Chromatographic Separation of Tröger's Base in a Batch Column

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Introduction

Separation of a mixture based on their relative interaction with a porous adsorbing medium is the basic principle of chromatography

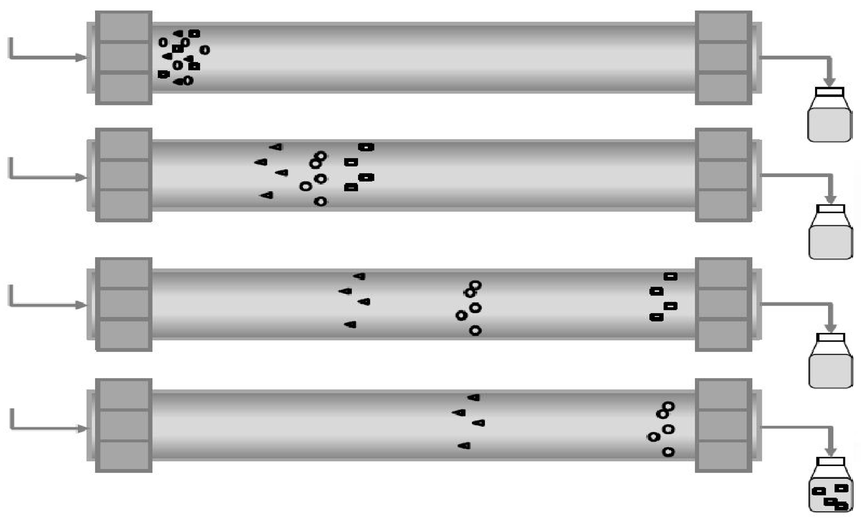

Figure 1. Pinciple of chromatography [1]

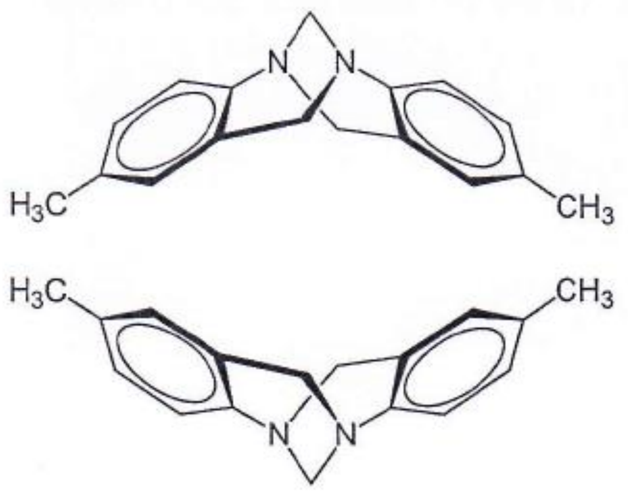

Figure 2. Tröger's base enantiomers

Here, chiral separation of Tröger's base enantiomers is considered, which has its applications in selective catalysis, enzyme inhibition etc. [2]

Computational Methods:

The equilibrium dispersive model shown in equation below is used to describe movement of solute through the column.

$$\varepsilon^*\frac{\partial c_i}{\partial t}+(1-\varepsilon^*)\frac{\partial n_i^*}{\partial t}+u\frac{\partial c_i}{\partial z}=\varepsilon^* D_{ap,i}\frac{\partial^2 c_i}{\partial z^2} \qquad n_i^*=\frac{a_{i,1}c_i}{1+\sum b_{j,1}c_j}+\frac{a_{i,2}c_i}{1+\sum b_{j,2}c_j} \quad (i=A,B)$$

This model can be simulated in COMSOL using the physics 'Species flow in porous media'.

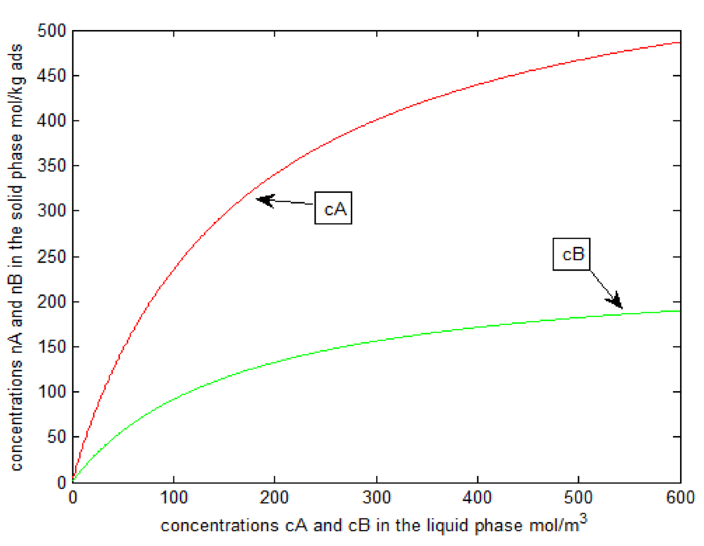

Figure 3. Isotherms(adapted from [3])

