

# OPERATING CONDITIONS OF A SIMULATED MOVING BED CHROMATOGRAPHY UNIT FOR THE PURIFICATION OF FRUCTO-OLIGOSACCHARIDES

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## INTRODUCTION

In recent times, the production of fructo-oligosaccharides (FOS) has gained large commercial interest due to its beneficial properties in the human health through modulation of the microbiota. Based on these benefits, FOS, such as kestose (GF<sub>2</sub>), nystose (GF<sub>3</sub>) and fructo-furanosilnystose (GF<sub>4</sub>), have been denominated as prebiotics (Gibson, 1998).

In large scale, FOS can be produced by fermentation of sucrose through fructosyltransferase that is present in several microorganisms. Fermentative processes have high production yields compared with other processes. However, the composition of the final broth from a fermentative process includes not only FOS, but also di and mono-saccharides, namely sucrose (S), fructose (F) and glucose (G) that do not contribute to the beneficial properties as prebiotics and must be removed from the oligosaccharides mixture.

Among other separation processes, simulated moving bed (SMB) chromatography appears to be an efficient downstream process for the fractionation of sugars in an industrial scale, since it is a continuous process and high productivities can be obtained with low consumption of reagents (Gomes *et al.*, 2006); see Figure 1.

The first step to study the separation of compounds by SMB is the choice of an efficient adsorbent. Ion exchange resins of sulfonated poly(styrene-co-divinylbenzene) (PS-DVB) have been largely used as adsorbent in the sugar industry due to their chemical inertness, higher capacity and selectivity (Luz *et al.*, 2008, Tiihonen *et al.*, 2002). These non-ionic resins can be functionalized with cations such as potassium. Potassium cations form weak complexes with sugars providing high kinetic adsorption rates (Pedruzzi *et al.*, 2008). The separation

using these resins occurs due to both size exclusion and restricted diffusion effects (Nobre *et al.*, 2009).

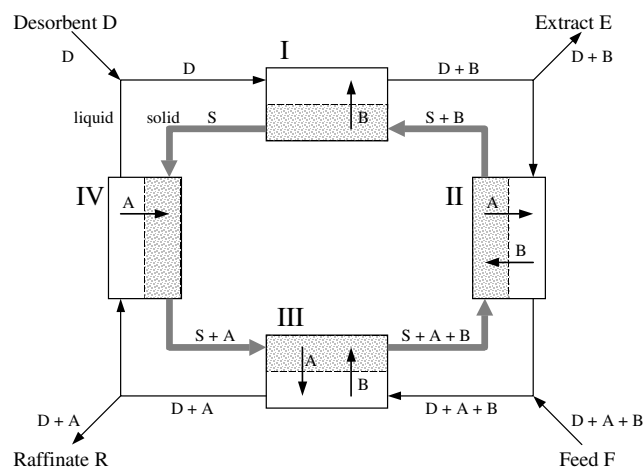


Figure 1. Equivalent counter-current representation of a simulated moving bed process – Material flows and adsorption-desorption phenomena in each section

## METHODS AND MATERIALS

In this work, two gel-type PS-DVB resins in the potassium form were studied namely, *Dowex 50W-X2* (particle size: 37-74  $\mu\text{m}$ ) and *Dowex Monosphere 99K/320* (particle size: 320  $\mu\text{m}$ ). Experiments were carried out in a batch column (1.6x30 cm) in order to determine adsorption parameters.

Salts present in the fermentative broth are mainly sodium (65%) and potassium (34%). Potassium resins were used so that sodium ions could replace potassium in the resin affecting its adsorption characteristics. To guarantee a minimum of 90% of potassium in respect to sodium ions in the final solution the broth was pre-treated. After removing the biomass by filtration (0.2  $\mu\text{m}$ ), 250 mL of broth, in batch steps, were saturated with potassium ions by passing the broth

through a column with 100 mL of *Dowex Monosphere 99K/320*. Before starting another batch, the column was washed with ultra-pure water and regenerated with  $K_2SO_4$  solution ( $0.5 \text{ mol/dm}^3$ )

## RESULTS AND DISCUSSION

In order to verify the separation performance, pulse tests of each sugar were performed in a batch column connected to an HPLC system equipped with an RI detector. Sugars were found to be adsorbed by both resins in the following order:  $F > G > S > GF_2 > GF_3 > GF_4$ . Moreover, with *Dowex 50W-X2* it was possible to separate salts from sugars. However, the chromatograms obtained for *Dowex Monosphere 99K/320* showed broader peaks for G, F and GF due to a slower kinetics caused by large particles.

Sugars adsorption showed linear equilibrium for the range of concentrations used. Thus, using the retention time method described in Guiochon *et al.*, 1994, it was possible to determine the Henry constants for the two groups present in the broth: FOS and SGF (sucrose+glucose+fructose).

Assays conducted with high flow-rates of eluent (above 20 mL/min) showed high compressibility of the particles for *Dowex 50W-X2*, causing a back pressure in the column up to the maximum allowed by the SMB system (60 bars). On the other hand, *Dowex Monosphere 99K/320* appeared to be stable at high flow-rates keeping a constant porosity. Therefore, *Dowex Monosphere 99K/320* was found to be suitable to work in the SMB unit.

