



Computer-assisted Optimization in Preparative SFC

Challenges, Pitfalls and Solutions

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Summary

We will demonstrate the insufficiency in the direct transfer of the simulation tools of HPLC to SFC.

Our long term goal is to determine the variable coefficients in a chromatographic column model in order to optimize preparative SFC.

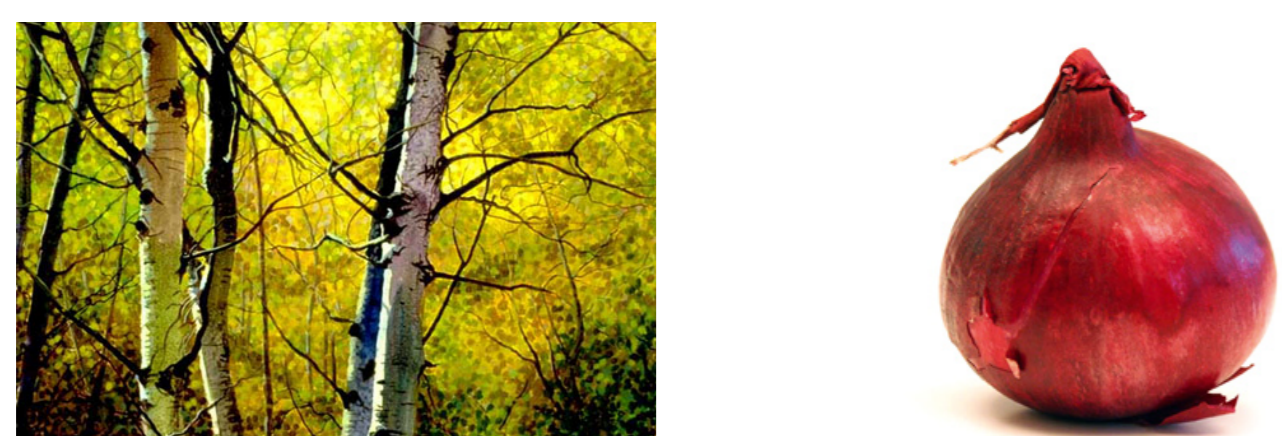
Background

Given the benign nature of carbon dioxide, and the potential economic incentives for application of SFC compared to HPLC, the physiochemical nature of SFC needs to be more thoroughly understood.

Today it is difficult to accurately model, simulate and optimize a preparative SFC process for all operating conditions. Because of the lack of understanding, the application of preparative SFC has been very limited compared to that of HPLC.

Introduction

Describing the migration of a molecule in packed column SFC is more complex than in HPLC. This is due to the sub- or supercritical nature of the mobile phase and its compressibility. Operating the system under non-negligible pressure drop will change the adsorption isotherm and the tools developed for HPLC cannot be used to optimize the process [1 - 3].

