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## Sulfuric acid - glucose separation using mixed-recycle steady state recycling chromatography

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## ABSTRACT

Batch chromatography is a widely used separation technique in a variety of fields meeting difficult separations. Several technologies for improving the performance of chromatography have been studied, including mixed-recycle steady state recycling (MR-SSR) chromatography. Design of MR-SSR has been commonly limited on 100 % purity constraint cases and empirical work. In this study a predictive design method was used to optimize feed pulse size and design a number of experimental MR-SSR separations for a solution of 20 % sulfuric acid and 100 g/L glucose. The design was under target product fraction purities of 98.7 % for H<sub>2</sub>SO<sub>4</sub> and 95 % for glucose. The experiments indicate a maximum of 59 % increase in sulfuric acid productivity and 82 % increase for glucose when compared to corresponding batch separation. Eluent consumption was lowered by approximately 50 % using recycling chromatography. Within this study the target purities and yields set in design were not completely met, and further optimization of the process is deemed necessary.

*Keywords:* Recycle chromatography, steady state, sulfuric acid, glucose

## NOMENCLATURE

$c$	concentration, mol L <sup>-1</sup>
$EC$	eluent consumption relative to produced component, L mol <sup>-1</sup>
$m$	mass, g
$n$	cycle number, -
$p^j$	purity of product fraction $j$ for target component, -
$PR$	productivity, mol L <sub>bed</sub> <sup>-1</sup> h <sup>-1</sup>
$t$	cut time relative to beginning of cycle, mL
$V$	volume, mL
$Y$	yield, -
$\varepsilon$	bed porosity, -
$\tau$	dimensionless time relative to the start of the cycle, -

### Subscripts and superscripts

0	initial column injection
1, 2	components to separate in order of least retention
A, B	product fractions
A1	beginning of product fraction A
A2	end of product fraction A
B1	beginning of product fraction B
B2	end of product fraction B
col	column
F0	fresh feed
inj	injection i.e. feed pulse
rec	recycle fraction

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## 1 INTRODUCTION

Chromatography is a widely used separation technique in fine chemicals, pharmaceuticals and biochemicals [1, 2]. Increasing batch chromatography throughput may result in larger unresolved portion on the chromatogram, discarding of which is usually unreasonable. Recycling this portion is a widely studied subject [3, 4], and may provide high productivity with less structural complexity compared to simulated moving bed (SMB) [5]. Several methods of recycling the unresolved fraction (for example closed-loop and mixed-recycle) have been presented elsewhere [3, 4].

The objective of this research was to study the practical application of mixed-recycle steady state recycling (MR-SSR) chromatography in sulfuric acid - sugar separation. The mixed-recycle mode was selected for the ability to predict the steady state and design the system using the method presented by Sainio and Kasperit [6]. The case of acid-sugar separation was due to its correlation with lignocellulosic biomass acid hydrolysis and biorefinery applications.

In this work the separation is carried out for an aqueous solution of 20 % by weight sulfuric acid with 100 g/L of glucose, eluent being Millipore grade water. The separation was carried out in a 100 mL column of Finex CS16GC SAC resin (capacity 1.84 eq/L).

## 2 OVERVIEW OF STEADY STATE RECYCLING CHROMATOGRAPHY

A simplified chart of steady state recycling (SSR) system is presented in Figure 1. Fresh feed ( $F_0$ ) and the recycle fraction ( $R$ ) are introduced into the column as feed pulses ( $F$ ) alongside with eluent ( $E$ ). The output is divided into product fractions  $A$  and  $B$ , with the recycle  $R$  returned. The actual installations ( $I$ ) to realize this are not described in this section.

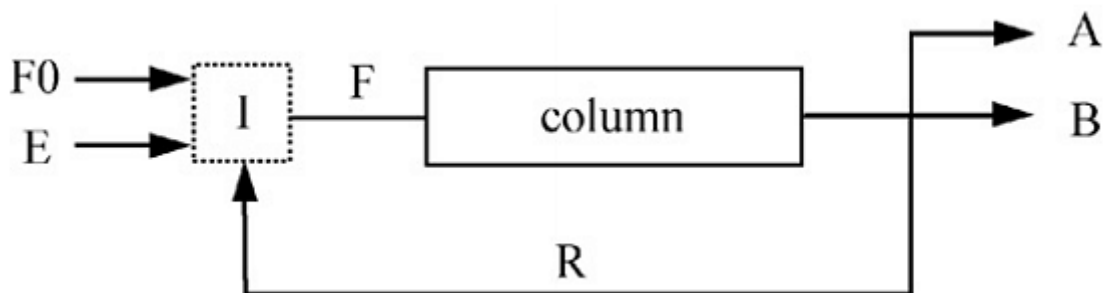


Figure 1. Schematic chart of a steady state recycling chromatography system.  $F_0$ , fresh feed;  $E$ , eluent;  $F$ , column feed;  $A$ , product fraction (component 1);  $B$ , product fraction (component 2);  $R$ , recycle fraction;  $I$ , installations for eluent and feed handling. [6]

Figure 2 presents an example of concentration profiles in the column output of the SSR system. In this specific example the process was initiated with a small injection of pure fresh feed and ran for 25 cycles. Each consecutive cycle is fractionated as per in Figure 1 along the constant cut times  $t_{A1}$ ,  $t_{A2}$ ,  $t_{B1}$  and  $t_{B2}$ . These cut times can be expressed in real time units, volume passed according to flow rate or commonly in equations as dimensionless time units  $\tau$ . The concentration profiles can be seen to gradually shift towards the steady state profile (thick line) of cycle 25.

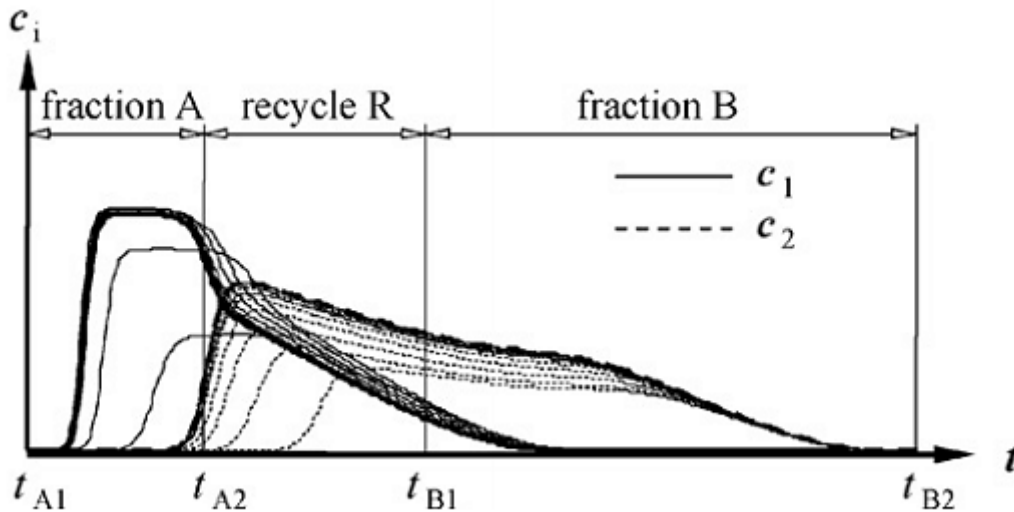


Figure 2. Example for concentration profiles and fraction division in a SSR process. The diagram shows 25 consecutive output profiles overlaid from startup to steady state (thick line). [6]

The actual method of recycling the fraction R into the feed F depends on application. In the closed-loop mode briefly mentioned in chapter 1 the recycle is re-injected into the column without disturbing the already formed profile, with fresh feed injected somewhere in the unresolved middle section [3]. In this case the recycle fraction is usually wider than in the example in Figure 2, with the relatively small amounts of resolved fractions A and B ‘shaved’ off both ends. In practice the recycled profile is difficult to keep undisturbed and design for such a system is usually based on empirical testing and time-consuming dynamic simulation [3].

In mixed-mode in contrast the recycle fraction is collected to a reservoir where it is thoroughly mixed with fresh feed before injecting to the column in the next cycle. This method has allowed for equilibrium based prediction in the limiting case of 100 % target purity and yield [7]. More recently a design method for arbitrary purity or yield constraints around the equilibrium framework has been presented by Sainio and Kaspereit [6]. This method allows for prediction of steady state and thus design of separation parameters (namely the cut times seen in Figure 2) without full dynamic simulations and is used as basis for designing the experimental part of this research.

