Understanding solvent-induced phase transformations driven by anomalous mass transfer

Research Celebration Event, 20/10/2023

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CMAC

1. Background and motivation

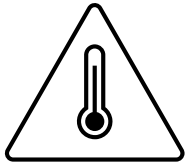
Nonsolvent Induced Phase Separation (NIPS)

- Nanomaterial synthesis [1]
- Polymeric membranes [2]
- Pharmaceuticals (ibuprofen [3], paracetamol [4])

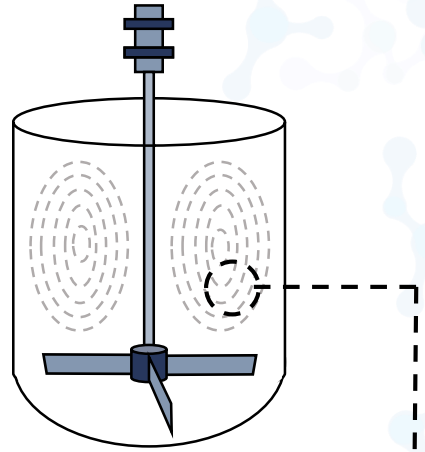
Gap in the fundamental understanding of how mixing processes occur

In particular, we focus on modelling and measuring **antisolvent crystallisation**, but can extend framework to **cooling crystallisation**

Mass transfer



Heat transfer



Macroscale

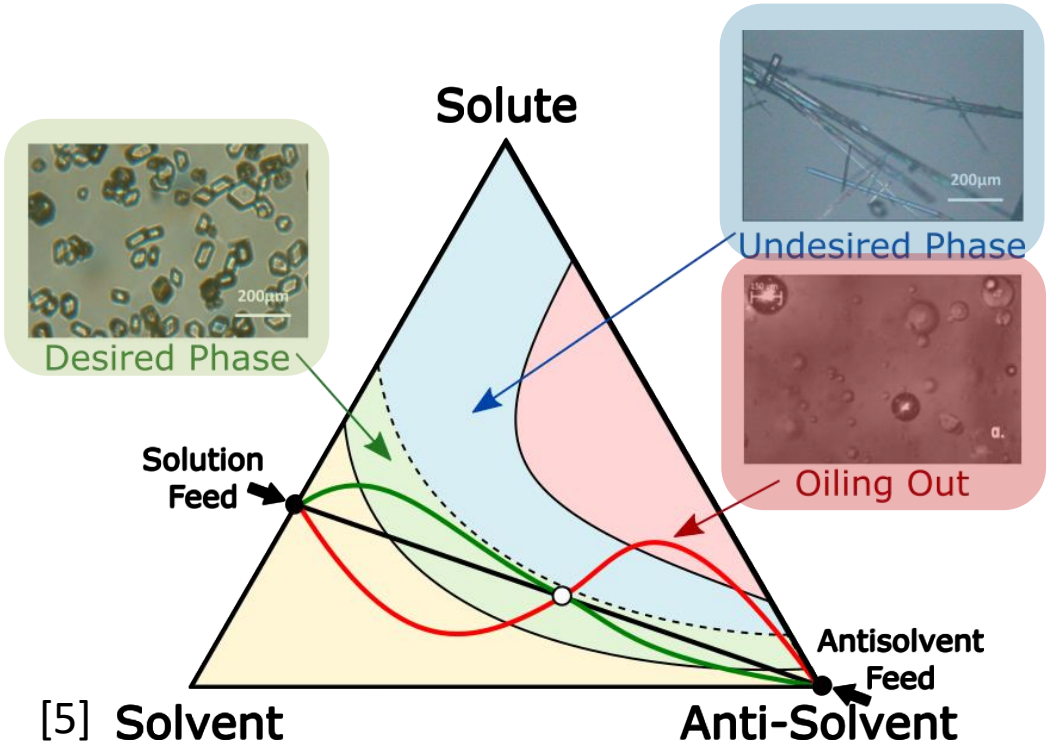
Convection dominates

Microscale

Diffusion dominates

[1] *International Journal of Pharmaceutics* 2007, 342(1–2), 26–32. **[2]** *Ind. Eng. Chem. Res.* 2011, 50, 7, 3798–3817.
[3] *International Journal of Chemical Engineering and Applications* 2013, 337–341. **[4]** *Cryst. Eng. Comm.* 2022, 24, 3122–3135.