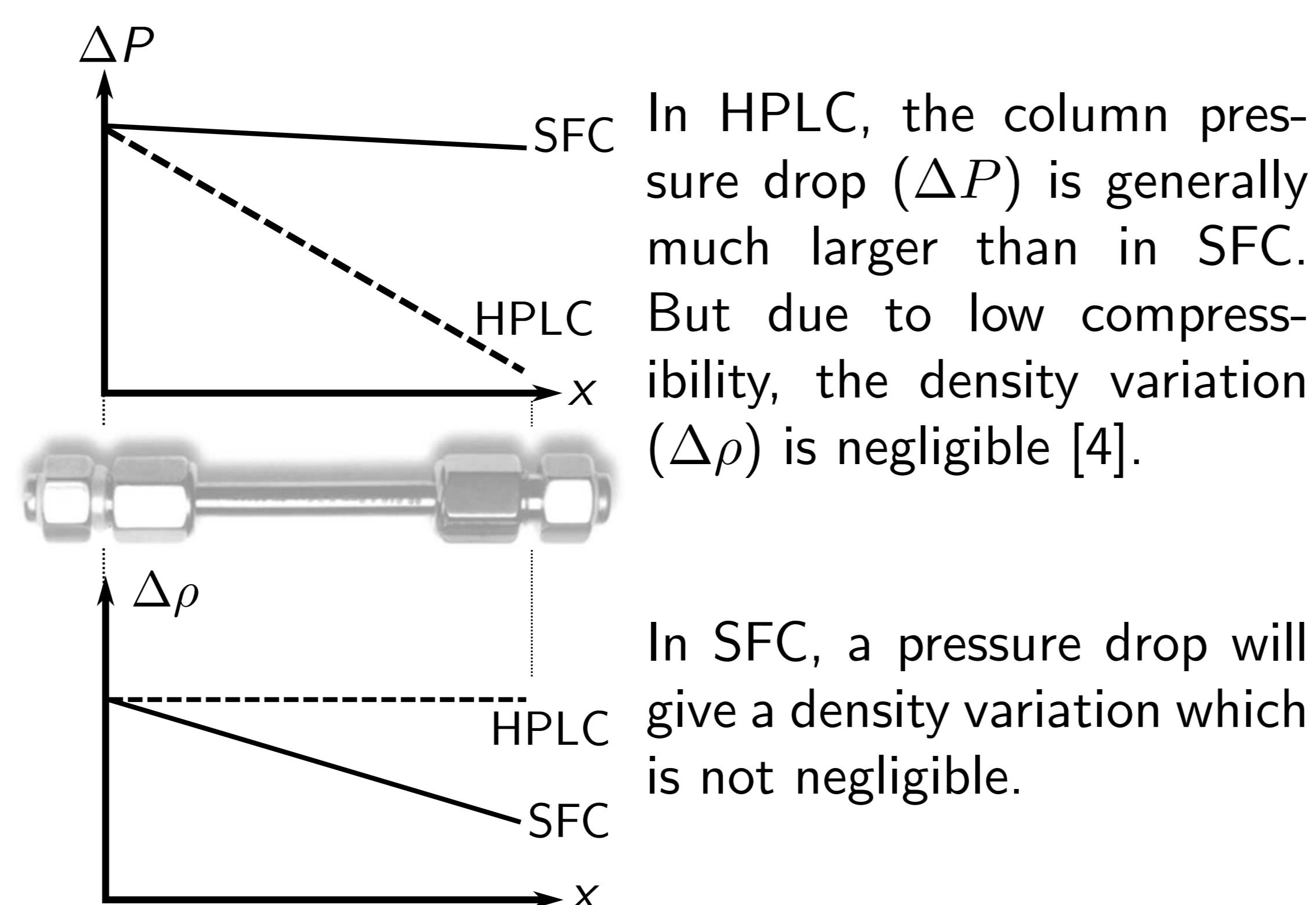


This research is a part of the newly initiated project,

"High-Value Compounds from Agricultural and Forestry Waste by Sustainable Methods- an Interdisciplinary Approach for Bioresource Utilization"

which aims at making an impact in recovery of high-value compounds, e.g. antioxidants, from agricultural byproducts and wastes using environmentally sustainable techniques.

The Column Pressure Drop



Theoretical Model HPLC/SFC

The Equilibrium-Dispersive model

$$\frac{\partial C}{\partial t} + F \frac{\partial q}{\partial t} + \frac{\partial (uC)}{\partial x} = \frac{\partial}{\partial x} \left(D_a \frac{\partial C}{\partial x} \right)$$

C mobile phase concentration
 F phase ratio
 q stationary phase concentration
 u linear velocity
 D_a apparent dispersion coefficient

For a given column, substance, eluent, set mass flow, working temperature T and back pressure P , the following table can be compiled.

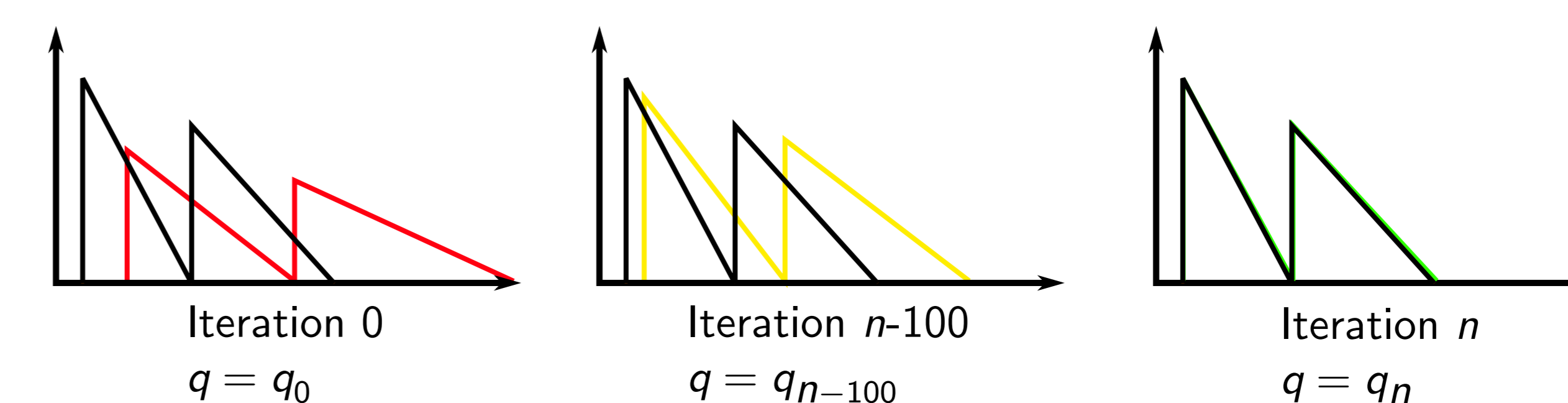
	HPLC	SFC
T	constant	$T = f(\Delta P)$
ρ	constant	$\rho = f(T, P)$
q	$q = f(C)$	$q = f(C, \rho, T)$
u	constant	$u = f(\rho)$
D_a	constant	$D_a = f(\rho, u)$

