

# Design and analysis of chromatographic separation of metal ions

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## Abstract

*The aim of this article was to develop a methodology for design and optimisation of a multi-component chromatographic separation. The case studied was an ion-exchange chromatographic separation of samarium, europium and gadolinium. The optimisation method used was differential evolution. It was concluded that it was difficult to incorporate all different variables into a single optimisation. Nonetheless, a broader optimisation can be necessary in order to get results that can be used as the basis for reduction of the problem. This methodology, to reduce the problem gradually is considered to be applicable to other design problems as well.*

**Keywords:** Optimisation, preparative chromatography, multi-component fractionising, differential evolution.

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## Introduction

It can be very beneficial to use simulations and optimisations as a tool in the design of industrial processes. Time and money can be saved by minimising the number of extensive and expensive experiments needed in the scale-up process from laboratory to pilot scale and from pilot to factory scale.

The aim of this article was to design a chromatographic separation step and to find a methodology that can be applied to other similar separation steps.

The case used to exemplify this is an ion-exchange chromatographic separation of Samarium (Sm), Europium (Eu) and Gadolinium (Gd). This is an interesting case since it is both considered to be a difficult separation [1] and that Eu has a high market price [2].

## Model

An extensive toolbox for chromatography simulations is developed at Lund University [3]. Models for e.g. dispersion and adsorption as well as programs for numerically solving the models, post- and pre-processing etc. are

implemented in the preparative chromatograph simulator (PCS).

The PCS were used for all simulations in this article. To describe the mobile phase a lumped kinetic dispersion model were used [4, p. 22 – 26].

$$\frac{\partial c_i(z,t)}{\partial t} = D_{AX} \cdot \frac{\partial^2 c_i(z,t)}{\partial z^2} - v_{lin,i} \cdot \frac{\partial c_i(z,t)}{\partial z} + \frac{1-\varepsilon_c}{\varepsilon_c + (1-\varepsilon_c) \cdot \varepsilon_{p,i}} \cdot \frac{\partial q_i(z,t)}{\partial t} \quad (\text{eq. 1})$$

where  $c_i$  is the concentration of component  $i$  in the mobile phase, [mole/m<sup>3</sup>];  $t$  is the time, [s];  $D_{AX}$  is the axial dispersion, [m/s];  $z$  is the axial position,  $v_{lin,i}$  is the interstitial velocity, [m/s];  $\varepsilon_c$  is the column porosity,  $\varepsilon_{p,i}$  is the particle porosity and  $q_i$  is the concentration of component  $i$  in the stationary phase, [mole/m<sup>3</sup> stationary phase].

The adsorption-desorption were described by Langmuir type kinetics with mobile phase modulators.

$$\frac{\partial q_i(z,t)}{\partial t} = k_{kin,i} \cdot s^{\beta_i} \cdot \left( K_{eq,i} \cdot q_{i,max} \cdot s^{-\beta_i} \cdot e^{-\gamma_i s} \cdot e^{-\delta_i(pH-pH_{ref})} \cdot c_i(z,t) \cdot \left( 1 - \sum \frac{q_i(z,t)}{q_{i,max}} \right) - q_i(z,t) \right) \quad (\text{eq. 2})$$

where  $k_{kin,i}$  is the adsorption reaction rate, [ $s^{-1}$ ];  $S$  is the eluent concentration, [ $mole/m^3$ ];  $\beta_i$  describes the ion-exchange characteristics,  $K_{eq,i}$  is the equilibrium constant for the adsorption reaction,  $q_{i,max}$  is the maximum possible concentration of component  $i$ , [ $mole/m^3$ ];  $\gamma_i$  describes hydrophobicity and  $\delta_i$  describes the pH dependency. [5, p. 6]

Ergun's equation [6] were used to calculate the pressure drop ( $\Delta P$ )

$$\frac{\Delta P}{L} = 150 \frac{(1-\varepsilon_c)^2}{\varepsilon_c^3} \frac{\mu_f v_0}{\phi^2 d_p^2} + 1.75 \frac{(1-\varepsilon_c) \rho_f v_0^2}{\varepsilon_c^3 \phi d_p} \quad (\text{eq. 3})$$

where  $L$  is the bed length, [m];  $\varepsilon_c$  is the fractional void volume, or porosity, of the bed;  $\mu_f$  is the dynamic viscosity of the fluid, [Pa s];  $v_0$  is the superficial velocity, [m/s];  $\phi$  is the sphericity factor;  $d_p$  is the particle diameter, [m]; and  $\rho_f$  is the fluid density, [ $kg/m^3$ ].