1. Background and motivation



[5]

- Undesired crystal properties (CSD, morphology)
- Downstream processing issues
- Differences in bioavailability

Current understanding: mixing process evolves through black line (ideal)

Green line: Desired outcome still achieved

Blue area: Appearance of undesired crystal phase

Red line: The system liquid-liquid phase splits

Aim Accurate modelling of antisolvent/cooling, seeded/unseeded crystallisation

[5] Graph created by D. McKechnie

2. Model comparison

Fick's second diffusion law

$$J_A = -D_{AB} c \cdot \nabla x_A$$

$$\frac{\partial x_A}{\partial t} + \nabla(\mathbf{v} x_A) = D_{AB} \cdot \nabla^2 x_A$$

Cahn-Hilliard-like phase-field model

$$J_A = -Đ_{AB} c_A \cdot \nabla \beta \mu_A$$

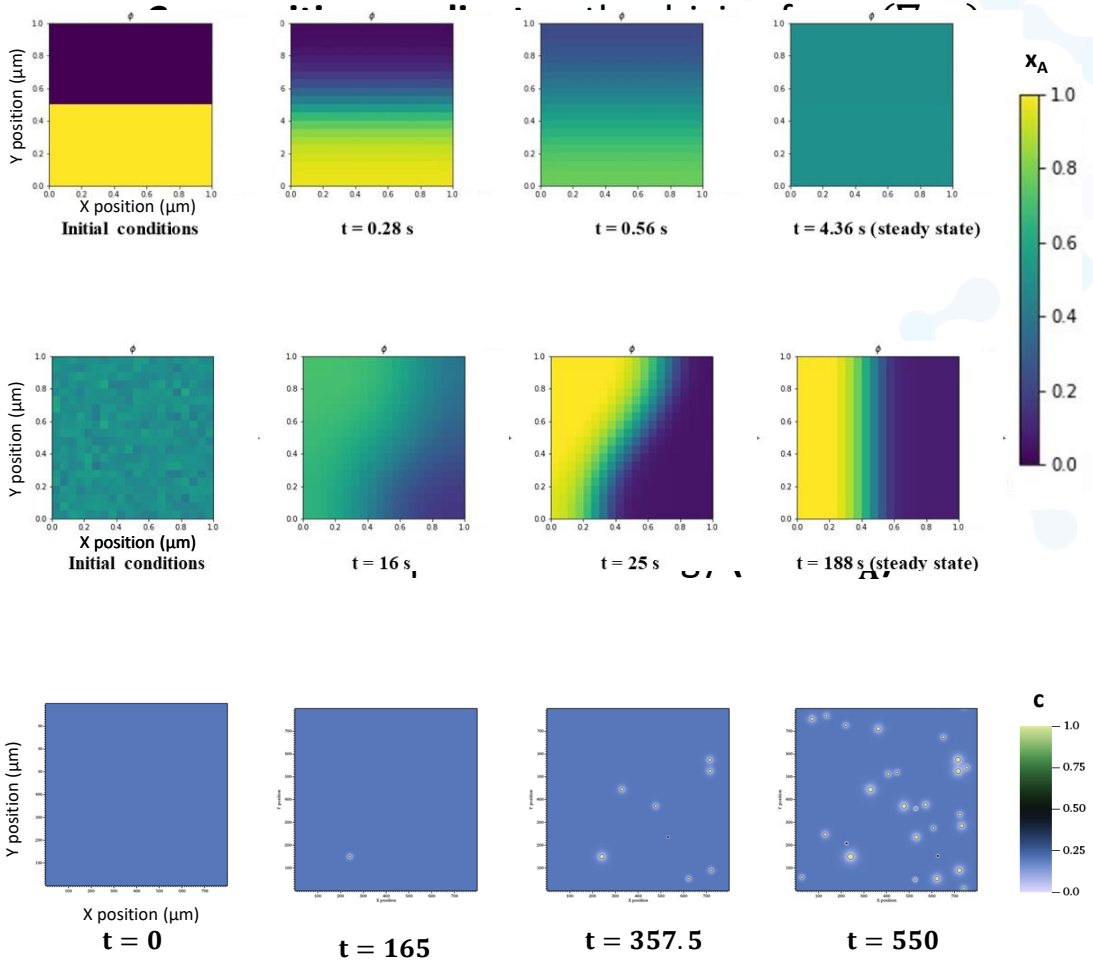
$$\frac{\partial x_A}{\partial t} + \nabla(\mathbf{v} x_A) = \nabla[Đ_{AB} \cdot \nabla x_A] + \nabla\left[Đ_{AB} x_A \cdot \nabla[A(1 - x_A)^2 - \varepsilon^2 \nabla^2 x_A]\right]$$

