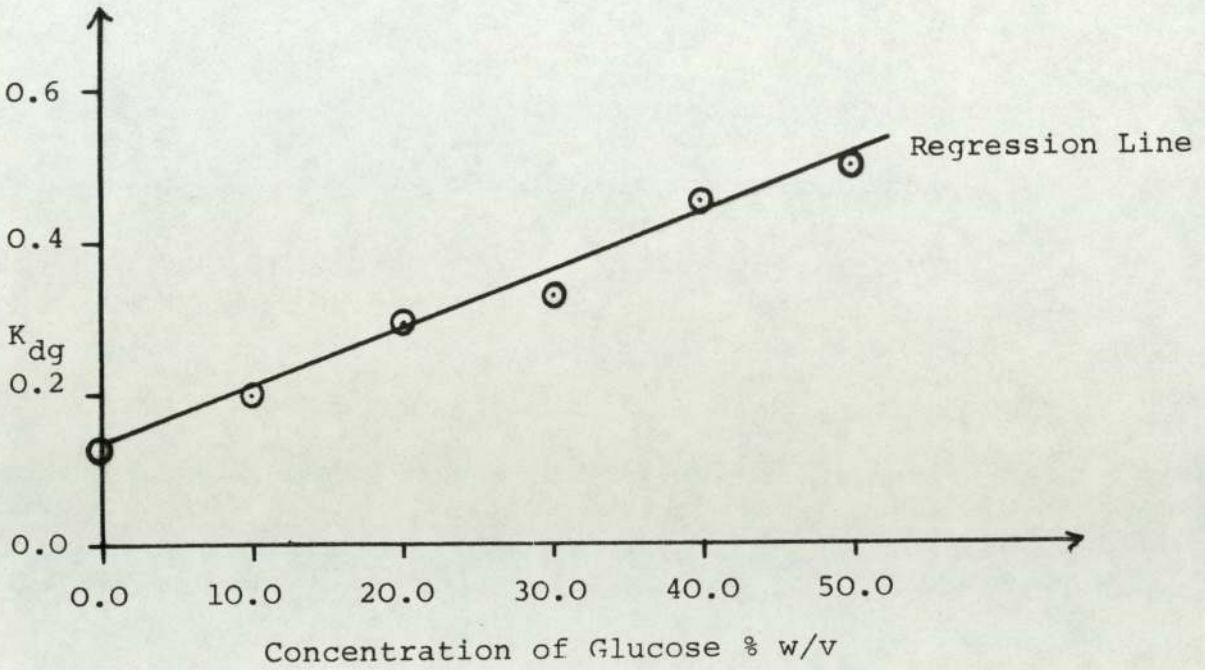


FIG. 3.3 VARIATION OF DISTRIBUTION COEFFICIENT OF FRUCTOSE WITH GLUCOSE CONCENTRATION AT AMBIENT TEMPERATURE

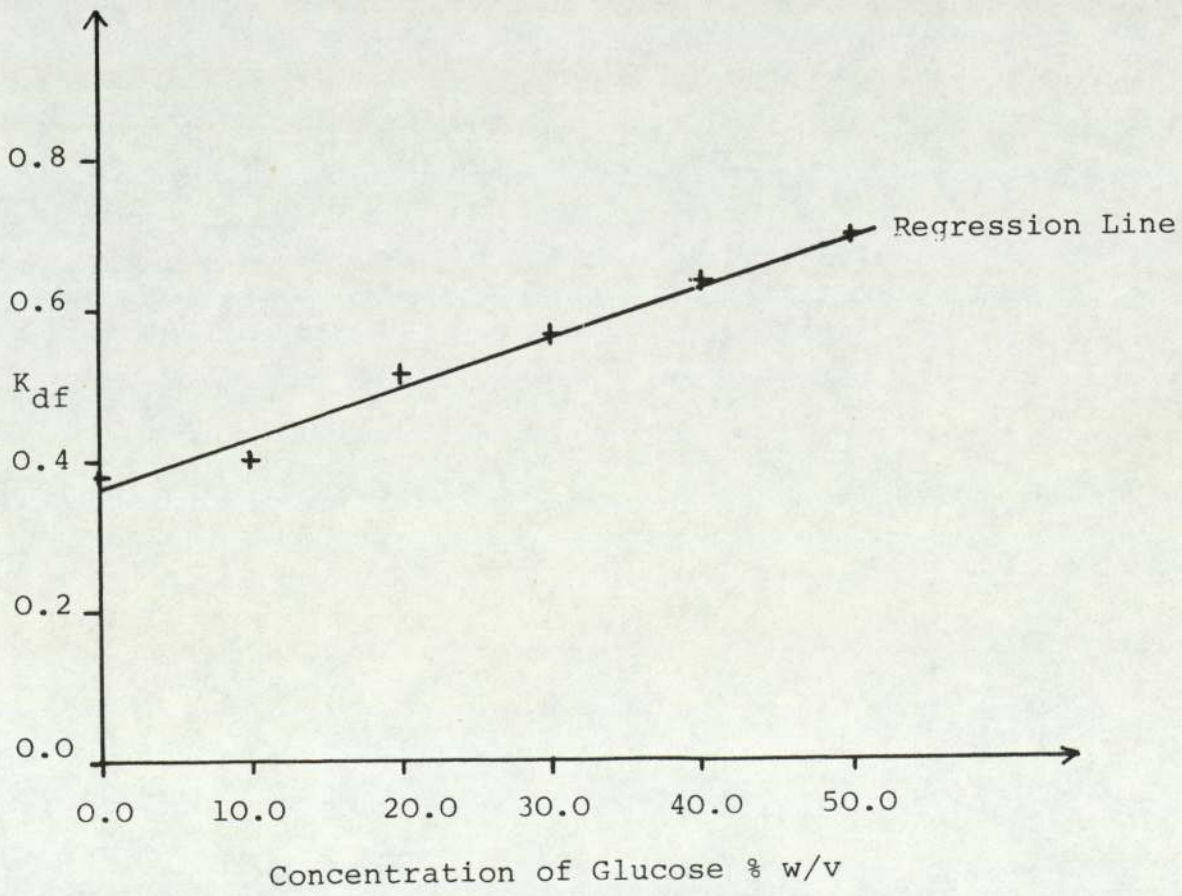


FIG. 3.4 VARIATION OF DISTRIBUTION OF GLUCOSE WITH FRUCTOSE CONCENTRATION AT AMBIENT TEMPERATURE

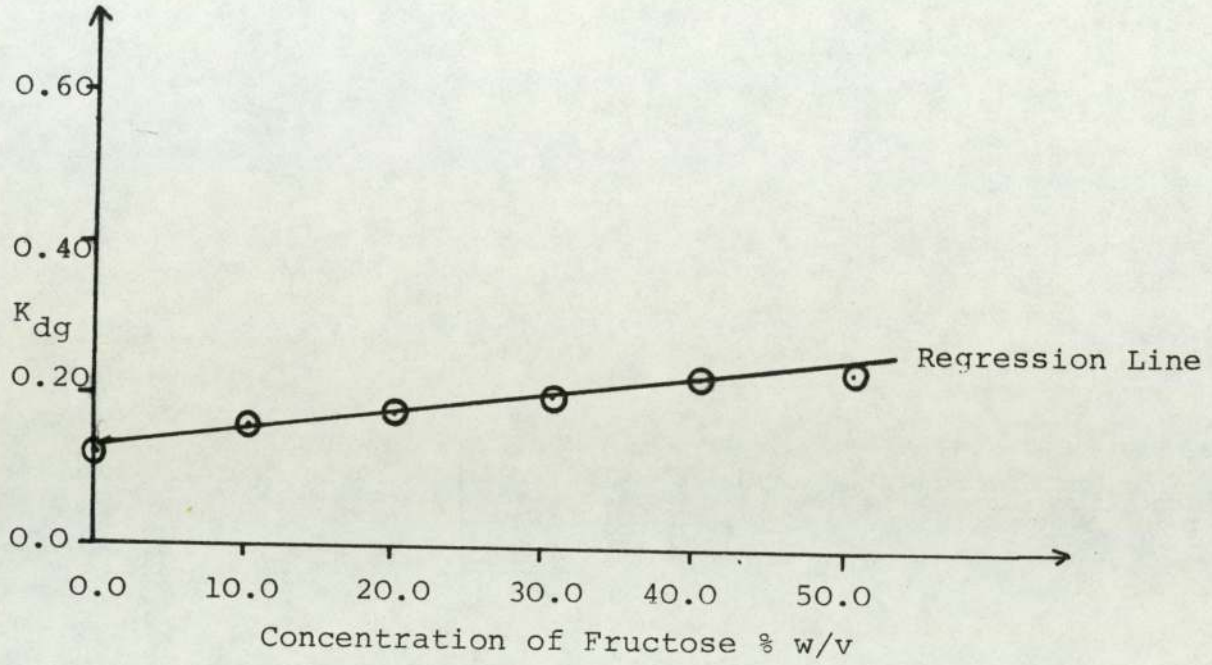


FIG. 3.5 VARIATION OF DISTRIBUTION COEFFICIENT OF FRUCTOSE WITH FRUCTOSE CONCENTRATION AT AMBIENT TEMPERATURE

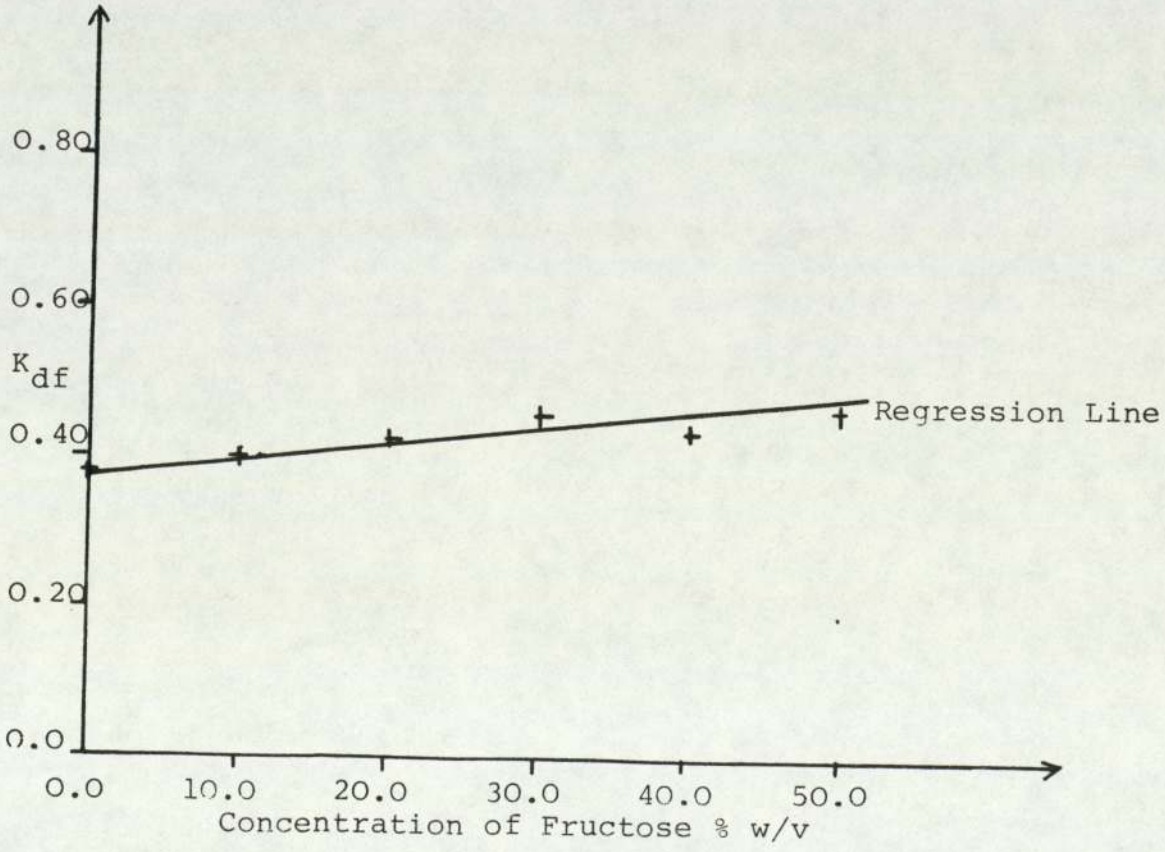


FIG. 3.6 VARIATION OF DISTRIBUTION COEFFICIENT WITH DEXTRAN CONCENTRATION

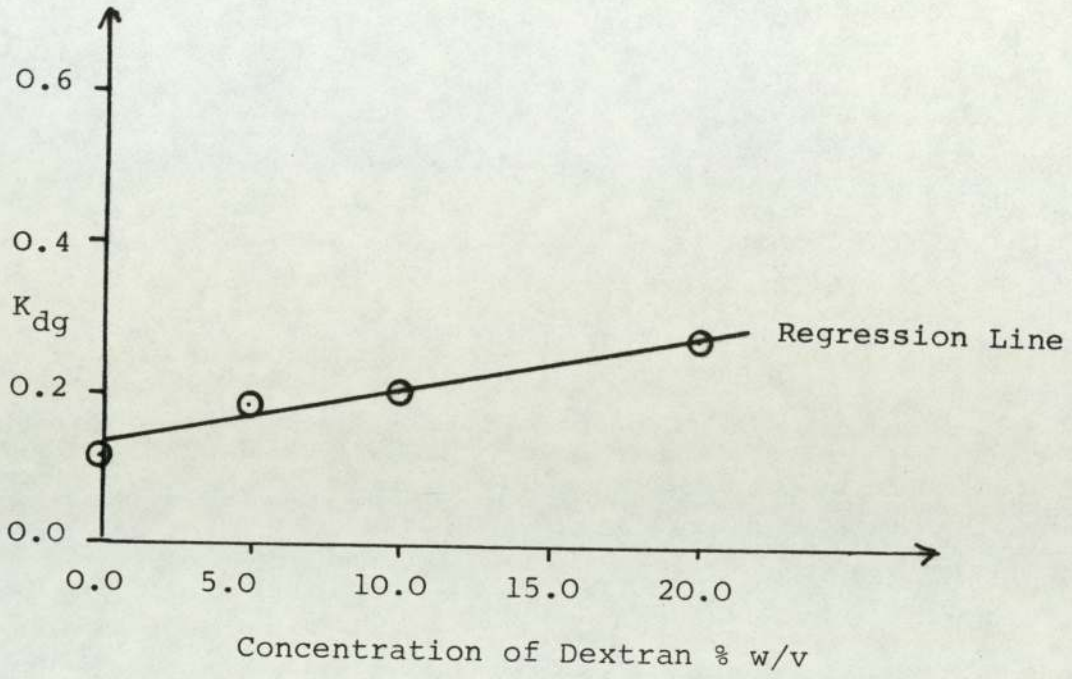
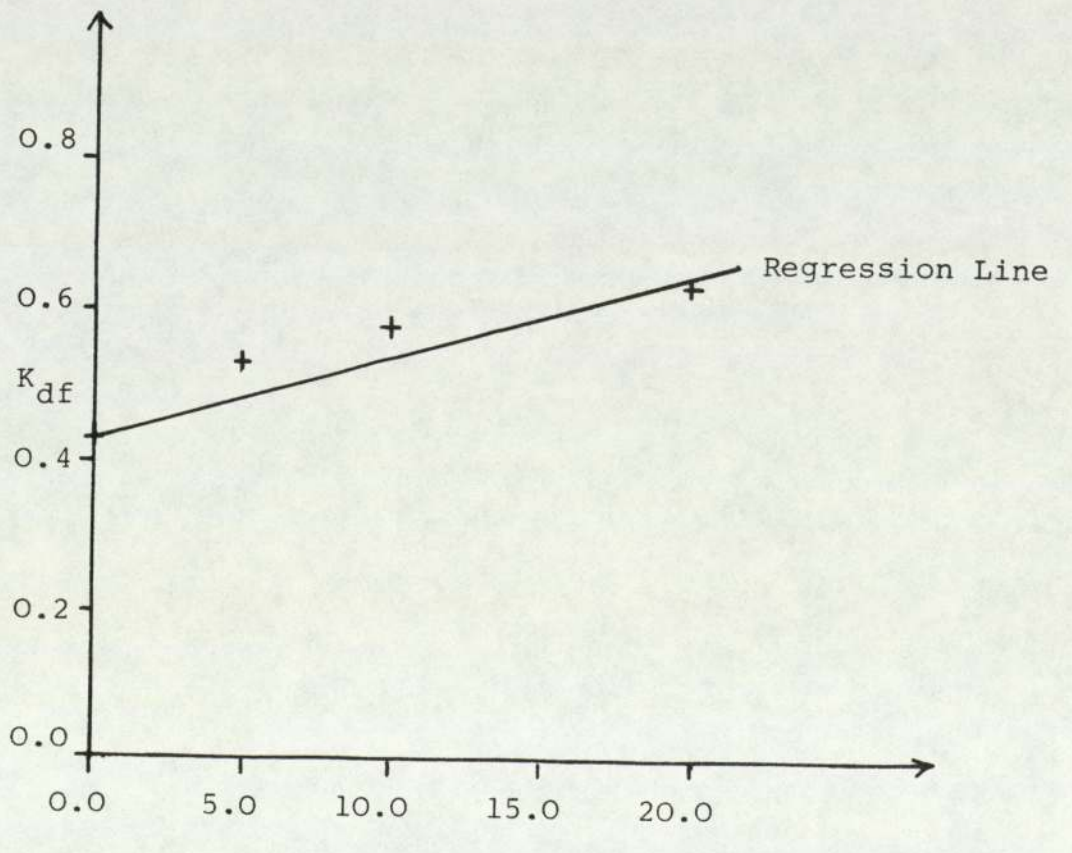


FIG. 3.7 VARIATION OF DISTRIBUTION COEFFICIENT WITH DEXTRAN CONCENTRATION



fructose molecules occurs due to formation of a complex between the fructose molecules and the calcium ions present within the resin particle.

The results can be explained in terms of three factors.

(i) viscosity effect:- Increasing the concentration of sugar increases the viscosity and an increase in viscosity increases the elution volume, hence the distribution coefficients of both glucose and fructose increase. There is a marked increase in viscosity of dextran with concentration causing a rapid increase in the partition coefficient of the components.

(ii) concentration effect:- A concentration gradient between the stationary and the mobile phase is created. This gradient is strong enough to force glucose to stay with the stationary phase either by diffusion or by osmosis. For fructose this effect is reduced since it is already chemisorbed by the resin to its limiting capacity.

(iii) the effect of chemical structure:- This applies only to fructose. β-D fructopyranose, a six membered ring structure is the only form of fructose that complexes with the calcium ions. The fraction of this form of fructose with other forms decreases with an increasing concentration, i.e. less fructose is likely to be chemisorped, at high concentration, by the calcium ions in the resin causing a decrease in the value of distribution coefficient.

In dextran solution viscosity effect is prominent together with the concentration effect causing an overall rapid increase in the distribution coefficient.

The viscosity effect is less marked in the glucose solution, so the increase in the distribution coefficient is mainly because of the concentration effect.

In a fructose medium, the increase in the distribution coefficient is caused by viscosity to some extent and the concentration effect. However the effect of change in chemical structure reduces the K_d value. The overall result is a less rapid increase in K_d value compared with glucose.

3.5 PARTITION COEFFICIENTS IN A MIXTURE OF SUGAR SOLUTIONS

Three experiments were carried out in an eluent medium containing glucose and fructose mixtures. The chromatograms produced for dextran, glucose and fructose were analysed and the information obtained presented in Table 3.5..

3.5.1 Results and Discussion

If the results in Table 3.5 are compared with those in Table 3.1 and 3.2, it will be seen that the value of the partition coefficients of glucose and fructose in a mixture are highly influenced by the presence of glucose, i.e. the K_d value for the mixture is approximately the same as that of the individual glucose K_d values.

ELUENT CONC.		Eluent Flow-Rate $cm^3 min^{-1}$	Dextran		Glucose		Fructose		Distribution Coefficient	
G % w/v	F % w/v		Elution Time (min)	Elution Volume (cm^3)	Elution Time (min)	Elution Volume (cm^3)	Elution Time (min)	Elution Volume (cm^3)	K_{dg}	K_{df}
10	10	.27	33.4	9.018	43.15	11.6505	53.35	14.4045	.22	.465
15	15	.266	34.3	9.261	43.95	11.88	53.45	14.4315	.23	.456
20	20	.29	33.2	9.628	44.4	12.875	51.0	14.79	.296	.47

TABLE 3.5 DISTRIBUTION COEFFICIENTS IN GLUCOSE/FRUCTOSE MIXTURES

This effect can be explained by means of the concentration effect described in Section 3.4.1. The effect of the concentration gradient is to bring about the dilution of the more concentrated components, hence no difference is observed whether the eluent is a mixture or merely glucose or fructose.

CHAPTER FOUR

DESCRIPTION AND OPERATION OF THE SCCR6 UNIT

4.1 INTRODUCTION

The first semi-continuous chromatographic refiner used for liquid-solid chromatographic work was built and commissioned by Ching (8), then modified and operated by Chuah (9). The refiner consisted of ten 2.54 cm ID x 70 cm high columns packed to a height of 65 cm with zerolit 225 of particle size 150-300 μm, containing 4% Di-vinyl benzene cross link, and charged to a calcium form. To assess scale up effects in terms of throughput, product purity and product concentration, another unit containing ten columns of 10.8 cm ID packed to a height of 65 cm, with zerolit 225 of same specification as described above, was built and commissioned by Gould (10). The modification and operation of the latter has been undertaken in this research project.

4.1.1 Principle of Operation

If a mixture containing glucose and fructose is eluted through a column packed with a cross linked polystyrene resin charged in the calcium form, a separation occurs (4). Glucose and fructose are isomers but the structure of fructose is such that it forms a chemical complex with calcium ions and has a relatively lower velocity through the column compared with glucose. A typical concentration profile of such a system is shown in Fig. 4.1. If on the other hand the

FIG. 4.1 CHROMATOGRAPHIC CONCENTRATION PROFILE FOR REPEATED BATCH CO-CURRENT OPERATION

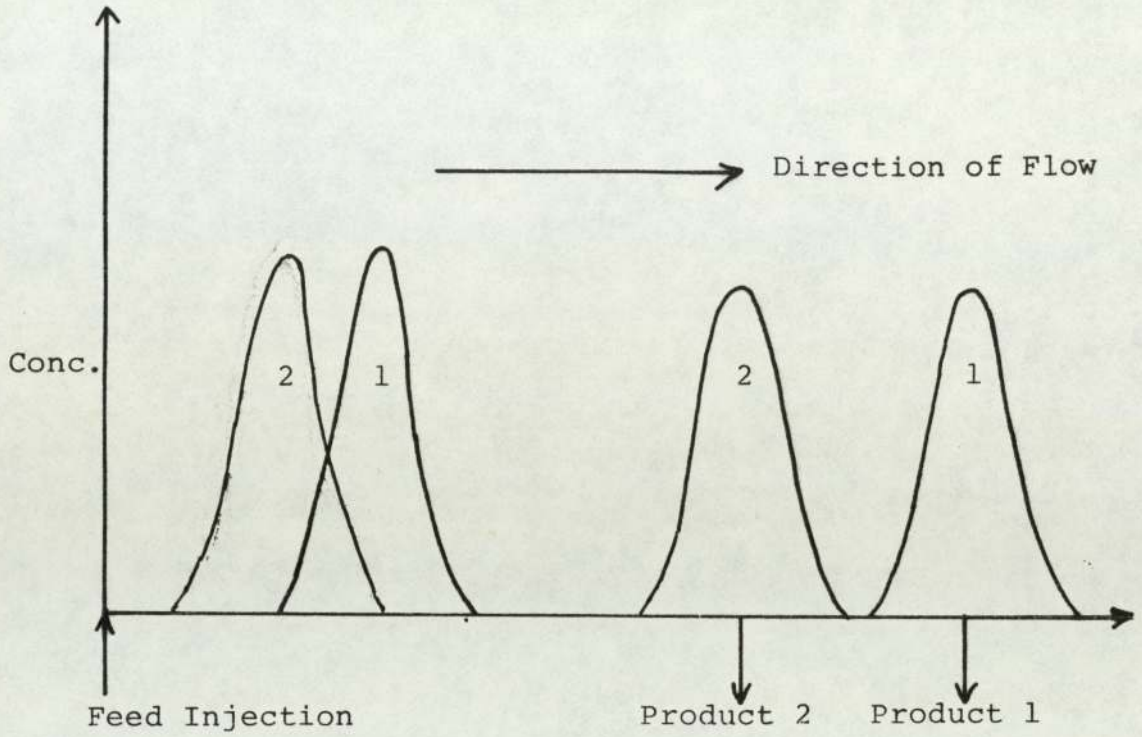
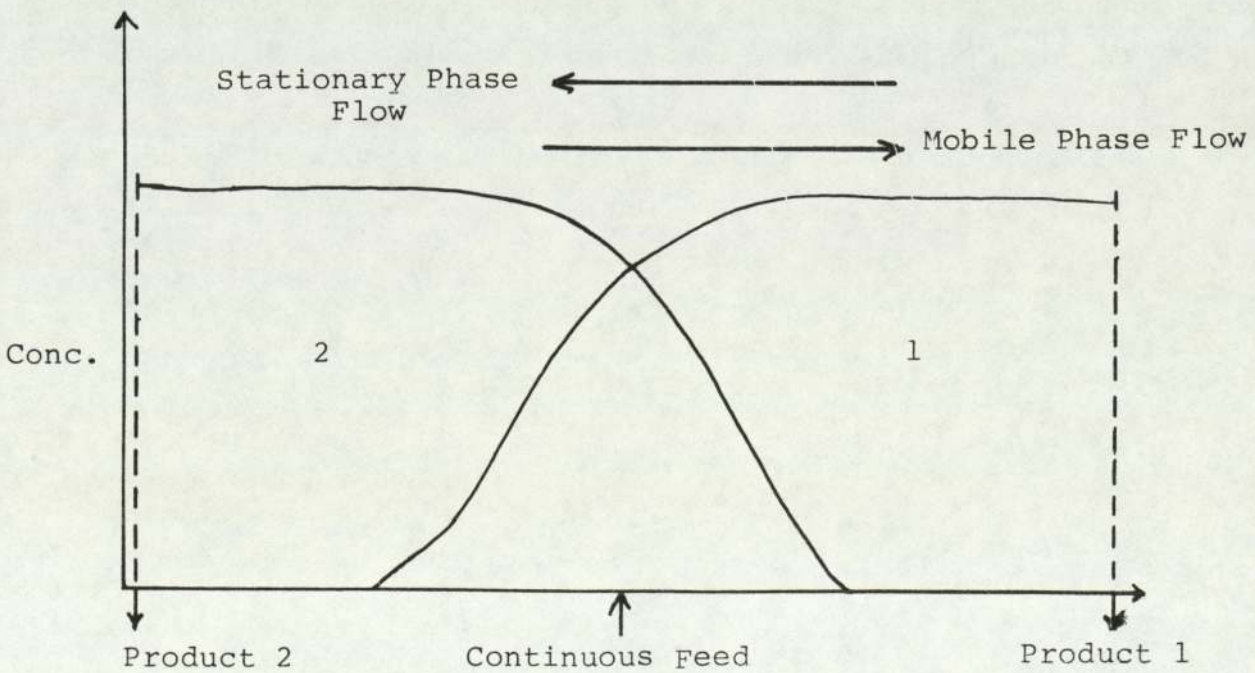


FIG. 4.2 CHROMATOGRAPHIC CONCENTRATION PROFILE FOR CONTINUOUS COUNTER-CURRENT OPERATION



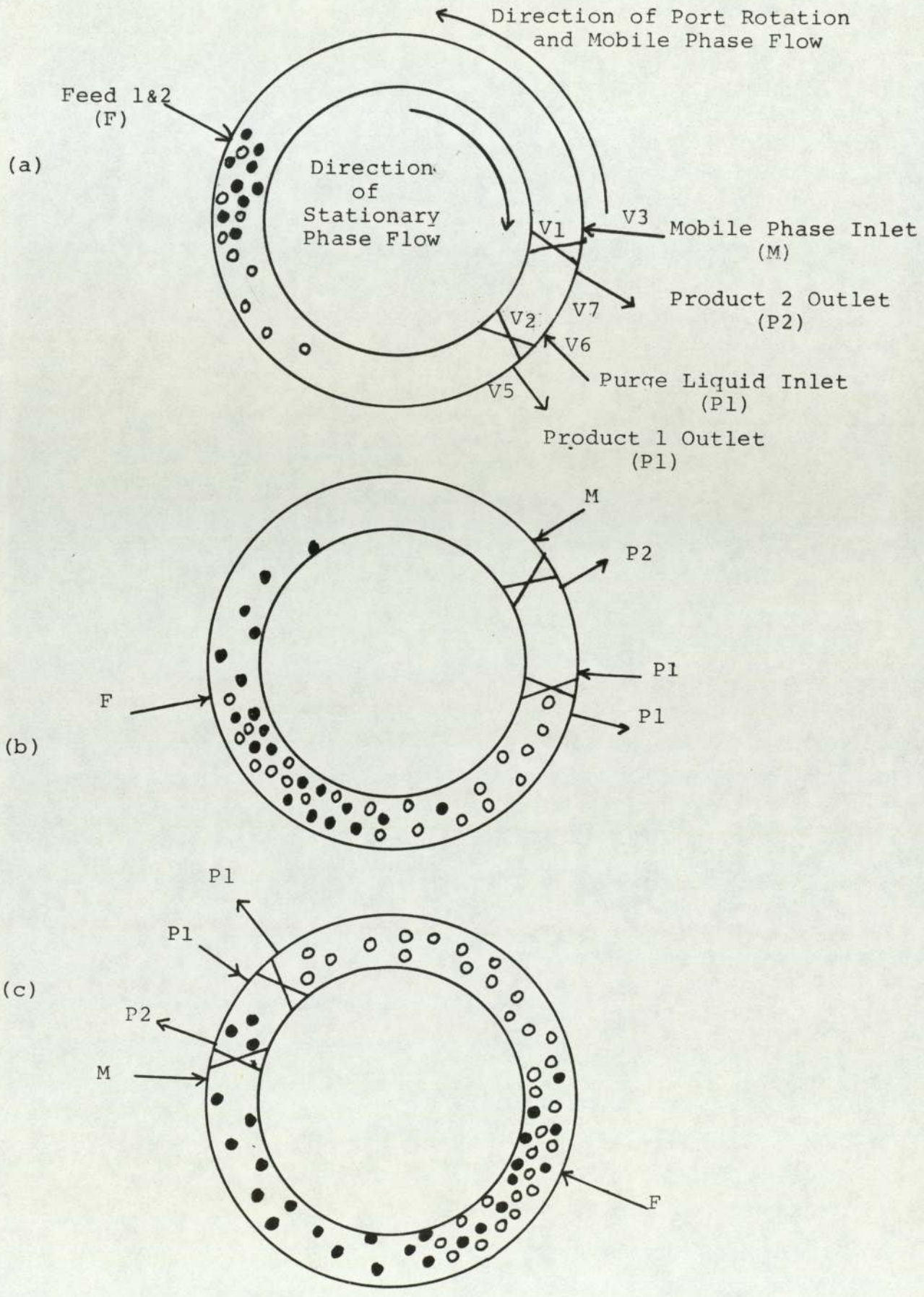
stationary phase and the mobile phase moved counter current to each other at suitable flow rates then a concentration profile similar to that shown in Fig. 4.2 would result.

4.1.2 Method of Operation

The operation of a semi-continuous refiner is schematically shown in Fig. 4.3. A mixture of glucose and fructose is fed into the system at port F. The least absorbed solute glucose is preferentially moved with the mobile phase fluid towards the glucose rich product offtake V5. Two locks V1 and V2 isolate a section of the closed loop column and here an independent purge fluid stream enters at port V6 and exits with more strongly absorbed fructose from port V7.

Fig. 4.3a represents the distribution of the two components within the system soon after start up. Fig. 4.3b presents the situation where all port functions have been advanced by one position in the direction co-current to the direction of mobile phase flow. This port advancement results in an 'effective' movement of the packed column in a direction counter current to the direction of the mobile phase flow. If the rate of this port advancement is less than the velocity of glucose migration through the bed but greater than the velocity of the fructose through the bed, two enriched products will emerge from each end of the separating section, Fig. 4.3c

FIG. 4.3 PRINCIPLE OF OPERATION OF THE SCCR



4.1.3 Idealised Operating Conditions

In the chromatographic unit glucose travels with the mobile phase and fructose with the stationary phase. These two phases move counter current to each other in a semi continuous fashion while a feed stream, an eluent stream and a purge stream enter the column and two product streams leave it continuously, (Fig. 4.4).

A model can be constructed relating flow rates of the mobile phase and stationary phase and component separation. A material balance on glucose about the feed point gives:

$$F_g = L_e.y_g + P.x_g \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (4.1)$$

where F_g = mass rate of glucose input at feed point (gm s^{-1})

L_e = eluent phase flow rate ($cm^3 s^{-1}$)

P = Stationary phase flow rate

y_g = concentration of glucose in eluent phase (gm cm^{-3})

x_g = concentration of glucose in stationary phase (gm cm^{-3})

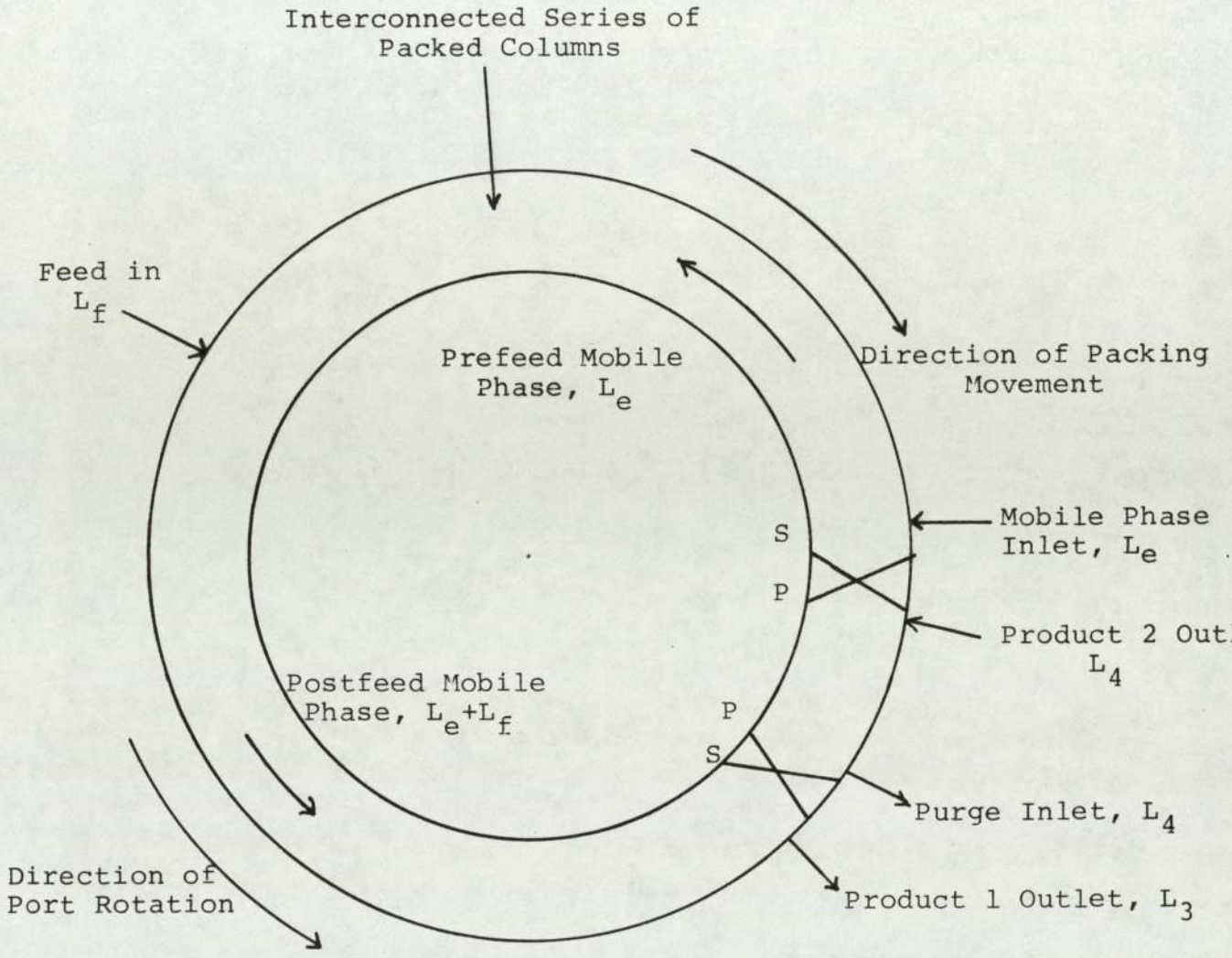
For a glucose molecule to move preferentially with the eluent phase then

$$L_e y_g > P x_g \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (4.2)$$

Rearranging

$$\frac{L_e}{P} > \frac{x_g}{y_g} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (4.3)$$

FIG. 4.4 SCHEMATIC DIAGRAM OF THE SCCR6 UNIT



S-S Separation Section
Product 1 Glucose Rich Product
P-P Purge Section
Product 2 Fructose Rich Product

and since

$$\frac{x_g}{y_g} = K_{dg} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (4.4)$$

Then

$$\frac{L_e}{P} > K_{dg} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (4.5)$$

Similarly for fructose to move with the stationary phase

$$\frac{L_e}{P} < K_{df} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (4.6)$$

Combining equation 4.5 and 4.6 we obtain the theoretical limits of eluent and stationary phase flow rates to achieve separation of fructose and glucose:

$$K_{dg} < \frac{L_e}{P} < K_{df} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (4.7)$$

In the refiner the stationary phase flow is achieved by the sequencing action at the end of every switch period. As each column contains eluent phase in the void volume the actual eluent phase flow rate is effectively reduced to:

$$L_e = L_i - \frac{V_o}{S} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (4.8)$$

where L_i = measured eluent phase flow rate, $cm^3 s^{-1}$

V_o = void volume

S = switch period

The equilibrium distribution coefficients K_ds were measured as described in Section 3.3.4 under dilute conditions.

To completely purge all the fructose from the isolated column it is therefore necessary to have

$$\frac{L_4}{P} > K_{df} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (4.9)$$

where L_4 = purge stream flow rate

4.1.4 Non-Idealities in a Practical System

A number of factors influence the ability of the SCCR equipment to separate a feed mixture. Some of the factors that cause departures from the idealised case are:

(a) Concentration interaction

(b) Zone broadening

(c) Discontinuous Operation

(d) Finite feed flow rate

(a) Concentration Interactions

Distribution coefficients are effected by on column sugar concentration. This effect has been studied in detail in Chapter 3.

(b) Zone Broadening

Zone broadening depends upon several factors, such as particle size, eluent velocity, packing density and the physical batch columns. The greater the zone broadening, the poorer the fractionation.

(c) Discontinuous Operation

Packing material is simulated to move in the opposite direction to the mobile phase in a discontinuous manner by the sequencing of the inlet and outlet ports. The degree to which this discontinuity affects the

system would be reduced if the number of sequencing steps (columns) were increased.

(d) Feed Flow Rate

The inequality shown in Eqn. 4.7 has to be extended to include the interaction of a finite volume of feed. Hence the practical inequality would be:

$$K_{dg} < \frac{Le}{P} < \frac{Le+Lf}{P} < K_{df} \quad \ldots\ldots\ldots\ldots \quad (4.10)$$

The closer the distribution coefficients, the closer the values of $\frac{Le}{P}$ and $\frac{Le+Lf}{P}$ thereby limiting the feed flow rate.

4.2 THE OVERALL DESCRIPTION OF THE CHROMATOGRAPHIC REFINER

A detailed flow diagram of the SCCR6 unit is shown in Fig. 4.5. The separation section is a series of ten discrete packed columns linked at the top and bottom to form a closed loop. It can be seen from Fig. 4.6 that during any particular switch seven valves need to be activated, five to open namely the inlets for feed, eluent and purge and outlets for glucose and fructose rich product. Two valves, the transfer valves at each end of the isolated columns, need to be closed to form a closed loop. Fig. 4.7 is a photograph of the apparatus as used by Gould (10).

FIG. 4.5 COMPLETE FLOW DIAGRAM

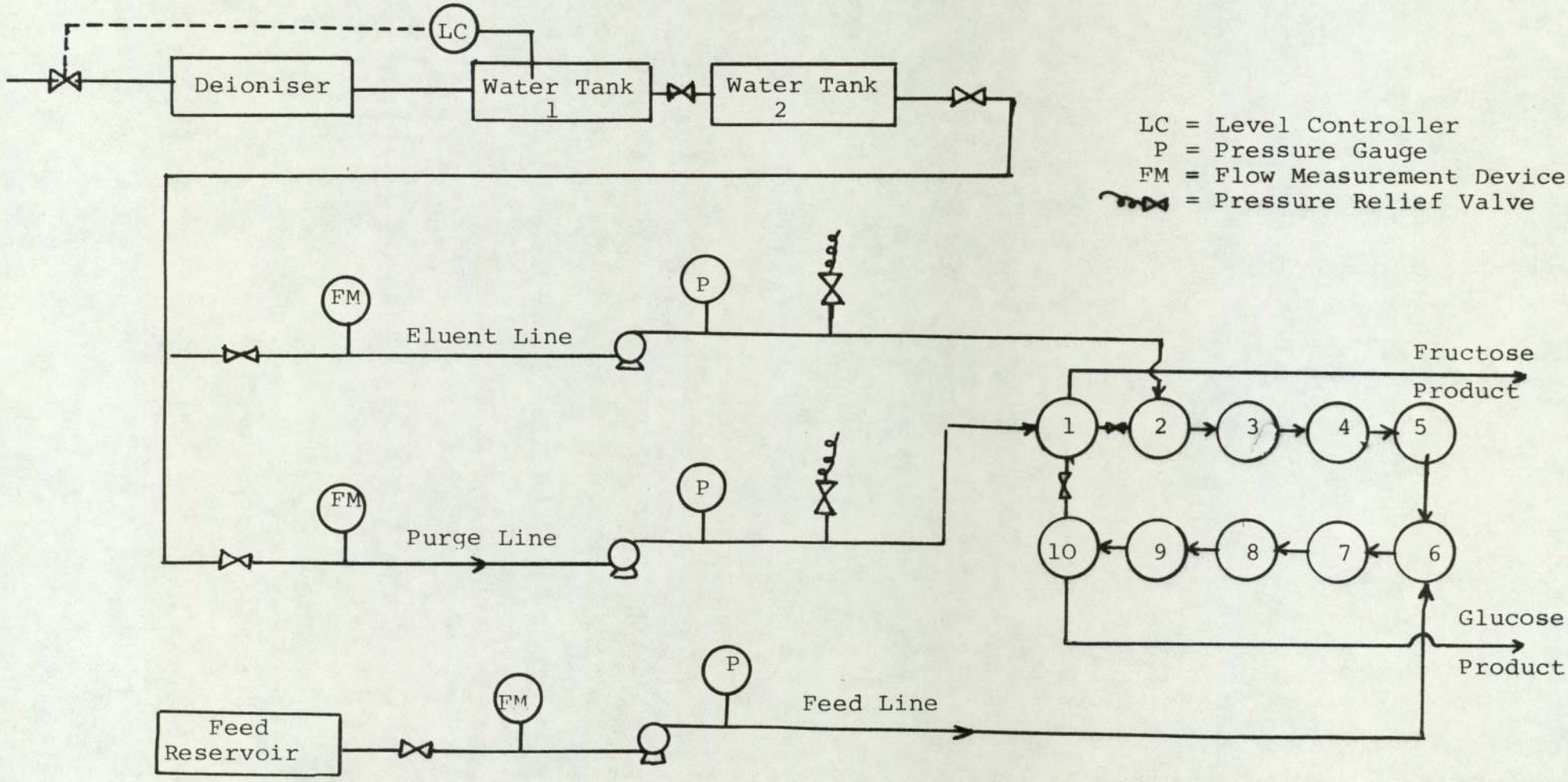
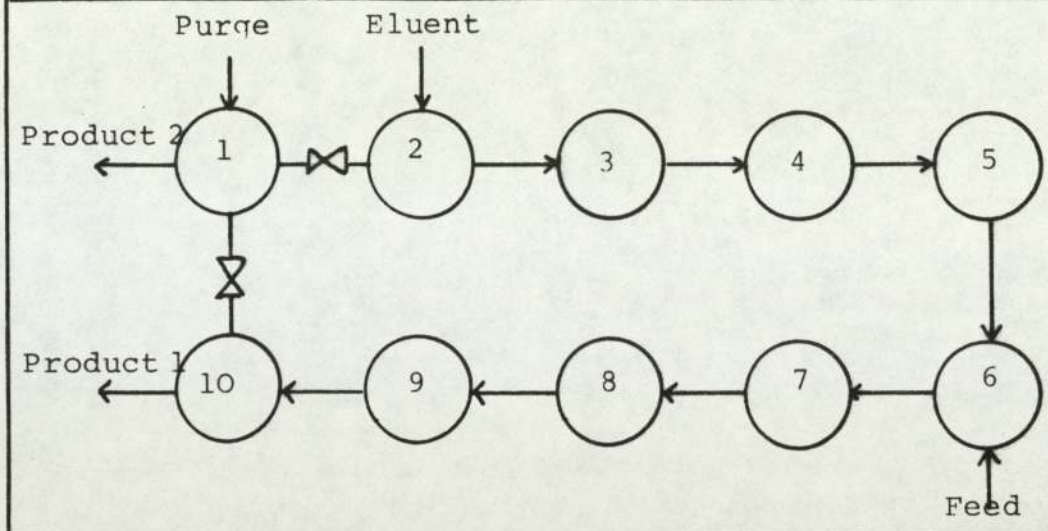
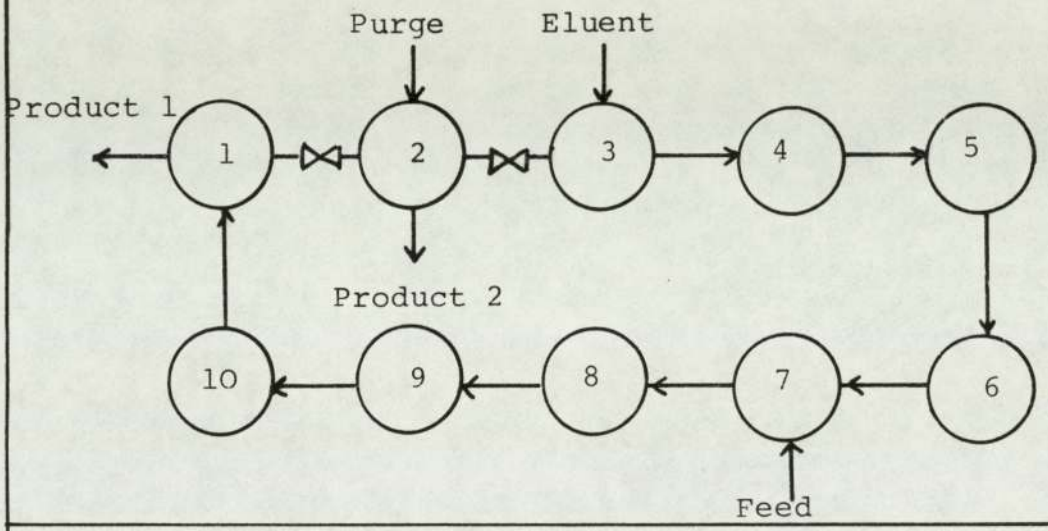


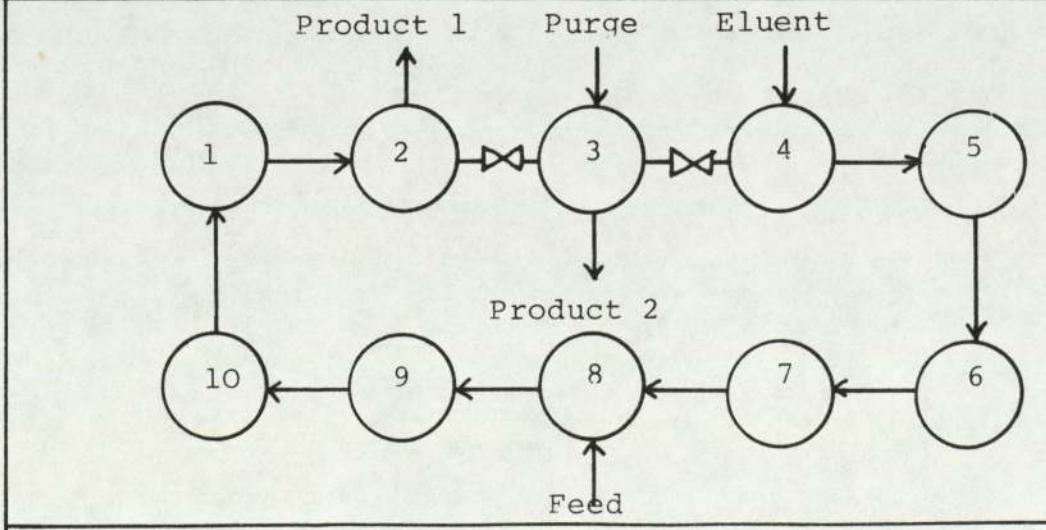
FIG. 4.6 DIAGRAMS SHOWING SEQUENCES OF OPERATION OF THE SCCR



Switch One: Column 1 Isolated Columns 2-10 Fractionating



Switch Two: Column 2 Isolated Columns 3-1 Fractionating

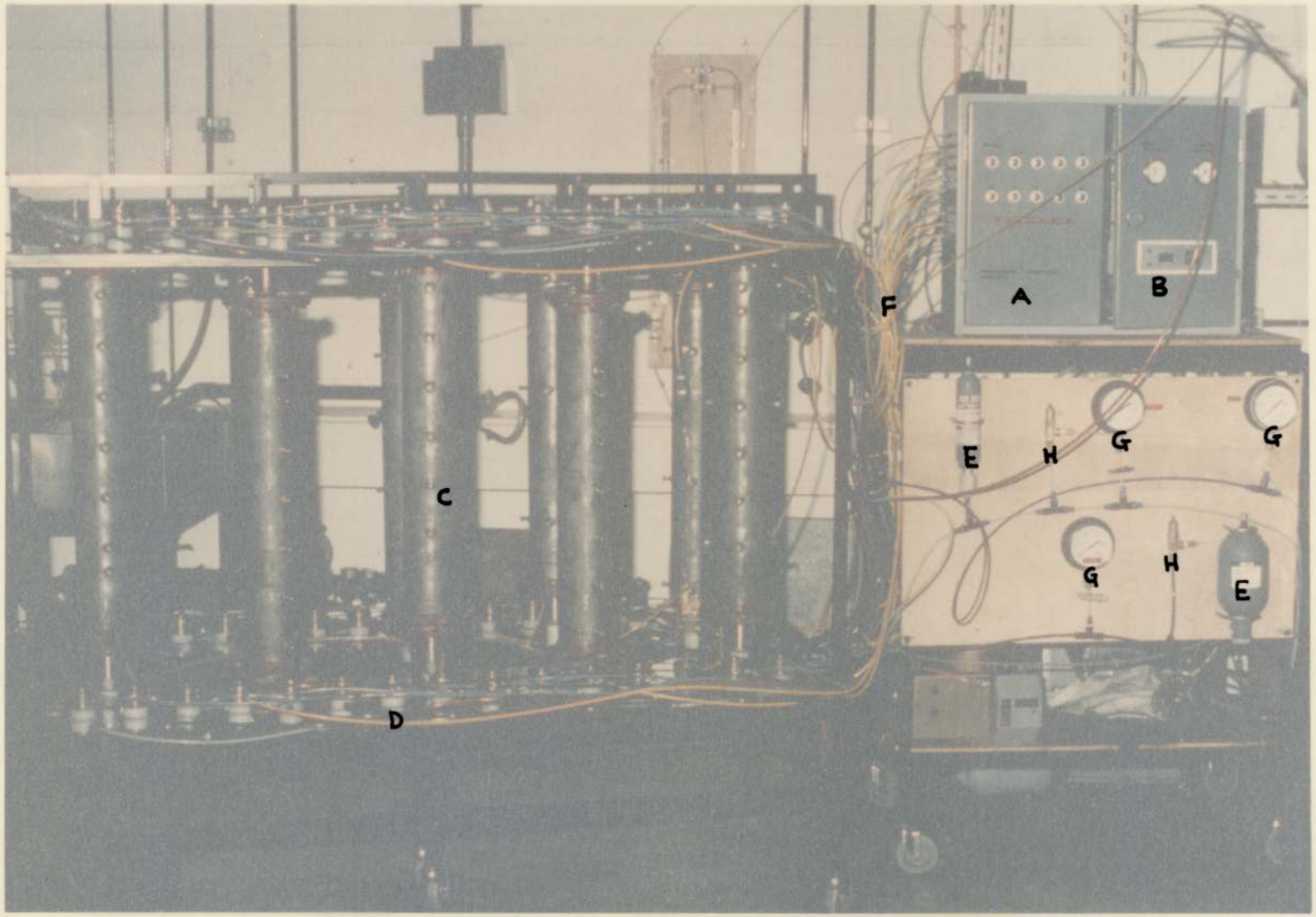


Switch Three: Column 3 Isolated Columns 4-2 Fractionating

Fig. 4.7 Photograph of the equipment used by Gould

Key for Fig. 4.7

A	Control box
B	Digital timer
C	Packed columns
D	Valve
E	Pulsation dampener
F	Pneumatic line
G	Pressure gauges
H	Pressure relief valve


A
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H

4.3 DETAILED DESCRIPTION OF THE SCCR6 UNIT

4.3.1 The Columns

The refiner designed and commissioned by Gould (10) consisted of ten stainless steel column of 10.8 cm internal diameter and 65 cm bed length. Stainless steel sampling points were constructed and welded to the sides of the columns radially and longitudinally. Mild steel flanges were welded to the top and bottom of each column to allow the inlet and outlet assemblies to be bolted into place (Fig. 4.8a).

4.3.2 The Column Inlets

To counteract any packing expansion and contraction Gould (10) decided to have a floating piston. This allowed a slight positive pressure to be kept on the bed at all times. A hydraulically operated piston constructed from polypropylene was designed to achieve this. The seal between the hydraulic fluid (deionised water) and the packed bed was effected by two rubber O rings.

The arrangement of inlet manifold is shown in Fig. (4.8b). The liquid passageway in the polypropylene was only 5 mm while the bed diameter was 10.8 cm, hence a distributor (4.8c) was introduced to promote a uniform velocity profile and thus increase the efficiency of the packed columns.

FIG. 4.8a SECTION THROUGH COLUMN ASSEMBLY

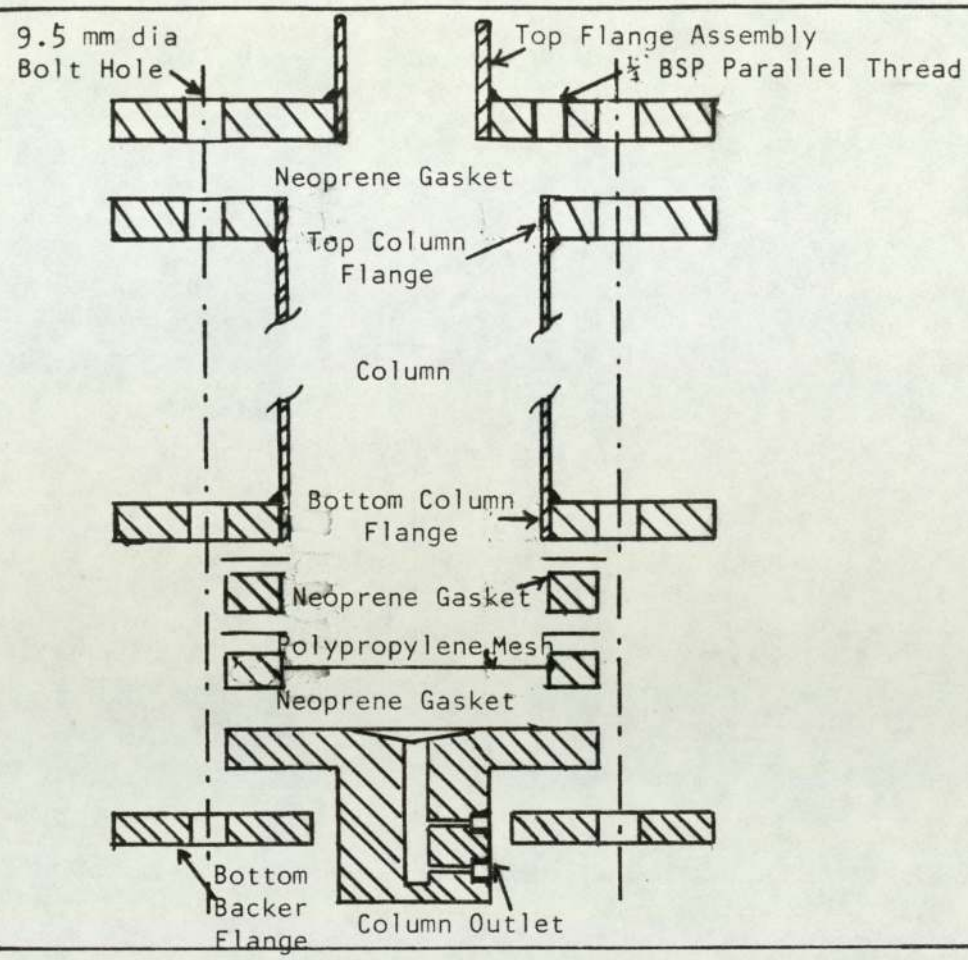
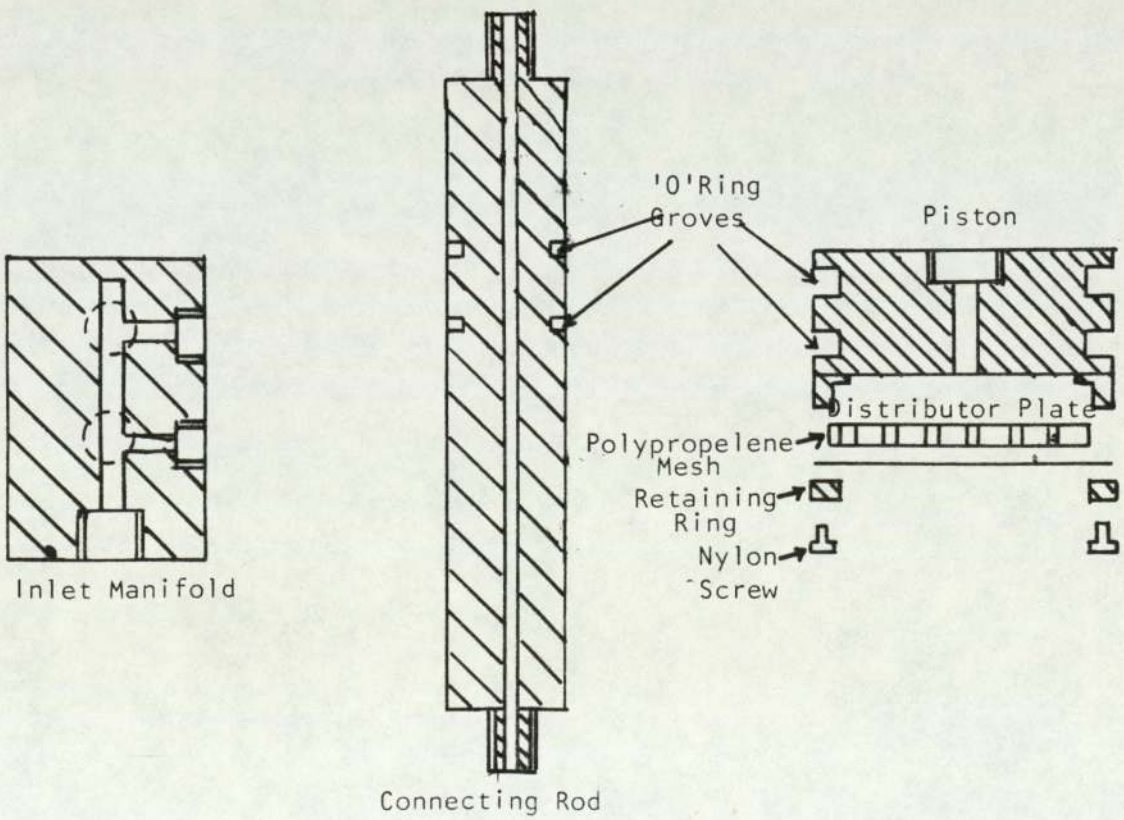


FIG. 4.8b SECTION THROUGH INLET ASSEMBLY



4.3.3 The Column Outlets

To prevent leakage of the resin from the column a polypropylene mesh of 100 μm aperture was welded between two polypropylene rings. Fig. 4.8a shows the arrangement of polypropylene mesh, outlet assembly block and the flange.

4.3.4 The Hydraulic System

The arrangement of column, piston, connecting rod and the inlet port is shown in Fig. 4.9a. Once the column was packed with the resin, the empty space between the top flange and the piston was filled with water pressurised to 200 psi (2800 kNm^{-2}) to keep the resin under compression. Further compression of the resin was achieved by tightening the screw onto the aluminium backing plate placed on top of the inlet manifold. Fig.4.9b represents part of the operating hydraulic system.

4.3.5 The Valves

The successful use of double acting poppet valves by Ching (8) and Chuah (9) encouraged Gould (10) to use similar valves with slight enlargement in the inlet and outlet ports for the 10.8 cm diameter column unit.

The double acting valve (Fig. 4.10) was operated pneumatically to either open or close the poppet valve. The design and operation of this valve is described in detail by Ching (8).