### 3 BASIS OF DESIGN SPECIFICATIONS

As mentioned in the previous chapter the design method presented by Sainio and Kasperit [6] allows for prediction of steady state. This holds for systems that follow the competitive Langmuir adsorption model. The sulfuric acid - glucose separation case in this study is known to follow that model, and the isotherms for the respective components are available from previous chromatographic separation work. The design method assumes that both product fraction purities  $p^A$  and  $p^B$  are known as constraints. As presented in the analysis [6] the key equations for these are

$$p^A = \frac{m_1^A}{m_1^A + m_2^A} = \int_{\tau_{A1}}^{\tau_{A2}} \frac{c_1}{c_1 + c_2} d\tau \quad (1)$$

$$p^B = \frac{m_2^B}{m_1^B + m_2^B} = \int_{\tau_{B1}}^{\tau_{B2}} \frac{c_2}{c_1 + c_2} d\tau \quad (2)$$

where  $m_i^j$  is the mass of component  $i = (1, 2)$  in product fraction  $j = (A, B)$  and  $c_i$  is the concentration of component  $i = (1, 2)$ . Alternatively the yields of both components are given by

$$Y_1 = \frac{m_1^A}{m_1^{F0}} = \frac{\int_{\tau_{A1}}^{\tau_{A2}} c_1 d\tau}{c_1^{F0} [\Delta\tau_{inj} - (\tau_{B1} - \tau_{A2})]} \quad (3)$$

$$Y_2 = \frac{m_2^B}{m_2^{F0}} = \frac{\int_{\tau_{B1}}^{\tau_{B2}} c_2 d\tau}{c_2^{F0} [\Delta\tau_{inj} - (\tau_{B1} - \tau_{A2})]} \quad (4)$$

where  $\Delta\tau_{inj} = (V_{F0} - V_{rec})/\varepsilon V_{col}$  is the dimensionless injection width i.e. the width of the feed pulse after mixing the recycle fraction with the fresh feed (F0). Since in the recycling process none of the binary system components are wasted, the connection between purities and yields can be derived from global mass balance as follows

$$Y_1 = \frac{p^A}{p^{F0}} \cdot \frac{p^{F0} + p^B - 1}{p^A + p^B - 1} \quad (5)$$

$$Y_2 = \frac{p^B}{1 - p^{F0}} \cdot \frac{p^A - p^{F0}}{p^A + p^B - 1} \quad (6)$$

where  $p^{F0} = c_1^{F0}/(c_1^{F0} + c_2^{F0})$ . Within the realm of this study the constraints could be arbitrarily selected around realistic figures. In the framework of hypothetical biorefinery application the targets were set to high purity sulfuric acid (the weaker adsorbing component 1) to be returned back

into hydrolysis stages while maintaining satisfactory sugar yield. The purity  $p^B$  to be used in the design method can be solved from the yield equation (6) as follows

$$p^B = \frac{Y_2(1 - p^{F0})(1 - p^A)}{Y_2(1 - p^{F0}) - p^A + p^{F0}} \quad (7)$$

Initially the target sulfuric acid fraction purity and glucose yield of 99 % and 95 % respectively were chosen. These figures do not produce a realistic solution for sugar fraction purity in equation (7) with the known fresh feed purity  $p^{F0} = 0.807$  for our acid-sugar solution presented in chapter 1, however. The fresh feed purity was calculated as per given under equation (6). The known sulfuric acid concentration of 20 % by weight was converted using the aqueous solution density in 20 °C of 1.1398 g/cm<sup>3</sup> obtained from a Mettler-Toledo concentration table [8].

Following this the target sulfuric acid purity  $p^A$  was gradually lowered into 98.7 % and the glucose purity  $p^B$  was iteratively set to 95 % producing a glucose yield of 94.55 % which was deemed satisfactory in the frames of this study. These purity constraints were then used as specifications in the following design simulations described in the next chapter.

#### 4 SIMULATED DESIGN OF PROCESS PARAMETERS

The first phase of the SSR experimental work was mapping out the process parameters for the practical experiments. Such model parameters as component isotherms, intraparticle diffusion coefficient, axial dispersion, bed porosity and swelling ratio were known from earlier work concerning sulfuric acid - glucose separation. The resin bed diameter was 25 mm and height 200 mm. The actual bed volume was thus 98.17 mL with an empirically determined porosity  $\varepsilon = 0.39$ . The column temperature was set to 50 °C. A constant flow rate of 2.655 mL/min was used.

The design method allows for determining the cut times needed to reach the desired steady state for any given feed pulse width (in this case practical pulse size in mL, since the column dimensions were known). The ideal feed pulse size was not known so extensive simulated runs of the steady state were required with variable pulse sizes to map out the optimal region for the separation under the purity constraints presented in chapter 3.

##### 4.1 SSR simulator in MATLAB

The simulations to find the optimal feed pulse size and cut times were carried out using a standalone simulator for single column chromatographic separation developed by Tuomo Sainio. The si-



simulator allows for column outlet simulation in batch mode or steady state prediction of SSR using the method presented by Sainio and Kaspereit [6], using a MATLAB interface.

The simulator was under continued development during this study, and the SSR model was not fully supported as of that time. The program did allow for two modes of SSR simulations, however; (i) a prediction of  $n$  cycles of SSR with given cut times for the recycle fraction, and (ii) a shortcut design mode treating either the front or the tail of the chromatogram as constant and finding the cut times that lead to the desired steady state with given purity constraints.

## 4.2 Design phase

The design phase consisted of several simulated runs of SSR for variable feed pulse sizes. First the corresponding batch separation pulse size – the feed pulse with which both product fraction purities were met with a single cut – was determined. This pulse size, 0.9 mL, was the minimum for the feasible range.

Several different pulse sizes were chosen from this range and a standard simulation procedure was carried out for each of them. In a nutshell this procedure was as follows:

1. The SSR simulator was used in shortcut design mode, with the purity constraints of  $p^A = 0.987$  and  $p^B = 0.950$ , using the front of the chromatogram as constant (the front of the sulfuric acid shock was known to remain relatively unchanged from previous work). The simulator was allowed to run until neither the cut times  $t_{A2}$  and  $t_{B1}$ , nor the key values (actual product purities  $p^A$  and  $p^B$ , component productivities  $PR$  and relative eluent consumptions  $EC$ ) varied significantly from cycle to cycle.
2. The final cut times reported by the shortcut design were inserted into the simulator, and the SSR simulation was carried out for  $n = 50$  cycles starting from pure fresh feed injection to ensure reaching of steady state.
3. The key values of interest were averaged from the last ten cycles as the SSR is rather an undulating pseudo-steady state than a constant one.
4. The end purities were compared to the design constraints. An error margin of 5 % was set for the purities in order for the simulation to be deemed of use. In some cases especially with larger feed pulse sizes suitable cut times were not found immediately. This was due to the characteristically steep end shock of sulfuric acid overlapping the glucose concentration profile (as can be seen for example in Figure 9 in chapter 6) causing minor variations to project major changes in the recycle.

If the error margin was exceeded, the cut times were manually slightly tweaked according to the concentration profiles and the procedure repeated from point 2. When the results were within error margin they were gathered to a table to produce optimization curves.

In reality the design simulation outcomes were often less than ideal, as can be seen from the resulting optimization charts in Figure 3 below. The objective was to find suitable parameters for experimental SSR work and then compare the experimental results back to the simulations to determine the feasibility of this design method for practical application of MR-SSR, not to produce highly optimized separation processes at this time.

The simulation outcomes provided with the cut times to use for any pulse sizes selected for the experimental part, as well as the averaged steady state recycle fraction composition. This composition allows for tailoring the first injection so as to leap straight to steady state and avoid the high number of start-up cycles needed when starting the process with pure fresh feed.

