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Optimization Studies by Solvent Gradient Modulation in the Simulated Moving Bed Separation of Amino Acids

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ABSTRACT

The phi-plot optimization approach has been used effectively as a search routine for solvent-gradient simulated moving bed process (SG-SMB) separation. In such process the solvent strength is modulated to improve the performance resulting in a significant increase in purities and productivity, as well as a reduction in solvent consumption. The amino acids mixtures tryptophan-tyrosine (T-T) and tryptophan-phenylalanine (T-P) were studied using the phi-plot optimization method to separate them, which has never been investigated before in the context of SG-SMB process separation. The mass transfer kinetic parameters were first determined for each mixture of amino acids through the chromatographic dynamic data and incorporated into the SG-SMB simulator for the validation of the optimization conditions by the Phi-plot method. A series of optimization studies were carried out varying the solvent concentration and the process flow rates in the context of triangle theory. The dynamic and optimization studies were compared and evaluated between both the amino acid mixtures (T-T and T-P). For the new conditions studied, for the separation of T-T and T-P, the new phi-plot optimization approach was also able to determine the optimal operational settings for producing high-purity separations in the extract and raffinate, which was validated by the dynamic simulator. The optimization results of the studied conditions were plotted in the triangle theory separation regions which confirms the optimization technique as a viable search routine for such complex task of determination of the best operational conditions of SG-SMB. From the concentration profiles along the columns can be observed wider regions in the extract as well as raffinate for the separation T-P, which indicate that such mixture can be separated more easily than the mixture T-T. Such evidence can be seen in the chromatographs of Tryptophan and Tyrosine which are closer than those of Tryptophan and Phenylalanine.

Keywords: Simulated moving-bed, optimization, solvent gradient, chromatography

I. I. Introduction

Simulated moving bed (SMB) processes are used widely in many industrial sectors through the separation of similar molecules in a continuous and productive manner. The continuous aspect has considerable interest and it is attractive also from an economic point of view. The SMB process mimics the movement of the solid (and adsorbent) phase throughout the columns to create a counter current movement with the fluid phase. Several studies report to SMB as a good approach to achieve separation of molecules that are difficult to work in other types of separation techniques [1].

In a SMB unit containing four zones and two columns per zone, the allocation of the two inlet streams (feed and desorbent) and the two outlet streams (extract and raffinate) are changed in the clockwise direction while the columns themselves remain fixed. It should be noted that in a true moving bed (TMB) unit there is no change in the inlet/outlet streams position as the solid phase is forced to move along the column. Reallocating the inlet/outlet streams, as shown in Fig. 1, is an approach for simulating counter current movement of the solid adsorbent phase. The extract and raffinate streams collect the more and less adsorbable compounds, respectively.

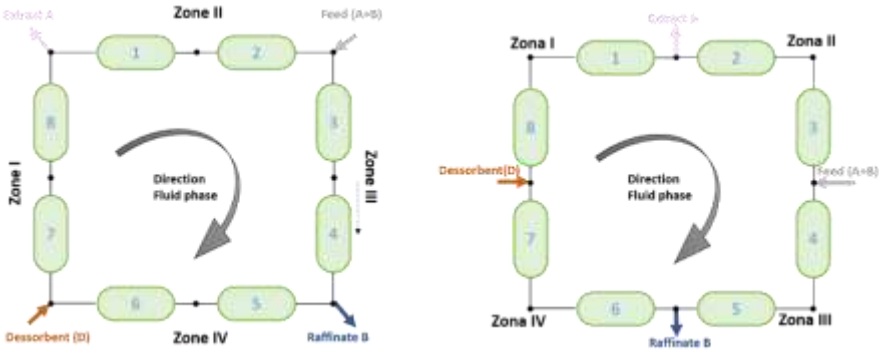

Figure 1- Representation of SMB in two different steps

Different methods of operation have been studied always looking for better productivity and efficiency. The optimization studies are usual in the development of SMB process as in the work of Azevedo and Rodrigues [2] which extended a previous algorithm to optimize the operation conditions for fructose-glucose separation case to obtain nearly pure streams of fructose and glucose in the extract and raffinate, respectively.