At a given  $\Delta P$  (10 bar) the flow velocity could be calculated and used in the simulations.

The model parameters are calibrated by Borg [7], the calibration was made as a visual adjustment to available experimental data. It is therefore not possible to speak of any real calibration. A real calibration would require numerical adjustment to several sets of experimental data. Nonetheless, the model used is considered to mimic a possible real separation case well enough to able to conduct the optimisations and to develop a useful methodology.

The partial differential equations were solved with *ode15s* implemented in Matlab, which is capable of handling stiff problems. The finite difference method was used as discretisation method, 200 grid points were used.

## Optimisation

The most crucial part of the optimisation is perhaps choosing the objective function, or objective functions. In this article productivity

(PR), specific productivity (SPR) and yield (Y) were used [4, p. 598 – 603].

$$PR_i = \frac{V_{inj} c_i^0 Y_i}{t_{cycle}} \quad (\text{eq. 4})$$

$$SPR_i = \frac{PR_i}{V_{solvent}} t_{cycle} \quad (\text{eq. 5})$$

$$Y_i = \frac{q \int_{t_c1}^{t_c2} c_i dt}{V_{inj} c_i^0} \quad (\text{eq. 6})$$

where  $V_i$  is volume [ $m^3$ ],  $c_i$  is the concentration of component  $i$  [ $mole/m^3$ ];  $t_i$  is time, [s] and  $q$  is the flow [ $m^3/s$ ].

PR is linked to fixed cost such as investments and equipment, SPR is linked to operating costs such as energy and solvent, and yield is linked to feed costs [4, p. 604 – 607].

## Optimisation method

The optimisation method used was differential evolution (DE) [8].

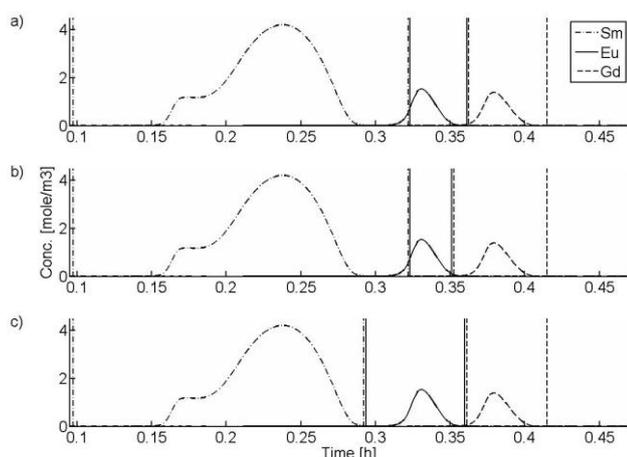
A simplified explanation of DE is that a population, consisting of a number of individuals, is created, this is the first generation. The objective function or functions are then calculated for said individuals. The individuals are then mutated and a new population, the second generation, is created. The objectives are then compared between the individuals of the first and second generation. The strongest individuals will survive and become the basis for generation three. Generation three will then be compared with generation two, the strongest will survive and a fourth generation will be created. This will continue either until an optimum is found or until the maximum number of iterations, generations, is reached. The population size will remain the same throughout all iterations. [8, p. 37 – 47]

The strengths of the DE are its ability to find global optimum even for a multi-modal objective functions. The drawback is the extensive computational power required.

## Multi-component fractionising

When all components are considered to be target components, as in this case the order in which they are collected (prioritisation order) are of great importance. An example is shown in figure 1.

Eu is the component that is affected the most by the prioritisation order. This was also expected since it is the middle component. Eu is also the most valuable and should therefore be given the highest prioritisation.



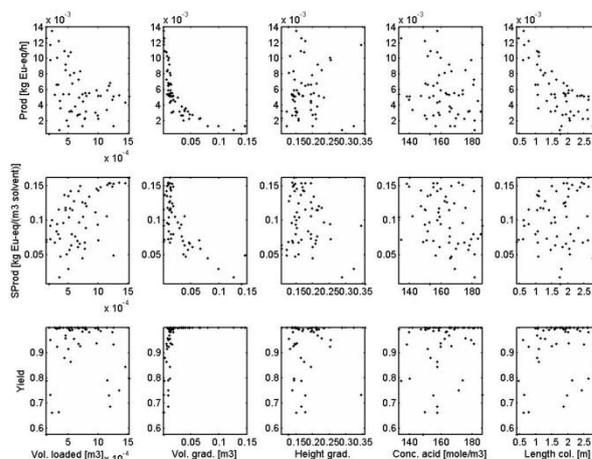
**Figure 1** Chromatogram with cut points for the components marked as vertical lines. The order in which the components are collected are; Sm, Eu and Gd (fig. a); Sm, Gd and Eu (fig. b) and Eu, Sm and Gd (fig. c).

