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Official URL: https://doi.org/10.1016/j.memsci.2004.05.007

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Study of biomolecules separation in an electrophoretic membrane contactor

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Abstract

In electrophoretic membrane contactors, a porous membrane is used to put into contact two flowing liquids between which an electrically driven mass transfer takes place. These processes offer the possibility to scale up electrophoresis as well as to extend the field of application of electrodialysis. This paper deals with the study of the mass transfer mechanisms involved in such electroseparation processes for the separation of binary mixtures. This study is carried out by associating an experimental work and a theoretical approach. The parameters involved in the model are calculated according from the experimental variations of the solvent and solute transfer. From the dependence of these parameters with the operating conditions, the importance of electrostatic interactions with respect to the separation performances is pointed out. Finally, the process performances are studied considering the separation of α-lactalbumin and bovine haemoglobin as a case study.

Keywords: Bioseparation; Membrane contactor; Electrophoresis; Electro-osmosis; Mass transfer

1. Introduction

Electrophoresis is an electrically driven operation that constitutes a purification step used at the later stage of the downstream process. Because of their high resolution at the analytical scale, different studies were devoted to find out operating modes to scale up electrophoretic separations.

One of them, continuous flow electrophoresis (CFE), is carried in a flowing film. Different experimental and theoretical studies were performed so as to understand the transport phenomena involved in the process [1–3]. From these works, the limitations of CFE were pointed out and their origin was also identified [4]. Whilst an interesting resolution was achieved under proper operating conditions [3], the limitation in terms of production capacity was demonstrated as well as the strong relationship between resolution and productivity [2]. Finally, it was found that the productivity could not be increased over a certain limit, typically about few milligrams per hour.

On the other hand, electromembrane operations offer the possibility to increase the productivity without damaging the separation efficiency.

The most common is electrodialysis, ED, in which ion exchange membranes are used. However, because of the properties of the membranes, the migration of molecules of molecular weight exceeding about 500 Da is forbidden.

The use of porous membranes in replacement of ion exchange ones was then investigated so as to extend the field of application of electrodialysis to biological molecules like polyamino acids, peptides or proteins. In that case, the porous membrane acts as a contactor and the separation is achieved with respect to the difference between the mass flow rates of the species. According to the membrane and solute properties, this difference can have various origins, like different electrophoretic mobility, sieving effects or a coupling of both [5–12]. One of these scalable preparative electrophoresis techniques is the Gradiflow apparatus [6]. It has been used for several applications like the separation of proteins from plasma and algal extracts [6] or from egg white [7,8]. The influence of the voltage, pH, solute concentration and membrane has been studied. However, no comprehensive work and no theoretical approach were devoted to the understanding of the transfer phenomena.

We have thus developed a proper methodology, associating a theoretical and an experimental approach carried out with a dedicated apparatus, to investigate the mass transfer...
phenomena involved in electrophoretic membrane contactors. The effects of solute charge and size as well as that of the different relevant parameters were investigated with single and binary solutions [13,14]. This study pointed out the influence of a characteristic parameter, $E\tau$, product of the electric field by the residence time, and the importance of electrostatic interactions between the solute and the membrane.

The objective of this paper is to go further through the understanding of the mass transfer mechanisms by investigating the separation of polyamino acids and proteins contained in binary solutions. The influence of the operating mode and the solute concentration is also studied. Then, the characteristic parameters involved in the model obtained in previous work and in this study are used to evaluate the process performances.

2. Principle of the process

The electrophoretic membrane contactor is schematically depicted in Fig. 1.

The separation chamber itself is composed of two compartments delimited by a porous membrane, acting as a contactor between the two streams between which the mass transfer takes place. The buffered solution to be purified is continuously fed into the chamber. The only driven force is a voltage, applied in a direction perpendicular to the feed flow. Two electrodes are located in dedicated compartments, which are separated from the separation chamber itself by ion exchange membranes. As soon as a voltage is applied, the charged components contained in the feed migrate along the chamber thickness from one compartment toward the other through the porous membrane. The solute mass flow depends on its electrophoretic mobility, which is fixed by the pH of the buffered solution. Then, solutes having distinct electrophoretic mobilities are carried through the membrane at different rates. Two outlet streams with different compositions are thus obtained.