FIG. 4.9a THE COLUMN INLET ASSEMBLY, HYDRAULIC SYSTEM AND RESIN COMPRESSION SYSTEM

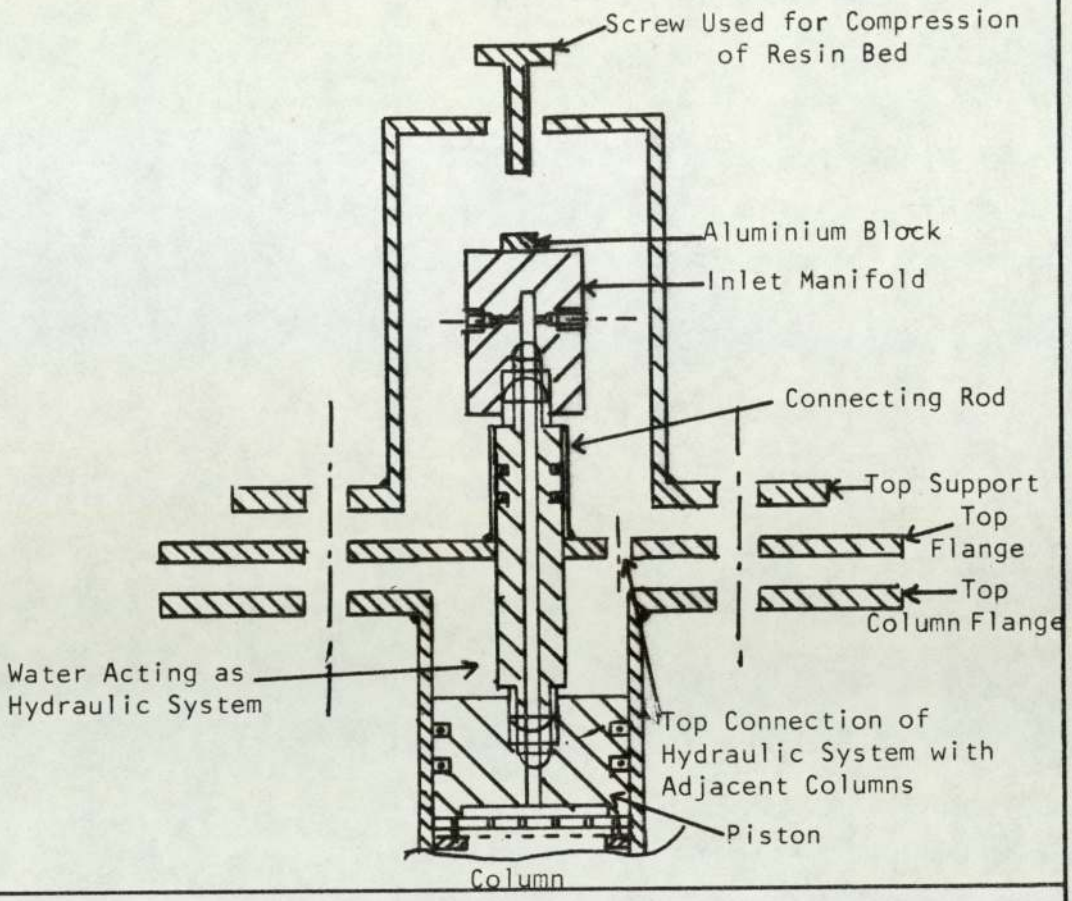


FIG. 4.9b THE HYDRAULIC SYSTEM

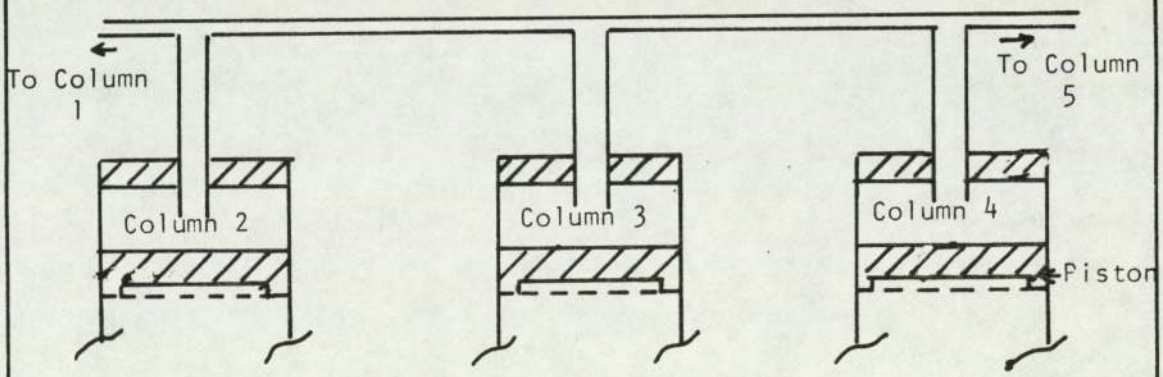
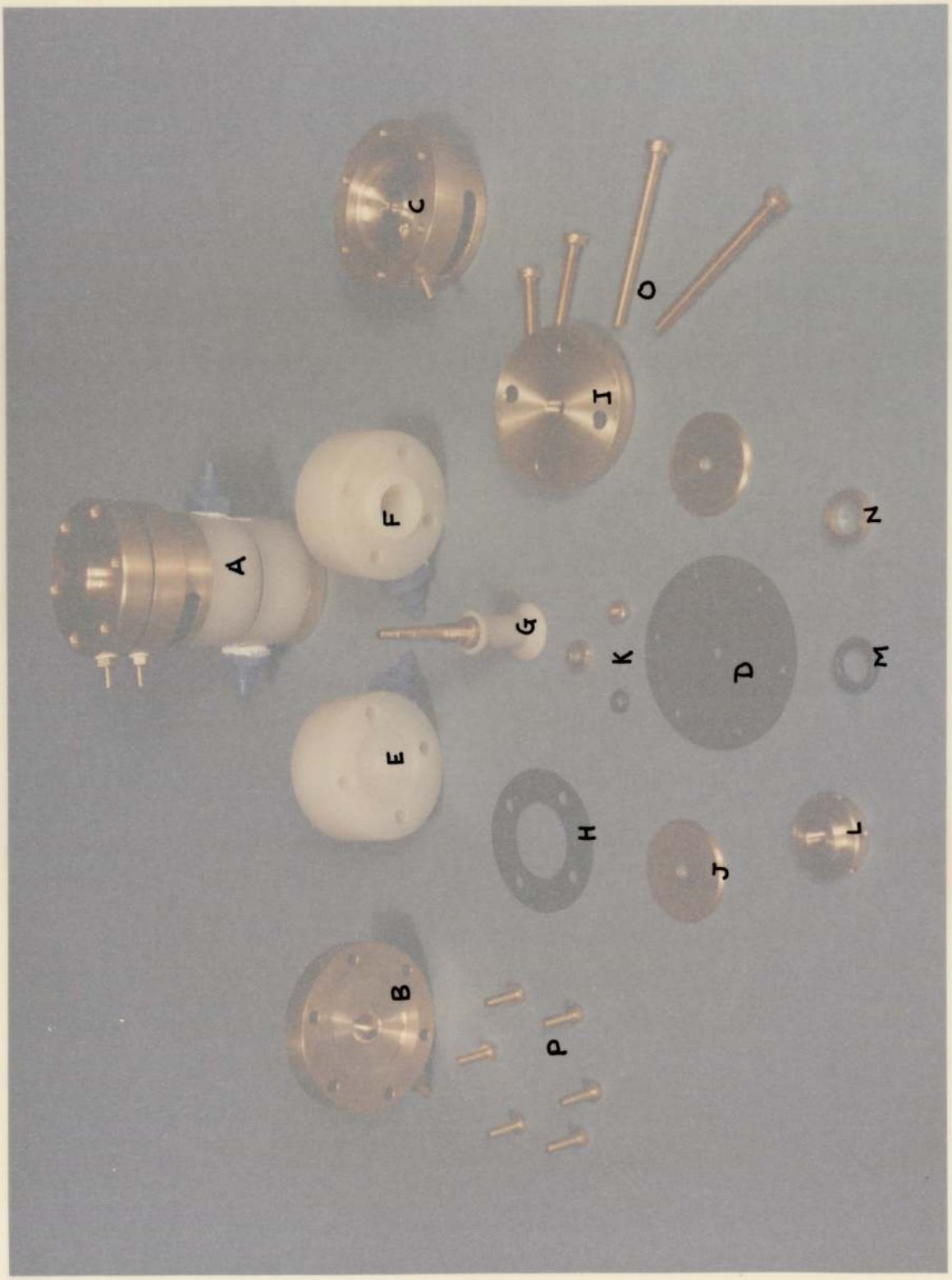


Fig. 4.10 Photograph of the Pneumatic Poppet Valve

Key for Fig. 4.10

A	Assembled valve
B	Upper diaphragm chamber
C	Lower diaphragm chamber
D	Neoprene rubber diaphragm
E	Liquid inlet chamber
F	Liquid outlet chamber
G	Poppet and stem
H	Viton rubber gasket
I	Valve base
J	Diaphragm backing plate
K	Diaphragm assembly component
L	Adjustment nut
M	Viton O ring
N	Thrust washer
O	4 x 2BA cheese head screw
P	6 x 4BA cap screw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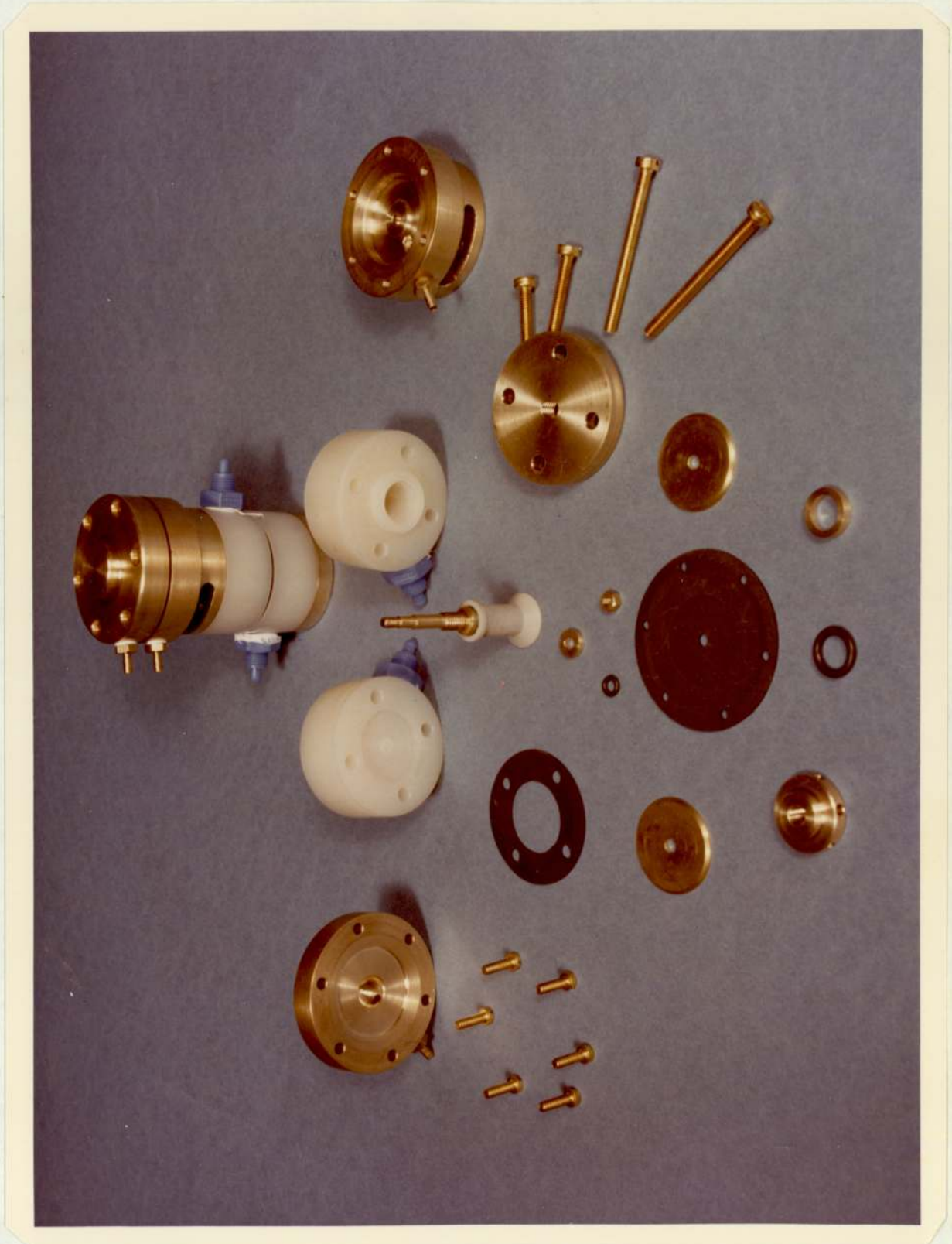


4.3.6 The Control System

Table 4.1 shows the valves which need to be operated during each switch period. Compressed air supplied to the refiner by a Broom and Wade Compressor at 540 kNm^{-2}, was divided into two streams namely the actuating and the bias streams. The pressure of these streams were controlled using Spirax pressure regulators at 540 kNm^{-2} for the actuating and 270 kNm^{-2} for the bias pressure.

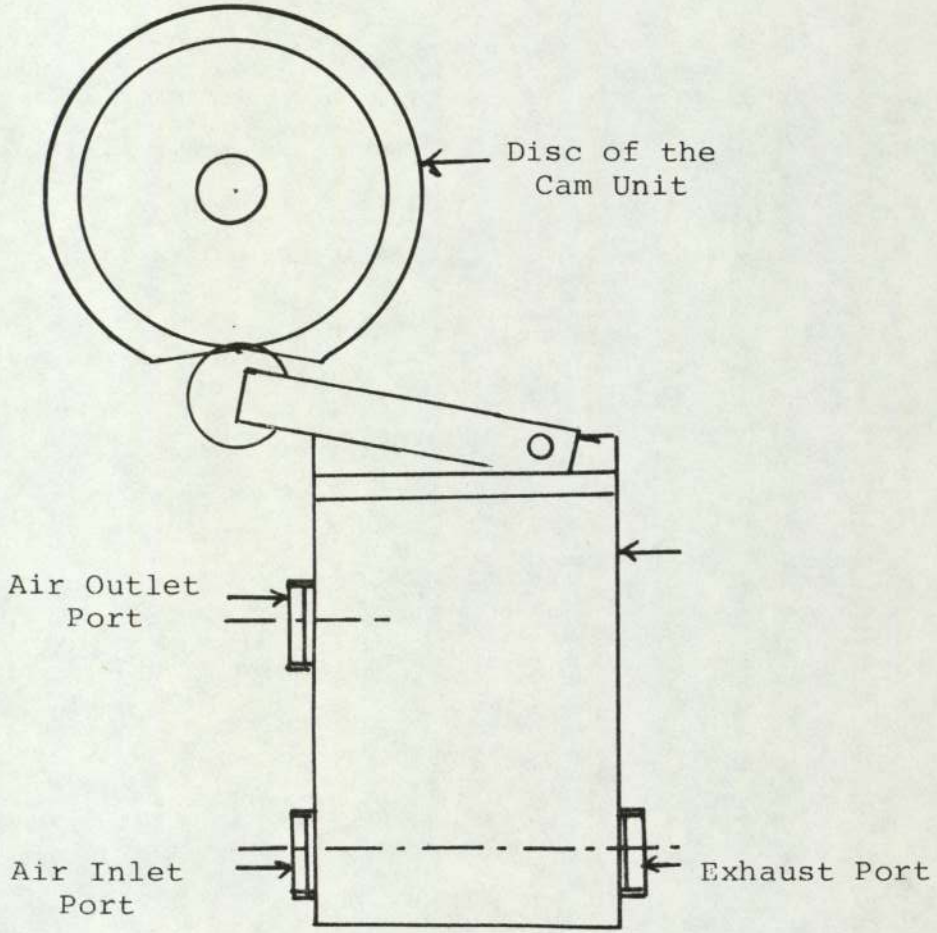
The heart of the central control system was a cam unit with ten programmable discs operating ten on/off valves. Fig. 4.11 illustrates how the on/off roller valves were operated by the discs. The gaps on consecutive discs were set at 36^{o} out of phase and each gear wheel movement represents one sequence of the SCCR6 process. The cam unit was driven by a single speed motor. When a particular cam opened its roller valve, the actuating air was allowed to flow through the valve and was then split into four streams; one stream entered a closed ring main which opened five functional valves, namely the inlets for feed, eluent and purge and outlets for glucose and fructose rich products. The second and third of the four streams were each attached to a shuttle valve and each one of these in turn closed an isolating valve. The fourth stream travelled to an indicator to aid visual display of the eluent entry column. A further branch allowed air to flow to a pneumatic/electric switch which stopped the voltage to the motor. The switch also zeroed and

TABLE 4.1

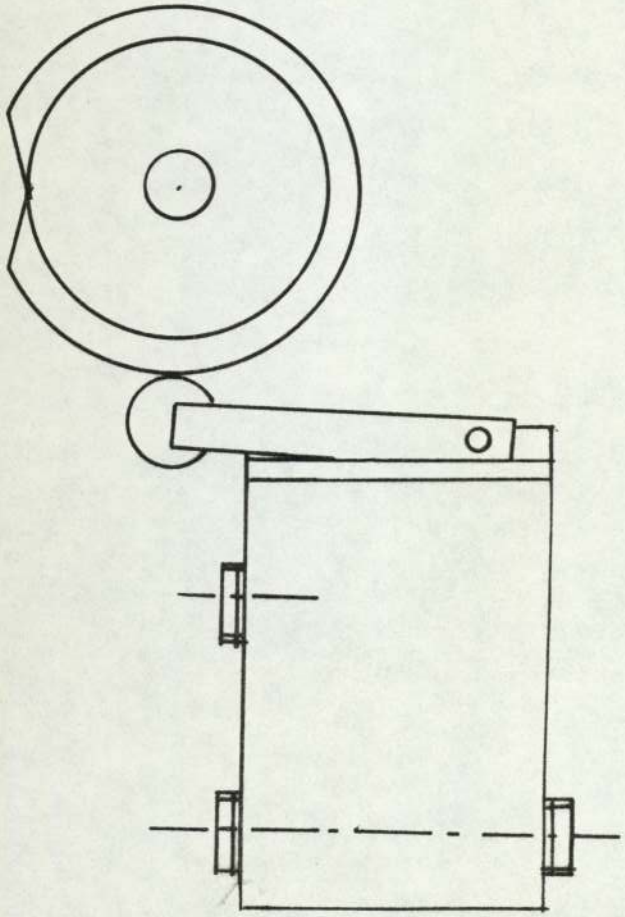
Switch Number	Valves Activated						
	To Open					To Close	
	Eluent	Feed	Purge	FRP	GRP	Transfer	Transfer
1	1	5	10	10	9	10	1
2	2	6	1	1	10	1	2
3	3	7	2	2	1	2	3
4	4	8	3	3	2	3	4
5	5	9	4	4	3	4	5
6	6	10	5	5	4	5	6
7	7	1	6	6	3	6	7
8	8	2	7	7	6	7	8
9	9	3	8	8	7	8	9
10	10	4	9	9	8	9	10

FIG. 4.11 THE OPERATION OF ON/OFF VALVE BY THE DISC OF CAM UNIT

(a) Valve in Open Position



(b) Valve in Closed Position



restarted a manually adjustable digital timer which permitted the various sequencing intervals.

At the end of the sequence the timer activated the electropneumatic switch which rotated the camshaft another 36^{o} and the sequence repeated itself.

4.3.7 Pumps

The success of the SCCR6 scheme rested heavily upon the accurate and reliable operation of the pumps. Three separate pumps were employed for each of the feed, eluent and purge streams.

Feed Pump - Two pumps were used for the pumping of the feed

1. Supplier - Hughes Micropumps, Epsom, Surrey
   Flow Range - 0-100 $cm^{3}min^{-1}$ with $\pm_{1}$% accuracy
   Maximum Operating Pressure - 1700 kNm^{-2}
   Specification - Two heads attached to a common drive which operated 180^{o} out of phase to smooth the flow
2. An alternative head in the K twin eluent pump (details are given below).

Eluent Pump

Supplier - Metering Pumps Ltd, Ealing, London
Type - K twin (two heads)
Stroking Speed - 96 strokes per minute
Flow Range - 0-360 $cm^{3}min^{-1}$ with $\pm_{1}$% accuracy
Maximum Operating Pressure - 1360 kNm^{-2}

Purge Pump

Supplier - Metering Pumps Ltd. Ealing, London

Type - L series

Stroking Speed - 150 strokes per minute

Flow Range - 0-6500 cm^3min^{-1} with ±5% accuracy

Maximum Operating Pressure - 1160 kNm^{-2}

During this research programme, the operation of the first feed pump was found unsatisfactory. After many unsuccessful attempts to reduce the noise level that occurred, its use was abandoned. The fault could not be detected. An alternative head in the K series eluent pump range was used for the feed.

4.3.8 Eluent Purge and Feed Supply

All deionised water used in the experimental programme was produced from an Elgastat B224 deioniser supplied by Elga Products Ltd., High Wycombe. Town's water was supplied to the deioniser at approximately 340 kNm^{-2}. The conductivity of the deionised water produced remained below 50 μs. If this value of conductivity was exceeded on exhaustion of the deionising resin in the cartridge, a solenoid valve in the control head on the cylinder was automatically activated to prevent a further flow of water. Deionised water was stored in two large stainless steel tanks of total capacity 750 litres. A feed back level controller was installed to prevent the tanks from overflowing. These storage pump tanks were elevated to give each pump a net positive suction head. The supplies to each pump

were fed by a 2.54 cm diameter pipeline in a ring main from the reservoir.

A polythene tank of capacity 150 litres was used to prepare the feed solution. It was transferred to a 15 litre glass aspirator approximately 2.5 metres above the feed pump to provide a net positive suction head.

4.3.9 Flow Rate and Pressure Measuring Device

Both the eluent and feed flows entering the refiner could be diverted via a three way valve into calibrated glass QVF pipes of 2.54 cm diameter and 0.5 m length. The purge flow rate was calculated by weighing the product. Two pulsation dampeners were installed at the eluent and purge entry line to smooth the flow. All inlet pressures generated could be monitored on the relevant gauges.

4.3.10 The Pipe Network and the Product Collection

All the process lines were made of nylon and piped so as to form a ring main. The tubing for eluent, feed and glucose product lines were 0.6 cm internal diameter and that of the purge supply and fructose product outlet were 0.8 cm internal diameter to carry the extra volume. All connectors, T pieces and other fittings were manufactured from either nylon or polypropylene. All lines were colour coded.

Collection of both products was into plastic containers.

4.4 MODIFICATIONS TO THE SCCR6 UNIT

In the last run on the SCCR6 unit, Gould used a very high feed flow rate of 70 $cm^3 min^{-1}$, causing a pressure build-up in the feed line as the sequencing took place, i.e. one feed valve closed and the next feed valve opened. This pressure build-up was too great for the air pressure to open the next feed valve. Consequently the feed line blew off frequently. The increase in the column pressure caused an upward movement of the piston and resulted in

(1) expansion of the resin bed in that column;

(2) as the top of the inlet manifold was fixed via a screw the bending of polystyrene connecting rod was unavoidable (Fig. 4.9a);

(3) the increase in the pressure of the hydraulic system of that column was transmitted to other columns causing the compression of the resin bed in those columns (Fig. 4.9b).

The overall result as the position of the feed column changed was chaotic, some of the resin beds were compressed to a significant extent and the others expanded to compensate.

4.4.1 The Connecting Rod

Since some of the polypropylene connecting rods were distorted, they were replaced by rods made of stainless steel.

4.4.2 The Hydraulic System

The hydraulic system was discarded and the compression of the resin bed was achieved via a screw mounted in a holder on the top of each column.

4.4.3 Polypropylene Mesh

As a result of the occurrence explained in Section 4.4, the columns needed to be repacked. While unpacking the column it was observed that the polypropylene mesh, used to prevent escape of resin particle, near to the outlet port had also cracked under pressure. The polypropylene mesh also replaced by stainless steel mesh mounted in a stainless steel ring.

4.5 HEATING EQUIPMENT

Gould (10) used the SCCR6 unit at ambient temperature only. A few modifications were essential for the operation of the equipment at higher temperature. The building and testing of the modifications to the SCCR6 along with the additional experimental techniques and safety precautions that were necessary are reported below.

4.5.1 Control and Heating of the Mobile Phase and Purge Stream

England (94) constructed the heating facilities for the mobile phase and the purge stream of the SCCR6 unit. The heating was performed in two stages, as Fig. 4.12 shows. Primary heating of the deionised

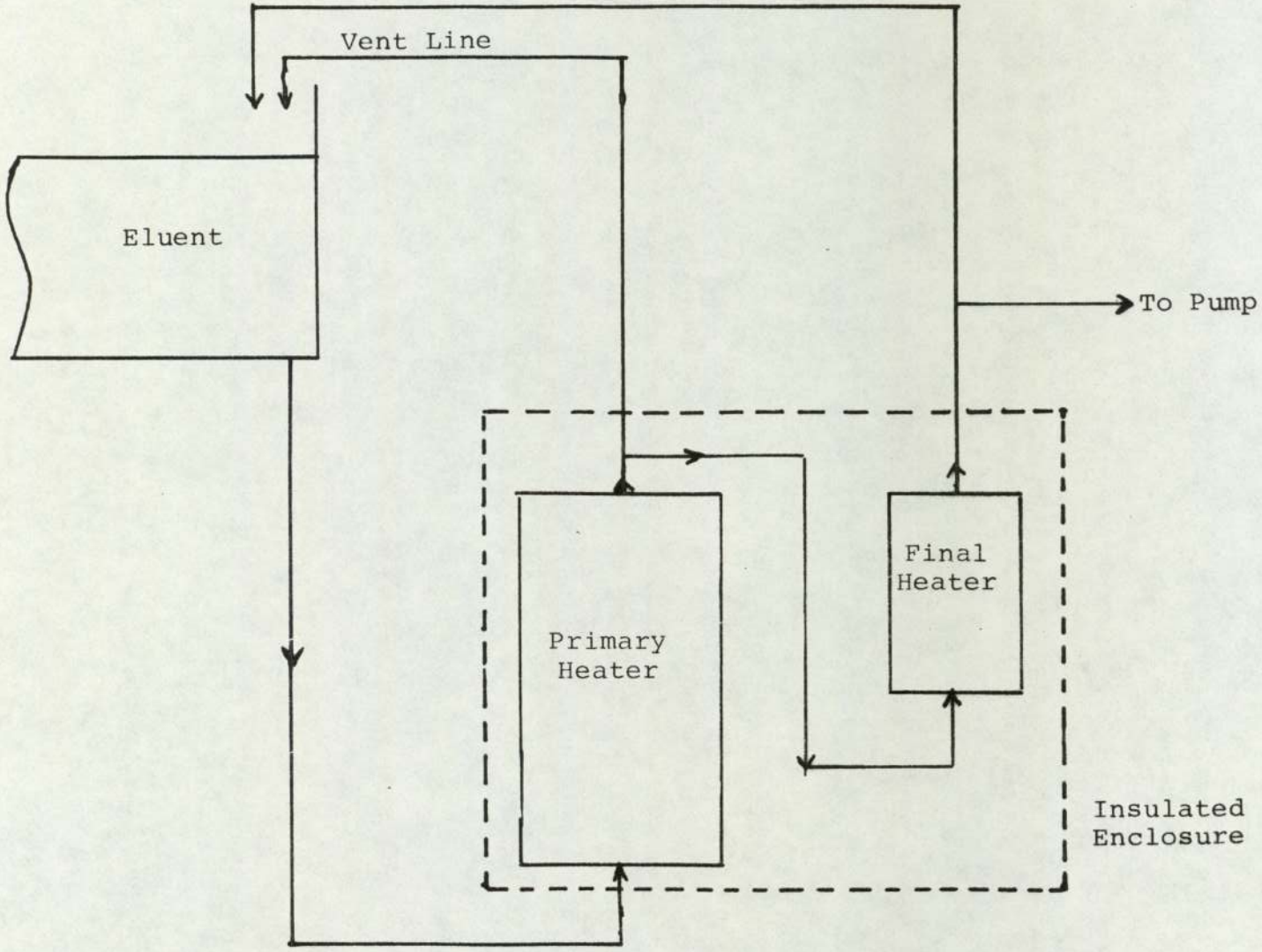


FIG. 4.12 ELUENT HEATING SYSTEM

water took place in a 30 cm I.D. x 31 cm long stainless steel vessel into which three stainless steel immersion heaters of 5 kw capacity were immersed. A thermostat was fitted to control the temperature. To prevent a pressure build-up a relief line was taken from this vessel and looped back over the mobile phase reservoir.

The second stage in the heating was performed in a smaller vessel, 13 cm I.D. x 38 cm long. Here an accurate and precise control of the temperature was achieved.

The insulated stainless steel pipe was laid from the vessels to the SCCR6 unit.

4.5.2 Control and Heating of the Feed Solution

The feed was heated in a 5.0 cm I.D. x 45 cm long stainless steel pipe in which an immersion heater of 5 k.w. capacity was screwed in through one end. The liquid flowed in via a 60 cm O.d. nylon tube and out from the other end of the pipe. The temperature of the feed was controlled using a proportional band controller supplied by Diamond H. Controls Ltd., Norwich. The input to the controller was measured as close as possible to the outlet arm of the feed heater by means of an hypodermic thermocouple.

4.5.3 Enclosure for the SCCR6 Unit

An enclosure for the SCCR6 was built around the chromatographic columns so that the air temperature surrounding them could be maintained at approximately

the same temperature as the mobile phase and feed streams. The final selection for the material of construction for the enclosure was galvanised steel sheets backed by an insulating layer of resin bonded fibre glass supplied by Kitsons, Perry Barr. The interior surface of the enclosure was coated with aluminium foil to prevent the escape of heat by radiation. The front and back section of the enclosure was split into two equal parts and could be opened as doors to reveal the chromatographic columns, as shown in Fig. 4.13. A 5 kw finned air heater supplied by Eltron Ltd., London, was used for heating and maintaining the temperature inside the enclosure. The air was circulated using an airotor. The control of the air temperature was by a proportional band controller supplied by Diamond H. Controls Ltd., Norwich. The input to the controller was via a NiCr/NiAl thermocouple placed inside the enclosure.

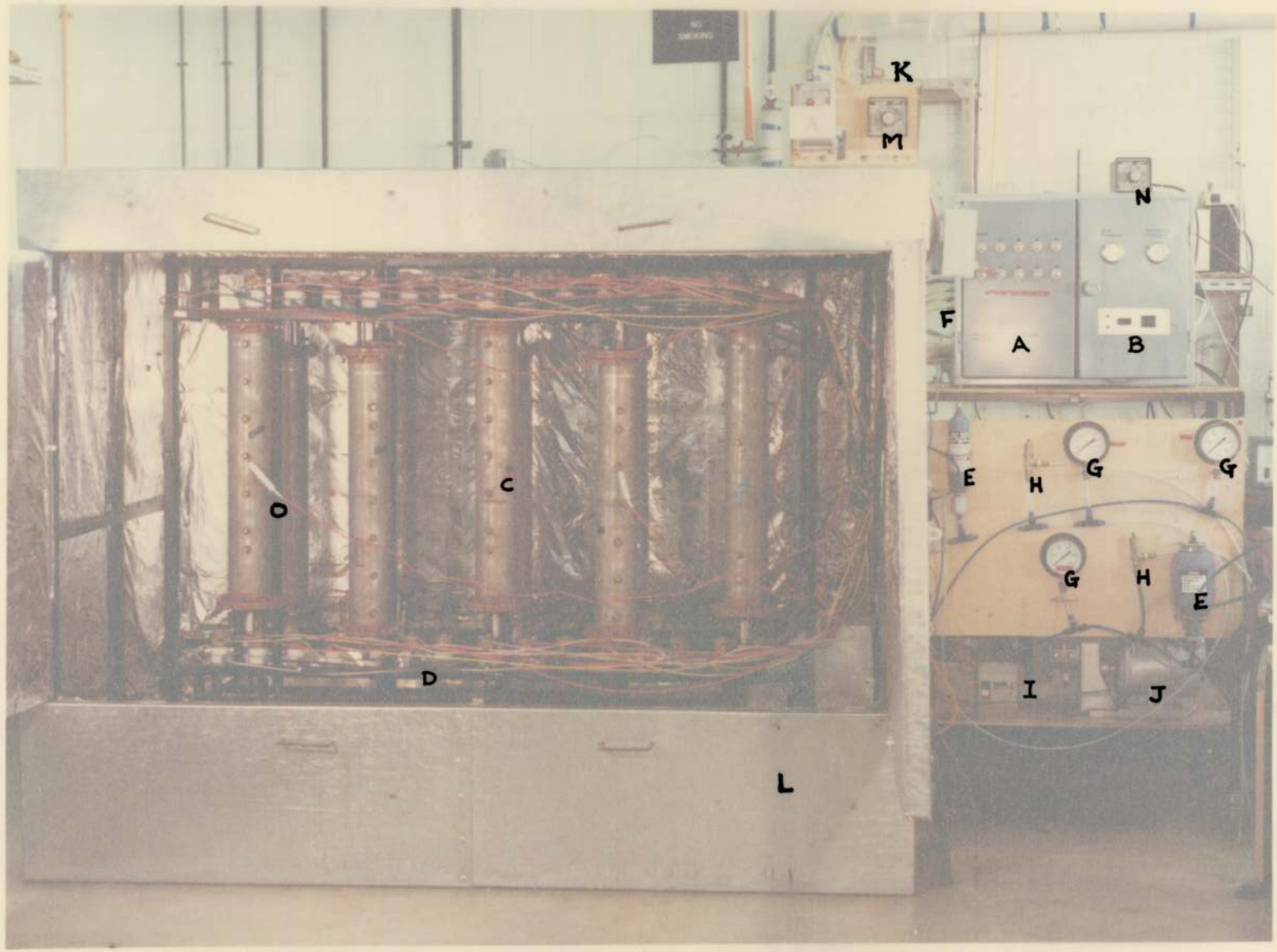
4.5.4 Temperature Indication and Control

All the temperature indications and controller inputs were from nickel chromium/nickel aluminium thermocouples supplied by Comark Electronics Ltd., Rustington. Two different types of thermocouples were used; hypodermic probes, similar to hypodermic syringe needles that were inserted through the rubber septum sample points into the resin bed; and fast response general purpose exposed junction thermo-couple used to monitor the temperature of each of the

Fig. 4.13 Photograph of equipment used in this research

Key for Fig. 4.13

A	Control box
B	Digital timer
C	Packed columns
D	Valve
E	Pulsation dampener
F	Pneumatic line
G	Pressure gauges
H	Pressure relief valve
I	Eluent pump
J	Feed pump
K	Feed reservoir
L	Constant temperature enclosure
M	Temperature controller for the enclosure
N	Feed temperature controller
O	Thermocouples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individual columns. The electrical potentials from the thermocouple were sent either to the respective temperature controller or to an electronic thermometer where the temperature could be recorded. The arrangement of the thermocouples is shown diagrammatically in Fig. 4.14.

4.6 CHARACTERISATION OF THE COLUMNS

The method adopted for the characterisation of the columns was similar to that used by Gould (10).

4.6.1 A Theoretical Basis for Comparison

The criterion used for comparing the performance of a chromatographic column is generally the height equivalent to a theoretical plate HETP. This is calculated by dividing the bed height L by the number of theoretical plates in a column. The number of plates in a column is calculated directly from a chromatogram using Gluekauf equation (16) as demonstrated in equation 2.10 ($N = 8(t_{Ri}/W_{h/e})^2$. Consequently to assess this parameter for both fructose and glucose, chromatograms were developed for each sugar.

4.6.2 Experimental Techniques for the Characterisation of the Columns

Three chromatograms per column were run: dextran, glucose and fructose.

T-pieces with injection and sampling points were fitted as closely as possible to the inlet and outlet

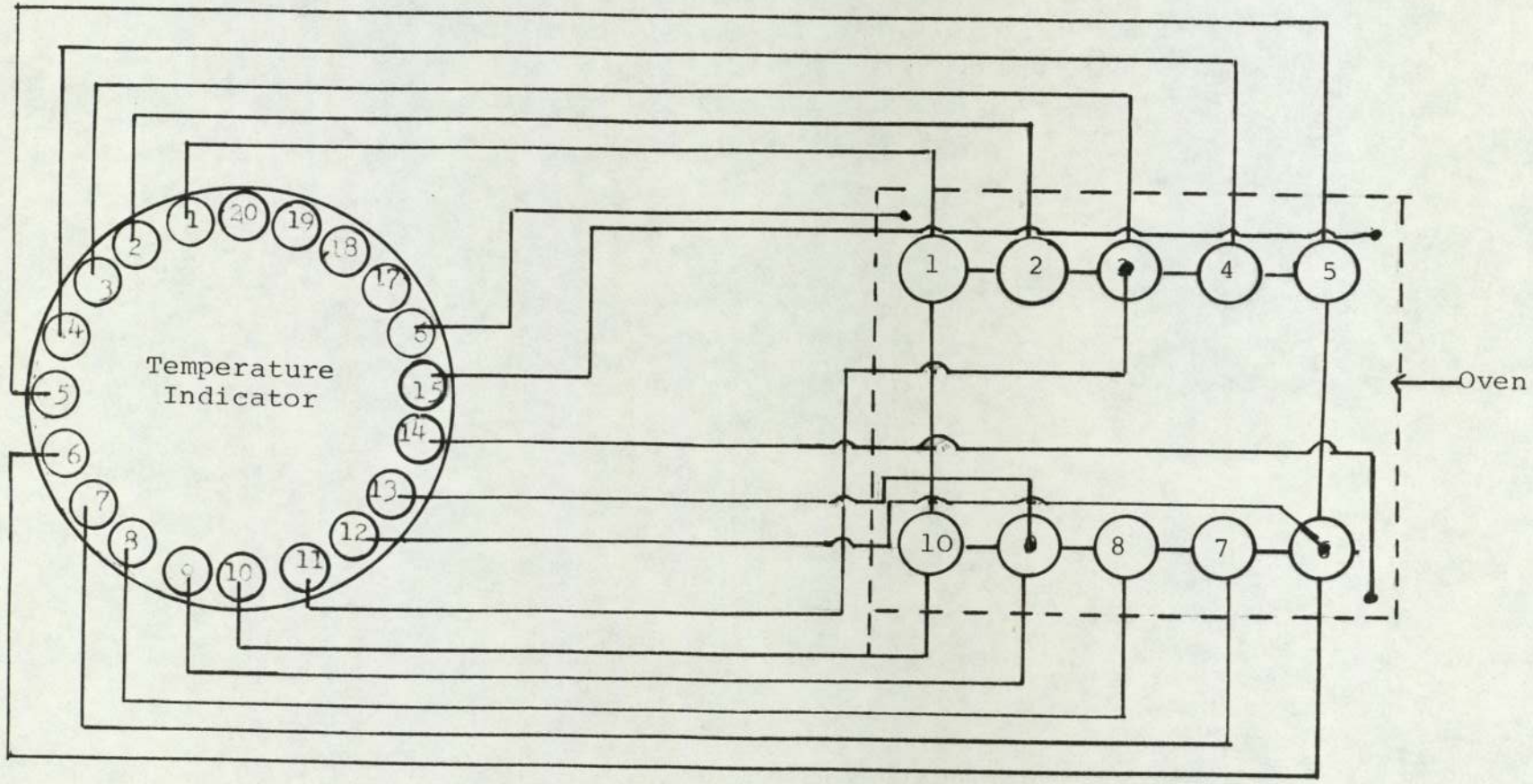


FIG. 4.14 THE SCHEMATIC ARRANGEMENT OF THERMOCOUPLE NETWORK

of the column under test. A sampling needle inserted into the rubber septum at the outlet allowed a small stream of the outlet stream to bypass through the refractive index detector which was linked to the chart recorder (See Fig. 4.15).

As the operating flow rate in future experiments was predicted to be 105 $cm^3 min^{-1}$, the eluent pump was set at this flow rate. When a steady base line had been established on the chart recorder, a 5 cm^3 slug of the feed containing 10% w/v sugar solids was injected into the inlet line through the rubber septum. A peak was produced on the chart recorder as the sugar was eluted. The chromatograms produced were analysed and the results are presented in Table 4.2.

4.6.3 Discussion of Results

The dextran molecules were too large to enter the intra-particle volume and travel through only the interstitial or void volume. The elution volume necessary for the removal of dextran from the column is the void volume. The wide range of void volumes obtained was due to different packing characteristics of each column. Repeatable packing becomes more difficult with increase in the diameter of columns (10).

The results obtained for the individual column properties were similar to that obtained by Gould (10).

The voidages ε, the ratio of the void volume V_o to the total bed volume, is considerably lower than those quoted in the literature (92) for spherical

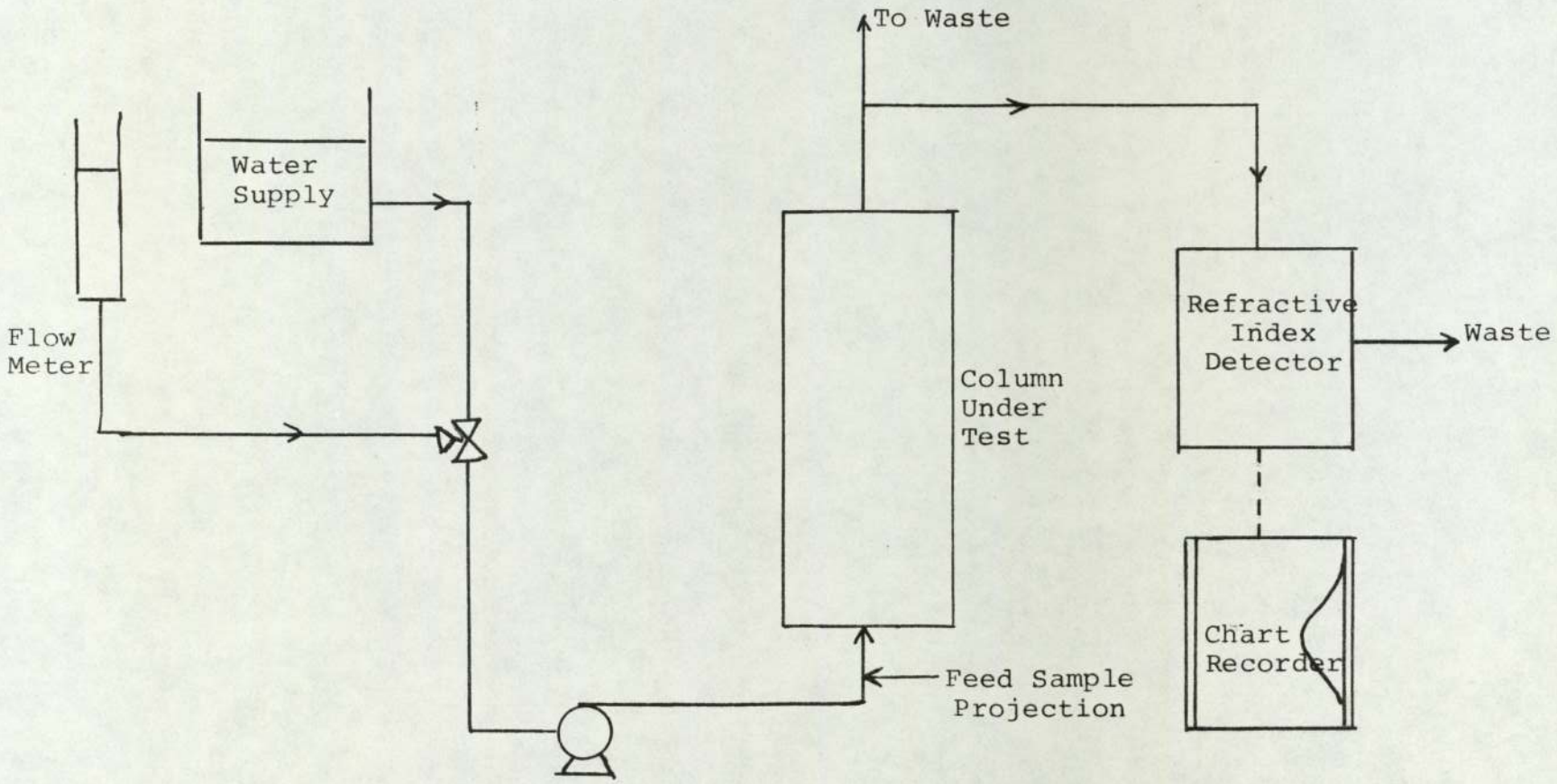


FIG. 4.15 FLOW DIAGRAM FOR THE COMPARISON OF INDIVIDUAL COLUMN PROPERTIES

TABLE 4.2 INDIVIDUAL COLUMN PROPERTIES

Column No.	Bed Volume (cm^3)	Bed Height (cm)	Void Volume V_o (cm^3)	Voidage	ELUTION VOLUMES (cm^3)		H.E.T.P.'s (cm)		Distributiuon Coefficient	
					Fructose	Glucose	Fructose	Glucose	Fructose	Glucose
1	5872	64.1	2258	.38	4077	2838	2.56	2.07	.5	.16
2	5964	65.1	1882	.32	3300	2411	2.41	1.14	.35	.13
3	5936	64.8	1886	.31	3424	2438	3.6	2.59	.38	.14
4	5845	63.8	1950	.33	3509	2671	2.09	0.97	.40	.19
5	5945	64.9	2171	.37	3791	2846	2.60	1.22	.43	.18
6	5781	63.1	1823	.32	3218	2370	2.87	1.11	.35	.14
7	5955	65.0	1659	.28	3622	2520	3.60	2.50	.46	.2
8	5872	64.1	2088	.36	3816	2809	1.64	1.03	.46	.19
9	5936	64.8	1830	.31	3595	2654	2.31	2.09	.41	.15
10	5781	63.1	1912	.33	3488	2495	2.10	1.40	.43	.2
Average	5889	64.28	1944	.331	3584	2604	2.58	1.617	.417	.168

particles. This is thought to be so for two reasons:

(i) the particle size range,

(ii) the compression by the piston.

The packing particle size range is 150-300 μm. Thus the smaller ones may well be dispersed to fill the volume between the larger ones more efficiently.

The variation in the retention volume of glucose is believed to reflect the difference in packing efficiency. The glucose molecules are small enough to diffuse in and out of the intra-particle volume. This is why the V_g values are greater than the V_o values, the non-uniformities in the packing give rise to variations in the flow velocities across the bed. This in turn gives rise to band spreading of the solute as it travels through the column (15). The velocity inequalities are dependent on the packing of each individual column and it is believed that these differences are reflected in the variation of V_g.

The retention volume of fructose V_f vary for the same two reasons as stated for glucose but the band is broadened even more because of the chemical complexing which occurs with the calcium ions. The variation may also be as a result of different amounts of calcium charge in each column.

The HETP values also vary. The method used to calculate their values basically compares the elution time in relation to the band-width. As the elution times vary somewhat, as shown in the elution volume measurements, some variation will automatically be

incurred. However the width of the solute band and its variation from column to column is a function of the velocity inequalities, the distribution within the column and possibly kinetics effects which occur as the band travels down the column.

4.7 EXPERIMENTAL PROCEDURE FOR THE OPERATION OF THE SCCR6 UNIT

4.7.1 Feed Preparation

The average volume of feed necessary for each run was 120 litres. Consequently the fructose and glucose were purchased in 25 kg bags from Kingsley Keith Ltd., Croydon, and L. Garvin Ltd., Isleworth, respectively. They were both of food grade purity. The glucose was available only as the monohydrate.

The feed solution of the required concentrations was prepared by dissolving the calculated weight of the sugars in deionised water. This water was preheated if the required concentration was greater than 40% w/v. After dissolution a sample was analysed to determine the exact concentration of the sugars.

In order to prevent any biological growth in the pipework or on the column an inhibitor, sodium azide, NaN_3 was used. The dose recommended by Fisons Ltd. was 0.02% w/v. This was selected because sodium ions did not displace calcium ions on the resin.

4.7.2 Preliminary Checks

The considerable quantities of deionised water necessary during operation (40 lh^{-1}) was produced by an Elgastat B224 deioniser. This with its level controlling device in the holding tanks was switched on. The conductivity of the produced water was checked to ensure it was below the level of 50 µs. The portable air compressor was activated and the bias and activating pressure checked.

4.7.3 Start Up Procedure

1. The eluent, feed and purge pump were set to the required flow rates.
2. The digital timer for controlling the switch period was set to the required value.
3. All the inlet values for eluent, feed and purge were opened and the collecting bins were positioned.
4. Pumps were turned on and the timer started.

4.7.4 Procedures During a Run

The following procedures were adopted during operation of the SCCR6 unit.

1. Flow rate and Pressure Measurements

Flow rate measurements were taken at regular intervals, usually every two or three switches, although more frequent measurements were taken during the first few cycles. The eluent and feed flow rates were measured at the inlet using the calibrated measuring device. The purge column flow rate was measured by monitoring

the outlet stream.

At the end of a cycle, the product collecting vessels were weighed and a mass balance carried out. The pressure drop of the eluent, feed and the purge stream through the rig was recorded every switch.

2. Sampling Technique

At the end of each cycle a sample was taken of the bulk switch period products of that cycle. These were analysed for purity and concentration as the run progressed. The sample points included along the length of each column allowed "on column" samples to be withdrawn by inserting an hypodermic needle through the silicone rubber septum and filling a 2 cm^3 syringe. These samples were removed at the same time from the same point on the same column in each switch period. These were immediately analysed and from the data obtained, an "on column" concentration profile constructed. This was possible because during the ten switch periods of a cycle, each column served every function, i.e. as the purge column, the eluent entry column, the feed column, the glucose exit or the part of a separating length.

3. Establishing Pseudo-Equilibrium

In a distillation column which is a truly counter-current mass transfer process, when equilibrium is established, the tray to tray composition remains constant along the column. In a semi-continuous process the same dynamic equilibrium is not possible because of the stepwise nature of operation. During

a switch period the concentration profile will be gradually changing along the column as it would be in a batch chromatograph. This is because only the mobile phase is physically moving. At the end of the switch period the stepwise counter-current movement of the stationary phase takes place and the concentration profile is consequently displaced by one column length. Therefore only a "pseudo equilibrium" can be achieved. Two tests were carried out to establish pseudo-equilibrium.

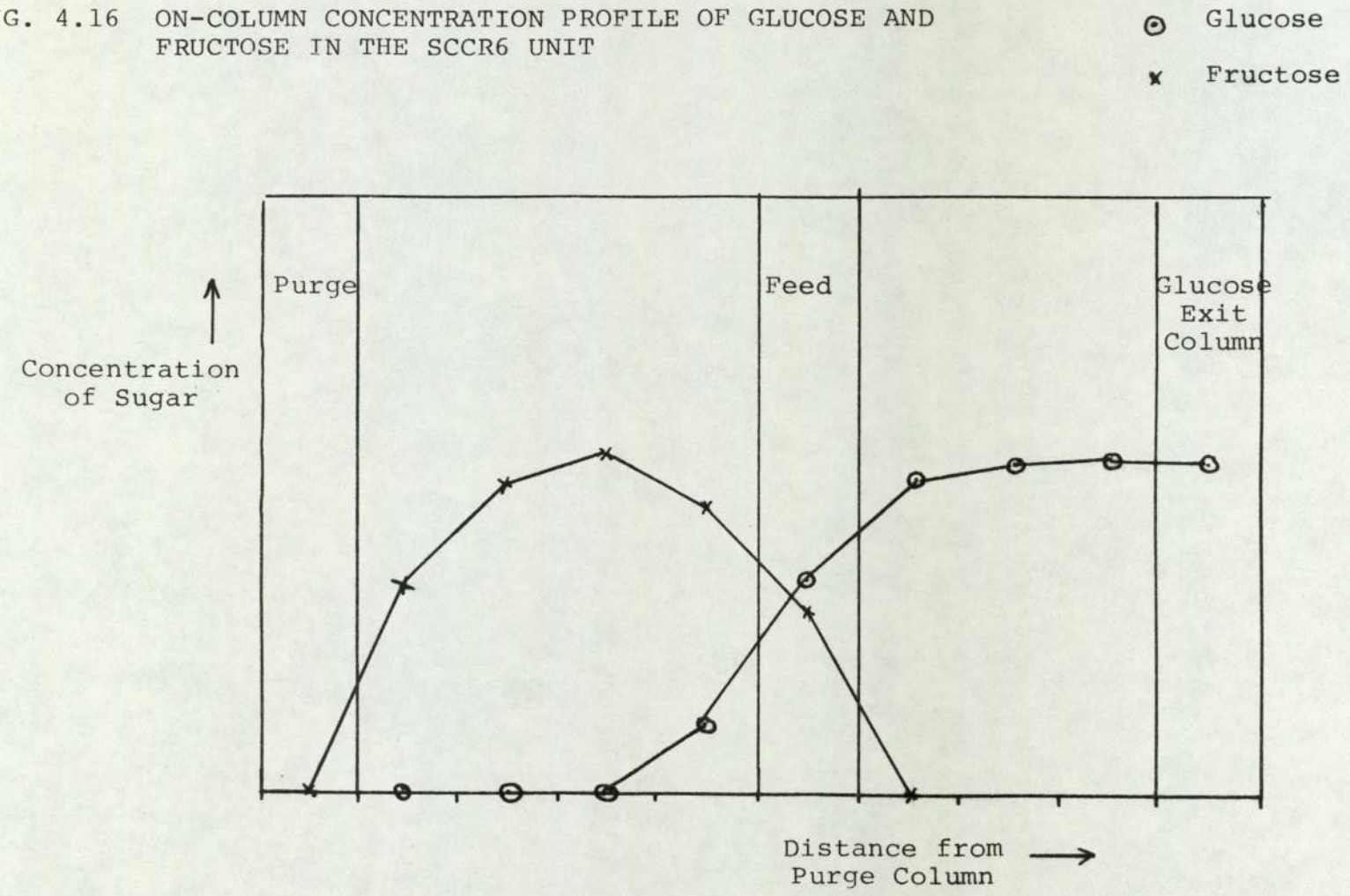
(i) Repeatable 'on column' concentration from one cycle to next.

(ii) Approximately 100% mass balance.

4.7.5 End of Run Profiles and Shut Down Procedure

As the last cycle was due to finish all pumps were switched off. The feed and eluent inlet valves were closed. The control system was switched to manual and moved one position. The purge pump was again activated and the product collected in a separate container. This was weighed and analysed. The procedure was repeated until all ten columns had been purged out and their products weighed and analysed. The analysis and weight enabled the mass of each sugar in each column to be calculated. From this data, an end of run average column concentration profiles could be constructed (see Fig. 4.16).

FIG. 4.16 ON-COLUMN CONCENTRATION PROFILE OF GLUCOSE AND FRUCTOSE IN THE SCCR6 UNIT



4.8 ADDITIONAL EXPERIMENTAL TECHNIQUES AT ELEVATED TEMPERATURES

4.8.1 Temperature Measurements

Regular monitoring of the temperature of the columns, the resin bed and the enclosure were performed. The temperatures of the columns altered slightly with their relative position from the inlet ports, because of this the temperatures were recorded at the same time through the switch. It was usual for the temperatures to be recorded at least three times per cycle.

4.8.2 Start-Up and Shut-Down Procedures

Amendments to the procedure outlined in Section 4.6.3 for the start-up of the SCCR6 were as follows:

(a) The air heater and airotor inside the enclosure were switched on and the temperature controller set.

(b) The air compressor was switched on and when the bias pressure and actuating pressure reached 40 psi (275 kNm^{-2}) and 80 psi (550 kNm^{-2}) respectively, the eluent and purge pumps were started. The water heaters were switched on and the temperature controllers were set. The pumping continued until the mobile phase temperature reached the set value. The flow rates were now adjusted.

(c) The start of the experiment was marked by switching the feed pump on.

During the shut down the liquid heaters were turned off approximately five minutes before the end

of the final switch. The pumps were switched off at the end of the switch and the delivery lines closed. The liquid pressures were allowed to decay. At the end of the experiment at this point the purge pump was switched on and the delivery line to the purge head was opened, the water heater turned on and the individual columns were purged.

4.9 THE ANALYTICAL SYSTEM

A carbohydrate analysis column manufactured by Bio-Rad Ltd was purchased for a fast and efficient analysis. This high performance liquid chromatographic column (HPLC), 250 mm in length and 4.0 mm in diameter, was packed with Animex HPX87, a polymer based ion exchange resin charged in the calcium form. The plate number as quoted by the manufacturer was 2700 giving an HETP of 9.25×10^{-3} mm.

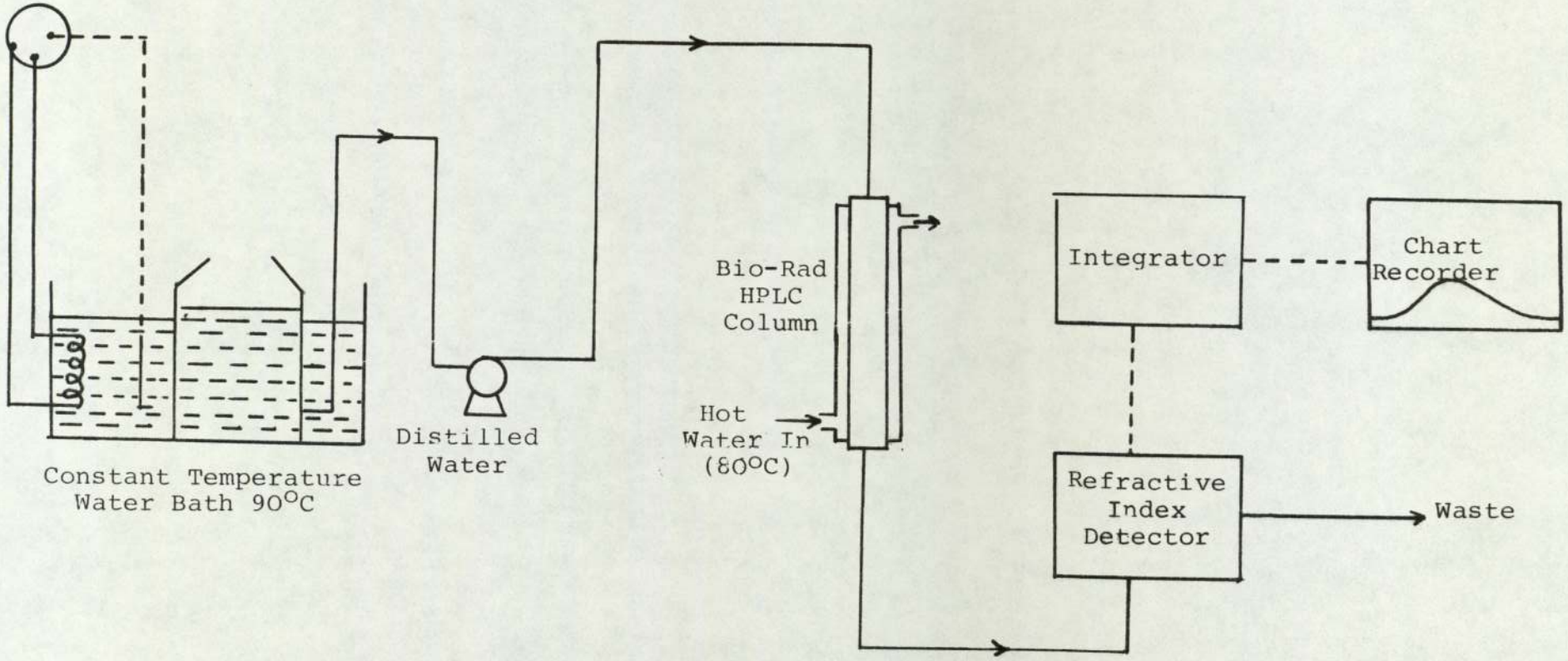
Before entry to the column the eluent, deionised water, was degassed at 65°C by placing a reservoir in a constant temperature water bath. To protect the column against any particulate matter, the eluent was filtered through a Whatman Grade 10 inline filter.

The column was operated at 85°C by means of a water jacket and heater circulator unit supplied by Tecam Ltd. of Cambridge. A six port sample injection valve with a 25 µl external loop was used to load the samples onto the column. Samples were filtered through a 0.45 µm filter before application. Eluent was supplied to the column by a micropump, supplied by

Metering Pumps Ltd. of Ealing, at a flow rate of 0.3 $cm^3 min^{-1}$ to produce a pressure drop through column of approximately 7800 kNm^{-2} (1000 psi).

A differential refractometer, supplied by LDC of Stone, was adopted to detect the sugar as they emerged. Its principle of operation was to compare the refractive index of the HPLC column outlet stream containing sugar with that of the pure eluent, deionised water. The detector was linked electrically to a Servoscribe Chart Recorder and a Hewlett Packard 337B Integrator, see Fig. 4.17. This arrangement gave a chromatogram of the separation on the chart together with the printout of the area under the curve by the integrator. The actual sample concentrations were calculated by comparing the areas obtained with those of known standard samples.

FIG. 4.17 THE ANALYTICAL SYSTEM



CHAPTER FIVE

SEMI-CONTINUOUS OPERATION OF THE SCCR6 UNIT

The semi-continuous operation of the SCCR6 unit is reported in three sections. The first two sections deal with the separation of a feed containing glucose and fructose at ambient and at elevated temperatures. The third section reports the separation of synthetic Fison's feed containing glucose, fructose and dextran.

5.1 SEMI-CONTINUOUS SEPARATION OF A GLUCOSE, FRUCTOSE MIXTURE AT AMBIENT TEMPERATURE

5.1.1 Scope

The experimental programme was concerned with the following objectives:

(i) to fill in the gaps in Dr. Gould's results in investigating the effect of changing the feed concentration

(ii) to investigate the effect of feed point location

(iii) to increase the throughput at ambient temperature

(iv) to increase concentration of the fructose rich product

A run was defined in the following manner, i.e.

Run 20-35-105-30-20

where

20 = feed concentration (% w/v solids)

35 = feed flow rate ($cm^3 min^{-1}$)

105 = eluent flow rate ($cm^3 min^{-1}$)

30 = switch period (min)

20 = temperature (^oC)

5.1.2 Effect of Changing the Feed Concentration

To investigate this parameter, Gould performed three experiments under identical operating conditions

with 20% w/v solids run 20-35-105-30-20

40% w/v solids run 40-35-105-30-20

and 60% w/v solids run 60-35-105-30-20

Three further experiments were performed to extend the range of information available

with 30% w/v solids run 30-35-105-30-20

35% w/v solids run 35-35-105-30-20

and 50% w/v solids run 50-35-105-30-20

The summaries of the conditions and results are given in Table 5.1. To highlight the effects of concentration change, the glucose and fructose profile has been plotted separately, Figs. 5.4 and 5.5 together with the individual profiles, Figs. 5.1, 5.2 and 5.3.

5.1.2.1 Results and Discussion

As the concentration of the feed increases the crossover point of glucose and fructose moves to the left towards the fructose product offtake, if the fructose profile alone is studied (Fig. 5.5), it may be seen that only very small quantities of fructose moves preferentially with the mobile phase into the post feed section. As the concentration of the feed increases,

TABLE 5.1 RUN CONDITIONS FOR VARYING FEED CONCENTRATION EXPERIMENTS												
Run Number	Average Flow Rates			Feed Conc. % w/v		Switch Period min	Average Pressure Drop			L/P Ratios		
	Eluent cm^3/min	Feed cm^3/min	Purge cm^3/min	Glucose	Fructose		Eluent KNm^{-2}	Feed kNm^{-2}	Purge kNm^{-2}	Pre-Feed	Post-Feed	Av.
20-35-105-30-20 G	105	35	550	10.0	10.0	30	190	55	61	.165	.475	.32
30-35-105-30-20	105	35	550	15.0	15.0	30	235	76	62	.165	.475	.32
35-35-105-30-20	105	35	550	17.5	17.5	30	255	84	61	.165	.475	.32
40-35-105-30-20 G	105	35	550	20.0	20.0	30	279	95	61	.165	.475	.32
50-35-105-30-20	105	35	550	25.0	25.0	30	286	117	65	.165	.475	.32
60-35-105-30-20 G	105	35	550	30.0	30.0	30	293	136	68	.165	.475	.32

RESULTS FOR VARYING FEED CONCENTRATION EXPERIMENTS							
Run Number	Fructose Product			Glucose Product			Feed T'Put kg/hr
	Purity %	Mass Bal.%	Prod. Conc.*	Purity %	Mass Bal.%	Prod. Conc.	
20-35-105-30-20 G	99.9	98	0.64	99.9	101	2.37	0.42
30-35-105-30-20	99.9	97	0.94	99.9	98	3.59	0.63
35-35-105-30-20	99.9	96	1.28	99.9	103	4.2	0.735
40-35-105-30-20 G	88.0	96	1.29	99.9	96	3.6	0.84
50-35-105-30-20	82.0	95	1.74	99.9	103	4.5	1.05
60-35-105-30-20 G	77.0	86	1.79	99.9	93	5.0	1.26

G denominates the run performed by Gould
* bulk product collected over the switch time of 30 minutes

the amount of fructose retained in the column is enhanced and consequently product concentrations increase.

When the glucose profiles are studied, Fig. 5.4, a marked effect is observed. At 20%, 30% and 35% w/v solids of 50-50 glucose fructose feed mixture only a negligible amount of glucose travels preferentially with the stationary phase, this is likely to be the glucose present in the feed column when the sequencing action occurs. At 40%, 50% and 60% solids feed concentrations a significant amount of glucose moves preferentially with the stationary phase to contaminate the fructose rich product.

The general shape of both glucose and fructose profiles individually remain similar; it is thought that the change in the distribution of the glucose and fructose is not caused by the hydration theory as explained by Gould (10).