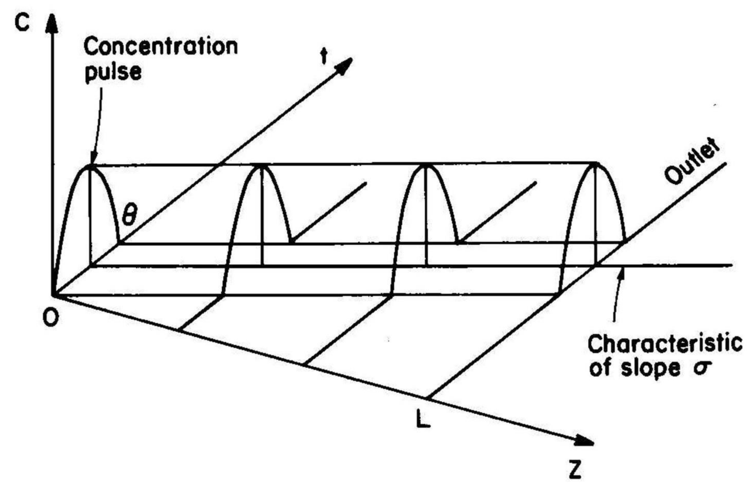

Figure 4. Graphical representation of solution

The relation between solute in adsorbent n_i^* and solute in mixture c_i is given by the bi-Langmuir isotherm shown in figure 3. The parameters required to solve the above model are given in table 1 ,2 . The dispersion coefficient $D_{ap,i}$ depends on superficial velocity. The solution to the above equation would look like figure 4.

Isotherm	Component A	Component B
ai,1	3.99	1.56
bi,1 [L/g]	0.0107	0.0132
ai,2	0.986	0.304
bi,2 [L/g]	0.601	0.136

Table 1. Isotherm parameters [3]

Column parameter	Value	Units
Diameter	0.46	cm
Cross sectional area	0.166	cm^2
length	15	cm
Overall void fraction	0.68	-

Table 2. Column parameters [3]