The compartments in which the outlet concentration of the target solute are, respectively, lower and higher than the inlet one will be further called “dilute” and “concentrate”.

Like in electrodialysis for instance, this process can be operated in two different ways, i.e. operating modes. The first one is that depicted in Fig. 1(a), where the same solution, containing the species to be separated, is fed on both sides of the membrane. This configuration will be further called “separation mode”.

The second mode of operation, illustrated for the purification of a negatively charged component A, is depicted in Fig. 1(b). In that case, the solution to be purified is fed in one compartment. The other compartment, which is the elution compartment, is fed with the buffer. The solute A, which migrates through the membrane, is then collected in that compartment. That configuration will be later called the “elution mode”.

These two modes of operation can be used to achieve different objectives, i.e. to favour quantitative or qualitative aspects.

Indeed, as far as the production is concerned, the separating mode will be preferable. On the contrary, for achieving higher purification, the eluting mode will be used.

3. Theoretical approach (mathematical model)

A mathematical model has been previously developed [13] to describe the solute mass transfer in such electrophoretic membrane contactors. This model gives expressions of the outlet concentrations as function of the operating parameters and solute characteristics. It is based on the description of the solvent and solute mass transfer, which results from the combination of different transport
phomena taking place in the separation chamber, i.e. in the solution and at the membrane/solution interface. It is considered that the two transport phenomena due to the electric field, i.e. electromigration of charged solutes on one hand and electro-osmosis through the charged porous membrane on the other hand, are predominant. It means that the contribution of osmosis and diffusion is neglected. This assumption has been validated [13].

The solute mass balance can be written at the steady state, in the solution and in the membrane, using the Nernst–Planck equation.

A partition coefficient $\phi$ is used to link the solute concentrations in and out of the membrane.

Then, for a solute and a membrane carrying negative charges, Eq. (1) is obtained for the expression of the solute concentration at the outlet in the dilute, where $C_d$, with respect to the system parameters:

$$
C_d = C_0 \left[ 1 - \frac{u_{eo} E \tau}{d} \right]^{\alpha (\infty / u_{eo} \alpha^{-1} - 1 - 1)}
$$

(1)

$C_0$ is the inlet solute concentration, $u_{eo}$ and $u_{eo}$ the absolute values of the electrophoretic and electro-osmotic mobilities, $\tau$ the mean residence time inside the chamber that is fixed by the flow rate and $d$ the compartment thickness.

From the qualitative point of view, the value of $\phi$, ranging from 0 to 1, enables to evaluate the strength of the membrane/solute interactions. A value close to unity means that the membrane/solute interactions are negligible while decreasing values of $\phi$ reveal stronger interactions.

The outlet concentration in the concentrate, $C_c$, is obtained from Eq. (1) and the solute mass balance.

A relationship between the electro-osmotic mobility and the characteristic parameter $E\tau$, product of the electric field by the residence time, was also proposed:

$$
u_{eo} = -\alpha E \tau + a_0
$$

(2)

where $a_0$ represents the electro-osmotic mobility corresponding to the feed solution ionic strength. This relationship is established for $E\tau$ values lower than $2 \times 10^3$ V s m$^{-1}$.

The characteristic parameters involved in the model to describe the variation of the solute concentration versus $E\tau$, are the partition coefficient $\phi$, $a_0$ and $\alpha$.

4. Materials and methods

4.1. Buffer and samples

All chemicals used are of analytical grade. Poly(\textepsilon-glutamic) acid (PLGA), \textalpha-lactalbumin (type III from bovine milk), bovine haemoglobin (HbH) and 2-(\textN-morpholino) ethane-sulfonic acid (MES) were purchased from Sigma (St. Louis, MO, USA). Tris(hydroxymethyl)aminomethane (Tris) was a product from Merck (Darmstadt, Germany).

The fluid used as separation buffer as well as electrode buffer is a Tris–Mes buffer at a pH of 8.0.

The electrical conductivities are $140$ and $220 \mu$S cm$^{-1}$

for the separation and electrode buffer, respectively. The solutions are prepared by dissolving the appropriate amount of poly(\textepsilon-glutamic) acid, \textalpha-lactalbumin and bovine haemoglobin in the separation buffer.