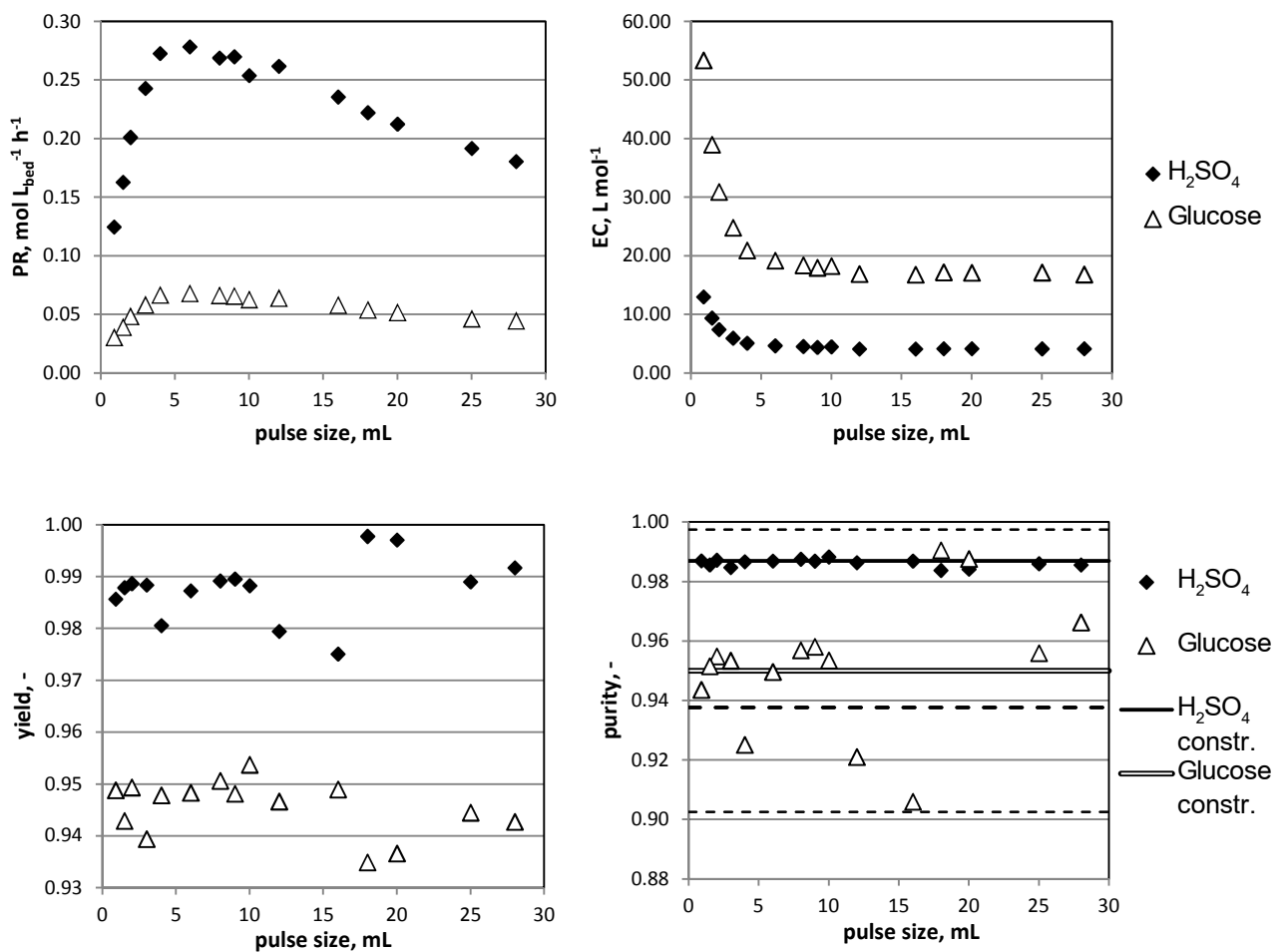


Figure 3. Key values for simulated MR-SSR sulfuric acid-glucose separations in 98.17 mL bed of Finex CS16GC SAC resin. A constant flow rate of 2.655 mL/min was used. (Top) Optimization curves for process productivity ( $PR$ ) and eluent consumption ( $EC$ ). (Bottom) Product yields and product fraction purities compared to the used design constraint values. 5 % error margins are shown in dashed lines for acid (thick line) and sugar (thin line) constraints. Pulse size is the total column feed pulse size in mL after mixing recycle and fresh feed.

## 5 SEPARATION EXPERIMENTS

The goal of the experimental part was to carry out a selection of separation tests using the parameters determined by simulated design presented in the previous chapter. The steady state concentration profiles, as well as product fraction purities, productivities, yields and eluent consumptions were determined and compared to the simulated predictions.

### 5.1 Experimental setup

The separation experiments were performed using custom made installations. A schematic flow chart of the process equipment is shown in Figure 4. Eluent is pumped from a glass container E-1 by the mobile phase pump P-1 through a motorized MV-7 injection valve (V-1). The flow passes through the column C-1 packed with Finex CS16GC resin. After the column are two on-line indicators; a conductivity detector (I-1) and a refractive index (RI) detector (I-2). The column outlet is fractionated by a motorized MV-8 valve (V-2). The outlet can be directed to waste, collected as product fractions, returned as recycle or directed entirely into an automated fraction collector E-4 for concentration profile samples.

The injection loop E-2 doubles as the recycle mixing reservoir. A GE Healthcare 50 mL Superloop was used. Fresh feed was introduced from the container E-3 alongside the collected recycle fraction via a three-way valve V-3, and the fresh feed solution was kept in constant flow with an additional pump P-2, usually circulating it back into the container. All wetted parts were glass, Teflon or PEEK. Further equipment specifications are presented in Table I.

Both liquid containers E-1 and E-3 were placed on balances to determine flow rate average in 5 minute measurement intervals prior to the experiments. The eluent flow rate was also measured during the experiments.

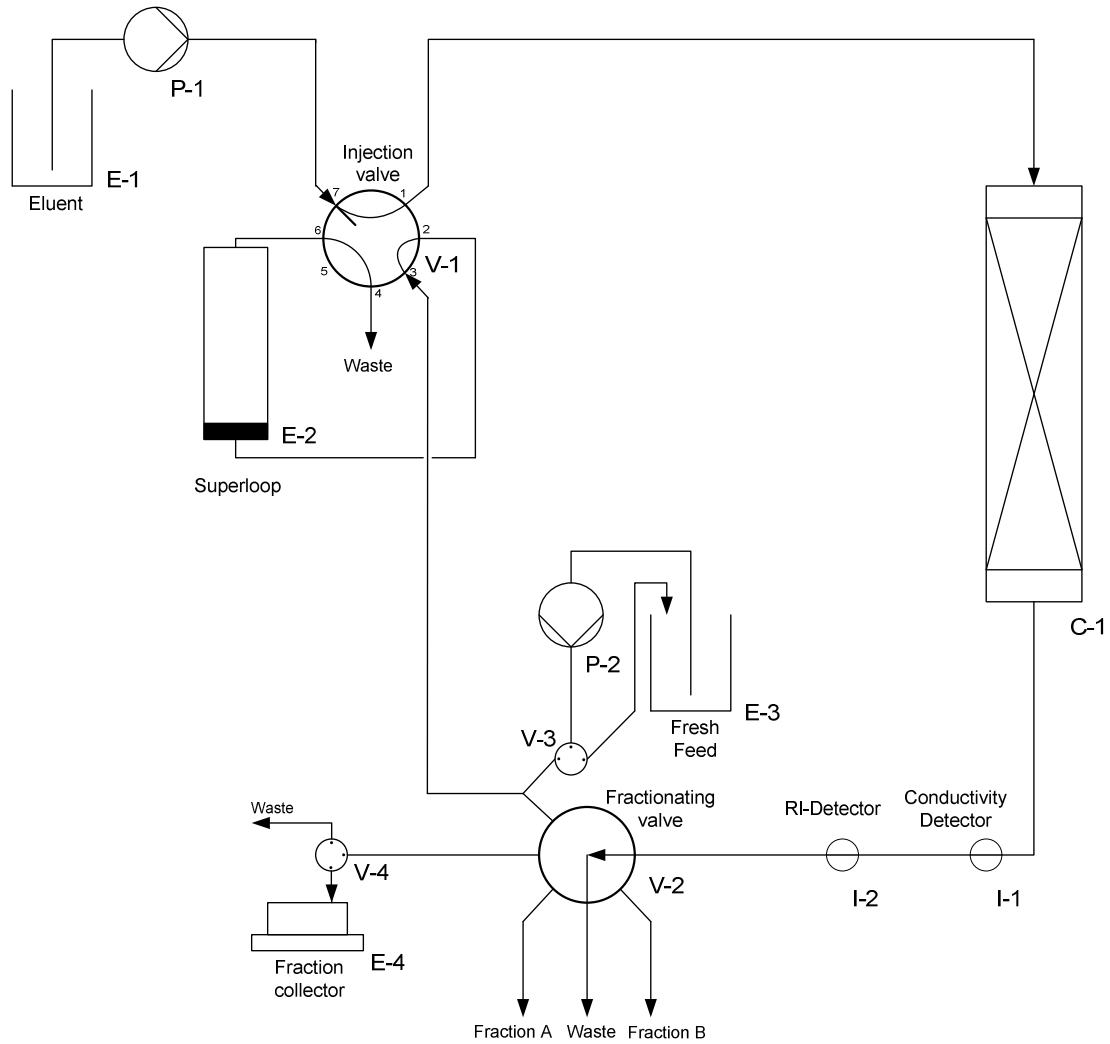


Figure 4. Schematic flow chart of the process equipment used in the SSR separation experiments.