Gould (10) suggested that, when the glucose molecules are in dilute solution, each glucose molecule is associated with fifteen to twenty molecules of water to attain the lowest energy of conformation and thus gain the greatest thermodynamic stability. Under conditions of higher sugar concentrations the number of water molecules in solution which are available for hydration decreases. Hence, there is a competition between the sugar molecules for water molecules in an attempt to totally hydrate and achieve the lowest conformational energy. As a result a weak bonding of glucose molecules with other glucose molecules, complexed fructose

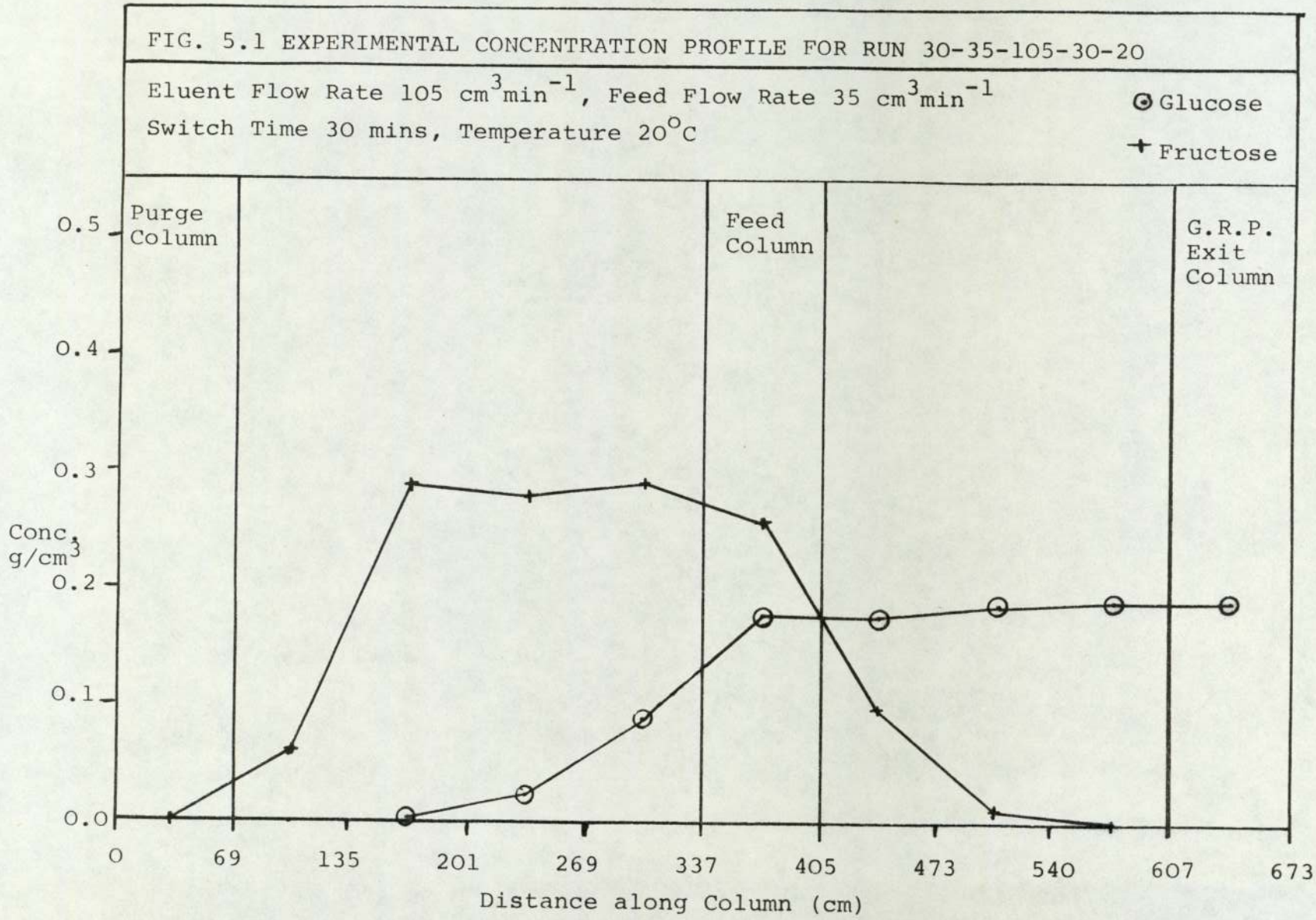
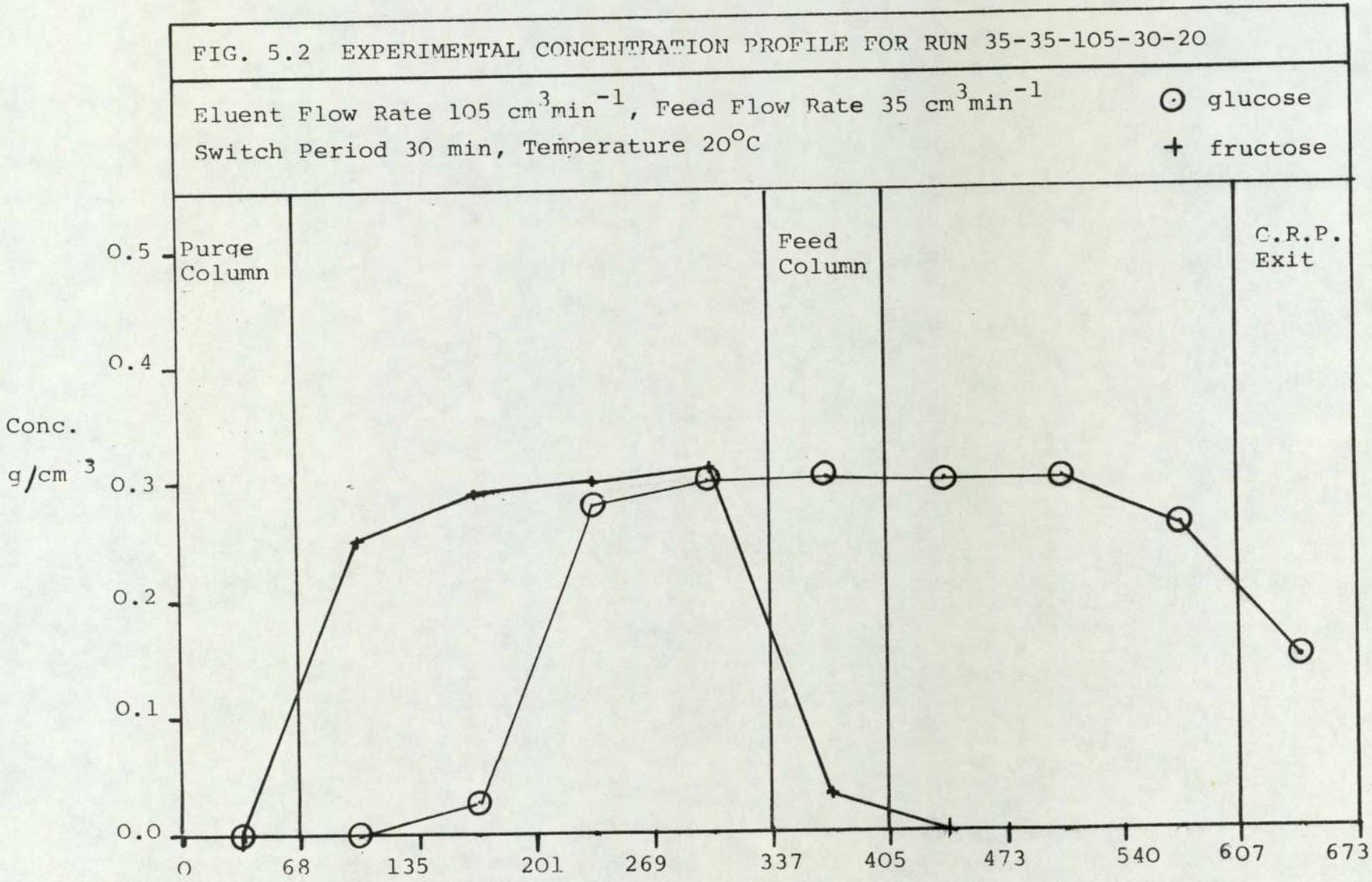


FIG. 5.1 EXPERIMENTAL CONCENTRATION PROFILE FOR RUN 30-35-105-30-20
Eluent Flow Rate 105 cm3min-1, Feed Flow Rate 35 cm3min-1
Switch Time 30 mins, Temperature 20°C
Glucose
Fructose
Purge Column
Feed Column
G.R.P. Exit Column
0.5
0.4
0.3
0.2
0.1
0.0
Conc, g/cm3
0
69
135
201
269
337
405
473
540
607
673
Distance along Column (cm)

FIG. 5.2 EXPERIMENTAL CONCENTRATION PROFILE FOR RUN 35-35-105-30-20



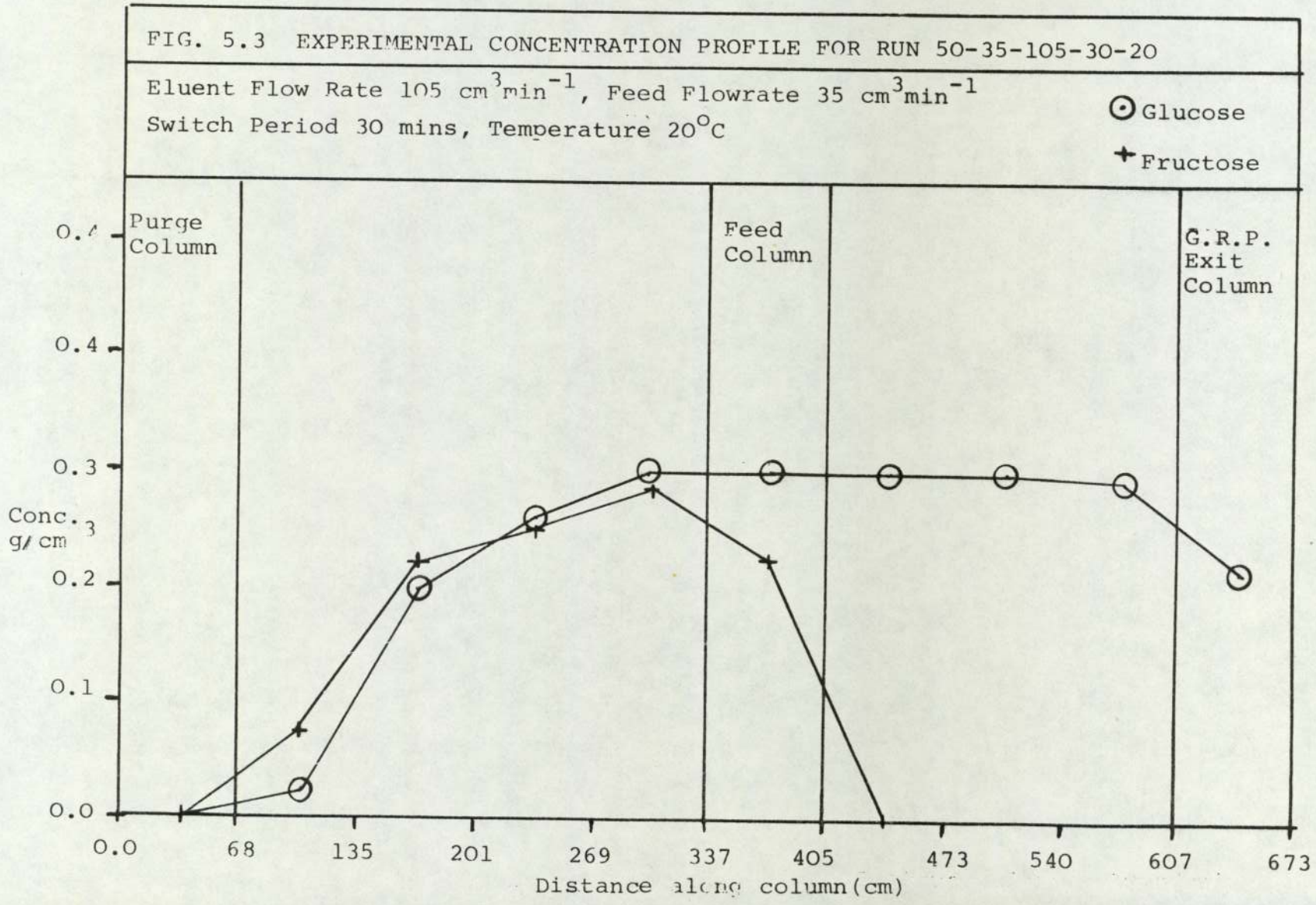
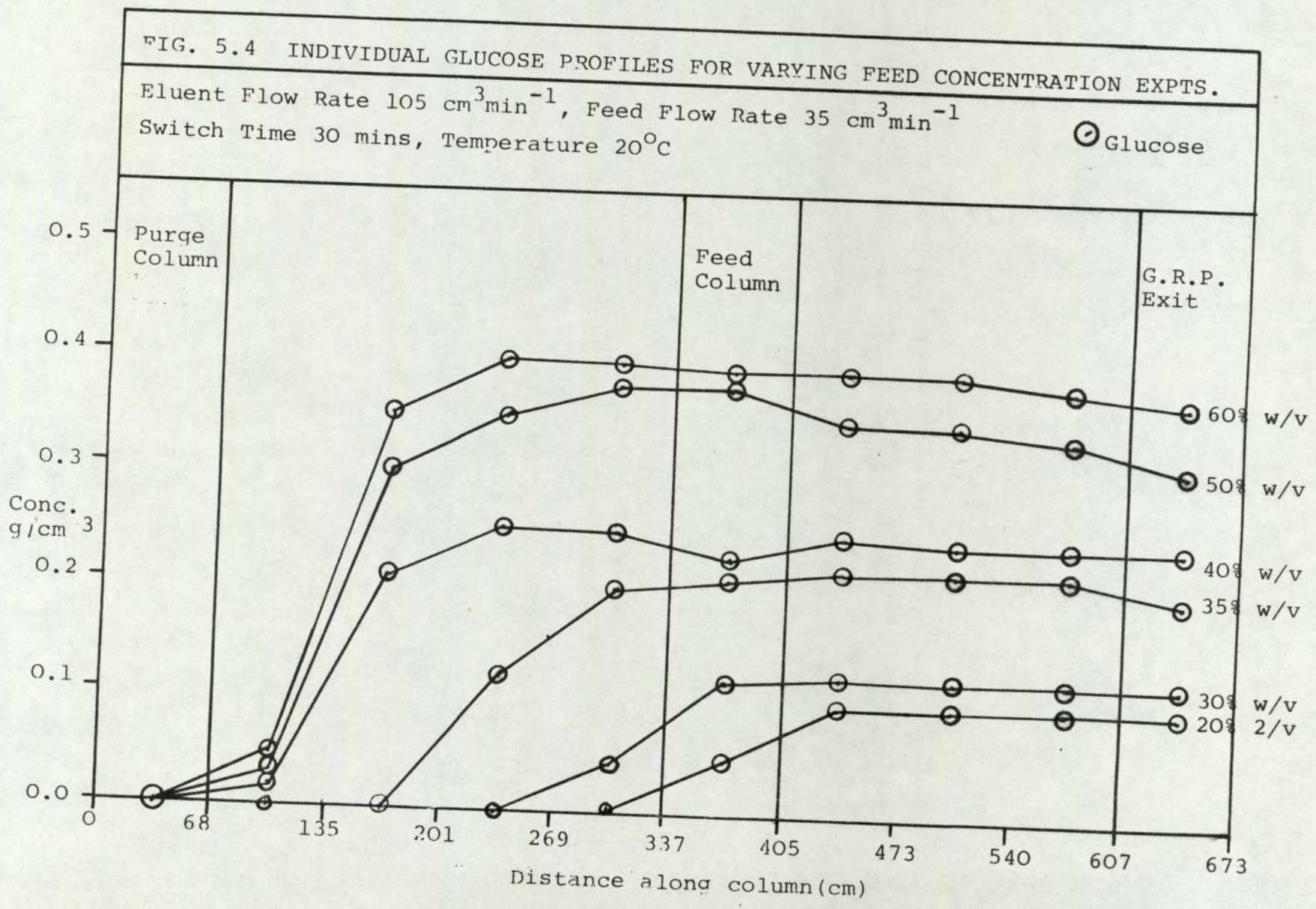


FIG. 5.3 EXPERIMENTAL CONCENTRATION PROFILE FOR RUN 50-35-105-30-20
Eluent Flow Rate 105 cm3min-1, Feed Flowrate 35 cm3min-1
Switch Period 30 mins, Temperature 20°C
Glucose
Fructose
Purge Column
Feed Column
G.R.P. Exit Column
Conc. g/cm3
0.0
0.1
0.2
0.3
0.4
0.0
68
135
201
269
337
405
473
540
607
673
Distance along column (cm)

FIG. 5.4 INDIVIDUAL GLUCOSE PROFILES FOR VARYING FEED CONCENTRATION EXPTS.

Eluent Flow Rate 105 $cm^3 min^{-1}$, Feed Flow Rate 35 $cm^3 min^{-1}$
Switch Time 30 mins, Temperature 20°C



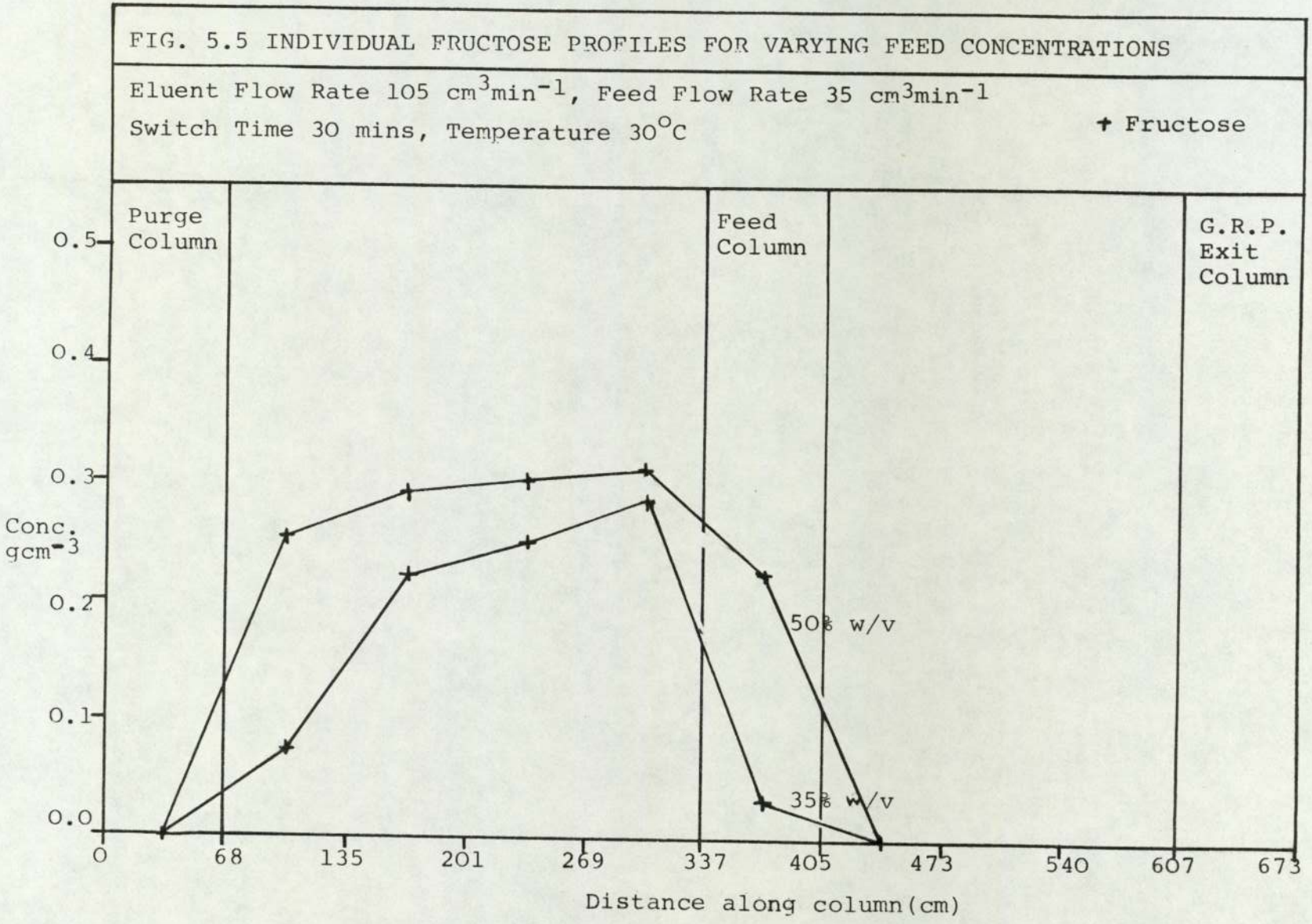


FIG. 5.5 INDIVIDUAL FRUCTOSE PROFILES FOR VARYING FEED CONCENTRATIONS
Eluent Flow Rate 105 cm3min-1, Feed Flow Rate 35 cm3min-1
Switch Time 30 mins, Temperature 30°C
+ Fructose
Purge Column
Feed Column
G.R.P. Exit Column
0.5
0.4
0.3
0.2
0.1
0.0
Conc. gcm-3
50% w/v
35% w/v
0
68
135
201
269
337
405
473
540
607
673
Distance along column(cm)

molecules and calcium ions may occur. This causes the glucose to move with the stationary phase. However, there is no evidence to support the hydration theory. On investigation of the variation of the distribution coefficient with on column sugar concentration, a linear relationship between the two was obtained. This increase in the distribution coefficient with on column sugar concentration causes the glucose to move with the stationary phase.

As the concentration of sugar solids in the column increases, the retention of component in the stationary phase increases. This results in an enhanced concentration of both glucose and fructose on the column and a marked movement of glucose with the stationary phase.

Under the set conditions and with the column length available for separation, the feed concentration of 35% w/v solid sugar utilises the column most efficiently to produce two 99.9% pure products.

5.1.3 Effect of Changing the Feed Point Location

In the experiments with higher feed concentrations 50%-60% (Figs. 5.3 and 5.8) w/v of sugar solids, contamination in the fructose rich product occurred as the glucose travelled with the stationary phase. Also noted from the fructose profiles was the fact that two columns in the post feed section were not utilised at all. Gould (10) recommended that the purity of the fructose product could be enhanced by moving the feed entry point nearer to the glucose exit column.

During his research program the feed was always introduced into the fifth column after the eluent entry column. This meant that there were four column lengths in the pre-feed section and five column lengths in the post feed section. The purge column was always isolated.

To obtain an indication of how changing the location of the feed point would affect product purity, Gould (10) used a mathematical model and computer to simulate the results. An experiment was performed using the same operating conditions as used by Gould in simulation work with a feed entry location shifted by two columns in the direction of the glucose exit column. The result obtained by both simulation and experimental runs are presented in Figs. 5.6 and 5.7 respectively, together with the profile of standard 60-35-105-30-20 run, Fig. 5.8. Table 5.2 shows the experimental operating conditions and results.

5.1.3.1 Results and Discussion

The simulated concentration profile by moving the feed point location by two column lengths in the direction of the glucose exit column (Fig. 5.6) looked very promising. The experimental result however proved otherwise (Fig. 5.8). Comparing Fig. 5.7 with the standard 60-35-105-30-20 no significant change in the end of run profile was observed.

In the mathematical modelling Gould (10) assumed a constant value for the distribution coefficient, experimentally however it has been proved to increase

TABLE. 5.2 RUN CONDITIONS FOR THE SHIFT IN FEED ENTRY LOCATION

RUN NUMBER	AVERAGE FLOW RATES			FEED CONC. % w/v		SWITCH PERIOD min	AVERAGE PRESSURE DROP			L/P RATIOS			Feed Point Location
	ELUENT cm^3/min	FEED cm^3/min	PURGE cm^3/min	G	F		ELUENT kNm^{-2}	FEED kNm^{-2}	PURGE kNm^{-2}	PRE FEED	POST FEED	AV	
60-35-105-30-20 G	105	35	550	30	30	30	190	55	61	0.165	0.475	0.32	6
60-35-105-30-20 FP2	105	35	550	30	30	30	190	25	61	0.165	0.475	0.32	8

RESULTS FOR SHIFT IN FEED ENTRY LOCATION

RUN NUMBER	FRUCTOSE PRODUCT			GLUCOSE PRODUCT			FEED T'PUT kg/hr
	Purity %	Mass Balance %	Conc.* % w/v	Purity %	Mass Balance %	Conc. % w/v	
60-35-105-30-20 G	77.0	86.	1.79	99.9	93	5.0	1.26
60-35-105-30-20 FP2	77.0	87.	2.35	99.0	86	6.7	1.26

G denotes experiment performed by Gould
FP2 indicates that feed point has been moved by two columns in the direction of GRP exti column
* bulk concentration for the product collected over a switch period of 30 minutes

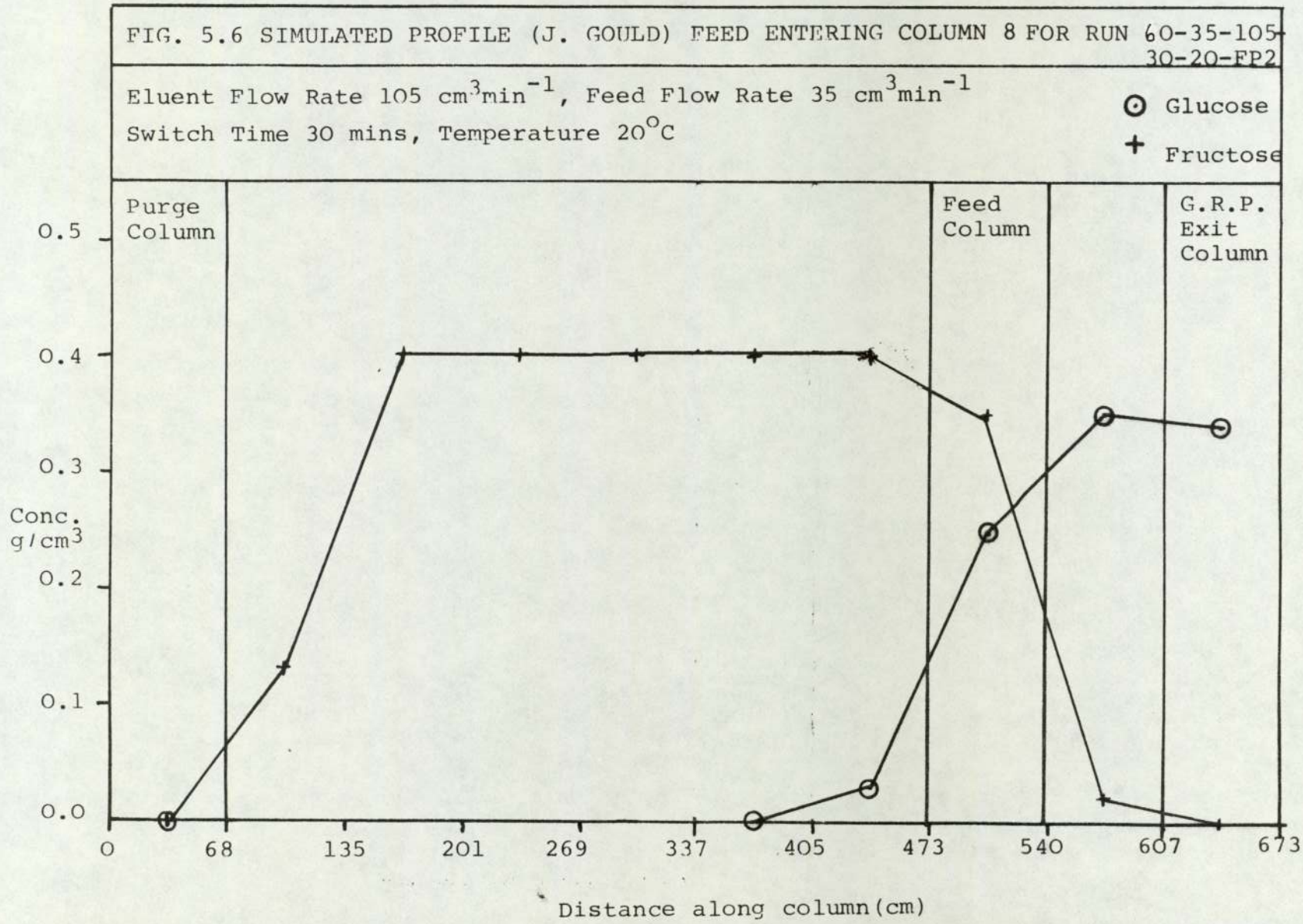


FIG. 5.6 SIMULATED PROFILE (J. GOULD) FEED ENTERING COLUMN 8 FOR RUN 60-35-105-30-20-FP2
Eluent Flow Rate 105 cm3min-1, Feed Flow Rate 35 cm3min-1
Switch Time 30 mins, Temperature 20°C
Glucose
Fructose
Purge Column
Feed Column
G.R.P. Exit Column
0.5
0.4
0.3
0.2
0.1
0.0
Conc. g/cm3
0
68
135
201
269
337
405
473
540
607
673
Distance along column(cm)

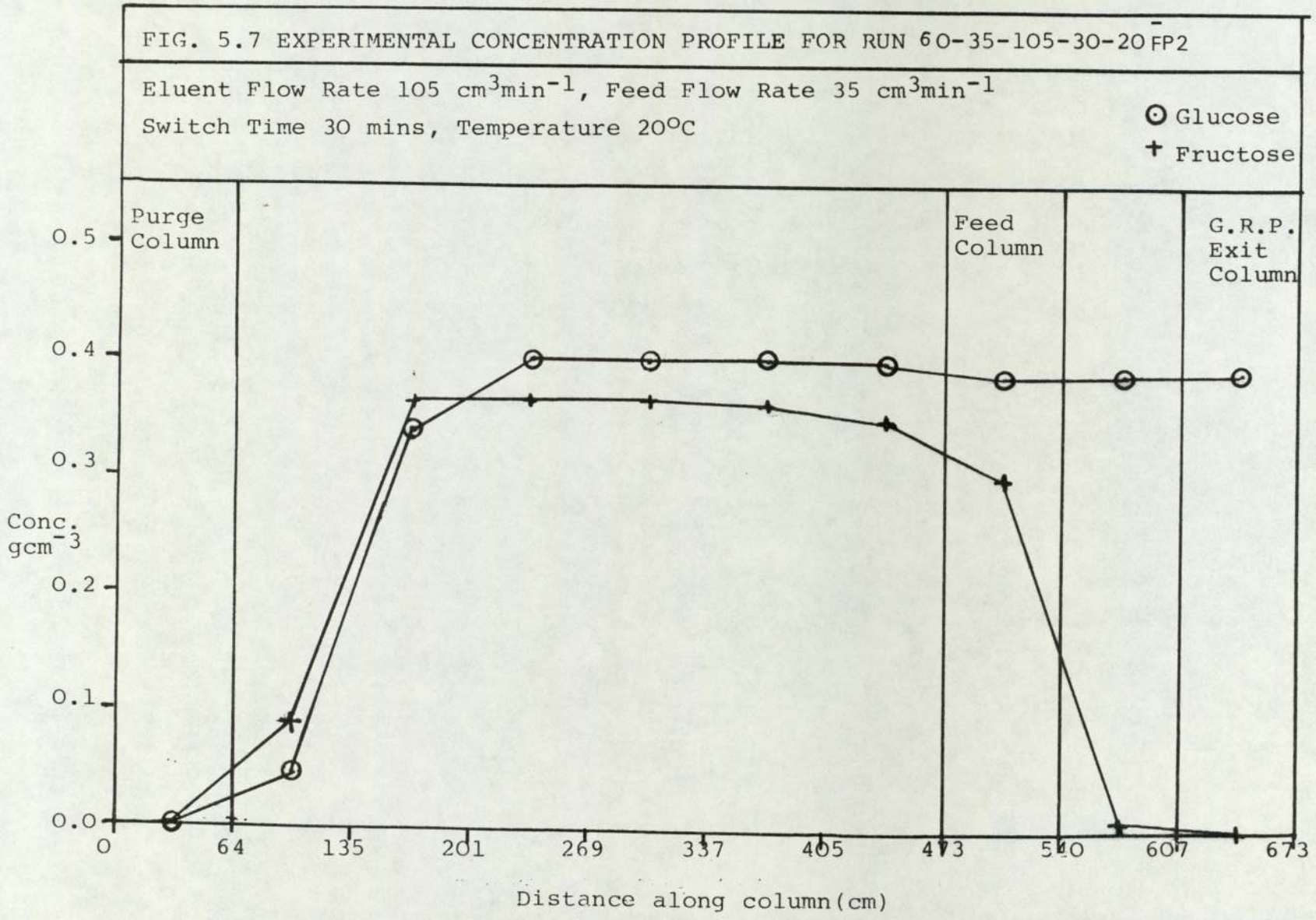


FIG. 5.7 EXPERIMENTAL CONCENTRATION PROFILE FOR RUN 60-35-105-30-20 FP2
Eluent Flow Rate 105 cm3min-1, Feed Flow Rate 35 cm3min-1
Switch Time 30 mins, Temperature 20°C
Glucose
Fructose
Purge Column
Feed Column
G.R.P. Exit Column
Conc. gcm-3
0.0
0.1
0.2
0.3
0.4
0.5
0
64
135
201
269
337
405
473
540
607
673
Distance along column (cm)

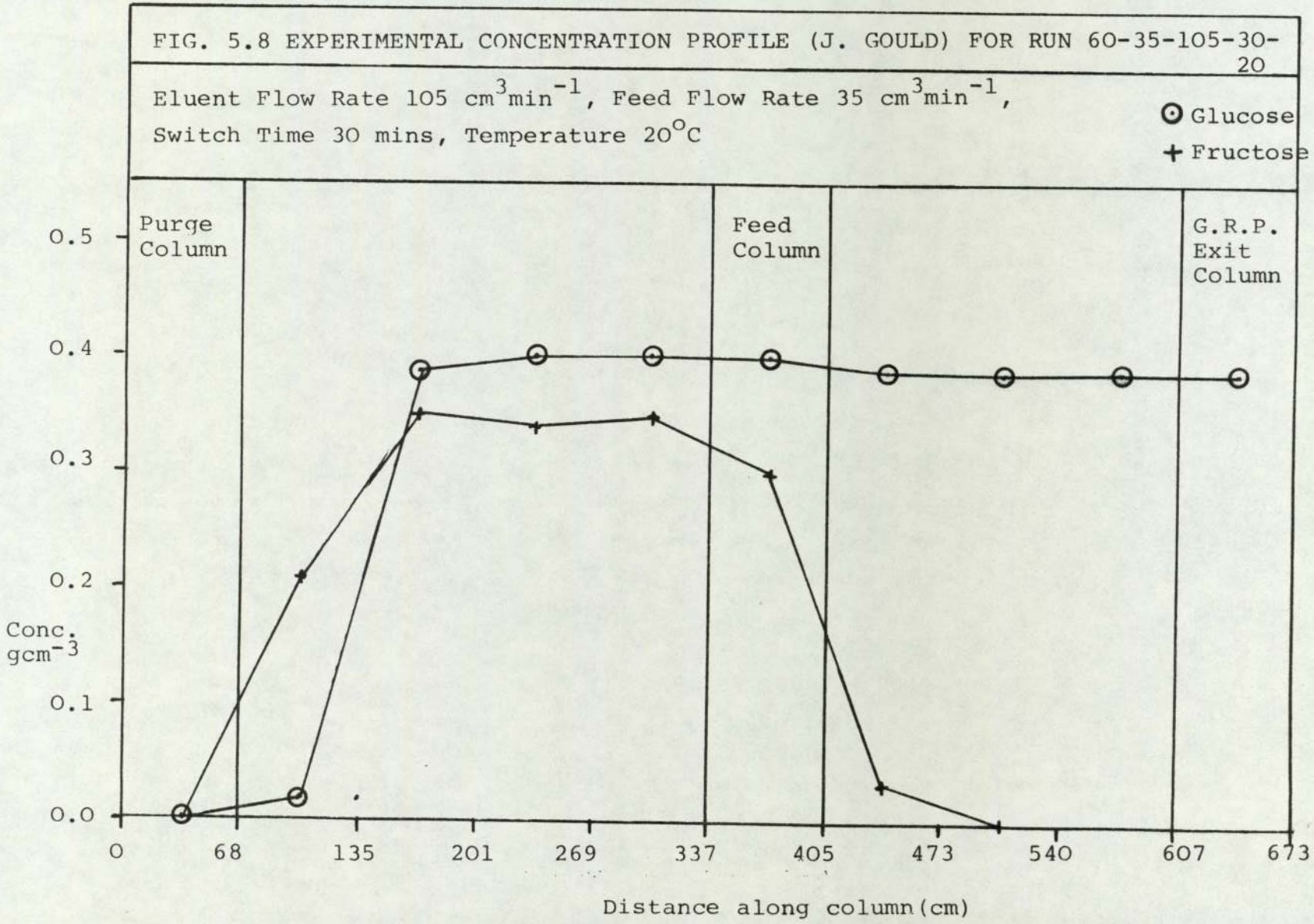


FIG. 5.8 EXPERIMENTAL CONCENTRATION PROFILE (J. GOULD) FOR RUN 60-35-105-30-20
Eluent Flow Rate 105 cm3min-1, Feed Flow Rate 35 cm3min-1,
Switch Time 30 mins, Temperature 20°C
Glucose
Fructose
Purge Column
Feed Column
G.R.P. Exit Column
0.5
0.4
0.3
0.2
0.1
0.0
Conc. gcm-3
0
68
135
201
269
337
405
473
540
607
673
Distance along column (cm)

linearly with concentration (Chapter 3). One possible explanation for the discrepancy in the simulated run could be due to the assumption made above. This will be investigated later in Chapter 7 when mathematical modelling on the SCCR6 unit is performed taking into account the variation of distribution coefficients with the concentration of sugar solids.

5.1.4 Attempts to Increase the Throughput at Ambient Temperature

One of the aims of this research programme was to compare the throughputs of the SCCR6 unit in batch and semi-continuous mode. For this reason attempts were made to increase the throughput in the semi-continuous mode.

A method of increasing the throughput at a particular feed concentration was by increasing the feed flow rate. The flow rates were doubled and the corresponding switch period was halved so that the $\frac{L}{P}$ ratio in the pre-feed and post-feed remained the same as in the previous experiments. In all the experiments the eluent to feed ratio was kept constant at 3:1 and a feed concentration of 40% and 50% solids was used. Run 20-70-210-15-20 was performed by Gould to study the effect of switch period. The conditions of the experiments, Run 20-70-210-15-20, Run 40-70-210-15-20 and Run 50-70-210-15-20 are shown in Table 5.3. The end of run concentration profiles are shown for run 40-70-40-15-20 and Run 50-70-210-15-20 in Figs. 5.9 and 5.10 respectively.

TABLE 5.3 RUN CONDITIONS FOR INCREASING THE THROUGHPUT OF THE SCCR6 UNIT												
RUN NUMBER	AVERAGE FLOW RATES			FEED CONC. % w/v		SWITCH PERIOD min	AVERAGE PRESSURE DROP			L/P RATIOS		
	ELUENT cm^3/min	FEED cm^3/min	PURGE cm^3/min	G	F		ELUENT kNm^{-2}	FEED kNm^{-2}	PURGE kNm^{-2}	PRE FEED	POST FEED	AV
20-70-210-15-20 G	210	70	550	10.2	9.8	15	269	100	61	0.165	0.475	0.32
40-70-210-15-20	210	70	550	19.6	20.2	15	500	195	62	0.165	0.475	0.32
50-70-210-15-20*	210	70	550	24.9	25.3	15	560	230	61	0.165	0.475	0.32

RESULTS FOR INCREASING THE THROUGHPUT OF THE SCCR6 UNIT								
RUN NUMBER	FRUCTOSE PRODUCT			GLUCOSE PRODUCT			FEED T'PUT kg/hr	
	PURITY %	MASS BALANCE	CONC. %w/v	PURITY %	MASS BALANCE	CONC.		
20-70-210-15-20 G	85	105	1.22+	99.9	69	1.4	0.84	EQUILIBRIUM NOT REACHED
40-70-210-15-20	76	102	3.2 +	99.9	98	2.98	1.68	
50-70-210-15-20*	70	111	7.6*	99.9	100	2.7	2.10	

* Fructose rich product collected over fifteen minutes switch period had been used as an eluent to increase the concentration of fructose product (see Section 5.1.5.2)

G denotes the experiments performed by Gould

\+ bulk concentration over fifteen minutes switch period

5.1.4.1 Results and Discussion

In Run 40-70-210-15-20 and 50-70-210-15-20, the pseudo equilibrium had been established, however Gould was unable to establish equlibrium with 20-70-210-15-20 due to the problem encountered with the equipment during the run.

Comparing run 50-70-210-15-20, Fig. 5.10 (Table 5.3) with run 50-35-105-30-20, Fig. 5.3 (Table 5.1), it can be seen that as the feed flow rate increases, the cross-over point has moved to the left towards the stationary phase. If the fructose profiles are studied, it may be seen that their basic shapes are the same and that very little fructose has travelled preferentially with the mobile phase into the post feed section. It can also be seen that the concentration of fructose product has also increased with increased feed flow rate. This is because the volume of purge water per cycle has decreased by decreasing the switch time.

If the glucose profiles are studied, it may be seen that as the feed flow rate increases and the switch time decreases more glucose travels preferentially with the stationary phase contaminating the fructose product. This is true even though the eluent to feed ratio remains constant at 3:1. The mass input of sugar changes from 17.5 gm per minute to 35.0 gm per minute. There is such a high quantity of sugar fed onto a feed column which only has a finite volume. As the sequencing of the columns takes place, more and more glucose is moved with the stationary phase into the pre-feed section. This is

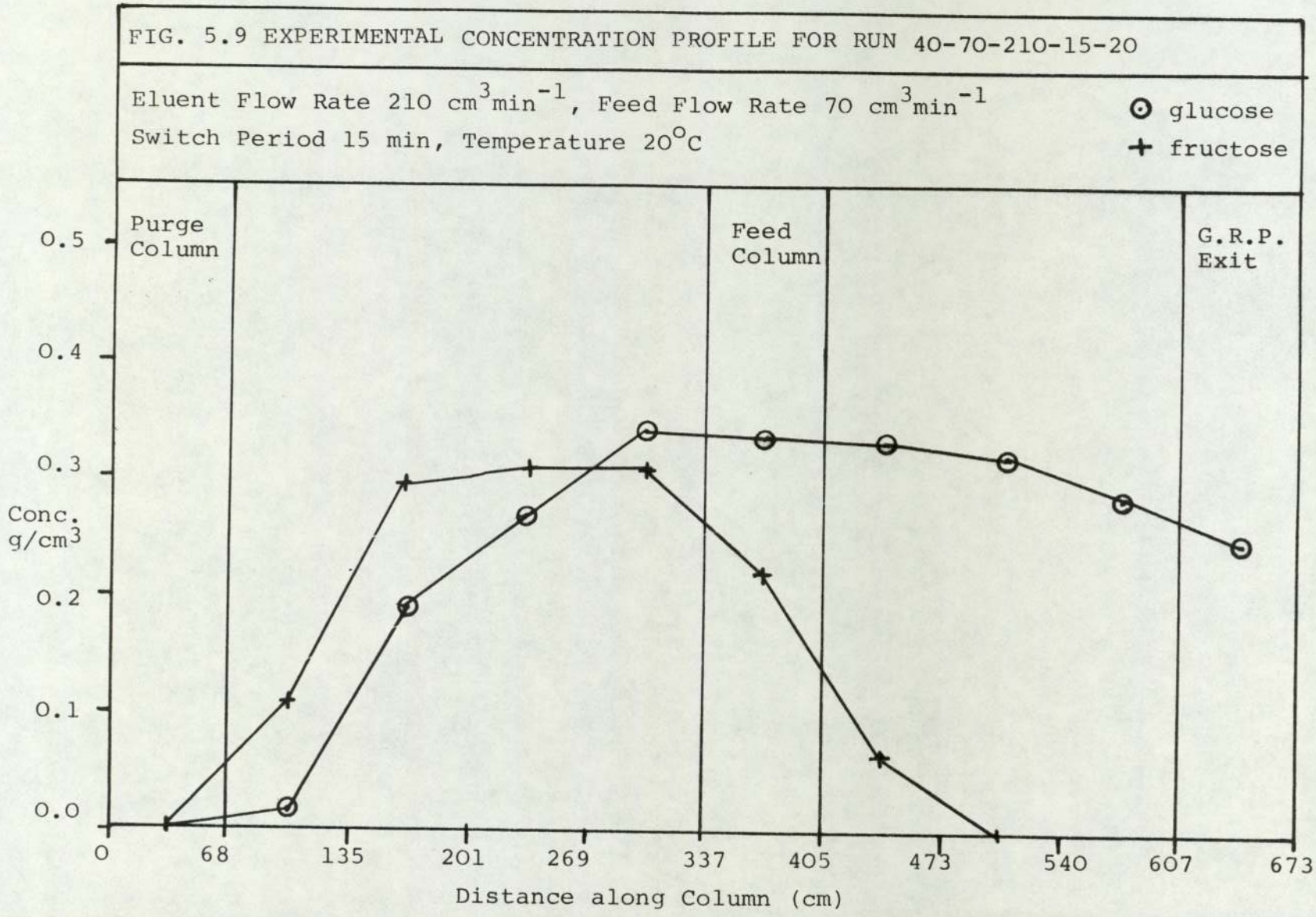


FIG. 5.9 EXPERIMENTAL CONCENTRATION PROFILE FOR RUN 40-70-210-15-20
Eluent Flow Rate 210 cm3min-1, Feed Flow Rate 70 cm3min-1
Switch Period 15 min, Temperature 20°C
glucose
fructose
Purge Column
Feed Column
G.R.P. Exit
0.5
0.4
0.3
0.2
0.1
0.0
Conc. g/cm3
0
68
135
201
269
337
405
473
540
607
673
Distance along Column (cm)

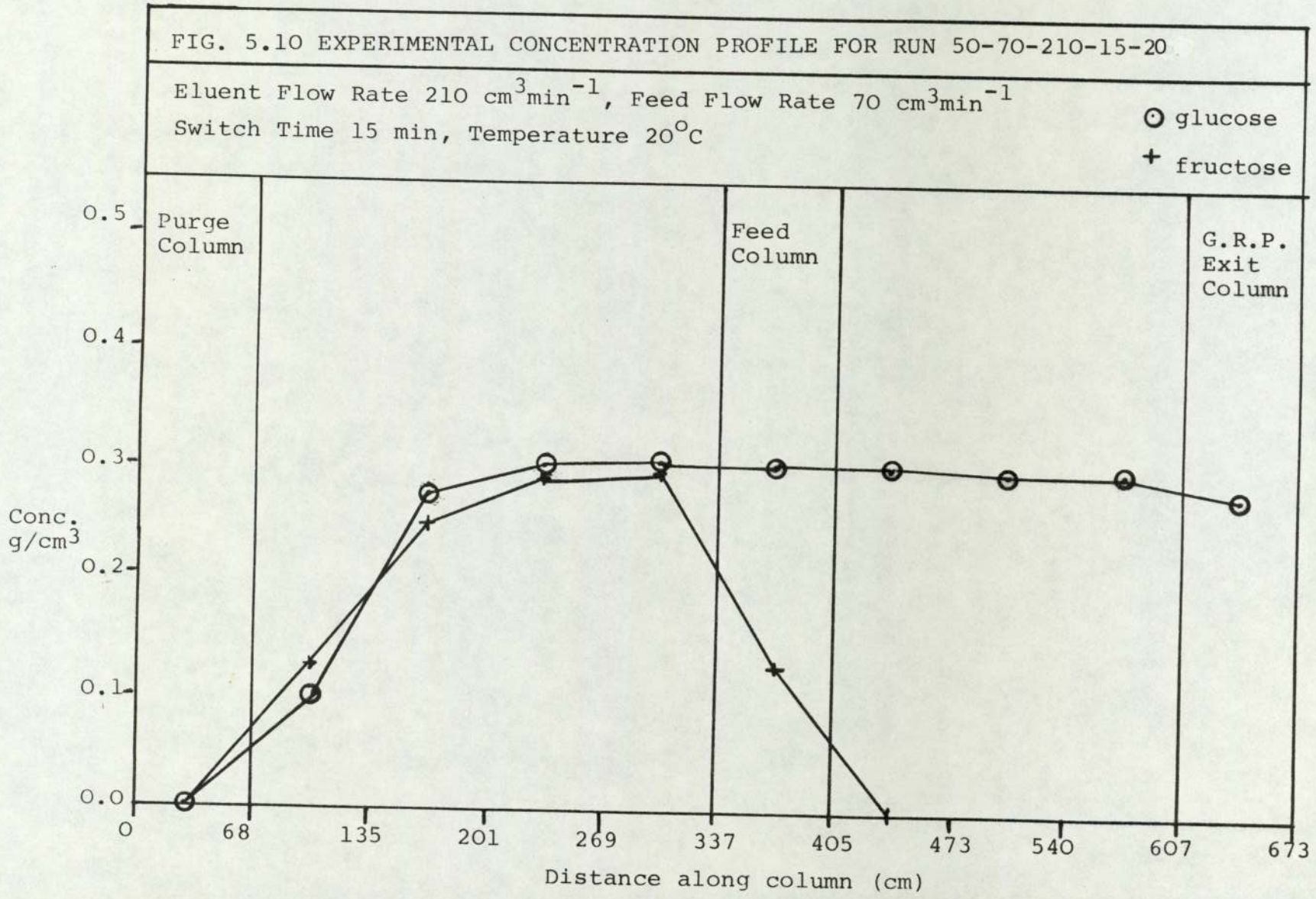


FIG. 5.10 EXPERIMENTAL CONCENTRATION PROFILE FOR RUN 50-70-210-15-20
Eluent Flow Rate 210 cm3min-1, Feed Flow Rate 70 cm3min-1
Switch Time 15 min, Temperature 20°C
glucose
fructose
Purge Column
Feed Column
G.R.P. Exit Column
Conc. g/cm3
0.0
0.1
0.2
0.3
0.4
0.5
0
68
135
201
269
337
405
473
540
607
673
Distance along column (cm)

directly as a result of glucose not being carried towards the glucose outlet at a high enough rate in such a short switch period. When the switching over occurs, all the glucose has not been removed and a concentration build up occurs. This results in the purity of fructose product decreasing from 82% with run 50-35-105-30-20 to 70% with run 50-70-210-15-20.

5.1.5 Attempts to Improve the Concentration of the Fructose Rich Product

Attempts were made to improve the concentration of fructose in the fructose product. This was essential to make the semi-continuous counter-current refiner commercially viable.

The concentration of feed is kept constant at 50% w/v solids containing 50-50 glucose and fructose. Three techniques were used to improve the concentration of fructose in the fructose product (Table 5.4).

5.1.5.1 By Fractional Product Collection

The concentration profile of the fructose product stream was constructed for run 50-35-105-30-20 (Table 5.4) over a thirty minute switch period. This is shown in Fig. 5.11. During the next cycle the fructose product stream was collected in two fractions of fifteen minutes each. The fructose product rose in concentration from 1.74% w/v solids in the 30 minute bulk product to 3.4% w/v solids in bulk product for the first fifteen minutes collection period. Further increase in concentration

TABLE 5.4 RUN CONDITIONS FOR IMPROVING THE FRUCTOSE CONCENTRATION IN FRUCTOSE PRODUCT

RUN NUMBER	AVERAGE FLOW RATES			FEED CONC. % w/v		SWITCH PERIOD min	AVERAGE PRESSURE DROP			L/P RATIOS		
	ELUENT cm^3/min	FEED cm^3/min	PURGE cm^3/min	G	F		ELUENT kNm^{-2}	FEED kNm^{-2}	PURGE kNm^{-2}	PRE FEED	POST FEED	AV
50-35-105-30-20-P-15	105	35	550	25	25	30	286	117	65	0.165	0.475	0.32
50-35-105-30-20-P-10	105	35	550	25	24.9	30	286	117	65	0.165	0.475	0.32
50-35-105-30-20-P-10-R	105	35	550	25	25.1	30	286	117	65	0.165	0.475	0.32
50-70-210-15-20-P-15-R	210	70	550	24.9	25.3	15	560	230	65	0.165	0.475	0.32
50-70-210-15-20-P-15-R-S	210	70	550	24.9	25.3	15	560	230	62	0.165	0.475	0.32

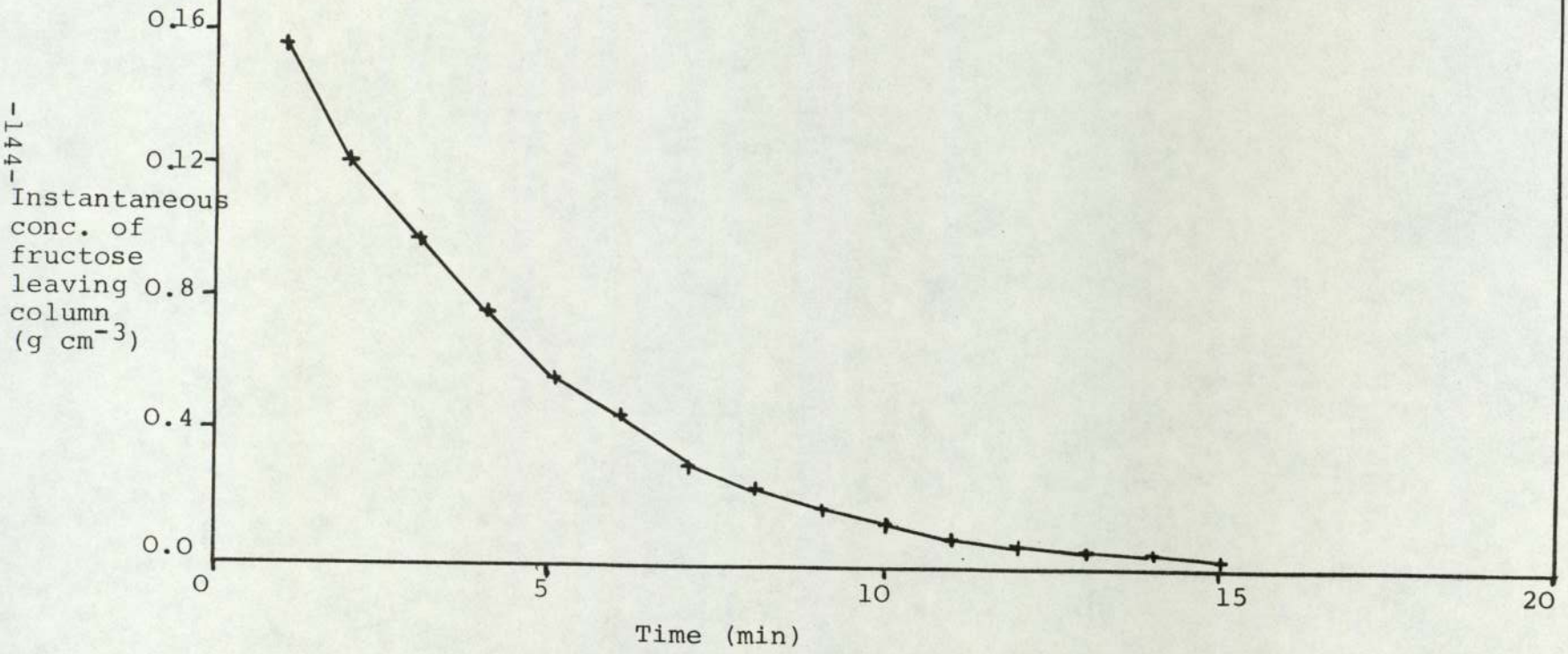
RESULTS FOR IMPROVING THE FRUCTOSE CONCENTRATION IN FRUCTOSE PRODUCT

RUN NUMBER	FRUCTOSE PRODUCT			GLUCOSE PRODUCT			Throughput kg/h
	Purity %	Mass Balance %	Conc. % w/v	Purity %	Mass Balance %	Conc. % w/v	
50-35-105-30-20-P-15	82.0	96	3.4	99.9	103	4.5	1.05
50-35-105-30-20-P-10	82.0	95	5.1	99.9	104	4.52	1.05
50-35-105-30-20-P-10-R	72.0	93	9.4	99.9	95	4.17	1.05
50-70-210-15-20-P-15-R	70.0	111	7.6	99.9	100	2.7	2.10
50-70-210-15-20-P-15-R-S	57.0	110	6.8	99.9	100	1.53	2.10

P-10 denotes that the fructose product is collected for the first 10 minutes
P-15-R denotes that the fructose product is collected in the first 15 minutes and is used as an eluent
P-15-R-S denotes that the fructose product is collected in the first 15 minutes and is used as an eluent and mixed with a sidestream product

FIG. 5.11 FRUCTOSE CONCENTRATION PROFILE FROM PURGE OUTLET OF COLUMN IN RUN 30-35-105-30-20

Eluent Flow Rate 105 $cm^3 min^{-1}$, Feed Flow Rate 35 $cm^3 min^{-1}$, Purge Rate 500 $cm^3 min^{-1}$



was achieved by collecting the fructose product stream in two fractions of the first 10 minutes and the last twenty minutes. The bulk fructose concentration in the first ten minute fraction rose to 5.1% w/v. The purity in each case remained the same at 82%.

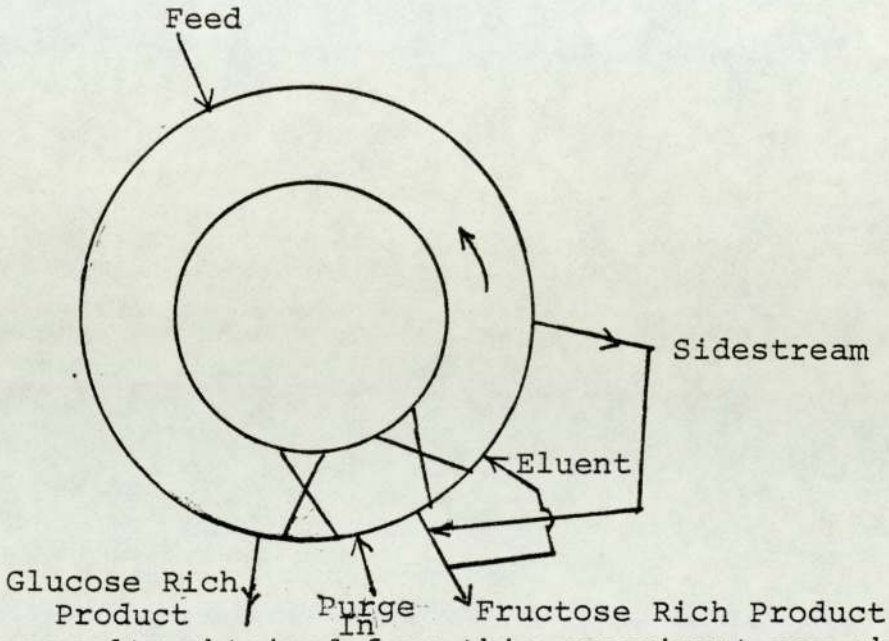
5.1.5.2 By using the Fructose Rich Product as an Eluent

In the operation of the SCCR6 unit the previous eluent entry column becomes the purge or fructose exit column at the end of the switch. By using deionised water as an eluent, the sugar concentration in the eluent entry column was reduced considerably and hence the fructose concentration in the fructose product was low. The use of fructose rich product, collected in the first ten minutes, as an eluent maintained the concentration of sugar in the eluent entry column. The concentration of fructose in the fructose rich product rose from 1.74% to 9.4% but the purity was reduced from 82% to 72%.

By increasing the concentration of sugar in the column, the distribution coefficients of the components were increased. As a result, a higher fraction of glucose and fructose was retained in the stationary phase. The distribution coefficient of glucose increases more rapidly than fructose (see Chapter 3), consequently reducing the purity of the fructose rich product.

5.1.5.3 By the Introduction of a Sidestream

In addition to using the fructose rich product as an eluent, a sidestream was introduced into the system. The sidestream product was collected from the outlet of the column next to the eluent entry column as shown below.



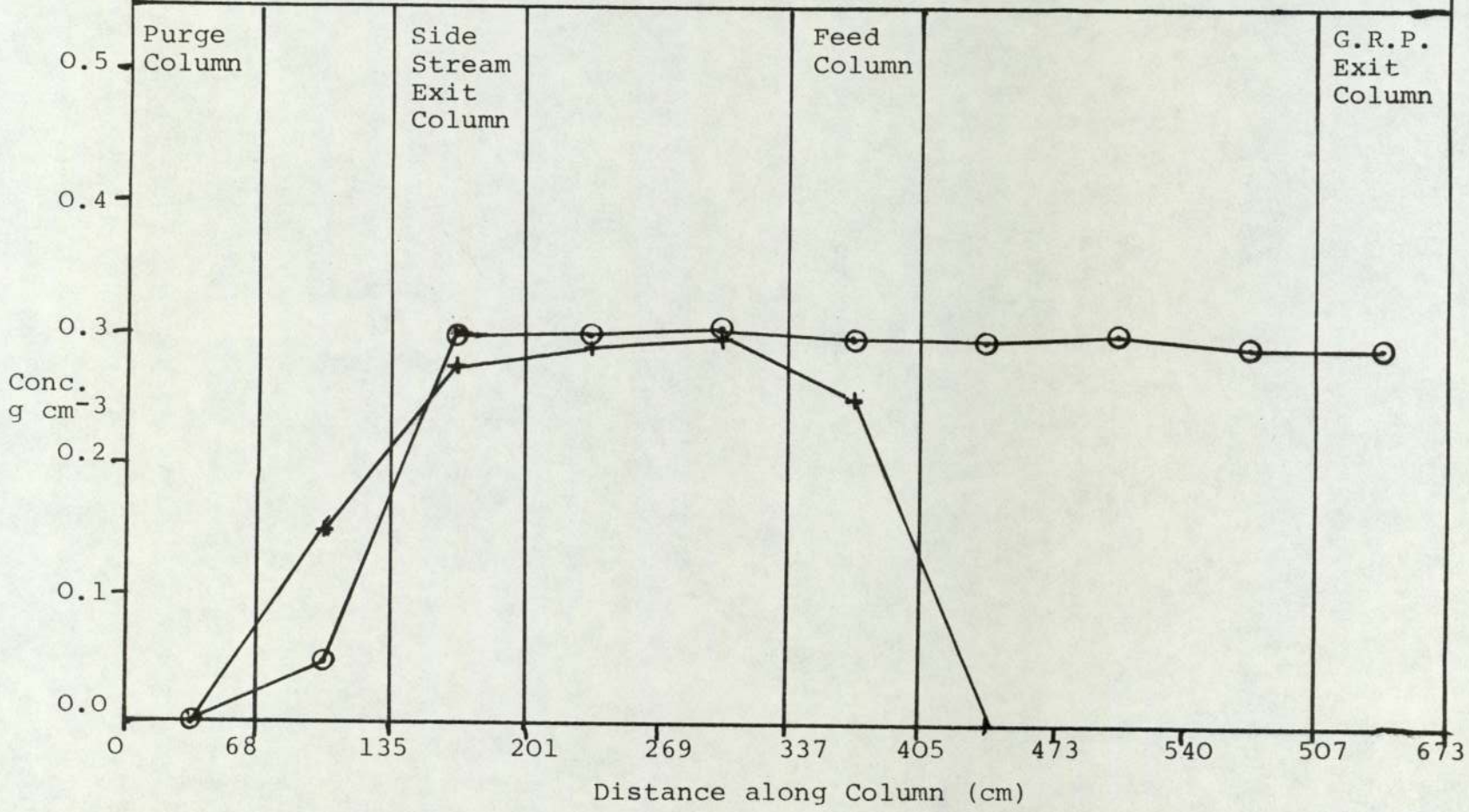
The results obtained from this experiment are shown in Table 5.4 together with the run conditions and the end of run profile in Fig. 5.12. The addition of a sidestream product into the fructose product had an adverse effect. In fact it reduced the concentration of fructose in the product from 7.6% to 6.8% as well as reduced the purity from 70% to 57%.