4.2. Electroseparation apparatus and set-up

The experimental set-up was depicted into details in a former paper [13]. The electrophoretic chamber has a membrane active area of $32$ cm$^2$. The thickness of the dilute and concentrate compartments is $0.2$ cm. The porous membrane, i.e. the contactor, is a derived cellulose membrane made in our laboratory. Its hydraulic permeability is equal to $4.0 \times 10^{-10}$ m$^2$ Pa$^{-1}$ s$^{-1}$ and its molecular weight cut off is estimated about 100 kDa. A cation exchange membrane and an anion exchange membrane are used at the anode and cathode side, respectively.

The two separation compartments are continuously fed from two distinct feed tanks using peristaltic pumps placed at the outlet of the cell. The outlet flow rates are set at constant and equal values. The electrode buffer is circulated in a closed loop from a single tank to the electrode compartments using a gear pump.

An automatic data acquisition system allows real-time recording of the main experimental data, i.e. inlet flow rates, and equal values. The electrode buffer is circulated in a closed loop from a single tank to the electrode compartments using a gear pump.

4.3. Experimental procedure and operating conditions

All experiments are carried out at the ambient temperature ($22 \pm 3$ °C).

The inlet solute concentration is generally set at a constant value of $0.1$ g l$^{-1}$. Only one experiment is carried out at a higher concentration of $0.5$ g l$^{-1}$ with \textalpha-lactalbumin and bovine haemoglobin.

The outlet flow rate in the separation chamber and the buffer flow rate in the electrode compartment are fixed at $100$ ml h$^{-1}$ (τ = 230 s) and $5.0$ l h$^{-1}$, respectively.

The experiments are carried out at a constant current density. Different values are used ranging from 10 to 70 mA (i.e. from 3 to 22 A m$^{-2}$).

The average electric field strength $E$ in the separation chamber is calculated from the following equation [15]:

$$
E = \frac{I}{\tau_{avg} S}
$$

(3)

where $I$ is the current, $S$ the membrane area and $\tau_{avg}$ the mean electrical conductivity, calculated from the inlet and outlet ones. For the operating conditions used, the average electric field is comprised between $100$ and $800\, \text{V} \text{m}^{-1}$.

Since the outlet flow rates are fixed and equal, the electro-osmotic flux $J_{eo}$ is obtained from the measurement
of the inlet flow rates in each compartment by the following relationship:

$$J_{eo} = \frac{|Q_{inlet} - Q_{outlet}|}{2S}$$  \hspace{1cm} (4)

Then, the electro-osmotic mobility $u_{eo}$ is deduced from the values of the electro-osmotic flux and of the electric field. The solute concentration at the outlet of each compartment is determined after reaching the steady state.

### 4.4. Data acquisition

Poly(L-glutamic) acid concentrations are determined by gel permeation chromatography with UV detection at 214 nm, using a Superdex peptide column (Pharmacia Biotech, Sweden). The eluent is a phosphate buffer at pH 7.2 adjusted with NaCl to get a conductivity of 10 mS cm$^{-1}$, at a flow rate of 0.80 ml min$^{-1}$.

For single solutions, the concentrations of α-lactalbumin and bovine haemoglobin are measured by ultraviolet spectroscopy at 280 and 406 nm, respectively. For binary solutions, the total protein concentration is calculated from the absorbance at 406 nm, since only bovine haemoglobin has an absorbance at 406 nm. Finally, the α-lactalbumin concentration is obtained from mass balance.

The electrophoretic mobilities of poly(L-glutamic) acid, α-lactalbumin and bovine haemoglobin are determined in the separation buffer by capillary electrophoresis (Spectra Phoresis 500, Spectra-Physics, United States).

### 5. Results and discussion

Experiments were carried out with buffered solutions of different compositions in order to investigate the influence of the fluid composition on the solvent and solute transfer.

The experimental value of the electro-osmotic flux is first used to calculate the electro-osmotic mobility. Then, the coefficients $a_0$ and $a_1$ described in Eq. (2) are determined.

The partition coefficient $\phi$ is obtained by fitting the experimental variations of the concentration versus the characteristic parameter $Et$ with the ones calculated from Eq. (1).

Table 1 provides the relevant characteristic of the selected solutes, i.e., their molecular weight (size), electrophoretic mobility (electrical charge) and isoelectric point. It was formerly mentioned that the membrane used as a contactor carries negative charges [13]. Since all the solutes are negatively charged, electrostatic interactions, if any, will be repulsive.