Other SMB applications can be observed in the area as the supercritical fluid simulated moving bed (SF-SMB) which utilizes a supercritical CO2 fluid to modulated the elution strength along the process through a pressure gradient [3].

Another type of SMB gradient process is the solvent gradient simulated moving bed process (SG-SMB), in which the main goal of the modification is to modulate the solvent strength within the desorbent stream, resulting in a significant increase in purities and productivity while lowering solvent consumption. This can be accomplished by utilising solvents of varying strengths in the desorbent and feed streams, with the modifier added to the desorbent stream carrying out the process [4-10].

When shown in Fig. 2, the solvent strength in the solvent gradient simulated moving bed (SG-SMB) process is adjusted along the sections as the volume fraction of the modifier (ϕ) changes. This configuration is the one used in the present study where it has one column per zone in which the species A e B are tryptophan and tyrosine, respectively. The distilled deionized water, W, is the main solvent in the desorbent stream and the ethanol the modifier. When a modifier (ethanol in this case) is added to the desorbent (water + modifier) stream, the modifier volume fraction increases in zones I and II, the mobile phase strength falls, and the adsorption affinity (partition coefficient) of the molecules in these regions drops. At this condition it is easier to desorb the retained specie from the solid matrix. Thus, the liquid outlet between these zones is rich in the more strongly adsorbed component (A) and it is called extract. In sections III and IV, the converse is true because there is no ethanol in the inlet feed stream, lowering the modifier volume percentage and increasing the adsorption affinity. Thus, the outlet stream between the zones will be rich in the less adsorbed component (B) and it is called raffinate.

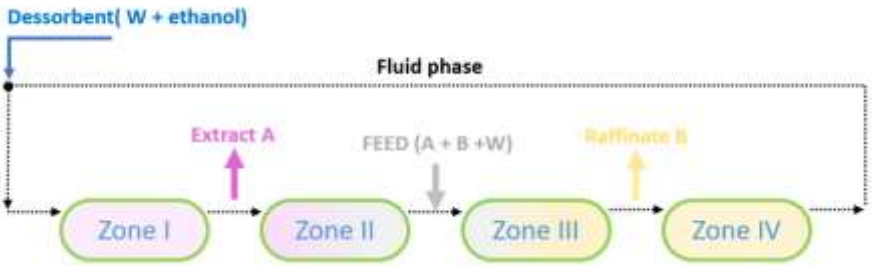

Figure 2- SG-SMB scheme with the ethanol as modifier in the desorbent stream

The optimization and design criteria studies are very important to determine the optimal operating conditions such as the switching time for the valves change and flowrate of the streams. The search for optimal operation conditions of a SMB unit is so important for maintaining the expected results of purity and productivity. For its operation it is necessary to develop a good control system and equipment capable of handle time-programmed complex valve switches and pumps control.

For the accomplishment of optimal operating conditions, several optimization studies use inverse routines combined with phenomenological mass transfer models for the columns and the overall system [4-6,9]. Inverse routines are useful in the SG-SMB process optimization field because they can account for more realistic phenomena such as mass transfer resistance, finite column efficiency, purity constraints, and other factors, as well as modifier interaction along the columns in terms of adsorption affinity. The main drawbacks of such methods are the large processing costs associated with numerical simulations, as well as the algorithm correctness and efficiency in the discovery for optimal solutions. In the work of Nam et al. [9] the authors used a genetic algorithm in conjunction with detailed mass transfer chromatographic rate models to optimise phenylalanine and tryptophan separation using SG-SMB. In this example, the optimization method was successful in determining the optimal operating parameters, which were then used and proven experimentally in a lab-scale SG-SMB unit.

Antos and Seidel-Morgenstern [7] studying a SG-SMB process utilized a design criteria strategy based on the triangle theory coupled to mass transfer models (mixed cells in series) in the determination of suitable operating conditions as a function of averaged desorbent concentrations. Long and Le [10] proposed a modified design method for SG-SMB separation of o-xylene and p-xylene by reversed-phase chromatography. They utilized a method of separation region on plane which is function of the volumetric content of organic modifier in the raffinate and the extract, achieving improvement in the process performance through a partial-discard strategy with the increase in the solvent gradient level.