The results obtained can be explained by looking at the end of run profile, Fig. 5.12. The concentration of glucose is higher in the sidestream exit column than that of fructose. The fructose has more or less the same concentration in the sidestream exit column as the eluent entry column. By adding the sidestream product no improvement to the fructose concentration could be

FIG. 5.12 EXPERIMENTAL CONCENTRATION PROFILE FOR RUN 50-70-210-15-20-R-S

Eluent Flow Rate 210 $cm^3 min^{-1}$, Feed Flow Rate 70 $cm^3 min^{-1}$

Switch Time 15 min, Temperature 20°C



made, but purity was decreased by the addition of extra glucose.

5.2 SEMI-CONTINUOUS SEPARATION OF GLUCOSE AND FRUCTOSE AT ELEVATED TEMPERATURES

The separation of glucose and fructose at ambient temperature has been reported in Section 5.1. In this section the effect of temperature on the semi-continuous separation of the glucose fructose mixture would be described. There are two main reasons for the use of higher temperature

(i) to reduce any biological growth in the columns;

(ii) to reduce the pressure drop across the column length by reducing the viscosity of the mobile phase at high feed concentrations.

The separation performance of the SCCR6 was studied at four temperatures, 20°, 30°, 45° and 60°C. Operating conditions were chosen with the aim of separating glucose and fructose from the feed material and also comparing the on-column concentration profiles at various temperatures.

5.2.1 Experimental Programme

5.2.1.1 Scope

The industrial interest associated with this project required that an evaluation of the SCCR6 capabilities to separate fructose from a mixture of glucose/fructose at an elevated temperature be made. A comparison was

made in terms of separation capability of the SCCR6 by varying the feed concentration in the range 200-600 g litre^{-1}. and the temperature from 20-60^{o}C. The aims of the experimental programme were:-

(i) to study the effect of temperature on the separation capability of the SCCR6 at a constant concentration;

(ii) to study the effect of concentration on the separation capability of the SCCR6 at an elevated temperature.

A run code has been defined in a manner similar to that described in Section 5.1.1.

5.2.2 The Effect of Temperature

Table 5.5 summaries the operating conditions and results for the experiments with an aim of investigating the effect of temperature on the separation capability of the SCCR6 unit at a fixed concentration of 200 g litre^{-1}.

To highlight the effect of temperature the fructose profiles have been plotted separately in Fig. 5.17 together with the individual profiles, Figs. 5.13, 5.14, 5.15 and 5.16 at a temperature of 20^{o}, 30^{o}, 45^{o} and 60^{o}C respectively.

5.2.2.1 Results and Discussion

As the temperature of operation increases, the cross-over point moves to the right towards the glucose exit column. If the glucose profile alone is studied, no significant difference is observed and the

TABLE 5.5 RUN CONDITION FOR STUDYING THE EFFECT OF TEMPERATURE													
RUN NUMBER	AVERAGE FLOW RATES			FEED CONC. % w/v		SWITCH PERIOD (min)	TEMP. °C	AVERAGE PRESSURE DROP			L/P RATIO		
	ELUENT cm^3/min	FEED cm^3/min	PURGE cm^3/min	G	F			ELUENT kN/m^2	FEED kN/m^2	PURGE kN/m^2	PRE FEED	POST FEED	AV
20-35-105-30-20 G	105	35	550	10.1	10.2	30	20	190	55	61	0.165	0.457	0.32
20-35-105-30-30	105	35	550	10.1	10.1	30	30	190	55	60	0.165	0.475	0.32
20-35-105-30-45	105	35	550	9.8	10.2	30	45	150	48	52	0.165	0.475	0.32
20-35-105-30-60	105	35	550	9.9	10.3	30	60	125	39	48	0.165	0.475	0.32

RESULTS FOR STUDYING THE EFFECT OF TEMPERATURE							
RUN NUMBER	FRUCTOSE PRODUCT			GLUCOSE PRODUCT			THROUGH-PUT kg/hr
	PURITY %	MASS BALANCE %	PROD.* CONC. % w/v	PURITY %	MASS BALANCE %	PROD. CONC. % w/v	
20-35-105-30-20 G	99.9	98	0.64	99.9	101	2.37	0.42
20-35-105-30-30	99.9	96	0.65	91.0	108	2.69	0.42
20-35-105-30-45	99.9	96	0.65	91.0	108	2.69	0.42
20-35-105-30-60	99.9	97	0.80	62.0	116	3.31	0.42

* bulk concentration for the product collected over a switch period of 30 minutes

G denotes experiment performed by Gould

FIG. 5.13 EXPERIMENTAL CONCENTRATION PROFILE FOR (J. GOULD'S) RUN 20-35-105-30-20

Eluent Flow Rate 105 $cm^3 min^{-1}$, Feed Flow Rate 35 $cm^3 min^{-1}$,
Switch Time 30 min, Temperature 20°C

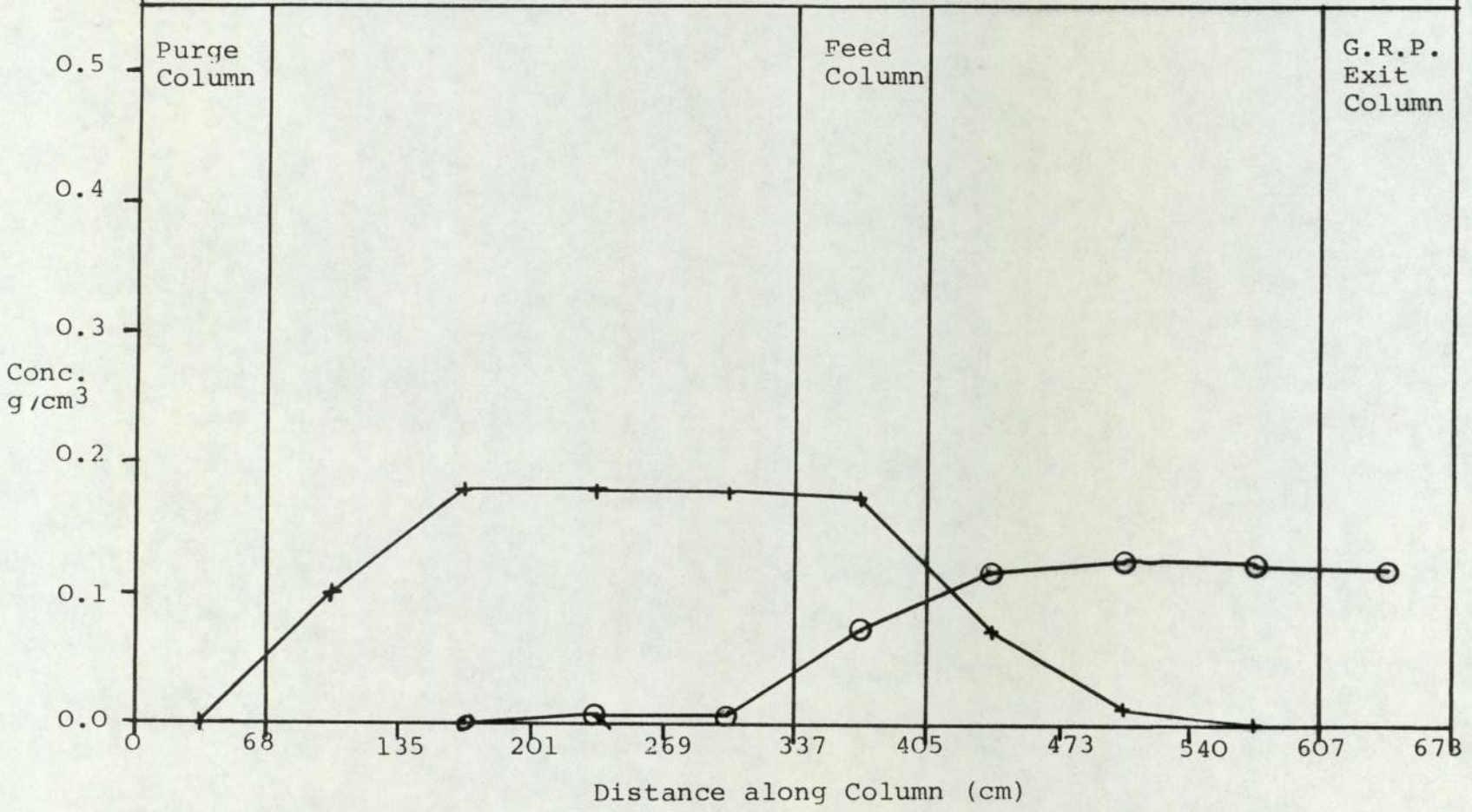
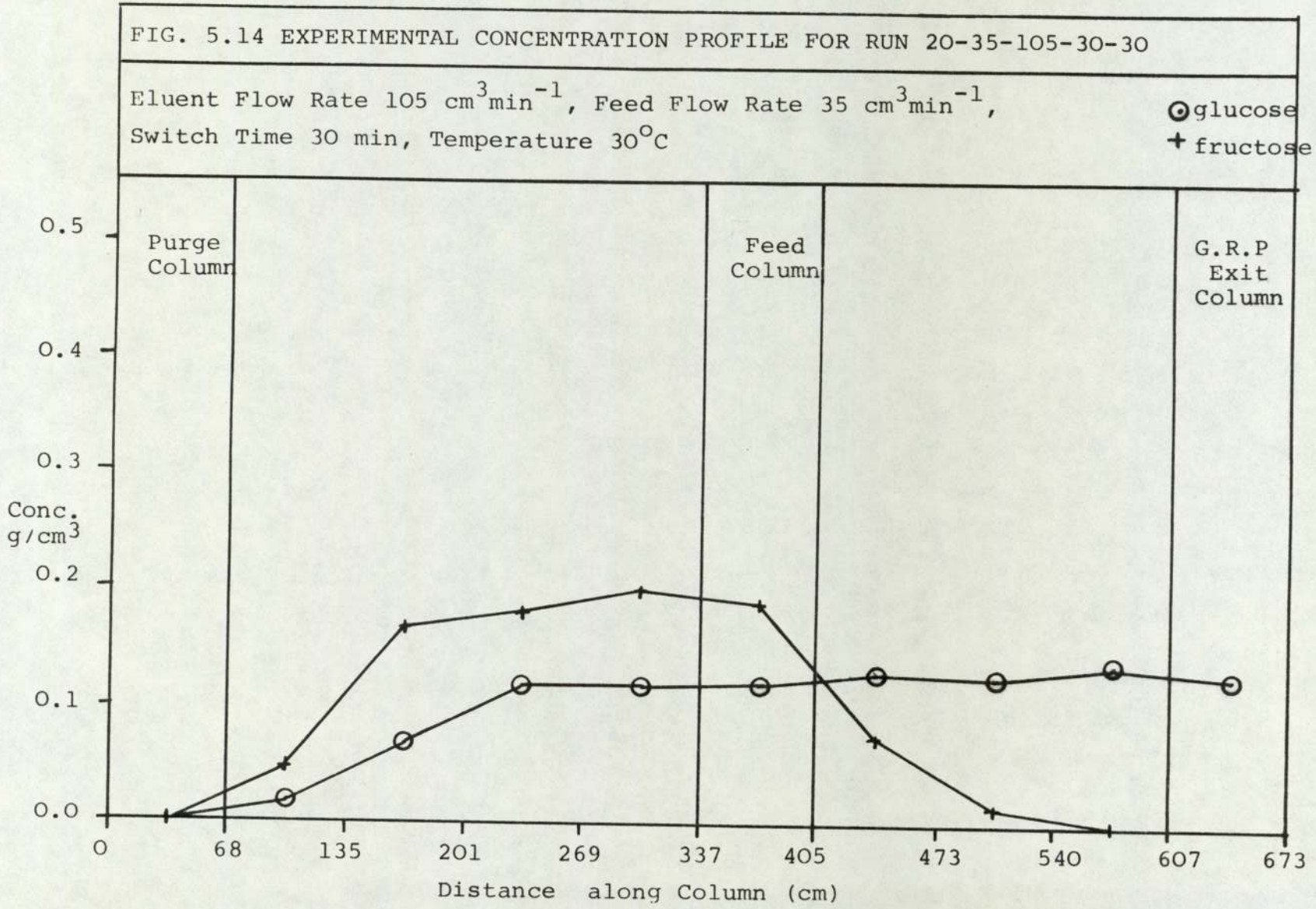


FIG. 5.14 EXPERIMENTAL CONCENTRATION PROFILE FOR RUN 20-35-105-30-30



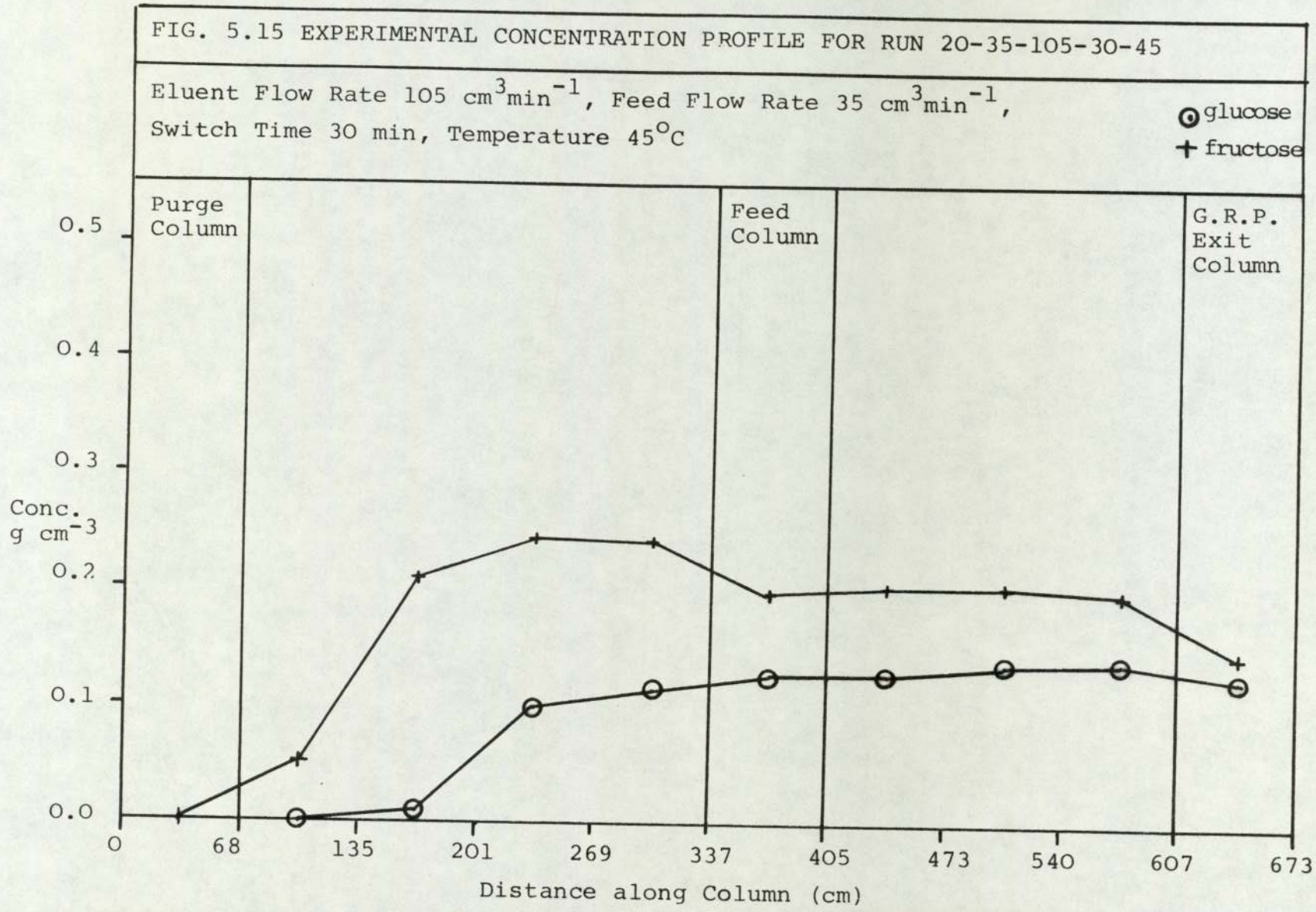


FIG. 5.15 EXPERIMENTAL CONCENTRATION PROFILE FOR RUN 20-35-105-30-45
Eluent Flow Rate 105 cm3min-1, Feed Flow Rate 35 cm3min-1,
Switch Time 30 min, Temperature 45°C
glucose
fructose
Purge Column
Feed Column
G.R.P. Exit Column
0.5
0.4
0.3
Conc. g cm-3
0.2
0.1
0.0
0
68
135
201
269
337
405
473
540
607
673
Distance along Column (cm)

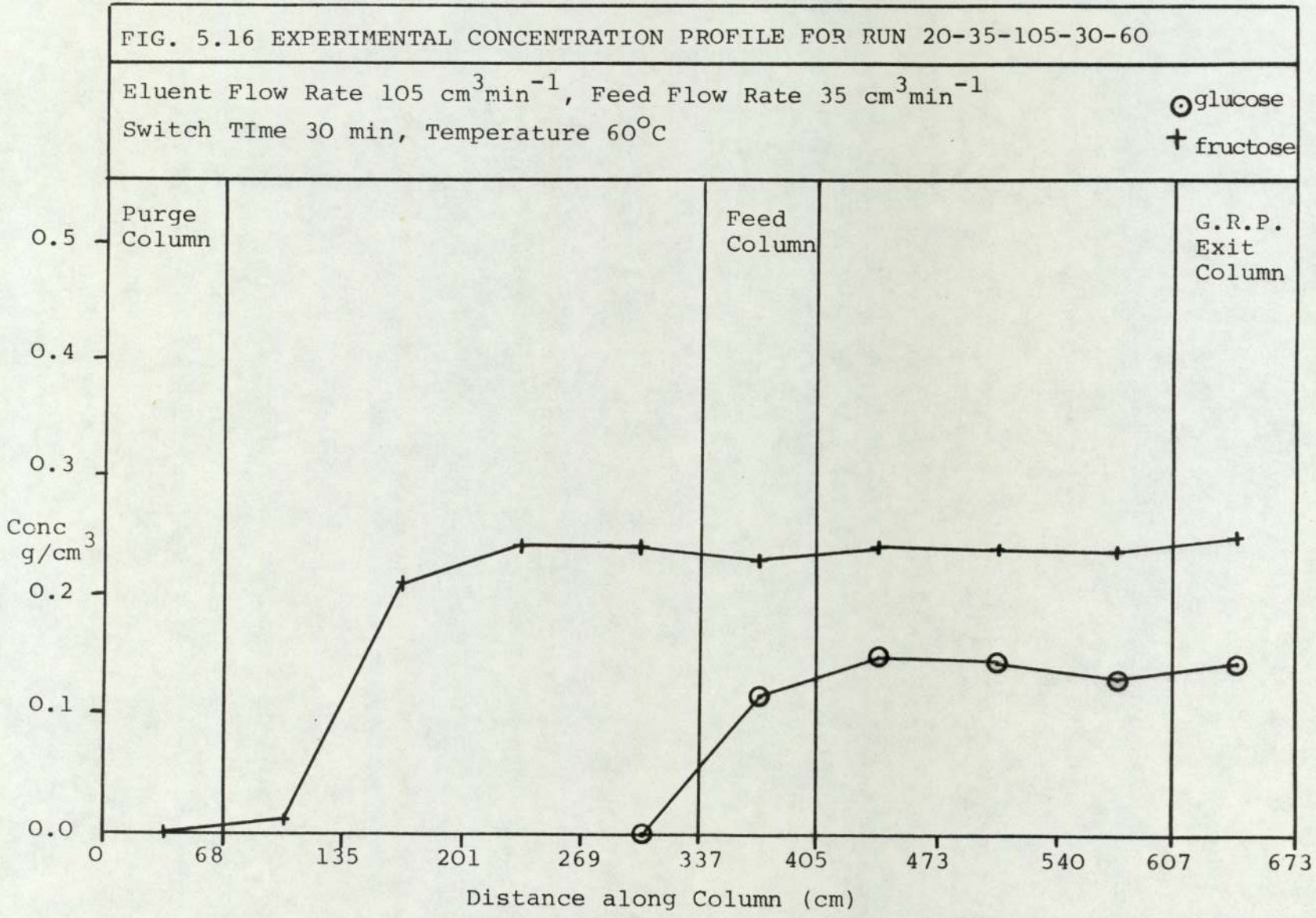
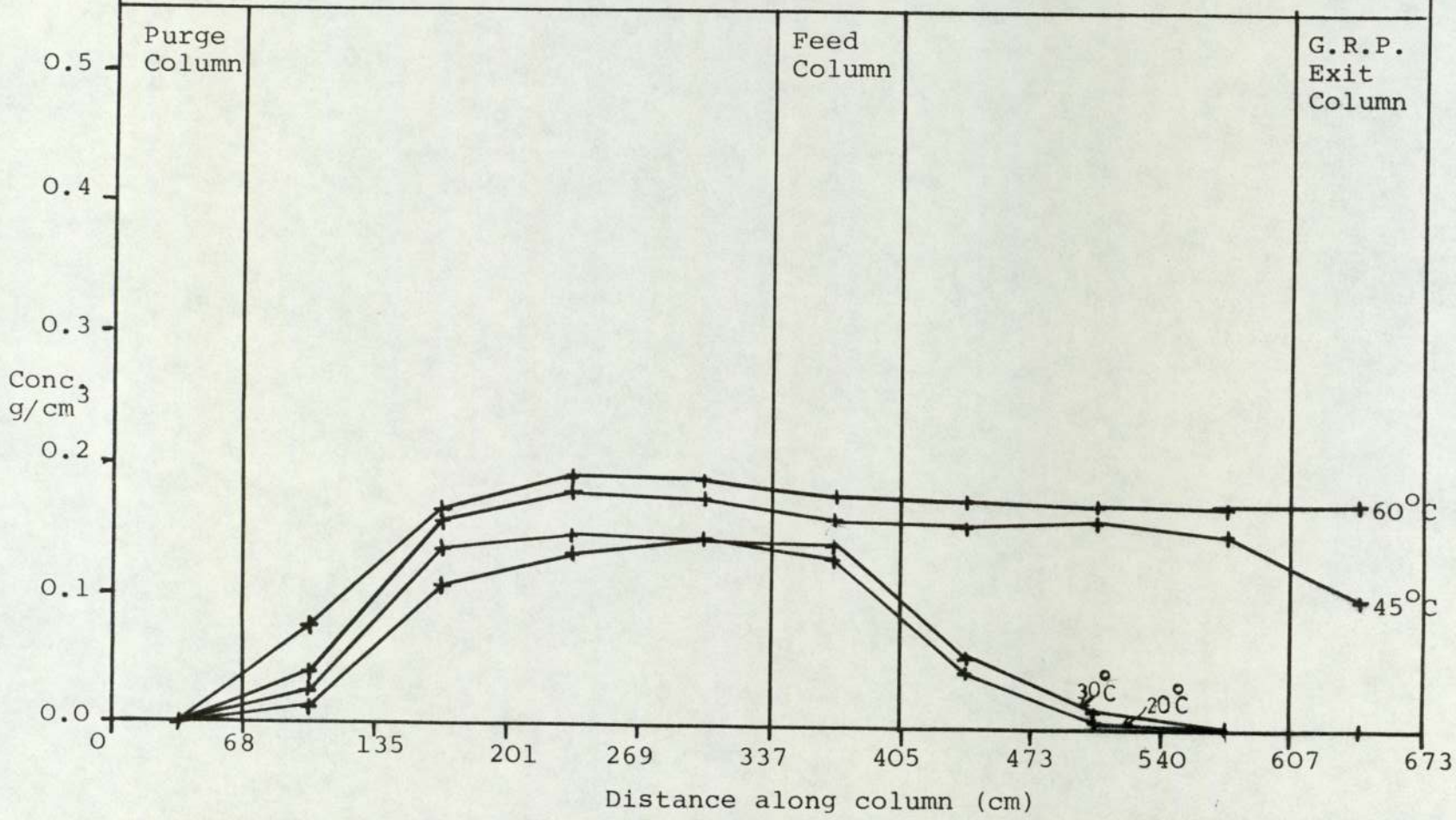


FIG. 5.16 EXPERIMENTAL CONCENTRATION PROFILE FOR RUN 20-35-105-30-60
Eluent Flow Rate 105 cm3min-1, Feed Flow Rate 35 cm3min-1
Switch TIme 30 min, Temperature 60°C
glucose
fructose
Purge Column
Feed Column
G.R.P. Exit Column
0.5
0.4
0.3
Conc g/cm3
0.2
0.1
0.0
0
68
135
201
269
337
405
473
540
607
673
Distance along Column (cm)

FIG. 5.17 INDIVIDUAL FRUCTOSE PROFILES FOR VARYING TEMPERATURE EXPERIMENTS

Eluent Flow Rate 105 $cm^3 min^{-1}$, Feed Flow Rate 35 $cm^3 min^{-1}$,
Feed Concentration 20 g cm^{-3}, Switch Time 30 min



concentrations of glucose in the glucose rich product remains the same. However when the fructose profile is studied, it may be seen that a significant amount of fructose has travelled preferentially with the mobile phase and into the post-feed section. As the temperature is increased, the amount of fructose travelling with the mobile phase is enhanced and consequently a contamination in the glucose rich product has occurred. The purity of the glucose rich product is reduced from 99.9% at 20°C to 62% at 60°C.

As discussed in Section 2.6.5, it is the $2C_5$ form of six ringed β-D fructofuranose, which forms a complex with the calcium ions. The concentration of this form of fructose in equilibrium decreases as the temperature increases; hence fewer fructose molecules are able to form a complex with the calcium ions (95). This lack of formation of complex reduces the retention of fructose, hence more fructose travels with the mobile phase.

5.2.3 The Effect of Concentration at an Elevated Temperature

Table 5.6 summaries the operating conditions and the results for experiments with an aim of investigating the effect of concentration on the separation capability of the SCCR6 unit at a constant temperature of 60°C.

To study the effect of concentration at a temperature of 60°C, the glucose and fructose profiles have been plotted separately in Figs. 5.20 and 5.21 and the individual profiles for feed containing 20, 40 and 60% w/v

TABLE 5.6 RUN CONDITIONS FOR STUDYING THE EFFECT OF FEED CONCENTRATION AT A TEMPERATURE OF 60°C													
RUN NUMBER	AVERAGE FLOW RATES			FEED CONC. % w/v		SWITCH PERIOD min	TEMP °C	AVERAGE PRESSURE DROP			L/P RATIO		
	ELUENT cm^3/min	FEED cm^3/min	PURGE cm^3/min	G	F			ELUENT kN/m^2	FEED kN/m^2	PURGE kN/m^2	PRE FEED	POST FEED	AV
20-35-105-30-60	105	35	550	9.9	10.3	30	60	125	39	48	0.165	0.475	0.32
40-35-105-30-60	105	35	550	20.2	19.7	30	60	235	76	50	0.165	0.475	0.32
60-35-105-30-60	105	35	550	30.0	29.1	30	60	279	95	51	0.165	0.475	0.32

RESULTS FOR STUDYING THE EFFECT OF FEED CONCENTRATION AT A TEMPERATURE OF 60°C							
RUN NUMBER	FRUCTOSE PRODUCT			GLUCOSE PRODUCT			THROUGH-PUT kg/h
	PURITY %	MASS BAL. %	PROD. CONC.* % w/v	PURITY %	MASS BAL. %	PROD. CONC. % w/v	
20-35-105-30-60	99.9	97	0.8	62.0	116	3.31	0.42
40-35-105-30-60	84.0	93	1.4	99.9	91	4.19	0.84
60-35-105-30-60	77.0	94	2.86	99.9	90	5.11	1.26

* bulk concentration for the product collected over a switch period of 30 minutes

sugar solids have been plotted in Figs. 5.16, 5.18 and 5.19 respectively.

5.2.3.1 Results and Discussion

As the concentration of sugar solids in the feed is increased, keeping a constant operating temperature of 60°C, the cross-over point moves to the left towards the fructose rich product exit column. If the individual glucose profile is studied, Fig. 5.20, then a resemblance is observed in comparison to Fig. 5.4. In Fig. 5.4, the effect of concentration on the glucose profile is studied at the ambient temperature. This movement of glucose with the stationary phase can be explained by an increase in the value of the distribution coefficients with on-column sugar concentration.

If the fructose profile alone is studied, Fig. 5.21, a marked pattern is observed. As the concentration of on-column fructose is increased less fructose travels with the mobile phase. The experimental fructose profile could be as a result of three reasons.

(i) as explained in Section 2.6.5, it is the $2C_5$ form of six ringed β-D fructofuranose which forms a complex with the calcium ions. The concentration of this form of fructose, in equilibrium, decreases with an increase in temperature, hence less fructose is available to form a complex.

(ii) as the concentration of fructose in the feed increases, proportionately a greater number of fructose molecules are likely to form a complex

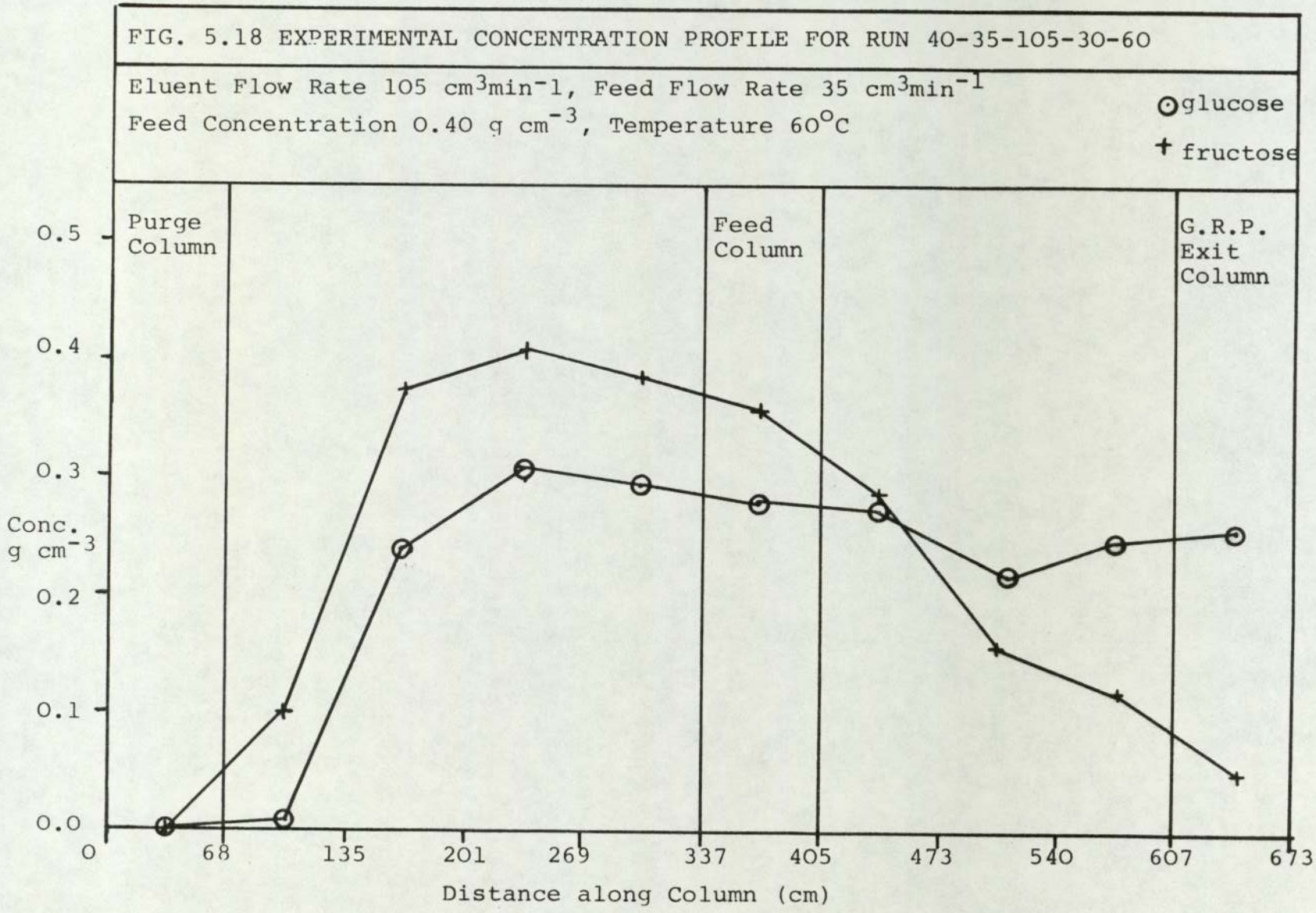


FIG. 5.18 EXPERIMENTAL CONCENTRATION PROFILE FOR RUN 40-35-105-30-60
Eluent Flow Rate 105 cm3min-1, Feed Flow Rate 35 cm3min-1
Feed Concentration 0.40 g cm-3, Temperature 60°C
glucose
fructose
Purge Column
Feed Column
G.R.P. Exit Column
0.5
0.4
0.3
0.2
0.1
0.0
Conc. g cm-3
0
68
135
201
269
337
405
473
540
607
673
Distance along Column (cm)

FIG. 5.19 EXPERIMENTAL CONCENTRATION PROFILE FOR RUN 60-35-105-30-60

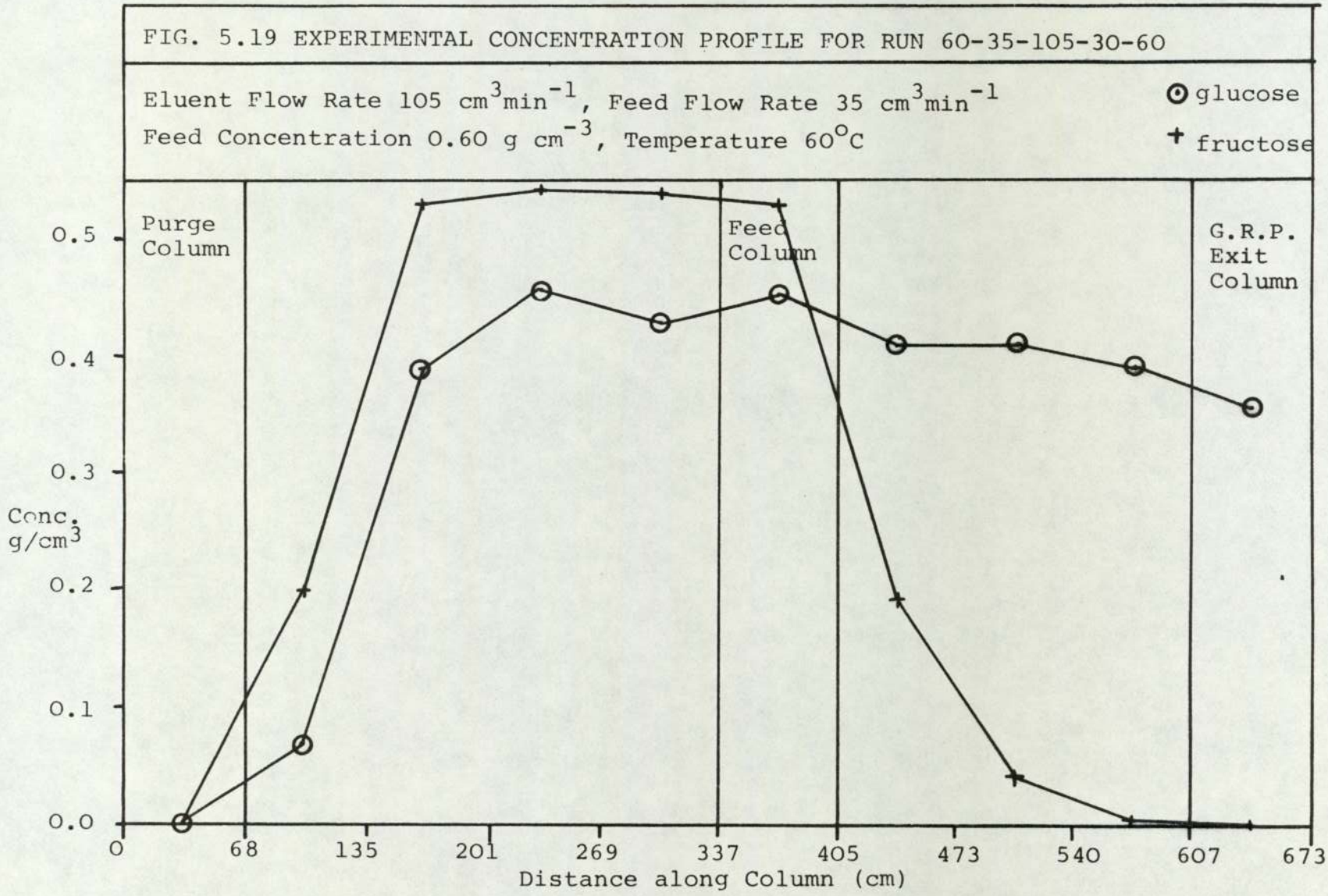


FIG. 5.20 INDIVIDUAL GLUCOSE PROFILES FOR VARYING FEED CONCENTRATION EXPERIMENTS AT AN ELEVATED TEMPERATURE OF 60°C

Eluent Flow Rate 105 $cm^3 min^{-1}$, Feed Flow Rate 35 $cm^3 min^{-1}$

Switch Time 30 min, Temperature 60°C

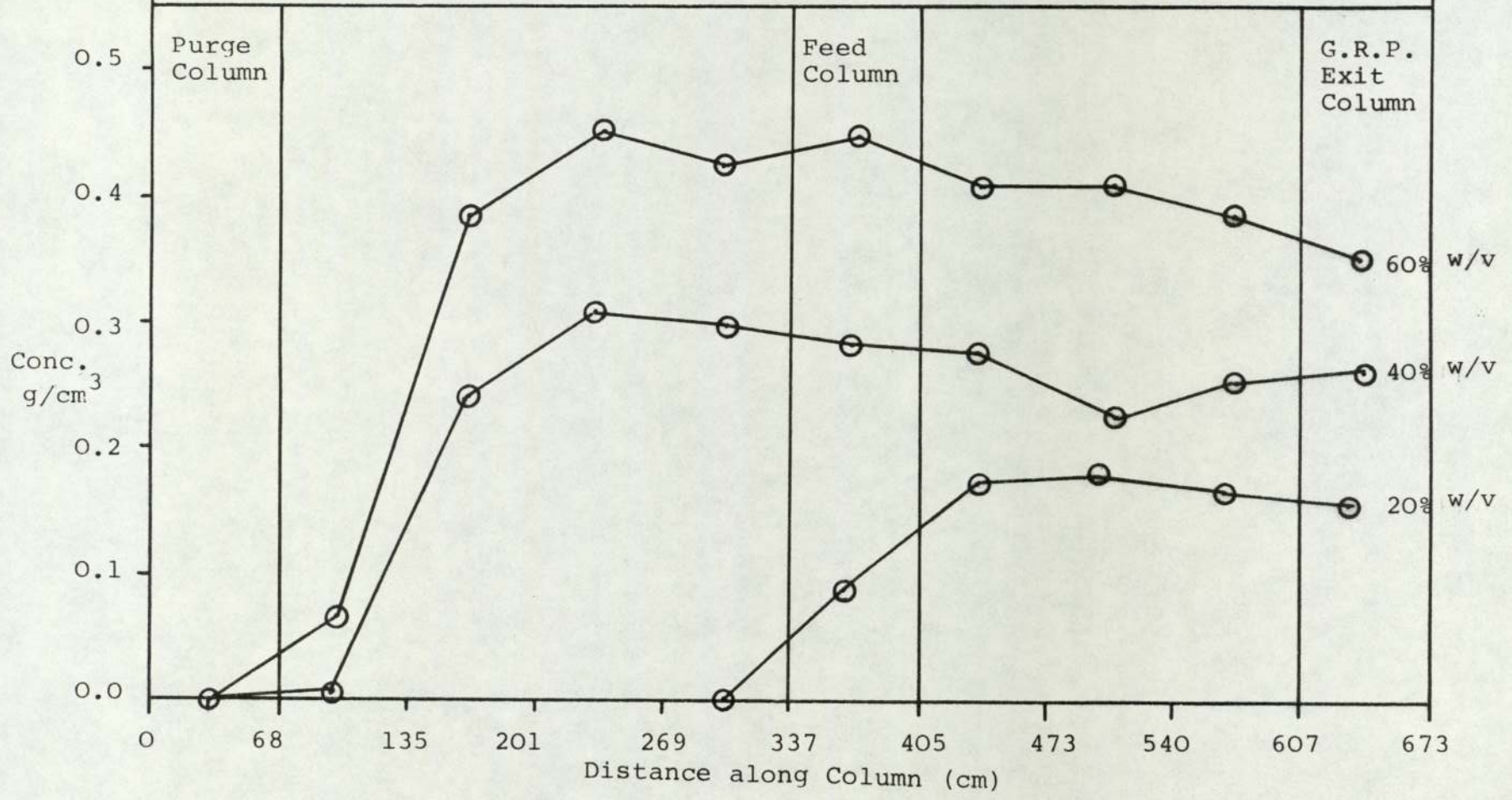
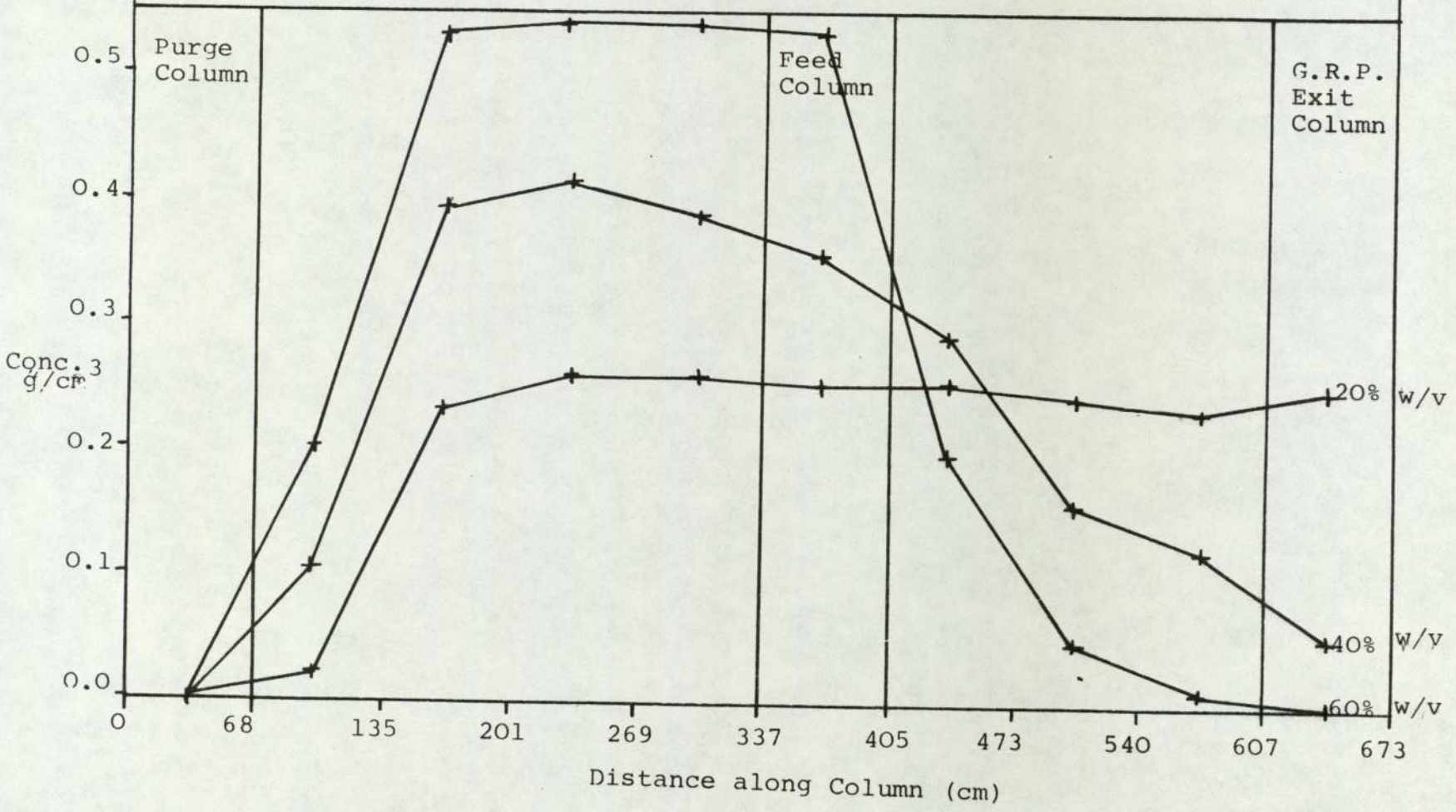


FIG. 5.21 INDIVIDUAL FRUCTOSE PROFILES FOR VARYING FEED CONCENTRATION EXPERIMENTS AT AN ELEVATED TEMPERATURE OF 60°C

Eluent Flow Rate 105 $cm^3 min^{-1}$, Feed Flow Rate 35 $cm^3 min^{-1}$, Switch Time 30 min, Temperature 60°C



with 60% w/v of sugar solids than with 20% w/v of sugar solids. Hence a greater retention is observed.

(iii) as the distributing coefficient of fructose increases with increasing on column sugar concentration (see Chapter 3), more fructose travels with the stationary phase.

When comparing the fructose profiles in Fig. 5.5 and Fig. 5.21, it can be seen that for a particular feed concentration, the fructose has travelled further with the mobile phase at 60^{o}C in comparison to ambient temperature emphasising the effect of reduced complexing at a higher temperature.

5.3 SEMI-CONTINUOUS RUNS WITH FISONS SYNTHETIC FEED

In the manufacture of dextran, a polyglucose, by Fisons Ltd., Pharmaceutical Division, Holmes Chapel, a fructose rich effluent is produced with a sugar solids content of 70% w/v containing:

fructose	68% of total sugar present
dextran	22% of total sugar present
glucose	8% of total sugar present

and reducing sugar 2% of total sugar present.

The commercial feedstock was contaminated by iron, copper, lead, zinc and calcium ions. To avoid any interference with ion exchange resins in this research an artificially produced Fisons feed was used. Work by Chuah (9) showed that the cation resins used in this

work were suitable for performing separations with the actual Fisons feed containing ions.

The feed composition was as follows:

A total of 70% w/v sugar solid in solution containing

Fructose - 69% (w/w)

Glucose - 9% (w/w)

Dextran - 22% (w/w)

Gould (10) performed a number of experiments to investigate the effect of Fisons feed flow rate on the separation efficiency of the SCCR6 unit. In this project two experiments were performed with a view:

(i) to increase the throughput of synthetic Fisons feed comparable to the batch mode;

(ii) to increase the fructose concentration in the fructose rich product by using fructose rich product as an eluent.

5.3.1 Results and Discussion

A run 70-70-210-15-20 was started to increase the throughput of the sugar solids while keeping the L/P ratio similar to the glucose, fructose separation. To increase the concentration of fructose in the fructose product, the fructose rich product was used as an eluent.

After the third cycle, as the concentration of sugar solids in the columns was built up, problems were encountered due to a high pressure drop of 675 kNm^{-2} (100 psi) in the eluent stream. As explained in Section 4.3.6, the control valves were operated by the

TABLE 5.7 RUN CONDITIONS FOR FISONS SYNTHETIC FEED

Run Number	AVERAGE FLOW RATES			FEED CONC. % w/v			SWITCH PERIOD min	AVERAGE PRESSURE DROP			L/P RATIOS		
	ELUENT cm^3/min	FEED cm^3/min	PURGE cm^3/min	D	G	F		ELUENT kNm^{-2}	FEED kNm^{-2}	PURGE kNm^{-2}	PRE FEED	POST FEED	AV
70-70-210-15-20	210	70	550	14.9	6.2	48.3	15	675	340	61	0.165	0.475	0.32
70-70-210-15-60R	210	70	550	14.9	6.2	48.3	15	470	235	61	0.165	0.475	0.32

RESULTS WITH FISONS SYNTHETIC FEED

RUN NUMBER	FRUCTOSE PRODUCT			GLUCOSE/DEXTRAN PRODUCT				TEMP	
	PURITY %	MASS BALANCE %	PRODUCT CONC. % w/v	PURITY %	MASS BALANCE %	PRODUCT CONC. G % w/v	PRODUCT CONC. D % w/v		
70-70-210-15-20	99.9	114	-	-	-	-	-	20	EQUILIBRIUM NOT REACHED
70-70-210-15-60R	99.9	114	16.3	72.0	101	9.7	4.2	60	

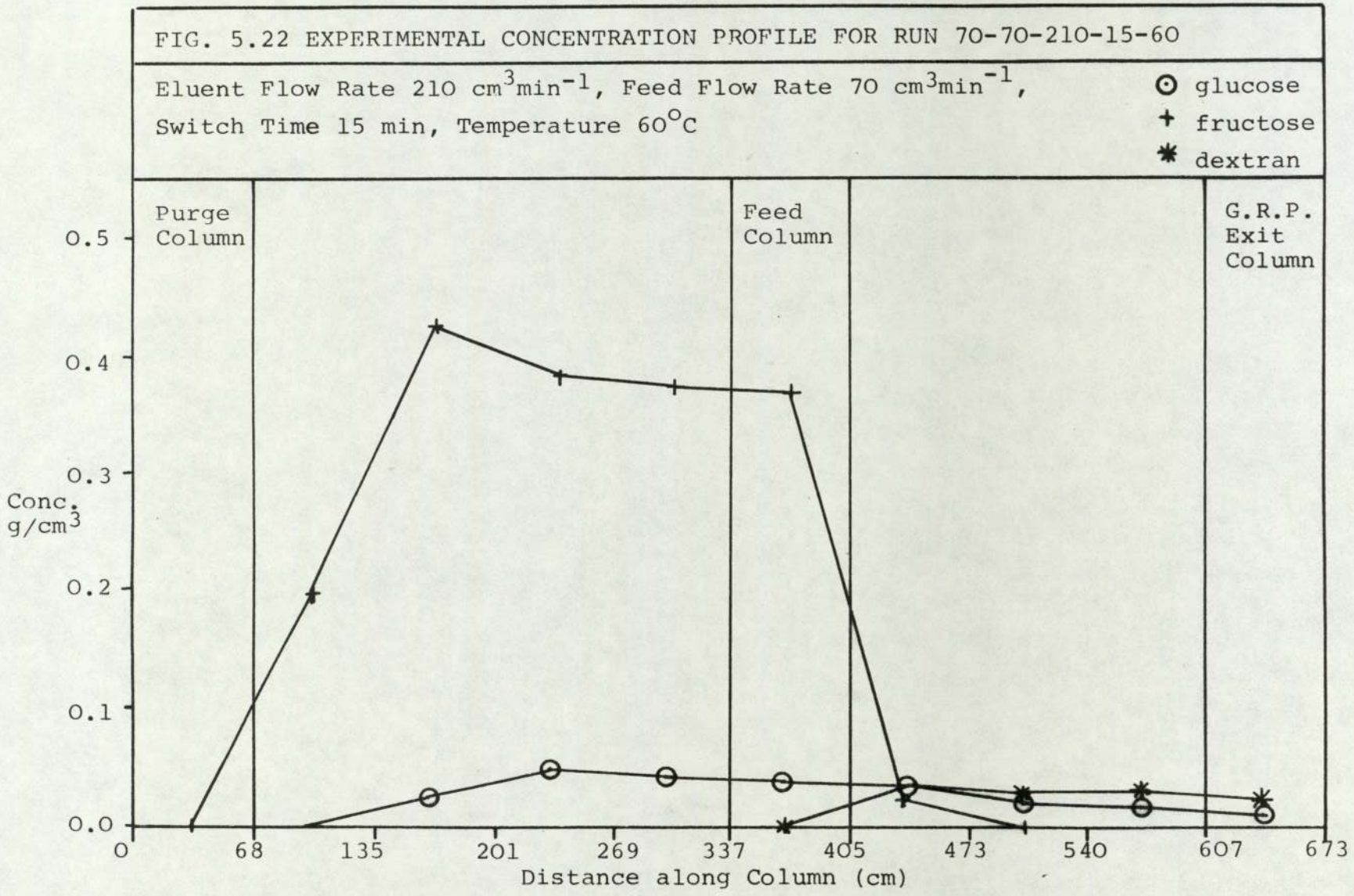
R - The fructose rich product was used as an eluent

differential pressure of the two air streams set at 540 kNm^{-2} (80 psi) and 270 kNm^{-2} (40 psi). With a high pressure drop in the eluent stream, the values did not open after the switching over process causing a rapid increase in the pressure drop.

The above problem encountered with high pressure drop was overcome by increasing the operating temperature from ambient to 60°C. This reduced the eluent pressure drop from 675 kNm^{-2} (100 psi) to 470 kNm^{-2} (70 psi). The results obtained from this run 70-70-210-15-60 is presented in Table 5.7 and the purge profile is shown in Fig. 5.22.

Using the conditions given in Table 5.7, the throughput of sugar solids has been increased to 2.9 kgh^{-1} compared with the maximum throughput by Gould (10) of 2.3 kgh^{-1}. But the best achievement has been recorded in comparing the fructose concentration in the fructose product where a fructose concentration of 16.3% w/v at 99.9% purity has been obtained compared with Gould's 5.1% w/v concentration at 99.9% purity. This is the highest concentration of fructose that has ever been achieved with 99.9% purity using a semi-continuous chromatography equipment similar to the SCCR6 unit.

FIG. 5.22 EXPERIMENTAL CONCENTRATION PROFILE FOR RUN 70-70-210-15-60



CHAPTER SIX

BATCH OPERATION OF THE SCCR6 UNIT

6.1 INTRODUCTION

Chromatography is used extensively as an analytical tool but its development into a viable commercial process is limited because of its low throughput compared with the other unit operations. The usual chromatographic technique normally operates in a small batchwise manner handling micrograms of material, whilst other separation processes such as distillation or solvent extraction are capable of handling tonnage quantities per day. For the last quarter of a century attempts have been made to increase the throughput in chromatography. Two principle approaches have been used:

(i) direct scale up of analytical equipment and introduction of repetitive feed injection into large diameter columns.

(ii) the development of novel designed equipment that permit continuous introduction of the feed, i.e. semi continuous chromatography (see Chapter 5).

This chapter deals with part (i) of this development.

6.1.1 Batch Chromatography

Batch chromatography involves injection of the feed into the column which is then eluted by the eluent. The product profile at the outlet has the shape as

FIG. 6.1 A SINGLE CHROMATOGRAM FOR GLUCOSE/FRUCTOSE MIXTURE

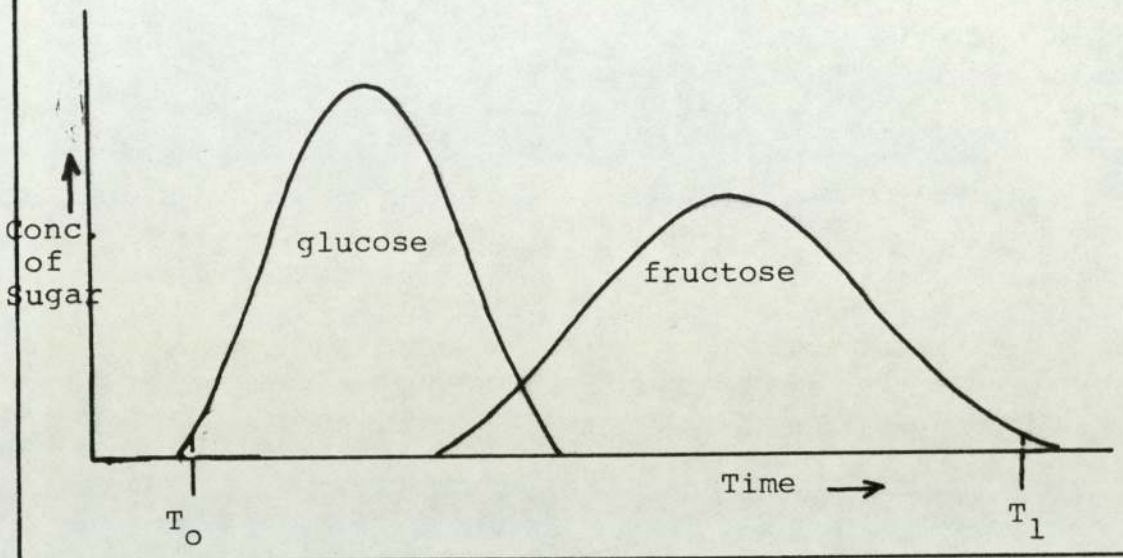
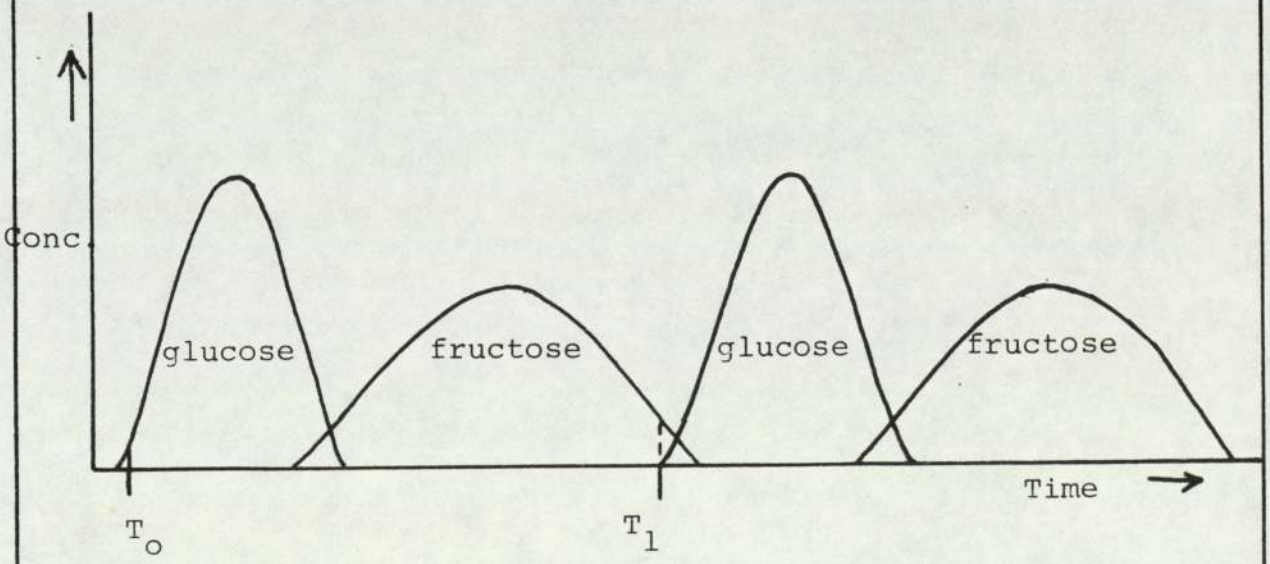


FIG. 6.2 REPETITIVE CHROMATOGRAPH FOR GLUCOSE FRUCTOSE MIXTURE



shown in Fig. 6.1.

6.1.2 Repetitive Batch Chromatography

Repetitive batch chromatography is effectively a continuous process because the discrete feed batches are injected repeatedly at a set time interval for as long as the plant is in operation. A typical chromatogram resulting from a repetitive batch process is shown in Fig. 6.2.

From the product concentration profile at the outlet it can be seen that if pure products are required then the valley section (overlap) containing the mixture of the two components must be recycled. This in fact limits the throughput in the repetitive batch chromatography, since the higher the throughput, the greater the overlap and hence an increase in recycling.

6.2 EQUIPMENT USED

6.2.1 Description of the Equipment

The same equipment SCCR6 (described in Chapter 5) which was used for semi-continuous operation was used for the batch experiments. It consisted of ten stainless steel columns (10.8 cm I.D. x 65 cm long) connected alternatively at the top and bottom to give an overall separation length of columns of 650 cm. Each column was packed with zerolit SRC14 (150-300 μm) resin conditioned to the calcium form.

6.2.1.1 Conversion of the SCCR6 Unit to Operate in the Batch Mode

Chapter 5 described the arrangement of valves when the equipment SCCR6 was operated in semi-continuous mode. Fig. 6.3 represents the arrangement of valves when the eluent enters into column 1 of the SCCR6 while it is operated in the semi-continuous mode. To convert the SCCR6 unit to operate in the batch mode a few adjustments were made, namely:

(a) A direct connection was made between the adjacent columns (except between columns 10 and 1), omitting the transfer valves to minimise the liquid hold-up in the system. To separate column 10 from 1, the transfer valve between the two was kept closed.

(b) The feed and eluent were introduced directly into column 1 via two three way valves which allowed an input of either the feed mixture or the eluent to the column.

(c) The valves (see Fig. 6.3)

(i) the feed entry to column 5

(ii) the product exit from column 9

(iii) the purge inlet to column 10

were closed allowing only one product outlet valve from column 10 to remain open.

The arrangement of the SCCR6 unit in the batch mode is shown in Fig. 6.4. A polarimeter was used qualitatively in the product line for identification of glucose/fructose in the eluent stream.