The injection valve V-1 has three positions: load, inject and wash. The load position is shown in Figure 4. In this position the Superloop E-2 can be loaded with either the initial feed pulse or the combination of recycle from valve V-2 and fresh feed from valve V-3. In the injection position the eluent flow is directed to the top on the loop through port 6 and the contents are pushed by a plunger separating the top and bottom parts of the loop, through ports 2 and 1 into the column. When the loop is empty the eluent will pass the plunger and purge the tubing before the valve V-1 is returned to load position.

Table I. List of equipment used in the experimental setup (see Fig. 4).

Description	Indication	Specification
Column	C-1	Kronlab ECO25 glass column
Eluent container	E-1	2 L glass bottle
Injection reservoir	E-2	GE Healthcare Superloop 50 mL
Fresh feed container	E-3	250 mL glass bottle
Fraction collector	E-4	Pharmacia Biotech FRAC 100
Conductivity detector	I-1	Pharmacia Biotech Conductivity Monitor 18 1500-00
Refractive index detector	I-2	Schambeck RI 2000 P Differential Refractive Index Detector
Mobile phase pump	P-1	Waters 515 HPLC Pump
Fresh feed pump	P-2	Waters 515 HPLC Pump
Injection valve	V-1	MV-7 motor valve
Fractionating valve	V-2	MV-8 motor valve
Fresh feed valve	V-3	Three-way solenoid valve
Fraction collector valve	V-4	Three-way solenoid valve
Tubing	N/A	Teflon/PEEK HPLC tubing

In mixed-mode SSR it is necessary that the fresh feed is thoroughly mixed in with the recycle fraction before injecting the mix into the column. Three tests were performed with the Superloop to evaluate the mixing of the contents. In all tests a 10 mL pulse of 20 w-%  $\text{H}_2\text{SO}_4$  was injected from the loop into the column, and the whole 26.55 mL wide outlet acid peak was collected back into the loop as recycle. An emulated fresh feed of 23.45 mL of 20 w-%  $\text{H}_2\text{SO}_4$  was pumped into the loop simultaneously during the collection of the ‘recycle’ via the valve V-3 (total volume of 50 mL in the loop). 1 minute after collection the mixture was injected through the conductivity detector I-1 without passing through the column. The flow rate in all tests was 2.655 mL/min.

The test conditions were varied in three key aspects: in one test the Superloop was loaded and injected as normal; in the second test the column outlet was taken out of the system, stirred thoroughly and injected back into the loop using a Luer Lock syringe; in the third test the Superloop was mounted upside-down so loading would induce a gravitational flow on the heavier  $\text{H}_2\text{SO}_4$  in water. The conductivity profiles overlaid for each test are shown in Figure 5. As seen from the profiles normal operation shows severe gradient inside the loop. However, simply operating the Superloop upside-down will provide nearly as good mixing as stirring in a system of sufficiently different density components.

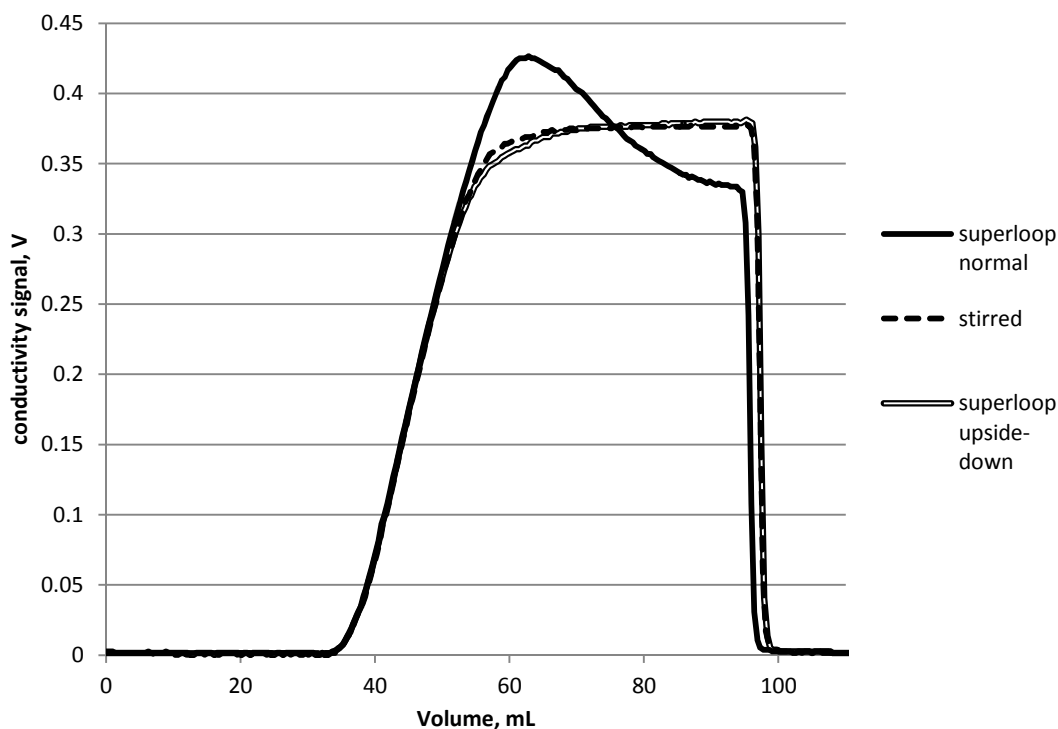


Figure 5. H<sub>2</sub>SO<sub>4</sub>-water mixing tests using the Superloop 50 mL. Flow rate was 2.655 mL/min. The acid profile was collected after injecting 10 mL of 20 w-% H<sub>2</sub>SO<sub>4</sub> through the column. A fresh feed of the acid was introduced simultaneously during the collection to fill the 50 mL loop and the resulting mixture's conductivity was measure leaving the Superloop.

### 5.1.1 Process control

The process was automated using a control program developed using National Instruments Labview software. All the valves and the fraction collector were controlled with a serial interface USB controller. The pumps in the system were calibrated to the correct constant flow rate prior to the experiments and monitored during the run. Initial feed was loaded manually into the Superloop with a Luer Lock syringe.

The control program was formed as a state machine and allowed the user to set all process parameters prior to the run. The injection and cut times were entered as volumes and the program used a constant flow rate to calculate times elapsed from cycle start for any valve position changes. A short safety delay was used before proceeding to the next cycle. The program allowed for directing the last cycle to fraction collector, where the profile could be collected as small samples at set intervals.

### 5.1.2 Data acquisition

The on-line detectors I-1 and I-2 in the system were connected to the control program via a NI SCXI interface. The control program collected the signal data at set intervals into graphs, overlaying the last three cycles so the user could monitor the development of steady state.

All detector data was stored into data files during a run. The program also formed a log file of the run that recorded all key control events and their time stamps.

### 5.1.3 MR-SSR experiments

Five different feed pulse (injection) sizes were selected for the practical experiments. Based on the simulated optimization charts shown in Figure 3, the smaller volume end was emphasized. In all experiments a constant flow rate of 2.655 mL/min was used. The column was regulated to 50 °C by a thermostat controlled water jacket. The resin bed porosity was determined prior to the experiments and checked that it was consistent with the value used in simulations. Other variable parameters in the experiments are presented in Table II. For practical reasons the cut times are presented as volumes passed and fraction widths as volumes.

The lowest pulse size used (0.9 mL) corresponds to a batch separation. This experiment was repeated twice. In the first run the product fraction A and B were collected in entirety, in the second run the outlet profile was collected with the fraction collector. Similarly in the SSR runs the product fractions A and B were collected from the sixth cycle and the profile samples were collected from the seventh cycle. Preliminary testing showed that five cycles were sufficient to reach a steady state when using the customized initial injection based on simulated data. The on-line detector data on each experiment confirmed the last cycles to be practically identical (see Appendix II). All results from the conducted experiments in comparison to corresponding simulated data are presented in Figures 6 to 11 in chapter 6.

Table II. Variable parameters used in the practical MR-SSR experiments. The start time of recycle  $t_{A2}$  is presented as volume passed from cycle start, the volumes of each fraction are relative to recycle start. Concentrations  $c^0$  are the used initial injection concentrations.

