The faculty of Engineering of the Vrije Universiteit Brussel invites you to attend the public defense leading to the degree of

DOCTOR OF ENGINEERING SCIENCES

of   **Timothy Januarius**

The public defense will take place on **Wednesday 28th August 2024 at 4:00 pm** in room **D.2.01** (Building D, VUB Main Campus)

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UNDERSTANDING AND PREDICTING AXIAL DISPERSION AND THE LIMITS OF SEPARATION PERFORMANCE OF SUPERCRITICAL FLUID CHROMATOGRAPHY SEPERATIONS

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Abstract of the PhD research

Supercritical fluid chromatography (SFC) is a separation technique where the major component of the mobile phase consists is compressed CO_2, either in the liquid or the supercritical state. Besides CO_2, current applications of analytical and preparative SFC in most cases require the addition of a polar co-solvent, such as methanol, ethanol, isopropanol and additives such as water or trifluoroacetic acid. Due to the low viscosity of the mobile phase, the technique is characterized by small pressure drops and high diffusion coefficients, allowing the use of longer columns or columns packed with smaller particles, operated at high velocities. However, due to complex nature of the supercritical solvent, of which the properties strongly vary with local pressure and temperature, it is difficult to characterize and predict its separation performance for current and future conditions. In addition, separation parameters such as retention factor are also affected by the operating pressure and thus vary with the pressure drop along the column. Unfortunately, there is a lack of physicochemical data (diffusion coefficients, viscosity, density…) of the binary solvent mixtures currently used in SFC. In addition, important parameters required to analyze separation performance in chromatographic separation such as the effective column bed and particle diffusion coefficients (D_{eff} and D_{part}) have not been reported in SFC.

To increase insight the separation performance of SFC separation, allowing to model and predict the axial dispersion for current and future separations, the first focus of this work was to develop an accurate and flexible method to measure diffusion coefficients (D_{mol}) in relevant SFC conditions using commercially available instrumentation. These results not only confirmed that the true diffusion coefficients in SFC mobile phase with organic modifiers are much lower than the often used reference values in neat CO_2, but also that small changes in the chemical structure can have a much larger effect on the actual D_{mol}-values than their molecular size. The measurements where extended to determine the effective column bed diffusion coefficient D_{eff} using a modified version of the peak parking experiment using two parallel columns and a switching values. Applying the effective medium theory, if was found that, contrary to liquid chromatography, the diffusion coefficient in the retained state is much smaller in SFC than LC. Using the insights in these diffusion parameters, the variation of the local plate in the SFC column was studied from a theoretical perspective using Computation Fluid Dynamics (CFD) simulations. These showed that the observed separation performance is the result of intricate interplay between the variation of the mobile phase properties and the retention factor with pressure. Experimental measurement of columns packed with different particles sizes finally showed the possibilities and limitations of using small particle diameter columns in SFC. Since standard gradient separation methods require a significant fraction of co-solvent, strongly increasing the mobile phase viscosity, and modern SFC instruments have a much lower pressure limit than their LC counterparts, the full potential of sub-2µm particles currently can't be exploited in SFC.