FIG. 6.3 ARRANGEMENT OF SCCR6 IN SEMI CONTINUOUS MODE WHEN COLUMN 10 IS BEING PURGED

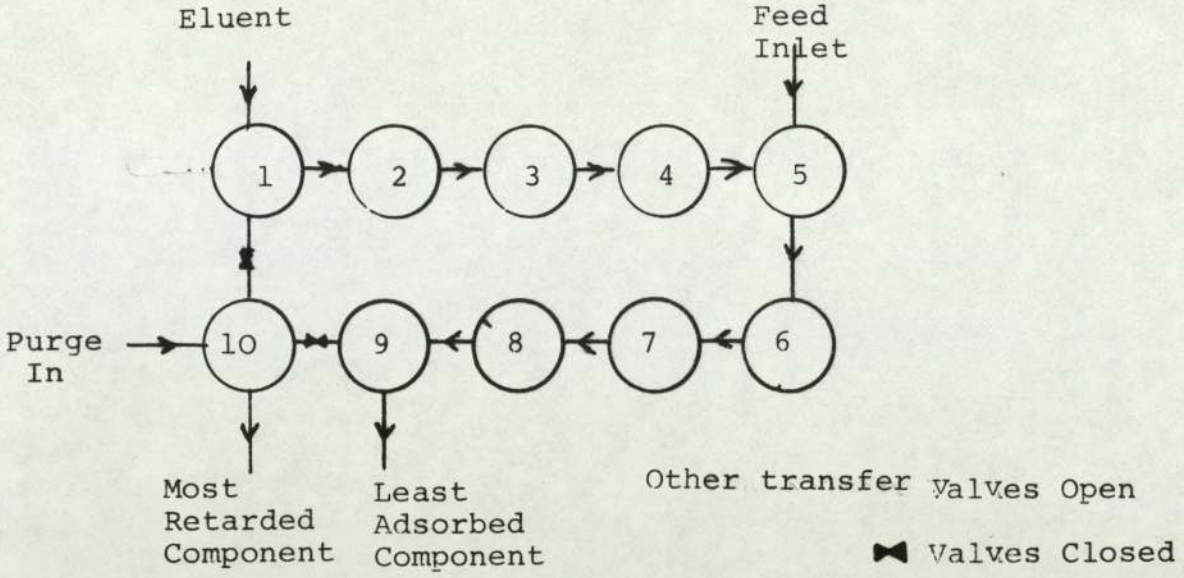
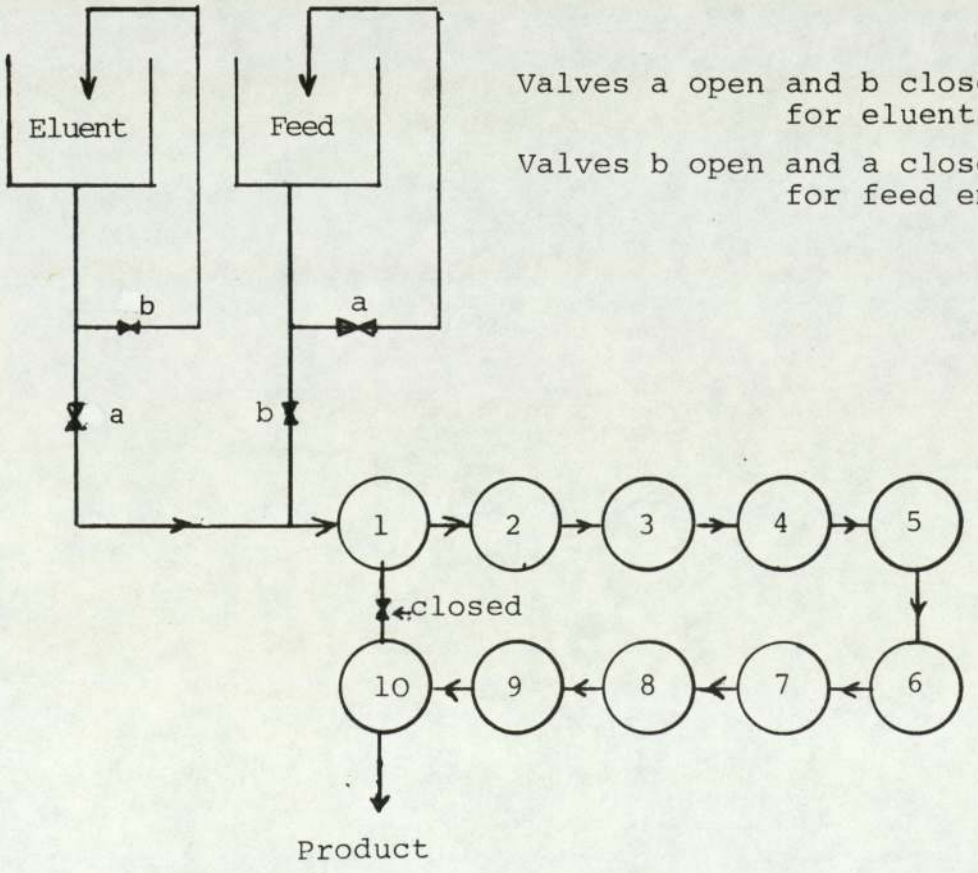


FIG. 6.4 BATCH ARRANGEMENT OF THE SCCR6 UNIT



Valves a open and b closed simultaneously for eluent entry

Valves b open and a closed simultaneously for feed entry

6.2.2 Eleunt and Feed System

Eluent, deionised water, passed from the reservoir via a positive displacement metering pump. Both the eluent and the feed solution were pumped by a 'M.P.L. KV TWIN METRIPUMP' supplied by Metering Pumps Limited, Ealing, London and fitted with a 2800 r.p.m. motor operating at 96 strokes per minute. The eluent left the pump via 4 mm i.d./6 mm o.d. polypropylene tubing through the three way valves where it was either directed onto the separating column or to the drain. In the case of the feed stream from the three way valve it was directed either to the separating column or back to the reservoir (see Fig. 6.4).

6.3 EXPERIMENTAL TECHNIQUES

6.3.1 Preparation of the Feed Solution

Approximately 110 litres of the feed was prepared to allow for a whole set of experiments to be performed. The amount of glucose, fructose and water required was calculated. The sugar was weighed out in the plastic tank of capacity 120 litres and water was added last. For a low concentration of sugar (<40% w/v of sugar) cold water could be used, but for the preparation of a concentrated feed mixture hot water was required. For any concentration of dextran, the heating of the feed mixture was essential. 0.02% w/v of sodium azide was added to the feed to avoid the growth of micro-organisms in the sugar solution.

6.3.2 Flowrate and Pressure Measurements

The flowrates of both the feed and the eluent were measured frequently to ensure that the pumps were operating correctly. The measurement of these flow rates were via the calibrated glass tubes. The tubes were filled with either the eluent or the feed from their respective reservoir via the glass three way valves. The time taken for the discharge of a known volume of the feed or the eluent was measured hence the flow rates calculated.

The discharge pressure from the feed and the eluent pump heads were continuously monitored by two Bourdon gauges, 0-1800 knm^{-2} (0-250 psi).

The pulsation produced by the metering pump was minimised by the restriction of the fluid movement to the gauges, by using screw clips on the polypropylene tubing immediately before the pressure gauge.

6.3.3 Sample Analysis

The feed, the bulk products, the waste fraction and the product samples collected at an interval of 5 minutes throughout the duration of the chromatogram were analysed using the bio-rad (HPLC) column (Section 4.9)

6.4 EXPERIMENTAL PROGRAMME

6.4.1 Scope

The principle aim of this experimental programme was to establish the throughput and concentration of

the glucose fructose and dextran, and glucose fructose mixtures that could be obtained by repetitive batch chromatography. This information would then be used to compare repetitive batch chromatography with a semi-continuous mode of operation.

The experimental programme concerned with the repetitive batch chromatography for the separation of glucose fructose and dextran, glucose and fructose mixtures had the following objective:

1. To produce suitable products of acceptable purity and concentration in a single pass of the feed solution through the apparatus.
2. To determine the maximum rate of separation by the given quantity of chromatographic packing; bounded by the constraints of producing an acceptable product and within the pressure limitation of the apparatus.
3. Also to investigate the effect of sample volume upon the separation ability of the apparatus and its effect upon the quality of the products.
4. Investigate the effect of sample concentration upon the separation ability of the apparatus and its effect upon the quality of the products.
5. Investigate the effect of temperature upon the separation ability of the apparatus and its effect upon the quality of the products.

6.4.2 Experimental Conditions

The experimental condition for the repetitive batch study were dominated by the requirement to maximise the throughput of sugar. When these columns were used in a semi-continuous mode by Gould, an eluent flow rate of 105 cm^3min^{-1} was frequently used (10). As a result of this the volumetric flow rate in the batch runs were chosen to be 105 cm^3min^{-1}. This produced a pressure drop of 504 kNm^{-2}(75 psi) across the columns. The maximum value of sample volume was bounded by the highest volume of feed that could be injected onto the column to produce an acceptable product. However the limitation on the concentration of feed sample was set by the solubility of the components in the feed mixture. Since Gould (10) used the feed concentration varying between 20-70% w/v of sugar, a similar concentration range was adopted for the batch experiments.

As soon as the polarimeter indicated the arrival of the first component from the outlet stream, the sample collection began at an interval of five minutes. The analysis of these samples produced a chromatogram, a graph of concentration of components vs time measured from the injection of sample, for a single batch (Fig. 6.1). From the chromatogram the time T_1-T_o (see Fig. 6.1) was measured. The feed was then introduced at an interval of time T_1-T_o to produce a product output trace as shown in Fig. 6.2. Using the repetitive batch technique and by collecting the products from the appropriate part of the chromatogram, the final

products and the recycle fractions were obtained.

The above procedure was repeated for each feed concentration and for all the different volumes of sample that were injected into the column.

Reports in the literature vary as to what size the volume of the injected feed can be as a percentage of the total column volume. Therefore a wide variation of the injected samples, equivalent to a 2 to 25% of the total column volume, were used.

6.4.3 Feed Solution

The glucose and fructose used to make feed solutions were bought in 25 kg bags. The glucose sold as mono-hydrate dextrose was supplied by L. Garvin Ltd., Isleworth, and fructose by Kingsley Keith Ltd., Croydon.

6.4.4 Overall Result

The details of repetitive batch experiments at ambient temperature are contained in Table 6.1. The following discussion will centre on three main points:

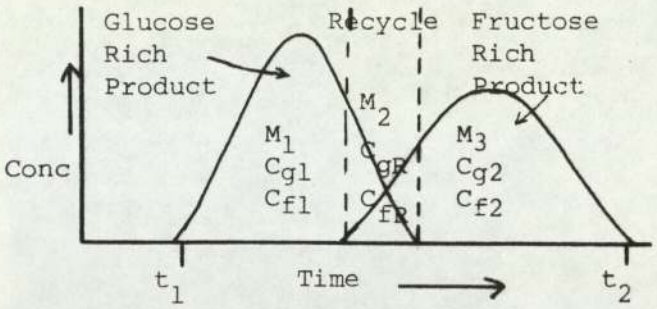
(a) What effect the volume of sample injected had upon the resulting products.

(b) What effect the concentration of the feed had upon the resulting products.

(c) What effect the temperature of the operation had upon the resulting product.

These topics will be discussed individually.

TABLE 6.1 EXPERIMENTAL DATA FOR BATCH EXPERIMENTS AT AMBIENT TEMPERATURE



M = Mass (kg)

C = bulk concentration (g/100 cm^3)

Subscript g - glucose
f - fructose
1 - glucose rich product
R - recycle
2 - fructose rich product

Expt No	Feed Conc	Vol Injected (l)	G.R.P.			RECYCLE			F.R.P.			$T=t_2-t_1$ (sec)
			M_1	C_{g1}	C_{f1}	M_2	C_{gR}	C_{fR}	M_3	C_{g2}	C_{f2}	
1	20	1.2	9.71	.98	-	1.72	.25	.13	17.87	-	.44	15500
2	20	2.4	13.91	1.78	.06	.68	.39	.44	20.26	.12	.93	15500
3	20	6	10.9	5.27	-	5.45	.72	3.35	12.5	-	3.57	16800
4	20	12	13.4	7.09	-	7.5	4.03	6.55	15.45	-	5.18	20520
5	20	15	12.5	7.65	-	9.77	5.78	6.84	15.9	-	5.44	21800
6	20	1.2	10.5	1.76	-	4.5	.24	.86	14.1	-	1.1	17700
7	20	2.4	10.0	3.2	-	5.45	.7	1.34	12.27	-	2.38	17700
8	20	6	11.8	8.2	-	2.7	.73	3.93	14.1	-	5.71	17040
9	20	12	11.8	13.28	-	5.3	3.15	10.1	14.77	-	8.0	20760
10	20	15	11.8	13.3	-	11.3	5.7	12.3	14.09	-	8.77	20760
11	40	1.2	11.01	2.48	-	.91	.79	.43	19.03	-	1.59	15840
12	40	2.4	12.18	4.42	-	1.28	1.7	1.19	19.05	.06	2.82	17950
13	40	6	13.64	8.51	-	3.64	1.31	5.6	14.54	-	5.89	15480
14	40	12	16.36	13.49	-	8.18	2.82	15.5	13.64	-	6.93	20280
15	40	15	14.55	15.52	-	8.18	5.67	15.02	14.1	.1	10.33	20280
16	50	1.2	16.5	3.04					18.41	.053	1.58	17400
17	50	2.4	11.14	4.67					18.41	.09	2.62	16200
18	50	3.6	12.27	7.11					18.64	.17	4.89	17100
19	50	4.8	13.18	8.52					19.77	.33	6.31	17220
20	50	6	13.4	10.29	-	3.6	1.52	6.37	15.09	-	7.04	16800
21	50	12	13.6	17.9	-	5.0	5.1	10.38	15.9	-	12.85	19080
22	50	15	14.8	21.9	-	7.95	5.97	18.66	15.0	-	12.9	20520
23	60	1.2	10.1	3.02	-	7.25	1.11	1.1	16.93	-	1.9	18600
24	60	2.4	10.35	6.74	-	8.0	2.01	3.47	15.65	-	3.95	19500
25	60	6	14.09	12.6	-	-	-	-	21.8	.15	8.03	17040
26	60	12	15.45	21.99	-	-	-	-	22.7	1.56	15.1	17400
27	60	15	15.9	21.85	-	7.27	9.72	23.98	17.73	.1	15.05	21600

Continuation - Table 6.1

A batch run is defined as 20-2-100-100-20

where

20 = Concentration of feed (% w/v)

2 = Volume of feed injected expressed as percentage of total empty column volume, i.e. 2% of total empty column volume

100 = Eluent flow rate ($cm^3 min^{-1}$)

100 = Feed flow rate ($cm^3 min^{-1}$)

20 = Temperature (^{o}C)

6.5 THE EFFECT OF SAMPLE VOLUME

In experiments 1,2,3,4,5 the quantity of sugar loaded onto the column during each injection ranged from 0.24-3.0 kg. The concentration of the feed solutions for each of the experiments was kept constant at approximately 200 g litre^{-1}. The variation of the sample loading was by virtue of changing the volume of feed injected from 1.2 litres to 15 litres. The resulting chromatograms from experiments 1-5 are presented in Figs. 6.5-6.9.

6.5.1 Results and Discussion

An increase in the volume eluted, prior to the product collection, was observed with increasing sample volume, Fig. 6.10, hence indicating an increase in the retention volume of the components. A study into the behaviour of resin at higher concentrations of sugar showed that the distribution coefficients of glucose and fructose increased with increasing on column concentrations (see Chapter 3). The distribution coefficient is defined as the ratio of the concentration of the component in the stationary phase to that of the same component in the mobile phase. The value of this parameter could therefore be interpreted as the measure of the strength with which a component is retained in the stationary phase. The higher the value of the distribution coefficient, the stronger the retention and the greater the elution volume. By increasing the volume of sample injected into the

FIG. 6.5 EXPERIMENTAL CONCENTRATION PROFILE FOR THE BATCH RUN 20-2-100-100-20

Feed Conc. 0.2 g/cm^3, Feed Volume Input 1200 cm^3 (2% of empty column volume)

Eluent Flow Rate 100 cm^{3}min^{-1}, Temperature 20°C

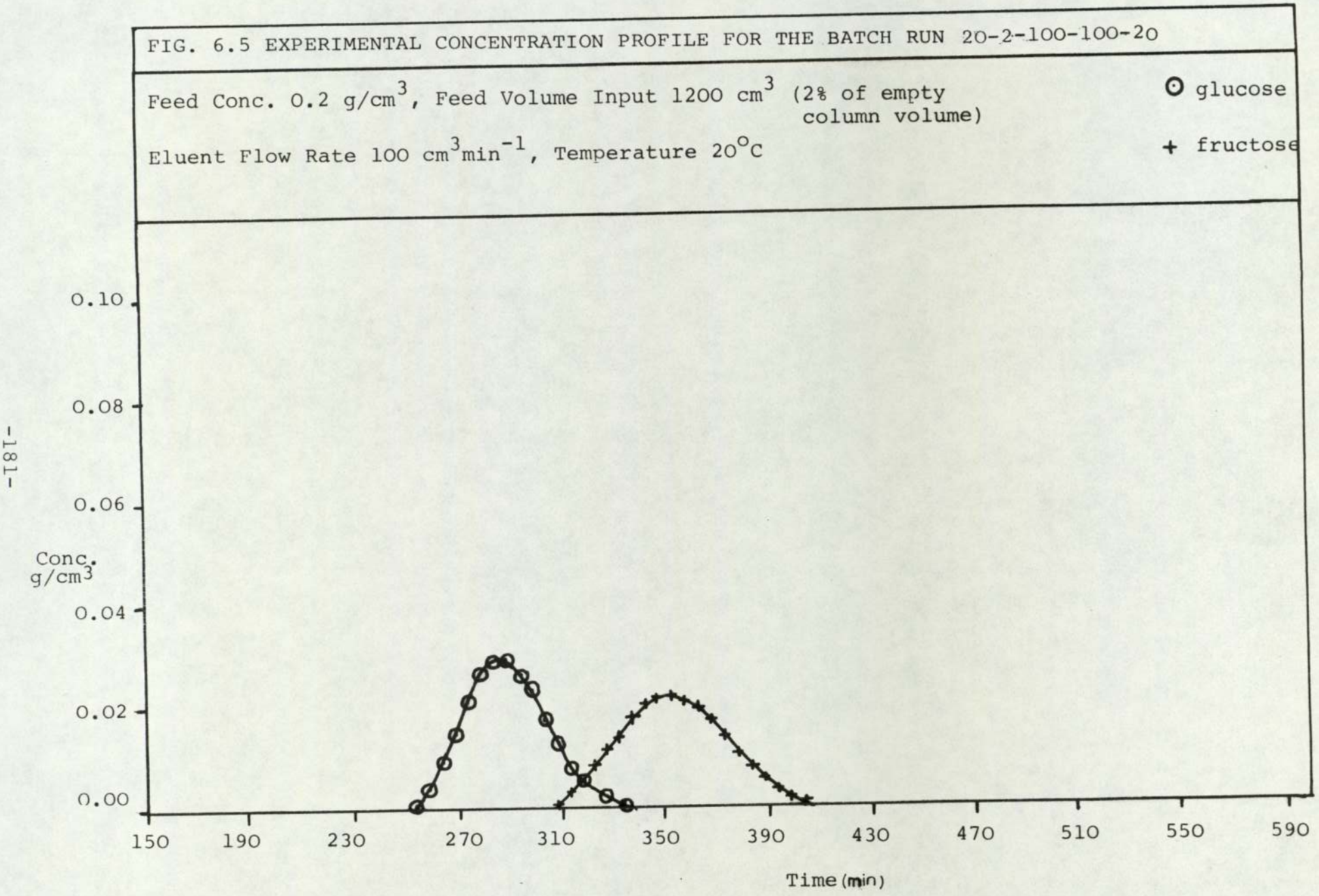


FIG. 6.6 EXPERIMENTAL CONCENTRATION PROFILE FOR THE BATCH RUN 20-4-100-100-20

Feed Conc. 0.20 g/cm^3, Feed Volume 2400 cm^3 (4% of total empty column volume)

Eluent Flow Rate 100 cm^{3}min^{-1}, Temperature 20^{o}C

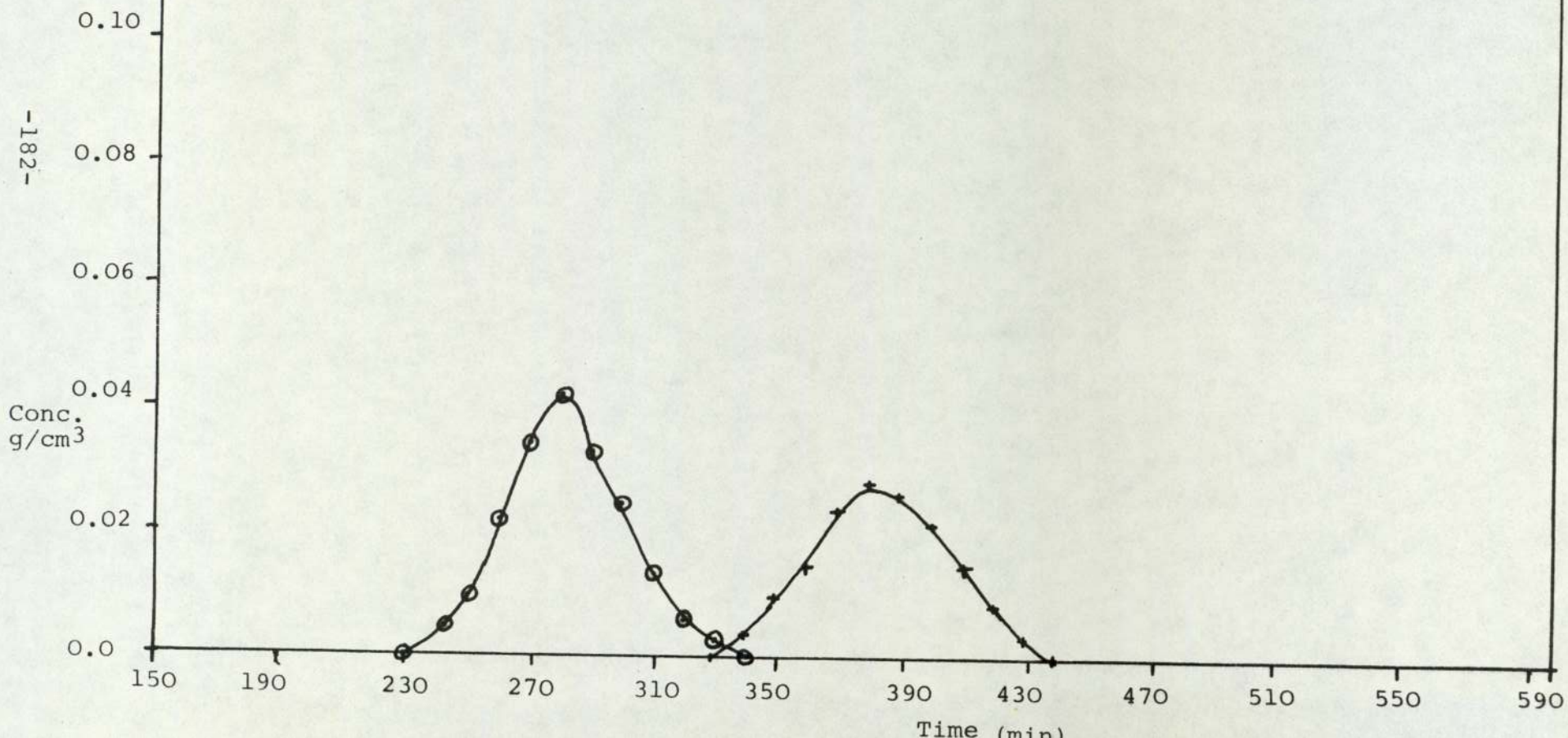


FIG. 6.7 EXPERIMENTAL CONCENTRATION PROFILE FOR BATCH RUN 20-10-100-100-20

Feed Conc. 0.2 g/cm^3, Feed Volume 6000 cm^3 (10% of total empty column volume)

Eluent FLow Rate 100 cm^{3}min^{-1}, Temperature 20^{o}C

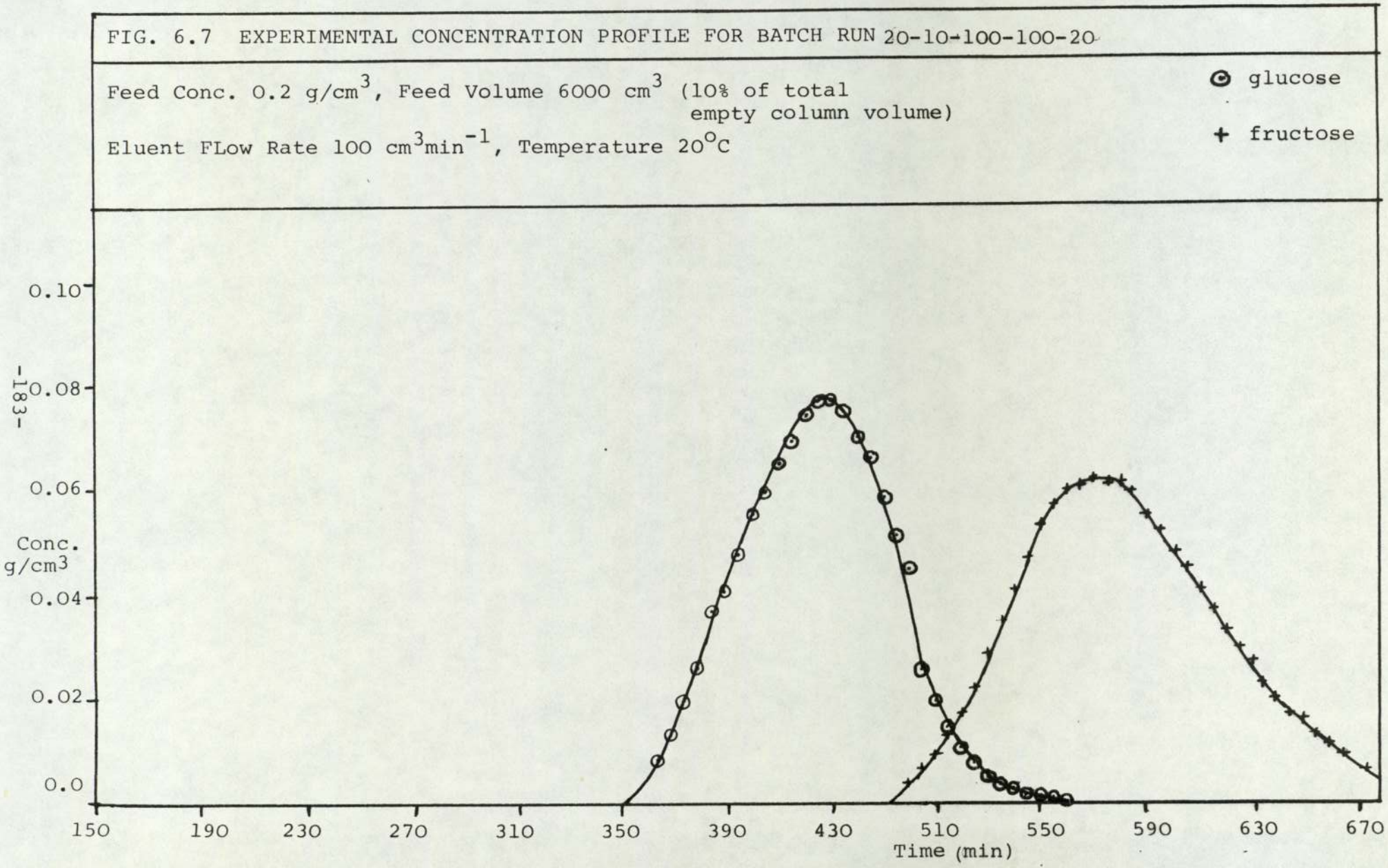


FIG. 6.8 EXPERIMENTAL CONCENTRATION PROFILE FOR BATCH RUN 20-20-100-100-20

Feed Conc. 0.20 g/cm^3, Feed Volume 1200 cm^3 (20% of total empty column volume)

Eluent Flow Rate 100 cm^{3}min^{-1}, Temperature 20^{o}C

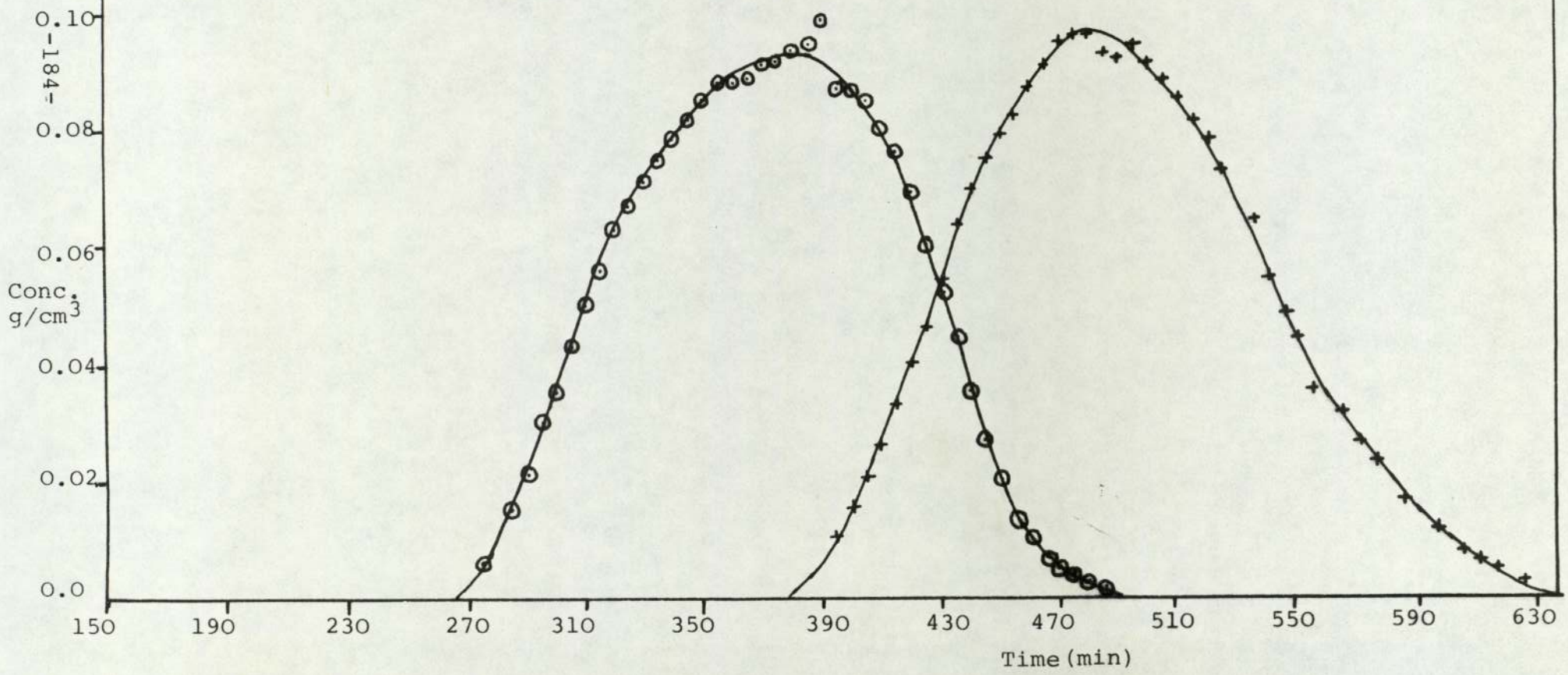


FIG. 6.9 EXPERIMENTAL CONCENTRATION PROFILE FOR BATCH RUN 20-25-100-100-20

Feed Concentration 0.2 g/cm^3, Feed Volume 15000 cm^3 (25% of total empty column volume)

Temperature 20^{o}C

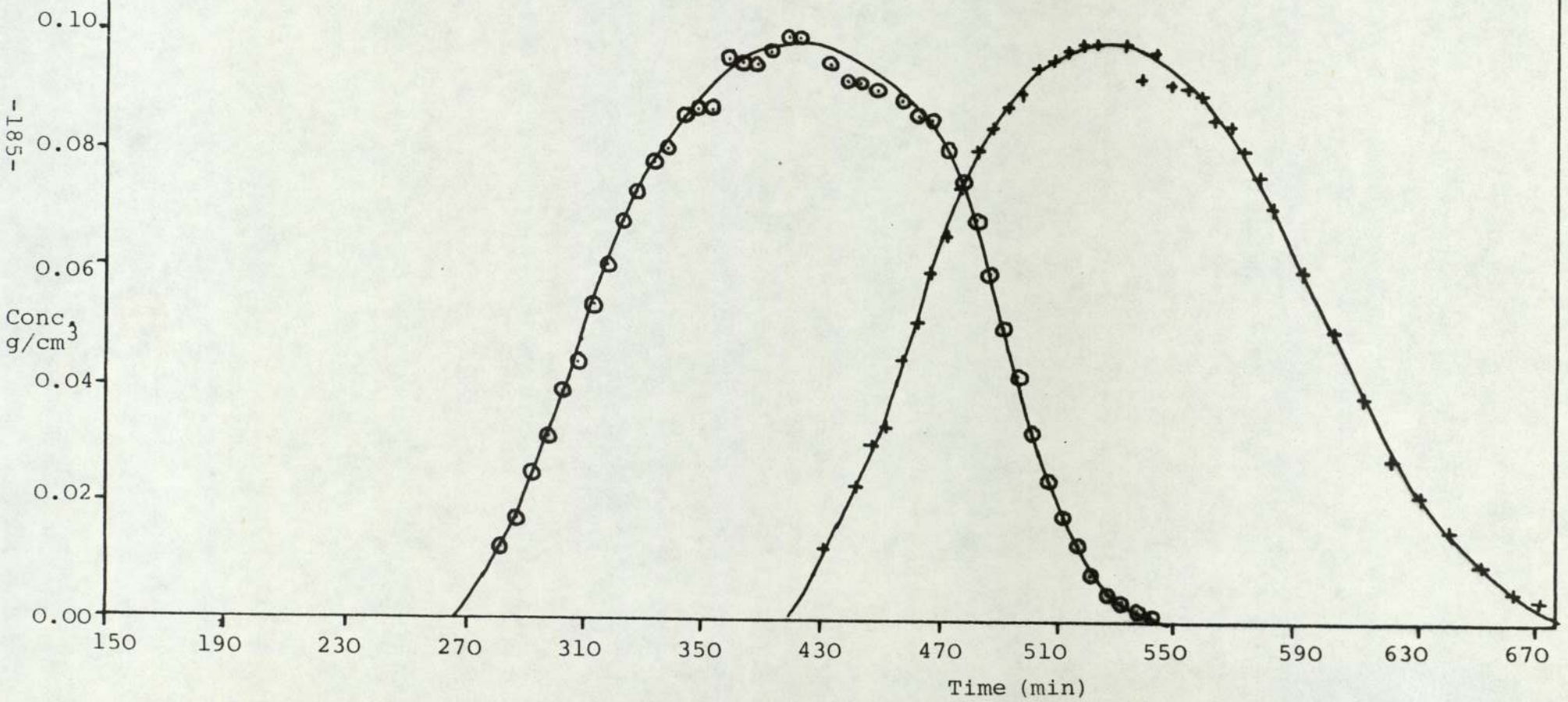
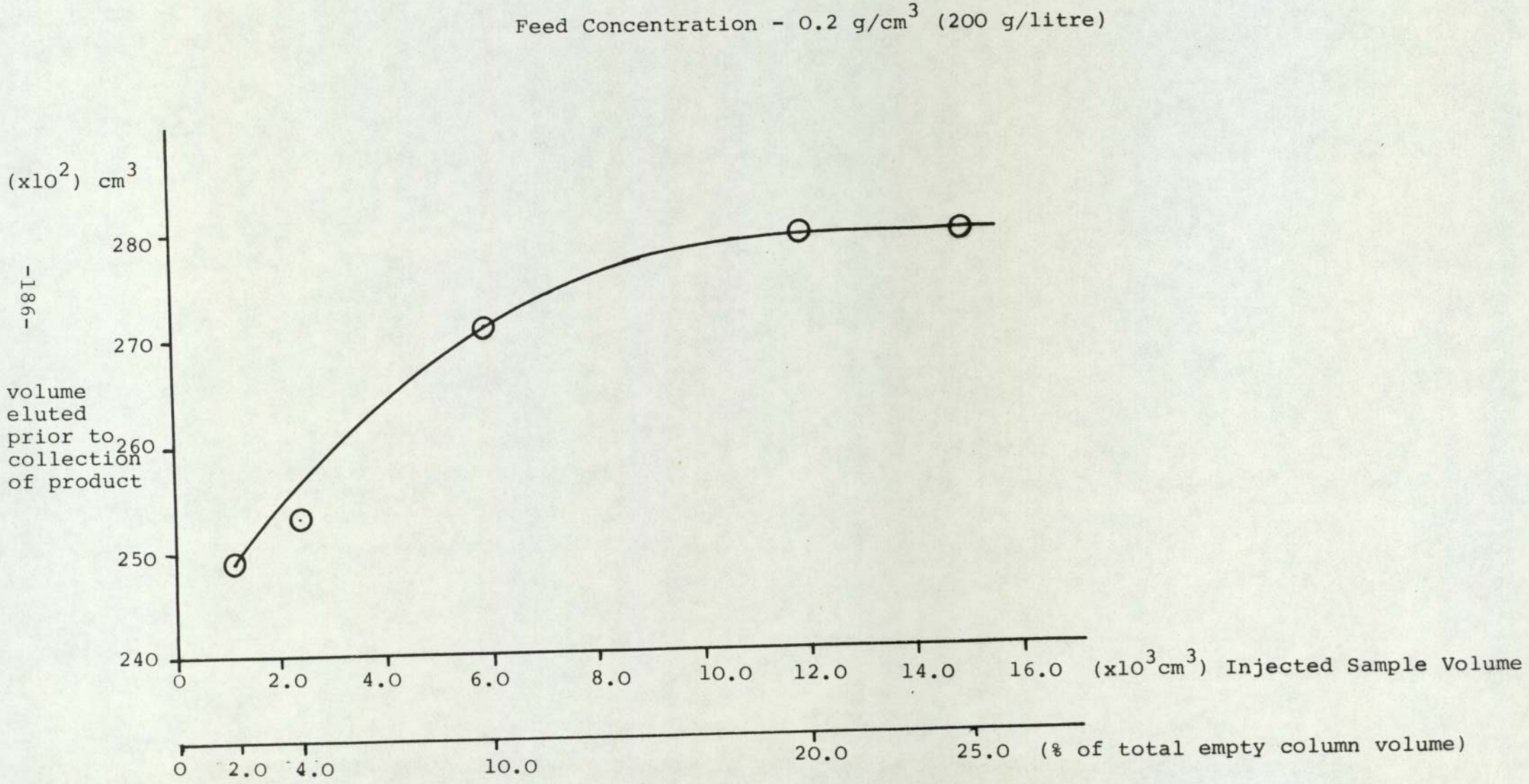


FIG. 6.10 THE EFFECT OF SAMPLE VOLUME ON VOLUME ELUTED PRIOR TO THE COLLECTION OF PRODUCTS



column effectively an increase in on-column concentration was created resulting in an increased distribution coefficient value and an increase in retention volume.

The percentage of the product which was not to the specification was named as the recycle product and increased with increasing sample volume (Fig. 6.11). A possible explanation for this could be due to the interference introduced into the chromatography of the products by the use of "large" injection volumes. When a small pulse of feed is introduced into an analytical column a chromatogram results. A large volume of feed could be considered as a series of non-interacting pulses similar to Fig. 6.1 where each pulse is separated individually. As a result of this the exit of the first molecule of glucose corresponds to the first pulse and the last to the last pulse. Similarly for fructose the first and last molecule would correspond to the first and last pulse respectively. This is shown diagrammatically in Fig. 6.12. The position of FF and GL in Fig. 6.12 effectively decide the percentage recycle. An increase in the feed volume would move the point FF to the left and point GL to the right resulting in an increase in the overall percentage recycle (See Figs. 6.5-6.9).

Directly as a result of increasing percentage recycle, a limit is reached on the "throughput" for a sample of particular concentration (Fig. 6.13), throughput being measured in terms of the pure products. Initially the increase in the percentage recycle had a

FIG. 6.11 THE EFFECT OF SAMPLE VOLUME ON THE PERCENTAGE RECYCLE OF THE PRODUCT, THE ACCEPTABLE PRODUCT BEING 100% PURE

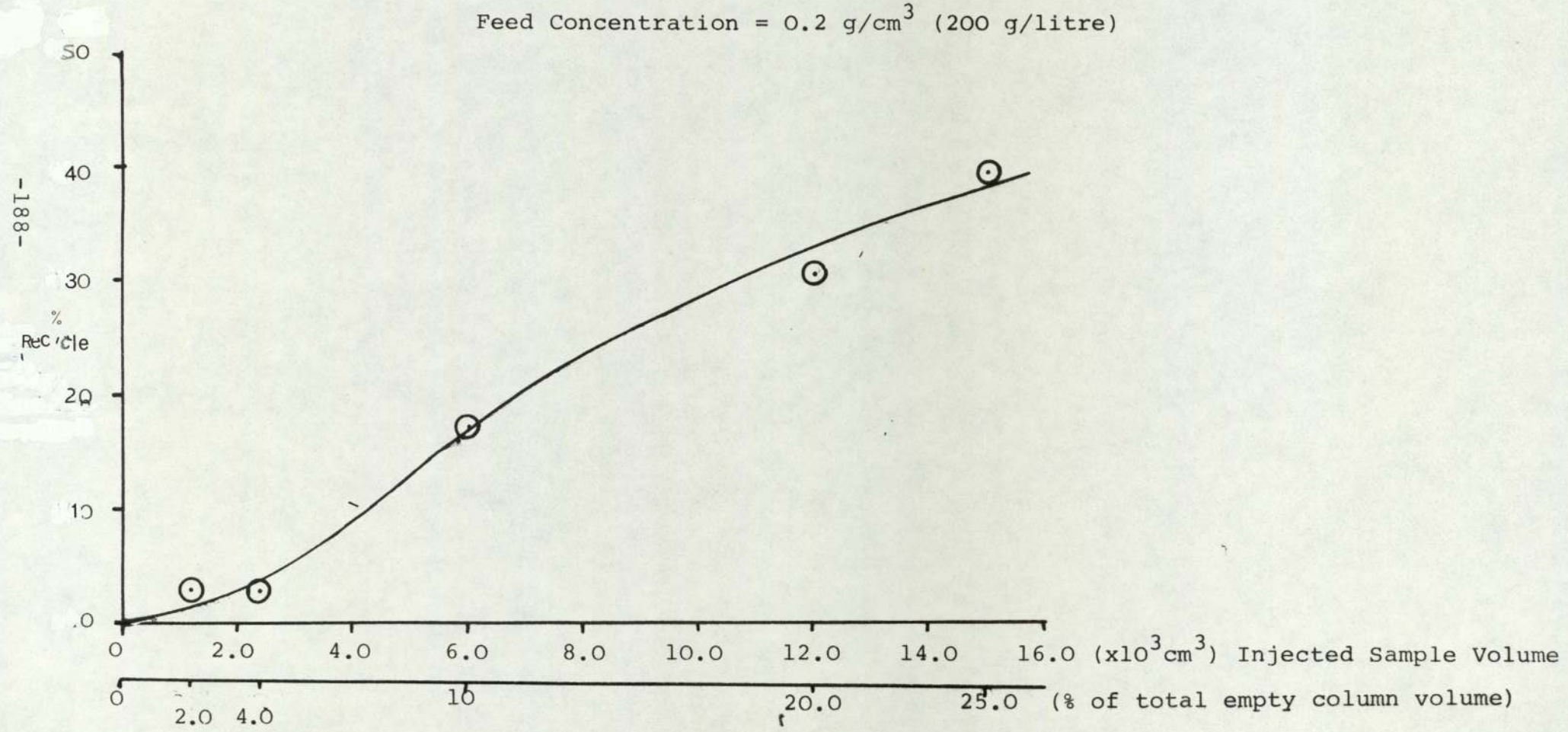


FIG. 6.12 PRODUCT PROFILE RESULTING FROM A "LARGE" VOLUME INJECTION

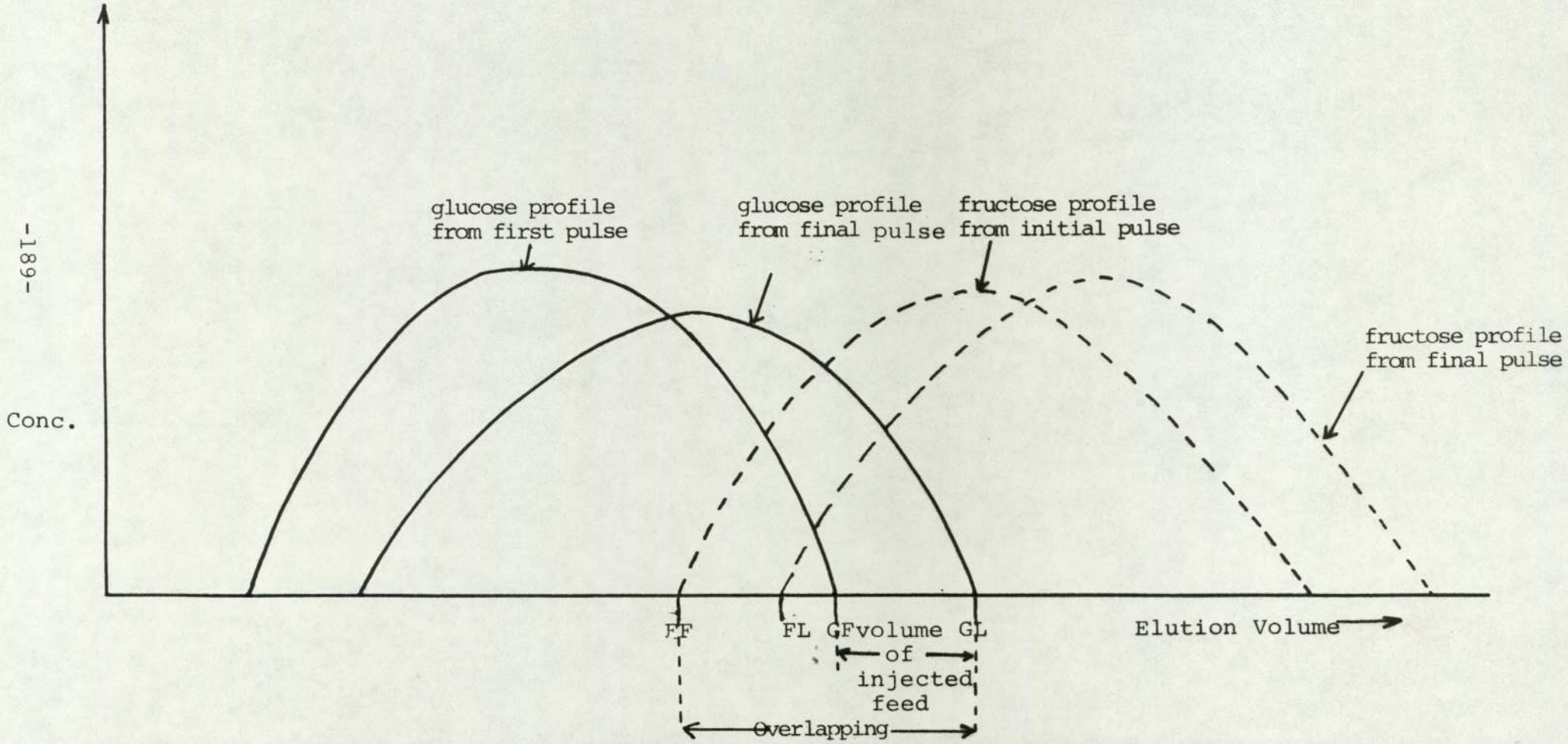
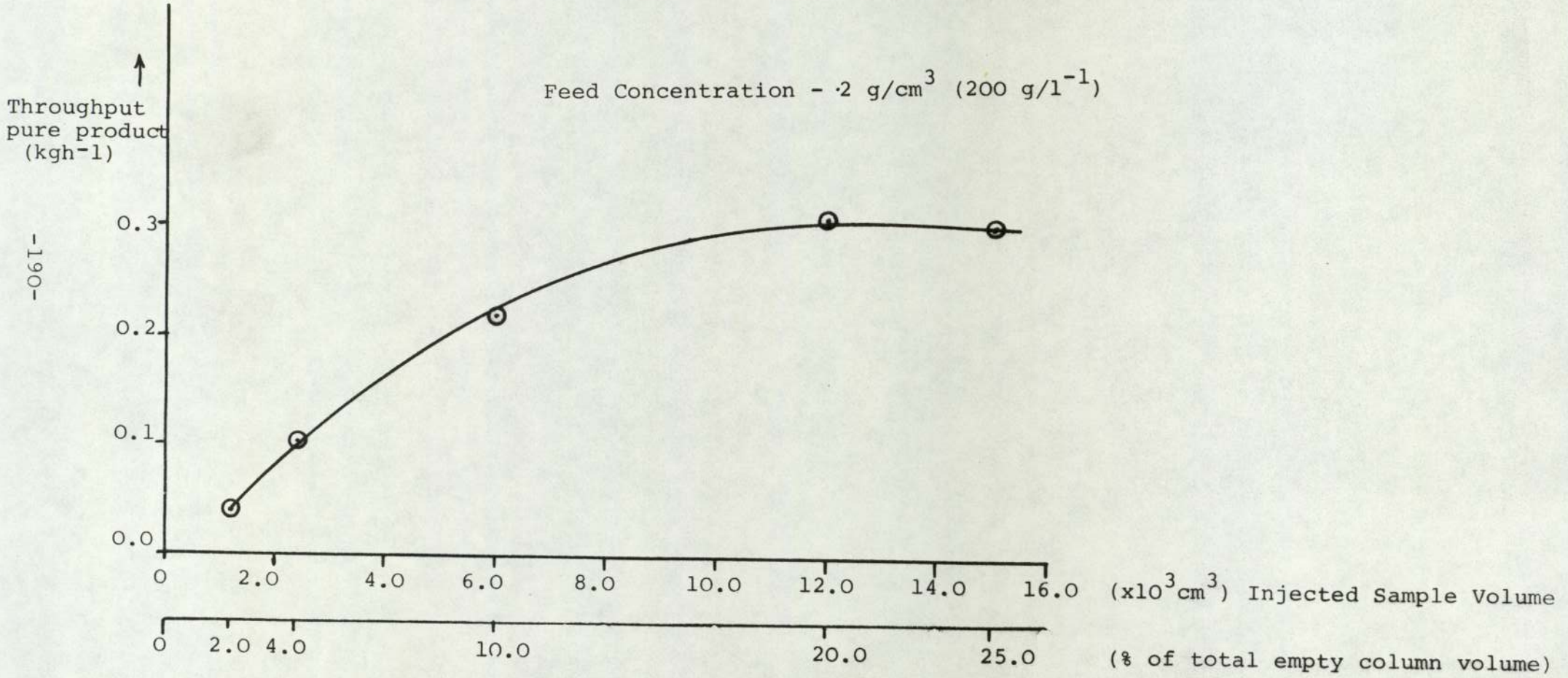


FIG. 6.13 EFFECT OF INJECTED SAMPLE VOLUME ON THE THROUGHPUT

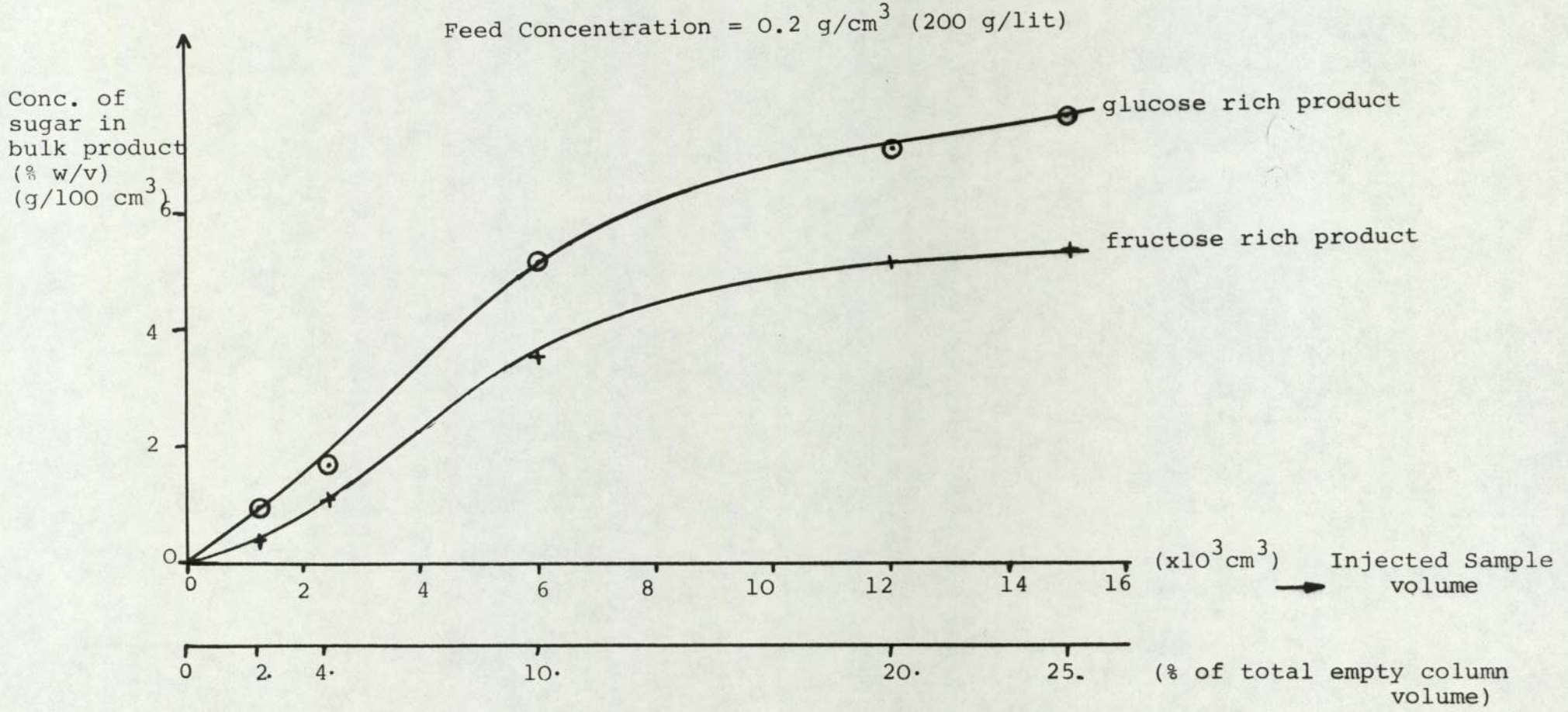


little effect on the throughput which increased rapidly. At higher sample volumes however the percentage recycle increased so rapidly reaching a value of 40% with 15 litres of sample volume that an increased feed volume had no significant effect on the throughput of sugar. This was taken as the optimum throughput corresponding to 40% recycle. Conder (47) while studying optimisation in gas chromatography also found that optimum throughput corresponded to 40% recycle.

Fig. 6.14 shows the variation for concentration of both glucose and fructose in their respective products plotted against the volume of feed injected. Initially a small change in the feed volume results in a sharp increase in the concentration of components in the products. However no significant change in the concentration of components in the products is observed by changing the sample volume from 12 to 15 litres. This indicates that an optimum feed volume of 15 litres has been reached in terms of throughput as well as the concentration of the sugar in the products.

The experiment that had the maximum volume of sample injected was experiment 5. In this experiment the total sample volume injected was equivalent to 25% of the total empty column volume. To obtain an acceptable product quality as much as 40% of the total sugar input needed recycling. Conder and Purnell (22) used large scale preparative batch chromatography and a gas-liquid system and suggested that for large volume samples three operating modes occur. Classification of these

FIG. 6.14 THE EFFECT OF SAMPLE VOLUME ON CONCENTRATION OF THE PRODUCTS



operating modes can be described by the value of the product of the number of plates occupied by the feed inlet band and the reciprocal of the root of the total number of plates in the column as discussed in Section 2.3.1.2.

Mode	Range
Elution	$\theta < \frac{1}{2}$
Overload Elution	$\frac{1}{2} < \theta < 6$
Eluto-Frontal	$\theta > 6$

where $\theta = N_f N_t^{-\frac{1}{2}}$

N_f = number of plates occupied by feed band

N_t = total number of plates in column

For the experimental programme the size of the injected sample volume in terms of θ ranged from .32 to 4.0, thus the operating mode changed from elution to overloaded elution. The advantage of operating in the overload elution mode was to increase the throughput.

6.6 EFFECT OF FEED CONCENTRATION

An increase in the throughput of the batch chromatographic equipment was also attempted by increasing the concentration of the feed solution from 200 to 600 g litre^{-1}. Experiments 1, 6, 11, 16 and 23 loaded identical volume of feed solution (1.2 litres) into the column, although experiment 23 loaded almost 66% more sugar than experiment 1. (See Table 6.1)

6.6.1 Result and Discussion

The volume eluted prior to the product collection increased with increasing sample concentration (Fig. 6.15). Enhancement of feed concentration would obviously result in an increase in on-column concentration. As explained in the previous section, the distribution coefficient increased with increasing on-column concentration which in turn enhanced the retardation.

The percentage of sugar in the feed which was recycled remained more or less constant with increasing feed concentration (Fig. 6.16). A possible explanation for this could be due to an identical amount of interference caused by identical sample volume. In terms of the diagram shown in Fig. 6.12 the position of FF and GL remain similar with respect to the peak of glucose and fructose. This would be possible if the position of FF and GL were dependent only on the feed volume. The change in the value of the partition coefficient does not cause any change in the shape of the chromatogram.

Directly as a result of constant percentage recycle, the 'throughput' increased linearly with increasing feed concentration. This could be a very useful result in terms of increasing the throughput of the equipment. The highest throughput of sugar would be obtained for the greatest concentration of feed that could be injected into the column (Fig. 6.17). The limitation on the feed concentration could arise for two main reasons. First would be the pressure drop across the

FIG. 6.15 EFFECT OF SAMPLE CONCENTRATION ON THE ELUTION VOLUME OF PRODUCT FRACTION

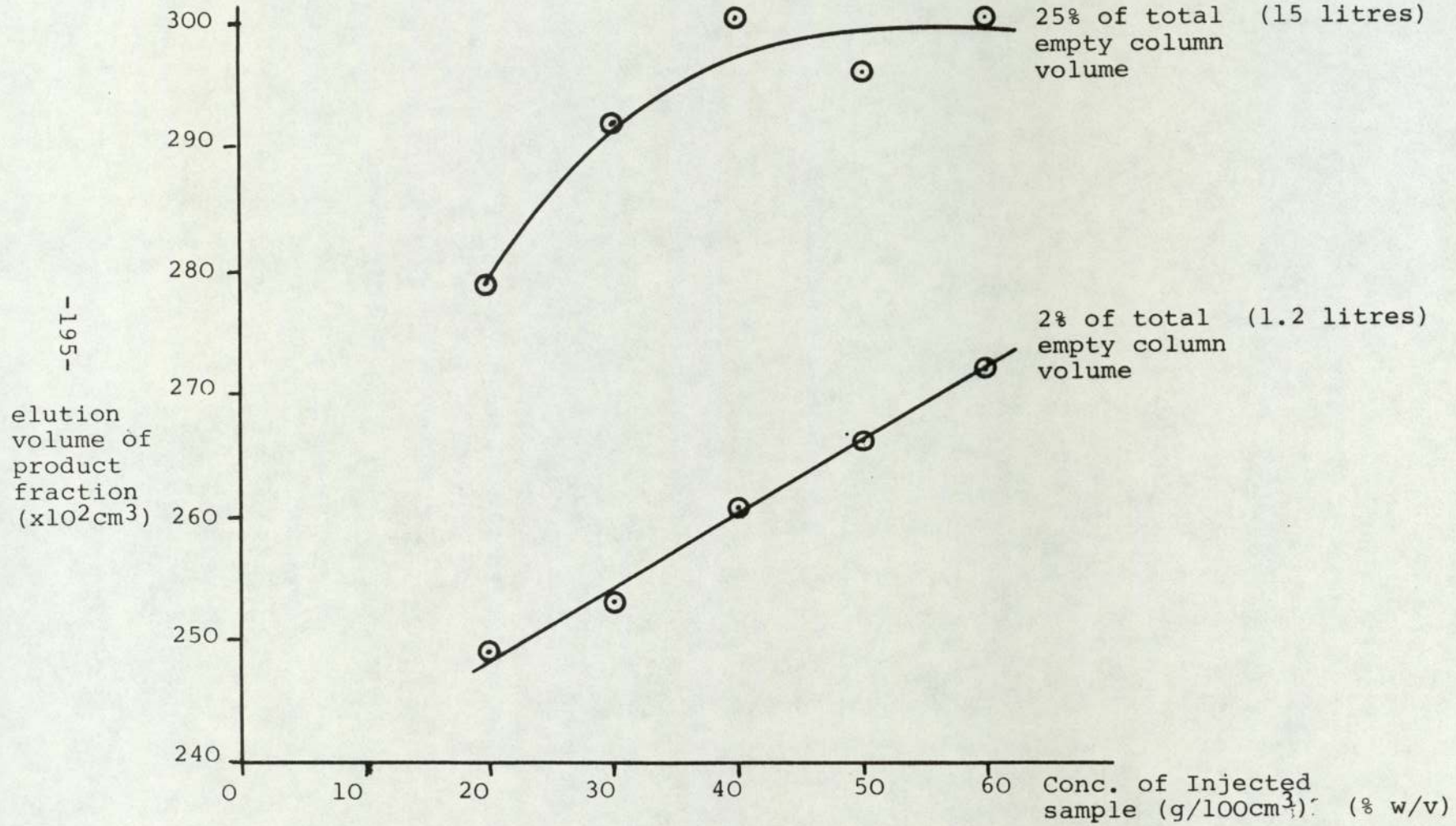


FIG. 6.16 EFFECT OF SAMPLE CONCENTRATION ON THE % RECYCLE OF THE PRODUCT

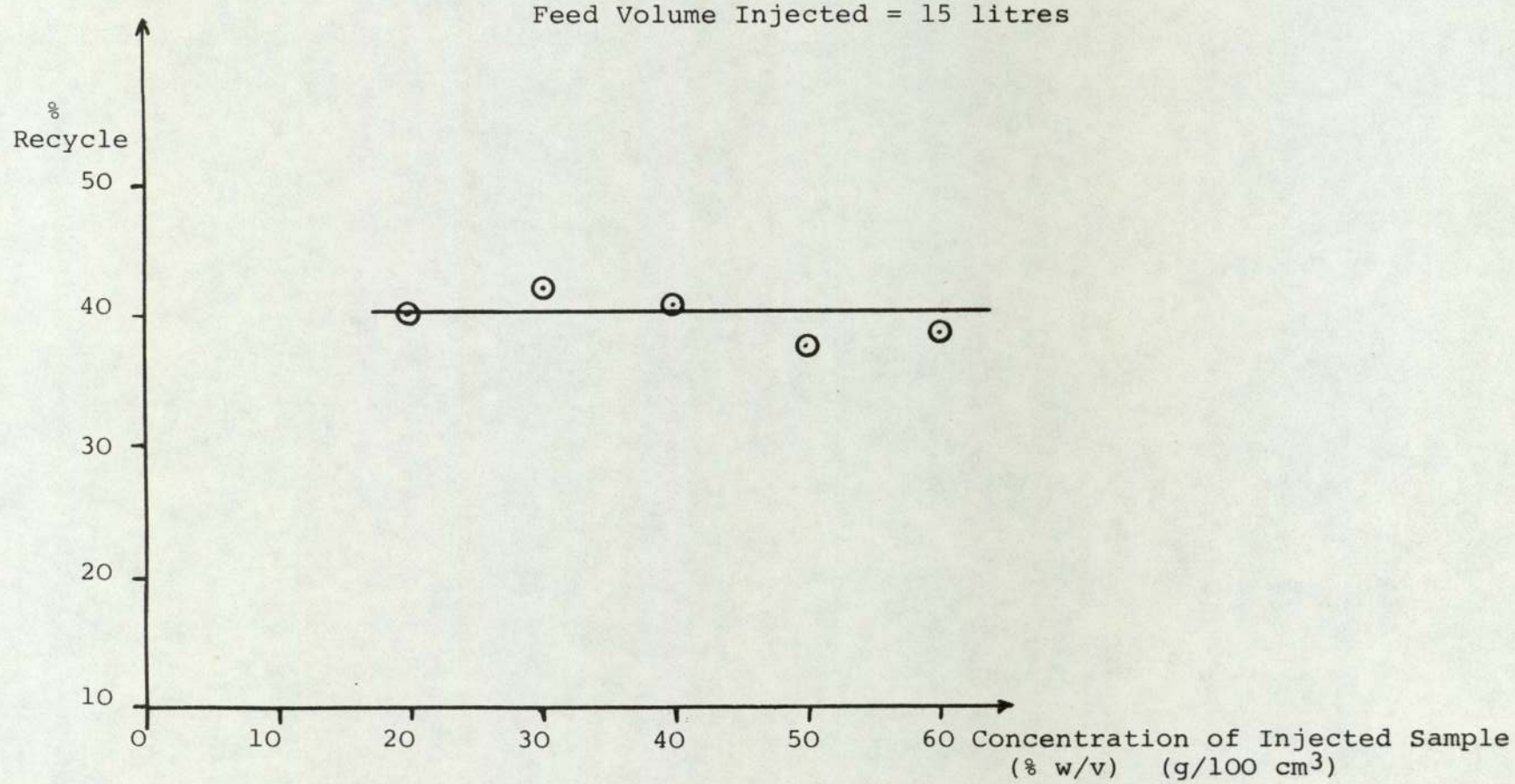
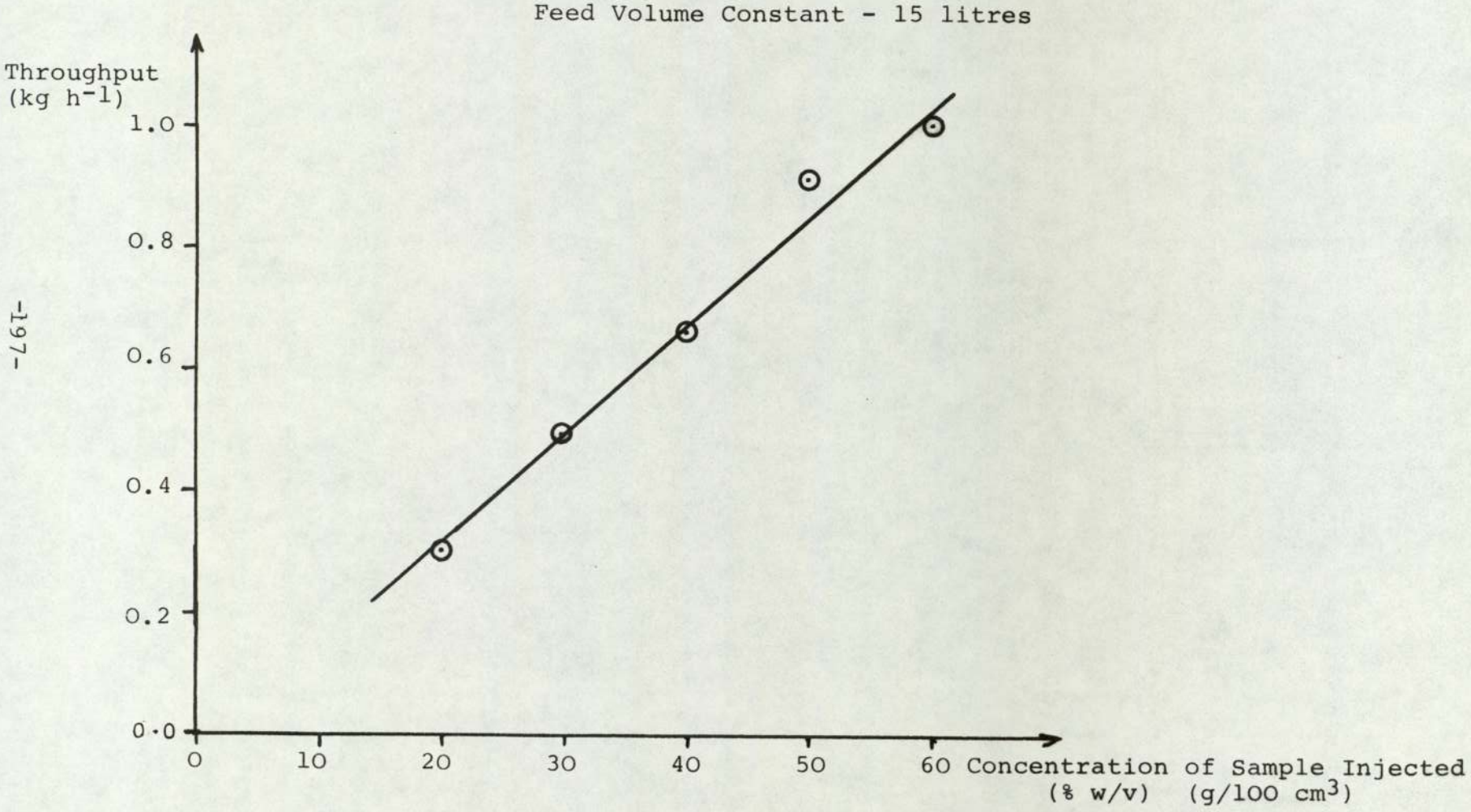


FIG. 6.17 EFFECT OF SAMPLE CONCENTRATION ON THROUGHPUT



columns that the equipment could withstand and the second would be the solubility of the components glucose and fructose in water. In view of Fig. (6.18) no significant increase in product concentration is achieved by increasing the feed concentration from 500 to 600 g litre^{-1}. Hence the throughput could be increased by increasing the feed concentration but with no significant improvement in the product concentrations.