AC-CH-KKS nucleation phase-field model [6]

$$\partial c/\partial t = \nabla(M/f, cc \cdot \nabla \mu_c);\ \mu_c = f_{\alpha,c}(1 - H) + f_{\beta,c} H$$

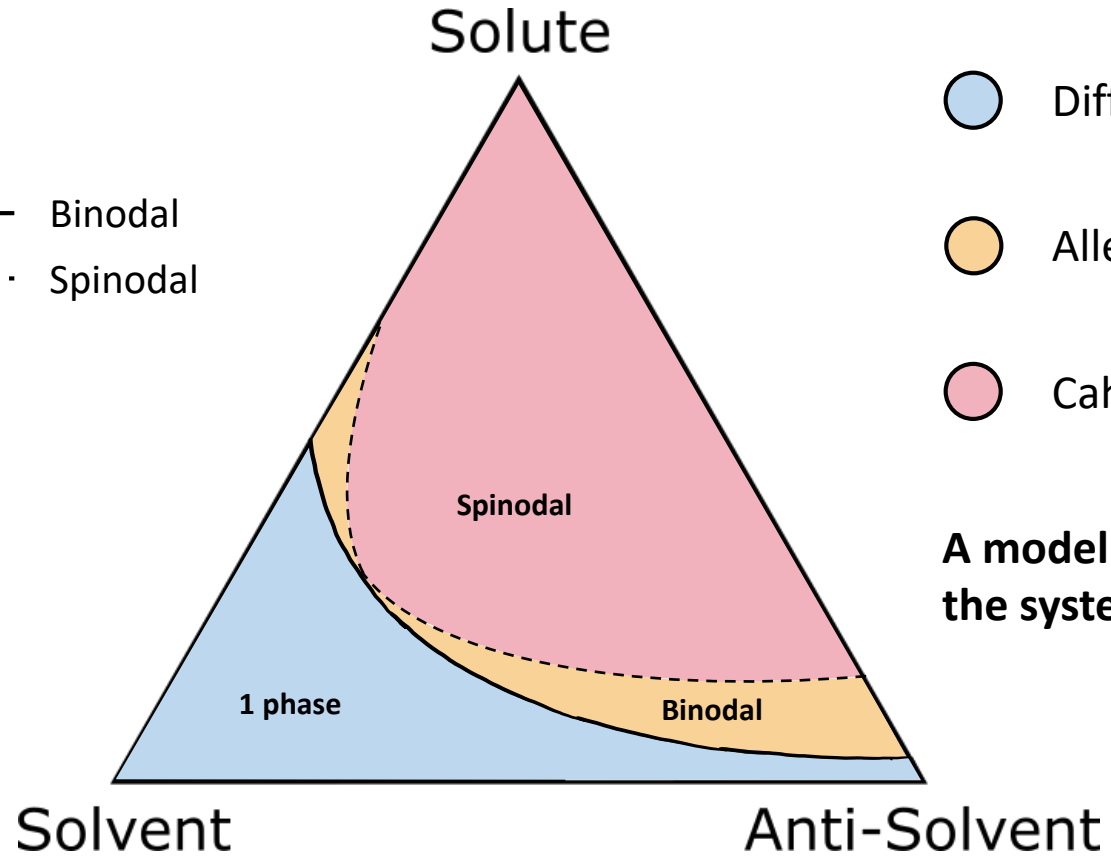
$$\partial \eta/\partial t = -L\mu_\eta;\ \mu_\eta = \left[f_\beta - f_\alpha - (c_\beta - c_\alpha) f_{\beta,c_\beta}\right] H + W f_{\mathrm{Land}} - \kappa\eta$$

- Mobilities
- Interpolation function (H(η))
- Barrier height for η double well
- Penalty coefficient for the α-β interface



[6] S. DeWitt, S. Rudraraju, D. Montiel, W.B. Andrews, and K. Thornton. PRISMS-PF: A general framework for phase-field modeling with a matrix-free finite element method. npj Computational Materials 6, 29 (2020).

