Unravelling anomalous mass transport in antisolvent crystallisation

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Objectives

- Simulate diffusive mixing in binary and ternary mixtures with Fick's law, the Maxwell-Stefan model and the Cahn-Hilliard equation.
- Adjust of the computational model to experimental data.
- Identify and understand effect of key process parameters

Introduction

Antisolvent crystallisation relies on the difference in solubility of a solute in the solvent and the antisolvent to create supersaturation [1]. The mixing process greatly impacts final product properties such as the CSD and the crystal polymorph obtained [2], as they are influenced by local supersaturation values. However, this process is not well understood, leading to unexpected and undesired phenomena such as oiling out or the formation of unwanted crystal phases, as illustrated in **Figure 1**.

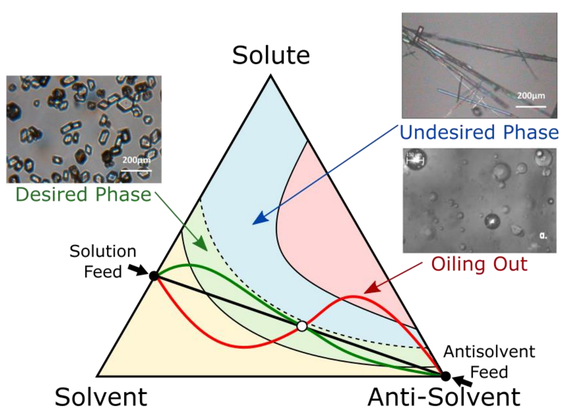


Figure 1. Ternary phase diagram illustrating that the crystallisation path dictates which outputs are obtained.

Traditionally, the mixing of solute, solvent and antisolvent at the microscale has been described through Fick's law of diffusion:

$$J_A = -D_{AB} \cdot \nabla x_A \qquad (1)$$

in which the concentration gradient is the driving force for mass transfer, instead of the more physically accurate gradient in chemical potential. Thus, it fails to explain anomalous behaviours such as uphill diffusion [3].

We will study diffusion in the microscale, comparing the performance of the Cahn-Hilliard (2) model coupled with Fick's law and with the Maxwell-Stefan equation (3). The studied system, in which these unwanted phenomena have been reported, is formed by water, ethanol and glycine.

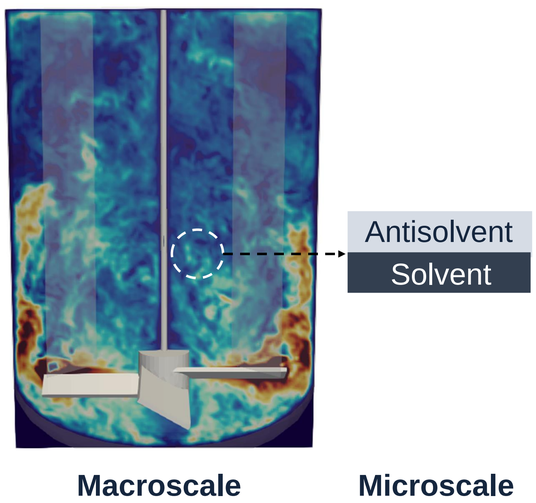


Figure 2. Diagram illustrating the different scales of mixing in a crystalliser.

$$\frac{\partial \phi}{\partial t} = \nabla \cdot D \nabla \left(\frac{\partial f}{\partial \phi} - \epsilon^2 \nabla^2 \phi \right), \qquad (2)$$

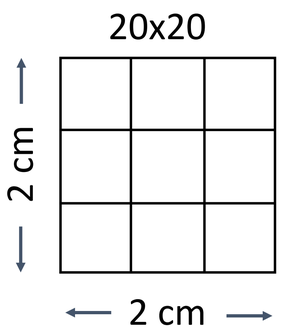
$$f = 0.5 a^2 \cdot \phi^2 \cdot (1 - \phi)^2$$

$$\frac{\nabla_{T,P} \mu_A}{RT} = \frac{x_B}{Đ_{AB}} (v_B - v_A) \qquad (3)$$

The Maxwell-Stefan framework considers the chemical potential as the driving force for diffusion, and thus better ability to predict non-idealities is expected. However, it cannot simulate the oiling-out phenomenon, as it does not account for the minimization of the interphase due to surface tension. In contrast, in the Cahn-Hilliard model, the term $\epsilon^2 \nabla^2 \phi$ is related to the Korteweg stress and penalizes steep changes in composition. Hence, this model could potentially simulate the oiling-out stage.

The simulation results will be compared to experimental diffusion measurements obtained through Raman spectroscopy. The model parameters will be tuned to replicate these results, acquiring more physical significance.