Then, the productivity, the purity and the product yield are calculated according to the characteristic parameters involved in the model ($\phi, a_0$ and $a_1$) to do a first evaluation of the process performances in the case of the separation of two proteins.

#### 5.1. Mass transfer

##### 5.1.1. Electro-osmotic flux

The experimental variations of the electro-osmotic flux versus the electrical field obtained with two binary buffered solutions, containing α-lactalbumin and PLGA on one hand, and α-lactalbumin and Hbb on the other hand, were presented and discussed in previous papers [13,14].

The values of $a_0$ and $a_1$ determined from experimental variations of $u_{eo}$ versus $Et$ are reported in Table 2 for the different fluids investigated.

It was concluded that the results obtained with binary mixtures are identical to those obtained with the single solution containing the solute having the highest electrical charge. Therefore, the electro-osmotic flux value is fixed by the solute, which has the highest electrophoretic mobility (electrical charge), i.e. PLGA for the α-lacta/PLGA solution and α-lacta for the α-lacta/Hbb solution [14].

Here, the influence of the solute concentration and of the operating mode are studied, considering the mixture α-lacta/Hbb as case study.

It was first observed that the operating mode has no influence on the electro-osmotic mobility. The results obtained for the elution mode are not shown but they are identical to that presented in Fig. 2 for the mixture α-lacta/Hbb at 0.1 g l$^{-1}$ for the separating mode.

Fig. 2 shows the variation of the electro-osmotic flux versus the electric field with the mixture α-lacta/Hbb for two different concentrations (0.1 and 0.5 g l$^{-1}$). These results are

Table 2: Values of $a$ and $a_0$ in Eq. (2) for different buffered solutions (Tris-Mes buffer at pH 8)

<table>
<thead>
<tr>
<th>Solution</th>
<th>$C_0 (g l^{-1})$</th>
<th>$a_0$ (m 2 V$^{-1}$ s$^{-1}$)</th>
<th>$a_1$ (m 2 V$^{-1}$ s$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hbb</td>
<td>0.1-0.5-1</td>
<td>$0.56 \times 10^{-10}$</td>
<td>$0.29 \times 10^{-10}$</td>
</tr>
<tr>
<td>α-Lacta/PLGA</td>
<td>0.1</td>
<td>$4.42 \times 10^{-10}$</td>
<td>$1.58 \times 10^{-10}$</td>
</tr>
<tr>
<td>α-Lacta/Hbb</td>
<td>0.1</td>
<td>$1.37 \times 10^{-10}$</td>
<td>$0.42 \times 10^{-10}$</td>
</tr>
<tr>
<td>α-Lacta/PLGA</td>
<td>0.5</td>
<td>$2.12 \times 10^{-10}$</td>
<td>$0.68 \times 10^{-10}$</td>
</tr>
</tbody>
</table>
compared to those obtained with a single solution of bovine haemoglobin at different concentrations (0.5 and 1 g l\(^{-1}\)). One can see that the electro-osmotic flux, i.e. the apparent charge of the membrane, increases with the solute concentration.

The corresponding values of \(\alpha\) and \(\alpha_0\) reported in Table 2 are compared to those obtained with the Tris–Mes buffer and the buffered solution of Hbb at different concentrations. One can observe that comparable values are obtained for different concentrations of Hbb. On the contrary, increasing electroosmotic fluxes are observed for increasing concentrations of \(\alpha\)-lactalbumin.

### 5.1.2. Solute mass transfer

The solute mass transfer is characterised by the value of the partition coefficient \(\phi\). This value is determined by fitting the experimental variations of the solute concentration versus \(E\tau\) with the ones calculated by Eq. (1). The electric field \(E\), the inlet solute concentration \(C_0\) and the mean residence time \(\tau\) are fixed operating parameters. The electro-osmotic mobility \(\mu_{eo}\), is calculated according to Eq. (2) with the values of \(\alpha\) and \(\alpha_0\) given in Table 2.

