Optimization strategies in the modelling of SG-SMB applied to separation of phenylalanine and tryptophan

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Abstract. The solvent-gradient simulated moving bed process (SG-SMB) is the new tendency in the performance improvement if compared to the traditional isocratic solvent conditions. In such SG-SMB process the modulation of the solvent strength leads to significant increase in the purities and productivity followed by reduction in the solvent consumption. A stepwise modelling approach was utilized in the representation of the interconnected chromatographic columns of the system combined with a lumped mass transfer model between the solid and liquid phase. The influence of the solvent modifier was considered applying the Abel model which takes into account the effect of modifier volume fraction over the partition coefficient. Correlation models of the mass transfer parameters were obtained through the retention times of the solutes according to the volume fraction of modifier. The modelling and simulations were carried out and compared to the experimental SG-SMB separation unit of the amino acids Phenylalanine and Tryptophan. The simulation results showed the great potential of the proposed modelling approach in the representation of such complex systems. The simulations showed great agreement fitting the experimental data of the amino acids concentrations both at the extract as well as at the raffinate. A new optimization strategy was proposed in the determination of the best operating conditions which uses the phi-plot concept.

1. Introduction
The simulated moving bed (SMB) process has been implemented successfully in the pharmaceutical industry to perform difficult separation of molecules. The simulated moving bed (SMB) is a continuous process of interconnected high-performance liquid chromatographic (HPLC) columns which can be used to separate enantiomeric mixtures with high purity and low solvent consumption. The process consists in the simulated countercurrent movement of solid adsorbent phase by switching the positions of the two inlet (Feed and solvent) and the two outlet (Extract and raffinate) streams in the clockwise direction. The more and less adsorbable molecules of enantiomers are collected at the extract and raffinate stream, respectively.

The solvent-gradient simulated moving bed process (SG-SMB) is the new tendency in the performance improvement if compared to the traditional isocratic solvent conditions [1-2]. In such SG-SMB process the modulation of the solvent strength leads to significant increase in the purities and productivity followed by reduction in the solvent. The solvent strength in the SG-SMB process is altered through the volume fraction of the modifier (φ) as can be seen in Fig. 1. Nam et al. [1] carried out SG-SMB experiments in the performance evaluation of phenylalanine and tryptophan separation which was compared to isocratic solvent conditions. Its operating conditions were determined from the SG-SMB optimization tool based on genetic algorithm.
The determination of the operation conditions of SG-SMB is a difficult task [2] and only numerical methods has been utilized as carried out by Nam et al. [1]. Therefore in this work it was proposed a new methodology to achieve the process operating conditions without heavy numerical calculations. A novel optimization strategy was proposed which considers the Henry’s constants as a function of the modifier volume fraction of the desorbent near the feed entrance. The influence of the solvent modifier was considered applying the Abel model which takes into account the effect of modifier volume fraction over the partition coefficient.

1. Modelling and optimization approaches

The chromatographic columns (Fig. 2A) of the SG-SMB process are modeled as a discrete representation of N mixed cells in series combined with lumped mass transfer solid-liquid model,

\[
\frac{dc_i^p}{dt} + \frac{dq_i^p}{dt} = (C_{i0}^p - C_i^p)\sigma_i^p
\]

in which \(C_i^p\), \(C_{i0}^p\), \(q_i^p\) and \(t\) represents the concentration of compound \(i\) in the liquid phase, the concentration of compound \(i\) in the liquid phase at the entrance of the mixed cell, the concentration of compound \(i\) in the solid adsorbent phase and the time, respectively, all at column \(p\). In Eq. 1 \(\sigma_i^p = F/\epsilon V\) with \(F\), \(\epsilon\) and \(V\) representing the volumetric flow rate, the total porosity and the volume of the mixed cell, respectively. It was utilized the Abel’s model for the determination of the partition coefficient (K)

\[
K = \frac{p_1}{(1+p_2\delta)p_3}
\]

where \(p_1\), \(p_2\) and \(p_3\) are the model parameters of either tryptophan or phenylalanine. The Mazzotti et al. [3] approach is the classical procedure determining the operating conditions of isocratic SMB process under linear mass transfer equilibrium. The classical Mazzotti’s approach [3] was extended analogously to solvent gradient condition (SG-SMB) assuming the Henry’s constant a function of the modifier volume fraction.