Mazzotti et al. [11] apply the triangle theory's isocratic principles to explore and improve an SMB gradient process, specifically the pressure gradient mode in supercritical fluid SMB (SF-SMB).

The relevance and importance of the triangle theory concepts in studying and evaluating the design criteria of solvent-gradient SMB (SG-SMB) processes motivated us to continue in the same direction using the concepts of the Phi-plot optimization routine proposed by Câmara [12] in 2014 for determining the optimal operating conditions of SG-SMB. The first studies published applying the Phi-plot optimization concepts [12,13] showed the great potential as powerful tool in the determination of the operating conditions of solvent gradient simulated moving bed process without numerical calculations. It was used as the basis for this work considering the evaluation of different operating conditions looking for performance improvement related to the separation of the amino acids tyrosine and tryptophan.

The SG-SMB separation of the aminoacids Tryptophan and Tyrosine (T-T) and Tryptophan and Phenylalanine (T-P) was studied previously by Castro and Câmara [14] which determined the process viability through the application of the phi-plot optimization method coupled with a global mass transfer SG-SMB dynamic simulator. Following the previous work, a series of optimization studies were carried out varying the solvent concentration and the process flow rates in the context of triangle theory. The best operational conditions of separation by phi-plot optimization approach were evaluated by the dynamic stepwise SG-SMB simulator.

II. II. METHODOLOGY

Optimization Routine

The Phi-plot optimization method is an analogous extension of the equilibrium theory [15] approach (Eqs. 1 to 4) in which is considered the Henry's constant a function of the modifier volume fraction.

$$H_{(+)}(\phi) < m_I < \infty \quad (1)$$

$$H_{(-)}(\phi) < m_{II} < H_{(+)}(\phi) \quad (2)$$

$$H_{(-)}(\phi) < m_{III} < H_{(+)}(\phi) \quad (3)$$

$$\frac{-\varepsilon_p}{(1-\varepsilon_p)} < m_{IV} < H_{(-)}(\phi) \quad (4)$$

in which ε_p, m_i, $H_{(+)}$, and $H_{(-)}$ correspond to intraparticle porosity, flow rate ratios in each section i, and the Henry constants for the more and less adsorbable molecules, respectively.

Fig. 3A shows a typical volume fraction distribution of modifier along columns with the drastic reduction of the modifier volume fraction after the feed inlet stream. This type of modifier volume fraction profile can be achieved whether or not the modifier is adsorbing to the solid adsorbent phase. The results of Fig. 3A were obtained by using a stepwise SG-SMB simulator [16] to simulate the separation of Phenylalanine and Tryptophan, without taking into account the modifier adsorption by the adsorbent phase and simply considering the convection of ethanol (modifier) through a stepwise approach (mixed cells in series). Similar results were reported in the study of Mun et al. [4] under the identical circumstance of modifier introduction in the desorbent inlet stream. The findings are close, but the authors used a robust chromatographic mass transfer rate model that included convection, dispersion, film mass-transfer, intra-particle diffusion, and adsorption for the ethanol (modifier). In the Phi-plot optimization approach it is assumed an average modifier volume fraction ($\hat{\phi}$) which is obtained from the arithmetic mean between the volume fraction of modifier in sections II (ϕ_{II}) and III (ϕ_{III}) using Eq. 5.

$$\hat{\phi} = \frac{\phi_{II} + \phi_{III}}{2} \quad (5)$$

According to the volume fraction of modifier along the columns (Fig. 3A), the Henry values can be plotted along sections II and III as a difference in terms of the inequalities of Eqs. 2 and 3, resulting in the inversion of the profiles (Fig. 3B).