The solute mass transfer has been studied in a previous work for a fixed buffer composition and single solute solutions in order to determine the influence of the solute charge and size [13]. Quite distinct partition coefficients were achieved for \(\alpha\)-lacta and PLGA on one hand and for \(\alpha\)-lacta and Hbb on the other hand. Consequently, experiments were carried out at a pH of 8 with mixed solution of theses solutes so as to investigate the separation of \(\alpha\)-lacta/PLGA and \(\alpha\)-lacta/Hbb.

#### 5.1.2.1. \(\alpha\)-Lactalbumin/poly(\(\gamma\)-glutamic) acid

The experimental variations of the solute concentrations versus \(E\tau\) (results not shown) were used to determine the value of the partition coefficient \(\phi\). The corresponding values obtained for each solute are reported in Table 3. It was demonstrated that the mass transfer of \(\alpha\)-lactalbumin and PLGA is limited by electrostatic interactions [13]. These interactions are strongly dependent on the apparent electrical charge of the membrane, that fixes the electro-osmotic flux, the variations of which where presented in the former section.

It was shown that the electro-osmotic flux obtained with a \(\alpha\)-lacta/PLGA solution is equal to that obtain with the PLGA solution [14]. Then identical partition coefficients are expected for PLGA with both solutions. On the contrary, because of the increase in electroosmotic flux, i.e. the enhancement of electrostatic interactions, the partition coefficient of \(\alpha\)-lactalbumin is expected to be lower in the case of the mixture compared to that obtained with a PLGA-free solution. These expectations are in agreement with experimental results, showing that similar values of the partition coefficient, close to zero, are obtained for both solutes.

Consequently, identical concentrations are achieved at the outlet of the separation chamber. For the operating conditions used, no separation can be obtained.

The increase of the concentration in the concentrate, which is experimentally observed, comes from the solvent

![Fig. 2. Variation of the electro-osmotic flux vs. the electric field. Influence of the solute concentration on the solvent transfer. Operating conditions: Tris–Mes buffer at pH 8; \(Q = 100 \text{ml h}^{-1}\); separating mode.](image-url)
transfer (electro-osmosis), directed from the concentrate to the dilute.

5.1.2.2. α-Lactalbumin/bovine haemoglobin. Figs. 3 and 4 show, for the separating and the elution mode, respectively, the variations of the solute concentration versus \( \varepsilon \tau \). Experimental concentrations are plotted together with those calculated from Eq. (1). The corresponding values of the partition coefficient \( \phi \) are reported in Table 3.

For any solute, the partition coefficient remains identical to that obtained with single solutions [13]. This result can be directly associated to that concerning the electro-osmotic flux. Indeed, it was shown in previous section that the electro-osmotic flux obtained with the mixed solution is comparable to that obtained with only α-lactalbumin.

Then, the electrostatic interactions that set the α-lactalbumin partition coefficient remain constant. On the other hand, it was concluded that the mass transfer of Hbb is limited by steric effects. Therefore, the electro-osmotic flux increase observed with the α-lacta/Hbb solution compared to that obtained with Hbb solution has negligible influence on the Hbb partition coefficient.

These results obtained with the mixed solution confirm that in the separating mode, an enriched fraction of α-lactalbumin can be obtained at the outlet of the concentrate. On the other hand, with the elution mode, one gets at the outlet of the concentrate a solution containing only α-lactalbumin, i.e. free of bovine haemoglobin.

Then, experiments were conducted with higher solute concentrations (0.5 g l\(^{-1}\)). The experimental variations of the solute concentration versus \( \varepsilon \tau \) are plotted in Fig. 5. The corresponding values of the partition coefficients are reported in Table 3.

One can state that no significant change is observed for the partition coefficient of bovine haemoglobin at different concentrations. On the other hand, a slight decrease from 0.8 to 0.6 is observed for the partition coefficient of α-lactalbumin as the concentration increases from 0.1 to 0.5 g l\(^{-1}\). It was already explained that this behaviour is due to the enhancement of the apparent charge of the membrane with the concentration of α-lactalbumin, which was pointed out from the electro-osmotic flux measurement (see former section).

5.2. Evaluation of the process performances

From the former experimental results, a first evaluation of the quantitative and qualitative process performances was done considering α-lactalbumin as the target solute.