3. Model summary



- Diffusion (Maxwell-Stefan: $\nabla\mu_A$) [7]
- Allen-Cahn dynamics
  + C-H to incorporate a nucleation model (in order to track c)
- Cahn-Hilliard dynamics

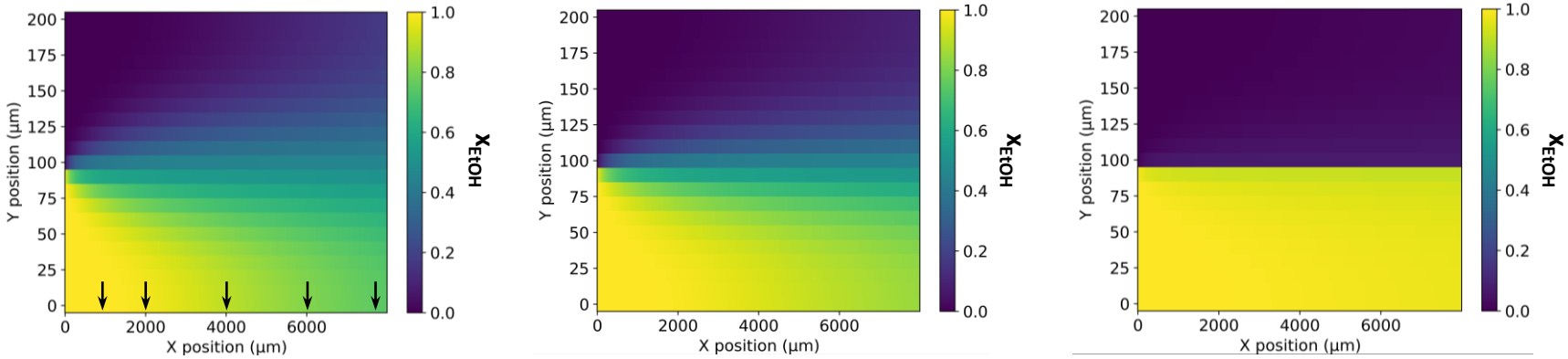
A model combining all of them should be able to track the system's pathway throughout a crystallization process

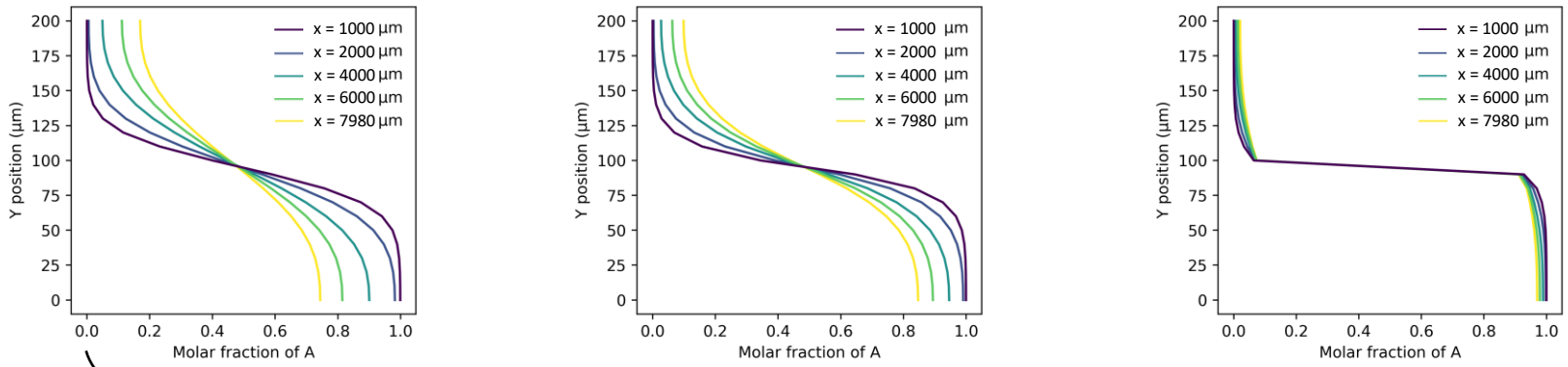
[7] *Cryst. Growth Des.* 2022, 22, 4, 2192–2207