## Results and discussion

At first an optimisation with three objective functions, or objectives, and five decision variables (dv) were used. The objectives were PR, SPR and Y and the dv were volume loaded, length of the gradient (i.e. volume), height of the gradient (i.e. end concentration), basic acid concentration and column length. The purity demand was set to 99 %.

Figure 2 shows the dv for the pareto points plotted against each objective. The pareto points are spread out over a relatively wide area which is an indication that the optimisation has not fully converged. A fully converged optimisation should display a clear trend between the pareto points and the

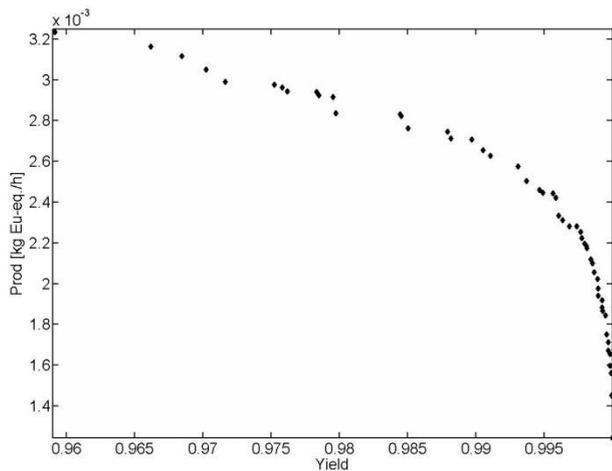
objective. This can, to some extent, be seen for length of the gradient.



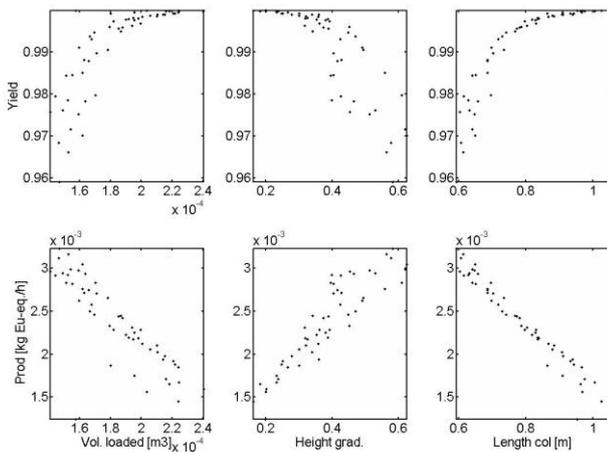
**Figure 2** The objectives plotted against the decision variables for the pareto points, one variable and objective at a time. The objectives are PR, SPR and Y respectively. The decision variables are volume loaded, length of the gradient, height of the gradient, acid concentration and column length.

Due to the fact that the optimisation does not converge and the sheer size of the optimisation some modifications of the problem and/or approach for solving it are called for. The first thing can be to reduce the number of dv. The results show a relatively narrow distribution of the basic acid concentration in the column. It is therefore assumed that this dv can be set as a parameter instead. Other means to further decrease the complexity and size of the optimisation is to reduce the number of objectives.

Another optimisation was done with two objectives, PR and Y, instead of the three previously used. Three dv were used, volume loaded, height of the gradient and column length. The gradient length was the same in all simulations and the gradient slope, which is the factor influencing separation, was thus only dependent on the height of the gradient. The cycle time was calculated as a post-process operation. A yield constraint for Eu was implemented ( $Y_{Eu} > 80\%$ ). Figure 3 shows the pareto created.



**Figure 3** Pareto front from the optimisation. The objectives are PR and Y respectively.



**Figure 4** The objectives plotted against the decision variables for the pareto points, one variable and objective at a time. The objectives are PR and Y respectively. The decision variables are volume loaded, height of the gradient (end concentration) and length of the column.

The pareto points plotted against the objectives can be found in figure 4. As can be seen, there are clear trends for all dv. Indicating that the solution is more converged compared to figure 2. The points are a bit spread out to speak of a fully converged optimisation.

## Conclusions

It was shown that it can be very difficult to incorporate all variables and other steps such as regeneration into an optimisation. The methodology used in this thesis therefore proved useful. First a broader search is

conducted and based on the results from that search the problem is reduced e.g. by reducing the number of decision variables. A new search is then conducted based on the conclusion from the first. This is thought to be applicable to other problems.

The design of the process is also considered to be successful under the given conditions, i.e. not a fully calibrated model.

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