From the quantitative point of view, the production capacity was estimated through the determination of the productivity, provided by the product of the outlet flow rate by the concentration of the target solute at the outlet of the concentrate:

\[
m_t = \dot{Q} \cdot C_t
\]

From the qualitative point of view, the separation efficiency was estimated through the calculation of the solute
purity, defined as the ratio of the target solute mass rate over the sum of all solute mass rates:

\[ p_i = \frac{(Q_i C_i)_y}{\sum_j (Q_j C_j)_y} \]  

Finally, the product yield, defined as the target solute mass recovered to the total target solute mass in initial feed, was also estimated:

- **Separating mode:**
  \[ \eta_i = \frac{C_i}{C_0} \times 100 \]  

- **Elution mode:**
  \[ \eta_i = \frac{Q_i C_i}{Q_d C_0} \times 100 \]

Since \( \alpha \)-lactalbumin migrates from the dilute to the concentrate, the process parameters, i.e. the productivity, the purity and the product yield, were calculated from the concentration in the concentrate. This concentration was obtained from the mathematical expression provided in Table 4. The parameters required for the calculation are the electrophoretic mobility \( u_{mi} \) (Table 1), the coefficients \( \alpha \) and \( \alpha_0 \) defined in Eq. (2) (Table 2) and the partition coefficient \( \phi \) (Table 3).

The variations of the productivity and purity versus \( E \tau \) are plotted in Fig. 6 for the two operating modes investigated. One can observe that in any case, the productivity increases with \( E \tau \). As expected, significant higher values are achieved in the separating mode. On the other hand, the purity remains almost constant and exceeding 99% for the elution mode. For the separating mode, the purity is lower and increases continuously with \( E \tau \). The corresponding variations of the product yield are plotted versus \( E \tau \) in Fig. 7. One can state that for any operating mode, increasing values of \( E \tau \) provide increasing product yields. It is obviously lower in the elution mode than in the separating one, but the difference decreases as \( E \tau \) increases.

The process parameters, i.e. the productivity, the purity and the yield, are provided for a fixed value of \( E \tau \) in Table 5. In this manner, the influence of the operating mode on the process performances can be quantitatively observed.

---

Table 4: Expressions of the outlet concentrations

<table>
<thead>
<tr>
<th>Outlet concentration in the dilute</th>
<th>[ C_d = C_0 \left[ 1 + \frac{u_{mE \tau}}{\phi (u_{mi})<em>{\alpha_0}} \right] ]  where ( u</em>{mE \tau} = -\alpha E \tau + \alpha_0 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outlet concentration in the concentrate</td>
<td>Separating mode: [ C_c = 2C_0 - C_d ]  Elution mode: [ C_c = \frac{(Q_d - Q_c) C_d - Q_c C_0}{Q_d} ]  where ( Q_{mE} = u_{mE} E )</td>
</tr>
</tbody>
</table>
As explained in the introduction, one of the main objectives for developing electrophoretic membrane contactors is to get the possibility to increase the productivity without damaging significantly the separation efficiency. One way to increase the productivity is to increase the inlet concentration. For instance, it was formerly stated with the Gradient apparatus that the transfer rate of bovine serum albumin (BSA) is proportional to the concentration up to 200 g l$^{-1}$ [8]. In that case however, no indication was provided concerning for instance the purity achieved.

Results obtained in the present work with the $\alpha$-lactalbumin/bovine haemoglobin mixture for two inlet concentrations are reported in Table 6. One can state that the productivity of $\alpha$-lactalbumin increases with the inlet concentration. Moreover, in the range of concentration investigated, the productivity is proportional to the inlet concentration. These results also show that this enhancement of productivity is achieved at a constant purity and product yield.

### 6. Conclusion

In this paper, we studied the mass transfer mechanisms involved in electrophoretic membrane contactors by investigating the separation of proteins in binary solutions. This was done using a methodology which was previously published, associating a theoretical and an experimental approach. The experimental study was here carried out with solution of increasing complexity, i.e. single solute and binary solutions.

This work clearly points out strong transfer limitations due to electrostatic interactions between the membrane and the solute. Therefore the application of such contactors to fractionate charged solutes like polyamino acids for instance still requires to manage such interactions. Different ways can be considered to do that like a modification of the pH, of the ionic strength or of the membrane material.