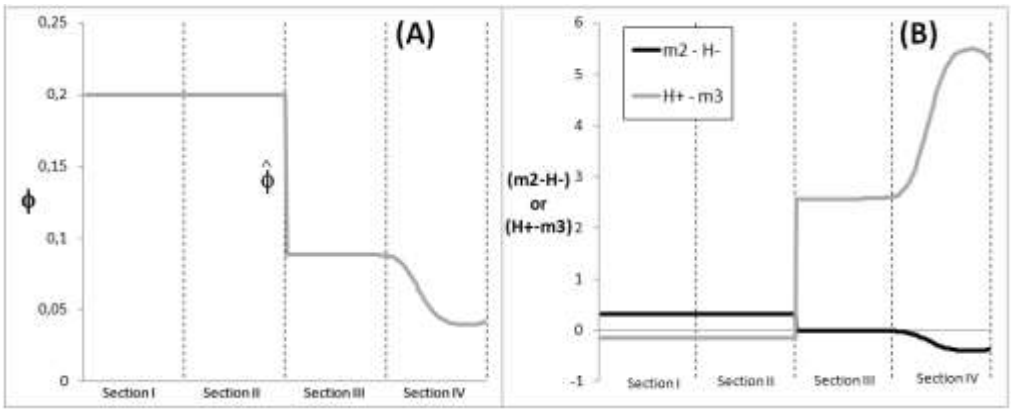

Figure 3- Modifier volume fraction along the sections (A); Inversion in the flow rates ratio difference near the feed inlet (B)

Along sections II and III the inequalities, for complete separation, should be as follows using Eq. 6:

$$m_{II} > H_{(-)}(\phi_{II}) \quad \text{and} \quad H_{(+)}(\phi_{III}) > m_{III} \quad (6)$$

or

$$m_{II} - H_{(-)}(\phi_{II}) > 0 \text{and} H_{(+)}(\phi_{III}) - m_{III} > 0 \quad (7)$$

and considering the limit near to zero the Eq. 7 can be equalized leading to Eq. 8

$$H_{(+)}(\hat{\phi}) + H_{(-)}(\hat{\phi}) = m_{II} + m_{III} \quad (8)$$

in which the Henry values for the more adsorbed, $H_{(+)}(\hat{\phi})$, and the less adsorbed molecules, $H_{(-)}(\hat{\phi})$, are functions of the average volume fraction of modifier. The Eq. (9) is described as the difference of the terms leading to the project design equation (χ equation)

$$\chi = H_{(+)}(\hat{\phi}) + H_{(-)}(\hat{\phi}) - m_{II} + m_{III} \quad (9)$$

in which the best operating condition corresponds to χ equation tending to zero, i. e, $\chi \to 0$.

The chromatographic columns volume, total porosity, and volume fraction of modifier are specified first in the optimization method (ϕ_0). The next step is the specification of the volumetric flow rates and the switching time that can be varied in order to minimize the χ equation, Eq. 9 ($\chi \to 0$). It is important to evaluate at the same time the Phi-Plot of the flow rate–Henry differences to identify the conditions that leads to curves in the positive regions which correspond to complete separation.

Process modeling

The chromatographic columns are modeled as a discrete representation of N mixed cells in series:

$$\left(\frac{dC_J}{dt}\right)_i - \left(\frac{dq_J}{dt}\right)_i = \frac{Q}{V.\varepsilon}(C_{j0} - C_j)_i \quad (10)$$

$$\left(\frac{dq_J}{dt}\right)_i = -r_j = k_{1j}.C_{ji} - k_{2j}.q_{ji} \quad (11)$$

$$\left(\frac{d\phi_J}{dt}\right)_i = \frac{Q}{V.\varepsilon}(\phi_0 - \phi)_i \quad (12)$$

Where q_J, C_J, C_{j0} represent the concentrations of compound j in the solid adsorbent phase, the concentration in the liquid phase and the concentration in the liquid phase at the entrance of a column (first mixed cell), respectively. The parameters Q, V, ε represent the volumetric flow rate, the volume of the mixed cell and the porosity, respectively. It's worth noting that during mass transfer between the liquid and solid phases, the molecules are considered to remain at the interface inside the liquid phase, therefore the concentrations are calculated using the same liquid volume. Furthermore, t denotes the passage of time, and i denotes the number of the stage (mixed cell). In the model shown above, a lumped mass transfer model is assumed to cover the effects of mass transfer between the liquid and solid adsorbent phases. As a result, the predominant and overwhelming effect of mass transfer between phases is the slow mass transfer kinetic (solid and liquid). The lumped mass transfer kinetic model presented in Eq. 11 depends on the concentrations as well as the mass transfer kinetic parameters of adsorption (k_{1j}) and desorption (k_{2j}).