4. Cahn-Hilliard analysis

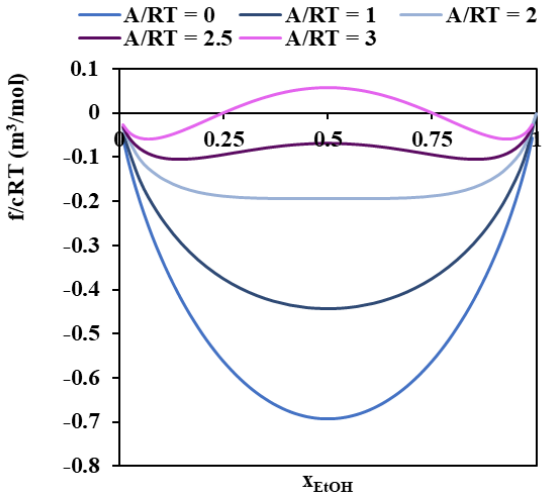
Effect of A — $\varepsilon = 1$, $D = 1600\ \mu m^2/s$ (H_2O-EtOH)

$A/RT = 0$ $A/RT = 1$ $A/RT = 3$





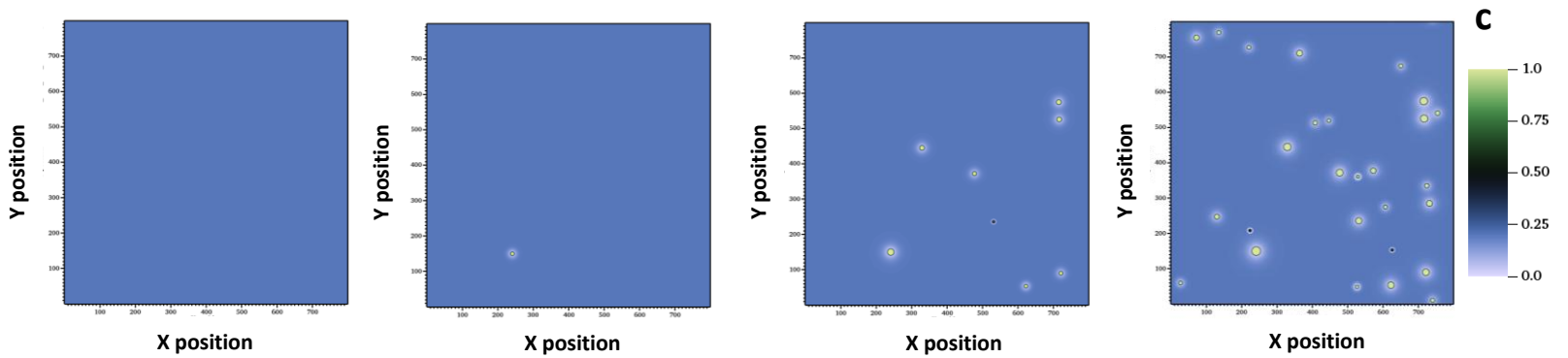
Vertical profiles along the channel taken at the black arrows

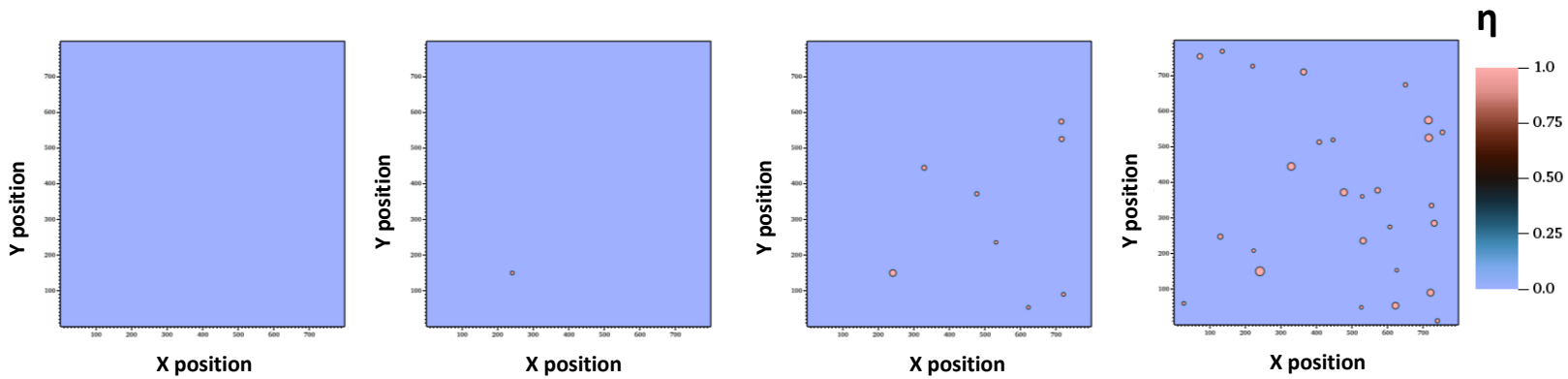


- $\mathbf{A > 2RT}$**:** the free energy favours having two phases
- $\mathbf{A < 2RT}$ **:** a homogeneous final state is reached [9]