$V_{inj}$ , mL	$t_{A2}$ , mL	$V_{rec}$ , mL	$V_A$ , mL	$V_B$ , mL	$c^0_{H_2SO_4}$ , mol L <sup>-1</sup>	$c^0_{Glu}$ , mol L <sup>-1</sup>
0.9	45.09	-	11.55	13.77	2.15	0.55
3	47.05	1.27	13.91	16.99	1.36	0.35
6	48.59	3.66	15.42	15.98	1.27	0.28
9	48.91	6.56	15.74	15.56	1.20	0.23
16	49.18	13.49	15.95	15.27	1.18	0.21

## 5.2 Concentration analysis

Both component concentrations (sulfuric acid and glucose) were analyzed from product fractions A and B from each experiment. In addition a number of samples from the collected profiles were ana-

lyzed to obtain sufficient outlet profile data points for comparison with the simulated concentration profiles.

Sulfuric acid concentrations were determined by titration. A Mettler-Toledo DL25 automatic titrator was used. The sample size was 0.5 mL. The titrant used was 0.1 M NaOH solution prepared from an ampoule. The profile samples for analysis were selected based on the conductivity detector data from the experiment in question.

Glucose concentrations were determined using Agilent series 1100 analytical HPLC equipment. The column used was Metacarb 87P in temperature 60 °C. The eluent was 0.005 M H<sub>2</sub>SO<sub>4</sub> and a constant flow rate of 0.6 mL/min was used. Injection volume for the samples was 10 µL and the glucose concentration was determined with provided peak integration software.

## **6 RESULTS AND DISCUSSION**

The productivity, eluent consumption, purity and yield data from the MR-SSR experiments described in chapter 5.1.3 are presented in Figure 6 below. The concentration profiles are presented in Figures 7 to 11. The experimental results are compared to corresponding simulated values also visible in the optimization charts in Figure 3. As can be seen from the charts in Fig. 6 Top, the productivity and eluent consumption for sulfuric acid and glucose follow the predicted trends.



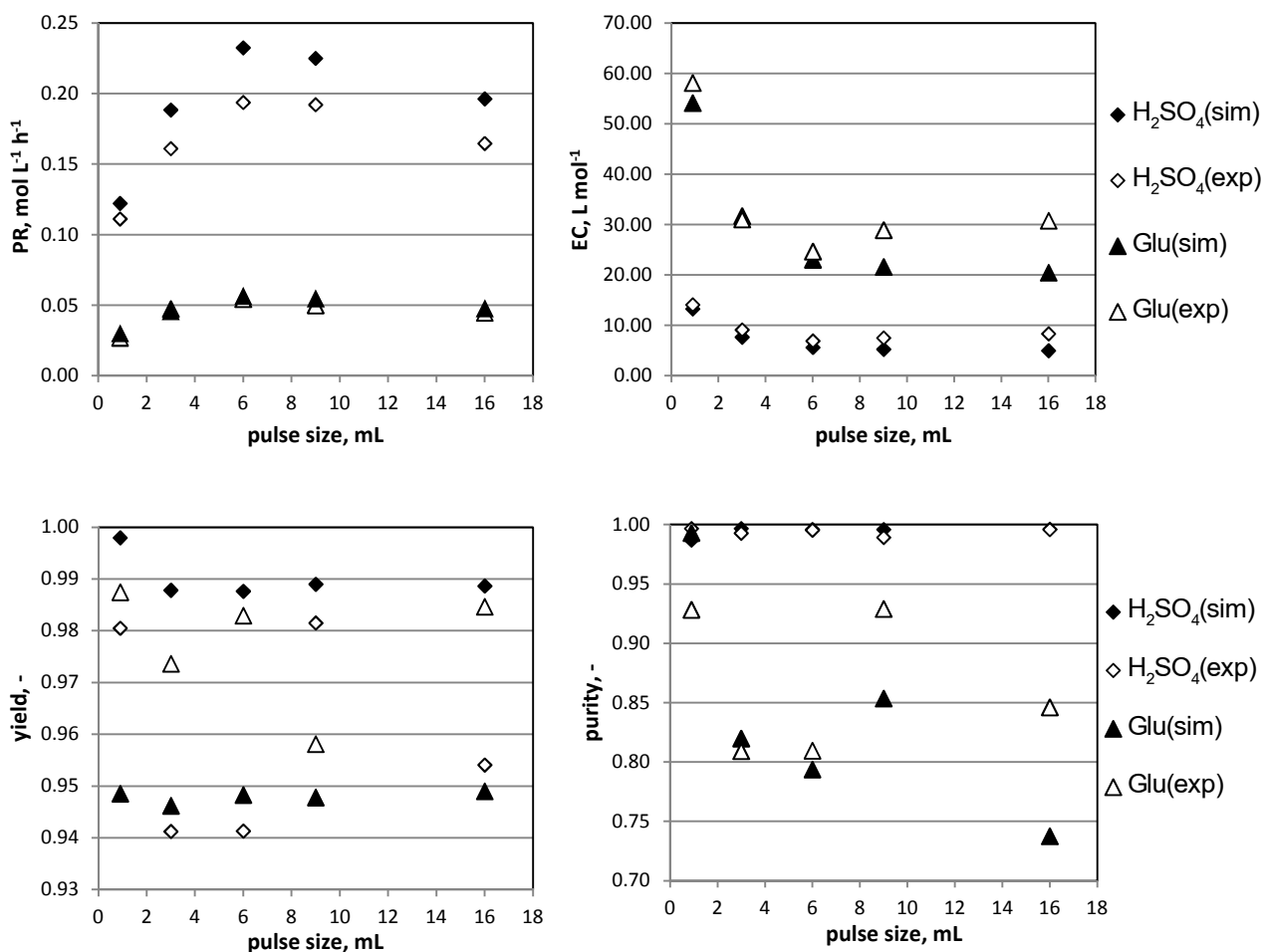


Figure 6. Experimental MR-SSR sulfuric acid-glucose separation results compared to corresponding simulated values. A 98.17 mL bed of Finex CS16GC SAC resin and constant flow rate of 2.655 mL/min was used. (Top) Results for process productivity (*PR*) and eluent consumption (*EC*). (Bottom) Product yields and product fraction purities.

The productivity of sulfuric acid is lower in practice than in the predictions. This is due to the shape of the acid concentration peak leaning more towards the end of the chromatogram, as seen in Figure 8 for instance. The case of sulfuric acid-sugar separation is very sensitive to small variations in the steep end of the acid shock, and with fixed cut times small deviations propagate further in SSR. Component isotherm model used in design does not completely fit the practical conditions in this case. Dynamic control of recycle cut times may also be required, a method that takes into account small variations in the profile due to erratic flow rate or temperature shifts.

Shifts of the concentration profiles towards the end of the chromatogram in steady state also lead to higher sugar fraction purities and lower acid yields than intended. The actual values for the data shown in Figure 6 can be found in a table in Appendix I. Figures showing the development of steady state in each SSR experiment according to the on-line detector data are included in Appendix II.