6.7 EFFECT OF TEMPERATURE

In order to study the behaviour of column performance with temperature, the two other conditions namely the concentration and the volume of sample injected were kept identical, 1200 cm^3 of sample of concentration 200 grams litre^{-1} were used. The temperature was varied in the range 20-60^{o}C.

6.7.1 Results and Discussion

The following observation could be recorded from the results:

(i) the elution volume prior to the collection of product decreased with increasing temperature (Fig. 6.19);

(ii) the repetitive injection time (t_1-t_o) decreased with increasing concentration (Fig. 6.20);

(iii) the glucose and fructose peaks moved closer together increasing overlapping (Figs. 6.9, 6.21, 6.22, 6.23).

FIG. 6.18 EFFECT OF SAMPLE CONCENTRATION ON CONCENTRATION OF THE PRODUCTS

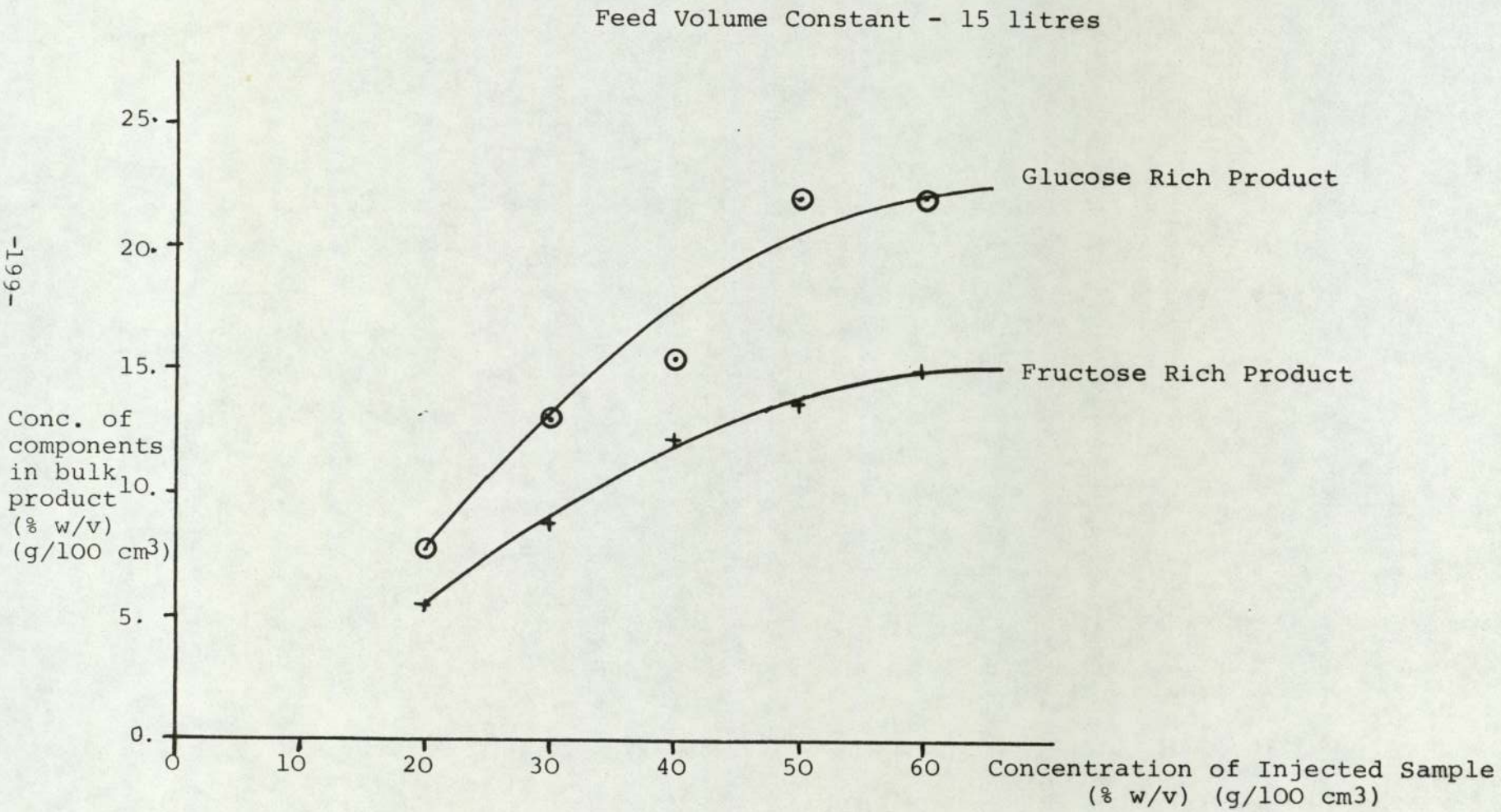


FIG. 6.19 THE EFFECT OF TEMPERATURE ON THE ELUTION VOLUME PRIOR TO THE PRODUCT COLLECTION AT A FEED CONCENTRATION OF 0.2 g/cm3 (20% w/v)

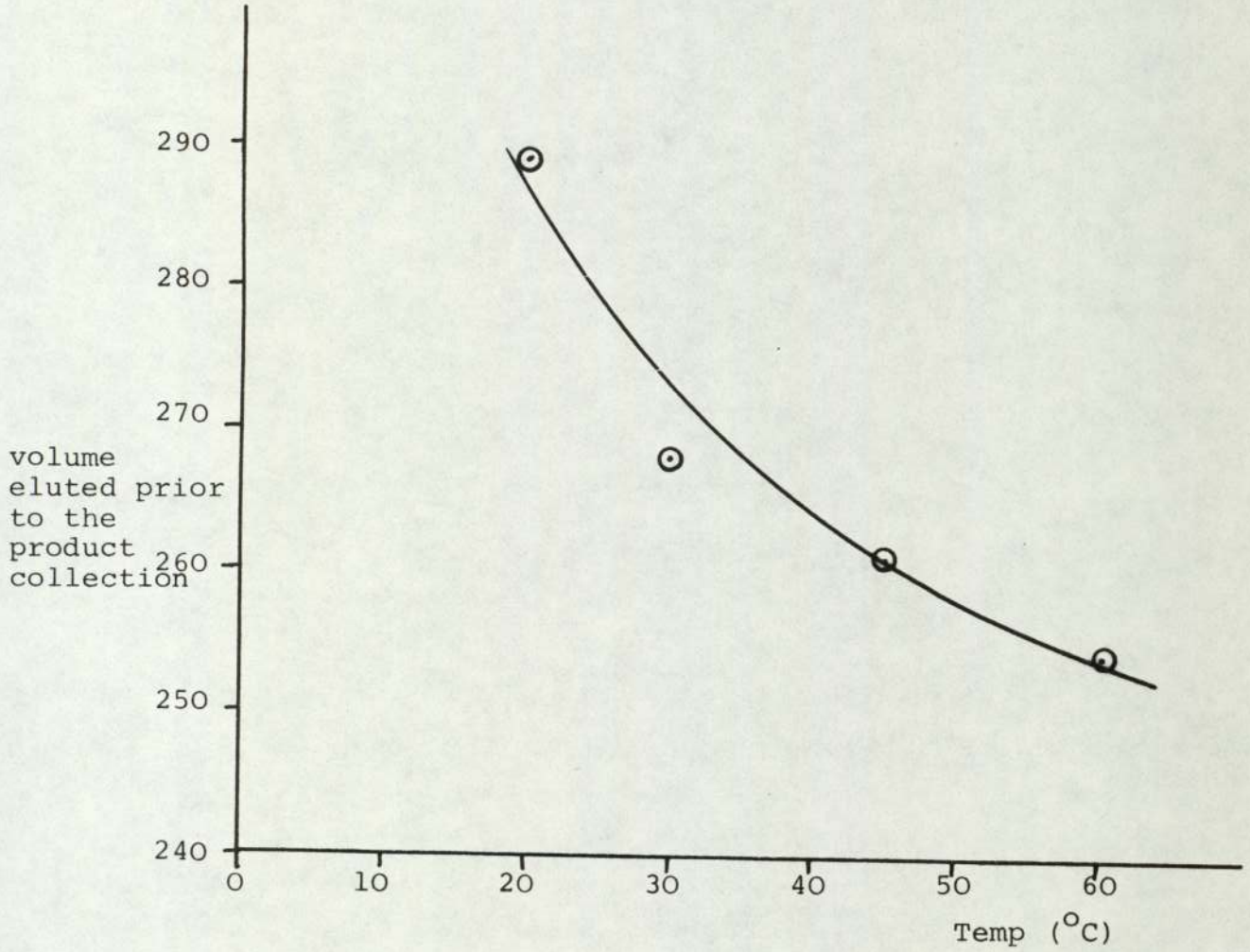


FIG. 6.20 THE EFFECT OF TEMPERATURE ON THE REPETITIVE INJECTION TIME OF THE BATCH

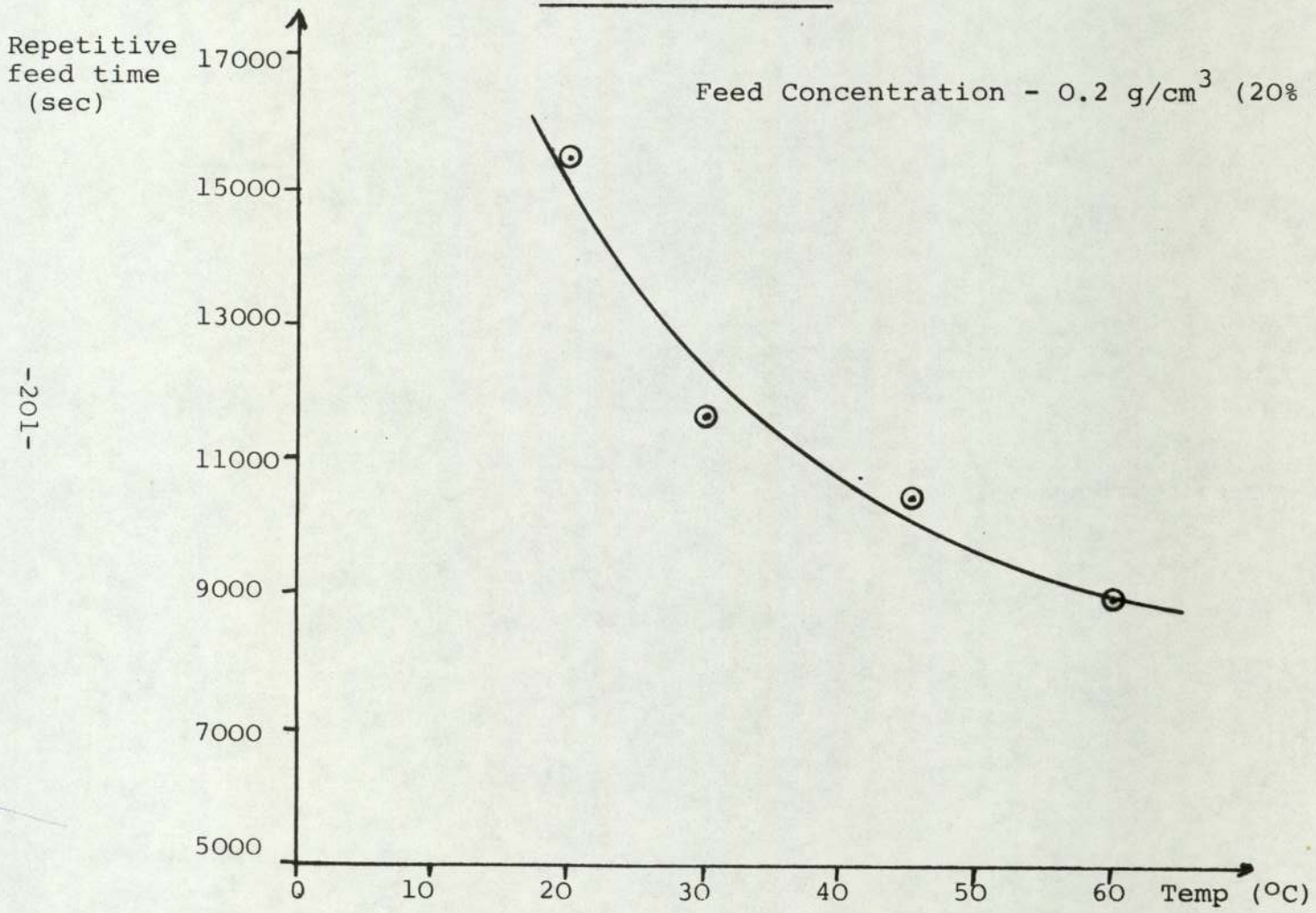


FIG. 6.21 EXPERIMENTAL CONCENTRATION PROFILE FOR BATCH RUN 20-25-100-100-30

Feed Concentration 0.2 g/cm^3, Feed Volume 15000 cm^3
(25% of total empty column volume)

Eluent Flow Rate 100 cm^{3}min, Temperature 30^{o}C

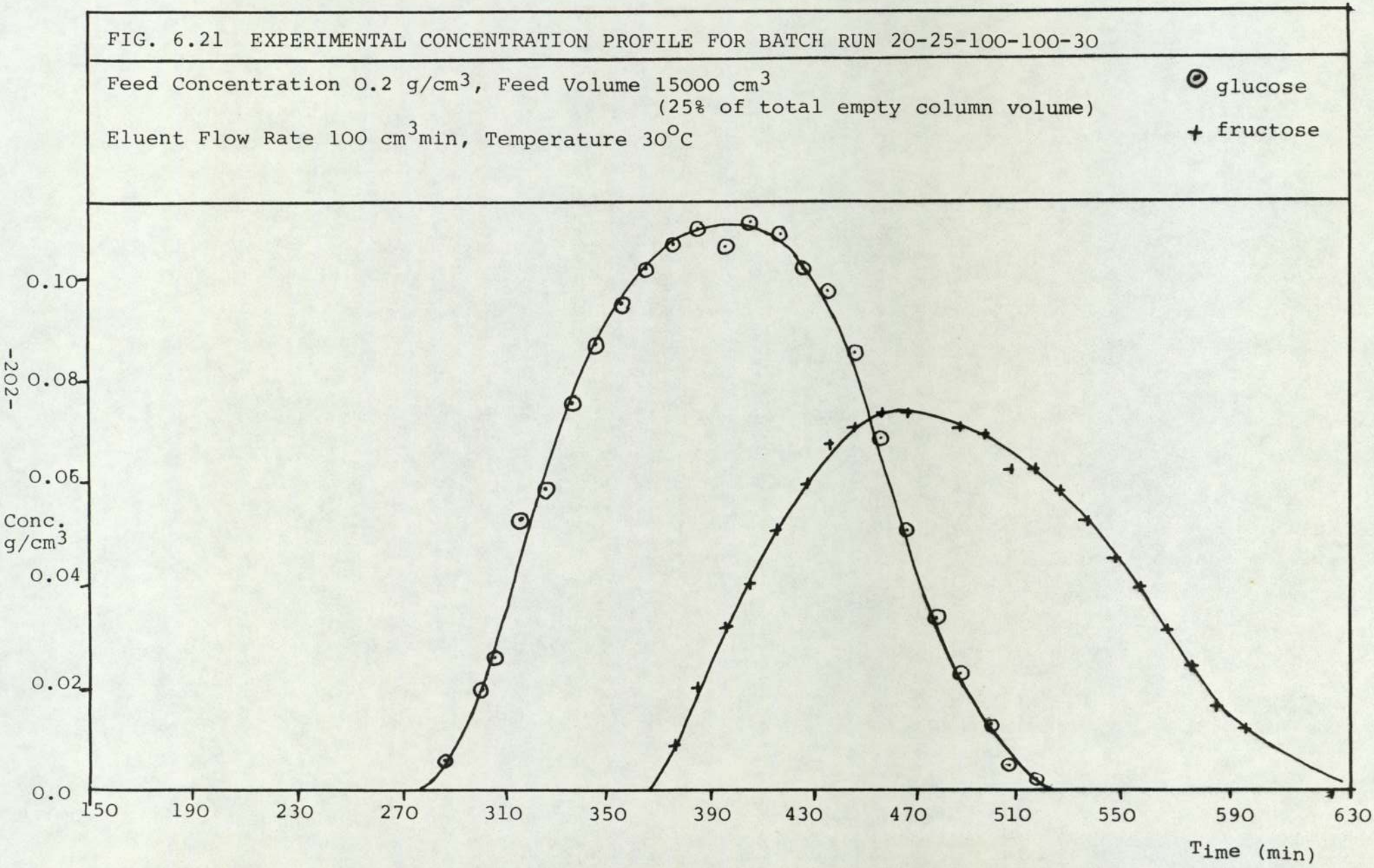


FIG. 6.22 EXPERIMENTAL CONCENTRATION PROFILE FOR BATCH RUN 20-25-100-100-45

Feed Concentration 0.2 g/cm^3 (200 g/lit), Feed Volume 15000 cm^3 (25% of total empty column volume)

Eluent Flow Rate 100 cm^{3}min^{-1}, Temperature 45^{o}C

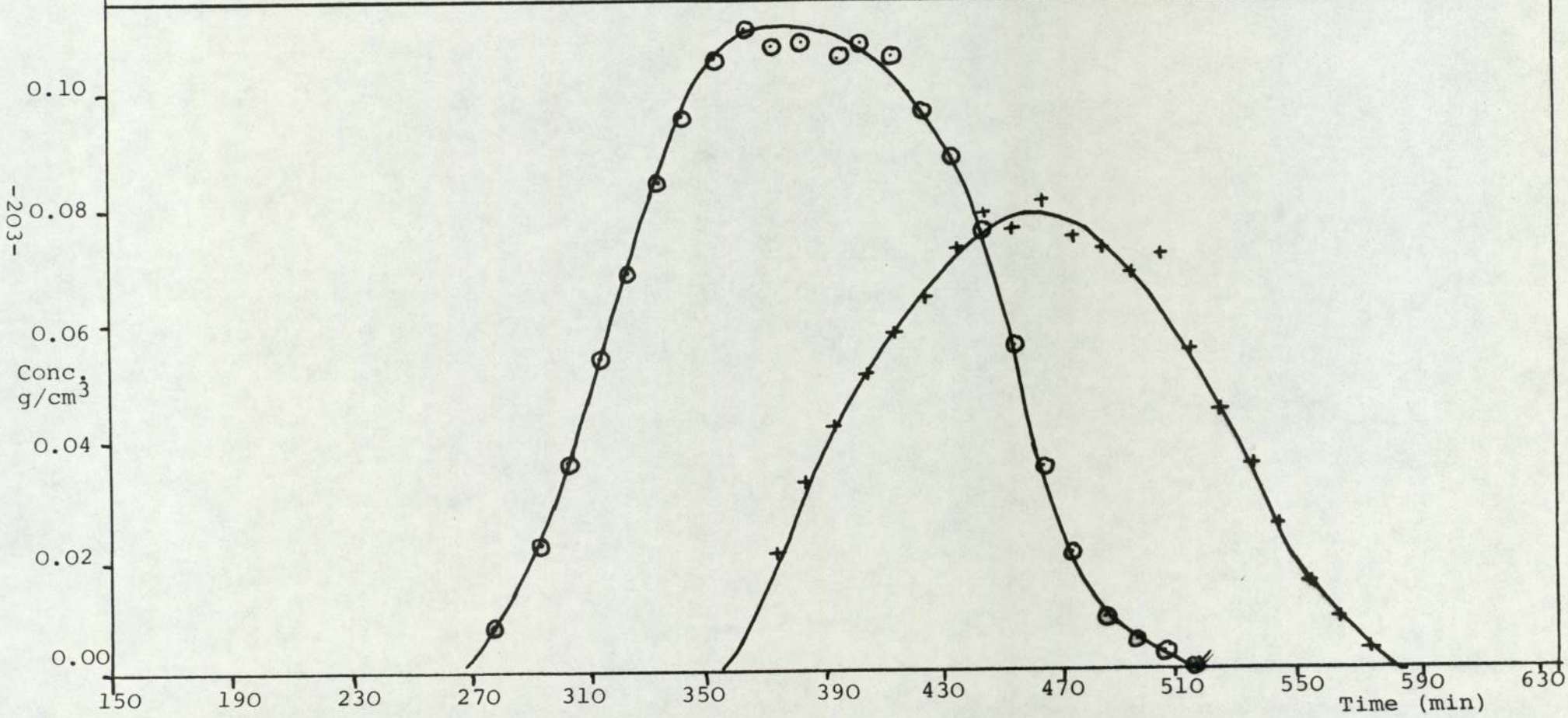
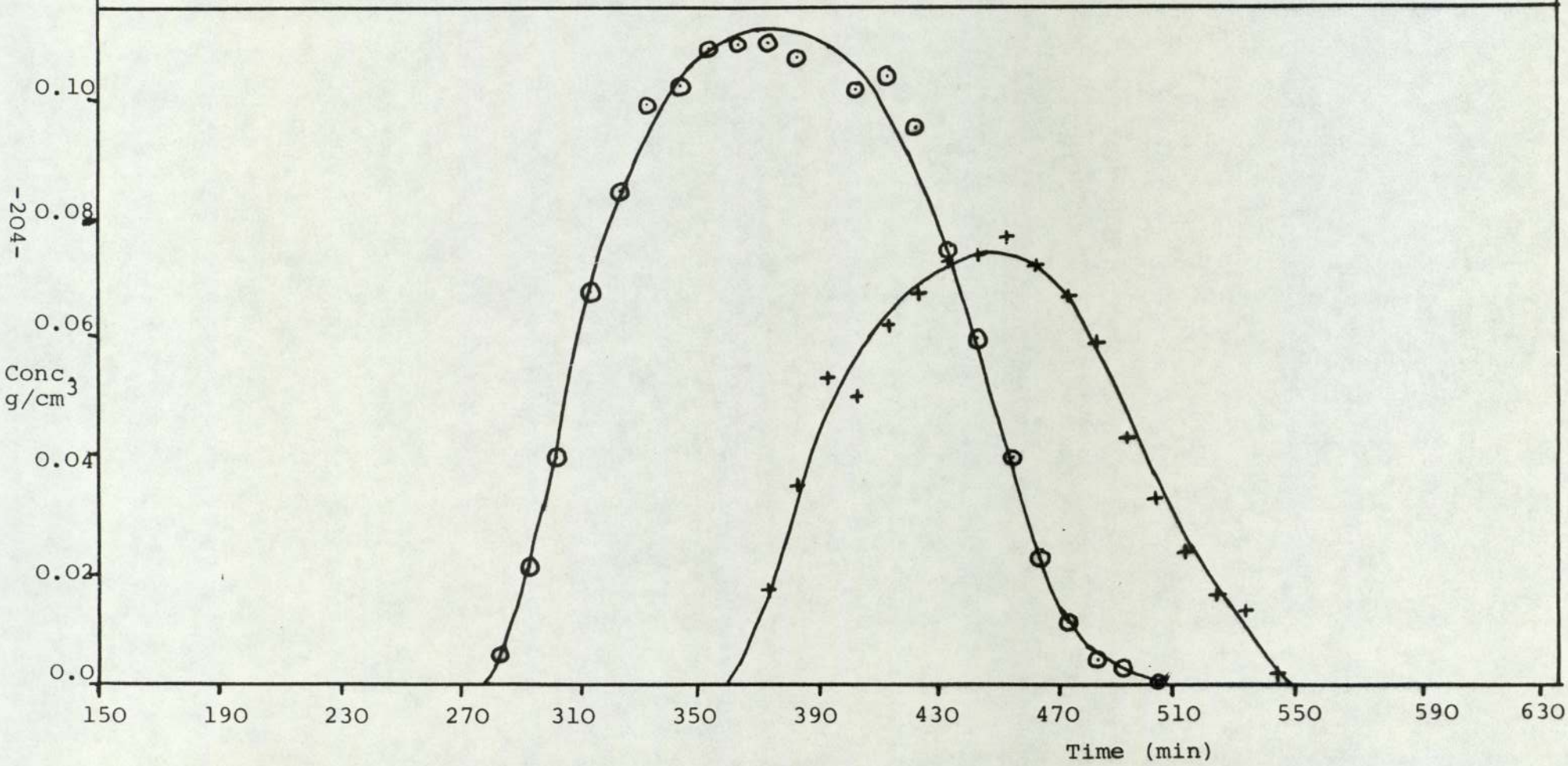


FIG. 6.23 EXPERIMENTAL CONCENTRATION PROFILE FOR BATCH RUN 20-25-100-100-60

Feed Concentration 0.2 g/cm^3 (20% w/v), Feed Volume 15000 cm^3 (25% of total empty column volume)

Eluent Flow Rate 100 cm^{3}min^{-1}, Temperature 60^{o}C



Ching (8) while studying the effect of temperature on HETP values found that the distribution coefficient of fructose decreased with increasing temperature. This decrease in the distribution coefficient reduces the elution volume of the fructose. In case of fructose the decrease in distribution coefficient is effected by the decrease in viscosity of the fructose solution with temperature. Also an enhanced reduction in the distribution coefficient is experienced due to the reduction in the $2C_5$ form of β D fructofuranose. It is the $2C_5$ form of fructofuranose which forms a complex with the calcium ions and the concentration of this form of fructose in equilibrium decreases with increasing temperature. This has an overall effect of bringing the glucose and fructose peaks closer and hence increases overlapping (see Figs. 6.9,6.21,6.22.6.23).

6.8 BATCH OPERATION WITH FISONS SYNTHETIC FEED

To complete the research programme it was decided to test the rig's ability to refine batchwise a synthetic feedstock with a similar carbohydrate content to a commercial by-product obtained by Fisons Ltd., Holmes Chapel, in the manufacture of dextran. It contained 70% w/v sugar solids content of which

69% was fructose

22% was dextran

9% was glucose

Two batch experiments were performed feeding 6 litres (10% of total column volume) and 12 litres

(20% of total column volume) of solution. The object of the experiment was to maximise the throughput of the three component feed.

6.8.1 Results and Discussion

Fig. 6.24 and 6.25 show the chromatograms when the feed injected was 6 litres and 12 litres respectively. As seen from Fig. 6.24 with a feed volume of 6 litres five products were obtained namely dextran rich product, recycle 1 containing dextran and glucose, glucose rich product, recycle 2 containing glucose and fructose and fructose rich product.

From Fig. 6.25, with an injected feed volume of 12 litres only three products are obtained - dextran rich product, recycle containing dextran, glucose and fructose and fructose rich product. The resolution of components has deteriorated considerably at this feed size. 48% of the total solid sugar input in the feed needed to be recycled when 12 litres of sample was injected compared to the 28% with 6 litres of sample.

The results giving details of product quality are shown in Table 6.2. In increasing the feed size from 6 litres to 12 litres the concentration of fructose in the fructose product was increased from 8.6% to 11.6%, an increase of 34% at a cost of an increase in the percentage recycle of 71%. An economic balance will have to be achieved to obtain an optimum feed size.

TABLE 6.2 BATCH OPERATION WITH FISONS SYNTHETIC FEED

Expt No.	Feed Conc.			Vol Injected (l)	D.R.P.			Recycle				G.R.P.				RECYCLE 2				F.R.P.			Mass Bal. Error			Throughput kgh^{-1}
	D	F	G		Purity %	C_D	C_G	Purity %	C_D	C_G	C_F	Purity %	C_D	C_G	C_F	Purity %	C_D	C_G	C_F	Purity %	C_G	C_F	D	G	F	
28	14.8	7.1	48.3	6	100	5.69	-	-	0.88	3.13	-	100	-	2.4	-	-	-	0.36	8.85	100	-	8.92	18	19	20	0.39
29	14.8	7.1	48.3	12	100	9.2	-	-	3.18	3.84	10.68	-	-	-	-	-	-	-	-	100	-	11.64	20	19	24	0.49

Where

C = bulk concentration of the component in the product (g/100 cm^3)

Subscripts

D = Dextran
G = Glucose
F = Fructose

FIG. 6.24 EXPERIMENTAL CONCENTRATION PROFILE FOR BATCH RUN WITH FISONS SYNTHETIC FEED 70-10-100-100-20

Feed Concentration 0.7 g/cm^3 (70% w/v), Feed Volume 6000 cm^3 (10% of total empty column volume)

Eluent Flow Rate 100 cm^{3}min^{-1}, Temperature 20^{o}C

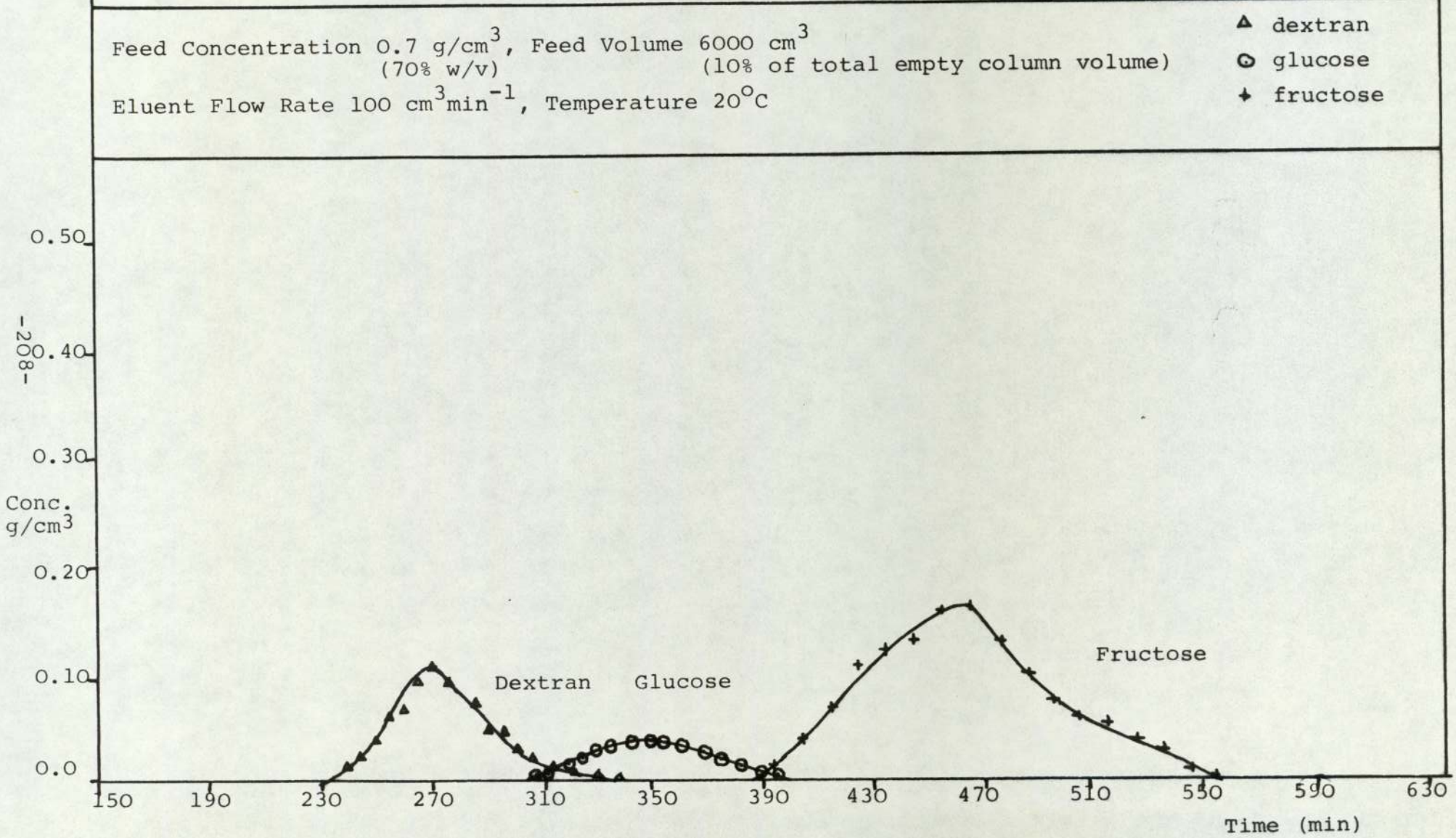
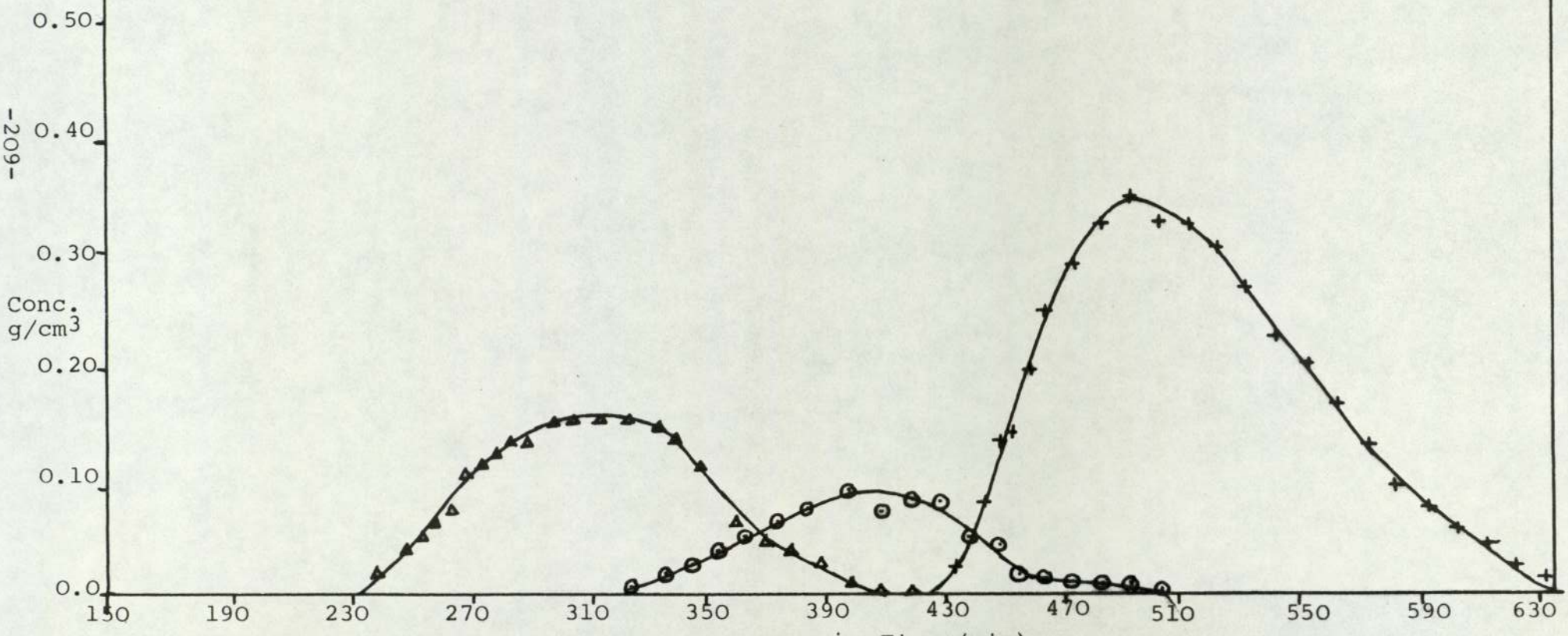


FIG. 6.25 EXPERIMENTAL CONCENTRATION PROFILE FOR BATCH RUN WITH SYNTHETIC FISONS FEED 70-20-100-100-20

Feed Concentration 0.7 g/cm^3 (70% w/v), Feed Volume 12000 cm^3 (20% of total empty column volume)

Eluent Flow Rate 100 cm^{3}min^{-1}, Temperature 20^{o}C



6.9 COMPARISON OF BATCH AND SEMI-CONTINUOUS OPERATION

The comparison of batch and semi-continuous operation will be based on two main headings, namely the throughput of sugar and the quality of product obtained.

6.9.1 Results and Discussion

Tables 6.3 and 6.4 show the results from the experiments which compare the batch and semi-continuous operation of the SCCR6 unit. For convenience the contents of Table 6.3 will be discussed first.

At 20% w/v feed concentration containing 50-50 glucose and fructose, the throughput in semi-continuous mode is twice as much as that in batch. With 40% and 60% w/v concentration the throughput ratio of semi-continuous to batch is 1.7:1. This indicates that the adaptation of semi-continuous chromatography is moving towards the production scale operation.

In terms of quality, i.e. concentration and the purity of product the batch looks promising. To make the product quality comparable to batch, further experiments have been devised to increase the concentration of fructose in the fructose rich product. These are described in Section 5.1.5. When using a feed containing 50% w/v of sugar solids the bulk concentration of fructose in the fructose product was increased from 1.74% w/v collected over a 30 minute switch period to 9.4% w/v by a combination of fractional collection over the first 10 minutes of the switch and by using the fructose rich product as an eluent.

TABLE 6.3 RESULTS FOR THE COMPARISON OF BATCH AND CONTINUOUS OPERATION OF GLUCOSE FRUCTOSE MIXTURE

Feed Conc % w/v		Batch							Semi-Continuous							
		F.R.P.			G.R.P.				F.R.P.			G.R.P.				
G	F	Purity %	Mass Bal. %	Fruct. Conc. % w/v	Purity %	Mass Bal. %	Gluc. Conc. % w/v	Throughput kg h^{-1}	Purity %	Mass Bal. %	Fruct. Conc. % w/v	Purity %	Mass Bal. %	Gluc. Conc. % w/v	Throughput kg h^{-1}	Throughput Ratio Semi/Batch
10.1	10.2	99.9	102	5.44	99.9	103	7.65	0.3	65.0	105	1.22	99.9	69	1.4	0.84	2.8
20.0	20.0	84.0	105	12.01	99.9	101	15.52	0.98	76.0	102	3.2	99.9	98	2.98	1.68	1.72
25.0	25.1	82.0	103	13.1	99.9	106	21.85	1.21	70.0	111	7.6	99.9	100	2.7	2.1	1.74

TABLE 6.4 RESULTS FOR THE COMPARISON OF BATCH/CONTINUOUS OPERATION FOR FISONS SYNTHETIC FEED

Feed Conc.			Batch								Semi-Continuous								
			F.R.P.			D.R.P.					F.R.P.			D.R.P.					
G	F	D	Purity %	Mass Bal. %	Fruct. Conc. % w/v	Purity %	Mass Bal.% D	Mass Bal.% G	Dext. Conc. % w/v	Throughput kgh $^{-1}$	Purity %	Mass Bal. %	Fruct. Conc. % w/v	Purity %	Mass Bal.% D	Mass Bal.% G	Dext. Conc. % w/v	Throughput kgh $^{-1}$	Throughput Ratio Semi/Batch
6.3	48.3	14.9	99.9	114	8.64	66	1.10	108	3.84	0.56	99.9	114	16.3	72	101	102	4.2	2.94	5.25

When comparing the batch and semi-continuous separation of the three components feed system the semi-continuous operation is extremely promising in terms of throughput and quality of the product. A throughput of five fold has been obtained by semi-continuous operation in comparison to the batch. In addition a better product quality is obtained in semi-continuous operation, namely the fructose rich product containing 16.3% w/v of fructose at 99.9% purity in semi-continuous compared to 11.64% w/v of fructose at 99.9% purity in batch and the dextran rich product containing 4.2% w/v of dextran at 72% purity in semi-continuous compared with 3.84% w/v of dextran at 66% purity.

The development of the semi-continuous refiner appears to be very promising when used for the separation of the three component system, but a further improvement to the product quality would be welcome in the case of the glucose, fructose feed. A change of the existing zerolit SRC14 resin to a better one might be one possibility.

Semi-continuous operation has a few more advantages in comparison to batch and these are:

(i) no recycle is necessary - two products continuously exit from the two product lines, while in batch the recycle of the overlapping section is essential.

(ii) repeatable product quality from cycle to cycle is obtainable in semi-continuous but

the batch product differs slightly in quality from batch to batch. In three batches at 50% w/v concentration of feed, the fructose concentration varied from 16.0 to 17.94% and its purity varied from 79 to 83%.

(iii) the semi-continuous system is more flexible. The product quality could be altered by changing the flowrates of eluent and feed.

CHAPTER SEVEN

MATHEMATICAL MODELLING AND COMPUTER SIMULATION OF THE SCCR6

7.1 INTRODUCTION

Mathematical modelling of the SCCR6 unit has been described in three sections. The first section deals with the performance of the SCCR6 unit in the batch mode, the second section models the unit in the semi-continuous mode, and the third section theoretically compares the performance of the SCCR6 unit in the batch and semi-continuous mode.

7.2 MATHEMATICAL MODEL OF THE SCCR6 UNIT IN THE BATCH MODE

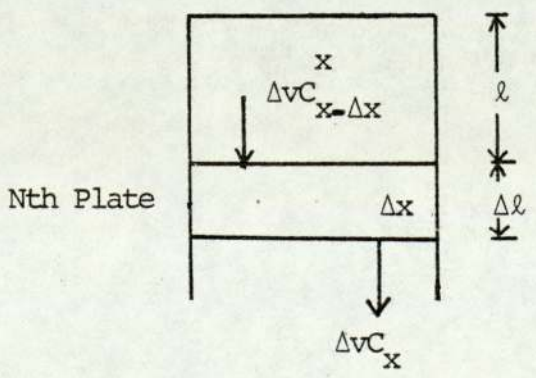
Various models for the prediction of plate heights in gas-liquid batch systems have been reviewed in Section 2.1. Martin and Synge (2) introduced the concept of a theoretical plate to the chromatographic system. They suggested that a chromatographic column could be considered to consist of a number of layers of packing, each of which was equivalent to a theoretical plate (HETP). To simplify the mathematical modelling of such a complicated system five assumptions were made, these are listed in Section 2.1.3.1. One of the assumptions was that the flow of the mobile phase was regarded as discontinuous that is, it consisted of a stepwise addition of a volume of mobile phase, each equal to the free volume per plate.

A modification to the previous model by Martin and Synge (2) was made by Gluekauf (16). He converted the discrete plate model to a continuous one by reducing the volume of the plate to an infinitesimally small value.

7.2.1 The Batch Model

Gluekauf (16) pictured the column as a discontinuous medium divided into units. Each unit represented an "effective theoretical plate" as a unit of length. Within a unit the concentration of solute could be taken as uniform, both in the stationary phase and in the mobile phase. A concentration equilibrium of a component was also set up between the two phases. He considered the material balance in such a unit of thickness $\Delta\ell$ cm, cross section A cm^2 hence a volume $\Delta x = A\Delta\ell$ cm^3. The amount adsorbed per unit volume of column (not necessarily at equilibrium) was signified as q. The distance from the top of the column was measured either in cm(ℓ) or in column volume (x) or by number of theoretical plates ($N = x/\Delta x = \ell/\Delta\ell$) above and including the theoretical plate concerned as shown in Fig. 7.1.

FIG. 7.1 THE BATCH MODEL



After a volume v of solution has already passed through the column, a further amount Δv will enter the Nth section with the concentration $C_{x-\Delta x}$ and leave it with the concentration C_x. The amount in the section Δx is thus changed by $\Delta v(C_{x-\Delta x}-C_x)$. When the volume v has passed, the section has the content $\Delta x.q_v$ which after a further amount Δv of solution has changed to $\Delta x q_{(v+\Delta v)}$. It follows that

$$\Delta x(q_{(v+\Delta v)}-q_v) = \Delta v(C_{(x-\Delta x)}-C_x) \quad \ldots\ldots\ldots (7.1)$$

Small differences of this type can generally be expressed by means of differentials, according to Taylors theorem

$$C_{(x-\Delta x)} = C_x - \left(\frac{\partial c}{\partial x}\right)_v.\Delta x + \left(\frac{\partial^2 c}{\partial x^2}\right).\frac{\Delta x^2}{2} \quad \ldots\ldots \text{etc} \qquad (7.2)$$

$$q_{(v+\Delta v)} = q_v+\left(\frac{\partial q}{\partial v}\right)_x.\Delta v + \left(\frac{\partial^2 q}{\partial v^2}\right)_x.\frac{\Delta v^2}{2} + \ldots\ldots \text{etc} \qquad (7.3)$$

third differentials being quite negligible if

$$\Delta x << x$$

Substituting (7.2) and (7.3) into (7.1) results in the following mass balance equation:

$$\left(\frac{\partial c}{\partial x}\right)_v + \left(\frac{\partial q}{\partial v}\right)_x - \frac{\Delta x}{2}\left(\frac{\partial^2 c}{\partial x^2}\right)_v + \frac{\Delta v}{2}\left(\frac{\partial^2 q}{\partial v^2}\right)_x = 0 \qquad (7.4)$$

If the solution flow is continuous, then this is equivalent to the volume units Δv being infinitessimally small and equation (7.4) simplifies to

$$\left(\frac{\partial c}{\partial x}\right)_v + \left(\frac{\partial q}{\partial v}\right)_x - \frac{\Delta x}{2}\left(\frac{\partial^2 c}{\partial x^2}\right)_v = 0 \quad \ldots\ldots\ldots (7.5)$$

By assuming a local equilibrium so that $\frac{q}{c} = k_d$, Gluekauf (16) applied the following boundary conditions to equation (7.5):

i) $M = 0 \quad 0 < N < N_o \quad C = C_o$

ii) $M = 0 \quad N = N_o \quad C = 0$

iii) $M > 0 \quad N = 0 \quad C = 0$

where

$\frac{x}{\Delta x} = N$ = the number of "theoretical plates" up to point x

$\frac{v}{K_d \Delta x} = M$ = the number of "theoretical plate elution volumes" contained in the volume V

K_d = the distribution coefficient

N_o = the number of "theoretical plates" in the feed band

and obtained

$$c = C_{max} \exp\{-\frac{N'}{2}\frac{(\bar{v}-v)^2}{\bar{v}v}\} \quad \ldots\ldots\ldots\ldots\ldots\ldots (7.6)$$

and

$$C_{max} = \frac{m}{\bar{v}}\sqrt{\frac{N'}{2\pi}} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (7.7)$$

where

C_{max} = maximum peak height

m = mass of solute loaded onto the column

$\bar{v}$ = peak elution volume

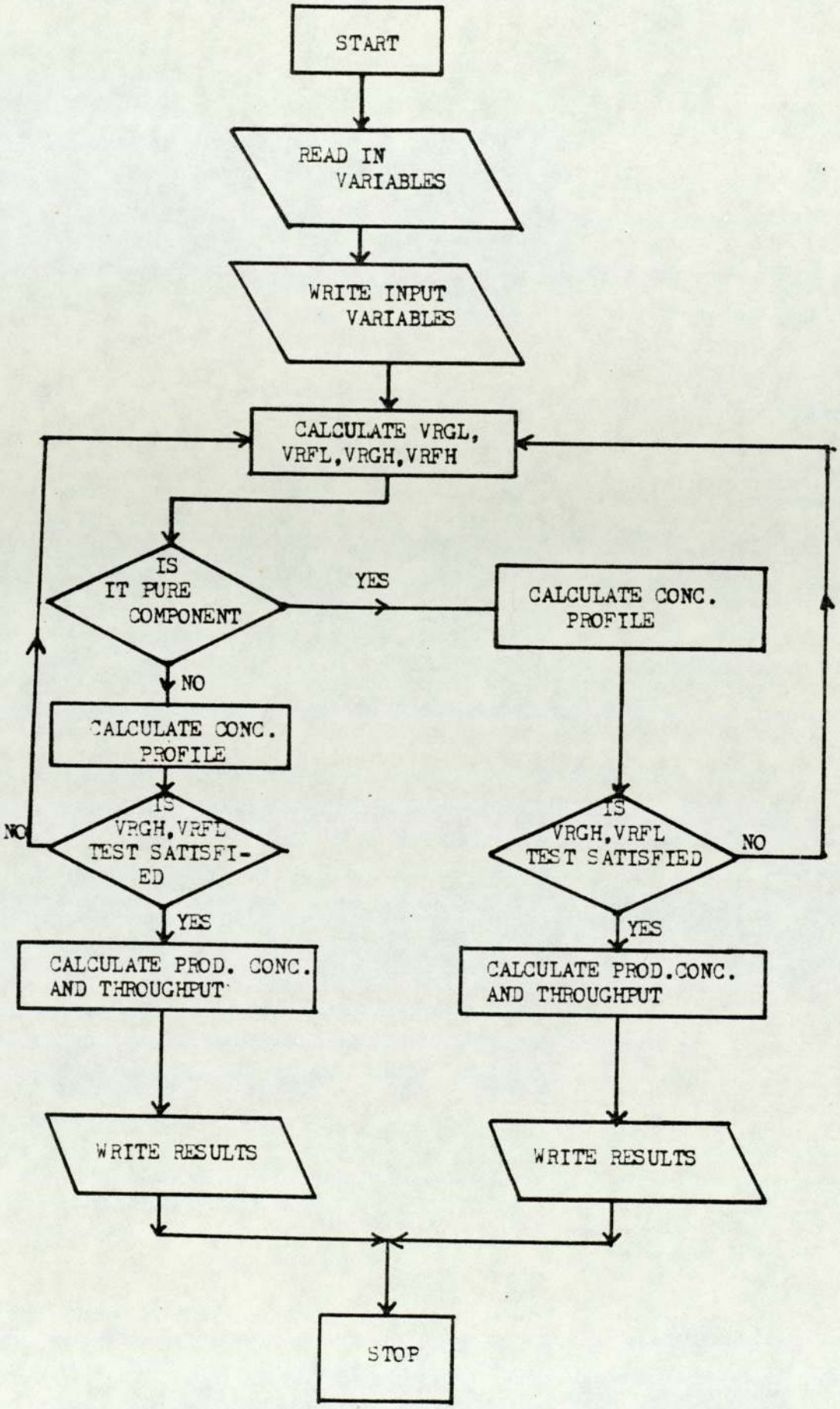
v = volume of eluting solution

N' = $N - \frac{1}{2}N_o$

c = concentration of solute

A flow chart for the programme is provided in Fig. 7.2. A listing of the programme and a sample of the print-out results is provided in Appendix 2.

FIG. 7.2 COMPUTER FLOW CHART FOR THE SIMULATION OF THE BATCH OPERATION OF THE S.C.C.R.6 UNIT



7.2.2 Simulation of Experimental Runs

The accuracy of the model and numerical method for the simulation of the batch chromatograph was investigated using glucose fructose and glucose fructose and dextran mixtures. The concentration profile of each component was computed using equation (7.6) and the mass of sugar in each product was obtained by integrating equation 7.6 with respect to volume v using Simpson's rule.

A number of batch runs were simulated with concentrations ranging from 200-700 g litre^{-1} and the sample volume injected changing from 1.2-15 litres. The experimental and simulated profiles of some of the runs are shown in Figs. 7.3-7.8.

7.2.3 Results and Discussion

If the simulated profiles are compared with the experimental profiles in Figs. 7.3-7.8, it can be seen that the simulated profile agrees closely with the experimental profile when the volume of sample injected was low. At higher sample volume (15 litres), the simulated peak becomes flatter at a maximum value lower than the experimental peak value.