Results

Rectangular pulse

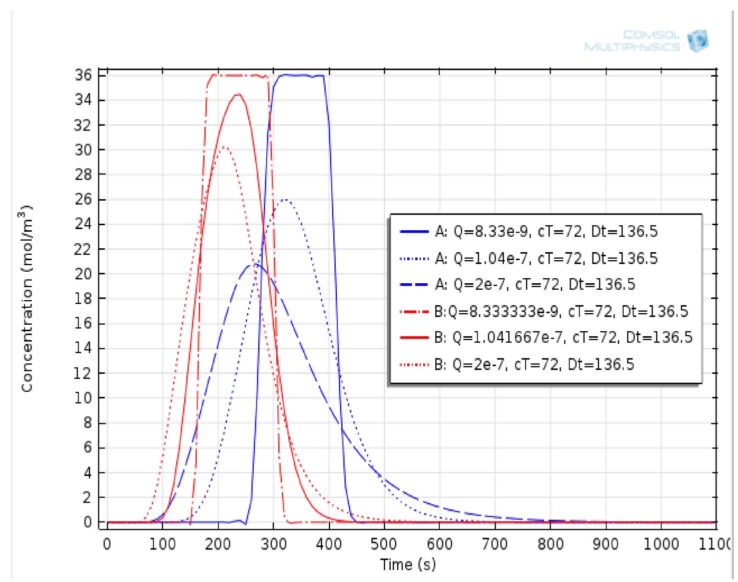

Figure 5. Variation of flow rate

Dirac pulse

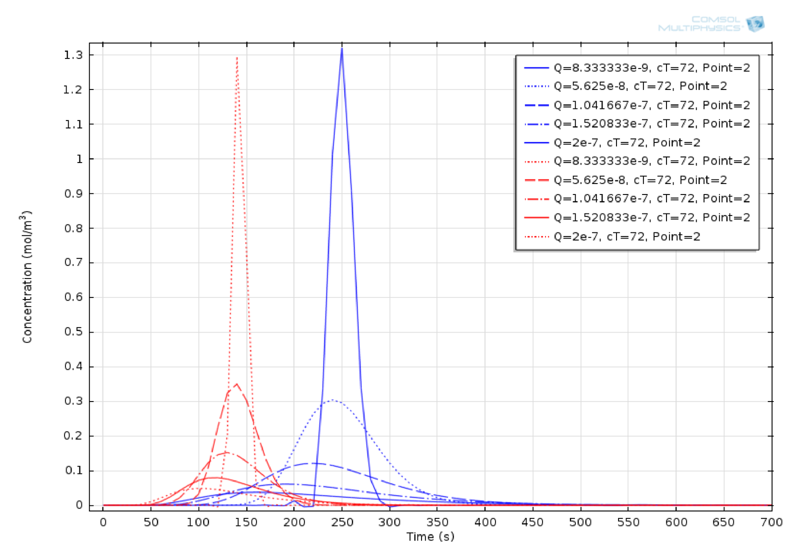

Figure 6. Variation of flow rate

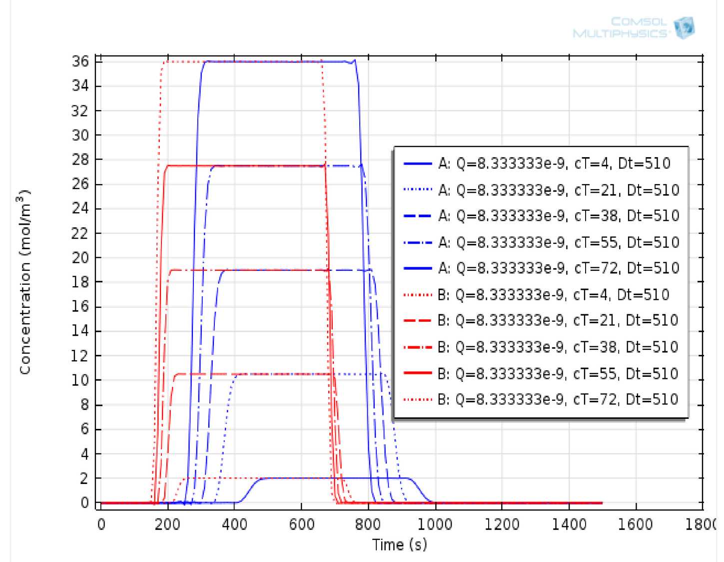

Figure 7. Variation of concentration

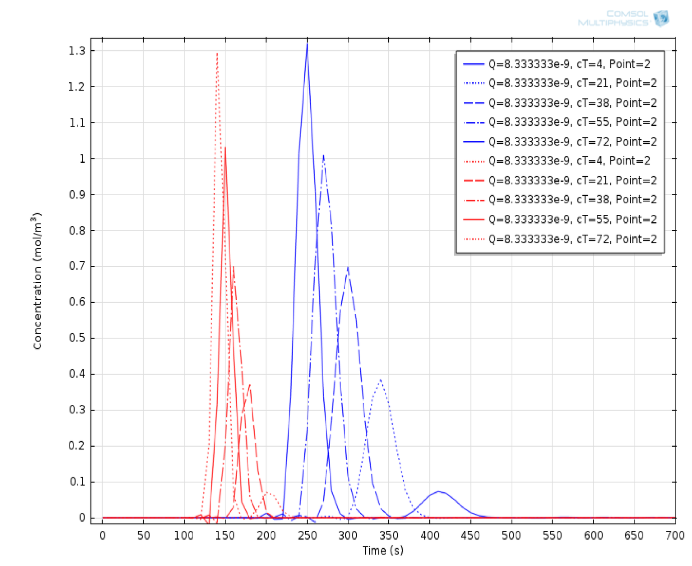

Figure 8. Variation of concentration

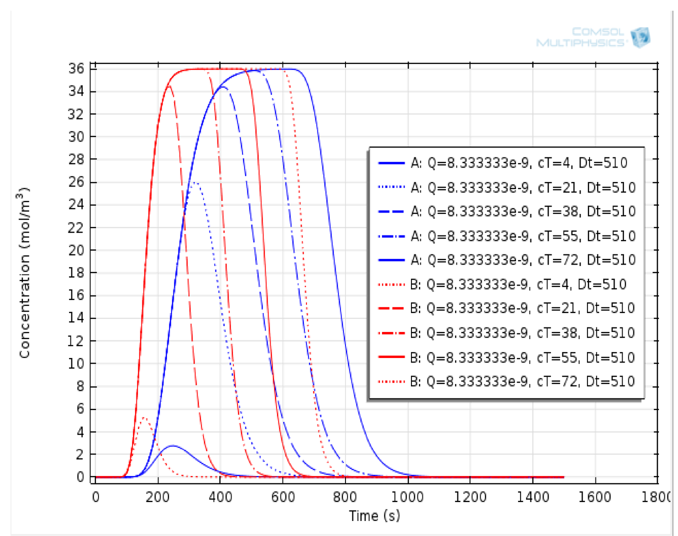

Figure 9. Variation of rectangular pulse width

Simulations have been run with a rectangular pulse and a dirac pulse. For all the runs, the outlet concentration profile has been plotted as a function of time. The following observations have been made:

- Increasing the flowrate reduced the retention time while dispersion was found to increase.
- Likewise, increasing the total concentration reduced the break through time.
- At lower pulse widths, the behavior looked similar to variation of concentration, but once completely developed, the width of the outlet increase parallel to the inlet.