A mathematical model was used to predict the elution profile and validated with experimental results. This model consists of 4 mass balance partial differential equations, 2 for the concentrations in the liquid phase and 2 for the concentrations in the solid phase:

$$\frac{\partial c_i}{\partial t} + \frac{1-\varepsilon}{\varepsilon} \frac{\partial q_i}{\partial t} = -v \frac{\partial c_i}{\partial z}$$

$$\frac{\partial q_i}{\partial t} = k_{F,i} (q_i^{eq} - q_i)$$

where  $c_i$  and  $q_i$  are the concentration of the component  $i$  in the liquid and solid phase respectively,  $t$  is the time,  $\varepsilon$  is the porosity,  $z$  is the axial coordinate,  $v$  is the fluid velocity and  $k_{F,i}$  is the mass transfer coefficient.

A LDF model (Ruthven, 1984) is used for mass transfer kinetics. The equilibrium concentration is given by a linear isotherm where  $H$  is the Henry coefficient.

$$q_i^{eq} = H_i c_i$$

These model PDEs are solved in Matlab with the toolbox MatMol ([www.matmol.org](http://www.matmol.org); (Wouwer *et al.*, 2004) using a method of lines approach, i.e. spatial discretization followed

by time integration of the resulting semi-discrete (discrete in space but continuous in time) equations.

As the concentration profiles develop steep moving fronts, the application of finite difference schemes lead to spurious oscillations in the concentration profiles, as illustrated in Figure 1, even when using upwind schemes for the convective terms and a relatively large number of spatial grid points.

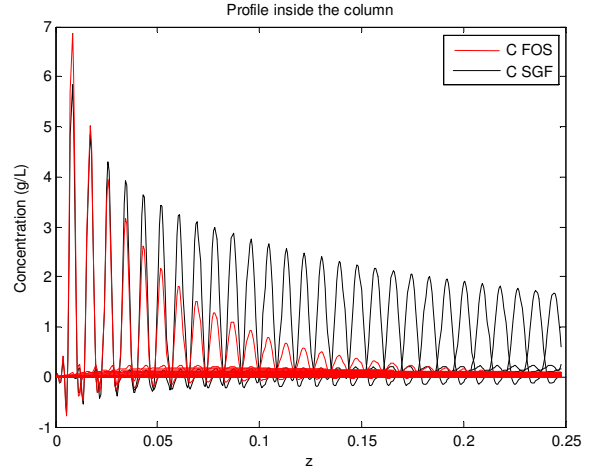


Figure 2: Time evolution of the spatial concentration profiles inside a chromatographic column, computed with finite differences with a 4-point biased upwind scheme, and  $N = 400$  grid points.

To alleviate this problem, nonoscillatory schemes can be used such as Koren slope limiters, as illustrated in Figure 2.

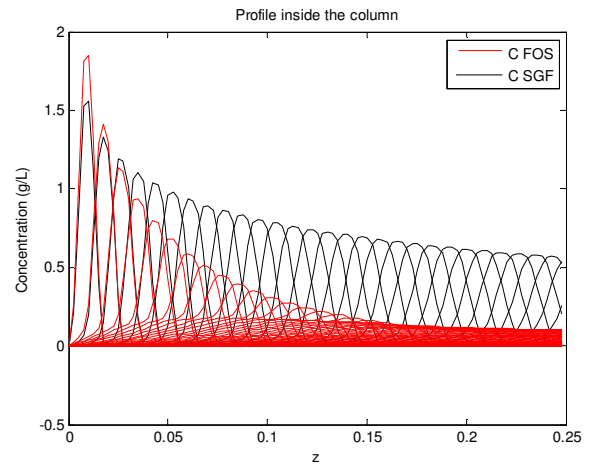


Figure 3: Time evolution of the spatial concentration profiles inside a chromatographic column, computed with a Koren slope limiter scheme, and  $N = 100$  grid points

The use of this scheme is quite efficient and leads to the following time evolution at the column outlet. The numerical simulation results are also compared with experimental data, showing a relatively good fit using the model parameters determined in the batch experiments.

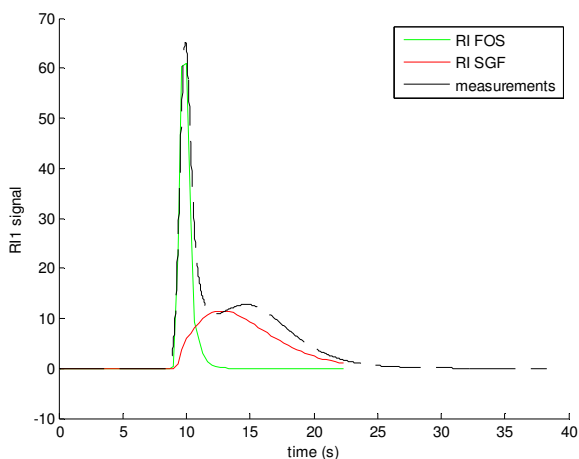


Figure 4: Time evolution of the (RI signal) at the column outlet. Comparison of real (measurements) and simulated data for FOS and SGF.

It is of interest to assess the model parameter sensitivity by a perturbation method, i.e., by making small changes in the isotherm parameters and by observing the effect on the concentration profiles.

This sensitivity analysis is a first step towards a parameter estimation procedure, using the numerical simulator and minimizing the distance to the experimental data in some sense (the most common approach being the least-squares). This is subject of current work, and will be reported at the time of the conference.

## CONCLUSIONS

*Dowex Monosphere 99K/320* was found to be more suitable to work in the SMB unit as compared to *Dowex 50W-X2* due to greater resistance at high pressure.

Batch experiments were carried out to estimate the adsorption parameters. The experimental results are compared with model prediction. The latter is computed by numerical solution of the mass balance equations of a kinetic model, using a method of lines approach and slope limiters for approximating the spatial operators. Indeed, very sharp concentration profiles travel through the column and non-oscillatory schemes are necessary to avoid spurious oscillations and unrealistic negative concentration values.

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