Although the programme takes into account the K_d variation with on column concentration, the viability of other assumptions made in the derivation of equation 7.6 has to be discussed. It is open to discussion whether the instantaneous equilibrium across the plate actually occurs. Plate volumes used in the simulations

FIG. 7.3 EXPERIMENTAL AND SIMULATED PROFILE FOR BATCH RUN 20-2-100-100-20

Feed Concentration 20% w/v , Feed Volume 1200 cm^3
0.2 g cm^3 (2% of total empty column volume)

Eluent Flow Rate 100 $cm^3 min^{-1}$, Temperature 20°C

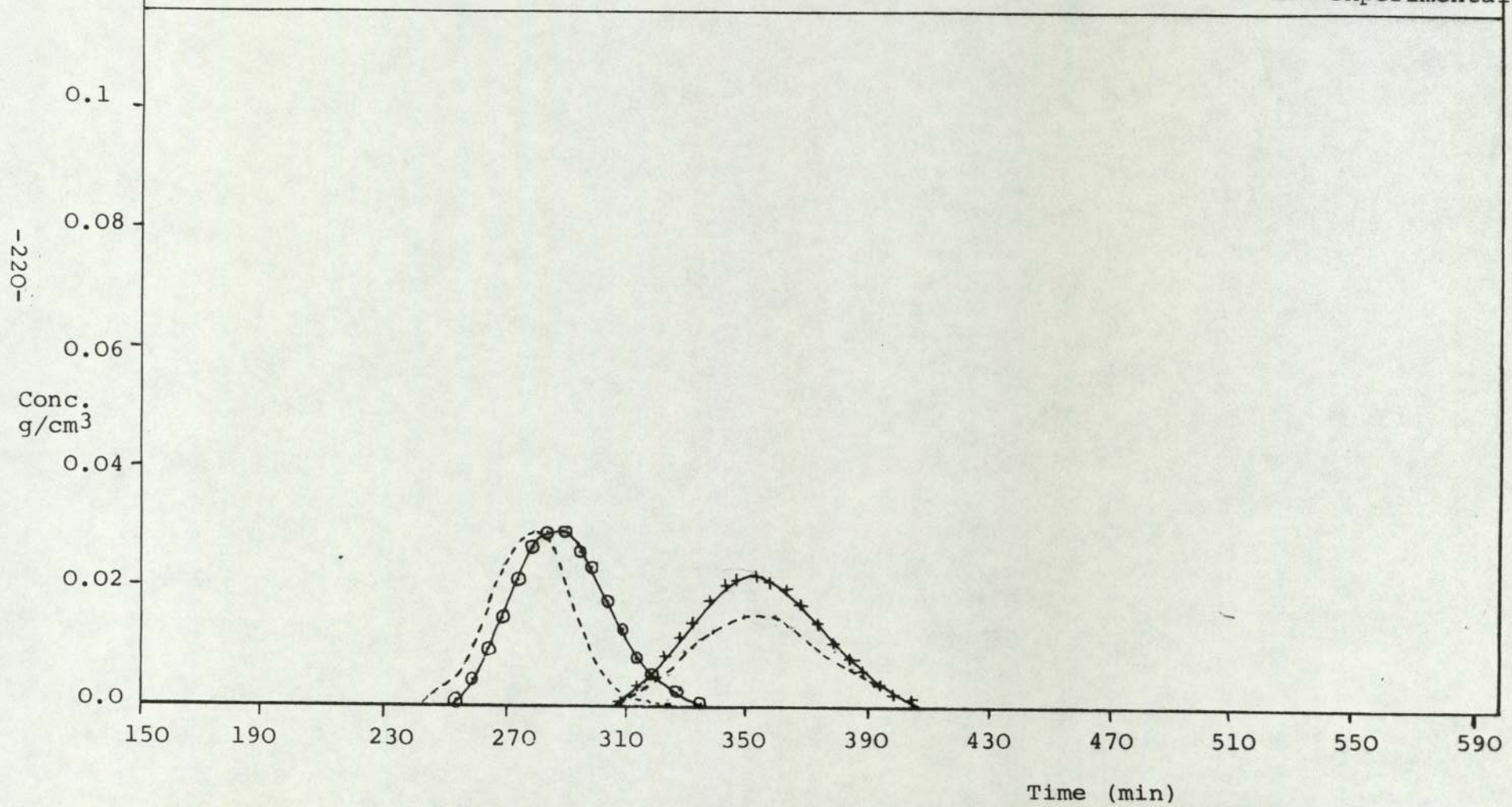


FIG. 7.4 EXPERIMENTAL AND SIMULATED CONCENTRATION PROFILE FOR BATCH RUN NO. 20-4-100-100-20

Feed Concentration 20% w/v , Feed Volume 2400 cm^3
0.2 g/cm^3 (4% of total empty column volume)

Eluent Flow Rate 100 $cm^3 min^{-1}$, Temperature 20°C

⊙ glucose
\+ fructose
-----simulated
——— experimental

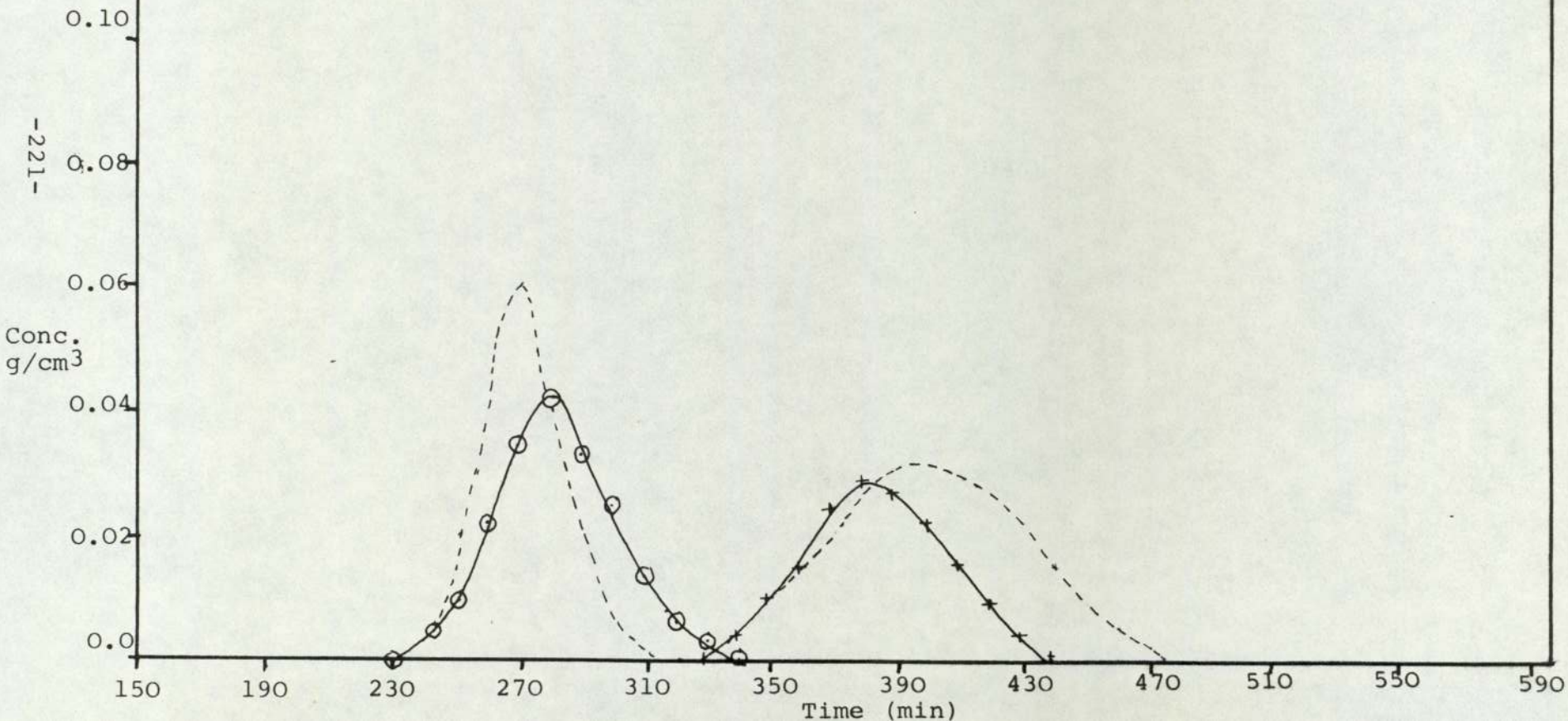


FIG. 7.5 EXPERIMENTAL AND SIMULATED PROFILE FOR BATCH RUN 20-10-100-100-20

Feed Concentration 20% w/v , Feed Volume 6000 cm^3
0.2 g/cm^3 (10% of total empty column volume)

Eluent Flow Rate 100 $cm^3 min^{-1}$, Temperature 20°C

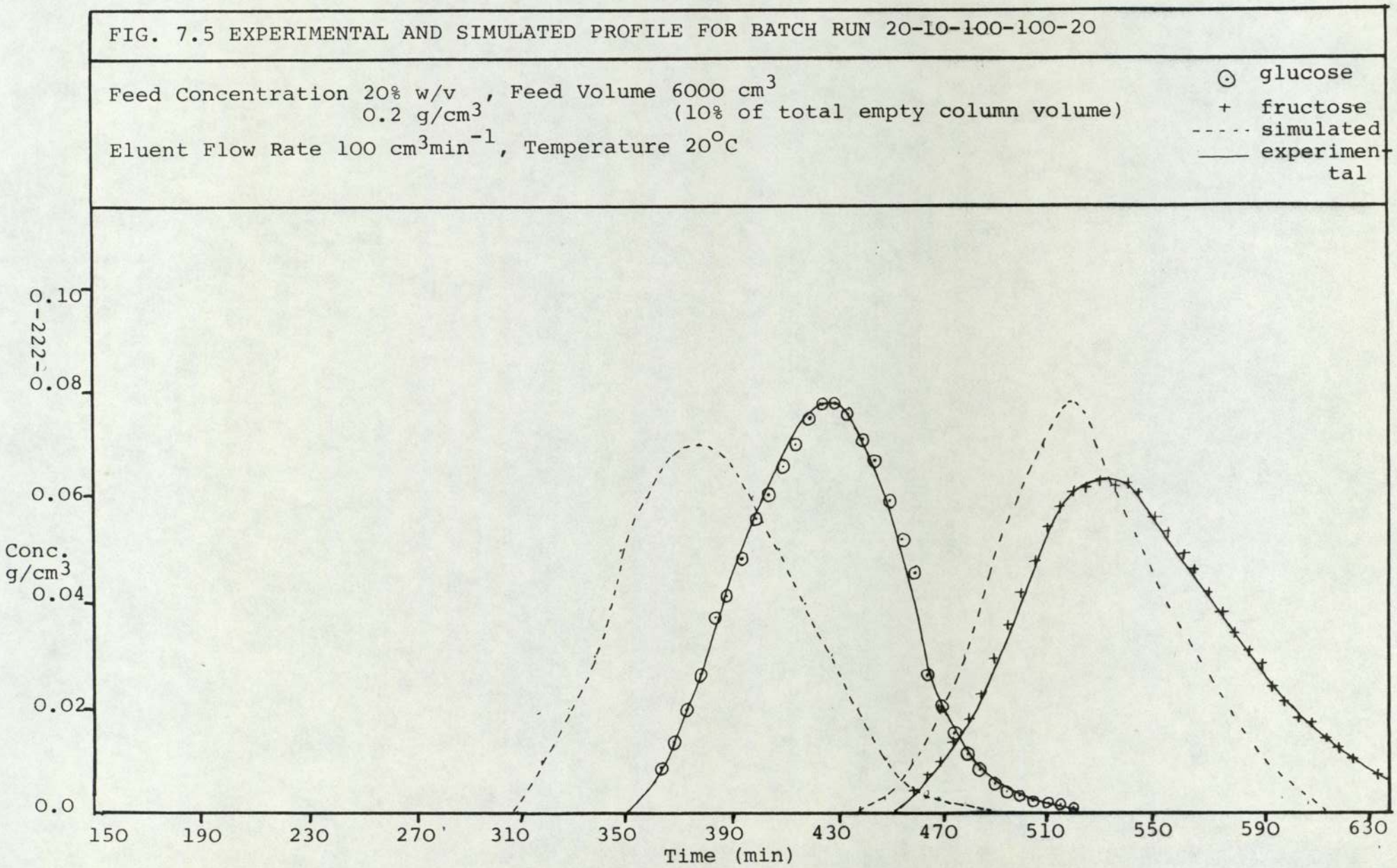


FIG. 7.6 EXPERIMENTAL AND ISMULATED PROFILE FOR BATCH RUN 20-20-100-100-20

Feed Concentration 20% w/v, Feed Volume 12000 cm^3
0.2 g/cm^3 (20% of total empty column volume)

Eluent Flow Rate 100 $cm^3 min^{-1}$, Temperature 20°C

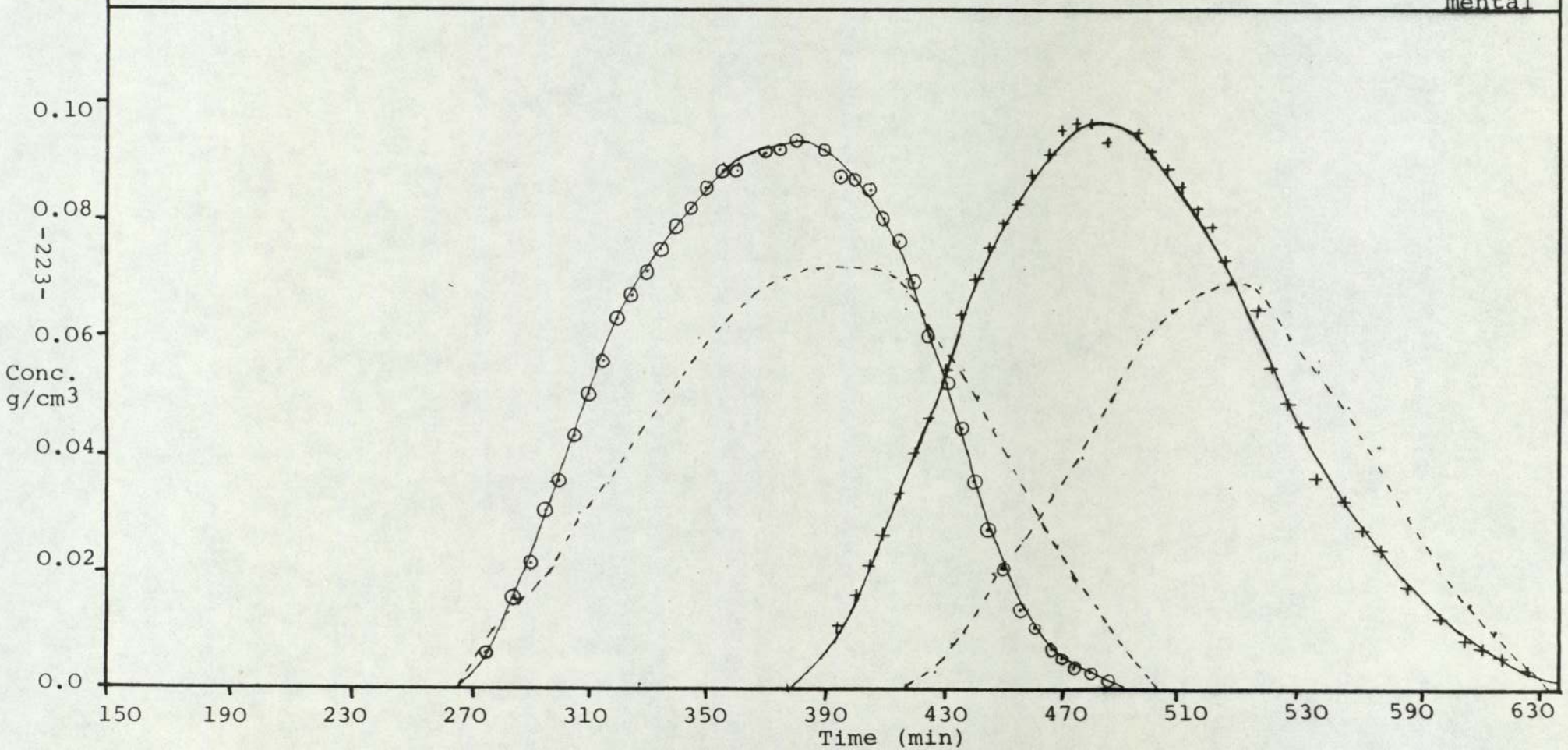


FIG. 7.7 EXPERIMENTAL AND SIMULATED PROFILE FOR BATCH RUN 20-25-100-100-20

Feed Concentration 20% w/v , Feed Volume 15000 cm^3
0.2 g/cm^3 (25% of total empty column volume)

Eluent Flow Rate 100 $cm^3 min^{-1}$, Temperature 20°C

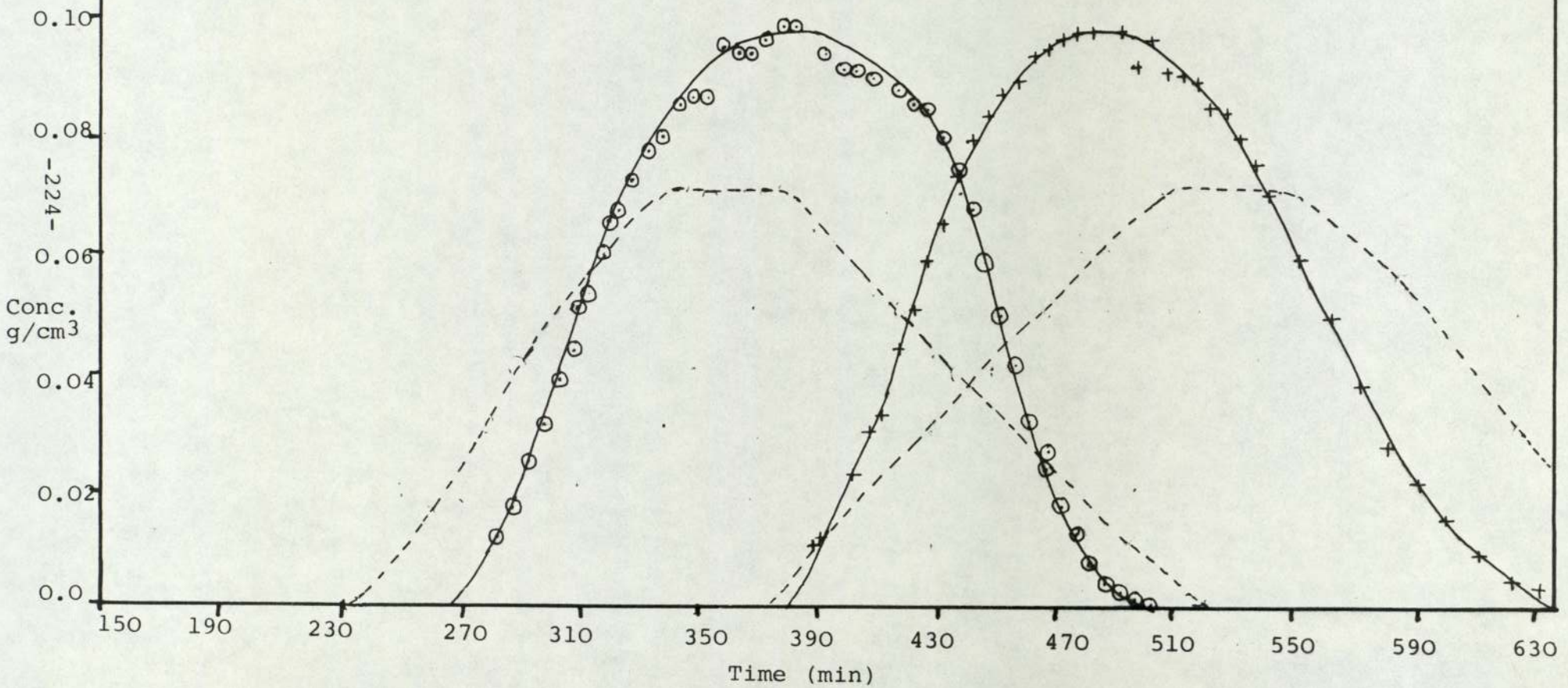
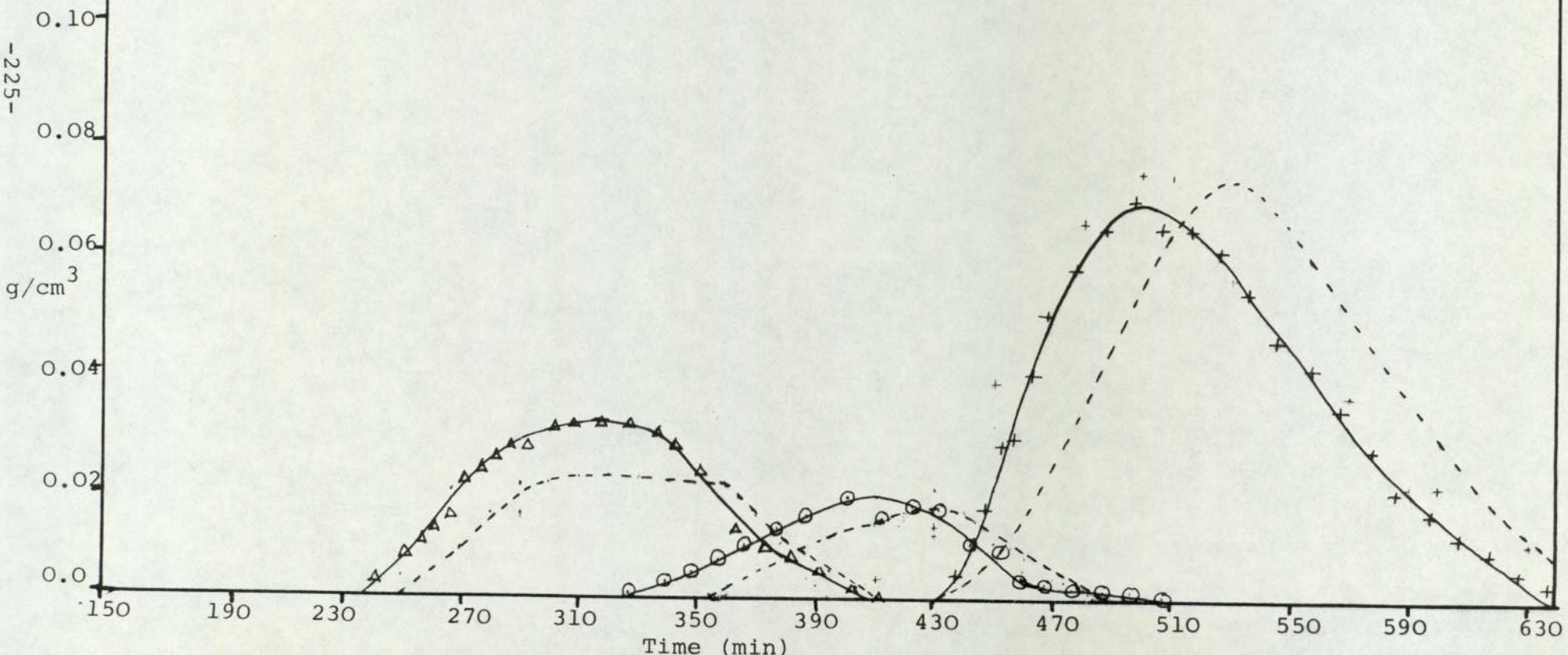


FIG. 7.8 EXPERIMENTAL AND SIMULATED PROFILE FOR BATCH RUN 70-20-100-100-20

Feed Concentration 70% w/v , Feed Volume 12000 cm^3
0.7 g/cm^3 (20% of total empty column volume)

Eluent Flow Rate 100 $cm^3 min^{-1}$, Temperature 20°C

⊙ glucose
\+ fructose
△ Dextran
---- simulated
—— experimental



are, for glucose, approximately 150 cm^3 which theoretically comprises 80 cm^3 of stationary phase and 70 cm^3 of mobile phase; and, for fructose, approximately 240 cm^3 of which 130 cm^3 is stationary phase and 110 cm^3 mobile phase.

In comparing the experimental and simulated profile a shift of the simulated peak to the left or right is observed. A chromatogram is a concentration vs. time curve. In calculation of time in the simulated result a constant flow rate of 100 $cm^3 min^{-1}$ is assumed, experimentally however an error of ±1% can easily occur. This error in the flow rate over a period of 7-8 hours, required to obtain the whole of the chromatogram, can cause a shift of ±40minutes.

Further improvements to the model can be made by considering other factors such as diffusion and band broadening effects. The literature survey in Chapter Two reveals that a considerable amount of work has been done in this field in gas chromatography but in liquid-solid chromatography no useful publications has been observed.

7.3 MATHEMATICAL MODELLING OF THE SCCR6 UNIT IN THE SEMI-CONTINUOUS MODE

Sciance and Crosser (96) proposed a probabilistic 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. In an example where the feed was introduced into the mid-section of the column, they proposed

$$\ln(u_Z)_A = \frac{0.5\ l\ K''_A}{u} = (K_A - \psi) \quad \ldots\ldots\ldots \quad (7.8)$$

$$\ln(1-(u_Z)_B = \frac{0.5\ l\ K''_B}{u} = (K_B - \psi) \quad \ldots\ldots\ldots \quad (7.9)$$

where

A refers to the faster moving component

B refers to the slower moving component

$(u_Z)_A$ = bottoms/feed mass flow rate ratio of A

$(u_Z)_B$ = tops/feed mass flow rate ratio of B

K" = rate constant of desorption

u = average mobile phase velocity

ψ = mobile phase/stationary phase velocity ratio

l = required column length

Experimental determination of K''_A and K''_B is difficult to determine and published values are rare. This has restricted the application of the model.

Al-Madfai (97) used the random walk approach developed by Giddings (15) and adopted it for predicting plate height in a continuous 'moving column' counter-current chromatography system. His proposed model is as follows:

$$H = d_p + \frac{2D_m}{u} + \frac{2\gamma_1\gamma_2}{(\gamma_1+\gamma_2)^2} \cdot \frac{(u+u_L)^2}{u\gamma_2 - u_L\gamma_1} \quad \ldots\ldots\ldots \quad (7.10)$$

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-Madfai also related the number of theoretical plates required to resolve binary mixtures in a batch column and in a continuous chromatographic system.

$$\frac{N_{cc}}{N_b} = 3(\alpha-1) \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (7.11)$$

where

N_{cc} = number of continuous plates

N_b = number of batch plates

α = separation factor of components

Barker and Lloyd (98) developed a transfer unit concept to simulate a continuous gas-liquid chromatographic system. They obtained equations to predict the number of overall transfer units in the moving column chromatograph for the rectifying and stripping section of the separating length.

$$(N_G)_R = \frac{1}{(V_G/K_oV_L^{-1})} \ln\left\{\frac{E_1/K_oV_L - C_1(V_G/K_oV_L^{-1})}{E_1/K_oV_L - C_2(V_G/K_oV_L^{-1})}\right\} \quad (7.12)$$

$$(N_G)_S = \frac{1}{(1-V_G/K_oV_L)} \ln\left\{\frac{E_2/K_oV_L - C_1(1-V_G/K_oV_L)}{E_2/K_oV_L - C_2(1-V_G/K_oV_L)}\right\} \quad (7.13)$$

where

$(N_G)_R, (N_G)_S$ = the number of overall gas phase transfer units in the rectifying and stripping sections respectively

E_1, E_2 = the mass flow rate of solute leaving in products 1 and 2 respectively

C_1, C_2 = gas phase solute concentrations at point 1 and 2 in the column

V_G, V_L = the gas and liquid volumetric flow rates

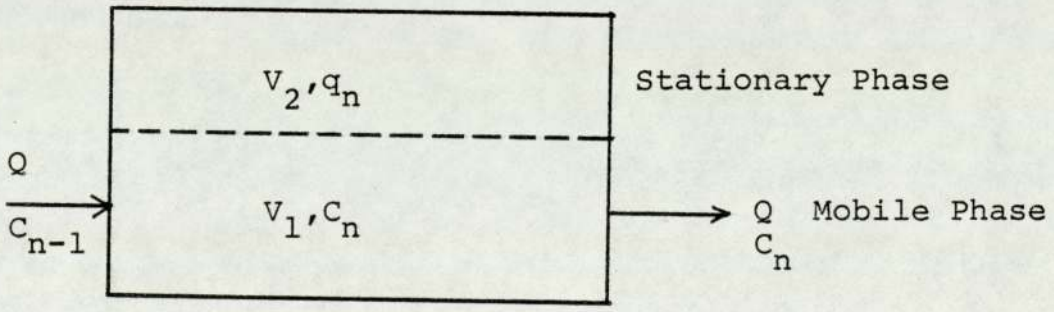
K_o = the partition coefficient

7.3.1 The Semi-Continuous Model

Ching (8) developed a model to describe the SCCR mode of operation. The model was based on the theoretical plate concept. A chromatographic column is considered to consist of a series of idealised mixing stages where the mobile phase leaving is in equilibrium with the stationary phase in the column.

Consider a stream of flow rate Q passing through the plate n having an initial solute concentration of C_{n-1} and an exit solute concentration of C_n. A mass balance over the plate n for the solute gives (Fig. 7.9).

FIG. 7.9 THE SEMI-CONTINUOUS MODEL



$$QC_{n-1} = QC_n + \frac{V_1 dC_n}{dt} + \frac{V_2 dq_n}{dt} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (7.14)$$

where

Q = volumetric flow rate of the mobile phase

C = solute 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 plate number

The distribution coefficient is defined as

$$K_d = \frac{q_n}{C_n}$$

Substituting this relationship into equation (7.14) gives

$$QC_{n-1} = QC_n + (V_1 + K_d V_2) \frac{dC_n}{dt} \quad \text{.....(7.15)}$$

This equation may now be integrated providing Δt is sufficiently small to allow C_{n-1} to be considered constant.

$$C_n = C_{n-1}\left(1 - \exp\left(\frac{-Q.\Delta t}{V_1+V_2K_d}\right)\right) + C_n^o \exp\left(\frac{-Q.\Delta t}{V_1+K_dV_2}\right) \quad (7.16)$$

where

C_n^o = initial concentration of the solute in plate, n

The first term on the right hand side of the equation (7.16) represents the material transferred to plate n from plate n-1 and the second term represents the material already present on plate n at the beginning of the time increment Δt.

For a feed plate, a mass balance on the solute yields a similar equation;

$$C_n = \left(\frac{QC_{n-1} + FC_f}{Q + F}\right)\left(1 - \exp\left(\frac{-Q.\Delta t}{V_1+K_dV_2}\right)\right) + C_n^o \exp\left(\frac{-Q.\Delta t}{V_1+K_dV_2}\right)$$

..... (7.17)

where

F = volumetric flow rate of feed

C_f = solute concentration in the feed

The sequencing action of the SCCR6 unit is simulated by stepping the system profile backwards, by one column, at the end of a sequencing interval. The model considers only one solute and the profile of the second solute is determined by duplicating the calculation at each plate with a different variable name. The assumption is made that there is no interaction between the components.

7.3.2 Improvements in the Model

Alternative to assuming that C_{n-1} remains constant over a small time increment Δt, K. England (94) obtained n number of simultaneous differential equations, for n plates, similar in form to equation (7.15), i.e.

$$(Q+F)C_n = QC_{n-1} + (V_1+K_dV_2)\frac{dC_n}{dt} + F.C_{fn} \quad \ldots \quad (7.18)$$

Rearranging equation 7.18 and dividing by $(V_1+K_dV_2)$ gives:

$$\frac{dC_n}{dt} = \frac{Q}{(V_1+K_dV_2)} C_{n-1} - \frac{(Q+F)}{(V_1+K_dV_2)} C_n + \frac{F}{(V_1+K_dV_2)} C_{fn}$$

or

$$\frac{dC_n}{dt} = x_n C_{n-1} + y_n C_n + Z_n C_{fn} \quad \ldots\ldots\ldots \quad (7.19)$$

where

$$x_n = \frac{Q}{(V_1+K_dV_2)}$$

$$y_n = \frac{Q + F}{(V_1+K_dV_2)}$$

$$Z_n = \frac{F}{(V_1+K_dV_2)}$$

For n number of plates, a set of equations was produced according to equation (7.19)

$$\dot{C}_1 = xC_o - yC_1 + zC_{f1}$$

$$\dot{C}_2 = xC_1 - yC_2 + zC_{f2}$$

$$\dot{C}_2 = xC_{n-1} - yC_n + zC_{fn}$$

or $$\dot{C}(t) = \underline{X}\,\underline{C}(t) + \underline{Y}\,C_f(t) \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (7.20)$$

Then the general equation (7.20) is solved and the solution is

$$C(t) = \exp^{\underline{X}t}\,\underline{C}_o + \int_o^t e^{\underline{X}(t-\tau)}\,\underline{Y}\,C_f(\tau)\,d\tau \quad \ldots \quad (7.21)$$

If the feed input is not time dependent equation (7.21) can be solved further to

$$C(t) = \exp^{\underline{X}t}\,\underline{C}_o + \underline{X}^{-1}(\exp^{\underline{X}t} - \underline{I})\,\underline{Y}\,C_f \quad \ldots\ldots \quad (7.22)$$

or

$$C(t) = \underline{\phi}(t)\,\underline{C}_o + \underline{\Delta}(t)\,\underline{Y}\,C_f \quad \ldots\ldots\ldots\ldots\ldots \quad (7.23)$$

where

$$\underline{\phi}(t) = \exp^{\underline{X}t}$$

$$\underline{\Delta}(t) = \underline{X}^{-1}(\exp^{\underline{X}t} - \underline{I}) = \underline{X}^{-1}(\underline{\phi}(t) - I$$

The detailed solution of equation 7.20 is given by England (94).

Using this model to simulate the SCCR6 unit with 250 theoretical plates and only 5 terms in the $\Delta(t)$ matrix, the computing time exceeded the maximum time allowed by CDC 7600 computer available by University of Manchester Regional Computer Centre. Later the same programme was transferred to Harris 500 available in

the University of Aston, but the programme failed to converge with only 5 terms. Increasing the terms in $\Delta(t)$ matrix increased the computing time but no satisfactory results were obtained for the glucose fructose system. For this reason the possible improvement to the existing model used by Gould (10) is considered in detail.

A significant improvement to the existing model used by Gould (10) is made by taking into account the concentration and temperature effect. This will be discussed shortly.

Further improvement is introduced by adopting the model to include a third component dextran - the non-sorbed species in the feedstock. This was accomplished by using a further mass balance equation in the feed and separating section of the programme.

An extra routine was introduced to compute the bulk concentration and purity of components in the individual products.

A flowsheet for the programme used in the simulation is shown in Fig. 7.10. A listing of the programme and a sample of the printout is included in Appendix 3.

7.3.2.1 Concentration and Temperature Effects

Because the separation performance of the SCCR6 unit changes significantly as the sugar concentration in the system increases, the computer programme used to simulate the operation of the SCCR6 unit, based on the theoretical model only was insufficient to predict the

FIG. 7.10 COMPUTER FLOW CHART FOR THE SIMULATION OF CONTINUOUS OPERATION OF THE S.C.C.R.6 UNIT

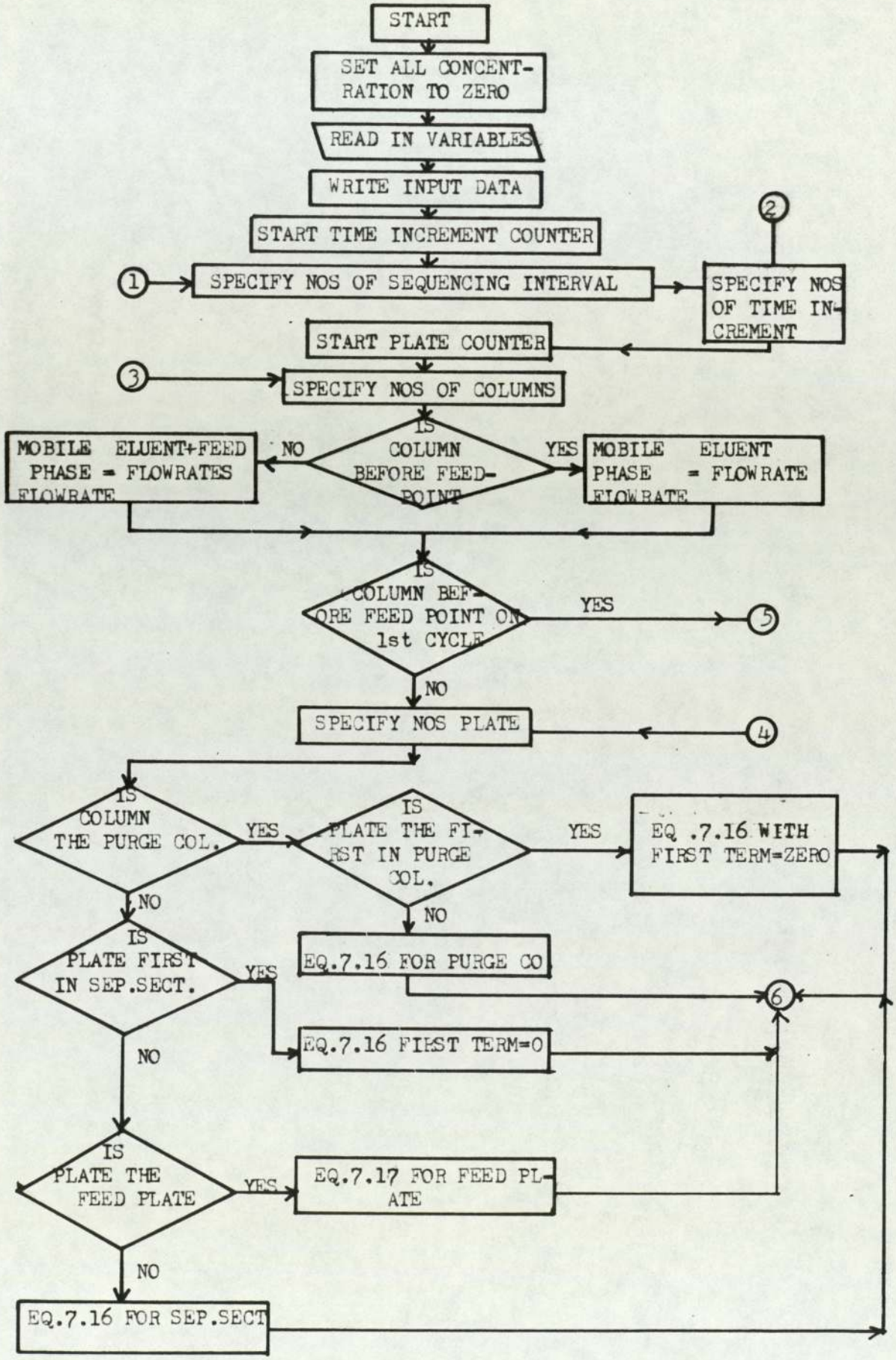


FIG. 7.10 Continued

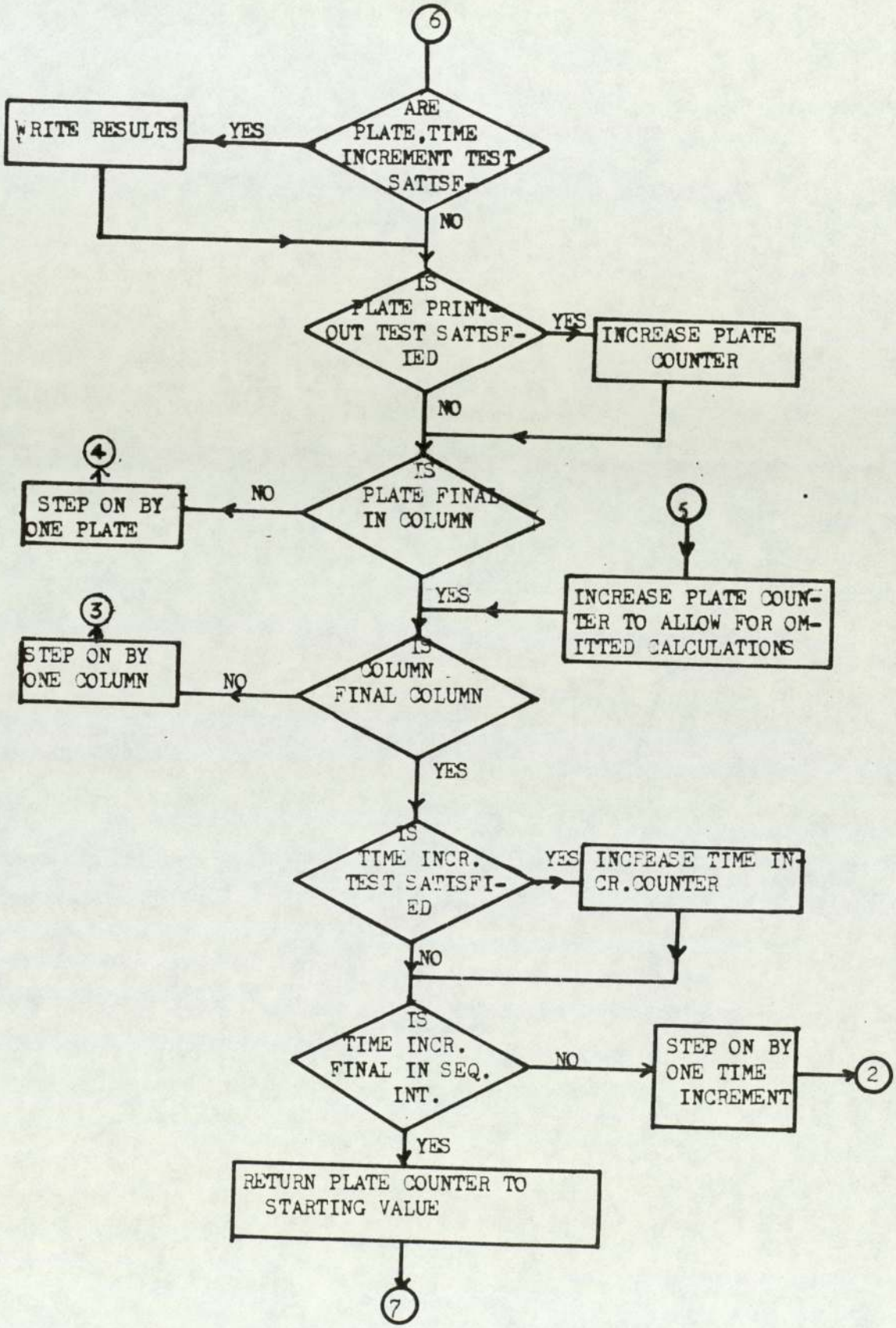
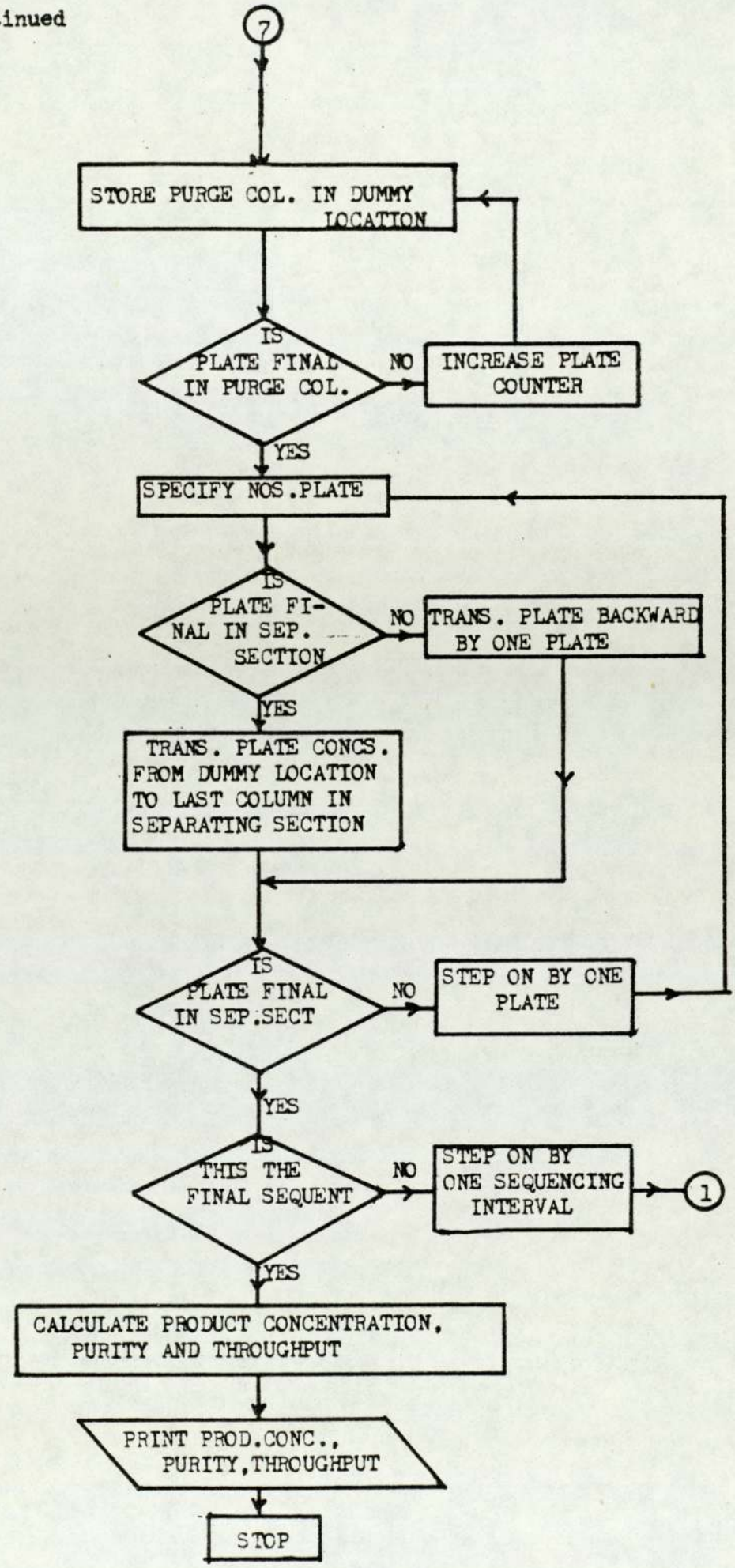


FIG. 7.10 Continued



separation of sugars on the SCCR6 unit (10). Hence the programme had to be modified to take into account the concentration and temperature effects.

Through lack of distribution coefficient data previous workers, Chuah (9) and Gould (10), assumed a value for K_d to get a best fit between the simulated and experimental profiles. In this project the data used for the concentration effects in the existing simulation programme was obtained by the experimental work carried out in the laboratory and is described in detail in Chapter 3. Table 3.4 gives the equations relating the concentration of the components to their distribution coefficients.

Chuah (9) performed a number of experiments in the laboratory to study the variation of distribution coefficients with temperature. It was calculated that for an increase in temperature from ambient to 30°C, the distribution coefficient of fructose was reduced to 95% of the value at ambient, at 45°C it was reduced to 91%, and at 60°C the reduction was down to 83% of the value at ambient temperature. The distribution coefficient of glucose remained more or less the same at all temperatures. Therefore the change in distribution coefficient of fructose K_{df} was defined as

$$K_{df}^{30^oC} = 0.95\ K_{df}^{20^oC} \quad \text{at } 30^oC$$

$$K_{df}^{45^oC} = 0.91\ K_{df}^{20^oC} \quad \text{at } 45^oC$$

$$K_{df}^{60^oC} = 0.83\ K_{df}^{20^oC} \quad \text{at } 60^oC$$

7.3.3 Simulation of Experimental Runs

The memory core available on the ICL 1904S computer at Aston University was not large enough for a programme of this size. The CDC 7600 computer from the University of Manchester Regional Computer Centre did not allow sufficient time for the execution of the programme. Instead the programme was transferred as a control point job on the Harris 500 interactive computer at Aston University. This allowed a maximum of 10,000 seconds for the execution of a programme and was found most satisfactory.

The experimental and simulated profiles of the simulated runs are shown in Fig. 7.11-7.22.

7.3.4 Results and Discussion

The model describes an idealised picture of the separation process taking place in the SCCR6 unit. Previous workers Chuah (9) and Gould (10) assumed a value for the distribution coefficient to get best fit between the simulated and experimental concentration profile. In this project variation of distribution coefficient with on column sugar concentration has been studied experimentally and the result has been incorporated in the existing model. The inclusion of concentration and temperature dependent distribution coefficient in the model provided a reasonable agreement between the simulated and experimental results but it failed to describe the process completely especially in case of change in feed point location. Further improvement to

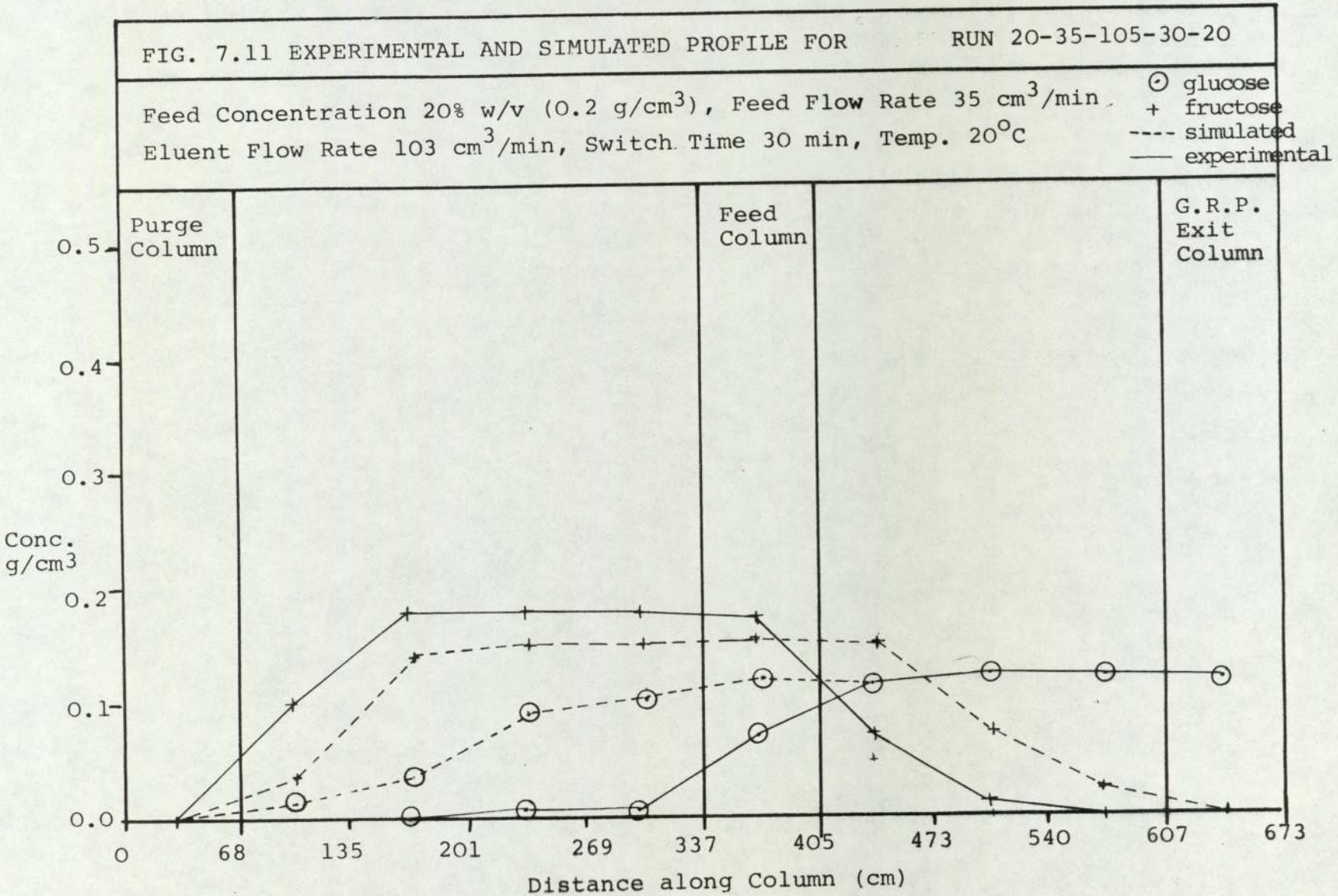


FIG. 7.11 EXPERIMENTAL AND SIMULATED PROFILE FOR RUN 20-35-105-30-20
Feed Concentration 20% w/v (0.2 g/cm3), Feed Flow Rate 35 cm3/min
Eluent Flow Rate 103 cm3/min, Switch Time 30 min, Temp. 20°C
glucose
fructose
simulated
experimental
Purge Column
Feed Column
G.R.P. Exit Column
Conc. g/cm3
0.5
0.4
0.3
0.2
0.1
0.0
0
68
135
201
269
337
405
473
540
607
673
Distance along Column (cm)

FIG. 7.12 EXPERIMENTAL AND SIMULATED PROFILE FOR RUN 30-35-105-30-2o

Feed Concentration 30% w/v (0.3 g/cm^3) Feed Flow Rate 35 cm^{3}min^{-1}
Eluent Flow Rate 105 cm^{3}min^{-1}, Switch Time 30 min, Temp. 2°C

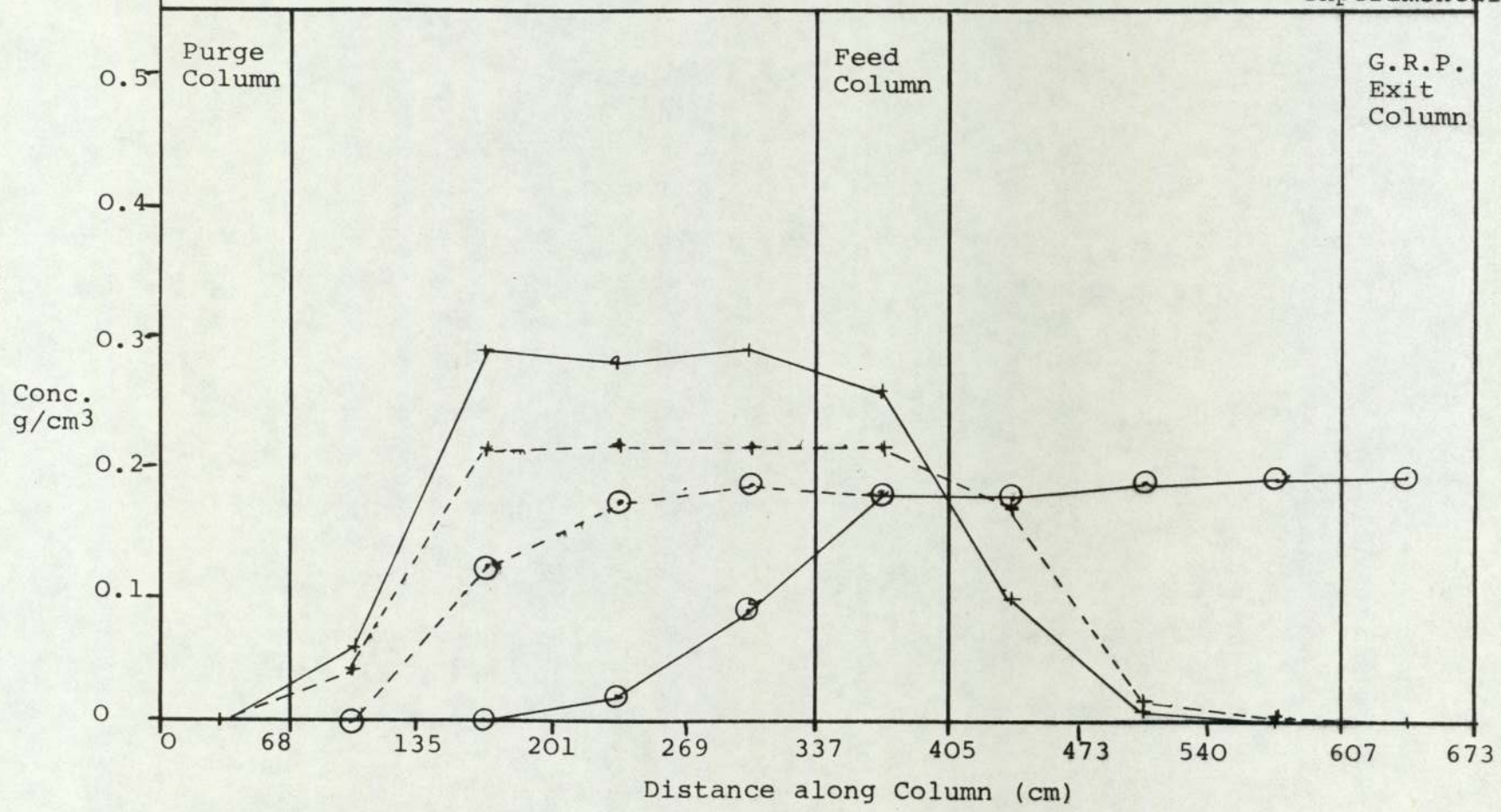


FIG. 7.13 EXPERIMENTAL AND SIMULATED CONCENTRATION PROFILE FOR RUN 40-35-105-30-20

Feed Concentration 40% w/v (0.4 g cm^{-3}), Feed Flow Rate 35 $cm^3 min^{-1}$
Eluent Flow Rate 105 $cm^3 min^{-1}$, Switch Time 30 min, Temp. 20°C

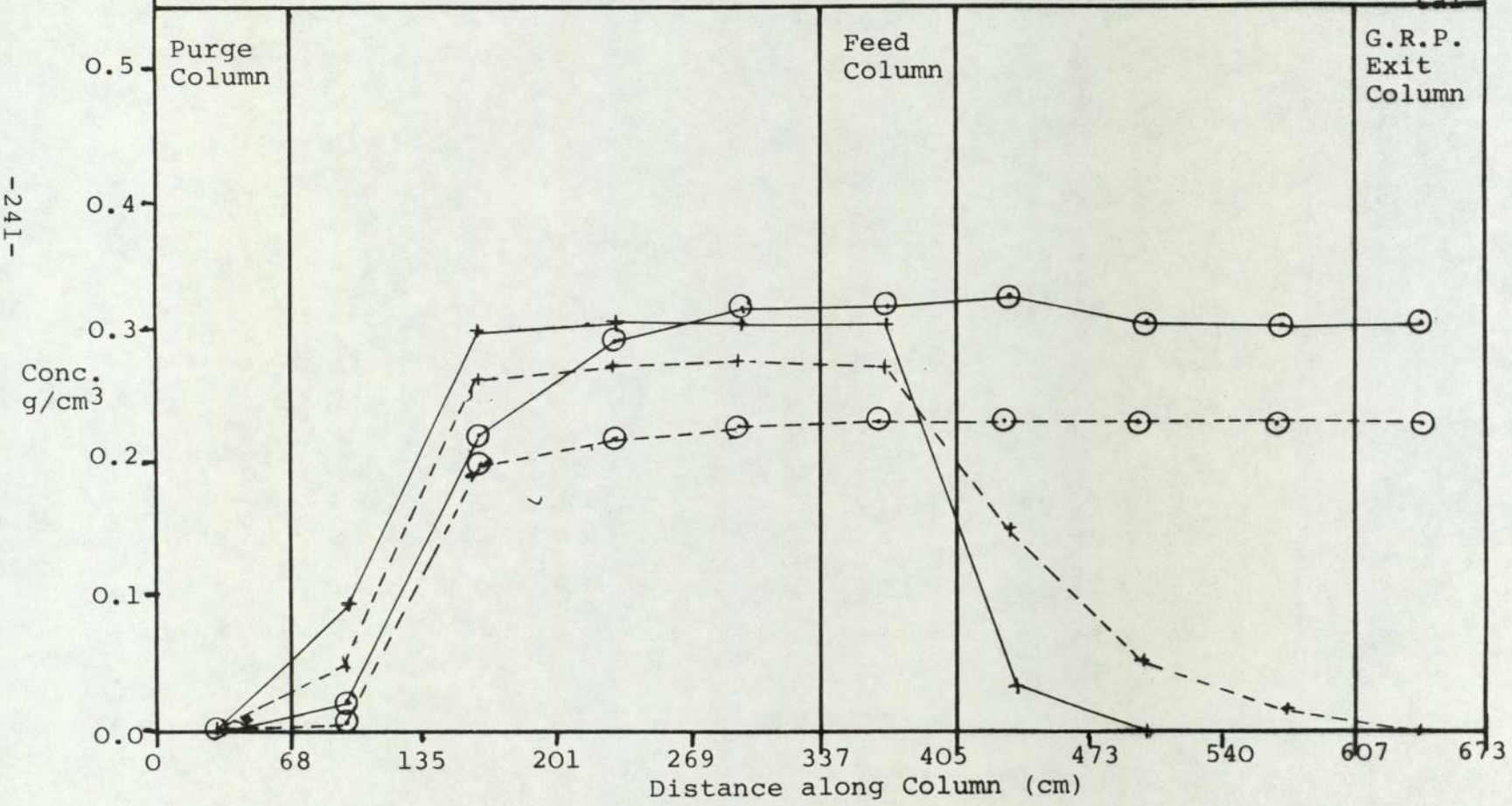


FIG. 7.14 EXPERIMENTAL AND SIMULATED CONCENTRATION PROFILE FOR RUN 50-35-105-30-20

Feed Concentration 50% w/v (0.5 g/cm^3), Feed Flow Rate 35 cm^{3}min^{-1}, Eluent Flow Rate 105 cm^{3}min^{-1}, Switch Time 30 min, Temp. 20^{o}C

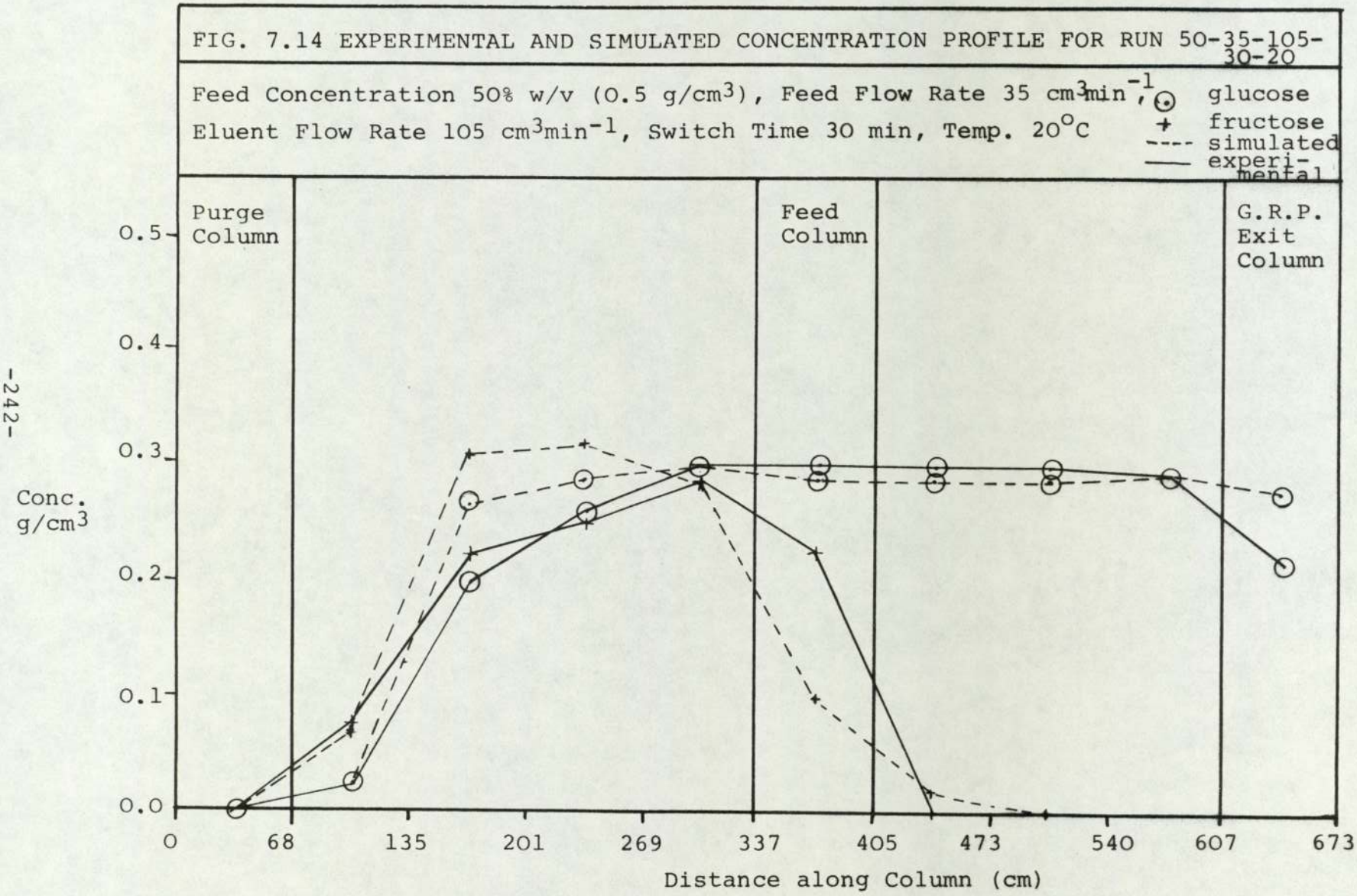
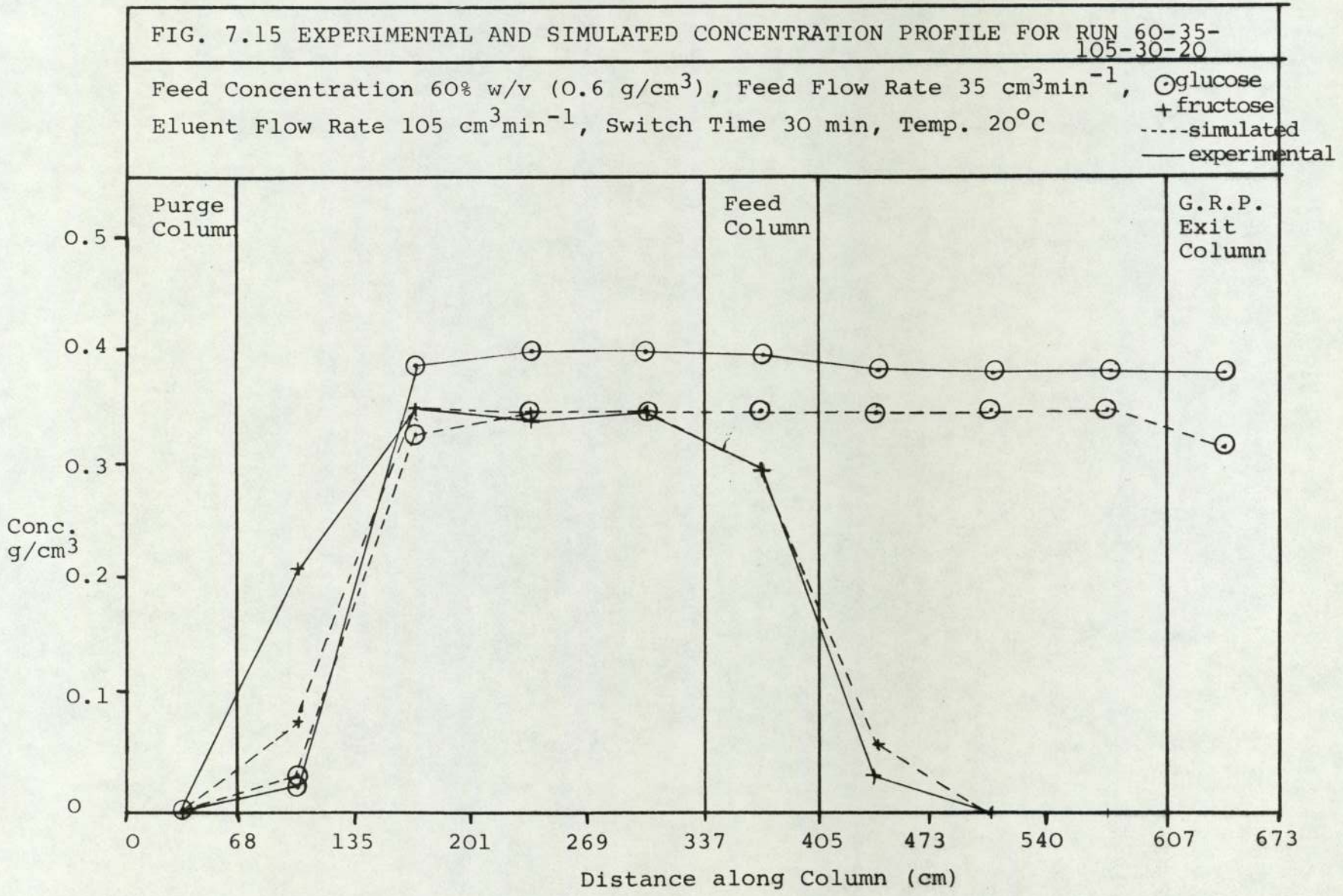


FIG. 7.15 EXPERIMENTAL AND SIMULATED CONCENTRATION PROFILE FOR RUN 60-35-105-30-20

Feed Concentration 60% w/v (0.6 g/cm^3), Feed Flow Rate 35 cm^{3}min^{-1}, Eluent Flow Rate 105 cm^{3}min^{-1}, Switch Time 30 min, Temp. 20°C



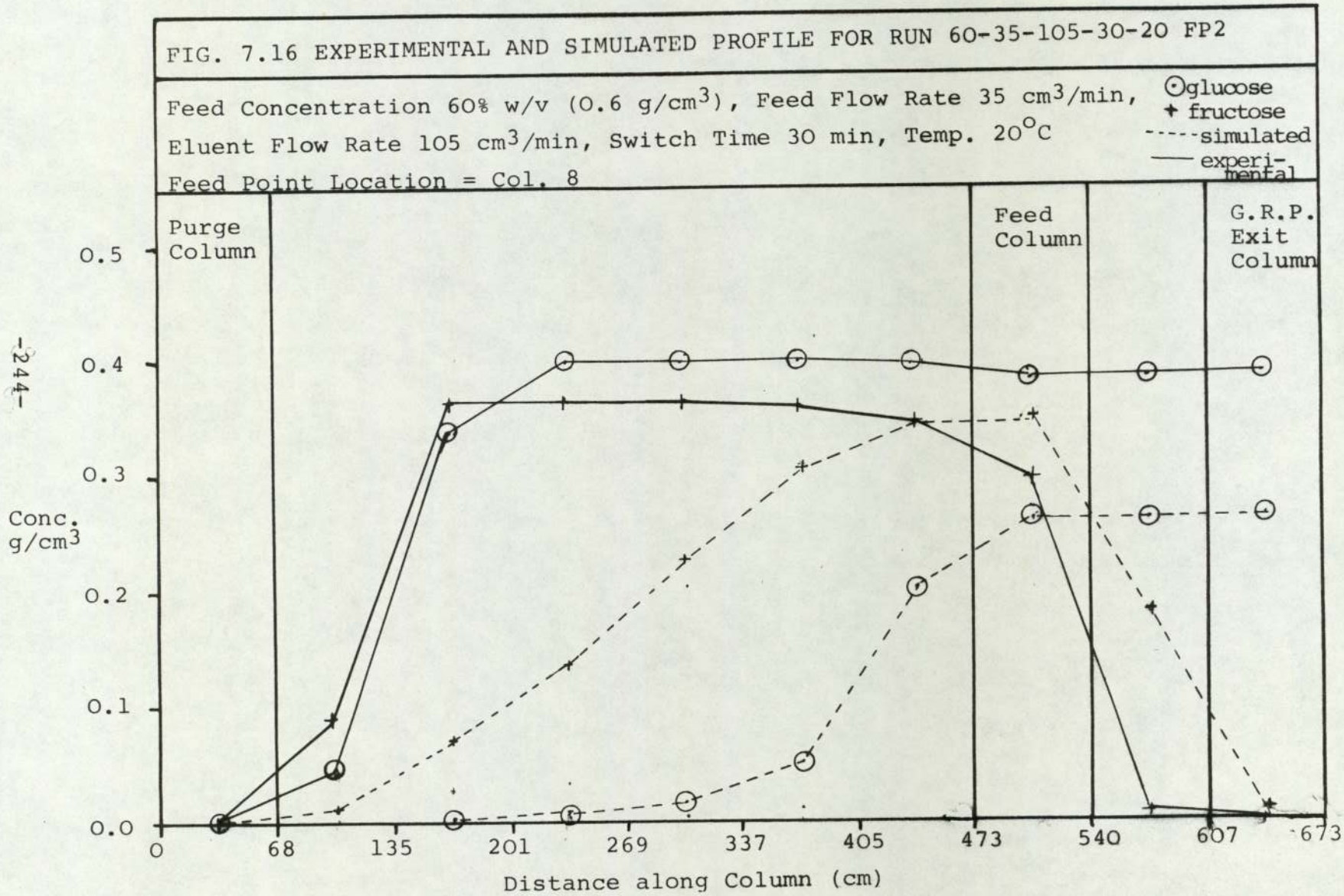


FIG. 7.16 EXPERIMENTAL AND SIMULATED PROFILE FOR RUN 60-35-105-30-20 FP2
Feed Concentration 60% w/v (0.6 g/cm3), Feed Flow Rate 35 cm3/min,
Eluent Flow Rate 105 cm3/min, Switch Time 30 min, Temp. 20°C
Feed Point Location = Col. 8
glucose
fructose
simulated
experimental
Purge Column
Feed Column
G.R.P. Exit Column
Conc. g/cm3
0.0
0.1
0.2
0.3
0.4
0.5
0
68
135
201
269
337
405
473
540
607
673
Distance along Column (cm)