The solute mass balances at the nodes (Fig. 1), are solved with the volumetric flow rates of each stream to represent the SG-SMB unit computationally (Feed, Desorbent, Extract and Raffinate). The new mass balance of solutes at the nodes is recalculated after each change in configuration and a switch time period. The equations 10 to 11 are organized explicitly according to a simple finite difference approach implemented in Fortran90/95 and solved numerically utilizing a 4th order Runge-Kutta method, with a time step equal to 10^{-4}.

For the calculation of the Henry coefficients, 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. The parameters for the Abel model considering such amino acids are available in the work of Nam et al. [17].

III. III. Results and discussion

The first step in the modeling and simulation was the mass transfer kinetic parameters determination from the chromatographic experimental data of Nam et al. [17]. The chromatograms of tryptophan and tyrosine and tryptophan and phenylalanine were correlated to the column models (Eqs. 10-12) in the determination of the mass transfer kinetic parameters according to modifier volume fraction (ethanol). The obtained mass transfer kinetic parameters were incorporated into mass transfer equations which are functions of volume fraction of modifier. In this work it was evaluated the operating conditions based on the flowrate values utilized by Nam et al. [9] in SG-SMB separation of amino acids. The mass transfer equations obtained in column characterization were applied in the SG-SMB simulator to evaluate the operational conditions obtained by the Phi-Plot optimization routine.

The Table 1 presents the not optimized simulation results with the respective values of X-equation, modifier concentration (ϕ_{des}), switch time (ST) etc. As it can be seen in Table 1 the X-equation values are far from zero which is not the ideal condition for complete separation. In the ideal condition, the X-equation value near zero, Eq. 9 ($\chi \to 0$), leads to the best operational condition as the raffinate and extract can lead to both purities closer to 100%.

Table 1. Not optimized simulation results

	Run	**ϕ_{des}**	**Q_{feed}**	**Q_{des}**	**Q_{ext}**	**Q_{raf}**	**ST**	**Pur. Raf.**	**Pur. Ext.**	**X-Eq.**
T-T	1	0.2	5.04	13.5	5.98	5.44	25.95	52.60%	100.00%	-3.342
T-T	2	0.2	5.04	15.0	5.98	5.44	25.95	35.55%	99.99%	-4.880
T-T	3	0.2	3.78	10.0	4.49	4.08	36.0	48.49%	100.00%	-3.550
T-T	4	0.2	3.78	12.0	4.49	4.08	36.0	32.93%	100.00%	-6.395
T-T	5	0.2	3.78	12.0	4.49	4.08	25.95	54.94%	99.99%	-2.847
T-T	6	0.2	10.0	15.0	8.00	8.0	10.0	68.74%	33.51%	+2.343
T-T	7	0.2	6.0	14.0	9.0	6.0	30.0	96.95%	99.99%	-2.260

T-P	1	0.2	5.04	13.5	5.98	5.44	25.95	48.31%	99.99%	-3.750
T-P	2	0.2	5.04	15.0	5.98	5.44	25.95	32.13%	100.00%	-5.286
T-P	3	0.2	6.3	15.0	7.48	6.8	25.95	47.83%	99.99%	-4.266
T-P	4	0.2	9.0	19.0	11.0	10.0	20.0	90.95%	99.99%	-3.100

Table 2. Optimized simulated results

	Run	**ϕ_{des}**	**Q_{feed}**	**Q_{des}**	**Q_{ext}**	**Q_{raf}**	**ST**	**Pur. Raf.**	**Pur. Ext.**	**X-Eq.**
T-P	1	0.2	6.3	12.5	7.475	6.8	20.8	99.99%	99.99%	-0.048
T-P	2	0.2	5.04	9	5.98	5.44	30	99.99%	99.03%	0.244
T-P	3	0.2	3.78	7.5	4.485	4.08	34	100.00%	99.90%	0.074
T-T	1	0.2	6.3	15	7.475	6.8	16.3	99.99%	99.59%	0.022
T-T	2	0.2	5.04	12	5.98	5.44	19.5	99.99%	99.55%	0.299
T-T	3	0.2	3.78	10	4.485	4.08	23	99.98%	99.91%	0.062