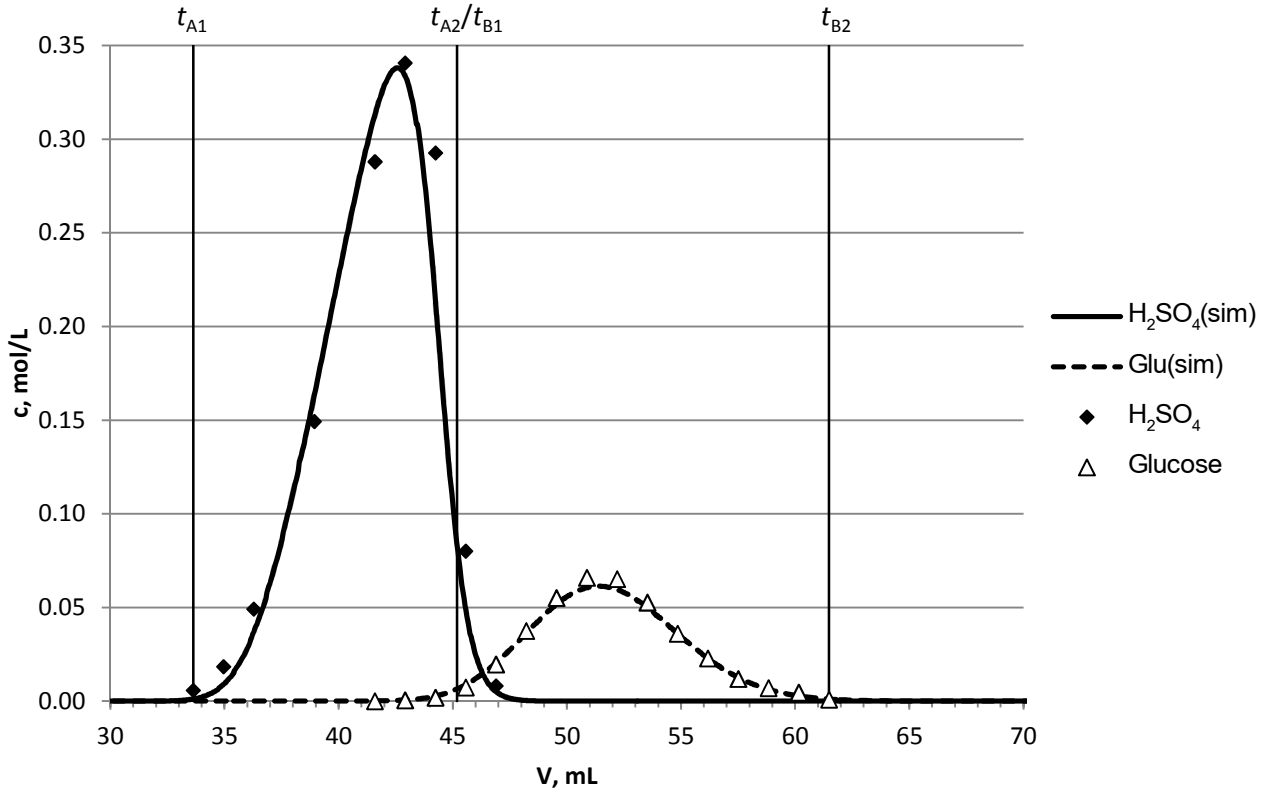


Figure 7. Concentration profiles from the 0.9 mL feed pulse size batch experiment. Lines represent simulated data; markers are analyzed concentrations from experiment samples.

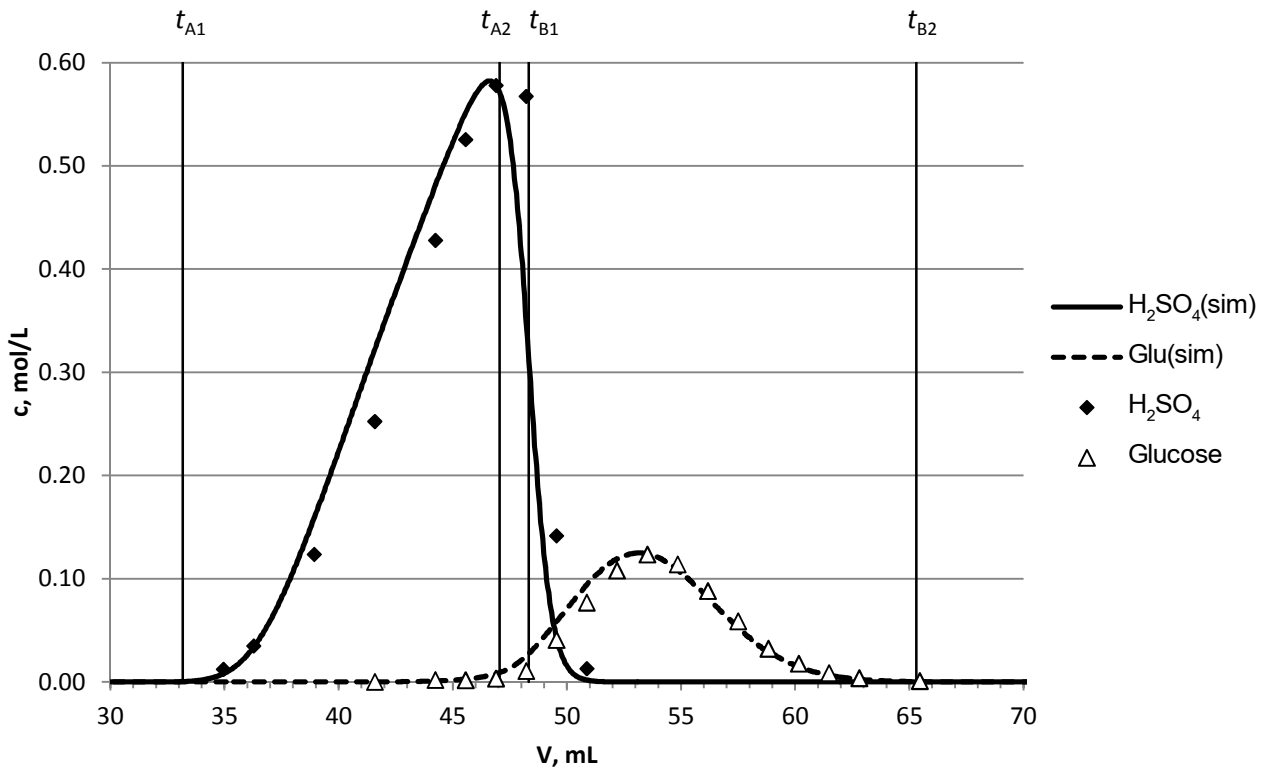


Figure 8. Concentration profiles from the 3 mL feed pulse size SSR experiment. Lines represent simulated data; markers are analyzed concentrations from experiment samples.

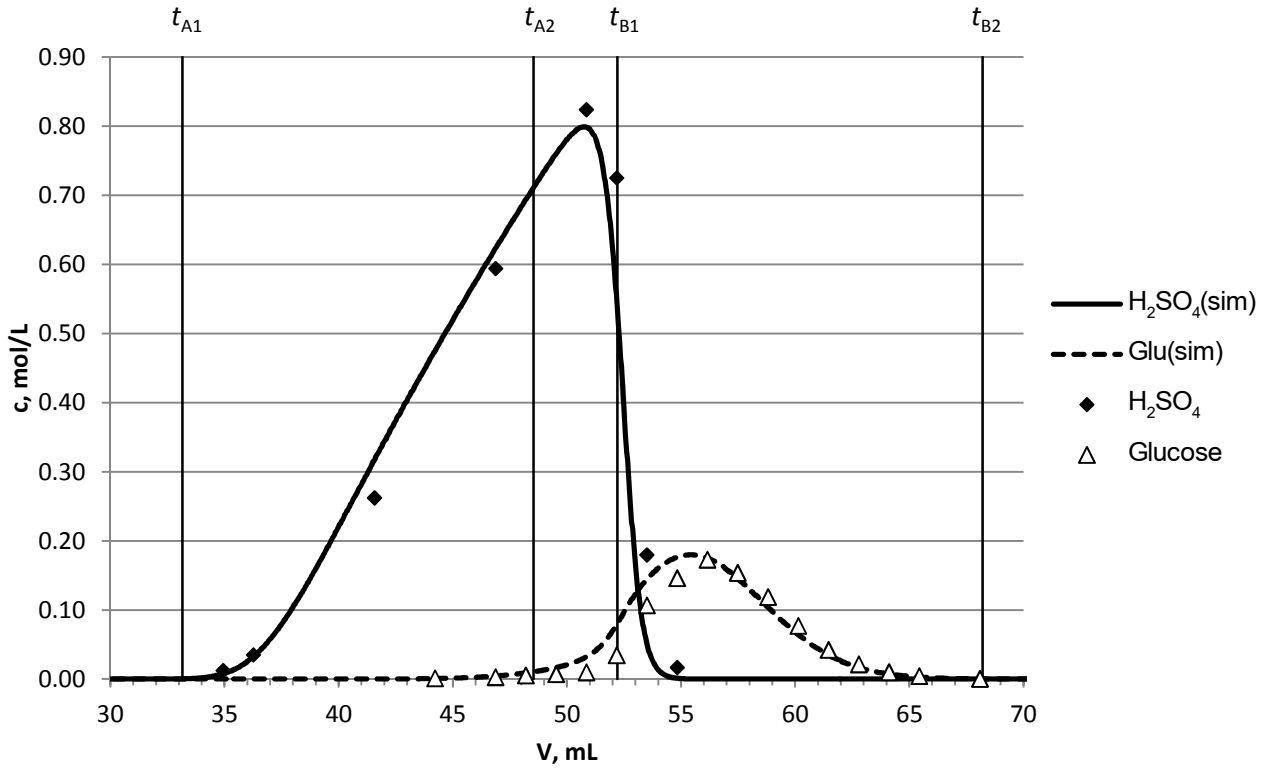


Figure 9. Concentration profiles from the 6 mL feed pulse size SSR experiment. Lines represent simulated data; markers are analyzed concentrations from experiment samples.