The process performances were studied considering the purification of $\alpha$-lactalbumin from a mixed solution containing $\alpha$-lactalbumin and bovine haemoglobin as case study. Three parameters were chosen to characterise the process performances, i.e. the productivity, the purity and the product yield.

It was confirmed that the productivity can be enhanced, at least by a factor of 5 for the conditions used in this study, by increasing the inlet concentration. It was further demonstrated that this increase of productivity is achieved without damaging the purity and the product yield. Consequently, this process appears to be scalable and its flexibility was demonstrated.

At this stage, any comparison of the performances presented here with those obtained with other systems is out of the scope. Indeed, several target parameters, like for instance the pH, the electric field, the membrane used as contactor, were considered as fixed conditions, and were thus not optimised. Moreover, the results were obtained in a continuous mode, i.e. single passage, so that there are hardly comparable as they stand to previous ones concerned with batch operating mode. Therefore, the performances of the process presented in this study are only indicative values and further work will be devoted to the improvement of the separation productivity and efficiency.

### Nomenclature

- $C$: solute concentration (kg m$^{-3}$ i.e. g l$^{-1}$)
- $C_0$: inlet solute concentration (kg m$^{-3}$ i.e. g l$^{-1}$)
- $d$: concentrate and dilute compartment thickness (m)
- $E$: electric field in the bulk solution (V m$^{-1}$)
- $I$: current (A)
- $I_{eo}$: electro-osmotic flux (m s$^{-1}$)
- $\eta$: purity
- $Q$: flow rate (m$^3$s$^{-1}$)

### Table 5

<table>
<thead>
<tr>
<th>Target solute</th>
<th>Operating mode</th>
<th>Productivity, $\eta_i$ (mg h$^{-1}$)</th>
<th>Purity, $\eta_i$ (%)</th>
<th>Product yield, $\eta_i$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\alpha$-Lactalbumin</td>
<td>Separation</td>
<td>17</td>
<td>60</td>
<td>86</td>
</tr>
<tr>
<td></td>
<td>Elution</td>
<td>5.5</td>
<td>99</td>
<td>66</td>
</tr>
</tbody>
</table>

Operating conditions: Tris–Mes buffer at pH 8; $E_T = 0.1$ g l$^{-1}$, Tris–Mes at pH 8.

### Table 6

<table>
<thead>
<tr>
<th>Target solute</th>
<th>$C_i$ (g l$^{-1}$)</th>
<th>Productivity, $\eta_i$ (mg h$^{-1}$)</th>
<th>Purity, $\eta_i$ (%)</th>
<th>Product yield, $\eta_i$ (%)</th>
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<tbody>
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<td>$\alpha$-Lactalbumin</td>
<td>0.1</td>
<td>17</td>
<td>60</td>
<td>86</td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>83</td>
<td>57</td>
<td>83</td>
</tr>
</tbody>
</table>

Operating conditions: Tris–Mes buffer at pH 8; $E_T = 150$000 V m$^{-1}$, separating mode.

Fig. 7. Variation of the product yield vs. the product of the electric field by the residence time (Ef). Target solute: $\alpha$-lactalbumin. Operating conditions: mixture $\alpha$-lactalbumin/bovine serum albumin (BSA) is proportional to the concentration up to 200 g l$^{-1}$ [8].
<table>
<thead>
<tr>
<th>Symbol</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>$S$</td>
<td>membrane area (m$^2$)</td>
</tr>
<tr>
<td>$u_{eo}$</td>
<td>electro-osmotic mobility (m$^2$V$^{-1}$s$^{-1}$)</td>
</tr>
<tr>
<td>$u_{mi}$</td>
<td>electrophoretic mobility (m$^2$V$^{-1}$s$^{-1}$)</td>
</tr>
<tr>
<td>$w_i$</td>
<td>productivity (g h$^{-1}$)</td>
</tr>
</tbody>
</table>

**Greek letters**
- $\alpha$ slope of the straight line $u_{eo} = f(E\tau)$
- $\alpha_0$ $y$-intercept of the straight line $u_{eo} = f(E\tau)$
- $\eta$ product yield
- $\tau$ mean residence time (s)
- $\phi$ partition coefficient
- $\chi$ electrical conductivity (S m$^{-1}$)

**Subscripts**
- avg average
- c concentrate
- d dilute
- eo electro-osmosis
- mi electromigration

**References**


