Modeling a problem in displacement mode centrifugal partition chromatography

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1 Introduction

Chromatography is a chemical method whose aim is the separation of the constituents of a mixture. Chromatography can be either analytical or preparative. The former solves chemical identification and quantification problems while the latter is performed to get grams (or kilograms, or tons) of pure chemical compounds.

Centrifugal partition chromatography (CPC) is a preparative technique based on the selective distribution of the analytes (the mixture constituents) between two immiscible liquid phases. One of them is said to be stationary and is maintained inside of the chromatographic apparatus (named "column" for historical reasons) by means of a centrifugal force field created by rotation of the column around its revolution axis. The column can be viewed as a collection of "cells" connected by "ducts". The column initially contains the stationary phase. Then, the mixture of analytes is introduced at the entry point of the column. The other liquid phase (the mobile one) is pumped through the stationary one. Depending on the chemical nature of the phases, the analytes will move inside of the column at individual speed, and will flow out of the column at separate times.

There are essentially two ways of using CPC: elution and displacement. Elution is the simplest to understand. The analytes that dissolve preferentially in the mobile phase are those who flow out first. The graph of the concentration of an analyte as a function of time is a Gaussian-like curve. The center of the Gaussian curve is positioned according to the affinity difference of the analyte for both liquid phases. In more chemical words, an analyte A will partition between the phases according to:

$$A_{stat} \rightleftharpoons A_{mob}$$

where A_{stat} and A_{mob} represent the chemical species A in the stationary and mobile phases, respectively. The existence of this chemical equilibrium leads to a particular relationship between their concentration (disregarding the subtle difference between concentration and chemical activity in its thermodynamic sense):

$$\frac{[A_{mob}]}{[A_{stat}]} = K_p$$

where [.] means concentration (in mol.l^{-1}) of a species and K_p a constant (the partition constant) that depends only of temperature (thus supposed to be constant). This relationship is a particular case of the "mass action" law that prevails for all chemical equilibriums:

$$aA + bB \rightleftharpoons cC + dD \quad \Rightarrow \quad \frac{[C]^c\,[D]^d}{[A]^a\,[B]^b} = K(T)$$

Therefore, each chemical equilibrium is governed by a particular relationship between the concentrations of the reacting species. Displacement CPC uses other equilibriums than the partition one to discriminate between analytes and thus to separate them. They can be acid-base equilibriums (giving rise to the so-called "pH zone-refining" technique) or ion-pair formation equilibriums. This latter case is of interest, and is also known as "ion-exchange chromatography".

2 Ion-exchange CPC

The presently described example uses an aqueous mobile phase and an organic stationary phase (an industrial solvent like methyl t-butyl ether, $CH_3OC(CH_3)_3$). An ion exchanger, benzalkonium chloride, is added to the stationary phase. This compound is a salt formally written (B^+,Cl^-), where B^+ is an ion that presents an high affinity for organic solvents. This affinity is so strong that one cannot find a trace of B^+ ions in the aqueous mobile phase.

Two (for example) mixed acidic substances are introduced in the column as benzalkonium salts (B^+,A_1^-) and (B^+,A_2^-) in the organic stationary phase. We consider that A_1^- and A_2^- never react with water, being ionic forms of strong acids. Their presence in water does not affect the pH value of the aqueous phase, that will stay at 7. The mobile phase will contain sodium iodide, (Na^+,I^-). Neither Na^+ and I^- do not react with water (this is strictly speaking incorrect in what concerns the I^- ions. The stability (defined below) order of ions pairs in the organic phase is (B^+,I^-) > (B^+,A_2^-)

$> (B^+,A_1^-) > (B^+,Cl^-)$. This means that iodides from the mobile phase will preferentially substitute the chloride ions of the stationary phase and that the chloride ions that are freed from the ion pairs (B^+,Cl^-) will be carried by the mobile phase. When all chloride ions are displaced (hence the name of the technique) A_1^- ions will be preferentially displaced, relatively to A_2^- ions. From the column, (Na^+,Cl^-), (Na^+,A_1^-), (Na^+,A_2^-), and(Na^+,I^-) will flow out in this order. The last one appears when the column contains only benzalkonium iodide, meaning that all what can be displaced was displaced.

Some experimental observations lead us to formulate the hypothesis that A_1^- et A_2^- ions in aqueous phase pair together by a mechanism named "π stacking" to form a new species C. Our recent motivation to search an efficient method for polynomial equation system solving originates in the exploration of this hypothesis (but was formulated a long time before).

3 The chemical equations of the problem

The chemical species in aqueous phase are Na^+ (never reacts and can be left out), I^-, Cl^-, A_1^-, A_2^-, and C (5 species). Those in organic phase are (B^+,I^-), (B^+,Cl^-), (B^+,A_1^-), and (B^+,A_1^-) (4 species). One needs to write 9 equations between species concentration to totally determine the state of such a system at equilibrium. Five equations are those describing the I^-, Cl^-, A_1^-, A_2^- and B^+ species preservation. The four other ones arise from mass action law.

Species preservation means invariance of number of moles for the cited species during the chemical reactions they undergo. A concentration being a mole/volume ratio, we define V_{mob} and V_{stat}, the volumes of mobile and stationary phase in each cell (supposed to be constants).

