Title version 1:

**Improved workflow of finding coefficients for equilibrium dispersive model of chromatography using multi-experimental data of preparative chromatography separation of carbohydrates and mannitol mixture**

**Annotation**

Preparative liquid chromatography on ion-exchanging resins is an effective method for the separation of various mixtures, e.g., various carbohydrates, sugar alcohols, and other organic compounds. Novel applications of preparative liquid chromatography accelerate the broad effort toward a sustainable future. The technology enables new concepts for traditional productions and opens the opportunities for new production approaches of various chemicals or new ways of utilization of side products or wastes in various biochemical and agri-food processes. However, the use of preparative chromatography on an industrial scale requires a well-defined and computationally evaluated equipment design with a limited amount of experimental data. Therefore, it is necessary to find and evaluate a mathematical model of the chromatographic system that reliably simulates the separation process under various conditions and dimensional parameters. This work improves an experimental and subsequent computational workflow for the selection of the sufficient noncompetitive linear or nonlinear isotherm and determination of the isotherm constants and coefficients of the equilibrium dispersive model (EDM). The experimental part consists solely of dynamic separation experiments because the proposed workflow does not require static sorption isotherm determination or specialized methods for sorbent porosity determination. The arising partial differential equations are solved separately using a sufficient implicit finite difference method. Arising 3-to-4-dimensional optimization problem of fitting the experimental curves into model solution is tackled by improved multiexperimental loss function definition, primal pre-analysis of the loss function space, and secondar fine simplex optimization.

Introduction

This work proposes an improved workflow of finding coefficients of equilibrium dispersive model for designing simulation of preparative chromatography process based on original experimental data utilizing laboratory- and semi-industrial scale equipment. Proposed workflow The simulation of the chromatography process is essential for the development of industrial-scale equipment.

Experimental data were obtained from dynamic chromatographic experiments performed with different concentrations of separated components in the injected mixture, flow rates, and column dimensions. The exact concentrations of the components in the output fraction have been analyzed with HPLC-PAD using an anion exchanger column. All of the experimental data form a complex data set that is used for the mathematical description of a specific chromatography process.

In the computational part of the work, the Equilibrium Dispersive Model of chromatography with nonlinear isotherms has been studied. A suitable numerical solution is proposed for nonlinear problems arising from a partial differential equation, and the computational time is analyzed in relation to the precision of the particular solution.

In addition, the work describes the fitting of the model curve into measured data and the arising three-dimensional optimization problem. The work proposes an extended loss function calculation in order to utilize all the available experimental data in one optimization step. The loss function solution space has been analyzed, and the fitting simplex optimization algorithm for minima finding has been proposed.

**Experimental System**

pump, columns, annex

**Experimental Data**

|  |  |  |  |
| --- | --- | --- | --- |
| Experiment # | Column | Flow rate | Concentration |
| 1 | Column 1 | Flowrate lower | Low conc. |
| 2 | Medium conc. |
| 3 | High conc. |
| 4 | Flowrate higher | Low conc. |
| 5 | Medium conc. |
| 6 | High conc. |
| 7 | Column 2 | Flowrate lower | Low conc. |
| 8 | Medium conc. |
| 9 | High conc. |
| 10 | Flowrate higher | Low conc. |
| 11 | Medium conc. |
| 12 | High conc. |

Numerical solution of the model

Optimization Problem

Results and Discussion

Con

Contents:

1. Problem definition – model description (unknown porosity !!)
2. Experimental and Analytical Set-up
3. Numerical solution of the model
4. Optimizer:
   1. Definition and analysis
   2. Optimization Procedure
5. Results
6. Conclusions

Experimental part concept:

* Separated mixture: Any binary solution of mono- or di- saccharides. (Gal/Man preferably)
* Column: Any 2 columns with different dimensions.
* Concentrations: Not too high to keep the presumption of linear isotherm (max. 20 g/L?)
* Flowrates: Not too high to achieve an observable separation effect (150 – 300 ml / h)
* Pump: Membrane Grundfos or self-made peristaltic pump (with dynamic control measurement).
* Fractions: 36 each 5 min (sum 180 min)

|  |  |  |  |
| --- | --- | --- | --- |
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Possible Journals:

* Chemical Engineering Science (IF 4.3)
* Computers & Chemical Engineering (IF 3.8)
* Chemical Engineering Journal (IF 13.2)
* Separation and Purification Technology (IF 7.3)
* Chemical Engineering Research and Design (IF 3.7)
* Journal of Chromatography A (IF 4.7)