The optimization results of Table 2 can be better visualized in next Fig. 4 in which there is a compilation of the pair values of purity of the raffinate (blue points) and extract (orange points) according to the X-equation values. The Fig. 4 was obtained varying previously the operational process variables by the Phi-plot analysis being evaluated such predetermined conditions through the stepwise lumped mass transfer solvent gradient simulator (SG-SMB simulator). As it can be seen in Fig. 4, as the X-equation approaches to zero the pair values of purity tend to 100% which is the ideal separation condition (near 100% of purity). This result shows the effectiveness of the Phi-Plot method in the determination of the best operational conditions of SG-SMB process. In the optimized results of Table 2 the purities in the extract as well as raffinate, are higher than 99.0% with X-equation values closer to zero. From Fig. 4 it can be observed that for positive values of the X-equation the raffinate stream purity (blue points) stays in values near 100% and for the extract stream there is a decrease in the purity. In this X-equation region the term (m_2-$H_{(-)}$) for the section II is negative, indicating a contamination of the extract stream due to retention of the less adsorbed molecules on the solid adsorbent phase. For negative values of the X-equation it is observed the contrary as the extract purity stays near 100% and the raffinate purity decreases. In this condition the term ($H_{(+)}$-m_3) for section III is negative indicating a contamination of the raffinate stream due to convection transport of the more adsorbed molecules by the liquid phase. Therefore the ideal condition corresponds to that in which X-equation tends to zero.

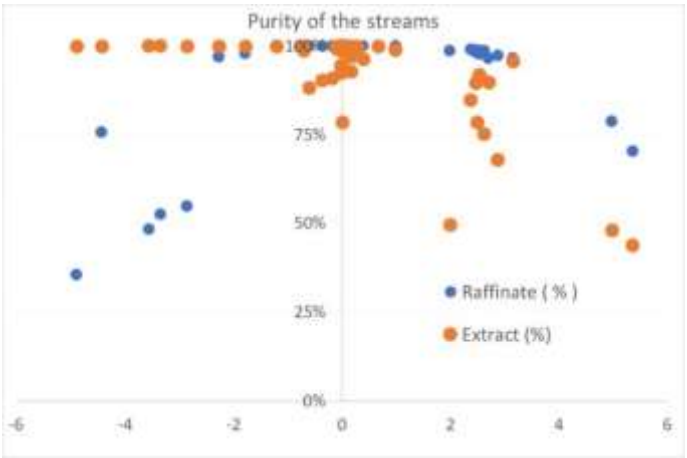

Figure 4- Purity versus X-equation for SG-SMB separation of tryptophan and tyrosine (T-T)

The next Fig. 5 presents the concentrations of tryptophan and tyrosine (Fig. 5A) and tryptophan and phenylalanine (Fig. 5B) along the columns in the steady state. As can be seen From Figs 5A and 5B the enrichment of the more adsorbable molecules of tryptophan in the extract streams while the less adsorbable molecules of tyrosine and phenylalanine are collected in the raffinate. The modifier concentration (phi) reduces in the raffinate direction as the feed stream do not introduce such molecules in the process. The modifier introduction in the desorbent stream favours the desorption of the more adsorbable molecules, the tryptophan, in this region which are collected in the extract.

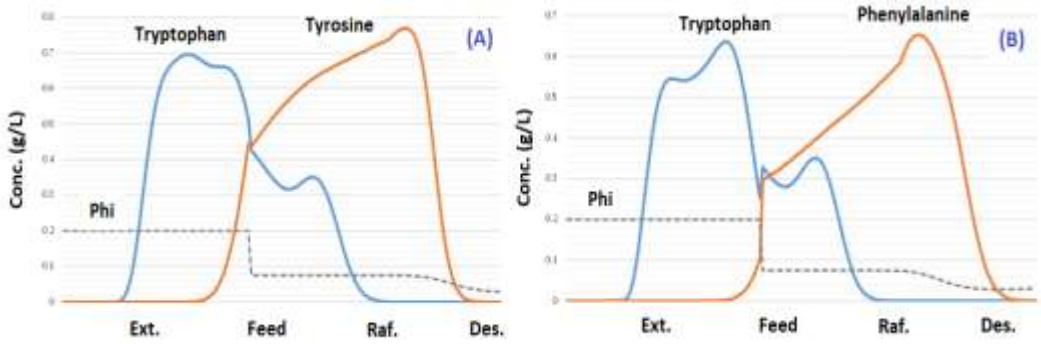

Figure 5- Concentration along columns for T-T (A) and T-P (B)