If n_I is the total number of I^- ions in a cell, then

$$n_I = V_{mob}\left[I^-\right] + V_{stat}\left[B^+, I^-\right]$$

Defining concentration $c_I = n_I/V_{mob}$ and the volume ratio $v = V_{stat}/V_{mob}$, we get:

$$c_I = \left[I^-\right] + v\left[B^+, I^-\right].$$

In the same way, with:

$$\begin{aligned} x_1 &= \left[I^-\right] \\ x_2 &= \left[Cl^-\right] \end{aligned}$$

$$
\begin{aligned}
x_3 &= \left[A_1^-\right] \\
x_4 &= \left[A_2^-\right] \\
x_5 &= v\left[B^+, I^-\right] \\
x_6 &= v\left[B^+, Cl^-\right] \\
x_7 &= v\left[B^+, A_1^-\right] \\
x_8 &= v\left[B^+, A_2^-\right] \\
x_9 &= [C]
\end{aligned}
$$

and with

$$
\begin{aligned}
a_1 &= c_I \\
a_2 &= c_{Cl} \\
a_3 &= c_{A1} \\
a_4 &= c_{A2} \\
a_5 &= c_B
\end{aligned}
$$

one gets the (linear) preservation equations:

$$
\begin{aligned}
a_1 &= x_1 + x_5 \\
a_2 &= x_2 + x_6 \\
a_3 &= x_3 + x_7 + x_9 \\
a_4 &= x_4 + x_8 + x_9 \\
a_5 &= x_5 + x_6 + x_7 + x_8.
\end{aligned}
$$

Ion exchange reactions are described by the equilibriums:

$$
\begin{aligned}
I^- + (B^+, Cl^-) &\rightleftharpoons Cl^- + (B^+, I^-) \\
I^- + (B^+, A_1^-) &\rightleftharpoons A_1^- + (B^+, I^-) \\
I^- + (B^+, A_2^-) &\rightleftharpoons A_2^- + (B^+, I^-)
\end{aligned}
$$

that are characterized by their thermodynamic constants:

$$
K_{Cl} = \frac{[Cl^-]\,[B^+, I^-]}{[I^-]\,[B^+, Cl^-]}
$$

$$
\begin{aligned}
K_{A1} &= \frac{\left[A_1^-\right]\left[B^+, I^-\right]}{\left[I^-\right]\left[B^+, A_1^-\right]} \\
K_{A2} &= \frac{\left[A_2^-\right]\left[B^+, I^-\right]}{\left[I^-\right]\left[B^+, A_2^-\right]}
\end{aligned}
$$

These equations are built taking iodide ions as reference. The ion pair (B^+, I^-) is much stabler than (B^+, Cl^-) and therefore $K_{Cl} >> 1$. The association between A_1^- and A_2^- in the pair C of the aquous phase:

$$A_1^- + A_2^- \rightleftharpoons C$$

is governed by:

$$K_C = \frac{[C]}{\left[A_1^-\right]\left[A_2^-\right]}.$$

Using:

$$
\begin{aligned}
a_6 &= K_C \\
a_7 &= K_{Cl} \\
a_8 &= K_{A1} \\
a_9 &= K_{A2}
\end{aligned}
$$

one gets the (polynomial) equilibrium equations:

$$
\begin{aligned}
a_6 x_3 x_4 &= x_9 \\
a_7 x_1 x_6 &= x_2 x_5 \\
a_8 x_1 x_7 &= x_3 x_5 \\
a_9 x_1 x_8 &= x_4 x_5
\end{aligned}
$$

4 CPC column modelling

A CPC column is made of N partition cells, each containing a stationary phase volume V_{stat} and a mobile phase volume V_{mob}. The continuous chromatographic process is split into a series of "matter transfer" – "chemical equilibration" cycles. Initially, a small number M of cells at column input

contain both stationary phase and the (B^+,A_1^-) et (B^+,A_2^-) ions pairs. Matter transfer is achieved by moving each mobile part of each cell into the following cell. The content of the last cell is collected (after at least N cycles, of course). The A_1^- and A_2^- concentration evolution as a function of the collected volume constitutes the fractogram of the experiment. At each transfer, fresh mobile phase containing (Na^+,I^-) is injected in the first cell. After each transfer step in cycles 1 to i ($i \leq N$) the content of the cell numbered from 1 to i is equilibrated using the equations in the last section. For the following cycles, those for which effluent collection makes sense, all N cell contents must be equilibrated.

Such an approach provides only a rough model because the phenomena that take place inside of the column are both chemical and hydrodynamic. The last aspect is presently totally ignored.

5 Conclusion

The resolution of the polynomial equation systems by means of non-iterative methods will bring a high robustness to process modeling. The chemical system can be made much more complex with more than two analytes, taking into account possible reactions of mobile phase ions with water, the repartition of neutral species between the liquid phases, ...

Beyond CPC modeling and the interpretation of experimental fractograms, the search of the equilibrium state of any chemical system can be described (approximately...) by a polynomial equation system like the particular one that is described in the present document. The efficient resolution of such equation systems will most probably have a positive effect in the field of solution chemistry.