Therefore

To be able to simulate a SFC process using the Equilibrium-Dispersive model, we need to determine the variations in T , ρ , q , u and D_a as a function of the column coordinate.

Inverse Method

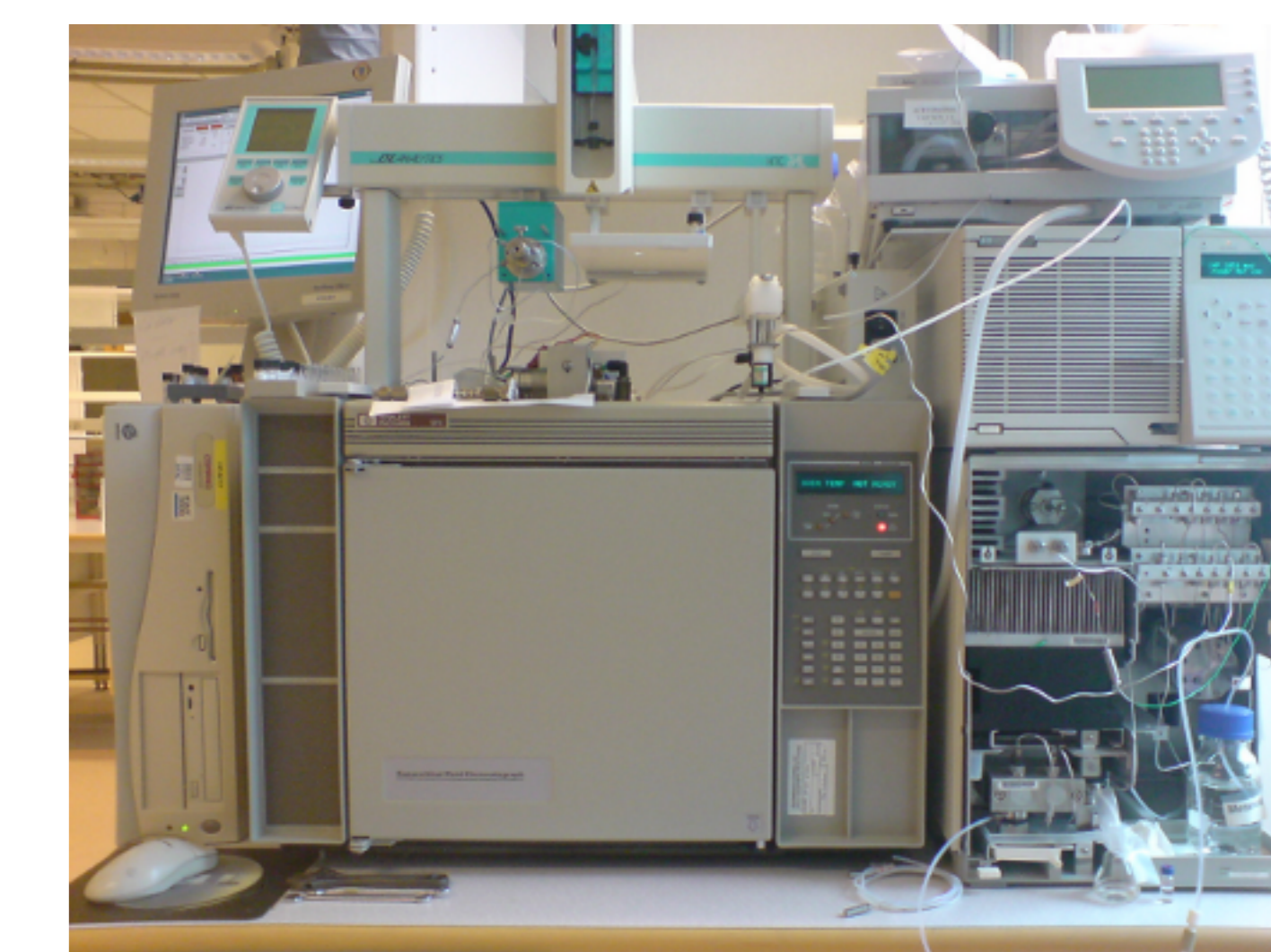
The inverse method of non-linear chromatography is a rapid method to determine the adsorption isotherm parameters, \mathbf{p} , directly from overloaded chromatograms. **Inverse Method Flowchart:**
 (1) Assume model $q(C, \mathbf{p})$, (2) Guess parameters \mathbf{p} , (3) Perturb \mathbf{p} to minimize difference, (4) Iterate (3) until convergence