The next Fig. 6 presents the regions of complete separation plotted in terms of equilibrium theory according to the modifier concentration (ϕ). The modifier concentration alters the region of complete separation of the molecules which corresponds to the area inside the triangles of Fig. 8. As the modifier concentration increases (ϕ), in the arrow direction, there is a variation in the partition coefficient which moves the region of complete separation in the direction of the origin. Also, there is a reduction in the region of complete separation as the modifier concentration increases. Such behaviour was also observed by Jensem et al. [18] which determined that the regions of complete separation are not triangular regions in the solvent gradient processes as in the isocratic ones (equilibrium theory).

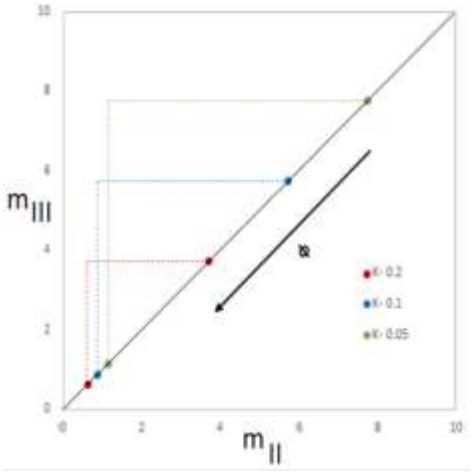

Figure 6- Regions of complete separation according to modifier concentration (ϕ)

The next Fig. 7 presents the results of Table 1 for separation of tryptophan and tyrosine (T-T) in terms of triangle theory. Fig. 7A shows the run results 1,3,5 and 7 while Fig. 7B the run results 2,4 and 6. As it can be seen in both figures, the coordinates m_{III}-m_{II}, for all the described runs, are not located inside the triangles which corresponds to the region of complete separation. Therefore, all runs presented in Table 1 do not have both values of purity for raffinate and extract higher than 99.0%.

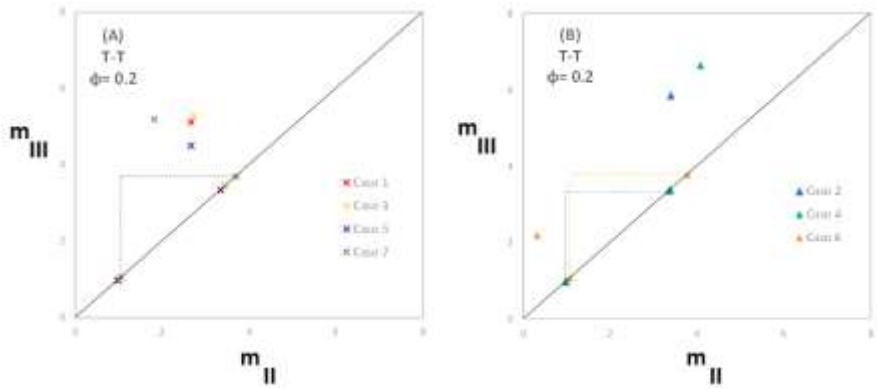

Figure 7- Table 1 results for separation of T-T in terms of triangle theory

The same behavior is observed in Fig. 8 for the separation of tryptophan and phenylalanine as the runs 1 to 4 of Table 1. Also, the coordinates m_{III}-m_{II}, for all the described runs, are not located inside the region of complete separation (inside the triangle). Therefore, all runs presented for T-P separation do not have both values of purity for raffinate and extract higher than 99.0%.