Optimisation

The cost function, $F=w_1.Pr+w_2.SC$ is optimised where Pr, productivity and SC, solvent consumption are defined as:

$$Pr=\frac{1}{V}\cdot\left[\int_{t_{a1}}^{t_{a2}}(C_a+C_b).Q.dt+\int_{t_{b1}}^{t_{b2}}(C_a+C_b).Q.dt\right]$$

$$SC=\frac{Q_{eluent}*(t_{b2}-t_{a1})}{\int_{t_{a1}}^{t_{b2}}(C_a+C_b).Q.dt}$$

The optimisation was done keeping purity of the components at 100%.

Solvent consumption being a recurring investment, was considered more important than productivity and hence, has been given higher weightage. The weights are thus chosen arbitrarily equal to $w_1=10$ and $w_2=-100$.

The best combination was found to be a flow rate of 6x10^{-7} m^3/s, a total concentration of 72 mol/m^3 and a rectangular step length of 136,5 s.

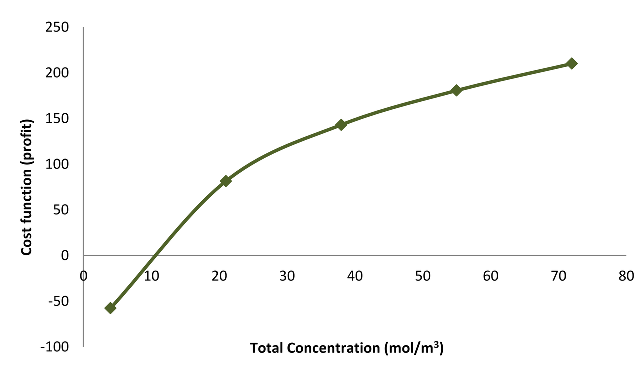

Figure 10. Cost with concentration

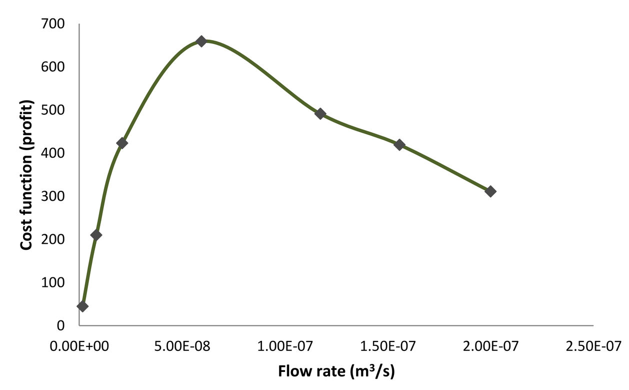

Figure 11. Cost with flow rate

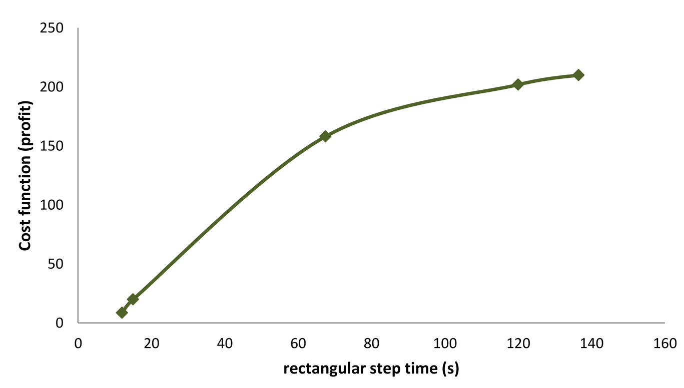

Figure 12.Cost with pulse width

Conclusions

- Comsol provides an efficient and user friendly platform for modelling chromatography columns. Input consists of adsorption isotherms typically obtained in laboratory experiments.
- The model allows for process design, optimization and scale-up, tasks that are typically approached in the fine chemical and pharmaceutical industry.
- For the specific example studied in this work, the process is optimally run at high feed concentration (only limited by solubility) and intermediate flow rate.

References:

1. Sylwester Czaplicki, Chapter 4- Chromatography in Bioactivity Analysis of Compounds, Column Chromatography, p. 99-122 (2013)
2. Ö. V. Rúnarsson, J. Artacho and K. Wärnmark, "The 125th Anniversary of the Tröger's Base Molecule: Synthesis," Eur. J. Org. Chem., p. 7015–7041 (2012)
3. S. Katsuo and M. Mazzotti, "Intermittent simulated moving bed chromatography: 2. Separation of Tröger's base enantiomers," Journal of Chromatography A, p. 3067-3075 (2010).