Experimental example

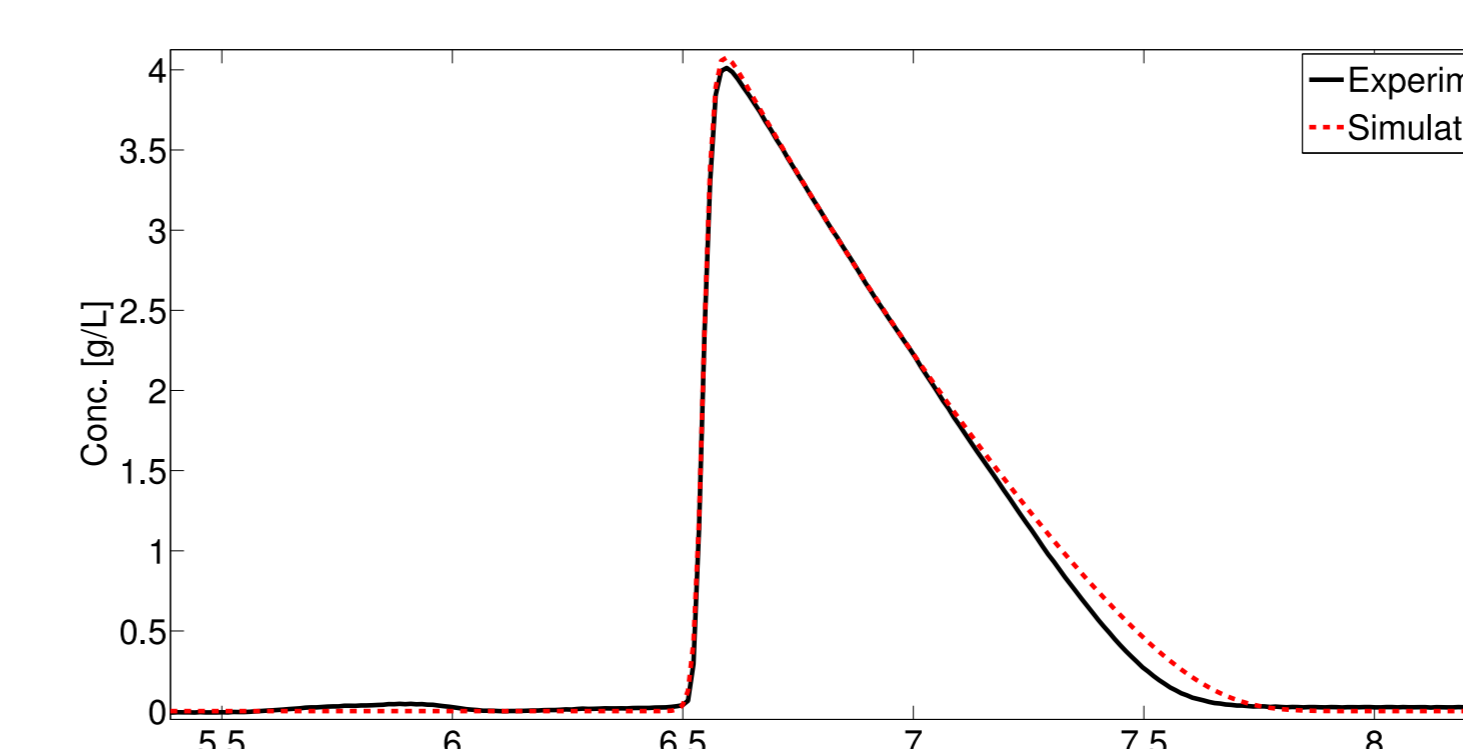
Experimental setup

Compound R(-)-methyl-mandelate
Column Kromasil CelluCoat 25x0.46cm 10 μm
Temperature 40 °C
Back pressure 150 bar
Mobile Phase CO₂ methanol 90/10
Flow 1 and 3 mL/min (nominal at pump)