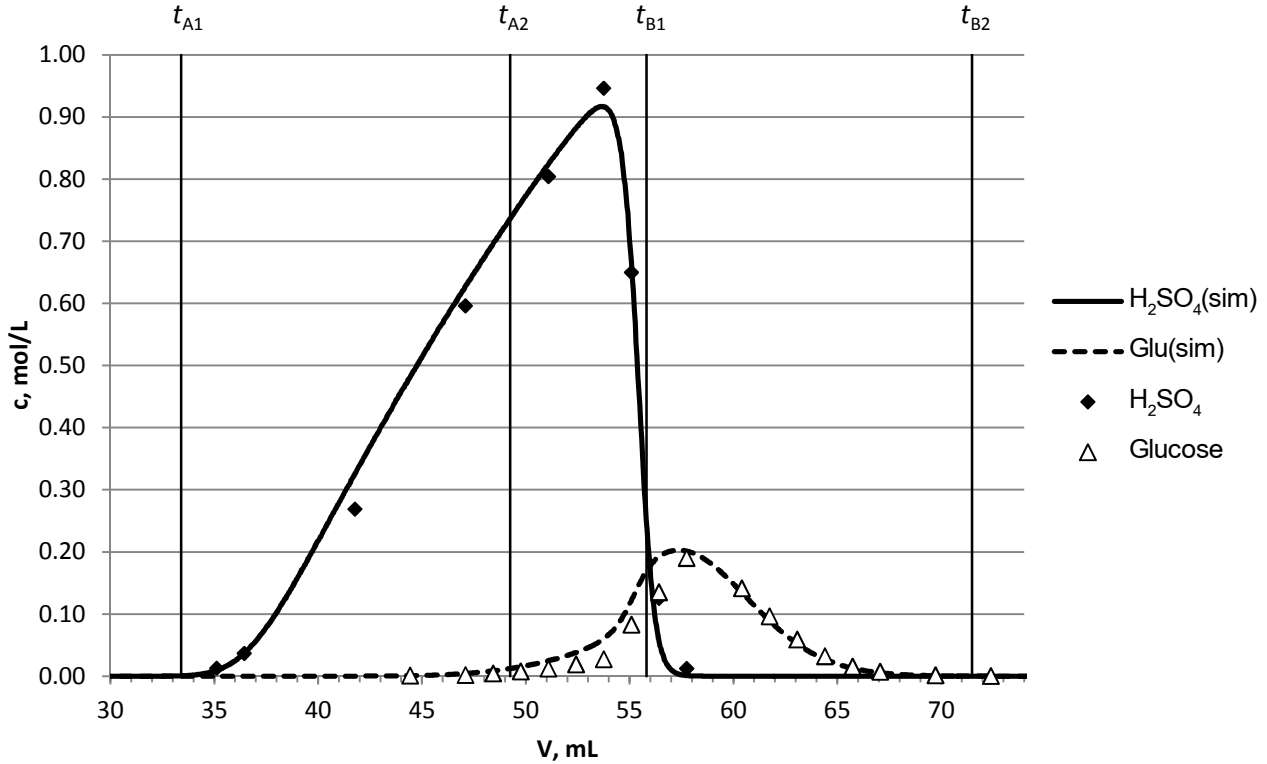


Figure 10. Concentration profiles from the 9 mL feed pulse size SSR experiment. Lines represent simulated data; markers are analyzed concentrations from experiment samples.

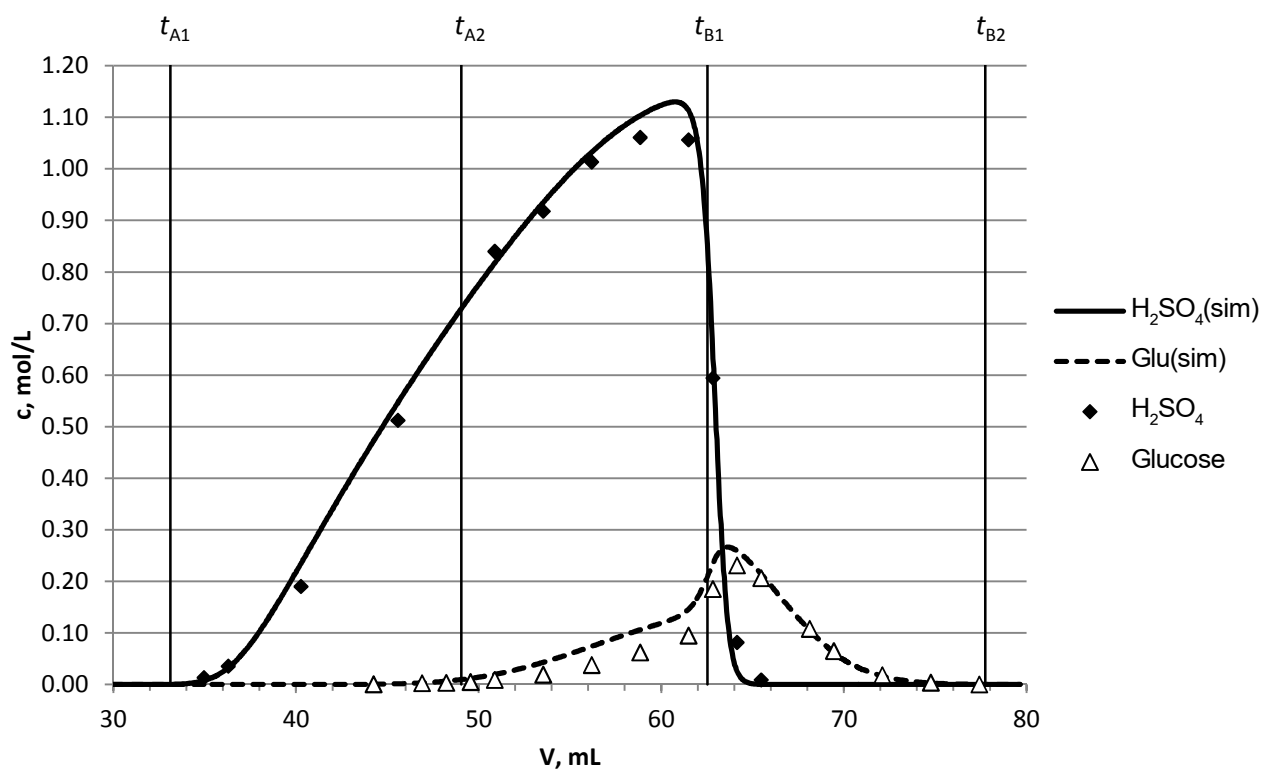


Figure 11. Concentration profiles from the 16 mL feed pulse size SSR experiment. Lines represent simulated data; markers are analyzed concentrations from experiment samples.

The results of this study indicate that the method [6] is useful for designing practical preparative MR-SSR. Simulated predictions indicate the optimal feed pulse size in this separation case to be approximately 6 mL, and the experimental results are consistent with this prediction. The productivity is 59 % higher for acid and 82 % higher for glucose in this case compared to ideal batch separation with a single cut. Eluent consumption is lowered approximately 50 % in SSR mode. The process design by simulation, namely choosing the correct cut times, is useful in avoiding extensive experimental work. However, further optimization in this case would be needed to reach the set constraints. Extremely accurate isotherm model is required to avoid propagation of small deviations.

The design method allows for narrowing down the correct pulse size, and setting the starting point for practical preparative SSR chromatographic separation, effectively reducing necessary empirical work in the early stages of process design and optimization.

## 7 SUMMARY

Mixed-recycle steady state recycling (MR-SSR) chromatography was used in sulfuric acid - glucose separation. The preparative separation experiments were designed using simulations based on a method to predict steady state, presented by Sainio and Kaspereit [6]. The design method allowed

for feed pulse size optimization, cut time determination and initial feed composition to short-cut start the steady state. Design was based on product fraction purity constraints less than 100 %. Even though the design values were not completely met in the experimental part, the approach displays higher productivity and lower eluent consumption compared to corresponding batch separation.