[8] J. E. Guyer, D. Wheeler & J. A. Warren, "FiPy: Partial Differential Equations with Python," *Computing in Science & Engineering* **11**(3) pp. 6—15 (2009)
[9] Poling, Bruce E., John M. Prausnitz, and John P. O'Connell. 2001. *Properties of Gases and Liquids*. 5th ed. New York: McGraw-Hill Education.

4. Allen-Cahn + Cahn-Hilliard + KKS





Composition evolution

- Light zone around the nuclei: supersaturation depletion in the area

Phase variable evolution

- Diffuse interphase within all nuclei
- No depletion zone – it is part of the liquid phase

[6] S. DeWitt, S. Rudraraju, D. Montiel, W.B. Andrews, and K. Thornton. PRISMS-PF: A general framework for phase-field modeling with a matrix-free finite element method. npj Computational Materials 6, 29 (2020).

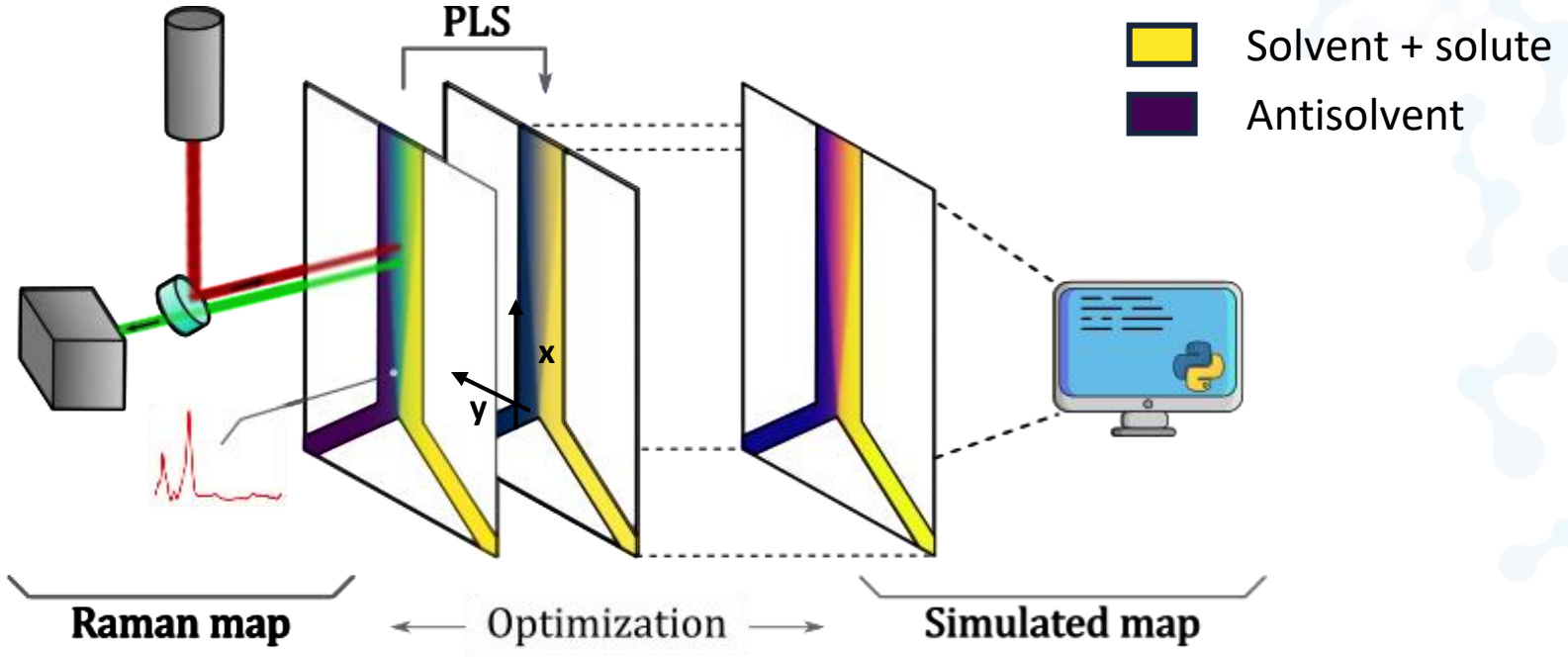
PRISMS-PF
An Open-Source Phase-Field Modeling Framework