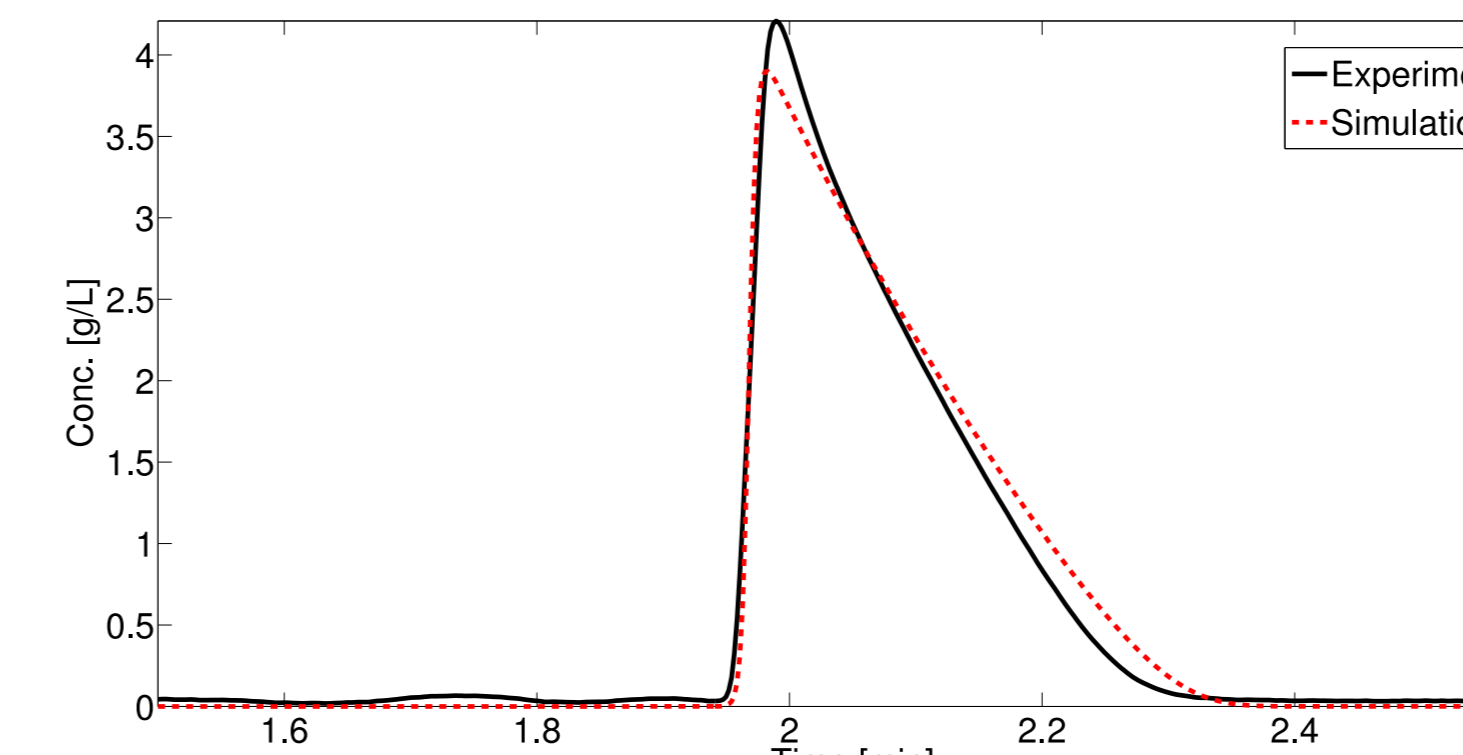
Case I

1 mL/min nominal
 $\Delta P \approx 0$ bar

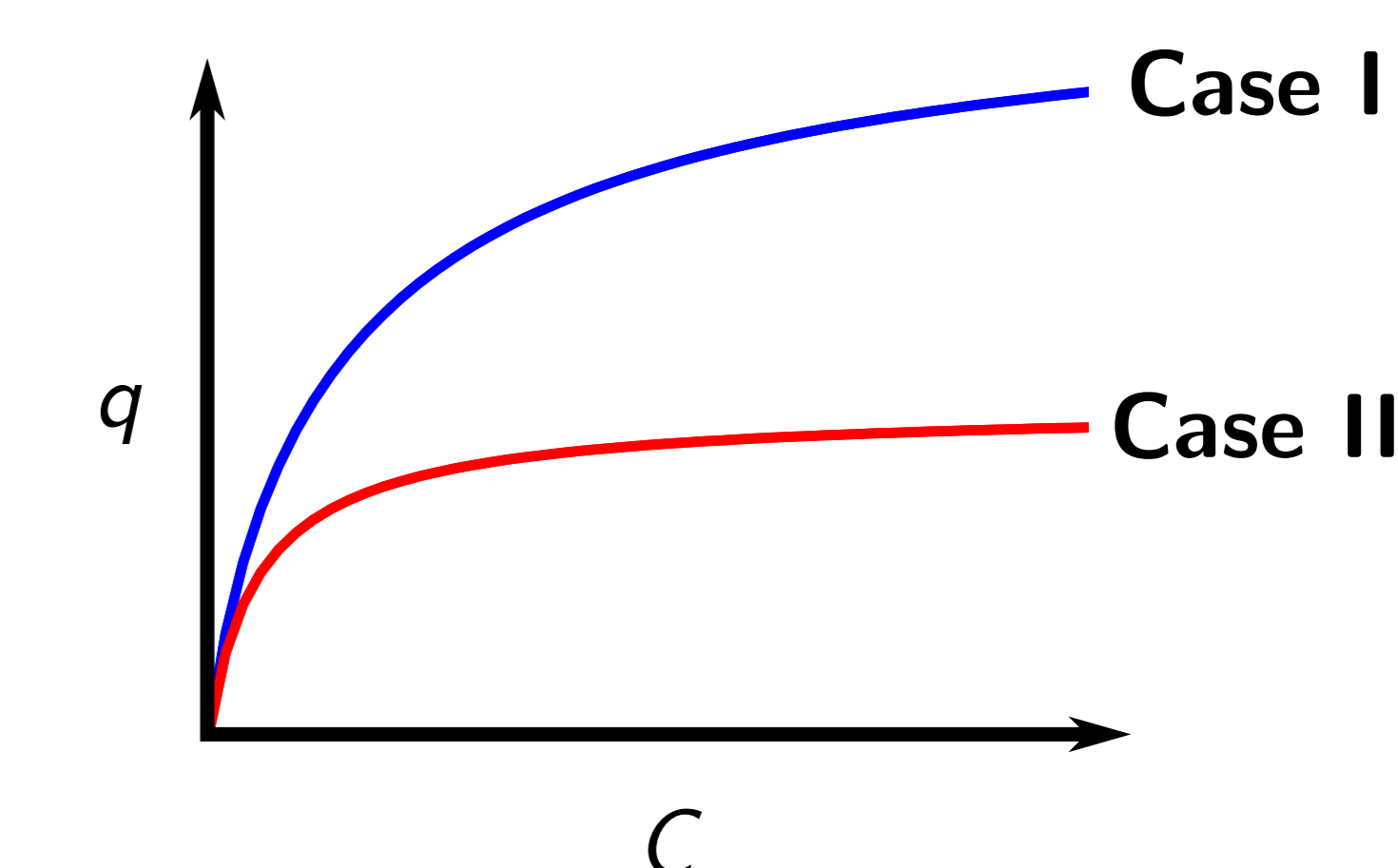


Case II

3 mL/min nominal
 $\Delta P \approx 20$ bar



Results



References

- (1) A. Rajendran, O. Kruchi, M. Mazzotti, M. Morbidelli, J Chromatogr., A, 1092 (2005) 149-160
- (2) S. Ottiger, J. Kluge, A. Rajendran, M. Mazzotti, J. Chromatogr., A 1162 (2007) 74-82
- (3) C. Wenda, A. Rajendran, J. Chromatogr., A 1216 (2009) 8750-8758
- (4) G. Guiochon, A. Felinger, D. G. Shirazi, A. M. Katti, Fundamentals of Preparative and Nonlinear Chromatography 2nd Ed, Elsevier Academic Press (2006).