Methodology



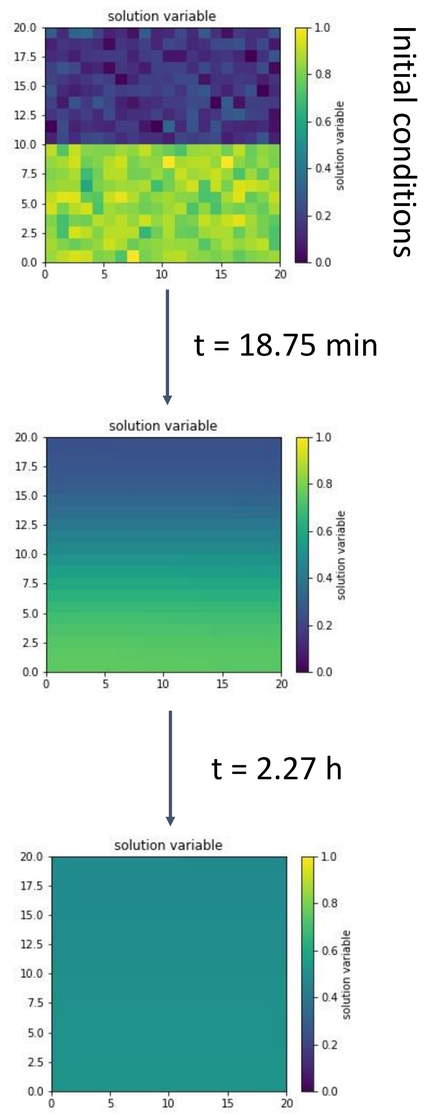
Both Fick's diffusion law and the Cahn-Hilliard model have been discretised through the finite volume method, using the FiPy library in Python.

The boundary conditions correspond to zero gradient, and the initial conditions resemble the microscale shown in **Figure 2**: a layer of solvent and a layer of antisolvent.

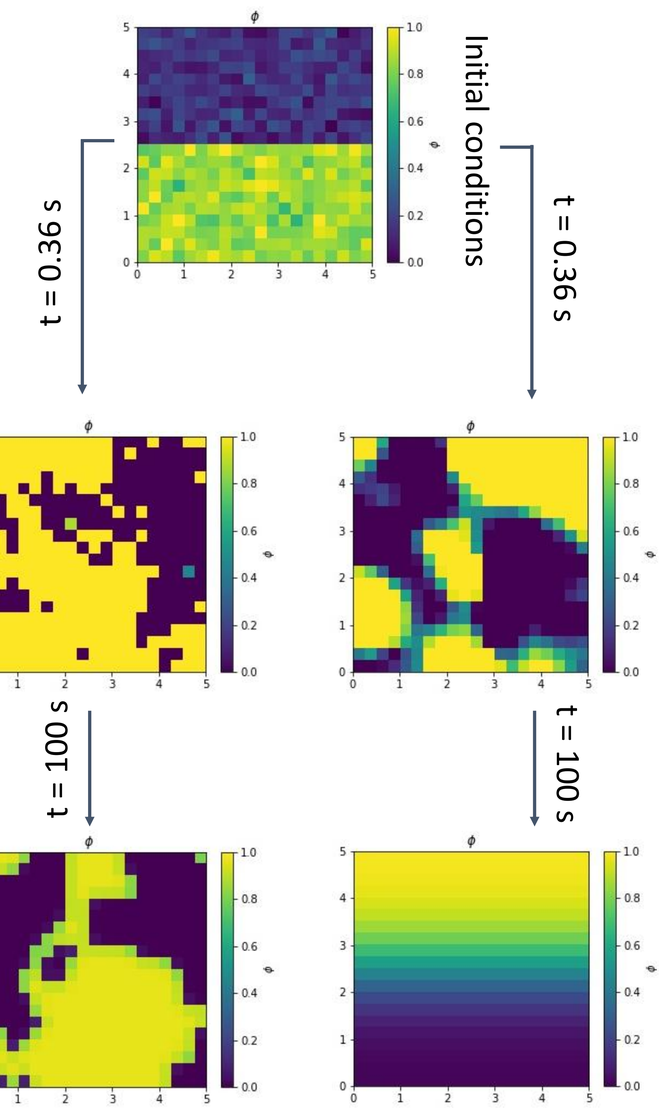
Preliminary results

2D diffusion in ethanol/water mixtures has been simulated using Fick's law. Initial simulations are also shown for the Cahn-Hilliard model.

2D Fickian diffusion



Cahn-Hilliard model



Conclusion

The preliminary results obtained for the Cahn-Hilliard model allow to simulate the oiling-out process, which occurrence depends on the value of ϵ in relation to a. In comparison, in Fick's law the system always results in homogeneous mixing. Incorporating Maxwell-Stefan diffusion and expanding the model to multicomponent mixtures will enable us to accurately simulate the L-L separation phenomenon for realistic systems.

Acknowledgements

- EPSRC Future Manufacturing Research Hub for Continuous Manufacturing and Advanced Crystallisation (CMAC)
- University of Strathclyde

References

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