5. Model validation framework

Only one experiment required for n components

Materials waste minimised

Information-rich output



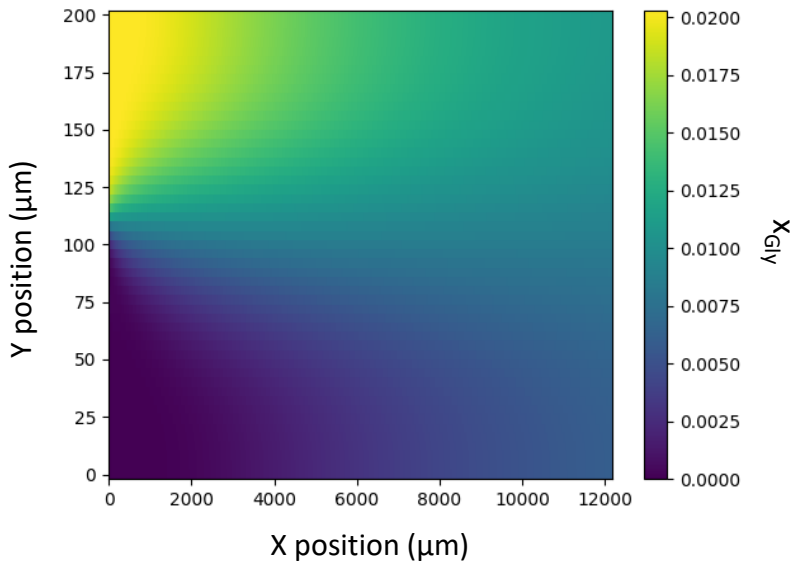
Raman & microfluidics: obtain mixing maps

Modelling: development of a better nonideal model, inform with experiments

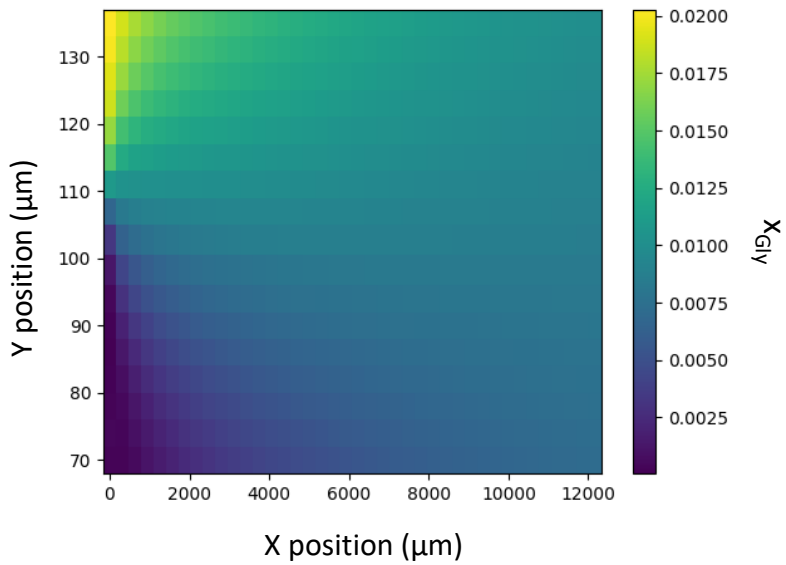
5. Model validation

Glycine – Water system [8]; Fick's law

The simulated map was **coarsened** through averaging to match the dimensions of the experimental map



Final simulated map



Final coarsened map

- **D: 920 µm²/s**.
- **Initial value:** 500 µm²/s
- **Method:** Nelder-Mead
- **Tolerance:** 0.0001

D = 877 µm²/s

Error < 5%

[8] Data collected by D. McKechnie

6. Future work

- Differentiate between oiling out and nucleation within the model – change in the free energy curves
- Add second equation for ternary system
- Add the temperature effect into the model

- Calibration and preliminary measurements obtained
- Solving problems with the setup (Raman was broken for a long time) – collect binary maps

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