FIG. 7.17 EXPERIMENTAL AND SIMULATED PROFILE FOR RUN 20-35-105-30-30

Feed Concentration 20% w/v (0.2 g/cm^3), Feed Flow Rate 35 cm^3/min,
Eluent Flow Rate 105 cm^3/min, Switch Time 30 min, Temp. 30^{o}C

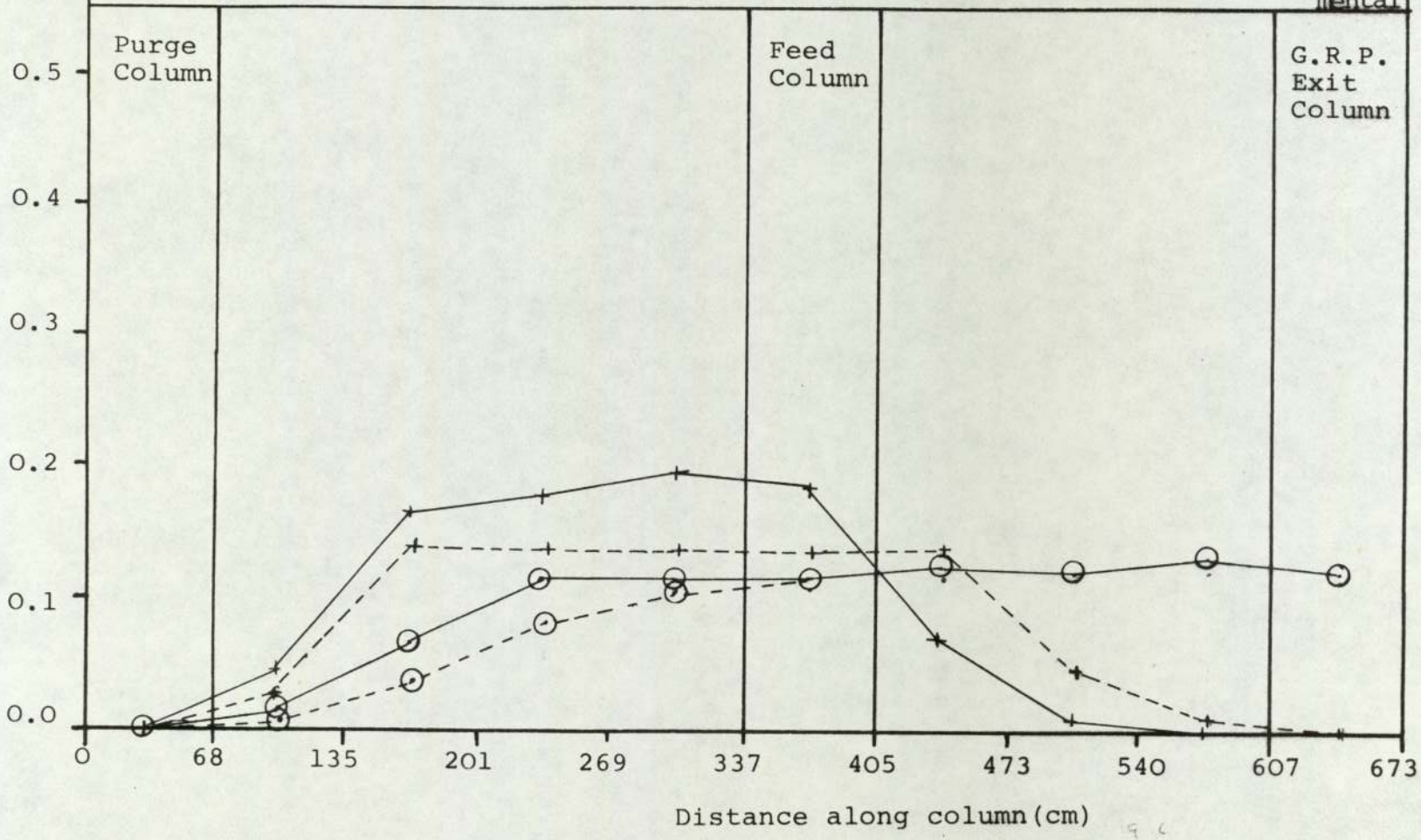


FIG. 7.18 EXPERIMENTAL AND SIMULATED PROFILE FOR RUN 20-35-105-30-45

Feed Concentration 20% w/v (0.2 g/cm^3), Feed Flow Rate 35 cm^3/min, Eluent Flow Rate 105 cm^3/min, Switch Time 30 min, Temp. 45°C

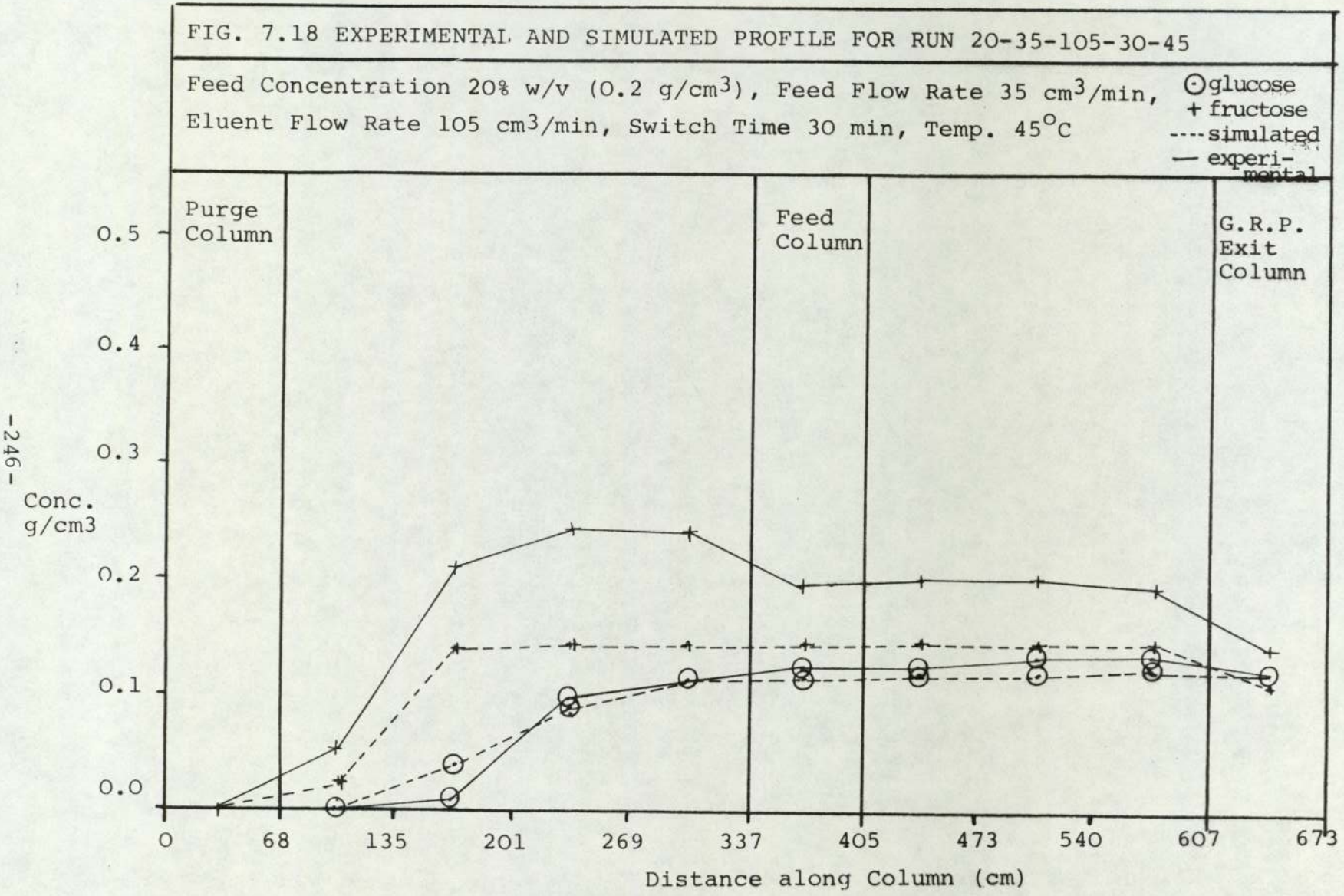


FIG. 7.19 EXPERIMENTAL AND SIMULATED PROFILE FOR RUN 20-35-105-30-60

Feed Concentration 20% w/v (0.2 g/cm^3), Feed Flow Rate 35 cm^3/min, Eluent Flow Rate 105 cm^3/min, Switch Time 30 min, Temp. 60°C

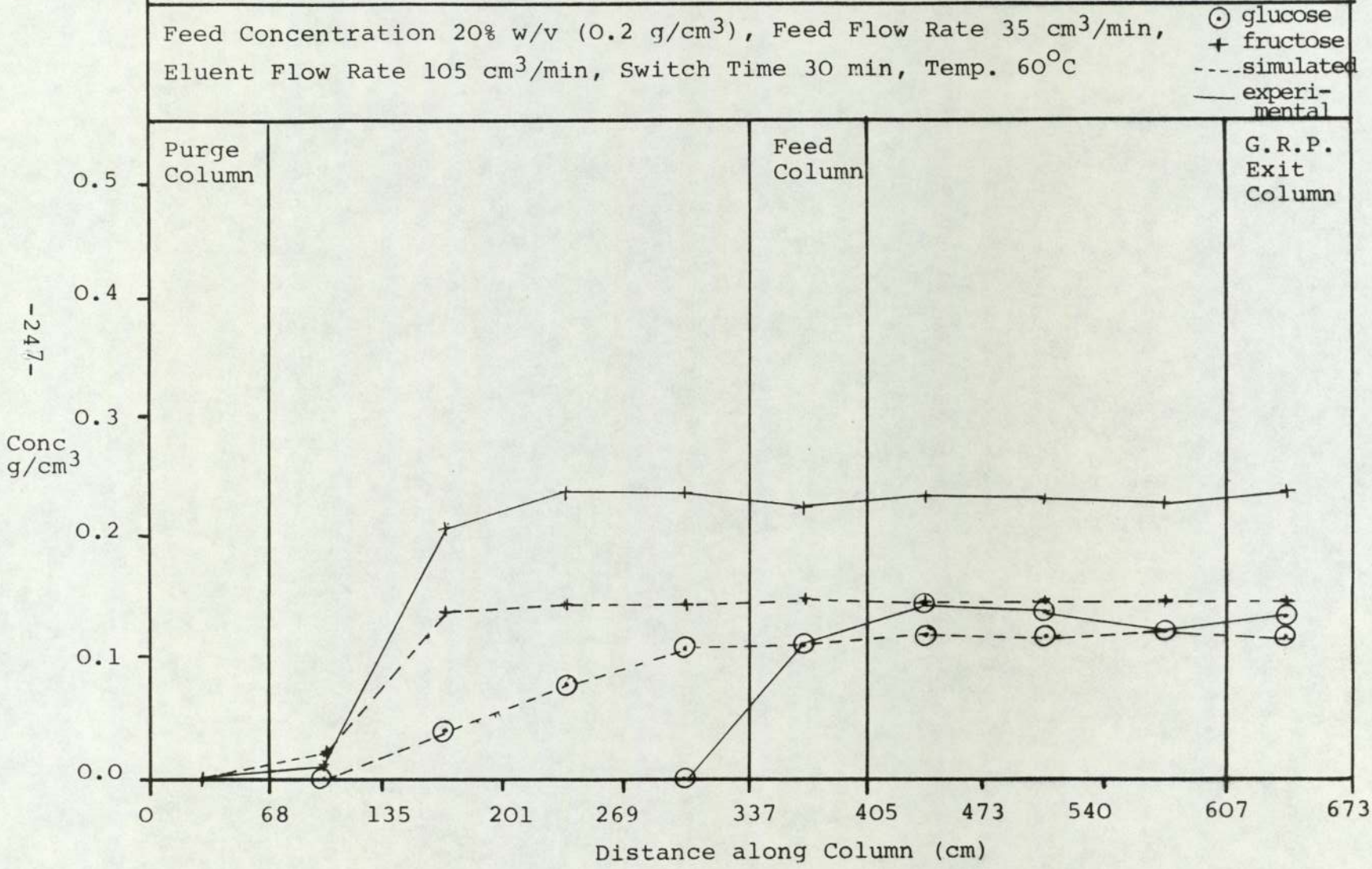


FIG. 7.20 EXPERIMENTAL AND SIMULATED PROFILE FOR RUN 40-35-105-30-60

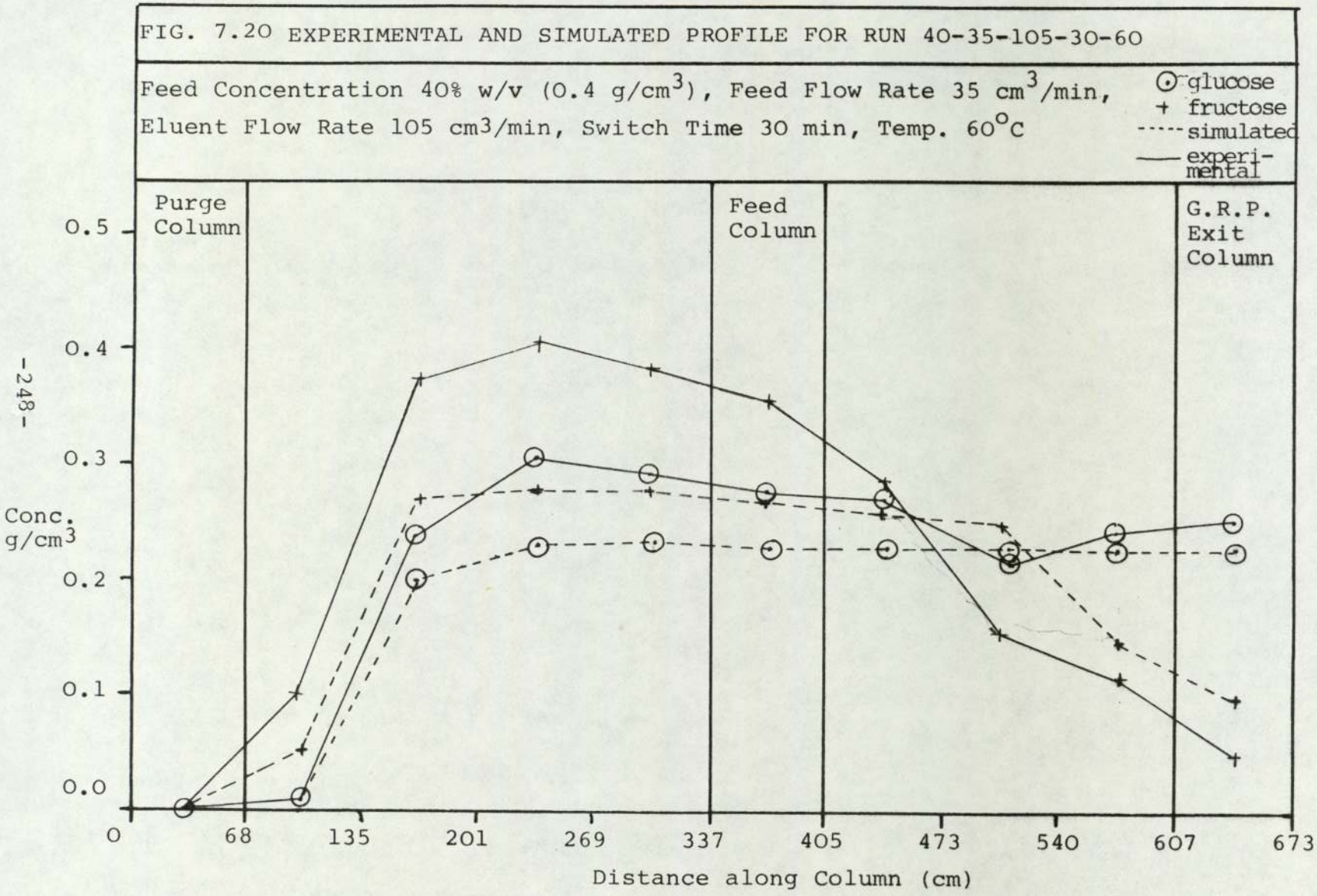


FIG. 7.21 EXPERIMENTAL AND SIMULATED PROFILE FOR RUN 60-35-105-30-60

Feed Concentration 60% w/v (0.6 g/cm^3), Feed Flow Rate 35 cm^3/min, Eluent Flow Rate 105 cm^3/min, Switch Time 30 min, Temp. 60^{o}C

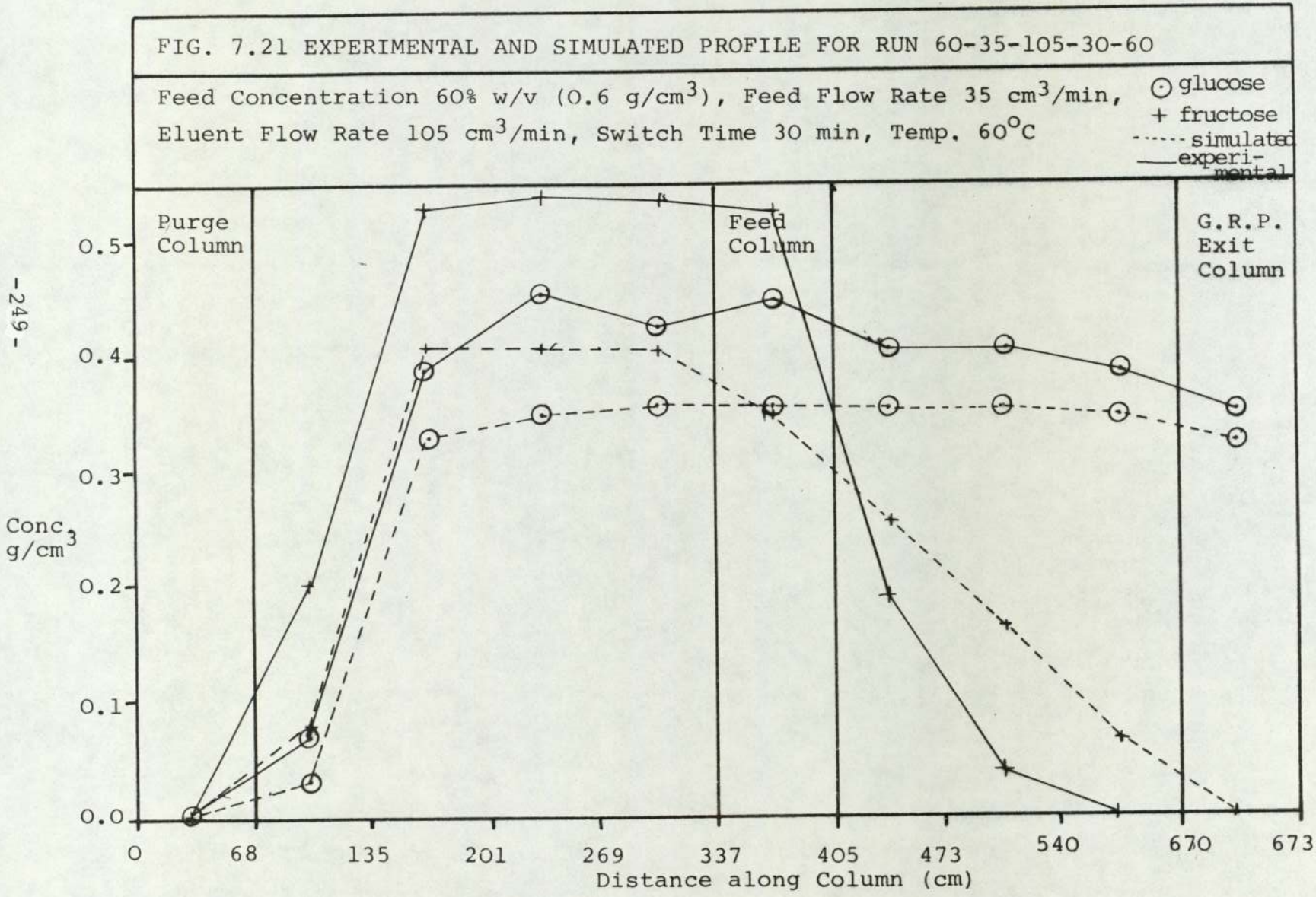
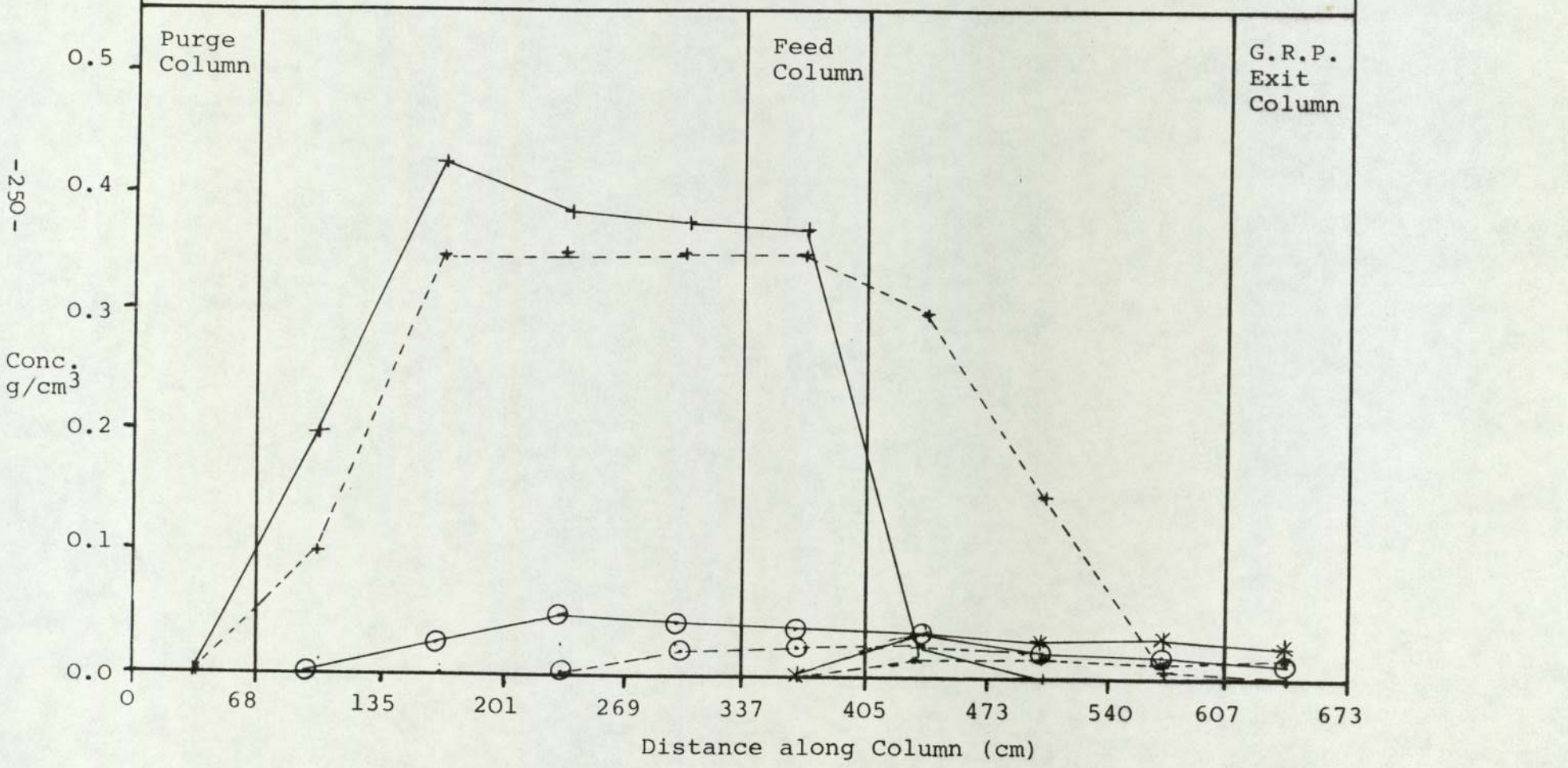


FIG. 7.22 EXPERIMENTAL AND SIMULATED PROFILE FOR RUN 70-70-210-15-60

Feed Concentration 70% w/v (0.7 g/cm^3), Feed Flow Rate 70 cm^3/min,
Eluent Flow Rate 210 cm^3/min, Switch Time 15 min, Temp. 60°C



the model can be made by considering other effects that take place simultaneously during the operation of the SCCR6 unit, such as diffusion. It is also open to discussion whether the instantaneous equilibrium, which the model assumes across the plate, actually occurs. The assumption that C_{n-1} remains constant over a small time increment Δt is also questionable and so is the assumption that the number of plates calculated for the individual components during a batch mode is identical to that in the semi-continuous mode. To evaluate these effects, it is preferable to carry out the experimental work on the SCCR6 unit under actual operating conditions instead of by batch mode technique.

7.4 THEORETICAL COMPARISON OF BATCH AND SEMI-CONTINUOUS OPERATION OF THE SCCR6 UNIT

The experimental comparison of batch and semi-continuous mode of operations in terms of throughput and quality of the product is performed in Section 6.9. In this section a theoretical comparison of the two modes of operations is made.

7.4.1 Simulation of the Experimental Runs

The computer programmes of both the batch and semi-continuous runs are designed in such a way that the throughput and product quality are printed out. The simulation of the experimental runs were chosen with a view to comparing the batch and semi-continuous runs theoretically as well as comparing the theoretical results

with the experimental results of Tables 6.3 and 6.4. The simulated results are presented in Tables 7.1 and 7.2.

7.4.2 Results and Discussion

By comparing Table 6.3 to 7.1 and 6.4 to 7.2, it can be seen that in terms of throughput ratio and purity of products the theoretical results falls very closely to the experimental results. However the model predicts lower concentrations in the bulk products. This can be explained by comparing the simulated and experimental concentration profiles for the same experiment in batch as well as in the continuous mode. The concentration in the simulated run is usually less than the experimental profile. The reason for this disagreement in the simulated and experimental profile is discussed in Section 7.3.4.

TABLE 7.1 THEORETICAL COMPARISON OF BATCH AND SEMI-CONTINUOUS OPERATION FOR GLUCOSE FRUCTOSE FEED AT AMBIENT TEMPRATURE

FEED CONC. %w/v		BATCH								SEMI CONTINUOUS									THROUGH-PUT RATIO
		SAMPLE VOLUME INJEC-TED (1)	FRUCTOSE PRODUCT			GLUCOSE PRODUCT			THROUGH-PUT kg/h	AVERAGE FLOW RATES		SWITCH PERIOD min	FRUCTOSE PRODUCT			GLUCOSE PRODUCT			THROUGH-PUT kg/h	
G	F		PURITY %	MASS BAL. %	PROD. CONC. %w/v	PURITY %	MASS BAL. %	PROD. CONC. %w/v		FEED $cm^3 min^{-1}$	ELU-ENT $cm^3 min^{-1}$		PURITY %	MASS BAL. %	PROD. CONC. %w/v*	PURITY %	MASS BAL. %	PROD. CONC. %w/v		SEMI CONT / BATCH
10.0	10.0	15.0	99.9	100	2.6	99.9	100	5.7	0.25	70.2	210	15	96.1	100	1.05	99.9	100	0.9	0.84	3.36
20.0	20.0	15.0	84.0	100	9.1	99.9	100	12.1	1.11	70.2	210	15	80.0	100	2.97	99.9	100	1.49	1.68	1.51
25.0	25.0	15.0	82.0	100	12.9	99.9	100	14.6	1.21	70.2	210	15	75.0	100	3.4	99.9	100	1.8	2.1	1.73

* fructose concentration in bulk fructose product over the switch period of 15 minutes

TABLE 7.2 THEORETICAL COMPARISON OF BATCH AND SEMI-CONTINUOUS OPERATION FOR GLUCOSE, FRUCTOSE, DEXTRAN FEED AT AMBIENT TEMPERATURE

FEED CONCENTRATION % w/v			BATCH								SEMI-CONTINUOUS										THROUGHPUT SEMI CONT / BATCH
			SAMPLE INJECTED (1)	FRUCTOSE PRODUCT			DEXTRAN PRODUCT				AVERAGE FLOW RATES		SWITCH PERIOD (min)	FRUCTOSE PRODUCT			DEXTRAN PRODUCT				
G	F	D		PUR. %	MASS BAL. %	FRUC. CONC. %w/v	PUR. %	MASS BAL. % D	MASS BAL. % G	D CONC. %	T'PUT kg/h	FEED $cm^3 min^{-1}$	EFFLUENT $cm^3 min^{-1}$		PUR. %	MASS BAL. %	FRUC. CONC. %w/v*	PUR. %	MASS BAL. % D	MASS BAL. % G	D CONC. %	T'PUT kg/h	
0.07	0.49	0.15	12	99.9	100	10.2	68	100	100	3.02	0.69	70.2	210	15	99.9	100	6.2	69.2	100	100	3.75	2.94	4.26

* fructose concentration in bulk fructose product over the switch period of 15 minutes

CHAPTER EIGHT

CONCLUSIONS AND RECOMMENDATIONS

8.1 CONCLUSIONS

As stated in the beginning of this thesis, this research project was aimed at recovering fructose, by batch and semi-continuous operation of the SCCR6 unit, from two types of feedstocks namely a mixture containing equi-concentrations of glucose and fructose and Fisons Pharmaceuticals dextran contaminated fructose rich effluent.

From the results obtained the following conclusions can be drawn.

1) In batch operation of the SCCR6 unit a feed volume of as much as 25% of the total empty column volume (15 litres) can be injected to obtain a reasonable separation of the components, but a recycle of as much as 40% of total sugar input was necessary.

2) For the continuous operation of the SCCR6 unit methods have been investigated to increase the throughput and the fructose concentration in the fructose rich product. The increase in throughput was achieved by increasing the feed flow rate, the eluent flow rate and decreasing the switch time to obtain reasonable L/P ratio for the separation of components. The increase in the concentration of fructose in the fructose rich product was achieved by collecting the fructose rich product over a switch period and using part of this product as an eluent.

In the experimental programme with the following conditions:

feed flow rate = 70 cm^3/min

eluent flow rate = 210 cm^3/min

switch period = 15 minutes

and eluent = part of fructose rich product collected over a switch period of 15 minutes.

The maximum throughput of sugar for 50% w/v binary glucose, fructose mixture was 2.1 kg/hr with a bulk fructose concentration of 7.6% w/v at 70% purity. When using a Fisons feedstock, however, under the same condition the sugar throughput was 2.94 kg/hr with a bulk fructose concentration of 16.3% w/v at 99.9% purity. This research has demonstrated, for the first time, that a fructose rich product containing 16.3% w/v fructose at 99.9% purity can be obtained from a Fisons feedstock using SCCR6 equipment.

3) In comparing batch and continuous operation of the SCCR6 unit, approximately twice the throughput has been achieved by operating the equipment in the semi-continuous mode.

4) Experimental work established that the 'cross over' point between solute profiles was influenced by the operating temperature. Under constant flow conditions, the 'cross over' point was shown to shift towards the glucose rich product exit as the operating temperature increased. Shifting of the 'cross over' point in such a manner has also accounted for a decrease in the

purity of the glucose rich product. However the adverse effect of operating at high temperatures was compensated by a reduction in the pressure drops for both the eluent and feed streams through the packed columns.

5) Experimental work was carried out to investigate the effect of on-column sugar concentrations at ambient temperature on the distribution coefficient of glucose and fructose. As predicted by Ching (8), Chuah (9) and Gould (10), the value of the distribution coefficient increased with increasing on column concentration of dextran, glucose and fructose. Statistical analysis showed that a technique of simple linear regression could be employed to obtain a linear relationship between the distribution coefficient and the concentration of each component, dextran, glucose and fructose.

6) The equilibrium plate model was adopted to simulate both the batch and semi-continuous mode of operation:

(i) For the simulation of the continuous operation of the SCCR6 unit, previous workers Ching (8), Chuah (9) and Gould (10) assumed a value for the distribution coefficient (K_d) to obtain a best fit between the simulated and experimental concentration profiles. An improvement in the existing model is made by the inclusion of actual K_d values found experimentally to replace the guessed values, thereby enabling a more accurate test of the model to be determined. A reasonable agreement between the simulated and experimental results was obtained.

(ii) For the simulation of the batch operation of the SCCR6 unit a close agreement between the simulated and experimental results was obtained for the small feed volume input, but the model failed to predict the concentration profile for the large feed volume input. A shift in the simulated profile was also observed in comparison to the experimental profile. It was thought that the fluctuation in the flow rate during the experimental run was the major reason for the shift.
(iii) In a theoretical comparison of the throughput and product quality for the carbohydrate separations mentioned, a very good agreement was obtained between the experimental and simulated result.

8.2 RECOMMENDATIONS FOR FUTURE WORK

The chromatographic method of separation is rapidly becoming an attractive commercial process. Therefore further research is required to ensure that this process is commercially viable. Recommendations for future work are

i) to find alternative packing with a greater resolving power for fructose and its isomers. It is suggested that the packing is chosen with consideration given to resolving power and cost.

ii) to introduce automation for collecting the fructose rich product in a reservoir and using a part of it as an eluent stream. Using this method, the concentration of fructose in the fructose product was increased considerably.

iii) to install a more accurate pump for the pumping of the eluent stream into the column to ensure a constant flow rate of that stream.

iv) to incorporate sensors and automatic control during the batch operation for the sample analysis and product collection, so that the whole process could be controlled by a computer. This will make the process more efficient, less labour intensive and hence less costly.

v) to adopt the same computer as in (iv) to control the operation in the semi-continuous mode.

vi) to modify the plate to plate model to account for the fructose entering the column as an eluent.

vii) to perform a cost study on the feasibility of constructing a production scale plant for the separation of fructose from a mixture of carbohydrate.

APPENDICES

1. Statistical Treatment of Experimental Partition Coefficient Data

2. Listing of Computer Program and Result for the Batch Operation of the SCCR6 Unit

3. Listing of Computer Program and Result for the Semi-COntinuous Operation of the SCCR6 Unit

APPENDIX 1

STATISTICAL TREATMENT OF EXPERIMENTAL PARTITION COEFFICIENT DATA

1.1 The Simple Linear Regression (91)

For the case where there is a single x and a single y, the data take the form of pairs of observation $((x_i, y_i);\ i = 1,2 \ldots\ldots, n)$. If the experiment is designed to choose the values of x, i.e. concentrations in advance and observe the corresponding y values. The regression line for n number of data can be represented by

$$y = a + bx \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad A(1.1)$$

where

$$b = \frac{n\sum_{i=1}^{n} x_i y_i - \left(\sum_{i=1}^{n} x_i\right)\left(\sum_{i=1}^{n} y_i\right)}{n\sum_{i=1}^{n} x_i^2 - \left(\sum_{i=1}^{n} x_i\right)^2} \quad \ldots\ldots\ldots\ldots\ldots \quad A(1.2)$$

$$\bar{y} = \sum_{i=1}^{n} y_i/n \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad A(1.3)$$

$$\bar{x} = \sum_{i=1}^{n} x_i/n \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad A(1.4)$$

and $$a = \bar{y} - b\bar{x} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad A(1.5)$$

1.2 The Correlation Coefficient

The measure of the linear relationship between two variables x and y is estimated by the sample correlation coefficient, r where

$$r = b \frac{\sum_{i=1}^{n} (x_i - \bar{x})^2}{\sum_{i=1}^{n} (y_i - y)^2} \quad \text{A(1.6)}$$

1.3 Confidence Limits and the Test of Significance (91)

Student t test on the correlation coefficient with

$$t = \frac{r\sqrt{n-2}}{\sqrt{(1-r^2)}} \quad \text{A(1.7)}$$

where r = correlation coefficient

n = number of data points

This value of t is checked with v, the value of freedom equal to n-2, at a significant level of 0.1% to test how the experiment data fit the regression line.

APPENDIX 2 LISTING OF COMPUTER PROGRAM AND RESULT FOR THE SIMULATION OF BATCH OPERATION OF SCCR6

```
 DIMENSION C1G(5000),C1F(5000)
REAL  MG,  MF,KDG1,KDF1,KDG2,KDF2,KDG,KDF
 READ(11,-)VO,VS,XG,XF,VG,VF,DV,N,NG,NF,TEMP,EF
READ(11,-)A1,C1,A2,C2,A3,C3,A4,C4,A,B,C,D
 KDG1=A1*XG+C1
 KDF1=A2*XG+C2
 KDG2=A3*XF+C3
 KDF2=A4*XF+C4
KDG=AMAX1(KDG1,KDG2)
KDF=AMAX1(KDF1,KDF2)
 IF((ABS(TEMP-30.)).LT.0.001)KDF=0.95*KDF
 IF((ABS(TEMP-45.)).LT.0.001)KDF=0.91*KDF
 IF((ABS(TEMP-60.)).LT.0.001)KDF=0.83*KDF
 VRG =VO+KDG*VS
 VRF =VO+KDF*VS
SG=VRG/SQRT(FLOAT(NG))
 SF=VRF/SQRT(FLOAT(NF))
 VRGL=VRG-(A*SG)
VRFL=VRF-(B*SF)
VRGH=VRG+(C*SG)
VRFH=VRF+(D*SF)
TI=(VRGL+VG)/EF
MG=(VG*XG)
MF=(VF*XF)
HG1=VG*FLOAT(NG)/VS
HF1=VF*FLOAT(NF)/VS
H1=(HG1*0.5+0.5)
H2=(HF1*0.5+0.5)
NG2=NG-INT(H1)
NF2=NF-INT(H2)
  WRITE(21,9)
9 FORMAT(1X,60("*"))
 P =XG*100.
 Q =XF*100.
   WRITE(21,1)P,Q
1  FORMAT(5X,"FOR FEED CONC IN % W/VOF ",/,30X,"GLUCOSE ="
   ,F10.5,/,30X,"FRUCTOSE =",F10.5,/)
   WRITE(21,2)VG,TEMP
2  FORMAT(10X,"FEED VOLUME INPUT(ML)=",F10.2,
  2X,"TEMPERATURE (DEG C)=",F10.2,/)
   WRITE(21,3)
3 FORMAT(1X,60("*"))
  IF(VRFL.GT.VRGH) GO TO 70
  CALL INTE(VRFL,VRGL,DV,DV1,M1)
  CALL INTE(VRGH,VRFL,DV,DV2,M2)
  CALL INTE(VRFH,VRGH,DV,DV3,M3)
   WRITE(21,100)
100 FORMAT(5X,"TIME(MIN)",10X,"GLU CONC(W/V)",/)
  VG1 =VRGL
   CALL CONC(VG1,VRG,C1G,1,M1,DV1,NG2,MG,XG,TI,EF)
  L1=M1+1
```

```
   L2=M1+M2
    VG1 =VRFL
    CALL CONC(VG1,VRG,C1G,L1,L2,DV2,NG2,MG,XG,TI,EF)
 13 WRITE(21,330)
330 FORMAT(2X,60("*"))
    WRITE(21,15)
 15 FORMAT(5X,"TIME(MIN)",10X,"FRU CONC(W/V)")
    WRITE(21,330)
    VF1 =VRFL
    CALL CONC(VF1,VRF,C1F,L1,L2,DV3,NF2,MF,XF,TI,EF)
 16 L3 =M2+1
    L4=M2+M3
    VF1 =VRGH
   CALL CONC(VF1,VRF,C1F,L3,L4,DV3,NF2,MF,XF,TI,EF)
   A1G1=0.
   CALL SUM(SG,A1G1,C1G,MG,1,M1,DV1)
   A1G2=0.
   CALL SUM(SG,A1G2,C1G,MG,L1,L2,DV2)
   A1F2=0.
   CALL SUM(SF,A1F2,C1F,MF,1,M2,DV2)
   A1F3=0.
   CALL SUM(SF,A1F3,C1F,MF,L3,L4,DV3)
   GO TO 60
 70CALL INTE(VRGH,VRGL,DV,DV1,M1)
   CALL INTE(VRFH,VRFL,DV,DV2,M2)
   WRITE(21,100)
    VG1 =VRGL
   CALL CONC(VG1,VRG,C1G,1,M1,DV1,NG2,MG,XG,TI,EF)
    VF1 =VRFL
   WRITE(21,330)
   WRITE(21,15)
   CALL CONC(VF1,VRF,C1F,1,M2,DV2,NF2,MF,XF,TI,EF)
   A1G1=0.
   CALL SUM(SG,A1G1,C1G,MG,1,M1,DV1)
   A1F1 =0.
   CALL SUM(SF,A1F1,C1F,MF,1,M2,DV2)
   GCONC=(A1G1/(VRGH-VRGL))*100.
   FCONC=(A1F1/(VRFH-VRFL))*100.
   THRT=(A1G1+A1F1)*60.*EF/((((VRGH-VRG)+(VRF-VRFL))*2.)*1000.)
   WRITE(21,350)
350FORMAT(15X,"GLU PRO",12X,"FRU PRO")
   WRITE(21,125) GCONC,FCONC,THRT
125FORMAT(5X,"TWO PURE COMPONENTS","GCONC(%W/V)=",F10.5,
  1" FCONC(%W/V)=",F10.5,/,5X,"TOTAL SUGAR THROUGHPUT(KG/HR)=",F1
  1,/)
   GO TO 210
 60 IF(N.NE.1)GO TO 65
   WRITE(21,351)
351FORMAT(15X,"GLU PRO",12X,"RECYCLE",15X,"FRU PRO")
   GCONC=(A1G1/(VRFL-VRGL))*100.
   FCONC=(A1F3/VRFH-VRGH)*100.
   RGCONC=(A1G2/(VRGH-VRFL))*100.
   RFCONC=(A1F2/(VRGH-VRFL))*100.
   THRT=(A1G1+A1F3)*60.*EF/((((VRGH-VRG)+(VRF-VRFL))*2.)*1000.)
    WRITE(21,140)GCONC,RGCONC,RFCONC,FCONC,THRT
140FORMAT(5X,"PURE","GCONC(%W/V)=",F10.5,2X,"RGCONC(%W/V)="
  1,F10.5,/,22X,"RFCONC(%W/V)=",F10.5,"FCONC(%W/V)="F10.5,
  1/,5X,"TOTAL SUGAR THROUGHPUT(KG/HR)=",F10.5,/)
   GO TO 210
 65 A1F2 =A1F2+A1F3
```

```
      PU=(A1F2/(A1F2+A1G2))*100.
      GCONC=(A1G1/(VRFL-VRGL))*100.
      FCONC=(A1F2/(VRFH-VRFL))*100.
      GFCONC=(A1G2/(VRFH-VRFL))*100.
      THRT=(A1G1+A1G2+A1F2)*EF*60./((((VRGH-VRG)+(VRF-VRFL))*2.)*1000.
      WRITE(21,352)
  352 FORMAT(10X,"GLU PRO",12X,"FRU PRO",/)
      WRITE(21,150)GCONC,GFCONC,FCONC,PU,THRT
  150 FORMAT(5X,"MIXED","GCONC(%W/V)=",F10.5,"GFCONC(%W/V)=",F10.5,
     1"FCONC(%W/V)=",F10.5,
     1"PURITY OF FRU PROD=",F10.5,/,5X,"TOTAL SUGAR THROUGHPUT(KG/HR)=
     1,F10.5,/)
  210 END
            TO CALCULATE THE NO OF INTERVALS
       SUBROUTINE INTE(VG,VF,DV,DV1,M1)
       AM1 =(VG-VF)/DV
       M1 =INT (AM1)
       DV1 =(VG-VF)/FLOAT(M1)
       RETURN
       END
            TO CALCULATE THE CONCENTRATION PROFILE OF COMPONENTS
        SUBROUTINE CONC(VF1,VRG,C1G,L1,L2,DV1,NG,GM,X,TI,EF)
       DIMENSION C1G(2500)
       M=1
       DO 20 I =L1,L2
       A1=((VF1-VRG)**2.)
       A2=(VF1*VRG)
       ZG=(A1*FLOAT(NG))/(A2*2.)
       A3=SQRT(FLOAT(NG)/(3.14159*2.))
       A4=EXP(-ZG)
      CMAX =A3*GM/VRG
        C1G(I) =A4*CMAX
   17 IF (M.NE.20)GO TO 15
      TI=TI+(20.*DV1/EF)
      WRITE(21,100)TI,C1G(I)
  100 FORMAT(F12.5,5X,F10.5)
        M =1
   15  VF1 =VF1+DV1
      M =M+1
   20  CONTINUE
       RETURN
       END
            TO SUM THE AREA UNDER THE CURVE USING THE SIMPSON"S RULE
       SUBROUTINE SUM(SG,A1G,C1G,GM,L1,L2,DV)
       DIMENSION C1G(2500)
       DO 20 I =L1,L2,2
      X1=C1G(I)
      X2=2*C1G(I+1)
      X3=C1G(I+2)
      A1G=A1G+((X1+X2+X3)*DV/2.0)
   20 CONTINUE
      RETURN
       END
```

FOR FEED CONC IN % W/VOF

GLUCOSE = 10.00000
FRUCTOSE = 10.00000

FEED VOLUME INPUT(ML)= 1200.00 TEMPERATURE (DEG C)=2

TIME(MIN)	GLU CONC(W/V)
303.37959	0.00488
306.38119	0.00692
309.38278	0.00943
312.38437	0.01236
315.38596	0.01559
318.38756	0.01894
321.38915	0.02219
324.39074	0.02510
327.39233	0.02744
330.39393	0.02902
333.39552	0.02971
336.39711	0.02946
339.39870	0.02834
342.40030	0.02645
345.40189	0.02398
348.40348	0.02113
351.40507	0.01812
354.40667	0.01511
357.40826	0.01228
360.40985	0.00973
363.41144	0.00752
366.41304	0.00567

TIME(MIN)	FRU CONC(W/V)
369.41395	0.00216
372.41487	0.00268
375.41579	0.00329
378.41671	0.00398
381.41763	0.00475
384.41855	0.00560
387.41947	0.00651
390.42039	0.00748
393.42131	0.00850
396.42223	0.00953
399.42315	0.01057
402.42407	0.01159
405.42499	0.01256
408.42591	0.01347
411.42683	0.01429
414.42775	0.01499
417.42867	0.01557

420. 42959	0. 01601
423. 43051	0. 01630
426. 43143	0. 01642
429. 43235	0. 01640
432. 43327	0. 01621
435. 43419	0. 01588
438. 43510	0. 01542
441. 43602	0. 01484
444. 43694	0. 01415
447. 43786	0. 01338
450. 43878	0. 01255
453. 43970	0. 01167
456. 44062	0. 01076
459. 44154	0. 00984
462. 44246	0. 00893
465. 44338	0. 00805
468. 44430	0. 00719
471. 44522	0. 00638
474. 44614	0. 00562
477. 44706	0. 00491
480. 44798	0. 00427
483. 44890	0. 00368
486. 44982	0. 00315

GLU PRO FRU PRO

TWO PURE COMPONENTSGCONC(%W/V)= 1. 78348 FCONC(%W/V)= 0. 98

TOTAL SUGAR THROUGHPUT(KG/HR)= 0. 07621

List of Symbols for the Simulation of Batch Operation of the SCCR6 Unit

VO	Total void volume
VS	Total stationary phase volume
C1G	Glucose concentration
C1F	Fructose concentration
KDG	Distribution coefficient of glucose
KDF	Distribution coefficient of fructose
XG	Glucose concentration in feed
XF	Fructose concentration in feed
DV	Volume increment
NG	Total number of plates for glucose
NF	Total number of plates for fructose
EF	Eluent flowrate
VRGL	Elution volume corresponding to beginning of glucose profile
VRFL	Elution volume corresponding to beginning of fructose profile
VRGH	Elution volume corresponding to the end of glucose profile
VRFH	Elution volume corresponding to the end of fructose profile
VRG	Elution volume corresponding to glucose peak
VRF	Elution volume corresponding to fructose peak
TI	Time counter
A1G	Mass of glucose
A1F	Mass of fructose
CMAX	Maximum concentration of the component

APPENDIX 3 LISTING OF COMPUTER PROGRAM AND RESULT FOR SEMI CONTINUOUS OPERATION OF SCCR6

```
      DIMENSIONG(500),F(500),AG(500),AF(500),GMASS(500),GCUM(500),
     1FMASS(500),FCUM(500) ,GCONC(500),FCONC(500),D(500),AD(500),
     2DMASS(500),DCUM(500),DCONC(500)
      REAL KD1,KD2,KDD,KD11,KD12,KD21,KD22,KD13,KD23
      READ(21,-)CFLOW,FFLOW,SFLOW,DT,TEMP
      READ(21,-)GFEED,FFEED,DFEED,KD1,KD2,KDD
      READ(21,-)NFEED,NNBED,KTOTAL,KKINK
      READ(21,-) E1,C1,E2,C2,E3,C3,E4,C4,E5,C5,E6,C6
      CFLOWM=CFLOW*60.0
      SFLOWM=SFLOW*60.0
      FFLOWM=FFLOW*60.0
      SWP=KKINK*DT/60.0
      KCYC=KTOTAL/10
      CFEED=(GFEED+FFEED)*100.0
      V1=2800.0/NNBED
      V2=3200.0/NNBED
      WRITE (22,5)
      WRITE(22,6)
      WRITE(22,7)
      WRITE(22,8)
      WRITE(22,51)CFEED,CFLOWM,FFLOWM,SFLOWM,SWP,NNBED,TEMP
      WRITE(22,9)
      WRITE(22,12)KCYC
      WRITE(22,10)
      WRITE(22,34)
    5 FORMAT(1H1,///,6X,'FEED',1X,'ELUENT',1X,'FEED',3X,'PURGE',2X,
     1'SWITCH',1X,'NO',6X,'TEMP')
    6 FORMAT(6X,'CONC',1X,'FLOW',3X,'FLOW',3X,'FLOW',3X,'PERIOD',1X,
     1'OF')
    7 FORMAT(8X,'%',2X,'RATE',3X,'RATE',3X,'RATE',3X,'MINS',3X,
     1'PLATES')
    8 FORMAT(11X,'ML/MIN',1X,'ML/MIN',1X,'ML/MIN',8X,'/ COL'//)
    9 FORMAT(//,10X,'AVERAGE  CONCENTRATION OF SUGARS ON EACH',
     11X,'COLUMN')
   12 FORMAT(10X,'AFTER',I3,'CYCLES')
   10 FORMAT(//,9X,'COL NO',2X,'AV GLUCOSE CONCN',2X,'AV',
     11X,'FRUCTOSE CONCN',2X,'AV DEXTRAN CONCN'/)
   34 FORMAT(22X,'GM/ML',15X,'GM/ML',15X,'GM/ML'/)
   51 FORMAT(6X,F4.1,1X,F5.1,2X,F4.1,3X,F5.1,2X,F4.1,3X,I2,4X,F6.2)
      DO 99 I=1,500
      G(I)=0.0
      F(I)=0.0
      D(I)=0.0
      AD(I)=0.0
      AG(I)=0.0
      AF(I)=0.0
   99 CONTINUE
      NNTOT=NNBED*10
      NNNINE=NNBED*9+1
      NNFEED=(NFEED-1)*NNBED+1
      DO 100 K=1,KTOTAL
```

```
      ISTKK=KKINK*(K-1)+1
      LSTKK=KKINK*K
      DO 200 KK=ISTKK,LSTKK
      DO 300 N=1,10
      IF(N.LE.5)CFLOWC=CFLOW
      IF(N.GE.6)CFLOWC=CFLOW+FFLOW
      IF(N.LE.(NFEED-K))GO TO 300
      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)=0.0
      F(NN-1)=0.0
      D(NN-1)=0.0
      GO TO 70
   50 A=CFLOWC* DT
      KD11=E1*G(NN)+C1
      KD12=E2*F(NN)+C2
      KD13=E5*D(NN)+C5
      KD21=E3*G(NN)+C3
      KD22=E4*F(NN)+C4
      KD23=E6*D(NN)+C6
      KD1=AMAX1(KD11,KD12,KD13)
      KD2=AMAX1(KD21,KD22,KD23)
      IF((ABS(TEMP-30.)).LT.0.001) KD2=0.95*KD2
      IF((ABS(TEMP-60.)).LT.0.001) KD2= 0.83*KD2
      IF((ABS(TEMP-45.)).LT.0.001) KD2    =0.91*KD2
      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+V2*KD1))
      SS=EXP(-A/(V1+V2*KD2))
      RD=EXP(-A/V1)
      G(NN)=(1.-RR)*((CFLOW*G(NN-1)+FFLOW*GFEED)/CFLOWC)+RR*G(NN)
      F(NN)=(1.-SS)*((CFLOW*F(NN-1)+FFLOW*FFEED)/CFLOWC)+SS*F(NN)
      D(NN)=(1.-RD)*((CFLOW*D(NN-1)+FFLOW*DFEED)/CFLOWC)+RD*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
      KD11=E1*G(NN)+C1
      KD12=E2*F(NN)+C2
      KD13=E5*D(NN)+C5
      KD21=E3*G(NN)+C3
      KD22=E4*F(NN)+C4
      KD23=E6*D(NN)+C6
      KD1=AMAX1(KD11,KD12,KD13)
      KD2=AMAX1(KD21,KD22,KD23)
      IF((ABS(TEMP-30.)).LT.0.001) KD2=0.95*KD2
      IF((ABS(TEMP-60.)).LT.0.001) KD2= 0.83*KD2
      IF((ABS(TEMP-45.)).LT.0.001) KD2    =0.91*KD2
      RR=EXP(-A/(V1+V2*KD1))
      SS=EXP(-A/(V1+V2*KD2))
      RD=EXP(-A/V1)
      G(NN)=(1.0-RR)*G(NN-1)+RR*G(NN)
      F(NN)=(1.0-SS)*F(NN-1)+SS*F(NN)
```

```
      D(NN)=(1.0-RD)*D(NN-1)+RD*D(NN)
      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*DT
      KD11=E1*G(NN)+C1
      KD12=E2*F(NN)+C2
      KD13=E5*D(NN)+C5
      KD21=E3*G(NN)+C3
      KD22=E4*F(NN)+C4
      KD23=E6*D(NN)+C6
      KD1=AMAX1(KD11,KD12,KD13)
      KD2=AMAX1(KD21,KD22,KD23)
      IF((ABS(TEMP-30.)).LT.0.001) KD2=0.95*KD2
      IF((ABS(TEMP-60.)).LT.0.001) KD2= 0.83*KD2
      IF((ABS(TEMP-45.)).LT.0.001) KD2    =0.91*KD2
      RR=EXP(-A/(V1+V2*KD1))
      SS=EXP(-A/(V1+V2*KD2))
      RD=EXP(-A/V1)
      D(NN)=(1.0-RD)*D(NN-1)+RD*D(NN)
      G(NN)=(1.0-RR)*((G(NN-1)))+RR*G(NN)
      F(NN)=(1.0-SS)*F(NN-1)+SS*F(NN)
  150 IF(K.EQ.KTOTAL.AND.KK.EQ.LSTKK)GO TO 160
      GO TO 400
  160 CONTINUE
  400 CONTINUE
  300 CONTINUE
  200 CONTINUE
      DO 500 NN=1,NNBED
      AG(NN)=G(NN)
      AF(NN)=F(NN)
      AD(NN)=D(NN)
  500 CONTINUE
      DO 600 NN=1,NNTOT
      IF(NN.GE.NNNINE)GO TO 2010
      NNADJ=NN+NNBED
      G(NN)=G(NNADJ)
      F(NN)=F(NNADJ)
      D(NN)=D(NNADJ)
      GO TO 600
 2010 NNADJ=NN+1-NNNINE
      G(NN)=AG(NNADJ)
      F(NN)=AF(NNADJ)
      D(NN)=AD(NNADJ)
  600 CONTINUE
  100 CONTINUE
   52 FORMAT(5X,I2,2X,I6,2X,I2,2X,I3,2X,F10.8,2X,F10.8)
      GCUM(1)=0.0
      FCUM(1)=0.0
      DCUM(1)=0.0
      DO 11 I=1,NNTOT
      KD11=E1*G(NN)+C1
      KD12=E2*F(NN)+C2
      KD13=E5*D(NN)+C5
```

```
      KD21=E3*G(NN)+C3
      KD22=E4*F(NN)+C4
      KD23=E6*D(NN)+C6
      KD1=AMAX1(KD11,KD12,KD13)
      KD2=AMAX1(KD21,KD22,KD23)
      IF((ABS(TEMP-30.)).LT.0.001) KD2=0.95*KD2
      IF((ABS(TEMP-60.)).LT.0.001) KD2= 0.83*KD2
      IF((ABS(TEMP-45.)).LT.0.001) KD2    =0.91*KD2
      GMASS(I)=G(I)*V1+G(I)*KD1*V2
      FMASS(I)=F(I)*V1+F(I)*KD2*V2
      DMASS(I)=D(I)*V1
   11 CONTINUE
      L=NNBED
   27 DO 14 I=1,NNTOT
      IF(I.EQ.(L+1))GCUM(I)=GMASS(I)
      IF(I.EQ.(L+1))FCUM(I)=FMASS(I)
      IF(I.EQ.(L+1))DCUM(I)=DMASS(I)
   14 CONTINUE
      L=L+NNBED
      IF(L.EQ.NNTOT)GO TO 15
      GO TO 27
   15 L=NNBED
      I=2
      GCUM(1)=0.0
      FCUM(1)=0.0
      DCUM(1)=0.0
   13 DO 16 M=I,L
      GCUM(M)=GMASS(M)+GCUM(M-1)
      FCUM(M)=FMASS(M)+FCUM(M-1)
      DCUM(M)=DMASS(M)+DCUM(M-1)
      GCONC(M)=GCUM(M)/2745.0
      FCONC(M)=FCUM(M)/2745.0
      DCONC(M)=DCUM(M)/2745.0
      KOLNO=M/NNBED
      IF(M.EQ.L) GO TO 18
      GO TO 16
   18 WRITE(22,4)KOLNO,GCONC(M),FCONC(M),DCONC(M)
    4 FORMAT(11X,I2,8X,F7.5,12X,F7.5,12X,F7.5)
   16 CONTINUE
      I=L+2
      L=L+NNBED
      IF(L.EQ.NNTOT)GO TO 17
      GO TO 13
17    P =SWP*60.
      FRU=FCONC(1)
      GLU=GCONC(1)
      DEX=DCONC(1)
      FRPC=FRU*2745./(P*SFLOW)
      GLPC=GLU*2745./(P*SFLOW)
      DRPC=DEX*2745./(P*SFLOW)
      DE=DFEED*FFLOW
      GL=GFEED*FFLOW
      FR=FFEED*FFLOW
      SG=(GL-(GLPC*SFLOW)/(CFLOW+FFLOW)
      SF=(FR-(FRPC*SFLOW)/(CFLOW+FFLOW)
      SD=(DE-(DRPC*SFLOW)/(CFLOW+FFLOW)
      PUF=FRPC/(FRPC+GLPC+DRPC)
      PUG=SG/(SG+SF+SD)
      PUD=SD/(SG+SF+SD)
      WRITE(22,83)
```

```
  83  FORMAT(15X,"FRU PRO ",15X,"GLU PRO ",/,2X,"FCONC",3X,"GCONC",
     13X,"PURITY",3X,"FCONC",3X,"G/DCONC",3X,"PURITY",/,37X,"GLU",
     16X,"DEX")
      WRITE(22,66) FRPC,GLPC,PUF,SF,SG,PUG,PUD
 66   FORMAT(7F8.4)
      STOP
      END
EOF.
```

FEED CONC %	ELUENT FLOW RATE ML/MIN	FEED FLOW RATE ML/MIN	PURGE FLOW RATE ML/MIN	SWITCH PERIOD MINS	NO OF PLATES / COL	TEMP
20.0	105.0	34.8	540.0	30.0	25	20.00

AVERAGE CONCENTRATION OF SUGARS ON EACH COLUMN
AFTER 9CYCLES

COL NO	AV GLUCOSE CONCN GM/ML	AV FRUCTOSE CONCN GM/ML	AV DEXTRAN CON GM/ML
1	0.00120	0.02981	0.0000
2	0.03575	0.14382	0.0000
3	0.08773	0.14673	0.0000
4	0.11210	0.14676	0.0000
5	0.11670	0.14660	0.0000
6	0.11688	0.14336	0.0000
7	0.11685	0.13278	0.0000
8	0.11682	0.11144	0.0000
9	0.11518	0.06700	0.0000

FRU PRO			GLU PRO			
FCONC	GCONC	PURITY	FCONC	G/DCONC	PURITY GLU	DEX
0.0040	0.0000	99.982	0.0000	0.0572	99.923	0.000

List of Symbols for the Simulation of

Continuous Operation of the SCCR6 Unit

D	Dextran concentration
G	Glucose concentration
F	Fructose concentration
V1	Volume of mobile phase per theoretical plate
V2	Volume of stationary phase per theoretical plate
CFLOW	Mobile phase flow rate
FFLOW	Feed flow rate
SFLOW	Purge flow rate
KDD	Distribution coefficient of dextran
KD1	Distribution coefficient of glucose
KD2	Distribution coefficient of fructose
DT	Time increment
DFEED	Dextran concentration in feed
GFEED	Glucose concentration in feed
FFEED	Fructose concentration in feed
NNBED	Number of plates per column
KTOTAL	Number of sequences
KKINK	Number of time increments in a sequence
NNTYPE	Number of plate increments between printout
NN	Counter for plate
N	Counter for column
NNTOT	Total number of plates
NNINE	First plate in last column of separating section
NNFEED	Number of feed plate
lSTKK	First time increment in sequencing interval
LSTKK	Last time increment in sequencing interval

KK	Counter for numberof time increments
CFLOWC	Post feed mobile phase flow rate
NFST	First plate in the column
NNLST	Last plate in the column

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_n^o	Initial concentration of solute in plate n used in continuous simulation of SCCR6
d	Dextran
D	Diffusion coefficient
d_p	Mean particle diameter
d_c	Diameter of column
E_1, E_2	Mass flowrate of solute leaving in product 1 and 2 streams respectively in Barker and Lloyd's H.T.U. model
f	Feed
F	Feed flowrate used in continuous simulation of SCCR6
G	Glucose
H	Plate height
H.E.T.P.	Height equivalent to a theoretical plate

K_d	Equilibrium distribution coefficient
k'	Capacity factor
k''	Rate constant of desorption
K_o	Distribution coefficient for a component in Barker and Lloyd's H.T.U. model
ℓ	Length of packed bed
L	Effective mobile phase flowrate in the SCCR6 unit
n	nth number of plate
N	Number of theoretical plate
N_{OC}	Number of counter current theoretical plates
$(N_G)_S$	Number of overall gas phase transfer units in the
$(N_G)_R$	stripping and rectifying sections respectively in Barker and Lloyd's model
P	Stationary phase flowrate in the SCCR6 unit
Q	Mobile phase flowrate in the SCCR6 unit
R_s	Resolution
t	Time
t_r	Retention time of a component
t_o	Retention time of a non-retained component
u	Mobile phase linear velocity
$(u_z)_A$	Mass flowrate ratio of component A and B used
$(u_z)_B$	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 phsae in the SCCR6 unit
V_S	Total volume of stationary phase in the SCCR6 unit
V_i	Pore volume
V_o	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
W	Solute band width of a component
$W_{h/e}$	Peak width at h/e of peak height (used to calculate N)

Greek symbols

σ	Standard deviation
λ	Packing characterisation term for eddy diffusivity
α	Relative retention factor
γ	Labyrinth factor to allow for the torous flow path
$\gamma_L \gamma_2$	Rate of transfer of molecules from gas to liquid and from liquid to gas in Al-Madfai's model
ψ	Operation mobile phase/stationary phase velocity ratio

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