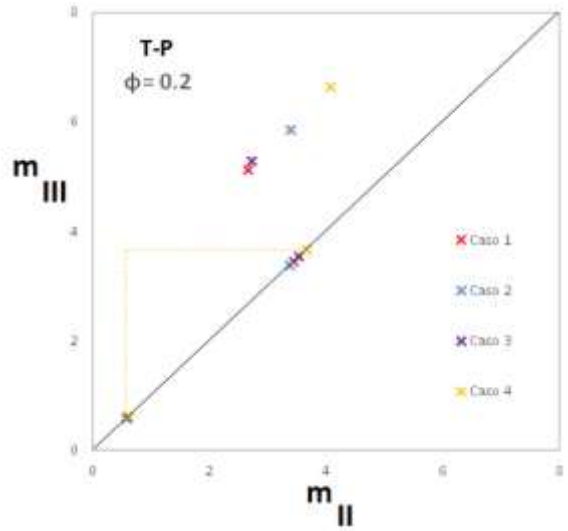

Figure 8- Table 1 results for separation of T-P in terms of triangle theory

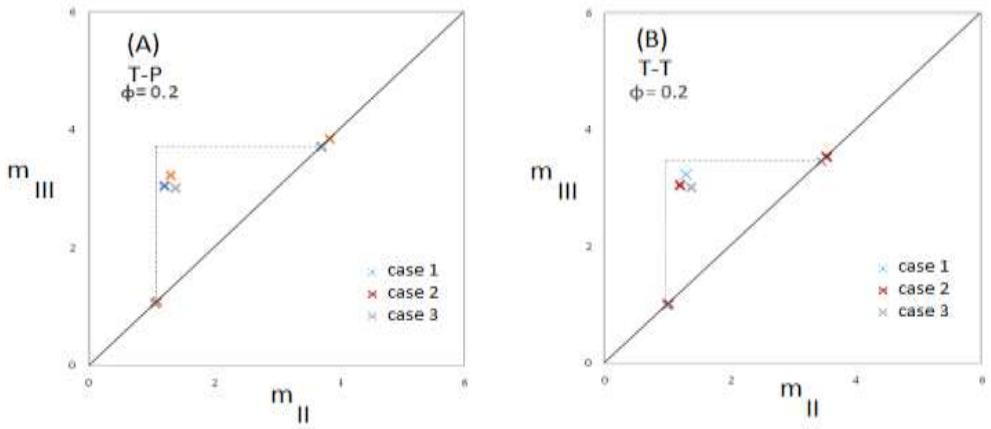

Figure 9- Table 2 results for separation of T-P in terms of triangle theory

The optimized results of Table 2 are evaluated in terms of the equilibrium theory for the separation of T-P (Fig. 9A) and T-T (Fig. 9B). The operational conditions of the runs presented in Table 2 were plotted against the equilibrium theory regions which are triangular. As it can be seen both in Fig. 9A and B all the optimized cases of Table 2 are inside the triangular region of complete separation so the extract and raffinate streams have purities near 100%. The optimized cases obtained by the Phi-plot method presented X-equation values around zero, indicating purities from the SG-SMB simulator higher than 99.0%. As described by Suvarov et al. [19] the optimal operation points are near the vertex of the triangle.

IV. Conclusions

The phi-plot optimization approach was found to be effective determining the ideal operational parameters for separating the amino acids tyrosine and tryptophan and phenylalanine and tryptophan. From the optimization results can be observed that the best conditions of purity (purity near 100%) corresponds to those in which the X-equation tends to zero. The simulation results showed concave and convex profiles, for the productivity and solvent consumption, respectively. Such results can be merged into tendency models in the optimization approach for the search of the best operational conditions. The triangle theory method were utilized through a series of optimization studies, varying the solvent concentration and the process flow rates. The best operational conditions of separation by phi-plot optimization approach were evaluated by the dynamic stepwise SG-SMB simulator. The new phi-plot optimization approach was able to establish the ideal operational conditions for achieving separations with high purities in the extract and raffinate, which was evaluated by the simulator, for the conditions tested. The optimization results of the studied conditions were plotted in the triangle theory separation regions which confirms the optimization technique as a viable search routine for such complex task of determination of the best operational conditions of SG-SMB. From the concentration profiles along the columns can be observed wider regions in the extract as well as raffinate for the separation T-P,

which indicate that such mixture can be separated more easily than the mixture T-T. Such evidence can be seen in the chromatographs of Tryptophan and Tyrosine which are closer than those of Tryptophan and Phenylalanine.

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