\[
m_{II} > H_{(-)}(\phi_{II}) \quad \text{and} \quad H_{(+)}(\phi_{III}) > m_{III}
\]

which can be organized as follow, where \(m_{II}, m_{III}, H_{(-)}, H_{(+)}\) are flow rates ratio at section II and II and the Henry’s constants of the less and more adsorbed compounds, respectively.

\[
m_{II} - H_{(-)}(\phi_{II}) > 0 \quad \text{and} \quad H_{(+)}(\phi_{III}) - m_{III} > 0
\]

The terms \(\phi_{II}\) and \(\phi_{III}\) are, respectively, the modifier volume fraction at section II and III. At the feed stream position the above Eq.(4) can be combined to give

\[
H_{(+)}(\hat{\delta}) + H_{(-)}(\hat{\delta}) = m_{II} + m_{III}
\]

The average modifier volume fraction,

\[
\hat{\delta} = \frac{\phi_{II} + \phi_{III}}{2}
\]
is determined from volume balance of modifier at the feed node.

The optimization approach follows the next steps: i) a feed flow rate and the volume fraction of modifier at desorbent ($\phi_0$) are specified; ii) as there is the volume fraction of the adsorbed ($\phi_a$), it can be obtained the volume fraction at section III ($\phi_{III}$) and also the average volume fraction of modifier ($\bar{\phi}$); iii) from the equation find the flow rates of desorbent, extract and raffinate with switch time to reach the equality of Eq. (5); iv) the phi-plot, which is the plot of Eqs. (4) versus phi ($\phi$), is evaluated to ensure the inequalities are true; The higher the inequalities of Eqs. (4) the better is the chance to achieve complete separation; v) the SG-SMB simulator is run to provide the modifier volume fraction profile along the columns and also the new phi-plot. The operating conditions can be altered to determine better results for the inequalities of Eqs. (5). In general only the steps i to iv are necessary to achieve the operating conditions for complete separation (purities at the extract and raffinate higher than 99.9%).

3. Results and discussions

The novel modelling and optimization procedure was correlated to the experimental data of Nam et al. [1] which utilized the SG-SMB process to separate the amino-acids phenylalanine and tryptophan. In a first moment it was evaluated the optimization strategy routine in the determination of the operating conditions of the SG-SMB process. From Fig. 2A to 2C can be seen the improvement in the extract and raffinate purities as the inequalities of Eq. (5) become higher than zero.

The purity values can be found in Table 1 so increasing the switch time leads to better separation performance of SG-SMB process.

| Switch time (min) | 10 (Fig. 2A) | 20(Fig. 2B) | 25(Fig. 2C) |
|-------------------|-------------|-------------|-------------|
| Eq.(5) diff.      | 4.47        | 1.35        | -0.22       |
| Raffinate purity (%) | 0.00        | 98.95       | 99.92       |
| Extract purity (%) | 31.43        | 97.94       | 99.98       |
| Productivity (g/h.L) | 0.1036       | 0.346       | 0.364       |

The high difference in terms of the left and right hand side of Eq. (5) indicates that the chosen operating conditions of Fig. 2A is not ideal leading to a poor separation of the solutes. In the other hand the low difference value of Eq. (5) leads to a high separation performance (Fig. 2C). The operating conditions of Nam et al. [1] were utilized which confirms the experimental operating conditions utilized to achieve a great separation performance (See Fig. 3). The Fig. 3 shows the good agreement between the present modelling and the experiments of Nam et al. [1] which validates the applied modelling approach. The present optimization routine was easily able to achieve the experimental conditions obtained by Nam et al. [1].
The next Fig. 4 shows the simulation results for concentrations of phenylalanine (less adsorbed), tryptophan (more adsorbed) and the volume fraction of ethanol (modifier) along the SG-SMB columns. As can be noted the modifier volume fraction reduces drastically at the feed as there is no injection of ethanol at this point. The Fig. 4 profile indicates the great separation performance as there are only the more adsorbed and the less adsorbed substances leaving the extract (E) and the raffinate (R), respectively.

3. Conclusions
The novel optimization approach showed potential determining the operating conditions of SG-SMB process without the utilization of numerical search algorithms. The new approach utilizes the concept of phi-plots to determine the ideal process conditions to achieve great separation performance.

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References
[1] Nam, H-G., Jo, S-H., Park, C., Mun, S. Process Biochemistry, 47 (2012) 401-409.
[2] Antos, D. Seidel-Morgenstern, A. Chemical Engineering Process, 56 (2001) 6667-6682.
[3] Mazzotti, M., Storti, G., Morbidelli, M., Journal of Chromatography A, 769 (1997) 3-24.