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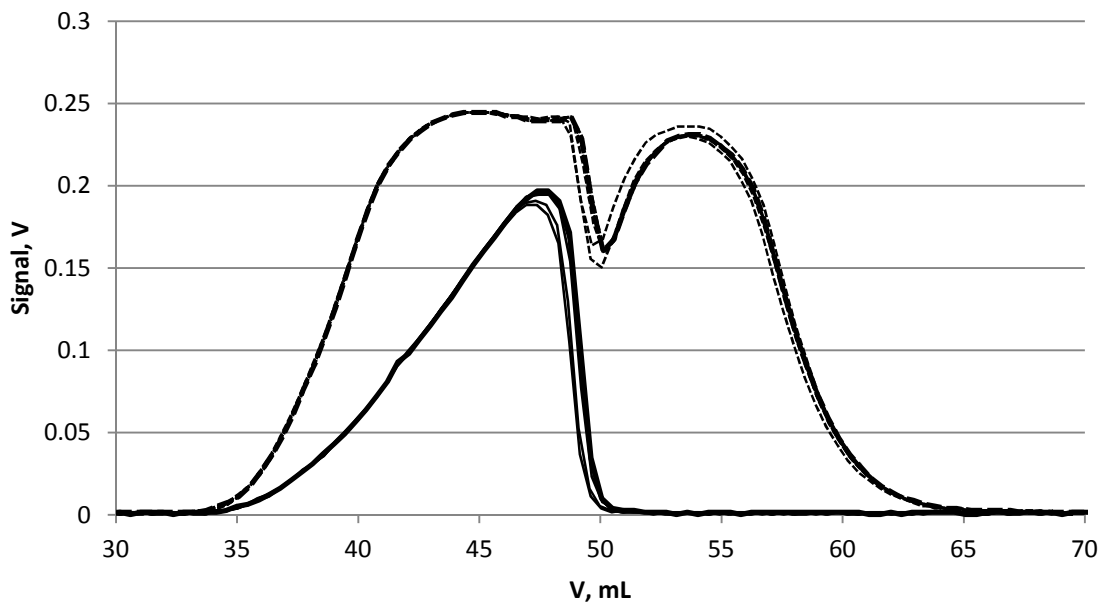
**Table of results for the MR-SSR, simulated and experimental values**

<b>Simulated</b>								
$V_{inj}$ , mL	$PR_1$ , mol $L_{bed}^{-1} h^{-1}$	$PR_2$ , mol $L_{bed}^{-1} h^{-1}$	$EC_1$ , L $mol^{-1}$	$EC_2$ , L $mol^{-1}$	$p^A$ , -	$p^B$ , -	$Y_1$ , -	$Y_2$ , -
0.9	0.122	0.030	13.270	54.167	0.987	0.993	0.998	0.949
3	0.189	0.046	7.669	31.715	0.997	0.820	0.988	0.946
6	0.233	0.057	5.605	23.067	0.996	0.794	0.988	0.948
9	0.225	0.055	5.262	21.636	0.996	0.854	0.989	0.948
16	0.196	0.048	4.973	20.488	0.996	0.738	0.989	0.949
<b>Experimental</b>								
$V_{inj}$ , mL	$PR_1$ , mol $L_{bed}^{-1} h^{-1}$	$PR_2$ , mol $L_{bed}^{-1} h^{-1}$	$EC_1$ , L $mol^{-1}$	$EC_2$ , L $mol^{-1}$	$p^A$ , -	$p^B$ , -	$Y_1$ , -	$Y_2$ , -
0.9	0.111	0.027	14.105	58.169	0.997	0.928	0.980	0.987
3	0.161	0.047	9.126	31.055	0.993	0.809	0.941	0.974
6	0.194	0.054	6.923	24.684	0.995	0.810	0.941	0.983
9	0.192	0.050	7.523	28.940	0.989	0.929	0.981	0.958
16	0.165	0.045	8.341	30.794	0.996	0.846	0.954	0.985

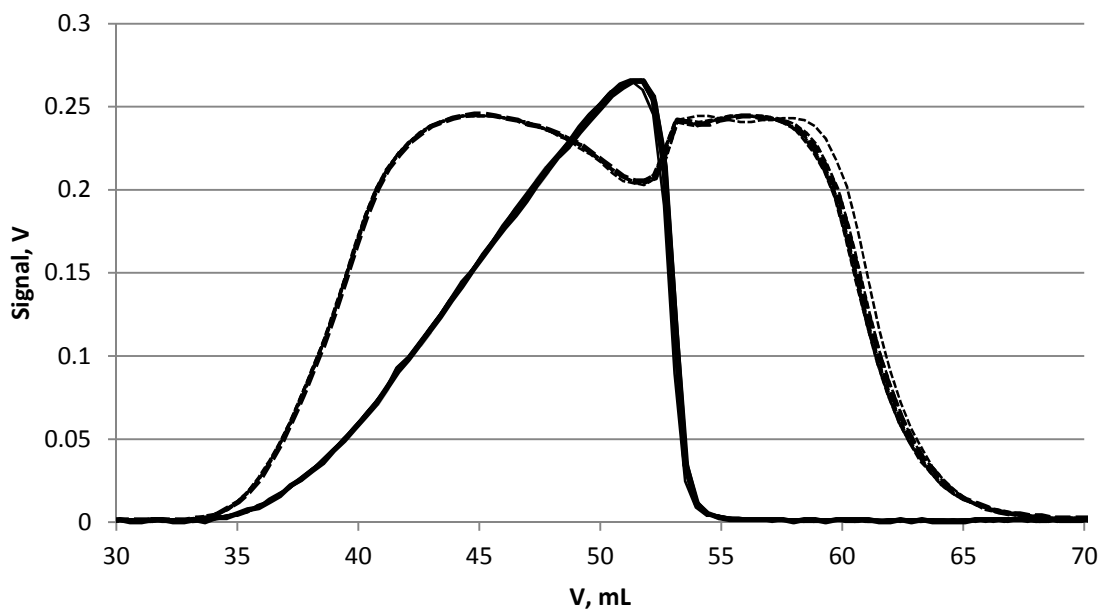
### Graphs for the on-line detector data from SSR experiments

Solid lines are conductivity data, dashed lines are refractive index. The last cycle (one used to collect profile samples) is marked with thick lines. Note that the data in the graphs is raw detector signal; different detector data are not scaled, and RI detector signal is capped at 2.444 V and changes polarity over that limit.

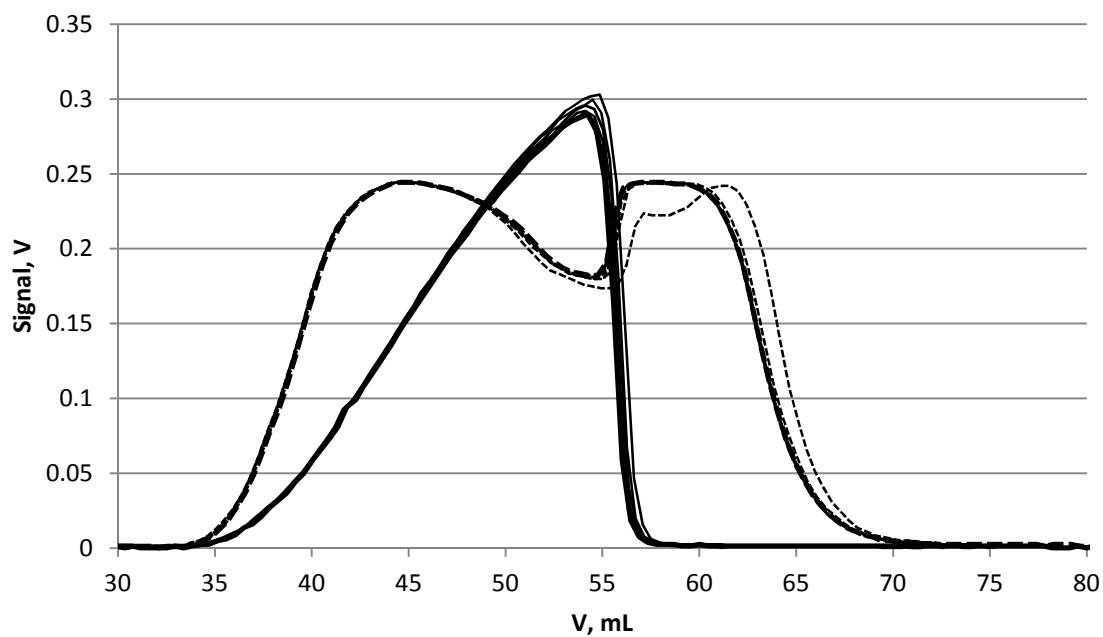
#### 3 mL SSR



#### 6 mL SSR





**9 mL SSR****16 mL SSR**